National Center for
Cancer Care and Research

Research Activities Book 2023

Cancer Services, Hamad Medical Corporation

المركز الوطني لعلاج وأبحاث السرطان
National Center for Cancer Care & Research

عضو في مؤسسة حمد الطبية
A Member of Hamad Medical Corporation

Contents

Preface

Dr. Mohammed Salem,

Medical Director, National Centre for Cancer Care and Research
Chairman, Cancer Services,
Hamad Medical Corporation

I am proud to present our research activities at the National Center for Cancer Care and Research for 2023.

This book is a testament to the contributions of our team of scientists, doctors, and nurses who have been instrumental in pushing the boundaries of cancer and non-hematological disease research. Our dedication to patient care has motivated us to continue our research activities and implement our findings. Our team has published in many journals with high impact factors and presented their findings at global conferences. Hamad Medical Corporation has played a role in many international collaborations and multi-center clinical trials that have had a profound impact on cancer research. I am enthusiastic about the role our team will continue to play in the advancement of cancer research.

With best wishes,

Introduction

Dr. Mohammed Ussama Al Homsi

Deputy Medical director and clinical research and education
National Center for Cancer Care and Research, Hamad Medical Corporation

It is my privilege to present our annual Research Activities Book for 2023

The research activities book has been a testament to the efforts of the National Center for Cancer Care and Research's (NCCCR) continued commitment to patient care. Research is the foundation supporting patient care and facilitating the advancement of healthcare. Our research teams have asked and investigated the major research questions in their respective fields, mainly: oncology, hematology, and non-malignant hematology. The number of cancer related publications has continuously increased, including the number of articles published in high impact factor journals.

The NCCCR's commitment to scientific excellence has gone beyond the regional commitment and towards global impact. Our research teams have been part of the global conversations on cancer care through their various publications and participation in conferences and seminars.

I would like to extend my appreciation to our clinical, research and support professionals for their efforts and dedication.

Research Areas of Focus

The National Centre for Cancer Care and Research (NCCCR) provides several services including Medical Oncology, Radiation Oncology, Hematology and Hemopoietic Stem Cell Therapy as well as hosting PET CT, Nuclear Medicine, Interventional Radiology and Cancer Genetics Services. NCCCR's physicians and scientists work closely to provide the best healthcare program for cancer patients in Qatar and some of them are also part of the Cancer Institute (CI) group which ultimately aims to improve cancer patient outcome through an advanced and innovative medical research work.

In accordance with the chapter 6 of the Qatar Cancer Plan 2023-2026 https://qcic.moph.gov.qa/nas/documents/QCPEnglish.pdf?csrt=4850885234744798392), the CI sets out priorities to focus all research efforts on patients healthcare, bringing together the best of clinical and academic thinking towards translational research that will deliver tangible benefits and improved services for the people of Qatar.

To enhance the quality and efficiency of patients' care, the CI research is exploring better ways to:

- Develop new diagnostics with Molecular Pathology and Precision Medicine.
- Develop and monitor cancer immunotherapy.
- Monitor treatment efficacy before clinically apparent (Dynamic Biomarkers).
- Identify the molecular and clinical features of cancer patients through omics research including proteomics, genomics, immunomics, metabolomics and microbiomics.
- Implement Stem Cell and other cell therapies (CAR-T, CAR-NK and TIL therapies).

Other cancer clinical research priorities at HMC are the following:

- Cancer Epidemiology Research
- Clinical Research and Real-World Evidence Research.
- New Diagnostics with advanced imaging and molecular pathology
- New Treatment Technologies in Radiotherapy and Surgical Oncology
- Special patient cohorts with familial and hereditary cancers patterns or disease clusters.

According to the Hamad Medical Research Centre (MRC) database, there were an average of 60 research projects per year.

The outcome of cancer research activities on cancer patients' health

The research and clinical team at the National Centre for Cancer Care and Research (NCCCR) are working closely on different clinical and translational research projects with the unique aim of improving cancer patients' outcomes. The Translational Cancer Research Facility (TCRF) is part

of the NCCCR medical oncology department. It undertakes immunology and immune-oncology research projects. During the last 5 years, the research group has been working on identifying, characterizing, and monitoring of circulating biomarkers in the blood/plasma of cancer patients in the Qatari population to define diagnostic/prognostic cancer panels. Soluble biomarkers extraction from patients' body fluids is considered as non-invasive technique that have the advantage of allowing continuous sampling and surveillance of molecular changes over the entire treatment course, thus avoiding the loss of response because of tumor heterogeneity, as well as improving the accuracy of the monitoring of treatment efficacy. Interestingly, this real-time monitoring is not only non-invasive and easily feasible from the diagnosis to the progression of the tumor, but it also allows the evaluation of the parameters which cannot be detected with conventional imaging techniques, such as Minimal Residual Diseases (MRD). Another advantage of these soluble biomarkers is their low-cost effectiveness. Additionally, liquid biopsy can be accessible to a wide range of patients and would allow HMC to dramatically reduce the cost of diagnostic and prognostic tools compared to the standard tissue biopsy tests. The recent data obtained by the TCFR team were published as 2 manuscripts in the peer-reviewed high impact scientific journal Frontiers in Immunology [1, 2]. These findings provided baseline data from Qatar on predictive biomarkers of response in non-small lung carcinoma (NSCLC) patients treated with immune checkpoint inhibitors (ICI) and will have high impact nationally and internationally to understand treatment response dynamics in patients treated with ICI.

Recently, the TCRF team has started the integration of "omics" approaches such as proteomics and transcriptomics to help in the comprehension of the biological mechanisms associated with response/resistance to novel treatment protocols for multiple myeloma. The ultimate objective of this project is the identification of novel prognostic/predictive biomarkers of response and relapse that would further be a key factor for precision medicine.

Moreover, many translational research projects undertaken at the TCRF are also focusing on the expression of immune cells inhibitory markers such as the programmed death protein-1 (PD-1) and its ligand PD-L1 and of tumor associated antigens, particularly the NY-ESO-1 cancer testis antigen. These projects aim at more accurate molecular diagnosis of the nature of the tumor and how it might progress over time to provide prognostic indicators. This research would also help to shape precision medicine therapeutic strategies by enabling the selection of the most effective treatments and the identification of patients who would most likely benefit from such treatments. Consequently, this research would play a role in the improvement in cancer patients' diagnosis and prognosis and in reducing toxicities and complications associated with treatments in non-responding patients. These investigations would also explore and identify the efficiency of new cancer therapeutic strategies such as combined immunotherapy with chemo- and/or radiotherapies.

Moreover, during the COVID-19 pandemic, using HMC cancer immunological research expertise, and

AHS financial support, the TCRF optimised and established cutting-edge novel technologies to study the patient's immune system response to COVID-19 infection, TB infection and targeted vaccines (the T-SPOT. COVID Assay and the multi-antigen serology assay for COVID-19 (Jess), the highly sensitive Ella Automated Immunoassay System to measure the cytokine storm, and the T-SPOT. TB assay). The first data generated in this topic was published in Frontiers in Immunology [3].

The major outcomes of the CI research activities fall into 3 categories:

1. Bolstering accuracy in diagnosis and improving prognosis.
2. Determining if a new treatment or approach is safe and effective.
3. Helping in developing novel therapeutic strategies.

We summarize in Table 1 some of the projects/publications that are carried out/published in 2023 by the CI and their relevant outcome on patients' health.

Table 2: The relevant outcome on patient's health of manuscripts published in 2023 by the Cancer Institute researchers

1. Bolstering accuracy in diagnosis and improving prognosis		
Sub-category	**Impact on patients' health**	**References**
1.1. Incidence and association of high-risk HPVs and EBV in patients with advanced stages of colorectal cancer from Qatar	1. Prevalence of human papillomaviruses (HPVs) and Epstein Barr virus (EBV) in colorectal cancer (CRC) patients in the Qatari population. High-risk HPVs and EBV are present in %69 and %21 of the CRC cases, respectively. 2. Correlation of co-presence of more than one HPV subtype can significantly worsen the prognosis of CRC patients. Suggesting the implementation of oncovirus screening in CRC patients as a key in down-staging CRC, selecting the proper treatment, and improving patient outcomes.	[4, 5]
1.2. BRCA-1specific machine learning model predicts variant pathogenicity with high accuracy	1. High prevalence of BRCA1 mutations in Qatari patients with breast cancer (BC) 2. Development of a BRCA-1specific machine learning model to predict the pathogenicity of all types of BRCA1 variants and to apply this model and previous BRCA-2specific model to assess BRCA variants of uncertain significance in Qatari BC patients and identify cancer patients at high pathogenicity risk.	[6]
1.3. An Artificial Intelligence-Based Diagnostic System for Acute Lymphoblastic Leukemia Detection	1. Advanced classification of Acute Lymphoblastic Leukemia (ALL). 2. Early ALL detection and timely treatment. 3. Replacement of manual procedures with intelligent diagnosis systems. 4. Optimization of diagnosis test outcomes	[7]

1.4. Machine Learning for Diagnosis and Screening of Chronic Lymphocytic Leukemia Using Routine Complete Blood Count (CBC) Results	1. Integration of AI-enabled smart and accurate diagnostic in hematological disease in NCCCR. 2. Early leukemia diagnosis and timely treatment. 3. Improved treatment response and survival rate with reduced cost. 4. Chance of cure or management of disease with easily available first-generation drugs	[8]
1.5. Applications of Artificial Intelligence in Philadelphia-Negative Myeloproliferative Neoplasms (MPNs)	1. More accurate diagnosis of Myeloproliferative Neoplasms (MPNs) 2. Easy differential diagnosis of Primary Myelofibrosis and Essential Thrombocythemia 3. Using AI in developing diagnostic panels that complement and confirm standard clinical diagnostic tools.	[9]
1.6. Applications of Machine Learning in Chronic Myeloid Leukemia	1. Machine learning high performance in diagnosing and subtyping leukemia. 2. Faster diagnosis and lower cost than traditional methods. 3. Use of blood smears or bone marrow aspirates, in large sample size of diverse hematological diseases. 4. Improved prognosis through early detection of the blood cancer and prediction of -5year survival.	[10]
1.7. An interesting case of chronic myeloid leukemia (CML) with T315I mutation raising suspicion of de novo AML, a diagnostic conundrum	1. The importance of karyotyping, PCR and sequencing, in accurately diagnosing and treating complex leukemia cases. 2. Highlighting the importance of targeted therapy in TKI resistant cases of CML as targeted therapy	[11]

2. Determining if a new treatment or approach is safe and effective		
Sub-category	**Impact on patients' health**	**References**
2.1. Serum immune mediators as novel predictors of response to anti-PD1-/PD-L1 therapy in non-small cell lung cancer patients with high tissue-PD-L1 expression	1. Identification of soluble biomarkers that can predict the effectiveness of immune checkpoint inhibitors (ICIs) in non-small lung cancer (NSCLC) patients. 2. Improving patient care and saving healthcare costs Dynamic 3. Establishing personalized treatment plans based on dynamic biomarkers expression for a better prognosis	[1, 2]
2.2. Differentiation syndrome in patients with acute promyelocytic leukemia	1. Importance of steroids to treat potentially fatal complication of APL. 2. Improving patient outcomes in APL treatment.	[12]
2.3. A Rare Case of Lambert-Eaton Myasthenia Syndrome (LEMS) Associated with Non-Hodgkin's Lymphoma: A Case Report and Review of the Literature	1. Improving patients' prognosis by better recognition and timely management of LEMS 2. Importance of immunosuppressive therapy and lymphoma treatment for rare cases of LEMS 3. The impact of specific epigenetic mutations on overall survival in AML and in tailoring treatment plans. 4. Critical insights for better patient outcomes in treating Acute Myeloid Leukemia (AML) and Myelodysplastic Syndromes (MDS) 5. The importance of R882 mutation as a significant prognostic factor and a novel therapeutic target in MDS 6. Safety and effectiveness of Venetoclax-based treatments for high-risk MDS patients.	[13]

2.4. Editorial: Uncovering the relationship between myelodysplastic syndromes and acute myeloid leukemia	1. The impact of specific epigenetic mutations on overall survival in AML and in tailoring treatment plans. 2. Critical insights for better patient outcomes in treating Acute Myeloid Leukemia (AML) and Myelodysplastic Syndromes (MDS). 3. The importance of R882 mutation as a significant prognostic factor and a novel therapeutic target in MDS. 4. Safety and effectiveness of Venetoclax-based treatments for high-risk MDS patients.	[14]
2.5. Carfilzomib-induced life-threatening lung injury in refractory multiple myeloma	1. Emphasizing the need for vigilance in monitoring rare but severe side effects of cancer treatments, in order to improve future patient outcomes	[15]
2.6. Predictors of community pharmacists' readiness to manage the effective and safe use of oral anticancer medicines in a developing setting	1. Emphasizing the limited understanding among pharmacists about chemotherapy cycles, targeted therapies, OAM side effects, and dosing. 2. Highlighting the significant role of clinical pharmacists in identifying and preventing OAMs side effects to improve overall health outcomes for hospitalized patients.	[16]
2.7. Polatuzumab Vedotin in a Patient with Refractory Burkitt Lymphoma, a Case Report	1. Improvement of Refractory Burkitt Lymphoma after starting the polatuzumab vedotin-based chemotherapy.	[17]

3. Helping in developing novel therapeutic strategies		
Sub-category	**Impact on patients' health**	**References**
3.1. Treatment with decitabine (DAC) induces the expression of stemness markers, PD-L1 and NY-ESO1- in colorectal cancer: potential for combined chemoimmunotherapy	1. Presenting the therapeutic potential of the combination of DAC and anti-PD1-/anti-PD-L1 antibodies treatment for CRC patients. 2. Role of DAC in inducing the epigenetic regulation of NY-ESO1- antigen, inhibiting cell proliferation, increasing apoptosis, and decreasing invasiveness.	[18, 19]
3.2. Studies on anti-colon cancer potential of nanoformulations of curcumin and succinylated curcumin in mannosylated chitosan	1. Development of novel drug delivery systems to improve absorption of oral drug in cancer patients	[20]
3.3. Persistence of spike-specific immune responses in BNT162b-2vaccinated donors and generation of rapid ex-vivo T cells expansion protocol for adoptive immunotherapy: A pilot study	1. Standardization of a fully automated assay, Jess Simple Western system, that detects human serum/plasma SARS-CoV2- binding antibodies in a large number of samples and very short time (3 hours). 2. Helping clinicians to identify the cancer patients who may benefit from a booster vaccination for efficient and durable protection against SARS-CoV2-.	[3]

3.4. Applying value-based strategies to accelerate access to novel cancer medications: guidance from the Oncology Health Economics Expert Panel in Qatar (Q-OHEP)	1. This is the first Qatar Oncology Health Economics Expert Panel consensus recommendations. 2. It provides a solid basis for evaluating, registering, and approving new cancer medications to accelerate patient access to novel cancer treatments in Qatar. 3. It facilitates the adoption and collection of patient-reported outcomes. 4. It enables the implementation of value-based cancer care in Qatar.	[21]
3.5. Strategic priorities for hematopoietic stem cell transplantation in the EMRO region	1. A collaborative work discussing the strategic priorities for hematopoietic stem cell transplantation in the Eastern Mediterranean Region (EMRO) 2. It highlights the importance of building capacities in countries with minimal resources and appropriately allocate the available resources to establish standards of practices.	[22]

Recently, the TCRF team has obtained MRC approval for 4 IRGC grants focusing on precision medicine in solid tumors including breast (MRC 01-22-404) and thyroid cancers (MRC 01-22-303, and MRC 01-22-304), and on hematological malignancies, particularly multiple myeloma (MRC 10-23-554). Recently, the management of cancers has been dramatically improved thanks to the molecular profiling of tumor tissues that aids in the selection of precise/personalized treatment for each patient. Such molecular profiling includes specific gene panels that have been validated by international studies. In this program, the TCRF researchers aim to use prognostic and predictive molecular profiling on retrospective and prospective collections of tumor tissues from cancer patients. The group will study tumor genome and apply transcriptome sequencing (whole exome sequencing) to characterize the molecular patterns of thyroid and breast cancer in Qatar. This program underscores the crucial role of precision medicine and lays the framework for research integration into clinical practice in HMC. This is pivotal in guiding treatment decisions, maximizing therapeutic effectiveness, minimizing risks, and ultimately improving the overall patient experience as per HMC's mission and vision for world-class healthcare excellence. Importantly, this program is under an alliance between HMC Cancer Services (NCCCR) and the Qatar Biomedical Research Institute/Hamad Bin Khalifa University (QBRI/HBKU), initiated to establish Precision Oncology in Qatar.

Summary

Research Projects

There were 48 active research projects in 2023..

Research Output: Publications

A total of 241 research communications have been published or presented in national, regional, international journals or conferences during 2023. Of these 72 original research articles, 46 case reports, 74 review articles, 13 Abstracts and 36 conference presentations.

Table 1- Research Publications in 2019-2023					
Publications	2019	2020	2021	2022	2023
Original Research Articles	32	44	25	74	72
Case Reports	28	64	52	49	46
Review Articles	16	35	22	55	74
Abstracts	13	10	14	5	13
Conference Presentations	60	37	14	25	36
Total	149	190	127	208	241

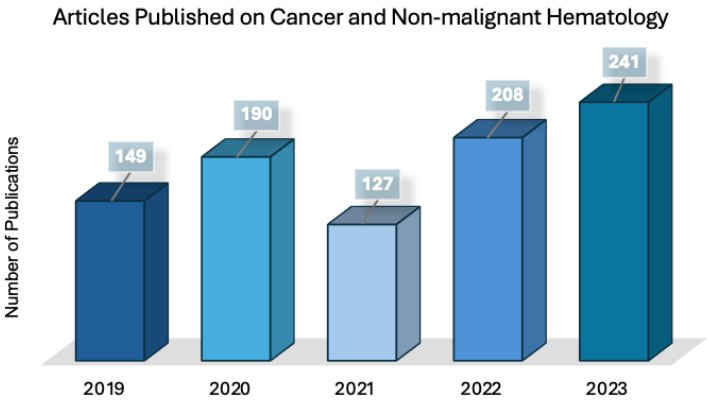

Figure 1: Total number of articles published on cancer and non-malignant between 2019 and 2023

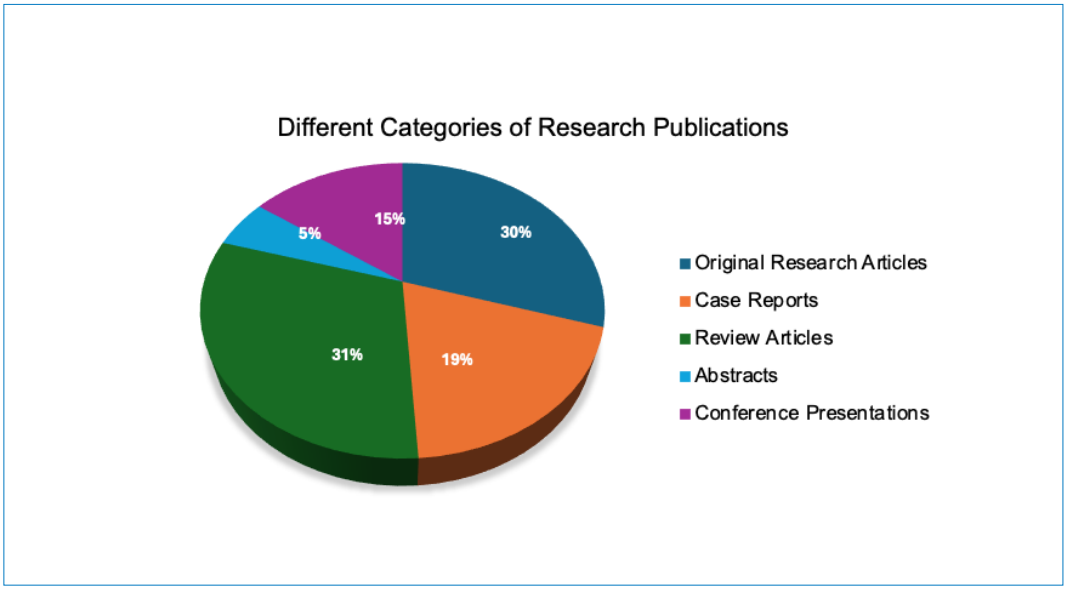

Figure 2: Classification of research publications in 2023

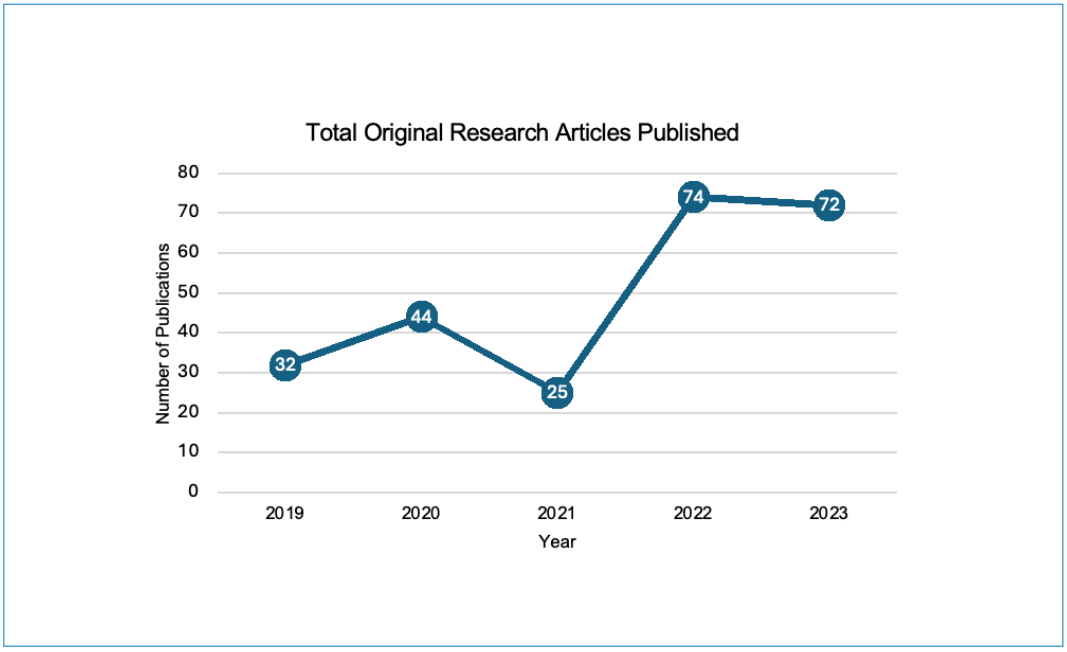

Figure 3: Total number of original research articles published 2019-2023

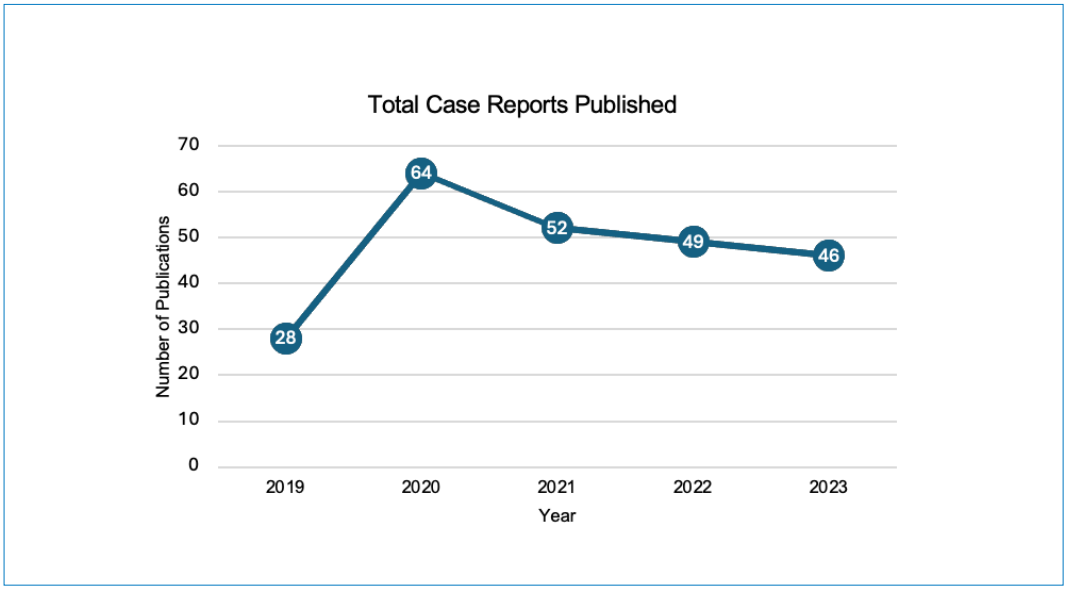

Figure 4: Total number of case reports published 2019-2023

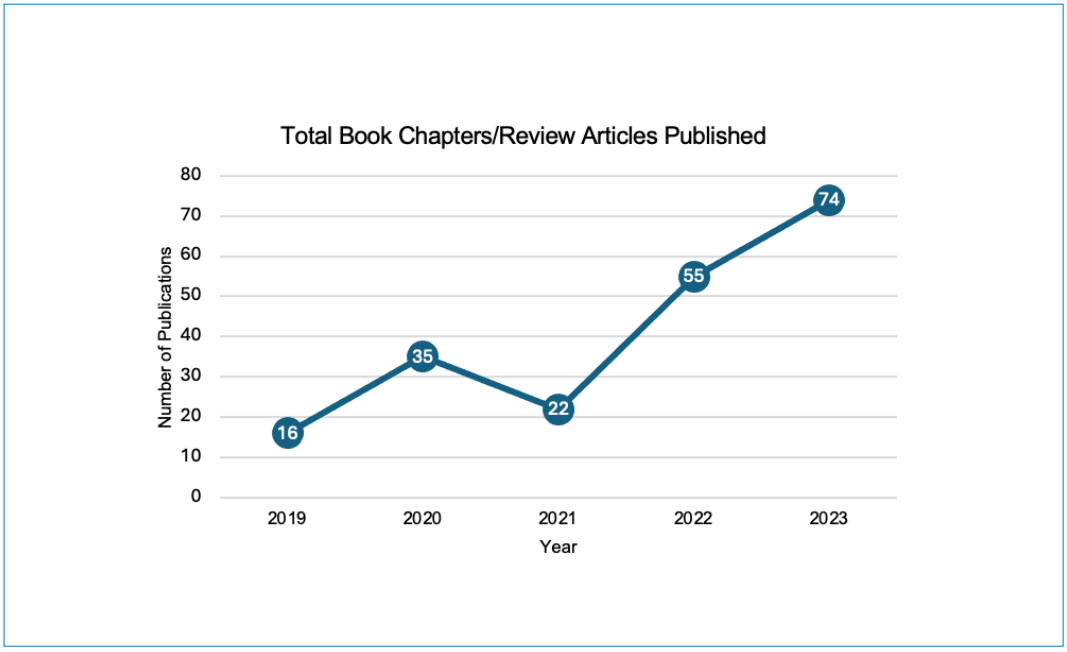

Figure 5: Total number of book chapter and review articles published 2019-2023

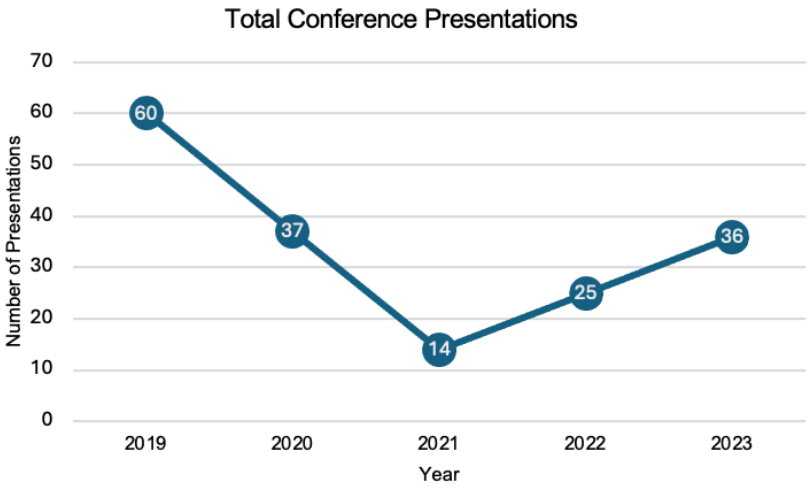

Figure 6: Total number of conference presentations 2019-2023

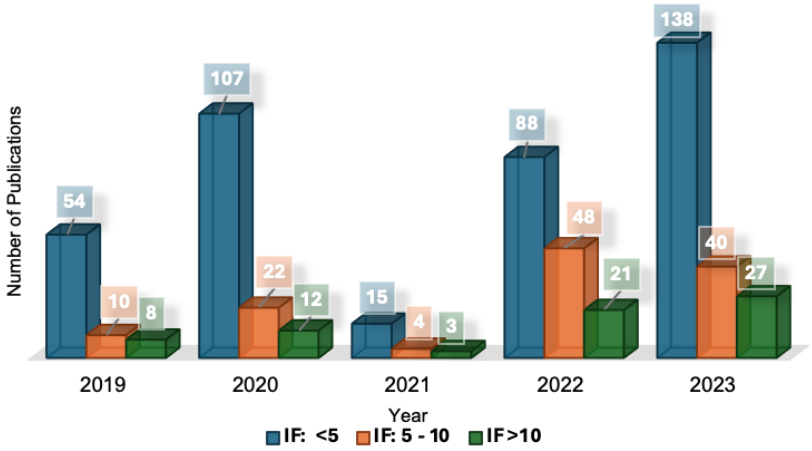

Figure 7: Classification of articles published 2019-2023 by impact factor (IF)

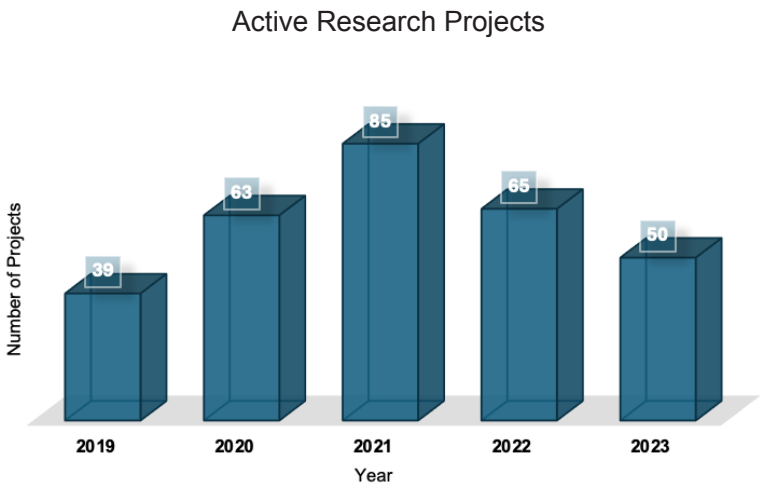

Figure 8: Number of Active Research Projects 2019-2023

ACTIVE RESEARCH PROJECTS

Active Research Projects 2023

No.	Protocol ID	Project Title	Funding Organization	Principle Investigator
1	16205	Precision Immunology Implications for Aggressive Types of Breast Cancer: Genomic Determinants Of Immune Response To Neoadjuvant Chemotherapy	None	Salha Bujassoum
2	IRGC-02-SI-010	Novel Tissue Classification Techniques for MR-only Image Guided Procedures of Brain and Head & Neck	None	Souha Aouadi
3	IRGC-04-SI-17-137	Modulatory Effects of KIR Surface Repertoire on the Effector Functions mediated by Chimeric Antigen Receptor-Engineered Natural Killer Cells	Hamad Medical Corporation (HMC)	Dr. Maysaloun Merhi
4	IRGC-04-SI-17-142	Investigation of immuno-regulatory mechanisms and biomarkers involved in anti-NY-ESO1- immune responses in colorectal cancer patients	Hamad Medical Corporation (HMC)	Dr. Said Dermime

5	IRGC-07-SI-20-716	Cloning of B cells secreting anti-SARS-CoV2- neutralizing antibodies and large-scale production of coronavirus-specific monoclonal antibodies from participants vaccinated with mRNA SARS-CoV2- vaccine	Hamad Medical Corporation (HMC)	Dr. Said Dermime
6	MRC-01-18-400	Chemotherapy-Induced Peripheral Neuropathic Pain (CIPN): Prospective Study From A Single Institute (i.e. NCCCR) In State Of Qatar	Hamad Medical Corporation (HMC)	Dr. Kakil Ibrahim Rasul
7	MRC-01-18-401	HLA-Haploidentical Hematopoietic Stem Cell Transplantation for Hematological Diseases: A Prospective Observational Study.	Hamad Medical Corporation (HMC)	Dr. Afraa Mustafa Sulieman Fadul
8	MRC-01-19-044	A Randomized, Multicenter, Open-Label Cross-Over Study To Evaluate Patient Preference And Satisfaction Of Subcutaneous Administration Of The Fixed-Dose Combination Of Pertuzumab And Trastuzumab In Patients With Her-2Positive Early Breast Cancer	Roche Pharmaceuticals, Switzerland	Dr. Salha Mohd. Bu Jassoum

9	MRC-01-19-273	The Effectiveness of Magic Mouthwash in Chemotherapy/ Radiotherapy-induced Mucositis: A Prospective Observational Study	Hamad Medical Corporation (HMC)	Ms. Taghrid Sahteh I Abou Hassan
10	MRC-01-19-293	First QChip-based expanded genetic newborn screening for Qatari newborns: HMC/ Heidelberg collaborative pilot study	(None)	Dr. Reem Jawad A A Al Sulaiman
11	MRC-01-19-300	Pilot study of dynamic biomarkers of response to anti-PD1- immune checkpoint inhibitors in head and neck squamous cell carcinoma patients	Hamad Medical Corporation (HMC)	Dr. Said Dermime
12	MRC-01-20-084	Screening of NY-ESO-1antibody at the National Center for Cancer Care and Research, HMC to determine its prevalence and utility as a potential predictive biomarker of cancer	Hamad Medical Corporation (HMC)	Dr. Varghese Philipose Inchakalody
13	MRC-01-20-267	Breast Cancer Survivorship Program: Benefits & Outcomes Study	Hamad Medical Corporation (HMC)	Dr. Salha Mohd. Bu Jassoum

14	MRC-01-20-418	The impact of Tyrosine Kinase inhibitors on fatherhood in patients with chronic myeloid leukemia	None	Dr. Mohammad Abdullah Moh'd Abu-Tineh
15	MRC-01-20-507	Soluble predictive biomarkers of response in Non-Small Cell lung cancer patients treated with immunotherapy in National Center for Cancer Care and Research, HMC	Hamad Medical Corporation (HMC)	Dr. Varghese Philipose Inchakalody
16	MRC-01-20-541	Predictive biomarkers of response and adverse events in Hepatocellular carcinoma patients treated with Sorefinib or Levnatinib and/ or Immunotherapy in National Center for Cancer Care and Research, HMC	Hamad Medical Corporation (HMC)	Dr. Varghese Philipose Inchakalody
17	MRC-01-20-800	Changes in microbiome expression and signatures after neoadjuvant therapy in colorectal cancers	Hamad Medical Corporation (HMC)	Dr. Mai Mostafa Hisham Ali Mostafa
18	MRC-01-21-067	Assessment of Radiation Anxiety and Radiation Protective Behaviors among nurses at NCCCR	None	Ms. Anite Philip

19	MRC-01-21-111	A pilot study of the immune response to the COVID19- vaccine in cancer patients in Qatar	Hamad Medical Corporation (HMC)	Dr. Salha Bujassoum Al-Bader
20	MRC-01-21-697	Assessment Of Organs Motion Impact On Brachytherapy Treatment Planning	Hamad Medical Corporation (HMC)	Ms. Souha Aoudi
21	MRC-01-22-230	Blood expression signatures with neo adjuvant therapy in rectal cancers (resubmission MRC801-20-01-)	Hamad Medical Corporation (HMC)	Dr. Mai Mostafa Hisham Ali Mostafa
22	MRC-01-22-296	Nurse-led medication self-management intervention in the improvement of medication adherence in adult patients with multimorbidity: A feasibility Randomized controlled trial	Hamad Medical Corporation (HMC)	Ms. Kalpana Singh
23	MRC-01-22-303	Towards precision oncology in advanced differentiated thyroid cancer (advanced DTC) and anaplastic thyroid cancer (ATC)	Hamad Medical Corporation (HMC)	Dr. Maysaloun Merhi
24	MRC-01-22-360	Assessment of quality of life of patients after cervix cancer treatment in NCCCR	None	Ms. Souha Aoudi

25	**MRC-01-22-404**	Towards precision oncology in breast cancer	Hamad Medical Corporation (HMC)	Dr. Said Dermime
26	**MRC-01-22-490**	Palbociclib Combinations in HR+ve/HER-2ve Metastatic Breast Cancer Patients: A Non-Interventional Prospective Study on the Treatment Patterns & Clinical Outcomes in Africa Middle East (PRECIOUS))	Pfizer Pharmaceutical company, US	Dr. Francois Calaud
27	**MRC-01-22-536**	Quality of life among patients with Colorectal cancer in Qatar: A Cross-Sectional Study	None	Dr. Nada Adli Adli Musa Abuhashem
28	**MRC-01-22-579**	Soluble circulating prognostic and predictive biomarkers of response in Nasopharyngeal Carcinoma patients in National Center for Cancer Care and Research, HMC	Hamad Medical Corporation (HMC)	Dr. Abdulrahman Zargul
29	**MRC-01-22-738**	Quality of life and its determinants among lung cancer patients in Qatar: A cross-sectional study	None	Dr. Elias Maan Tayar

30	MRC-01-22-789	Pilot study screening soluble Immunogenic Cell Death and Immune Checkpoint dynamic biomarkers in Colorectal cancer patients treated with chemotherapy in National Center for Cancer Care and Research, HMC	Hamad Medical Corporation (HMC)	Dr. Alaaeldin Shablak
31	MRC-01-22-796	Real-World Analysis of Granulocyte Colony Stimulating Factors Use Among Oncology Patients Receiving Chemotherapy Stratified by Febrile Neutropenia Risk Levels: Mixed design study at the national level in Qatar	None	Dr. Afnan Radi Said Alnajjar
32	MRC-01-22-804	Outcome of Infection and Suspected Sepsis in Adult Patients with Hematological Malignancies and Hematopoietic stem cell Transplantation in National Center for Cancer Care and Research (NCCCR)	Hamad Medical Corporation (HMC)	Dr. Mohammed Mahmoud Mohammad Bakr

33	MRC-01-22-805	Outcome of Infection and Suspected Sepsis in Patients with solid tumors in National Center for Cancer Care and Research (NCCCR)	Hamad Medical Corporation (HMC)	Dr. Cicy Mary Jacob
34	MRC-01-22-810	Pharmacy Based Analysis of Antibiotics' Use Among Cancer Patients with Suspected infection/Sepsis: A Single Center experience in Qatar	None	Ms. Farah Imadeddin Mohammed Jibril
35	MRC-01-23-139	Prevalence of CAM use among HMC breast cancer patients in Qatar: a 2023 cross-sectional study	None	Dr. Layla Jedea Al-Mansoori
36	MRC-01-23-387	The patients' perspective about Cancer Clinical Nurse Specialist: A Qualitative Study	None	Ms. Nahrida Nazir Band
37	MRC-01-23-452	Personalized Medicine: Cardiomyopathy Predictors Biomarkers	None	Ms. Asma Mohammad Younus

38	MRC-01-23-637	Exploring reporting of oncology-related medication errors at the National center for cancer care and Research	None	Ms. Neda Jafari Takhtinejad
39	MRC-02-18-054	Triple Negative Breast Cancer Prospective Registry in Middle East, and Africa	Merck Sharp & Dohme (MSD), UK	Dr. Salha Mohd. Bu Jassoum
40	MRC-02-20-655	Genetic determinants of high-risk non-BRCA2/1 familial breast cancer in Qatar.	Qatar Biomedical Research Institute (QBRI), Qatar	Dr. Julie Decock
41	MRC-02-21-1022	Influence of Pharmacogenetics on the Clinical Outcome of Patients with Early Breast Cancer Treated with Neoadjuvant Chemotherapy in Qatar	Hamad Medical Corporation (HMC)	Dr. Salha Mohd. Bu Jassoum Dr. Moza Sulaiman H Al Hail
42	MRC-02-21-462	Prospective, observational study in Sickle Cell Disease patients on Crizanlizumab treatment in Middle East countries and India (SPOTLIGHT)	Novartis Pharmaceutical company, Switzerland	Dr. Mohd. Abdeldaem Mohd. Yassin

43	MRC-02-21-562	A Cross-sectional, Noninterventional, Multicentre Study to Determine the Prevalence of Homologous Recombination Deficiency Among Women With Newly Diagnosed, High-grade, Serous or Endometrioid Ovarian, Primary Peritoneal, and/or Fallopian Tube Cancer	AstraZeneca Pharmaceuticals Company, UK	Dr. Salha Mohd. Bu Jassoum
44	MRC-02-21-878	Exploring Drug Resistance Mechanisms in Triple Negative Breast Cancers: From Patient Derived Organoids towards Precision Medicine	Qatar Foundation (QF), Qatar	Prof. Lotfi Chouchane/ Salha Mohd. Bu Jassoum
45	MRC-02-22-251	Identification of inflammation related Treg signatures in myelodysplastic syndrome patients	Qatar University (QU), Qatar	Dr. Mohd. Abdeldaem Mohd. Yassin
46	MRC-03-17-150	Mapping Genotype To Phenotype For Colorectal Cancer Stem Cells: Implications And Perspectives In Cancer Therapy	Qatar National Research Fund (QNRF), Qatar	Dr. Cristina Maccalli

47	MRC-03-20-580	Towards personalized cancer medicine: Immunoscore and immunogenomic score in primary and metastatic colorectal cancer patients from Europe and Qatar	Qatar National Research Fund (QNRF), Qatar	Dr. Davide Bedognetti
48	MRC-03-21-400	Pre-implementation of a smartphone application to support the delivery of antimicrobial prescribing policy	Qatar National Research Fund (QNRF), Qatar	Dr. Anas Ahmad E A Hamad

ONCOLOGY

ORIGINAL ARTICLES

An integrated tumor, immune and microbiome atlas of colon cancer

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Abstract

The lack of multi-omics cancer datasets with extensive follow-up information hinders the identification of accurate biomarkers of clinical outcome. In this cohort study, we performed comprehensive genomic analyses on fresh-frozen samples from 348 patients affected by primary colon cancer, encompassing RNA, whole-exome, deep T cell receptor and 16S bacterial rRNA gene sequencing on tumor and matched healthy colon tissue, complemented with tumor whole-genome sequencing for further microbiome characterization. A type 1 helper T cell, cytotoxic, gene expression signature, called Immunologic Constant of Rejection, captured the presence of clonally expanded, tumor-enriched T cell clones and outperformed conventional prognostic molecular biomarkers, such as the consensus molecular subtype and the microsatellite instability classifications. Quantification of genetic immunoediting, defined as a lower number of neoantigens than expected, further refined its prognostic value. We identified a microbiome signature, driven by Ruminococcus bromii, associated with a favorable outcome. By combining microbiome signature and Immunologic Constant of Rejection, we developed and validated a composite score (mICRoScore), which identifies a group of patients with excellent survival probability. The publicly available multi-omics dataset provides a resource for better understanding colon cancer biology that could facilitate the discovery of personalized therapeutic approaches.

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The Global, Regional, and National Burden of Adult Lip, Oral, and Pharyngeal Cancer in 204 Countries and Territories: A Systematic Analysis for the Global Burden of Disease Study 2019

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Abstract

Importance: Lip, oral, and pharyngeal cancers are important contributors to cancer burden worldwide, and a comprehensive evaluation of their burden globally, regionally, and nationally is crucial for effective policy planning.

Objective: To analyze the total and risk-attributable burden of lip and oral cavity cancer (LOC) and other pharyngeal cancer (OPC) for 204 countries and territories and by Socio-demographic Index (SDI) using 2019 Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study estimates.

Evidence review: The incidence, mortality, and disability-adjusted life years (DALYs) due to LOC and OPC from 1990 to 2019 were estimated using GBD 2019 methods. The GBD 2019 comparative risk assessment framework was used to estimate the proportion of deaths and DALYs for LOC and OPC attributable to smoking, tobacco, and alcohol consumption in 2019.

Findings: In 2019, 370 000 (95% uncertainty interval [UI], 338 000-401 000) cases and 199 000 (95% UI, 181 000-217 000) deaths for LOC and 167 000 (95% UI, 153 000-180 000) cases and 114 000 (95% UI, 103 000-126 000) deaths for OPC were estimated to occur globally, contributing 5.5 million (95% UI, 5.0-6.0 million) and 3.2 million (95% UI, 2.9-3.6 million) DALYs, respectively. From 1990 to 2019, low-middle and low SDI regions consistently showed the highest age-standardized mortality rates due to LOC and OPC, while the high SDI strata exhibited age-standardized incidence rates decreasing for LOC and increasing for OPC. Globally in 2019, smoking had the greatest contribution to risk-attributable OPC deaths for both sexes (55.8% [95% UI, 49.2%-62.0%] of all OPC deaths in male individuals and 17.4% [95% UI, 13.8%-21.2%] of all OPC deaths in female individuals). Smoking and alcohol both contributed to substantial LOC deaths globally among male individuals (42.3% [95% UI, 35.2%-48.6%] and 40.2% [95% UI, 33.3%-46.8%] of all risk-attributable cancer deaths, respectively), while chewing tobacco contributed to the greatest attributable LOC deaths among female individuals (27.6% [95% UI, 21.5%-33.8%]), driven by high risk-attributable burden in South and Southeast Asia.

Conclusions and relevance: In this systematic analysis, disparities in LOC and OPC burden existed across the SDI spectrum, and a considerable percentage of burden was attributable to tobacco and alcohol use. These estimates can contribute to an understanding of the distribution and disparities in LOC and OPC burden globally and support cancer control planning efforts.

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Association of Axillary Dissection With Systemic Therapy in Patients With Clinically Node-Positive Breast Cancer

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Abstract

Importance: The role of axillary lymph node dissection (ALND) to determine nodal burden to inform systemic therapy recommendations in patients with clinically node (cN)-positive breast cancer (BC) is currently unknown.

Objective: To address the association of ALND with systemic therapy in cN-positive BC in the upfront surgery setting and after neoadjuvant chemotherapy (NACT).

Design, setting, and participants: This was a prospective, observational, cohort study conducted from August 2018 to June 2022. This was a preplanned study within the phase 3 randomized clinical OPBC-03/TAXIS trial. Included were patients with confirmed cN-positive BC from 44 private, public, and academic breast centers in 6 European countries. After NACT, residual nodal disease was mandatory, and a minimum follow-up of 2 months was required.

Exposures: All patients underwent tailored axillary surgery (TAS) followed by ALND or axillary radiotherapy (ART) according to TAXIS randomization. TAS removed suspicious palpable and sentinel nodes, whereas imaging-guidance was optional. Systemic therapy recommendations were at the discretion of the local investigators.

Results: A total of 500 patients (median [IQR] age, 57 [48-69] years; 487 female [97.4%]) were included in the study. In the upfront surgery setting, 296 of 335 patients (88.4%) had hormone receptor (HR)-positive and Erb-B2 receptor tyrosine kinase 2 (ERBB2; formerly HER2 or HER2/neu)-negative disease: 145 (49.0%) underwent ART, and 151 (51.0%) underwent ALND. The median (IQR) number of removed positive lymph nodes without ALND was 3 (1-4) nodes compared with 4 (2-9) nodes with ALND. There was no association of ALND with the proportion of patients undergoing adjuvant chemotherapy (81 of 145 [55.9%] vs 91 of 151 [60.3%]; adjusted odds ratio [aOR], 0.72; 95% CI, 0.19-2.67) and type of systemic therapy. Of 151 patients with NACT, 74 (51.0%) underwent ART, and 77 (49.0%) underwent ALND. The ratio of removed to positive nodes was a median (IQR) of 4 (3-7) nodes to 2 (1-3) nodes and 15 (12-19) nodes to 2 (1-5) nodes in the ART and ALND groups, respectively. There was no observed association of ALND with the proportion of patients

undergoing postneoadjuvant systemic therapy (57 of 74 [77.0%] vs 55 of 77 [71.4%]; aOR, 0.86; 95% CI, 0.43-1.70), type of postneoadjuvant chemotherapy (eg, capecitabine: 10 of 74 [13.5%] vs 10 of 77 [13.0%]; trastuzumab emtansine-DM1: 9 of 74 [12.2%] vs 11 of 77 [14.3%]), or endocrine therapy (eg, aromatase inhibitors: 41 of 74 [55.4%] vs 36 of 77 [46.8%]; tamoxifen: 8 of 74 [10.8%] vs 6 of 77 [7.8%]).

Conclusion: Results of this cohort study suggest that patients without ALND were significantly understaged. However, ALND did not inform systemic therapy recommendations.

Citation: Weber WP, Matrai Z, Hayoz S, Tausch C, Henke G, Zimmermann F, Montagna G, Fitzal F, Gnant M, Ruhstaller T, Muenst S, Mueller A, Lelièvre L, Heil J, Knauer M, Egle D, Sávolt Á, Heidinger M, Kurzeder C; TAXIS Study Writing Group; Zwahlen DR, Gruber G, Ackerknecht M, Kuemmel S, Bjelic-Radisic V, Smanykó V, Vrieling C, Satler R, Hagen D, Becciolini C, Bucher S, Simonson C, Fehr PM, Gabriel N, Maráz R, Sarlos D, Dedes KJ, Leo C, Berclaz G, Fansa H, Hager C, Reisenberger K, Singer CF, Loibl S, Winkler J, Lam GT, Fehr MK, Kohlik M, Clerc K, Ostapenko V, Maggi N, Schulz A, Andreozzi M, Goldschmidt M, Saccilotto R, Markellou P. Association of Axillary Dissection With Systemic Therapy in Patients With Clinically Node-Positive Breast Cancer. JAMA Surg. 2023 Oct 1;158(10):1013-1021. doi: 10.1001/jamasurg.2023.2840. PMID: 37466971; PMCID: PMC10357358.

Impact Factor: 16.9

The clinical value of progesterone receptor expression in luminal breast cancer: A study of a large cohort with long-term follow-up

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Abstract

Background: The routine assessment of progesterone receptor (PR) expression in breast cancer (BC) remains controversial. This study aimed to evaluate the role of PR expression in luminal BC, with emphasis on the definition of positivity and its prognostic significance as compared to Ki67 expression.

Methods: A large cohort (n = 1924) of estrogen receptor (ER)-positive/HER2-negative BC was included. PR was immunohistochemically (IHC) stained on full face sections and core needle biopsies (CNB) where the optimal scoring cutoff was evaluated. In addition, the association of PR with other clinicopathological factors, cellular proliferation, disease outcome, and response to adjuvant therapy were analyzed.

Results: Although several cutoffs showed prognostic significance, the optimal cutoff to categorize PR expression into two clinically distinct prognostic groups on CNB was 10%. PR negativity showed a significant association with features of aggressive tumor behavior and poor outcome. Multivariate analyses indicated that the association between PR negativity and poor outcome was independent of tumor grade, size, node stage, and Ki67. PR negativity showed independent association with shorter survival in patients who received endocrine therapy whereas Ki67did not.

Conclusion: PR IHC expression provides independent prognostic value superior to Ki67. Routine assessment of PR expression in BC using 10% cutoff in the clinical setting is recommended.

Plain language summary: In this study, we have established an optimal approach to determine the prognostic value of progesterone receptor expression in estrogen receptor-positive breast cancer patients. To do this, the levels of progesterone receptor were measured in a large cohort of estrogen receptor-positive breast cancer patients. We have refined the definition of progesterone receptor positivity in estrogen receptor-positive breast cancer. We show that progesterone receptor expression adds prognostic and predictive value of endocrine therapy in estrogen receptor-positive breast cancer patients, and our results show that the absence of progesterone receptor is associated with poorer outcomes independent of tumor grade, size, node stage, and Ki67 expression.

Keywords: Ki67; PR; assessment; breast cancer; endocrine therapy.

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Impact Factor: 11.2

Deep Learning Approaches for Automatic Quality Assurance of Magnetic Resonance Images Using ACR Phantom

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Abstract

Background: In recent years, there has been a growing trend towards utilizing Artificial Intelligence (AI) and machine learning techniques in medical imaging, including for the purpose of automating quality assurance. In this research, we aimed to develop and evaluate various deep learning-based approaches for automatic quality assurance of Magnetic Resonance (MR) images using the American College of Radiology (ACR) standards.

Methods: The study involved the development, optimization, and testing of custom convolutional neural network (CNN) models. Additionally, popular pre-trained models such as VGG16, VGG19, ResNet50, InceptionV3, EfficientNetB0, and EfficientNetB5 were trained and tested. The use of pre-trained models, particularly those trained on the ImageNet dataset, for transfer learning was also explored. Two-class classification models were employed for assessing spatial resolution and geometric distortion, while an approach classifying the image into 10 classes representing the number of visible spokes was used for the low contrast.

Results: Our results showed that deep learning-based methods can be effectively used for MR image quality assurance and can improve the performance of these models. The low contrast test was one of the most challenging tests within the ACR phantom.

Conclusions: Overall, for geometric distortion and spatial resolution, all of the deep learning models tested produced prediction accuracy of 80% or higher. The study also revealed that training the models from scratch performed slightly better compared to transfer learning. For the low contrast, our investigation emphasized the adaptability and potential of deep learning models. The custom CNN models excelled in predicting the number of visible spokes, achieving commendable accuracy, recall,

precision, and F1 scores.

Keywords: Deep learning; MRI; Quality control.

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Impact Factor: 9.3

Transcriptome profiling and network enrichment analyses identify subtype-specific therapeutic gene targets for breast cancer and their microRNA regulatory networks

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Abstract

Previous studies have suggested that breast cancer (BC) from the Middle East and North Africa (MENA) is presented at younger age with advanced tumor stage, indicating underlying biological differences. Given the scant transcriptomic data on BC from the MENA region and to better understand the biology of this disease, we performed mRNA and microRNA (miRNA) transcriptomic profiling on a local cohort of BC (n = 96) from Qatar. Our data revealed the differentially expressed genes and miRNAs as function of BC molecular subtypes (HR+, HER2+, HER2+HR+, and TNBC), tumor grade (GIII vs GI-II), patients' age (young (≤40) vs old (>40)), and ethnicity (MENA vs

non-MENA). Our profiling data revealed close similarity between TNBC and HER2+, while the transcriptome of HER2+HR+ tumor was resemblant of that from HR+ tumors. Network analysis identified complex miRNA-mRNA regulatory networks in each BC molecular subtype, in high vs low grade tumors, in tumors from young vs old patients, and in tumors from MENA vs non-MENA, thus implicating miRNA-mediated gene regulation as an essential mechanism in shaping the transcriptome of BC. Integration of our transcriptomic data with CRISPR-Cas9 functional screen data and the OncoKB database identified numerous dependencies and therapeutic vulnerabilities in each BC molecular subtype, while CDC123 was functionally validated as potential therapeutic target for TNBC. Cox regression survival analyses identified mRNA and miRNA-based signatures predicative of worse and better relapse free survival (RFS), which were validated in larger BC cohorts. Our data provides comprehensive transcriptomic profiling and unraveled the miRNA-mRNA regulatory networks in BC patients from the region and identified novel actionable gene targets, employing integrated approach. Findings from the current study have potential implications to improve the current standard-of-care for BC from the MENA as well as patients from other ethnicities.

Citation: Elango R, Rashid S, Vishnubalaji R, Al-Sarraf R, Akhtar M, Ouararhni K, Decock J, Albagha OME, Alajez NM. Transcriptome profiling and network enrichment analyses identify subtype-specific therapeutic gene targets for breast cancer and their microRNA regulatory networks. *Cell Death Dis.* 2023 Jul 12;14(7):415. doi: 10.1038/s41419-023-05908-8. PMID: 37438342; PMCID: PMC10338679.

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Evaluation of tumour infiltrating lymphocytes in luminal breast cancer using artificial intelligence

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Abstract

Background: Tumour infiltrating lymphocytes (TILs) are a prognostic parameter in triple-negative and human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC). However, their role in luminal (oestrogen receptor positive and HER2 negative (ER + /HER2-)) BC remains unclear. In this

study, we used artificial intelligence (AI) to assess the prognostic significance of TILs in a large well-characterised cohort of luminal BC.

Methods: Supervised deep learning model analysis of Haematoxylin and Eosin (H&E)-stained whole slide images (WSI) was applied to a cohort of 2231 luminal early-stage BC patients with long-term follow-up. Stromal TILs (sTILs) and intratumoural TILs (tTILs) were quantified and their spatial distribution within tumour tissue, as well as the proportion of stroma involved by sTILs were assessed. The association of TILs with clinicopathological parameters and patient outcome was determined.

Results: A strong positive linear correlation was observed between sTILs and tTILs. High sTILs and tTILs counts, as well as their proximity to stromal and tumour cells (co-occurrence) were associated with poor clinical outcomes and unfavourable clinicopathological parameters including high tumour grade, lymph node metastasis, large tumour size, and young age. AI-based assessment of the proportion of stroma composed of sTILs (as assessed visually in routine practice) was not predictive of patient outcome. tTILs was an independent predictor of worse patient outcome in multivariate Cox Regression analysis.

Conclusion: AI-based detection of TILs counts, and their spatial distribution provides prognostic value in luminal early-stage BC patients. The utilisation of AI algorithms could provide a comprehensive assessment of TILs as a morphological variable in WSIs beyond eyeballing assessment.

Keywords:

Citation: Makhlouf S, Wahab N, Toss M, Ibrahim A, Lashen AG, Atallah NM, Ghannam S, Jahanifar M, Lu W, Graham S, Mongan NP, Bilal M, Bhalerao A, Snead D, Minhas F, Raza SEA, Rajpoot N, Rakha E. Evaluation of tumour infiltrating lymphocytes in luminal breast cancer using artificial intelligence. Br J Cancer. 2023 Nov;129(11):1747-1758. doi: 10.1038/s41416-023-02451-3. Epub 2023 Sep 30. PMID: 37777578; PMCID: PMC10667537.

Impact Factor: 9.0

Ubiquitin specific peptidase 37 and PCNA interaction promotes osteosarcoma pathogenesis by modulating replication fork progression

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Abstract

Background: Osteosarcoma is a type of bone cancer that predominantly affects young individuals,

including children and adolescents. The disease progresses through heterogeneous genetic alterations, and patients often develop pulmonary metastases even after the primary tumors have been surgically removed. Ubiquitin-specific peptidases (USPs) regulate several critical cellular processes, such as cell cycle progression, transcriptional activation, and signal transduction. Various studies have revealed the significance of USP37 in the regulation of replication stress and oncogenesis.

Methods: In this study, the Cancer Genome Atlas (TCGA) database was analyzed to investigate USP37 expression. RNA sequencing was utilized to assess the impact of USP37 overexpression and depletion on gene expression in osteosarcoma cells. Various molecular assays, including colony formation, immunofluorescence, immunoprecipitation, and DNA replication restart, were employed to examine the physical interaction between USP37 and PCNA, as well as its physiological effects in osteosarcoma cells. Additionally, molecular docking studies were conducted to gain insight into the nature of the interaction between USP37 and PCNA. Furthermore, immunohistochemistry was performed on archived tissue blocks from osteosarcoma patients to establish a correlation between USP37 and PCNA expression.

Results: Analysis of the TCGA database revealed that increased expression of USP37 was linked to decreased progression-free survival (PFS) in osteosarcoma patients. Next-generation sequencing analysis of osteosarcoma cells demonstrated that overexpression or knockdown of USP37 led to the expression of different sets of genes. USP37 overexpression provided a survival advantage, while its depletion heightened sensitivity to replication stress in osteosarcoma cells. USP37 was found to physically interact with PCNA, and molecular docking studies indicated that the interaction occurs through unique residues. In response to genotoxic stress, cells that overexpressed USP37 resolved DNA damage foci more quickly than control cells or cells in which USP37 was depleted. The expression of USP37 varied in archived osteosarcoma tissues, with intermediate expression seen in 52% of cases in the cohort examined.

Conclusion: The results of this investigation propose that USP37 plays a vital role in promoting replication stress tolerance in osteosarcoma cells. The interaction between USP37 and PCNA is involved in the regulation of replication stress, and disrupting it could potentially trigger synthetic lethality in osteosarcoma. This study has expanded our knowledge of the mechanism through which USP37 regulates replication stress, and its potential as a therapeutic target in osteosarcoma merits additional exploration.

Keywords: Deubiquitinating enzymes; Metastasis; Proliferating cell nuclear antigen; Replication stress; Ubiquitin specific protease 37.

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Marzooqi SK, Batra A, Bakhshi S, Sharma MC, Tanwar P, Khan SA, Samath EA, Uddin S, Akil ASA, Haris M, Macha MA, Pandita TK, Singh M. Ubiquitin specific peptidase 37 and PCNA interaction promotes osteosarcoma pathogenesis by modulating replication fork progression. J Transl Med. 2023 Apr 28;21(1):286. doi: 10.1186/s12967-023-04126-2. PMID: 37118828; PMCID: PMC10142227.

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Characterisation of luminal and triple-negative breast cancer with HER2 Low protein expression

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Abstract

Background: Breast cancer (BC) expressing low levels of human epidermal growth factor receptor 2 (HER2 Low) is an emerging category that needs further refining. This study aims to provide a comprehensive clinico-pathological and molecular profile of HER2 Low BC including response to therapy and patient outcome in the adjuvant and neoadjuvant settings.

Methods: Two different independent and well-characterised BC cohorts were included. Nottingham cohort (A) (n = 5744) and The Cancer Genome Atlas (TCGA) BC cohort (B) (n = 854). The clinical, molecular, biological and immunological profile of HER2 Low BC was investigated. Transcriptomic and pathway enrichment analyses were performed on the TCGA BC cohort and validated through next-generation sequencing in a subset of Nottingham cases.

Results: Ninety percent of HER2 Low tumours were hormone receptor (HR) positive (HR+), enriched with luminal intrinsic molecular subtype, lacking significant expression of HER2 oncogenic signalling genes and of favourable clinical behaviour compared to HER2 negative (HER2-) BC. In HR+ BC, no significant prognostic differences were detected between HER2 Low and HER2- tumours. However, in HR- BC, HER2 Low tumours were less aggressive with longer patient survival. Transcriptomic data showed that the majority of HR- /HER2 Low tumours were of luminal androgen receptor (LAR) intrinsic subtype, enriched with T-helper lymphocytes, activated dendritic cells and tumour associated neutrophils, while most HR-/HER2- tumours were basal-like, enriched with tumour associated macrophages.

Conclusion: HER2 Low BC is mainly driven by HR signalling in HR+ tumours. HR-/HER2 Low tumours tend to be enriched with LAR genes with a unique immune profile.

Keywords: Breast cancer; CIBERSORT; HER2 Low; Intrinsic molecular subtype; Transcriptomic analysis.

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Deciphering the Morphology of Tumor-Stromal Features in Invasive Breast Cancer Using Artificial Intelligence

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Abstract

Tumor-associated stroma in breast cancer (BC) is complex and exhibits a high degree of heterogeneity. To date, no standardized assessment method has been established. Artificial intelligence (AI) could provide an objective morphologic assessment of tumors and stroma, with the potential to identify new features not discernible by visual microscopy. In this study, we used AI to assess the clinical significance of (1) stroma-to-tumor ratio (S:TR) and (2) the spatial arrangement of stromal cells, tumor cell density, and tumor burden in BC. Whole-slide images of a large cohort (n = 1968) of well-characterized luminal BC cases were examined. Region and cell-level annotation was performed, and supervised deep learning models were applied for automated quantification of tumor and stromal features. S:TR was calculated in terms of surface area and cell count ratio, and the S:TR heterogeneity and spatial distribution were also assessed. Tumor cell density and tumor size were used to estimate tumor burden. Cases were divided into discovery (n = 1027) and test (n = 941) sets for validation of the findings. In the whole cohort, the stroma-to-tumor mean surface area ratio was 0.74, and stromal cell density heterogeneity score was high (0.7/1). BC with high S:TR showed features characteristic of good prognosis and longer patient survival in both the discovery and test sets. Heterogeneous spatial distribution of S:TR areas was predictive of worse outcome. Higher tumor burden was associated with aggressive tumor behavior and shorter survival and was an independent predictor of worse outcome (BC-specific survival; hazard ratio: 1.7, P = .03, 95% CI, 1.04-2.83 and distant metastasis-free survival; hazard ratio: 1.64, P = .04, 95% CI, 1.01-2.62) superior to absolute tumor size. The study concludes that AI provides a tool to assess major and subtle morphologic stromal features in BC with prognostic implications. Tumor burden is more prognostically informative than tumor size.

Keywords: ER-positive breast cancer; artificial intelligence; stroma-to-tumor ratio; tumor-associated stroma.

Citation: Atallah NM, Wahab N, Toss MS, Makhlouf S, Ibrahim AY, Lashen AG, Ghannam S, Mongan NP, Jahanifar M, Graham S, Bilal M, Bhalerao A, Ahmed Raza SE, Snead D, Minhas F, Rajpoot N, Rakha E. Deciphering the Morphology of Tumor-Stromal Features in Invasive Breast Cancer Using Artificial Intelligence. Mod Pathol. 2023 Oct;36(10):100254. doi: 10.1016/j.modpat.2023.100254. Epub 2023 Jun 26. PMID: 37380057.

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The Clinical and Biological Significance of Estrogen Receptor-Low Positive Breast Cancer

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Abstract

Estrogen receptor (ER) status in breast cancer (BC) is determined using immunohistochemistry (IHC) with nuclear expression in ≥1% of cells defined as ER-positive. BC with 1%-9% expression (ER-low-positive), is a clinically and biologically unique subgroup. In this study, we hypothesized that ER-low-positive BC represents a heterogeneous group with a mixture of ER-positive and ER-negative tumor,

which may explain their divergent clinical behavior. A large BC cohort (n = 8171) was investigated and categorized into 3 groups: ER-low-positive (1%-9%), ER-positive (≥10%), and ER-negative (<1%) where clinicopathological and outcome characteristics were compared. A subset of ER-low-positive cases was further evaluated using IHC, RNAscope, and RT-qPCR. PAM50 subtyping and ESR1 mRNA expression levels were assessed in ER-low-positive cases within The Cancer Genome Atlas data set. The reliability of image analysis software in assessment of ER expression in the ER-low-positive category was also assessed. ER-low-positive tumors constituted <2% of BC cases examined and showed significant clinicopathological similarity to ER-negative tumors. Most of these tumors were nonluminal types showing low ESR1 mRNA expression. Further validation of ER status revealed that 45% of these tumors were ER-negative with repeated IHC staining and confirmed by RNAscope and RT-qPCR. ER-low-positive tumors diagnosed on needle core biopsy were enriched with false-positive ER staining. BCs with 10% ER behaved similar to ER-positive, rather than ER-negative or low-positive BCs. Moderate concordance was found in assessment of ER-low-positive tumors, and this was not improved by image analysis. Routinely diagnosed ER-low-positive BC includes a proportion of ER-negative cases. We recommend repeat testing of BC showing 1%-9% ER expression and using a cutoff ≥10% expression to define ER positivity to help better inform treatment decisions.

Keywords: assessment; breast cancer; estrogen receptor; low expression; pitfalls.

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Studies on anti-colon cancer potential of nanoformulations of curcumin and succinylated curcumin in mannosylated chitosan

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Abstract

Colon cancer (CRC) is the second leading cause of death and the third most diagnosed cancer worldwide. Although curcumin (CUR) has demonstrated a potent anticancer activity, it is characterized by its poor solubility, low bioavailability, and instability. This study is a projection from a previous investigation where CUR and succinylated CUR (CUR.SA) were separately encapsulated in mannosylated-chitosan nanoparticles (CM-NPs) to form CUR-NPs and CUR.SA-NPs, respectively. Here, we aim to assess the anti-CRC activity of these two nanoformulations. Cytotoxicity studies using CCK-8 assay indicated that both CUR-NPs and CUR.SA-NPs have a dose and time-dependent toxicity towards CRC human cell-lines (HCT116 and SW480), and more cytotoxic compared to free CUR or CUR-SA in a time-dependent manner. A significant induction of early and late apoptosis in the CUR-NPs and CUR.SA-NPs treated CRC cell lines compared to untreated cells was observed. Western blotting analyses confirmed the induction of apoptosis through activation of Caspase signaling compared to untreated cells. Based on the physicochemical properties of CUR-NPs and CUR.SA-NPs along with the data from the in vitro studies, we may conclude these nanoparticle formulations hold very promising attributes, worthy of further investigations for its role in the management of CRC.

Keywords: Chitosan nanoparticles; Colorectal cancer; Curcumin; Cytotoxicity; Mannose.

Citation: Idoudi S, Bedhiafi T, Sahir F, Hijji Y, Uddin S, Merhi M, Dermime S, Billa N. Studies on anti-colon cancer potential of nanoformulations of curcumin and succinylated curcumin in mannosylated chitosan. Int J Biol Macromol. 2023 Apr 30;235:123827. doi: 10.1016/j.ijbiomac.2023.123827. Epub 2023 Feb 27. PMID: 36858085.

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Treatment with decitabine induces the expression of stemness markers, PD-L1 and NY-ESO-1 in colorectal cancer: potential for combined chemoimmunotherapy

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Abstract

Background: The mechanism of tumor immune escape and progression in colorectal cancer (CRC) is widely investigated in-vitro to help understand and identify agents that might play a crucial role

in response to treatment and improve the overall survival of CRC patients. Several mechanisms of immune escape and tumor progression, including expression of stemness markers, inactivation of immunoregulatory genes by methylation, and epigenetic silencing, have been reported in CRC, indicating the potential of demethylating agents as anti-cancer drugs. Of these, a chemotherapeutic demethylating agent, Decitabine (DAC), has been reported to induce a dual effect on both DNA demethylation and histone changes leading to an increased expression of target biomarkers, thus making it an attractive anti-tumorigenic drug.

Methods: We compared the effect of DAC in primary 1076 Col and metastatic 1872 Col cell lines isolated and generated from patients' tumor tissues. Both cell lines were treated with DAC, and the expression of the NY-ESO-1 cancer-testis antigen, the PD-L1 immunoinhibitory marker, and the CD44, Nanog, KLF-4, CD133, MSI-1 stemness markers were analyzed using different molecular and immunological assays.

Results: DAC treatment significantly upregulated stemness markers in both primary 1076 Col and meta-static 1872 Col cell lines, although a lower effect occurred on the latter: CD44 (7.85 fold; ***p = 0.0001 vs. (4.19 fold; *p = 0.0120), Nanog (4.1 fold; ***p < 0.0001 vs.1.69 fold; ***p = 0.0008), KLF-4 (4.33 fold; ***p < 0.0001 vs.2.48 fold; ***p = 0.0005), CD133 (16.77 fold; ***p = 0.0003 vs.6.36 fold; *p = 0.0166), and MSI-1 (2.33 fold; ***p = 0.0003 vs.2.3 fold; ***p = 0.0004), respectively. Interestingly, in the metastatic 1872 Col cells treated with DAC, the expression of both PD-L1 and NY-ESO-1 was increased tenfold (*p = 0.0128) and fivefold (***p < 0.0001), respectively.

Conclusions: We conclude that the upregulation of both stemness and immune checkpoint markers by DAC treatment on CRC cells might represent a mechanism of immune evasion. In addition, induction of NY-ESO-1 may represent an immuno-therapeutic option in metastatic CRC patients. Finally, the combination of DAC and anti-PD-1/anti-PD-L1 antibodies treatment should represent a potential therapeutic intervention for this group of patients.

Keywords: Chemoresistance; Colorectal cancer; Decitabine; Immune escape; NY-ESO-1; PD-L1; Stemness markers.

Citation: Taib N, Merhi M, Inchakalody V, Mestiri S, Hydrose S, Makni-Maalej K, Raza A, Sahir F, Azizi F, Nizamuddin PB, Fernandes Q, Yoosuf ZSKM, Almoghrabi S, Al-Zaidan L, Shablak A, Uddin S, Maccalli C, Al Homsi MU, Dermime S. Treatment with decitabine induces the expression of stemness markers, PD-L1 and NY-ESO-1 in colorectal cancer: potential for combined chemoimmunotherapy. J Transl Med. 2023 Mar 31;21(1):235. doi: 10.1186/s12967-023-04073-y. PMID: 37004094; PMCID: PMC10067322.

Impact Factor: 7.4

Circulating exosomal immuno-oncological checkpoints and cytokines are potential biomarkers to monitor tumor response to anti-PD-1/PD-L1 therapy in non-small cell lung cancer patients

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Abstract

Immune checkpoint inhibitors (ICIs) including anti-PD-1 and anti-PD-L1 antibodies, have significantly

changed the treatment outcomes of NSCLC patients with better overall survival. However, 15-40% of the patients still fail to respond to ICIs therapy. Identification of biomarkers associated with responses are mandated in order to increase the efficacy of such therapy. In this study we evaluated 27 serum-derived exosomal immuno-oncological proteins and 44 cytokines/chemokines before and after ICIs therapy in 17 NSCLC patients to identify surrogate biomarkers for treatment/monitoring patient stratification for maximum therapeutic benefit. We first confirmed the identity of the isolated exosomes to have their specific markers (CD63, CD81, HSP70 and CD91). We have demonstrated that baseline concentration of exosomal-PD-L1 ($p<0.0001$), exosomal-PD-L2 ($p=0.0413$) and exosomal-PD-1 ($p=0.0131$) from NSCLC patients were significantly higher than their soluble-free forms. Furthermore, the exosomal-PD-L1 was present in all the patients (100%), while only 71% of patients expressed tissue PD-L1. This indicates that exosomal-PD-L1 is a more reliable diagnostic biomarker. Interestingly, exosomal-PD-L2 expression was significantly higher ($p=0.0193$) in tissue PD-L1-negative patients compared to tissue PD-L1-positive patients. We have also shown that immuno-oncological proteins isolated from pre-ICIs treated patients were significantly higher in exosomes compared to their soluble-free counterparts (CD152, $p=0.0008$; CD80, $p=0.0182$; IDO, $p=0.0443$; Arginase, $p<0.0001$; Nectin-2, $p<0.0001$; NT5E, $p<0.0001$; Siglec-7, $p<0.0001$; Siglec-9, $p=0.0335$; CD28, $p=0.0092$; GITR, $p<0.0001$; MICA, $p<0.0001$). Finally, the changes in the expression levels of exosomal immuno-oncological proteins/cytokines and their correlation with tumor response to ICIs treatment were assessed. There was a significant downregulation of exosomal PD-L1 ($p=0.0156$), E-Cadherin ($p=0.0312$), ULBP1 ($p=0.0156$), ULBP3 ($p=0.0391$), MICA ($p=0.0391$), MICB ($p=0.0469$), Siglec7 ($p=0.0078$) and significant upregulation of exosomal PD-1 ($p=0.0156$) and IFN-γ ($p=0.0156$) in responding patients. Non-responding patients showed a significant increase in exosomal-PD-L1 ($p=0.0078$). Furthermore, responding-patients without liver-metastasis showed significant-upregulation of PD-1 ($p=0.0070$), and downregulation of ULBP1 ($p=0.0137$) and Siglec-7 ($p=0.0037$). Non-responding patients had significant-downregulation of ULBP3 ($p=0.0317$) in patient without brain-metastasis and significant-upregulation/downregulation of PD-L1 and ULBP3 ($p=0.0262/0.0286$) in patients with pulmonary-metastasis. We demonstrated for the first time that exosomal immuno-oncological proteins/cytokines are potential biomarkers to monitor response to ICIs therapy and can predict the clinical outcomes in NSCLC patients.

Keywords: NSCLC; biomarkers; cytokines; exosomes; follow-up; immune-checkpoint inhibitors; immune-oncological-checkpoints.

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therapy in non-small cell lung cancer patients. Front Immunol. 2023 Jan 18;13:1097117. doi: 10.3389/fimmu.2022.1097117. PMID: 36741391; PMCID: PMC9890181.

Impact Factor: 7.3

Serum immune mediators as novel predictors of response to anti-PD-1/PD-L1 therapy in non-small cell lung cancer patients with high tissue-PD-L1 expression

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Abstract

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related morbidity and mortality worldwide. Immune checkpoint inhibitors (ICIs) including anti-PD-1 and anti-PD-L1 antibodies, have

significantly changed the treatment outcomes with better overall survival, but only 15-40% of the patients respond to ICIs therapy. The search for predictive biomarkers of responses is warranted for better clinical outcomes. We aim here to identify pre-treatment soluble immune molecules as surrogate biomarkers for tissue PD-L1 (TPD-L1) status and as predictors of response to anti-PD-1/PD-L1 therapy in NSCLC patients. Sera from 31 metastatic NSCLC patients, eligible for anti-PD-1/PD-L1 or combined chemoimmunotherapy, were collected prior to treatment. Analysis of soluble biomarkers with TPD-L1 status showed significant up/down regulation of the immune inhibitory checkpoint markers (sSiglec7, sSiglec9, sULBP4 and sPD-L2) in patients with higher TPD-L1 (TPD-L1 >50%) expression. Moreover, correlation analysis showed significant positive linear correlation of soluble PD-L1 (sPD-L1) with higher TPD-L1 expression. Interestingly, only responders in the TPD-L1 >50% group showed significant down regulation of the immune inhibitory markers (sPD-L2, sTIMD4, sNectin2 and CEA). When responders vs. non-responders were compared, significant down regulation of other immune inhibitory biomarkers (sCD80, sTIMD4 and CEA) was recorded only in responding patients. In this, the optimal cut-off values of CD80 <91.7 pg/ml and CEA <1614 pg/ml were found to be significantly associated with better progression free survival (PFS). Indeed, multivariate analysis identified the cutoff-value of CEA <1614 pg/ml as an independent predictor of response in our patients. We identified here novel immune inhibitory/stimulatory soluble mediators as potential surrogate/predictive biomarkers for TPD-L1 status, treatment response and PFS in NSCLC patients treated with anti-PD-1/PD-L1 therapy.

Keywords: CEA; anti-PD-1; anti-PD-L1; non-small cell lung cancer; predictive soluble biomarkers; tissue PD-L1.

Citation: Raza A, Mohsen R, Kanbour A, Zar Gul AR, Philip A, Vijayakumar S, Hydrose S, Prabhu KS, Al-Suwaidi AK, Inchakalody VP, Merhi M, Abo El-Ella DM, Tauro MA, Akbar S, Al-Bozom I, Abualainin W, Al-Abdulla R, Sirriya SA, Hassnad S, Uddin S, Mohamed Ibrahim MI, Al Homsi U, Demime S. Serum immune mediators as novel predictors of response to anti-PD-1/PD-L1 therapy in non-small cell lung cancer patients with high tissue-PD-L1 expression. Front Immunol. 2023 May 15;14:1157100. doi: 10.3389/fimmu.2023.1157100. PMID: 37256148; PMCID: PMC10225547.

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Artificial Intelligence-Based Mitosis Scoring in Breast Cancer: Clinical Application

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Abstract

In recent years, artificial intelligence (AI) has demonstrated exceptional performance in mitosis identification and quantification. However, the implementation of AI in clinical practice needs to be evaluated against the existing methods. This study is aimed at assessing the optimal method of using AI-based mitotic figure scoring in breast cancer (BC). We utilized whole slide images from a large cohort of BC with extended follow-up comprising a discovery (n = 1715) and a validation (n = 859) set (Nottingham cohort). The Cancer Genome Atlas of breast invasive carcinoma (TCGA-BRCA) cohort (n = 757) was used as an external test set. Employing automated mitosis detection, the mitotic count was assessed using 3 different methods, the mitotic count per tumor area (MCT; calculated by dividing the number of mitotic figures by the total tumor area), the mitotic index

(MI; defined as the average number of mitotic figures per 1000 malignant cells), and the mitotic activity index (MAI; defined as the number of mitotic figures in 3 mm2 area within the mitotic hotspot). These automated metrics were evaluated and compared based on their correlation with the well-established visual scoring method of the Nottingham grading system and Ki67 score, clinicopathologic parameters, and patient outcomes. AI-based mitotic scores derived from the 3 methods (MCT, MI, and MAI) were significantly correlated with the clinicopathologic characteristics and patient survival ($P < .001$). However, the mitotic counts and the derived cutoffs varied significantly between the 3 methods. Only MAI and MCT were positively correlated with the gold standard visual scoring method used in Nottingham grading system ($r = 0.8$ and $r = 0.7$, respectively) and Ki67 scores ($r = 0.69$ and $r = 0.55$, respectively), and MAI was the only independent predictor of survival ($P < .05$) in multivariate Cox regression analysis. For clinical applications, the optimum method of scoring mitosis using AI needs to be considered. MAI can provide reliable and reproducible results and can accurately quantify mitotic figures in BC.

Keywords: algorithm; artificial intelligence; mitosis.

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Novel 2 Gene Signatures Associated With Breast Cancer Proliferation: Insights From Predictive Differential Gene Expression Analysis

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Abstract

The use of proliferation markers provides valuable information about the rate of tumor growth, which can guide treatment decisions. However, there is still a lack of consensus regarding the optimal molecular markers or tests to use in clinical practice. Integrating gene expression data with

clinical and histopathologic parameters enhances our understanding of disease processes, facilitates the identification of precise prognostic predictors, and supports the development of effective therapeutic strategies. The purpose of this study was to apply an integrated approach that combines morphologic, clinical, and bioinformatic data to reveal effective regulators of proliferation. Whole-slide images generated from hematoxylin-and-eosin-stained sections of The Cancer Genome Atlas (TCGA) breast cancer (BC) database (n = 1053) alongside their transcriptomic and clinical data were used to identify genes differentially expressed between tumors with high and low mitotic scores. Genes enriched in the cell-cycle pathway were used to predict the protein-protein interaction (PPI) network. Ten hub genes (ORC6, SKP2, SMC1B, CDKN2A, CDC25B, E2F1, E2F2, ORC1, PTTG1, and CDC25A) were identified using CytoHubba a Cytoscape plugin. In a multivariate Cox regression model, ORC6 and SKP2 were predictors of survival independent of existing methods of proliferation assessment including mitotic score and Ki67. The prognostic ability of these genes was validated using the Molecular Taxonomy of Breast Cancer International Consortium, Nottingham cohort, Uppsala cohort, and a combined multicentric cohort. The protein expression of these 2 genes was investigated on a large cohort of BC cases, and they were significantly associated with poor prognosis and patient outcome. A positive correlation between ORC6 and SKP2 mRNA and protein expression was observed. Our study has identified 2 gene signatures, ORC6 and SKP2, which play a significant role in BC proliferation. These genes surpassed both mitotic scores and Ki67 in multivariate analysis. Their identification provides potential opportunities for the development of targeted treatments for patients with BC.

Keywords: breast cancer; differential expression; genes; proliferation.

Citation: Ibrahim A, Toss MS, Alsaleem M, Makhlouf S, Atallah N, Green AR, Rakha EA. Novel 2 Gene Signatures Associated With Breast Cancer Proliferation: Insights From Predictive Differential Gene Expression Analysis. Mod Pathol. 2024 Feb;37(2):100403. doi: 10.1016/j.modpat.2023.100403. Epub 2023 Dec 15. PMID: 38104894.

Impact Factor: 6.98

Coinfection of HPVs Is Associated with Advanced Stage in Colorectal Cancer Patients from Qatar

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Abstract

High-risk human papillomaviruses (HPVs) are considered risk factors in the origin of several human malignancies, such as breast, cervical, head and neck, as well as colorectal cancers. However, there are no data reported on the HPV status in colorectal cancer in the State of Qatar. Therefore, we herein examined the presence of high-risk HPVs (16, 18, 31, 33, 35, 45, 51, 52, and 59), using polymerase chain reaction (PCR) in a cohort of 100 Qatari colorectal cancer patients, and their association with tumor phenotype. We found that high-risk HPV types 16, 18, 31, 35, 45, 51, 52, and 59 were present in 4, 36, 14, 5, 14, 6, 41, and 17% of our samples, respectively. Overall, 69 (69%) of the 100 samples were HPV positive; among these, 34/100 (34%) were positive for single HPV subtypes, while 35/100 (35%) of the samples were positive for two or more HPV subtypes. No significant association was noted between the presence of HPV and tumor grade, stage, or location. However, the presence of coinfection of HPV subtypes strongly correlated with advanced stage (stage 3 and 4) colorectal cancer, indicating that the copresence of more than one HPV subtype can significantly worsen the prognosis of colorectal cancer. The results from this study imply that coinfection with high-risk HPV subtypes is associated with the development of colorectal cancer in the Qatari population.

Keywords: Qatar; colorectal cancer; high-risk HPV coinfection; human papillomavirus.

Citation: Fernandes Q, Gupta I, Murshed K, Abo Samra H, Al-Thawadi H, Vranic S, Petkar M, Babu

GR, Al Moustafa AE. Coinfection of HPVs Is Associated with Advanced Stage in Colorectal Cancer Patients from Qatar. Pathogens. 2023 Mar 8;12(3):424. doi: 10.3390/pathogens12030424. PMID: 36986346; PMCID: PMC10053117.

Impact Factor: 6.58

Unmet needs in cancer patients: Creating recommendations to overcome geographical disparities in economic growth.

Middle East Panel for the Optimal Nutritional Management of Patients with Cancer

Collaborators

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Abstract

Cancer is a major clinical, economic and societal challenge across different world regions. Effective anticancer therapies are now available, yet the impact of these treatments on the needs of patients with cancer remains questionable, since improved survival is not frequently associated with improved quality of life. In an effort to raise patients' needs at the core of anticancer therapies, the importance of nutritional support has become recognized by international scientific societies. It is recognized that the needs of patients with cancer are universal, yet the economic and societal status of any country influence the availability and implementation of nutritional care. The Middle East is a geographic area in which major differences in economic growth coexist. Consequently, it appears reasonable that international guidelines on nutritional care in oncology are reviewed to highlight

those recommendations which could be universally adopted and those which may need a progressive implementation. To this end, a group of Middle East healthcare professionals working in cancer centers across the region gathered to develop a list of recommendations to be implemented in daily practice. This would translate in a likely better acceptance and delivery of nutritional care, aligning all Middle East cancer centers to the quality standards now available only in selected hospital across the region.

Keywords: Cancer patients; Clinical practice; Economic status; Malnutrition; Nutritional support; Social status.

Citation: Middle East Panel for the Optimal Nutritional Management of Patients with Cancer. Unmet needs in cancer patients: Creating recommendations to overcome geographical disparities in economic growth. Clin Nutr ESPEN. 2023 Jun;55:267-276. doi: 10.1016/j.clnesp.2023.03.009. Epub 2023 Mar 21. PMID: 37202056.

Impact Factor: 6.402

Characteristics and prognostic significance of polo-like kinase-1 (PLK1) expression in breast cancer

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Abstract

Aim: Polo-like kinase-1 (PLK1) plays a crucial role in cell cycle progression, and it is considered a potential therapeutic target in many cancers. Although the role of PLK1 is well established in triple-negative breast cancer (TNBC) as an oncogene, its role in luminal BC is still controversial. In this study, we aimed to evaluate the prognostic and predictive role of PLK1 in BC and its molecular subtypes.

Methods: A large BC cohort (n = 1208) were immunohistochemically stained for PLK1. The association with clinicopathological, molecular subtypes, and survival data was analysed. PLK1 mRNA was evaluated in the publicly available datasets (n = 6774), including The Cancer Genome Atlas and the Kaplan-Meier Plotter tool.

Results: 20% of the study cohort showed high cytoplasmic PLK1 expression. High PLK1 expression was significantly associated with a better outcome in the whole cohort, luminal BC. In contrast, high PLK1 expression was associated with a poor outcome in TNBC. Multivariate analyses indicated that high PLK1 expression is independently associated with longer survival in luminal BC, and in poorer prognosis in TNBC. At the mRNA levels, PLK1 expression was associated with short survival in TNBC

consistent with the protein expression. However, in luminal BC, its prognostic value significantly varies between cohorts.

Conclusion: The prognostic role of PLK1 in BC is molecular subtype-dependent. As PLK1 inhibitors are introduced to clinical trials for several cancer types, our study supports evaluation of the pharmacological inhibition of PLK1 as an attractive therapeutic target in TNBC. However, in luminal BC, PLK1 prognostic role remains controversial.

Keywords: ER positive; PLK1; TNBC; breast cancer; luminal; polo-like kinase-1; triple-negative.

Citation: Lashen AG, Toss MS, Wootton L, Green AR, Mongan NP, Madhusudan S, Rakha E. Characteristics and prognostic significance of polo-like kinase-1 (PLK1) expression in breast cancer. Histopathology. 2023 Sep;83(3):414-425. doi: 10.1111/his.14960. Epub 2023 May 24. PMID: 37222669.

Impact Factor: 6.4

PD-1 expression, among other immune checkpoints, on tumor-infiltrating NK and NKT cells is associated with longer disease-free survival in treatment-naïve CRC patients

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Abstract

A variety of variables, such as microsatellite instability or inflammatory mediators, are critical players in the development and progression of colorectal cancer (CRC). Natural killer (NK) and natural killer T (NKT) cells are involved in the prognoses of CRC. Immunological components of the tumor microenvironment (TME) impact cancer progression and therapeutic responses. We report that CRC patients with higher frequencies of tumor-infiltrating PD-1+ NK and NKT cells had significantly longer disease-free survival (DFS) than patients with lower frequencies. In agreement with that, patients with higher frequencies of tumor-infiltrating PD-1- NK and NKT cells showed shorter DFS. There were no significant associations between tumor-infiltrating PD-1+TIM-3+, PD-1+TIGIT+, PD-1+ICOS+, PD-1+LAG-3+ NK cells, and PD-1+TIM-3+, PD-1+TIGIT+, and PD-1+LAG-3+ NKT cells with DFS. This study highlights the significance of PD-1 expression on tumor-infiltrating NK and NKT cells and its association with disease prognoses in CRC patients.

Keywords: Colorectal cancer; Disease-free survival; Natural killer T cells; Natural killer cells; Programmed cell death-1.

Citation: Al-Mterin MA, Murshed K, Elkord E. PD-1 expression, among other immune checkpoints, on tumor-infiltrating NK and NKT cells is associated with longer disease-free survival in treatment-

naïve CRC patients. Cancer Immunol Immunother. 2023 Jun;72(6):1933-1939. doi: 10.1007/s00262-022-03337-8. Epub 2022 Nov 27. PMID: 36436018; PMCID: PMC10198836.

Impact Factor: 5.8

Identification of MicroRNAs Associated with Histological Grade in Early-Stage Invasive Breast Cancer

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Abstract

This study aimed to identify microRNAs associated with histological grade using comprehensive microRNA analysis data obtained by next-generation sequencing from early-stage invasive breast cancer. RNA-seq data from normal breast and breast cancer samples were compared to identify candidate microRNAs with differential expression using bioinformatics. A total of 108 microRNAs were significantly differentially expressed in normal breast and breast cancer tissues. Using clinicopathological information and microRNA sequencing data of 430 patients with breast cancer from The Cancer Genome Atlas (TCGA), the differences in candidate microRNAs between low- and high-grade tumors were identified. Comparing the expression of the 108 microRNAs between low- and high-grade cases, 25 and 18 microRNAs were significantly upregulated and downregulated, respectively, in high-grade cases. Clustering analysis of the TCGA cohort using these 43 microRNAs identified two groups strongly predictive of histological grade. miR-3677 is a microRNA upregulated

in high-grade breast cancer. The outcome analysis revealed that patients with high miR-3677 expression had significantly worse prognosis than those with low miR-3677 expression. This study shows that microRNAs are associated with histological grade in early-stage invasive breast cancer. These findings contribute to the elucidation of a new mechanism of breast cancer growth regulated by specific microRNAs.

Keywords: histological grade; invasive breast cancer; microRNA.

Citation: Kurozumi S, Seki N, Narusawa E, Honda C, Tokuda S, Nakazawa Y, Yokobori T, Katayama A, Mongan NP, Rakha EA, Oyama T, Fujii T, Shirabe K, Horiguchi J. Identification of MicroRNAs Associated with Histological Grade in Early-Stage Invasive Breast Cancer. Int J Mol Sci. 2023 Dec 19;25(1):35. doi: 10.3390/ijms25010035. PMID: 38203206; PMCID: PMC10779190.

Impact Factor: 5.6

Co-expression of PD-1 with TIGIT or PD-1 with TIM-3 on tumor-infiltrating CD8+ T cells showed synergistic effects on improved disease-free survival in treatment-naïve CRC patients.

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Abstract

Immune checkpoints (ICs) are highly expressed on tumor-infiltrating immune cells (TIICs) in different malignancies, including colorectal cancer (CRC). T cells play crucial roles in shaping CRC, and their presence in the tumor microenvironment (TME) has proven to be one of the best predictors of clinical outcomes. A crucial component of the immune system is cytotoxic CD8+ T cells (CTLs), which play decisive roles in the prognosis of CRC. In this study, we investigated associations of immune checkpoints expressed on tumor-infiltrating CD8+ T cells with disease-free survival (DFS) in 45 naïve-treatment CRC patients. First, we examined the associations of single ICs, and found that CRC patients with higher levels of T-cell immunoglobulin and ITIM-domain (TIGIT), T-cell immunoglobulin and mucin domain-3 (TIM-3) and programmed cell death-1 (PD-1) CD8+ T cells tended to have longer DFS. Interestingly, when PD-1 expression was combined with other ICs, there were more evident and stronger associations between higher levels of PD-1+ with TIGIT+ or PD-1+ with TIM-3+ tumor-infiltrating CD8+ T cells and longer DFS. Our findings for TIGIT were validated in The Cancer Genome Atlas (TCGA) CRC dataset. This study is the first to report on the association of co-expression of PD-1 with TIGIT and PD-1 with TIM-3 in CD8+ T cells and improved DFS in treatment-naïve CRC patients. This work highlights the significance of immune checkpoint expression on tumor-infiltrating CD8+ T cells as critical predictive biomarkers, especially when co-expression of different ICs is considered.

Keywords: CD8(+) T cells; Colorectal cancer; Disease-free survival; Immune checkpoints; Tumor-infiltrating lymphocytes.

Citation: Meyiah A, Mahmoodi Chalbatani G, Al-Mterin MA, Malekraeisi MA, Murshed K, Elkord E. Co-expression of PD-1 with TIGIT or PD-1 with TIM-3 on tumor-infiltrating CD8+ T cells showed synergistic effects on improved disease-free survival in treatment-naïve CRC patients. Int Immunopharmacol. 2023 Jun;119:110207. doi: 10.1016/j.intimp.2023.110207. Epub 2023 Apr 24. PMID: 37099940.

Impact Factor: 5.6

The expression of high mobility group protein 3 (HMGB3) in breast cancer with emphasis on its role in lymphovascular invasion

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Abstract

Lymphovascular invasion (LVI) is a common phenomenon in breast cancer (BC), and it is correlated to poor outcome. However, the biomarkers that influence the development of LVI remain to be defined. Through rigorous bioinformatics analyses, *high mobility group protein 3 (HMGB3)* was revealed as a driver gene that is associated with the presence of LVI. The purpose of this study was to further investigate the role of *HMGB3* in the pathogenesis of LVI in BC. *In vitro* functional assays were performed to investigate the effect of *HMGB3* silencing on cell proliferation, migration, adherence and transmigration of BC cell lines with dermal lymphatic endothelial cells (DLECs) and human vascular endothelial cells (HUVECs). The correlation of HMGB3 expression with clinicopathological parameters was also assessed at the transcriptomic and the proteomic levels using large BC cohorts with well-characterised LVI status. Silencing *HMGB3* reduced cell proliferation, migration, adherence

and transmigration across endothelial cell lines. At the mRNA and protein levels, high HMGB3 expression was significantly correlated with LVI-positivity, higher tumour grade, lymph nodal stage, hormone receptor negativity, HER2 positivity and poor outcome. Moreover, high HMGB3 expression was an independent predictor of shorter breast cancer-specific survival. *HMGB3* plays an oncogenic function and contributes to the development of LVI in BC. Results warrant further investigation as a potential target to inhibit LVI in BC.

Keywords: Breast cancer; HMGB3; LVI; prognosis; progression.

Citation: Aljohani AI, Alsaeed SA, Toss MS, Raafat SA, Green AR, Rakha EA. The expression of high mobility group protein 3 (*HMGB3*) in breast cancer with emphasis on its role in lymphovascular invasion. Am J Cancer Res. 2023 Nov 15;13(11):5334-5351. PMID: 38058796; PMCID: PMC10695817.

Impact Factor: 5.3

Kidney Cancer Diagnosis and Surgery Selection by Machine Learning from CT Scans Combined with Clinical Metadata

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Abstract

Kidney cancers are one of the most common malignancies worldwide. Accurate diagnosis is a critical step in the management of kidney cancer patients and is influenced by multiple factors including tumor size or volume, cancer types and stages, etc. For malignant tumors, partial or radical surgery of the kidney might be required, but for clinicians, the basis for making this decision is often unclear. Partial nephrectomy could result in patient death due to cancer if kidney removal was necessary, whereas radical nephrectomy in less severe cases could resign patients to lifelong dialysis or need for future transplantation without sufficient cause. Using machine learning to consider clinical data alongside computed tomography images could potentially help resolve some of these surgical ambiguities, by enabling a more robust classification of kidney cancers and selection of optimal surgical approaches. In this study, we used the publicly available KiTS dataset of contrast-enhanced CT images and corresponding patient metadata to differentiate four major classes of kidney cancer: clear cell (ccRCC), chromophobe (chRCC), papillary (pRCC) renal cell carcinoma, and oncocytoma (ONC). We rationalized these data to overcome the high field of view (FoV), extract tumor regions of interest (ROIs), classify patients using deep machine-learning models, and extract/post-process CT image features for combination with clinical data. Regardless of marked data imbalance, our combined approach achieved a high level of performance (85.66% accuracy, 84.18% precision, 85.66% recall, and 84.92% F1-score). When selecting surgical procedures for malignant tumors (RCC), our method proved even more reliable (90.63% accuracy, 90.83% precision, 90.61% recall, and 90.50% F1-score). Using feature ranking, we confirmed that tumor volume and cancer stage are

the most relevant clinical features for predicting surgical procedures. Once fully mature, the approach we propose could be used to assist surgeons in performing nephrectomies by guiding the choices of optimal procedures in individual patients with kidney cancer.

Keywords: cancer surgery; classification; computerized tomography (CT); kidney; machine learning; malignant tumor; object detection; partial nephrectomy; radical nephrectomy.

Citation: Mahmud S, Abbas TO, Mushtak A, Prithula J, Chowdhury MEH. Kidney Cancer Diagnosis and Surgery Selection by Machine Learning from CT Scans Combined with Clinical Metadata. Cancers (Basel). 2023 Jun 14;15(12):3189. doi: 10.3390/cancers15123189. PMID: 37370799; PMCID: PMC10296307.

Impact Factor: 5.2

High Inner Centromere Protein Expression Correlates with Aggressive Features and Predicts Poor Prognosis in Patients with Invasive Breast Cancer

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Abstract

Introduction: Inner centromere protein (INCENP) is a member of the chromosomal passenger complex and plays a key role in mitosis and cell proliferation. This study aimed to evaluate the clinical and prognostic significance of INCENP in invasive breast cancer (BC).

Methods: INCENP expression was evaluated on a tissue microarray of a large BC cohort (n = 1,295) using immunohistochemistry. At the mRNA level, INCENP expression was assessed using the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) (n = 1,980) and The Cancer Genome Atlas (TCGA) BC cohorts (n = 854). The correlations between INCENP expression, clinicopathological parameters, and patient outcome were investigated.

Results: INCENP expression was detected in the nucleus and cytoplasm of the tumour cells. Its expression was significantly associated with features characteristic of aggressive BC behaviour including high tumour grade, larger tumour size, and high Nottingham prognostic index scores. High INCENP nuclear expression was a predictor of shorter BC-specific survival in the whole cohort, as well as in the luminal subtype (p < 0.001). High INCENP nuclear expression was predictive of poor prognosis in BC patients who received hormone treatment or chemotherapy.

Conclusion: High INCENP expression is a poor prognostic biomarker in BC with potential therapeutic benefits.

Keywords: Chromosomal passenger complex; Inner centromere protein; Invasive breast cancer; Prognosis.

Citation: Ibrahim A, Miligy IM, Toss MS, Green AR, Rakha EA. High Inner Centromere Protein Expression Correlates with Aggressive Features and Predicts Poor Prognosis in Patients with Invasive Breast Cancer. Pathobiology. 2023;90(6):377-388. doi: 10.1159/000529628. Epub 2023 Apr 7. PMID: 37031675.

Impact Factor: 5.0

The molecular mechanisms of apoptosis accompanied with the epigenetic regulation of the NY-ESO-1 antigen in non-small lung cancer cells treated with decitabine (5-aza-CdR)

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Abstract

Dysregulated epigenetic modifications are common in lung cancer but have been reversed using demethylating agent like 5-Aza-CdR. 5-Aza-CdR induces/upregulates the NY-ESO-1 antigen in lung cancer. Therefore, we investigated the molecular mechanisms accompanied with the epigenetic regulation of NY-ESO-1 in 5-Aza-CdR-treated NCI-H1975 cell line. We showed significant induction of the NY-ESO-1 protein (**$p < 0.0097$) using Cellular ELISA. Bisulfite-sequencing demonstrated 45.6% demethylation efficiency at the NY-ESO-1 gene promoter region and RT-qPCR analysis confirmed the significant induction of NY-ESO-1 at mRNA level (128-fold increase, *$p < 0.050$). We then investigated the mechanism by which 5-Aza-CdR inhibits cell proliferation in the NCI-H1975 cell line. Upregulation of the death receptors TRAIL (2.04-fold *$p < 0.011$) and FAS (2.1-fold *$p < 0.011$) indicate activation of the extrinsic apoptotic pathway. The upregulation of Voltage-dependent anion-selective channel protein 1 (1.9-fold), Major vault protein (1.8-fold), Bax (1.16-fold), and Cytochrome C (1.39-fold) indicate the activation of the intrinsic pathway. We also observed the differential expression of protein Complement C3 (3.3-fold), Destrin (-5.1-fold), Vimentin (-1.7-fold), Peroxiredoxin 4 (-1.6-fold), Fascin (-1.8-fold), Heme oxygenase-2 (-0.67-fold**$p < 0.0055$), Hsp27 (-0.57-fold**$p < 0.004$), and Hsp70 (-0.39-fold **$p < 0.001$), indicating reduced cell growth, cell migration, and metastasis. The upregulation of 40S ribosomal protein S9 (3-fold), 40S ribosomal protein S15 (4.2-fold), 40S ribosomal protein S18 (2.5-fold), and 60S ribosomal protein L22 (4.4-fold) implied the induction of translation machinery. These results reiterate the decisive role of 5-Aza-CdR in lung cancer treatment since it induces the epigenetic regulation of NY-ESO-1 antigen, inhibits cell proliferation, increases apoptosis, and decreases invasiveness.

Keywords: 5 Aza-CdR; Apoptosis; Epigenetic regulation; Intrinsic and extrinsic apoptotic pathway; NY-ESO-1; Non small lung cancer.

Citation: Inchakalody VP, Hydrose SP, Krishnankutty R, Merhi M, Therachiyil L, Sasidharan Nair V, Elashi AA, Khan AQ, Taleb S, Raza A, Yoosuf ZSKM, Fernandes Q, Al-Zaidan L, Mestiri S, Taib N, Bedhiafi T, Moustafa D, Assami L, Maalej KM, Elkord E, Uddin S, Al Homsi U, Dermime S. The molecular mechanisms of apoptosis accompanied with the epigenetic regulation of the NY-ESO-1 antigen in non-small lung cancer cells treated with decitabine (5-aza-CdR). Eur J Pharmacol. 2023 Apr 15;945:175612. doi: 10.1016/j.ejphar.2023.175612. Epub 2023 Feb 22. PMID: 36822455.

Impact Factor: 5.0

Novel Tetrahydro-[1,2,4]triazolo[3,4-a]isoquinoline Chalcones Suppress Breast Carcinoma through Cell Cycle Arrests and Apoptosis

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Abstract

Chalcones are interesting anticancer drug candidates which have attracted much interest due to their unique structure and their extensive biological activity. Various functional modifications in chalcones have been reported, along with their pharmacological properties. In the current study, novel chalcone derivatives with the chemical base of tetrahydro-[1,2,4]triazolo[3,4-a]isoquinolin-3-yl)-3-arylprop-2-en-1-one were synthesized, and the structure of their molecules was confirmed through NMR spectroscopy. The antitumor activity of these newly synthesized chalcone derivatives was tested on mouse (Luc-4T1) and human (MDA-MB-231) breast cancer cell lines. The antiproliferative effect was evaluated through SRB screening and the MTT assay after 48 h of treatment at different concentrations. Interestingly, among the tested chalcone derivatives, chalcone analogues with a methoxy group were found to have significant anticancer activity and displayed gradient-dependent inhibition against breast cancer cell proliferation. The anticancer properties of these unique analogues were examined further by cytometric analysis of the cell cycle, quantitative PCR, and the caspases-

Glo 3/7 assay. Chalcone methoxy derivatives showed the capability of cell cycle arrest and increased Bax/Bcl2 mRNA ratios as well as caspases 3/7 activity. The molecular docking analysis suggests that these chalcone methoxy derivatives may inhibit anti-apoptotic proteins, particularly cIAP1, BCL2, and EGFRK proteins. In conclusion, our findings confirm that chalcone methoxy derivatives could be considered to be potent drug candidates against breast cancer.

Keywords: Luc4T1; MDA; breast cancer; cIAP1; cell cycle; chalcones; cytotoxicity; docking; methoxy group effect.

Citation: Darwish MIM, Moustafa AM, Youssef AM, Mansour M, Yousef AI, El Omri A, Shawki HH, Mohamed MF, Hassaneen HM, Abdelhamid IA, Oishi H. Novel Tetrahydro-[1,2,4]triazolo[3,4-a] isoquinoline Chalcones Suppress Breast Carcinoma through Cell Cycle Arrests and Apoptosis. Molecules. 2023 Apr 10;28(8):3338. doi: 10.3390/molecules28083338. PMID: 37110575; PMCID: PMC10144155.

Impact factor: 4.927

Incidence and association of high-risk HPVs and EBV in patients with advanced stages of colorectal cancer from Qatar

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Abstract

High-risk Human Papillomaviruses (HPVs) and Epstein - Barr virus (EBV) are present and involved in several types of human carcinomas, including cervical and, head and neck cancers. Nevertheless, their presence and association in the pathogenesis of colorectal cancer is still nascent. The current study explored the association between the high-risk HPVs and EBV and tumor phenotype in colorectal cancers (CRCs) in the Qatari population. We found that high-risk HPVs and EBV are present in 69/100 and 21/100 cases, respectively. Additionally, 17% of the cases showed a copresence of high-risk HPVs and EBV, with a significant correlation only between the HPV45 subtype and EBV ($p = .004$). While the copresence did not significantly associate with clinicopathological characteristics, we identified that coinfection with more than two subtypes of HPV is a strong predictor of advanced stage CRC, and the confounding effect of the copresence of EBV in such cases strengthens this association. Our results indicate that high-risk HPVs and EBV can co-present in human CRCs in the Qatari population where they could plausibly play a specific role in human colorectal carcinogenesis. However, future studies are essential to confirm their copresence and synergistic role in developing CRCs.

Keywords: Colorectal cancer; Epstein–Barr virus; Qatar; human papillomavirus; oncoviral coinfection; oncovirus.

Citation: Fernandes Q, Gupta I, Murshed K, Samra HA, Al-Thawadi H, Vranic S, Petkar M, Babu

GR, Moustafa AA. Incidence and association of high-risk HPVs and EBV in patients with advanced stages of colorectal cancer from Qatar. Hum Vaccin Immunother. 2023 Aug 1;19(2):2220626. doi: 10.1080/21645515.2023.2220626. Epub 2023 Jun 9. PMID: 37293893; PMCID: PMC10332205.

Impact Factor: 4.8

The effectiveness and safety of palbociclib and ribociclib in stage IV HR+/HER-2 negative breast cancer: a nationwide real world comparative retrospective cohort study

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Abstract

Introduction: Palbociclib and ribociclib are indicated in the first-line treatment of hormonal receptor-positive HER-2 negative (HR+/HER2- negative) advanced breast cancer. Although randomized-controlled trials (RCTs) proved their clinical efficacy, there are no observational studies yet to validate the clinical findings in the real-world. Therefore, this study aimed to evaluate and compare the clinical effectiveness and safety profiles of palbociclib and ribociclib in Qatar.

Materials and methods: A retrospective observational study was conducted on HR+/HER-2-negative stage-IV breast cancer patients receiving palbociclib or ribociclib in the state of Qatar. Clinical data were collected from the National Center for Cancer Care and Research (NCCCR) in Qatar using Cerner®. Primary outcomes were progression-free-survival (PFS) and overall-survival (OS) generated by Kaplan-Meier curves. Moreover, safety profiles of both two treatments were evaluated.

Results: The data from 108 patients were included in the final analysis. There was no statistically significant difference in PFS between the palbociclib and ribociclib groups; PFS was 17.85 versus 13.55 months, respectively($p > 0.05$). Similarly, there was no statistically significant difference in OS between the two medications, 29.82 versus 31.72 months, respectively($p>0.05$). Adverse events

were similar between the two groups. Neutropenia was the most common side effect in the study population accounting for 59.3% of the patients.

Conclusions: Therefore, both treatments have similar efficacy and safety profiles. Further research on a larger-scale population and longer follow-up period is recommeneded.

Keywords: CDK4/6 cell cycle inhibitors; HR+/HER-2 negative; advanced breast cancer (ABC); cyclin-dependent-kinase 4/6 inhibitors; effectiveness & efficiency (E&E).

Citation: Al-Ziftawi NH, Elazzazy S, Alam MF, Shafie A, Hamad A, Bbujassoum S, Mohamed Ibrahim MI. The effectiveness and safety of palbociclib and ribociclib in stage IV HR+/HER-2 negative breast cancer: a nationwide real world comparative retrospective cohort study. Front Oncol. 2023 Dec 15;13:1203684. doi: 10.3389/fonc.2023.1203684. PMID: 38162489; PMCID: PMC10757634.

Impact factor: 4.7

BRCA1-specific machine learning model predicts variant pathogenicity with high accuracy

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Identification of novel BRCA1 variants outpaces their clinical annotation which highlights the importance of developing accurate computational methods for risk assessment. Therefore our aim was to develop a BRCA1-specific machine learning model to predict the pathogenicity of all types of BRCA1 variants and to apply this model and our previous BRCA2-specific model to assess BRCA variants of uncertain significance (VUS) among Qatari patients with breast cancer. We developed an XGBoost model that utilizes variant information such as position frequency and consequence as well as prediction scores from numerous in silico tools. We trained and tested the model with BRCA1 variants that were reviewed and classified by the Evidence-Based Network for the Interpretation of Germline Mutant Alleles (ENIGMA) consortium. In addition we tested the model's performance on an independent set of missense variants of uncertain significance with experimentally determined functional scores. The model performed excellently in predicting the pathogenicity of ENIGMA-classified variants (accuracy: 99.9%) and in predicting the functional consequence of the independent set of missense variants (accuracy: 93.4%). Moreover it predicted 2 115 potentially pathogenic variants among the 31 058 unreviewed BRCA1 variants in the BRCA exchange database. Using two BRCA-specific models we did not identify any pathogenic BRCA1 variants among those found in patients in Qatar but predicted four potentially pathogenic BRCA2 variants, which could be prioritized for functional validation.

Keywords: BRCA2; VUS; breast cancer; in silico predictions; ovarian cancer.

Citation: Khandakji M, Habish HHA, Abdulla NBS, Kusasi SAA, Abdou NMG, Al-Mulla HMMA, Al Sulaiman RJAA, Bu Jassoum SM, Mifsud B. BRCA1-specific machine learning model predicts variant pathogenicity with high accuracy. Physiol Genomics. 2023 Aug 1;55(8):315-323. doi: 10.1152/physiolgenomics.00033.2023. Epub 2023 Jun 19. PMID: 37335020; PMCID: PMC10393322.

Impact Factor: 4.297

Knowledge toward ovarian cancer symptoms among women in Syria: Cross-sectional study

Haidara Bohsas [1], Hidar Alibrahim [1], Sarya Swed [1], Amro A El-Sakka [2], Mohammad Alyosef [3], Haia Haitham Sarraj [1], Bisher Sawaf [4], Mhd Baraa Habib [4], Sherihan Fathey [5], Gowhar Rashid [6], Ahmed Thabet Daraghmi [7], Angham Thabet Daraghmi [7], Wael Hafez [7 8]

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Abstract

Background: Ovarian cancer is the second most prevalent malignancy in women over 40, especially in low-income nations. For every 100,000 women in Syria, 473 new cases of ovarian cancer are diagnosed. This study aims to investigate the knowledge of ovarian cancer symptoms among Syrian women and determine the factors associated with good knowledge.

Methods: An online cross-sectional was performed between July 29 and August 17, 2022. The inquired participants in the study were Syrian females above 18 years. The questionnaire consists of 41 questions organized into three sections: sociodemographic information, Confidence in recognizing ovarian cancer symptoms, and women's Awareness of the symptoms of ovarian cancer.

Results: This research included 557 Syrian women, and the average age was 23. Only 20.5% of involved women demonstrated a good knowledge of the symptoms of ovarian cancer. The participants who agreed that abdominal pain and pelvic pain are ovarian cancer symptoms formed (36.8%), and (63.9%), respectively. Regarding the additional presenting symptoms of ovarian cancer, "extreme generalized fatigue" was the most often reported symptom (66.1%). Divorced women

showed greater knowledge scores than other marital status groups (7.13 ± 3.31, P-value<0.05), while public sector participants scored higher than other occupational groups (6.38 ± 2.5, P-value<0.05).

Conclusion: Our findings indicate that Syrian females have inadequate knowledge regarding ovarian cancer symptoms. More ovarian cancer awareness programs for Syrian women of all ages are needed to increase the early identification of this illness.

Keywords: Awareness; Cross-sectional study; Ovarian cancer; Symptoms.

Citation: Bohsas H, Alibrahim H, Swed S, A El-Sakka A, Alyosef M, Haitham Sarraj H, Sawaf B, Baraa Habib M, Fathey S, Rashid G, Thabet Daraghmi A, Thabet Daraghmi A, Hafez W. Knowledge toward ovarian cancer symptoms among women in Syria: Cross-sectional study. Heliyon. 2023 Aug 12;9(8):e19076. doi: 10.1016/j.heliyon.2023.e19076. PMID: 37636422; PMCID: PMC10457438.

Impact factor: 4.0

COVID-19 in patients with neuroendocrine neoplasms: 2-year results of the INTENSIVE study

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Abstract

We conducted a retrospective/prospective worldwide study on patients with neuroendocrine neoplasms (NENs) and a molecularly proven SARS-CoV-2 positivity. Preliminary results regarding 85 patients of the INTENSIVE study have been published in 2021. Now we are reporting the 2-year analysis.Here, we are reporting data from consecutive patients enrolled between 1 June 2020, and 31 May 2022. Among the 118 contacted centers, 25 were active to enroll and 19 actively recruiting at the time of data cut-off for a total of 280 patients enrolled. SARS-CoV-2 positivity occurred in 47.5% of patients in 2020, 35.1% in 2021, and 17.4% in 2022. The median age for COVID-19 diagnosis was 60 years. Well-differentiated tumors, non-functioning, metastatic stage, and gastroenteropancreatic (GEP) primary sites represented most of the NENs. COVID-19-related pneumonia occurred in 22.8% of the total, with 61.3% of them requiring hospitalization; 11 patients (3.9%) needed sub-intensive or intensive care unit therapies and 14 patients died (5%), in 11 cases (3.9%) directly related to COVID-19. Diabetes mellitus and age at COVID-19 diagnosis > 70 years

were significantly associated with COVID-19 mortality, whereas thoracic primary site with COVID-19 morbidity. A significant decrease in both hospitalization and pneumonia occurred in 2022 vs 2020. In our largest series of NEN patients with COVID-19, the NEN population is similar to the general population of patients with NEN regardless of COVID-19. However, older age, non-GEP primary sites and diabetes mellitus should be carefully considered for increased COVID-19 morbidity and mortality. Relevant information could be derived by integrating our results with NENs patients included in other cancer patients with COVID-19 registries.

Keywords: COVID-19; SARS-CoV-2; coronavirus; neuroendocrine neoplasms; neuroendocrine tumors.

Citation: Fazio N, Gervaso L, Halfdanarson TR, Sonbol M, Eiring RA, Pusceddu S, Prinzi N, Lombardi Stocchetti B, Grozinsky-Glasberg S, Gross DJ, Walter T, Robelin P, Lombard-Bohas C, Frassoni S, Bagnardi V, Antonuzzo L, Sparano C, Massironi S, Gelsomino F, Bongiovanni A, Ranallo N, Tafuto S, Rossi M, Cives M, Rasul Kakil I, Hamid H, Chirco A, Squadroni M, La Salvia A, Hernando J, Hofland J, Koumarianou A, Boselli S, Tamayo D, Mazzon C, Rubino M, Spada F. COVID-19 in patients with neuroendocrine neoplasms: 2-year results of the INTENSIVE study. Endocr Relat Cancer. 2023 Apr 26;30(6):e220395. doi: 10.1530/ERC-22-0395. PMID: 36930250.

Impact factor: 3.9

Trends in use of neoadjuvant systemic therapy in patients with clinically node-positive breast cancer in Europe: prospective TAXIS study (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101)

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Abstract

Purpose: The aim of this study was to evaluate clinical practice heterogeneity in use of neoadjuvant systemic therapy (NST) for patients with clinically node-positive breast cancer in Europe.

Methods: The study was preplanned in the international multicenter phase-III OPBC-03/TAXIS trial (ClinicalTrials.gov Identifier: NCT03513614) to include the first 500 randomized patients with confirmed nodal disease at the time of surgery. The TAXIS study's pragmatic design allowed both the neoadjuvant and adjuvant setting according to the preferences of the local investigators who were encouraged to register eligible patients consecutively.

Results: A total of 500 patients were included at 44 breast centers in six European countries from August 2018 to June 2022, 165 (33%) of whom underwent NST. Median age was 57 years (interquartile range [IQR], 48-69). Most patients were postmenopausal (68.4%) with grade 2 and 3 hormonal receptor-positive and human epidermal growth factor receptor 2-negative breast cancer with a median tumor size of 28 mm (IQR 20-40). The use of NST varied significantly across the countries ($p < 0.001$). Austria (55.2%) and Switzerland (35.8%) had the highest percentage of patients undergoing NST and Hungary (18.2%) the lowest. The administration of NST increased significantly over the years (OR 1.42; $p < 0.001$) and more than doubled from 20 to 46.7% between 2018 and 2022.

Conclusion: Substantial heterogeneity in the use of NST with HR+/HER2- breast cancer exists in Europe. While stringent guidelines are available for its use in triple-negative and HER2+ breast cancer, there is a need for the development of and adherence to well-defined recommendations for HR+/HER2- breast cancer.

Keywords: Breast cancer surgery; Clinically node-positive; Neoadjuvant chemotherapy; Neoadjuvant systemic therapy; TAXIS trial; Tailored axillary surgery.

Citation: Tausch C, Däster K, Hayoz S, Matrai Z, Fitzal F, Henke G, Zwahlen DR, Gruber G, Zimmermann F, Andreozzi M, Goldschmidt M, Schulz A, Maggi N, Saccilotto R, Heidinger M, Mueller A, Tampaki EC, Bjelic-Radisic V, Sávolt Á, Smanykó V, Hagen D, Müller DJ, Gnant M, Loibl S, Markellou P, Bekes I, Egle D, Ruhstaller T, Muenst S, Kuemmel S, Vrieling C, Satler R, Becciolini C, Bucher S, Kurzeder C, Simonson C, Fehr PM, Gabriel N, Maráz R, Sarlos D, Dedes KJ, Leo C, Berclaz G, Fansa H, Hager C, Reisenberger K, Singer CF, Montagna G, Reitsamer R, Winkler J, Lam GT, Fehr MK, Naydina T, Kohlik M, Clerc K, Ostapenko V, Lelièvre L, Heil J, Knauer M, Weber WP. Trends in use of neoadjuvant systemic therapy in patients with clinically node-positive breast cancer in Europe: prospective TAXIS study (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101). Breast Cancer Res Treat. 2023 Sep;201(2):215-225. doi: 10.1007/s10549-023-06999-9. Epub 2023 Jun 25. PMID: 37355526; PMCID: PMC10361860.

Impact Factor: 3.8

Virtual pretreatment patient-specific quality assurance of volumetric modulated arc therapy using deep learning

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Abstract

Background: Automatic patient-specific quality assurance (PSQA) is recently explored using artificial intelligence approaches, and several studies reported the development of machine learning models for predicting the gamma pass rate (GPR) index only.

Purpose: To develop a novel deep learning approach using a generative adversarial network (GAN) to predict the synthetic measured fluence.

Methods and materials: A novel training method called "dual training," which involves the training of the encoder and decoder separately, was proposed and evaluated for cycle GAN (cycle-GAN) and conditional GAN (c-GAN). A total of 164 VMAT treatment plans, including 344 arcs (training data: 262, validation data: 30, and testing data: 52) from various treatment sites, were selected for prediction model development. For each patient, portal-dose-image-prediction fluence from TPS was used as input, and measured fluence from EPID was used as output/response for model training. Predicted GPR was derived by comparing the TPS fluence with the synthetic measured fluence generated by the DL models using gamma evaluation of criteria 2%/2 mm. The performance of dual training was compared against the traditional single-training approach. In addition, we also developed a separate classification model specifically designed to detect automatically three types of errors (rotational, translational, and MU-scale) in the synthetic EPID-measured fluence.

Results: Overall, the dual training improved the prediction accuracy of both cycle-GAN and c-GAN. Predicted GPR results of single training were within 3% for 71.2% and 78.8% of test cases for cycle-GAN and c-GAN, respectively. Moreover, similar results for dual training were 82.7% and 88.5% for cycle-GAN and c-GAN, respectively. The error detection model showed high classification accuracy (>98%) for detecting errors related to rotational and translational errors. However, it struggled to differentiate the fluences with "MU scale error" from "error-free" fluences.

Conclusion: We developed a method to automatically generate the synthetic measured fluence and identify errors within them. The proposed dual training improved the PSQA prediction accuracy of both the GAN models, with c-GAN demonstrating superior performance over the cycle-GAN. Our results indicate that the c-GAN with dual training approach combined with error detection model, can accurately generate the synthetic measured fluence for VMAT PSQA and identify the errors. This approach has the potential to pave the way for virtual patient-specific QA of VMAT treatments.

Keywords: QA; VMAT; automatic; deep learning; gamma evaluation.

Citation: Yoganathan SA, Ahmed S, Paloor S, Torfeh T, Aouadi S, Al-Hammadi N, Hammoud R. Virtual pretreatment patient-specific quality assurance of volumetric modulated arc therapy using deep learning. Med Phys. 2023 Dec;50(12):7891-7903. doi: 10.1002/mp.16567. Epub 2023 Jun 28. PMID: 37379068.

Impact Factor: 3.8

Coinfection of HPVs Is Associated with Advanced Stage in Colorectal Cancer Patients from Qatar

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Abstract

High-risk human papillomaviruses (HPVs) are considered risk factors in the origin of several human malignancies, such as breast, cervical, head and neck, as well as colorectal cancers. However, there are no data reported on the HPV status in colorectal cancer in the State of Qatar. Therefore, we herein examined the presence of high-risk HPVs (16, 18, 31, 33, 35, 45, 51, 52, and 59), using polymerase chain reaction (PCR) in a cohort of 100 Qatari colorectal cancer patients, and their association with tumor phenotype. We found that high-risk HPV types 16, 18, 31, 35, 45, 51, 52, and 59 were present in 4, 36, 14, 5, 14, 6, 41, and 17% of our samples, respectively. Overall, 69 (69%) of the 100 samples were HPV positive; among these, 34/100 (34%) were positive for single HPV subtypes, while 35/100 (35%) of the samples were positive for two or more HPV subtypes. No significant association was noted between the presence of HPV and tumor grade, stage, or location. However, the presence of coinfection of HPV subtypes strongly correlated with advanced stage (stage 3 and 4) colorectal cancer, indicating that the copresence of more than one HPV subtype can significantly worsen the prognosis of colorectal cancer. The results from this study imply that coinfection with high-risk HPV subtypes is associated with the development of colorectal cancer in the Qatari population.

Keywords: Qatar; colorectal cancer; high-risk HPV coinfection; human papillomavirus.

Citation: Fernandes Q, Gupta I, Murshed K, Abo Samra H, Al-Thawadi H, Vranic S, Petkar M, Babu

GR, Al Moustafa AE. Coinfection of HPVs Is Associated with Advanced Stage in Colorectal Cancer Patients from Qatar. Pathogens. 2023 Mar 8;12(3):424. doi: 10.3390/pathogens12030424. PMID: 36986346; PMCID: PMC10053117.

Impact factor: 3.7

Generating synthetic images from cone beam computed tomography using self-attention residual UNet for head and neck radiotherapy

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Abstract

Background and purpose: Accurate CT numbers in Cone Beam CT (CBCT) are crucial for precise dose calculations in adaptive radiotherapy (ART). This study aimed to generate synthetic CT (sCT) from CBCT using deep learning (DL) models in head and neck (HN) radiotherapy.

Materials and methods: A novel DL model, the 'self-attention-residual-UNet' (ResUNet), was developed for accurate sCT generation. ResUNet incorporates a self-attention mechanism in its long skip connections to enhance information transfer between the encoder and decoder. Data from 93 HN patients, each with planning CT (pCT) and first-day CBCT images were used. Model performance was evaluated using two DL approaches (non-adversarial and adversarial training) and two model types (2D axial only vs. 2.5D axial, sagittal, and coronal). ResUNet was compared with the traditional UNet through image quality assessment (Mean Absolute Error (MAE), Peak-Signal-to-Noise Ratio (PSNR), Structural Similarity Index (SSIM)) and dose calculation accuracy evaluation (DVH deviation and gamma evaluation (1 %/1mm)).

Results: Image similarity evaluation results for the 2.5D-ResUNet and 2.5D-UNet models were: MAE: 46±7 HU vs. 51±9 HU, PSNR: 66.6±2.0 dB vs. 65.8±1.8 dB, and SSIM: 0.81±0.04 vs. 0.79±0.05. There were no significant differences in dose calculation accuracy between DL models. Both models demonstrated DVH deviation below 0.5 % and a gamma-pass-rate (1 %/1mm) exceeding 97 %.

Conclusions: ResUNet enhanced CT number accuracy and image quality of sCT and outperformed UNet in sCT generation from CBCT. This method holds promise for generating precise sCT for HN ART.

Keywords: Adaptive Radiotherapy; Attention; CBCT; Deep-learning; Synthetic CT; UNet.

Citation: Yoganathan SA, Aouadi S, Ahmed S, Paloor S, Torfeh T, Al-Hammadi N, Hammoud R. Generating synthetic images from cone beam computed tomography using self-attention residual UNet for head and neck radiotherapy. Phys Imaging Radiat Oncol. 2023 Nov 17;28:100512. doi: 10.1016/j.phro.2023.100512. PMID: 38111501; PMCID: PMC10726231.

Impact Factor: 3.7

Characteristics and predictors associated with cancer-related fatigue among solid and liquid tumors

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Abstract

Purpose: Cancer-related fatigue (CRF) is a devastating complication with limited recognized clinical risk factors. We examined characteristics among solid and liquid cancers utilizing Machine learning (ML) approaches for predicting CRF.

Methods: We utilized 2017 National Inpatient Sample database and employed generalized linear models to assess the association between CRF and the outcome of burden of illness among hospitalized solid and non-solid tumors patients. And further applied lasso, ridge and Random Forest (RF) for building our linear and non-linear ML models.

Results: The 2017 database included 196,330 prostate (PCa), 66,385 leukemia (Leuk), 107,245 multiple myeloma (MM), and 41,185 cancers of lip, oral cavity and pharynx (CLOP) patients, and among them, there were 225, 140, 125 and 115 CRF patients, respectively. CRF was associated with a higher burden of illness among Leuk and MM, and higher mortality among PCa. For the PCa patients, both the test and the training data had best areas under the ROC curve [AUC = 0.91 (test) vs. 0.90 (train)] for both lasso and ridge ML. For the CLOP, this was 0.86 and 0.79 for ridge; 0.87 and 0.84 for lasso; 0.82 for both test and train for RF and for the Leuk cohort, 0.81 (test) and 0.76 (train) for both ridge and lasso.

Conclusion: This study provided an effective platform to assess potential risks and outcomes of CRF in patients hospitalized for the management of solid and non-solid tumors. Our study showed ML methods performed well in predicting the CRF among solid and liquid tumors.

Keywords: Cancer-related fatigue; Characteristics; Machine learning, Burden of illness; Prediction; Solid and liquid tumors.

Citation: Satheeshkumar PS, Pili R, Epstein JB, Thazhe SBK, Sukumar R, Mohan MP. Characteristics and predictors associated with cancer-related fatigue among solid and liquid tumors. J Cancer Res Clin Oncol. 2023 Nov;149(15):13875-13888. doi: 10.1007/s00432-023-05197-w. Epub 2023 Aug 4. PMID: 37540252.

Impact Factor: 3.6

Comparison of four commercial dose calculation algorithms in different evaluation tests

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Abstract

Background: Accurate and fast dose calculation is crucial in modern radiation therapy. Four dose calculation algorithms (AAA, AXB, CCC, and MC) are available in Varian Eclipse and RaySearch Laboratories RayStation Treatment Planning Systems (TPSs).

Objectives: This study aims to evaluate and compare dosimetric accuracy of the four dose calculation algorithms applying to homogeneous and heterogeneous media, VMAT plans (based on AAPM TG-119 test cases), and the surface and buildup regions.

Methods: The four algorithms are assessed in homogeneous (IAEA-TECDOCE 1540) and heterogeneous (IAEA-TECDOC 1583) media. Dosimetric evaluation accuracy for VMAT plans is then analyzed, along with the evaluation of the accuracy of algorithms applying to the surface and buildup regions.

Results: Tests conducted in homogeneous media revealed that all algorithms exhibit dose deviations within 5% for various conditions, with pass rates exceeding 95% based on recommended tolerances. Additionally, the tests conducted in heterogeneous media demonstrate high pass rates for all algorithms, with a 100% pass rate observed for 6 MV and mostly 100% pass rate for 15 MV, except for CCC, which achieves a pass rate of 94%. The results of gamma index pass rate (GIPR) for dose calculation algorithms in IMRT fields show that GIPR (3% /3 mm) for all four algorithms in all evaluated tests based on TG119, are greater than 97%. The results of the algorithm testing for the accuracy of superficial dose reveal variations in dose differences, ranging from -11.9% to 7.03% for 15 MV and -9.5% to 3.3% for 6 MV, respectively. It is noteworthy that the AXB and MC algorithms demonstrate relatively lower discrepancies compared to the other algorithms.

Conclusions: This study shows that generally, two dose calculation algorithms (AXB and MC) that

calculate dose in medium have better accuracy than other two dose calculation algorithms (CCC and AAA) that calculate dose to water.

Keywords: Acuros (AXB); Anisotropic Analytical Algorithm (AAA); Monte Carlo (MC).; Treatment Planning System (TPS); collapsed cone convolution (CCC).

Citation: Rostami A, Neto AJC, Paloor SP, Khalid AS, Hammoud R. Comparison of four commercial dose calculation algorithms in different evaluation tests. J Xray Sci Technol. 2023;31(5):1013-1033. doi: 10.3233/XST-230079. PMID: 37393487.

Impact Factor: 3.0

Applying value-based strategies to accelerate access to novel cancer medications: guidance from the Oncology Health Economics Expert Panel in Qatar (Q-OHEP)

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Abstract

Background: In line with global trends, cancer incidence and mortality may have decreased for specific types of cancer in Qatar. However, the cancer-related burden on patients, healthcare systems, and the economy is expected to expand; thus, cancer remains a significant public healthcare issue in Qatar. Qatar's free access to cancer care represents a considerable economic burden. Ensuring the best utilization of financial resources in the healthcare sector is important to provide unified and fair access to cancer care for all patients. Experts from the Qatar Oncology Health Economics Expert

Panel (Q-OHEP) aimed to establish a consistent and robust base for evaluating oncology/hematology medications; involve patients' insights to accelerate access to cutting-edge medications; increase the value of cancer care; and reach a consensus for using cost-effective strategies and efficient methodologies in cancer treatment.

Methods: The Q-OHEP convened on 30 November 2021 for a 3-hour meeting to discuss cancer management, therapeutics, and health economics in Qatar, focusing on four domains: (1) regulatory, (2) procurement, (3) treatment, and (4) patients. Discussions, guided by a moderator, focused on a list of suggested open-ended questions.

Results: Some of the salient recommendations included the development of a formal, fast-track, preliminary approval pathway for drugs needed by patients with severe disease or in critical condition; and encouraging and promoting the conduct of local clinical trials and real-world observational studies using existing registry data. The Q-OHEP also recommended implementing a forecast system using treatment center data based on the supply/demand of formulary oncology drugs to detect treatment patterns, estimate needs, expedite procurement, and prevent shortages/delays. Furthermore, the panel discussed the needs to define value concerning cancer treatment in Qatar, implement value-based models for reimbursement decision-making such as health technology assessment and multiple-criteria decision analysis, and promote patient education and involvement/feedback in developing and implementing cancer management guidelines.

Conclusion: Herein, we summarize the first Q-OHEP consensus recommendations, which aim to provide a solid basis for evaluating, registering, and approving new cancer medications to accelerate patient access to novel cancer treatments in Qatar; promote/facilitate the adoption and collection of patient-reported outcomes; and implement value-based cancer care in Qatar.

Keywords: Cancer; Health economics; Health policy; Hematology; Oncology; Patient access; Patient-reported outcomes; Pharmaceutical procurement; Precision medicine; Qatar.

Citation: Hamad A, Elazzazy S, Bujassoum S, Rasul K, Gaziev J, Cherif H, Al-Boloshi Z, Hanssens Y, Saleh A, Rasheed HA, Al-Badriyeh D, Babiker A, Hmaidan AA, Al-Hail M. Applying value-based strategies to accelerate access to novel cancer medications: guidance from the Oncology Health Economics Expert Panel in Qatar (Q-OHEP). BMC Health Serv Res. 2023 Jan 6;23(1):15. doi: 10.1186/s12913-022-08981-5. PMID: 36609388; PMCID: PMC9816531.

Impact Factor: 2.8

The Experience of Palliative Care Nurses in Qatar During the Time of COVID-19: A Qualitative Study

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Abstract

Background: The COVID-19 pandemic has been a source of significant confusion and fear for healthcare workers as they try to maintain some sense of normalcy within their daily practices. One of the many areas affected by this pandemic has been palliative care. Palliative care nurses were thrust into a world of chaos as they faced increasing numbers of patients who were in the process of dying.

Purpose: The aim of this research was to explore the caring experiences of palliative care nurses during the COVID-19 pandemic.

Methods: A qualitative interpretive description design was used to explore the experience of nurses caring for dying patients in a palliative care unit during the COVID-19 pandemic. Twenty-two nurses working in a palliative care unit participated in this study. Data were collected during 1.5- to 2-hour focus group sessions that were guided by open-ended questions.

Results: The collected data were analyzed and coded into themes, including (a) transitioning to the new normal, (b) ethical dilemmas, and (c) collaboration and support for fellow colleagues.

Conclusions: Although the COVID-19 pandemic has not yet ended, this study provides relevant implications for practice. These implications include (a) holding continuing education sessions to help nurses better understand the meaning of pandemic conditions and how best to respond and (b)

supporting nurses to better cope with the additional burdens faced because of increased patient loads. Overall, the nurses in this study were shown to have demonstrated reliance and resilience in the face of COVID-19.

Citation: Johnson J, Al Bulushi A, Idris Z, Essa ZA, Hassan A. The Experience of Palliative Care Nurses in Qatar During the Time of COVID-19: A Qualitative Study. J Nurs Res. 2023 Feb 1;31(1):e256. doi: 10.1097/jnr.0000000000000534. PMID: 36692835.

Impact Factor: 2.65

The role of multiparametric MRI in differentiating uterine leiomyosarcoma from benign degenerative leiomyoma and leiomyoma variants: a retrospective analysis

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Abstract

Aim: To assess qualitative and quantitative magnetic resonance imaging (MRI) factors that can help distinguish leiomyosarcoma (LMS) from benign degenerative leiomyoma (BDL) and leiomyoma variants (LV) and assess the interobserver agreement for the proposed quantitative factors.

Materials and methods: Retrospective analysis of all histopathology proven cases of LV, BDL, and LMS with a preoperative MRI was performed. Twenty-seven cases were included (five LMS, three LV, and 19 BDL) with each case independently read by a pair of radiologists. Lesion size, margins, presence or absence of degeneration, necrosis, and haemorrhage were assessed on MRI along with quantitative factors such as mean T2-weighted (W) and T1W signal intensity, T1W signal heterogeneity, diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) ratios as well as dynamic contrast enhancement (DCE) characteristics along with the presence or absence of lymphadenopathy and extra-uterine and peritoneal spread. Mean and standard deviation for quantitative variables and frequency with percentages for qualitative variables were assessed.

Results: Infiltrative margins were seen exclusively in the LMS group (n=1), with the remaining LMS cases showing lobulate or rounded smooth margins similar to BDL or LV. A high T2W signal <25% was seen exclusively in the BDL group (n=8). The presence of concomitant necrosis and haemorrhage was seen exclusively in the LMS group (n=2). Quantitative MRI had good inter-reader correlation but was not significantly different between the LMS, BDL, and LV groups.

Conclusion: LMS, BDL, and LV may have overlapping features on multiparametric MRI making differentiation difficult.

Citation: Mahmood NS, Al Rashid AA, Ladumor SB, Mohamed MA, Kambal AS, Saloum N, Mohamed SEMK, Al Hyassat S, Singh R. The role of multiparametric MRI in differentiating uterine leiomyosarcoma from benign degenerative leiomyoma and leiomyoma variants: a retrospective analysis. Clin Radiol. 2023 Jan;78(1):47-54. doi: 10.1016/j.crad.2022.08.144. Epub 2022 Oct 8. PMID: 36220736.

Impact Factor: 2.6

Cisplatin-induced ototoxicity: a novel approach to an ancient problem

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Abstract

With the scarcity of pharmacological otoprotective agents against cisplatin-induced ototoxicity (CIO), researchers find themselves compelled to look at and navigate all possible strategies to identify ways to prevent CIO. One of these promising strategies is pharmacogenomic implementation. This strategy aims for identifying and detecting high-risk genetic variants to tailor cisplatin therapy to reach the best survival outcomes with the least risk of ototoxicity.

Citation: Omar NE, Elewa H. Cisplatin-induced ototoxicity: a novel approach to an ancient problem. Pharmacogenet Genomics. 2023 Jul 1;33(5):111-115. doi: 10.1097/FPC.0000000000000497. Epub 2023 Apr 10. PMID: 37068004.

Impact Factor: 2.6

Assessing Syrian women's knowledge of breast cancer risk factors, warning signs, and barriers to preventive measures: A cross-sectional study

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Abstract

Background: This study aims to investigate the knowledge of Syrian women about breast cancer risk factors, warning signals, and barriers. Breast cancer is the most common cancer worldwide and the leading cause of cancer death among women. It develops when cells in the breast tissue grow uncontrollably, forming a tumor that can spread to other parts of the body.

Materials and methods: This survey was conducted online from September 3 to September 27, 2022,

and focused on Syrian women over the age of 18. It was divided into two sections, one focusing on sociodemographic characteristics and the other on breast cancer risk factors, warning signals, and barriers.

Results: This study found that the majority of the 1305 participants had inadequate knowledge of breast cancer risk factors, warning signs, and barriers. Those with higher levels of education, such as Ph.D. students, had the highest overall scores. The sample was mostly made up of housewives, married women, and women with moderate monthly incomes.

Conclusion: This research found that Syrian women have inadequate knowledge about breast cancer, including risk factors, warning signs, and barriers. To reduce mortality rates, increase survival rates, and improve early diagnosis, local health organizations should provide awareness courses to emphasize the importance of annual breast exams.

Keywords: Barriers; Breast cancer; Risk factors; Syria; Warning signs.

Citation: Bohsas H, Alibrahim H, Swed S, Khan U, Al Ibrahim M, Nashwan AJ, Hodaifah S, AlAli A, Alhalaky N, Sawaf B, Habib MB, Fathey S, Rashid G, Hafez W. Assessing Syrian women's knowledge of breast cancer risk factors, warning signs, and barriers to preventive measures: A cross-sectional study. Cancer Treat Res Commun. 2023;36:100717. doi: 10.1016/j.ctarc.2023.100717. Epub 2023 May 4. PMID: 37159973.

Impact Factor: 2.52

Combined proliferation and apoptosis index provides better risk stratification in breast cancer

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Abstract

Aims: Breast cancer (BC) risk stratification is critical for predicting behaviour and guiding management decision-making. Despite the well-established prognostic value of cellular proliferation in BC, the interplay between proliferation and apoptosis remains to be defined. In this study, we hypothesised that the combined proliferation and apoptosis indices can provide a more accurate in-vivo growth rate measure and a precise prognostic predictor.

Methods and results: Apoptotic and mitotic figures were counted in whole slide images (WSI) generated from haematoxylin and eosin-stained sections of 1545 BC cases derived from two well-defined BC cohorts. Counts were carried out visually within defined areas. There was a significant correlation between mitosis and apoptosis scores. High apoptotic counts were associated with features of aggressive behaviour, including high grade, high pleomorphism score and hormonal receptor negativity. Although the mitotic index (MI) and apoptotic index (AI) were independent prognostic indicators, the prognostic value was synergistically higher when combined. BC patients with a high combined AI and MI had the shortest survival. Replacing the mitosis score with the mitosis-apoptosis index in the Nottingham grading system revealed that the modified grade with the new score had a higher significant association with BC-specific survival with a higher hazard ratio.

Conclusion: Apoptotic figures count provides additional prognostic value in BC when combined with MI; such a combination can be implemented to assess the behaviour of BC and provides an accurate prognostic indicator. This can be considered when using artificial intelligence algorithms to assess proliferation in BC.

Keywords: apoptosis; breast cancer; count; methods.

Citation: Ibrahim A, Toss MS, Atallah NM, Al Saleem M, Green AR, Rakha EA. Combined proliferation and apoptosis index provides better risk stratification in breast cancer. Histopathology. 2023 Jun;82(7):1029-1047. doi: 10.1111/his.14887. Epub 2023 Mar 6. PMID: 36779253.

Impact Factor: 2.0

Gastrointestinal stromal tumor in North Africa and the middle east: updates in presentation and management from an 11-year retrospective cohort

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Abstract

Objectives: This study described the epidemiological, clinical, and survival profiles of patients with gastrointestinal stromal tumor (GIST) in North Africa and the Middle East (AfME).

Methods: This regional, multicenter, observational, retrospective study collected 11-year data on demographics, medical history, disease characteristics, current treatment approaches of GIST, the safety of the most common tyrosine kinase inhibitors (TKIs), second cancers, and survival status.

Results: Data of 201 eligible patients were analyzed: mean age was 56.9 ± 12.6 years; 111 (55.2%) patients were men, 21 (10.4%) patients had previous personal malignancy. The most common clinical presentation of GIST was dysphagia [92 (45.8%) patients]. The stomach was the most common primary site in 120 (60.7%) patients, 171 (85.1%) patients had localized disease at diagnosis. 198 (98.5%) GIST cases were CD117/CD34-positive. Imatinib was used in the neoadjuvant (18/21 patients), adjuvant (85/89 patients), and first-line metastatic treatment (28/33 patients) settings. The most common non-hematological toxicity associated with TKIs was vomiting in 32/85 (37.6%) patients. Overall, 100 (49.8%) patients (95%CI: 42.8-56.7%) were alive and disease-free while 30 (14.9%) patients were alive with active disease.

Conclusion: Presentation of GIST in our AfME population is consistent with global reports, being more frequent in patients >50 years old and having the stomach as the most common primary site. Unlike what is usually reported, though, we did have more patients with lymphatic spread of the disease. Despite the global trend and advances in the treatment of GIST according to molecular profile, this is still far to happen in our population given the lack of access to molecular profiles and the high associated cost.

Keywords: Diagnosis; epidemiology; gastrointestinal stromal tumor (GIST); markers; mutational analyses; tyrosine kinase inhibitors.

Citation: Farhat F, Hussein M, Sbaity E, Alsharm A, Rasul K, Khairallah S, Assi T, Allahverdi N, Othman A, Kattan J. Gastrointestinal stromal tumor in North Africa and the middle east: updates in presentation and management from an 11-year retrospective cohort. Hosp Pract (1995). 2023 Dec;51(5):275-287. doi: 10.1080/21548331.2023.2277682. Epub 2024 Jan 10. PMID: 38112178.

Impact Factor: 1.63

Transanal minimally invasive surgery for benign and malignant rectal lesions: midterm outcomes from a tertiary center

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Abstract

Background: Although transanal minimally invasive surgery (TAMIS) for rectal neoplasia has gained wide acceptance, the mid-term and long-term outcomes are not widely reported in the literature.

Objective: Describe the mid-term outcomes of patients who underwent TAMIS for benign and malignant rectal lesions in a single center.

Design: Retrospective cohort study.

Settings: Tertiary referral center.

Patients and methods: Demographic, clinical, and oncological outcomes of patients who underwent TAMIS between January 2015 and December 2022 were prospectively collected. The indication for TAMIS was based on the National Comprehensive Cancer Network guidelines. The follow up for the cancer patients included clinical examination, tumor markers every 6 months and MRI rectum at the end of one year. In addition, colonoscopy and CT scan at years one and three and a final CT scan and colonoscopy at year five.

Main outcome measures: Mid-term oncological and clinical outcome.

Results: Thirty elective TAMIS procedures included adenocarcinoma for 33.3% (n=10) of the patients, 20% (n=6) neuroendocrine tumor and the 40% (n=12) were adenomatous lesions. Negative resection margins were achieved in all malignant lesions. Perioperative complications occurred in 2 patients (6.6%), one patient had breaching into the peritoneal cavity, and postoperative hypotension occurred in another patient. The median follow-up time was 23 months (range: 5-72 months). Two patients with adenoma and positive margins developed recurrent adenoma (6.6%) and one patient with initial polypectomy biopsy of adenocarcinoma, had TAMIS with histopathology of adenoma and

distant metastasis had developed.

Conclusions: TAMIS for local excision of rectal neoplasia is a valid option with favorable mid-term outcomes provided there is adherence to careful selection criteria.

Limitations: Retrospective nature and small number of the patients.

Citation: Al-Dhaheri M, Al-Ishaq F, Toffaha A, Nada MA, Parvaiz A, Kurer M. Transanal minimally invasive surgery for benign and malignant rectal lesions: midterm outcomes from a tertiary center. Ann Saudi Med. 2023 Nov-Dec;43(6):348-351. doi: 10.5144/0256-4947.2023.348. Epub 2023 Dec 7. PMID: 38071443.

Impact Factor: 1.6

Generation of synthetic CT from CBCT using deep learning approaches for head and neck cancer patients

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Abstract

Purpose.To create a synthetic CT (sCT) from daily CBCT using either deep residual U-Net (DRUnet), or conditional generative adversarial network (cGAN) for adaptive radiotherapy planning (ART). Methods.First fraction CBCT and planning CT (pCT) were collected from 93 Head and Neck patients who underwent external beam radiotherapy. The dataset was divided into training, validation, and test sets of 58, 10 and 25 patients respectively. Three methods were used to generate sCT, 1. Nonlocal means patch based method was modified to include multiscale patches defining the multiscale patch based method (MPBM), 2. An encoder decoder 2D Unet with imbricated deep residual units was implemented, 3. DRUnet was integrated to the generator part of cGAN whereas a convolutional PatchGAN classifier was used as the discriminator. The accuracy of sCT was evaluated geometrically using Mean Absolute Error (MAE). Clinical Volumetric Modulated Arc Therapy (VMAT) plans were copied from pCT to registered CBCT and sCT and dosimetric analysis was performed by comparing Dose Volume Histogram (DVH) parameters of planning target volumes (PTVs) and organs at risk (OARs). Furthermore, 3D Gamma analysis (2%/2mm, global) between the dose on the sCT or CBCT and that on the pCT was performed.Results. The average MAE calculated between pCT and CBCT was 180.82 ± 27.37HU. Overall, all approaches significantly reduced the uncertainties in CBCT. Deep learning approaches outperformed patch-based methods with MAE = 67.88 ± 8.39HU (DRUnet) and MAE = 72.52 ± 8.43HU (cGAN) compared to MAE = 90.69 ± 14.3HU (MPBM). The percentages of DVH metric deviations were below 0.55% for PTVs and 1.17% for OARs using DRUnet. The average Gamma pass rate was 99.45 ± 1.86% for sCT generated using DRUnet.Conclusion.DL approaches outperformed MPBM. Specifically, DRUnet could be used for the generation of sCT with accurate intensities and realistic description of patient anatomy. This could be beneficial for CBCT based ART.

Keywords: CBCT; adaptive radiotherapy; deep learning; head and neck; patch method; synthetic CT.

Citation: Aouadi S, Yoganathan SA, Torfeh T, Paloor S, Caparrotti P, Hammoud R, Al-Hammadi N. Generation of synthetic CT from CBCT using deep learning approaches for head and neck cancer patients. Biomed Phys Eng Express. 2023 Aug 4;9(5). doi: 10.1088/2057-1976/acea27. PMID: 37489854.

Impact Factor: 1.4

Investigation of radiomics and deep convolutional neural networks approaches for glioma grading

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Abstract

Purpose.To determine glioma grading by applying radiomic analysis or deep convolutional neural networks (DCNN) and to benchmark both approaches on broader validation sets.Methods.Seven public datasets were considered: (1) low-grade glioma or high-grade glioma (369 patients, BraTS'20) (2) well-differentiated liposarcoma or lipoma (115, LIPO); (3) desmoid-type fibromatosis or extremity soft-tissue sarcomas (203, Desmoid); (4) primary solid liver tumors, either malignant or benign (186, LIVER); (5) gastrointestinal stromal tumors (GISTs) or intra-abdominal gastrointestinal tumors radiologically resembling GISTs (246, GIST); (6) colorectal liver metastases (77, CRLM); and (7) lung metastases of metastatic melanoma (103, Melanoma). Radiomic analysis was performed on 464 (2016) radiomic features for the BraTS'20 (others) datasets respectively. Random forests (RF), Extreme Gradient Boosting (XGBOOST) and a voting algorithm comprising both classifiers were tested. The parameters of the classifiers were optimized using a repeated nested stratified cross-validation process. The feature importance of each classifier was computed using the Gini index or permutation feature importance. DCNN was performed on 2D axial and sagittal slices encompassing the tumor. A balanced database was created, when necessary, using smart slices selection. ResNet50, Xception, EficientNetB0, and EfficientNetB3 were transferred from the ImageNet application to the tumor classification and were fine-tuned. Five-fold stratified cross-validation was performed to evaluate the models. The classification performance of the models was measured using multiple indices including area under the receiver operating characteristic curve (AUC).Results.The best radiomic approach was based on XGBOOST for all datasets; AUC was 0.934 (BraTS'20), 0.86 (LIPO), 0.73 (LIVER), (0.844) Desmoid, 0.76 (GIST), 0.664 (CRLM), and 0.577 (Melanoma) respectively. The best DCNN was based on EfficientNetB0; AUC was 0.99 (BraTS'20), 0.982 (LIPO), 0.977 (LIVER), (0.961) Desmoid, 0.926 (GIST), 0.901 (CRLM), and 0.89 (Melanoma) respectively.Conclusion.Tumor classification can be accurately determined by adapting state-of-the-art machine learning algorithms to the medical context.

Keywords: CT; benchmarking; deep learning; glioma grading; multi-contrast MRI; radiomics.

Citation: Aouadi S, Torfeh T, Arunachalam Y, Paloor S, Riyas M, Hammoud R, Al-Hammadi N. Investigation of radiomics and deep convolutional neural networks approaches for glioma grading. Biomed Phys Eng Express. 2023 Mar 23;9(3). doi: 10.1088/2057-1976/acc33a. PMID: 36898146.

Impact Factor: 1.4

Characteristics of the clinical pharmacist interventions at the National Center for Cancer Care and Research Hospital in Qatar

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Abstract

Introduction: Drug-related problems (DRPs) affect the health outcomes of patients during hospitalization. We sought to analyze the clinical pharmacist-documented interventions among hospitalized patients in the cancer hospital in Qatar.

Methods: A retrospective analysis of electronically reported clinical pharmacist interventions of patients admitted to cancer units at Hamad Medical Corporation, Qatar was conducted. Extracted data was based on an overall 3-month follow-up period; March 1-31, 2018, July 15-August 15, 2018 and January 1-31, 2019. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD).

Results: A total of 281 cancer patients with 1354 interventions were included. The average age of the study participants was 47 years (SD ± 17.36). The majority of the study population was females (n = 154, 54.80%). The prevailing pharmacist intervention was the addition of a drug therapy (n = 305, 22.53%), followed by medication discontinuation (n = 288, 21.27%) and the addition of a prophylactic agent (n = 174, 12.85%). This pattern was similar across all subgroups (i.e., gender, age, ward), except for the urgent care unit, where an increase in medication dose was the third highest frequently identified intervention (n = 3, 0.22%). The two medication groups associated with the majority of interventions were the anti-infective and fluid/electrolyte agents. Most of the interventions documented were in the oncology ward (73.19%), while the urgent care unit had the least documented interventions (1.62%).

Conclusions: Our analysis showed that clinical pharmacists can effectively identify and prevent DRPs among hospitalized cancer patients.

Keywords: Clinical pharmacy; cancer; drug-related problems; intervention.

Citation: Al Dali S, Al-Badriyeh D, Gulied A, Hamad A, Hail MA, Rouf PVA, El-Kassem W, Abushanab D. Characteristics of the clinical pharmacist interventions at the National Center for Cancer Care and Research Hospital in Qatar. J Oncol Pharm Pract. 2023 Jul 11:10781552231187305. doi: 10.1177/10781552231187305. Epub ahead of print. PMID: 37431260.

Impact Factor: 1.3

Cost savings and cost avoidance with the inpatient clinical pharmacist interventions in a tertiary cancer care hospital

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Abstract

Background: The economic benefit of the clinical pharmacist's role in ensuring the optimum use of medicines is potentially considerable, particularly when it comes to cancer management. We sought to evaluate the overall economic impact of clinical pharmacist interventions in the main cancer setting in Qatar.

Methods: The total economic benefit of the clinical pharmacy interventions were analyzed from the public hospital perspective. Patient records in March 2018, July/August 2018, and January 2019 were retrospectively reviewed at the National Center for Cancer Care and Research, Qatar. The total benefit from interventions was the total cost avoidance due to preventable adverse drug events plus any cost savings associated with therapeutic-based resource use. Sensitivity analyses confirmed the results' robustness and increased generalizability.

Results: A total of 1352 interventions based on 281 patients were analyzed. The majority of the drug-related problems were related to the appropriateness of therapy, followed by dosing and administration. The total population benefit over the 3-months study period was QAR 4,879,185 (USD 1,336,763), constituting cost avoidance of QAR 4,234,012 (USD 1,160,003) and negative resource-use cost savings of -QAR 645,174 (-USD 176,760). Projected annual overall benefit was QAR 14,355,354 (USD 3,932,974). The increase in resource use with therapies was mostly

because of the addition of other medications. Cost avoidance was mostly driven by recommending additional medications and discontinuation of medications. The uncertainty analysis demonstrated the robustness of outcomes.

Conclusions: The clinical pharmacist intervention increased resource use and its cost. In overall, however, taking avoided cost of adverse drug events in consideration, it is an economically beneficial practice in the National Center for Cancer Care and Research setting, associated with adverse drug events prevention and substantial economic benefits.

Keywords: Adverse drug event; cancer; cost savings; economics; intervention; pharmacis

Citation: Abushanab D, Gulied A, Hamad A, Abu-Tineh M, Abdul Rouf PV, Al Hail M, El-Kassem W, El Hajj MS, Al-Badriyeh D. Cost savings and cost avoidance with the inpatient clinical pharmacist interventions in a tertiary cancer care hospital. J Oncol Pharm Pract. 2023 Dec;29(8):1935-1943. doi: 10.1177/10781552231160275. Epub 2023 Mar 22. PMID: 36946146.

Impact Factor: 1.3

Analyzing Mortality Patterns and Location of Death in Patients With Malignant Esophageal Neoplasms: A Two-Decade Study in the United States

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Abstract

Background Esophageal neoplasm carries significant implications for end-of-life care. Despite medical advancements, disparities in the location of death persist. Understanding the factors influencing the place of death for esophageal neoplasm patients is crucial for delivering patient-centered care. Objectives The primary objective of this study is to inspect and evaluate mortality patterns in patients with malignant esophageal neoplasms over the past two decades. Materials and methods Using the CDC-WONDER database, the authors analyzed 309,919 esophageal neoplasm-related deaths. Data was categorized by age, gender, race, and location of death, enabling a detailed examination of the factors influencing the place of death. Result This analysis revealed significant disparities in death locations. Age, gender, race, and geographic region all played substantial roles in determining where esophageal neoplasm patients spent their final moments. Notably, males consistently experienced higher mortality rates across all settings. Geographic disparities indicated varying mortality rates by census region, with the Southern region reporting the highest rates. Racial disparities were also evident, with white individuals having the highest number of deaths. Conclusion This study underscores the importance of recognizing and addressing disparities in the place of death among esophageal neoplasm patients in the United States. By shedding light on the demographic influences on end-of-life decisions, it paves the way for more targeted and patient-centered approaches to end-of-life care for this patient population.

Keywords: age; esophageal neoplasms; gender; location; mortality patterns; racial disparities.

Citation: Vijayakumar S, Saravanan A, Sayeed N, Rusizana Kirezi NG, Duggirala NK, El-Hashash AH, Al Hussein H. Analyzing Mortality Patterns and Location of Death in Patients With Malignant Esophageal Neoplasms: A Two-Decade Study in the United States. Cureus. 2023 Dec 13;15(12):e50455. doi: 10.7759/cureus.50455. PMID: 38226107; PMCID: PMC10788881.

Impact Factor: 1.2

ONCOLOGY

CASE REPORTS

Tracheoesophageal fistula and esophageal perforation in a patient with advanced gastroesophageal junction tumor post ramucirumab treatment. A case report and literature review

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Abstract

Background: Ramucirumab is an anti-angiogenic drug that received Food and Drug Administration (FDA)-approvals for treatments of many cancers. Gastrointestinal fistulas and perforations are recognized side effects of anti-angiogenic therapies, however, there are very few reported cases of these conditions in patients managed with Ramucirumab. Here we report a case of a 46-year-old gentleman with a stage four gastroesophageal junction tumor, who developed multiple tracheoesophageal fistulas post ramucirumab containing regimen. To the best of our knowledge, this is the first case report that describes a serious uncommon complication of ramucirumab in a patient with a gastroesophageal junction tumor.

Keywords: Tracheoesophageal fistula Gastroesophageal junction tumor Ramucirumab Anti-angiogenic FOLFOX GEJ PD-L1 HER2 EGD MMR VEGF NSCLC

Citation: Ahmed Abdalhadi, Mouhammad J Alawad, Nabil E. Omar, Muhammed Hajmusa, Mohammed Gaber, Alaaeldin Shablak,Tracheoesophageal fistula and esophageal perforation in a patient with advanced gastroesophageal junction tumor post ramucirumab treatment. A case report and literature review, Current Problems in Cancer: Case Reports, Volume 9, 2023,100214

Impact Factor: 2.6

Testicular choriocarcinoma with small bowel metastasis and active gastrointestinal bleeding

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Abstract

Testicular choriocarcinomas make up less than 1% of all germ-cell tumors and are highly malignant, attributable to hematogenous spread. While the most common sites of metastasis are the lungs and liver, metastatic spread to the gastrointestinal tract is rare wherein patients may present with GI distress or even an upper GI bleed. In this report, we present a case of known testicular choriocarcinoma in a 40-year-old male who presented to the emergency room with severe anemia and a suspected upper GI bleed.

Keywords: Case report; Choriocarcinoma; Gastrointestinal bleed; Germ-cell tumor; Metastasis.

Citation: Fatimi AS, Anns KM, Khan F, Memon WA, Iqbal J, Aman M, Ahmad I, Fatima S. Testicular choriocarcinoma with small bowel metastasis and active gastrointestinal bleeding. Radiol Case Rep. 2023 Jan 6;18(3):1117-1120. doi: 10.1016/j.radcr.2022.12.019. PMID: 36684620; PMCID: PMC9849866.

Impact factor: 1.9

Delayed cervical spine metastasis from intracranial solitary fibrous tumor

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Abstract

Cervical spine metastasis from primary intracranial solitary fibrous tumors (SFTs) is an extremely rare clinical entity. This report focuses on its metastatic tendency, radiological imaging, management plan, and follow-up strategies in view of its long latency period for metastasis. A 35-year-old female presented with right-side cervical radiculopathy. Magnetic resonance imaging spine showed C7 vertebral body collapse with retropulsion and neural compression. Two years ago, the patient had surgical resection of intracranial SFT (World Health Organization grade 3) with no evidence of recurrence on follow-up imaging. Cervical C7 metastasis has been decompressed and fused by the anterior cervical approach. Histopathology confirmed SFT metastasis to the spine, and the patient received adjuvant radiotherapy. Cervical metastasis from well-controlled primary intracranial SFT poses a significant challenge for its diagnostic and management planning. Serial pre-emptive surveillance is warranted with regular imaging and appropriate patient counseling.

Keywords: Anaplastic hemangiopericytoma; Cervical; Delayed; Intracranial; Metastasis; Solitary fibrous tumor; Spine.

Citation: Arshad MM, Ali A, Thabet A, Ai-Bozom IA. Delayed cervical spine metastasis from intracranial solitary fibrous tumor. J Neurosci Rural Pract. 2023 Oct-Dec;14(4):750-753. doi: 10.25259/JNRP_252_2023. Epub 2023 Aug 5. PMID: 38059253; PMCID: PMC10696358.

Impact Factor: 1.4

Primary Ewing Sarcoma of the Cervical Spine: A Case Report and Literature Review

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Abstract

Ewing sarcoma is a rare neoplasm that mostly grows in bones or soft tissues around bones. Most cases of Ewing sarcoma occur in intra-skeletal locations (long bones, pelvis, or ribs) and rarely in extra-skeletal regions such as paravertebral or epidural space, whereas a primary intradural extramedullary Ewing sarcoma (IEES) is extremely rare. Fifty cases of primary IEES including our case were identified in the literature, so far, of which two-thirds are in the lumbosacral region, while only 12 reports described a cervical location of the tumor. Herein, we are presenting a case of C7-T1 primary IEES for a 24-year-old male, followed by a review of updated literature about the primary IEES in the cervical spine.

Keywords: ewing sarcoma; intradural extramedullary spine tumors; neurosurgery; spine oncology; spine surgery.

Citation: Shihadeh OM, Khan MM, Salih H, Thabet A, Belkhair S. Primary Ewing Sarcoma of the Cervical Spine: A Case Report and Literature Review. Cureus. 2023 Jul 30;15(7):e42687. doi: 10.7759/cureus.42687. PMID: 37649939; PMCID: PMC10464919.

Impact Factor: 1.2

Metastatic sigmoid adenocarcinoma to the larynx: A case report and updated literature review

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Abstract

Metastatic laryngeal cancer is a rare entity, usually indicating an advanced disease once discovered. In this report, we are describing a case of a 60-year-old male patient with stage IV colorectal cancer (CRC), who presented to our clinic with dysphonia; further workups showed metastatic CRC.

Keywords: colorectal adenocarcinoma; dysphonia; laryngeal metastasis; secondary laryngeal tumors.

Citation: Aljariri AA, Nashwan AJ, Hammoud R, Wazwaz B, Al Hyassat S, Haidar H. Metastatic sigmoid adenocarcinoma to the larynx: A case report and updated literature review. Clin Case Rep. 2023 Feb 8;11(2):e6942. doi: 10.1002/ccr3.6942. PMID: 36789305; PMCID: PMC9909257.

Impact factor: 1.089

Colonic medullary carcinoma: an exceedingly rare type of colorectal malignancy: a case report and review of the literature

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Abstract

Background: Medullary carcinoma of the colon is a rare subtype of colorectal cancer that has a unique, and sometimes varied, clinical and histologic profile. It usually presents in adult patients older than 50 years. Here, we report a unique case of young male patient who initially presented with abdominal pain followed by a large bowel obstruction.

Case presentation: A 40-year-old SriLankan male presented with right-sided abdominal pain and on examination, there was a palpable right iliac fossa mass. Colonoscopy and a computed tomography scan revealed cecal mass. Later, while waiting for elective resection, the patient developed symptoms and signs of a large bowel obstruction. He underwent a laparoscopic right hemicolectomy with an uneventful postoperative course. The histopathologic evaluation of the resected specimens showed invasive carcinoma with syncytial growth pattern, foci of lymphoid host response, and dirty necrosis, in keeping with a medullary carcinoma pT4a pN2b. Unlike most reported medullary carcinoma cases, this patient was young and caudal-related homeobox transcription factor 2 positive.

Conclusion: We have reported another case of medullary carcinoma of the colon in a young patient with unique histologic characteristics. Reporting such cases helps in refine understanding of the histologic and genetic, as well as clinical, phenotypes of medullary carcinoma of the colon.

Keywords: Colon cancer; Immunohistochemistry; Medullary carcinoma; Microsatellite instability.

Citation: Al-Ishaq F, Al-Dhaheri M, Toffaha A, Awad S, Rizvi S, AbuNada M, Kurer M. Colonic medullary carcinoma: an exceedingly rare type of colorectal malignancy: a case report and review of the literature. J Med Case Rep. 2023 Oct 18;17(1):434. doi: 10.1186/s13256-023-04160-0. Erratum in: J Med Case Rep. 2023 Nov 1;17(1):483. PMID: 37849007; PMCID: PMC10583308.

Impact Factor: 1.0

Large Ascites in a Cirrhotic Patient Reveal an Isolated and Late Metastasis of Ductal Breast Cancer: A Case Study

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Abstract

Breast cancer is the most prevalent cancer in women worldwide, and its prevalence has increased since the introduction of screening programs. Most cases are discovered at an early stage; however, despite effective treatment, some cases progress to metastasis. The most common breast cancer metastatic locations are the bone, liver, and lungs. Ascites malignant due to peritoneal involvement is a rare manifestation of metastatic breast cancer. After 8 years of well-controlled breast cancer, we report a 54-year-old woman who presents with malignant ascites and is known to have cirrhosis of the liver.

Keywords: Breast cancer; Case report; Invasive ductal carcinoma; Malignant ascites; Peritoneal carcinomatosis.

Citation: Mostafa S, Habib MB, Ahmed N, Sawaf B, Sadik N, Abdulhadi AM. Large Ascites in a Cirrhotic Patient Reveal an Isolated and Late Metastasis of Ductal Breast Cancer: A Case Study. Case Rep Oncol. 2023 Aug 8;16(1):585-590. doi: 10.1159/000531835. PMID: 37900789; PMCID: PMC10601764.

Impact Factor: 0.8

Esophageal Adenocarcinoma: An Unusual Pericardial and Pulmonary Metastasis - A Case Report

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Abstract

Introduction: Esophageal adenocarcinoma (EAC) manifests in the glandular cells present in the lining of the esophagus and usually forms in the distal portion of the esophagus. The metastasis of EAC has been reported to occur in surrounding lymphovascular structures, the liver, brain, and bones.

Case presentation: We present the rare case of a 52-year-old Hispanic male with EAC metastasis to the pericardium and lungs. The patient presented with shortness of breath off and on for the last 6 weeks without any usually reported symptoms of EAC like chest pain, vomiting, or chronic cough. Respiratory examinations of this patient were significant for bilateral bronchial breathing and coarse crackles. The patient had been given numerous courses of oral antibiotics over the previous weeks with the provisional diagnosis of atypical pneumonia. Cardiac tamponade pathophysiology was also observed in this patient, for which a pericardial window was created to relieve the patient's symptoms. A final diagnosis of EAC with an unusual metastasis in the lungs and pericardium was made based on radiological and pathological findings. The patient chose palliative care instead of curative care because of the advanced stage of this cancer. The patient received cancer diagnosis counseling and was sent to hospice care for further management.

Conclusion: The metastasis of EAC to the pericardium and lungs instead of usual sites constitutes an important prognostic factor in the overall survival of patients.

Keywords: Adenocarcinoma; Esophageal adenocarcinoma; Esophageal cancer; Medical oncology; Metastasis.

Citation: Rasheed W, Usman O, Rehman OU, Fatima E, Nashwan A. Esophageal Adenocarcinoma: An Unusual Pericardial and Pulmonary Metastasis - A Case Report. Case Rep Oncol. 2023 Oct 31;16(1):1253-1258. doi: 10.1159/000534359. PMID: 37915994; PMCID: PMC10618010.

Impact Factor: 0.8

Lung Cancer Mimicking Aspergilloma: A Case Report

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Abstract

An aspergilloma is a conglomeration of Aspergillus hyphae, fibrin, mucus, and cellular debris, typically found within a pulmonary cavity or ectatic bronchus. Computerized tomography (CT) scans often depict a cavity containing a solid mass and a notable crescent sign. Though these signs are indicative of aspergilloma, the European Respiratory Society emphasizes the need for a more detailed diagnostic criteria. A patient with a history of hemoptysis was initially diagnosed with an aspergilloma based on CT chest findings, showing a cavitary lesion in the left upper lobe with an intracavitary lobular opacity. Post resection, histological examination contradicted the initial diagnosis, revealing lung cancer instead. This case underscores the importance of tissue diagnosis from the outset or employing a multifaceted diagnostic criteria encompassing radiological findings, serology and microbiology tests. In the absence of an initial tissue diagnosis, rigorous follow-up, including early interval scanning, is crucial.

Keywords: Aspergilloma; Cavitary lung lesion; Lung cancer.

Citation: Wasim Jamal SM, Aboukamar MR, Khatib M, Al Maslamani M, Nashwan AJ. Lung Cancer Mimicking Aspergilloma: A Case Report. Case Rep Oncol. 2023 Nov 7;16(1):1318-1323. doi: 10.1159/000534527. PMID: 37942406; PMCID: PMC10629857.

Impact Factor: 0.8

Pulmonary Enteric Adenocarcinoma: A Very Rare Case Report from Qatar

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Abstract

A 78-year-old male patient presented with dyspnea, loss of appetite, and weight loss. Workup and imaging showed suspected malignant lung lesion. Biopsy was done and showed features of pulmonary enteric adenocarcinoma (PEAC). This is a very rare disease and its diagnosis is challenging.

Keywords: Immunohistochemistry; Lung cancer; Pulmonary enteric adenocarcinoma.

Citation: Yasin AKA, Mohamed A, Mohamed A, Elamin N, Al-Tikrity MA, Wazwaz B. Pulmonary Enteric Adenocarcinoma: A Very Rare Case Report from Qatar. Case Rep Oncol. 2023 Aug 30;16(1):759-764. doi: 10.1159/000533220. PMID: 37933317; PMCID: PMC10625813.

Impact Factor: 0.8

Intra-Abdominal Paraganglioma and Primary Thyroid Lymphoma in a Single Patient: The First Case Report

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Abstract

Rare diseases such as primary thyroid lymphoma (PTL) and paragangliomas exist. Although only 0.5% of patients experience a transformation from thyroiditis to PTL, patients with Hashimoto's thyroiditis have a higher risk of developing PTL than the general population. Primary non-Hodgkin lymphoma of the thyroid is rare. Paragangliomas are neuroendocrine tumors that originate from chromaffin cells situated along the sympathetic and parasympathetic chains. This paper reports the first case of primary diffuse large B-cell lymphoma with nonfunctional paraganglioma. A 29-year-old female presented with an enlarged neck and recurrent compressive symptoms. Ultrasonography results showed a nodule in the right lobe of the thyroid gland. Emergency thyroidectomy was performed after obtaining inconclusive fine-needle aspiration results. Immunohistopathology of the biopsy specimen confirmed the presence of a large diffuse B-cell lymphoma. Computed tomography revealed a nonfunctional mass in the adrenal gland. The team then proceeded with the appropriate treatment.

Keywords: Case report; Hashimoto's thyroiditis; Nonfunctional paraganglioma; Primary thyroid lymphoma.

Citation: Zakkor MD, Swed S, Salem R, Zayat H, Sultan R, Al Hussein H, Rezkallah V, Nashwan AJ. Intra-Abdominal Paraganglioma and Primary Thyroid Lymphoma in a Single Patient: The First Case Report. Case Rep Oncol. 2023 Aug 29;16(1):753-758. doi: 10.1159/000533300. PMID: 37933315; PMCID: PMC10625811.

Impact Factor: 0.8

Pembrolizumab-Induced Rhabdomyolysis in a Clear Cell Renal Cell Carcinoma Patient: A Case Report

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Abstract

Pembrolizumab is one of the approved treatments for many types of cancer including clear cell renal cell carcinoma (ccRCC). It has improved the prognosis of renal cell carcinoma, yet has many possible immune-related side effects. We discuss a rare case of rhabdomyolysis in an ccRCC patient treated with pembrolizumab. The case was complicated with acute kidney injury and severe hypothyroidism, which can be attributed to pembrolizumab.

Keywords: Oncology; Pembrolizumab; Renal cell carcinoma; Rhabdomyolysis.

Citation: Altermanini M, Ali K, Alwassiti W, Almohtasib S, Omar NE, Zafar A. Pembrolizumab-Induced Rhabdomyolysis in a Clear Cell Renal Cell Carcinoma Patient: A Case Report. Case Rep Oncol. 2023 Aug 25;16(1):728-733. doi: 10.1159/000532100. PMID: 37900826; PMCID: PMC10601742.

Impact Factor: 0.75

Langerhans Cell Histiocytosis with Good Response to Low-Dose Imatinib: Case Report and Literature Review

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Abstract

Langerhans cell histiocytosis (LCH) is a rare neoplastic disease characterized by infiltration of histiocytes and dendritic cells into body organs. While treatment is better established in pediatrics, there is still no consensus on therapy in the adult population. Imatinib has shown promising results in some case reports and a small clinical trial. We present here a fifty-nine-year-old patient with LCH in the lung, liver, and bone who responded well to an imatinib dose of 100 mg daily. Her symptoms improved within 3 months of treatment, and subsequent positron emission tomography-computed tomography (PET/CT) showed resolution of 18F-fluorodeoxyglucose (FDG)-avid lesions.

Keywords: Dendritic cell neoplasms; Histiocytic cell neoplasms; Histiocytosis; Positron emission tomography scan; Tyrosine kinase inhibitors.

Citation: Abdulgayoom M, Mudawi D, Lengyel Z, Abo Samra H, Alshurafa A, Yassin MA. Langerhans Cell Histiocytosis with Good Response to Low-Dose Imatinib: Case Report and Literature Review. Case Rep Oncol. 2023 Jul 12;16(1):511-518. doi: 10.1159/000531230. PMID: 37476563; PMCID: PMC10355039.

Impact Factor: 0.75

Aggressive Fibromatosis of the Left Mesocolon Mimicking a Gastrointestinal Stromal Tumor: A Case Report

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Abstract

Mesenteric fibromatosis (MF) is a proliferative fibroblastic lesion of the intestinal mesentery. It constitutes 8% of all desmoid tumors, representing 0.03% of all neoplasms. It is benign histologically, although it could infiltrate locally and recur following excision; however, it is free from the potential to metastasize. It is spontaneous or associated with familial adenomatous polyposis (FAP]) mutation as a part of Gardner's syndrome. This case report discusses the radiological, intraoperative, and histopathological findings from a 45-year-old male patient who presented with abdominal pain and a palpable mass in the left hemiabdomen. The pain was dull and aching, extending to the back and unrelated to any other gastrointestinal symptoms. There was no history of severe weight reduction. Furthermore, he is not a smoker. There were no comorbidities, severe medical diseases, or prior surgical procedures. Computerized tomography revealed a well-defined, lobulated, heterogeneously enhancing altered signal intensity mass at the mesocolon. Ultrasonography of the abdomen showed an intra-abdominal mass. Macroscopic mass characteristics include a well-defined mass measuring 22 × 14 × 11 cm connected to a small intestine segment measuring 21 × 2 × 2 cm. Histopathological and immunohistochemical examinations of the resected tumor, including positive nuclear immunostaining for beta-catenin, confirmed a postoperative diagnosis of desmoid-type fibromatosis. Based on its clinical presentation and computed tomography results, this case demonstrated how desmoid-type fibromatosis of the colon might mimic gastrointestinal stromal tumors (GISTs). Due to the varied therapies and follow-up methods used for these lesions, the differential diagnosis between desmoid-type fibromatosis and GIST is clinically significant.

Keywords: Fibromatosis; Gastrointestinal stromal tumor; Mesocolon; Preoperative diagnosis.

Citation: Abu-Jeyyab M, Al-Asbahi H, Al-Jafari M, Al-Tarawneh BK, Nashwan AJ. Aggressive Fibromatosis of the Left Mesocolon Mimicking a Gastrointestinal Stromal Tumor: A Case Report. Case Rep Oncol. 2023 Oct 16;16(1):1148-1155. doi: 10.1159/000534038. PMID: 37900798; PMCID: PMC10601818.

Impact Factor: 0.75

An Intestinal Type Gastric Neuroendocrine Tumor: A Case Report

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Abstract

Neuroendocrine tumors (NETs) represent a diverse set of malignancies, originating from the neuroendocrine cells dispersed throughout the body. Their symptoms are associated with the secretion of bioactive peptides by tumor cells. Five-year survival rates depend on the disease stage: 93% for local, 74% for regional, and 19% for metastatic disease. This report describes a case involving a 64-year-old male patient, who was enduring high blood pressure and anemia. His symptomatology included frequent fainting and bloody vomiting without prior bleeding, coupled with persistent abdominal pain and weight loss. A complete blood count revealed microcytic anemia. His condition improved postoperatively after the transfusion of two units of packed red blood cells, normalizing all parameters. Further biochemistry and serology tests did not provide significant insights. However, an upper endoscopy unveiled a deep ulcer below the gastroesophageal junction with ulcer desquamation. A combination of clinical, laboratory, and radiographic data initially indicated a gastric carcinoma of the intestinal type, characterized by extensive extracellular mucin secretion. The surgical intervention led to the extraction of multiple tumors from lymph nodes, culminating in a postoperative diagnosis of a gastrointestinal (GI) mesenchymal tumor. NETs predominantly manifest in the GI tract, initiating primarily in the small intestine but can also originate in the stomach, appendix, colon, and other parts of the GI tract. Their development from neuroendocrine cells enables them to produce high concentrations of hormone-like substances such as neuropeptides and amines.

Keywords: Carcinoma; Computed tomography; Neuroendocrine cells; Neuroendocrine tumors.

Citation: Abu-Jeyyab M, Kakish R, Alkatib M, Alshawabkeh L, Bani Hamad R, Almadani M, Santarisi M, Al-Jafari M, Nashwan AJ. An Intestinal Type Gastric Neuroendocrine Tumor: A Case Report. Case Rep Oncol. 2023 Oct 16;16(1):1113-1120. doi: 10.1159/000533761. PMID: 37900795; PMCID: PMC10601806.

Impact Factor: 0.75

A rare synchronous of dual primary genitourinary carcinoma manifested with a rapidly progressive renal failure

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Abstract

Non-urothelial carcinoma accounts for <5% of urinary bladder tumors, and primary bladder adenocarcinoma accounts for 0.5-2%, but the variant primary signet-ring cell is extremely rare. We present a rare case of a synchronous of dual primary malignancy from a rare variant of urinary bladder adenocarcinoma (signet-ring cell) with indolent prostate adenocarcinoma in a 61-year-old male. The patient presented with a rapidly progressive renal failure due to a non-dilated obstructive uropathy that formed a dilemma in the course of diagnosiswhich was relieved transiently by a high-dose methylprednisolone. Primary signet-ring cell adenocarcinoma of the urinary bladder is a very rare malignancy manifests as a high-grade, high-stage lesion, which takes a vague course and has a poor prognosis. It is often managed with radical cystectomy due to its aggressive nature.

Citation: Affas A, AlBitar S, Alyyan F, Affas MN. A rare synchronous of dual primary genitourinary carcinoma manifested with a rapidly progressive renal failure. Oxf Med Case Reports. 2023 Jun 26;2023(6):omad052. doi: 10.1093/omcr/omad052. PMID: 37377716; PMCID: PMC10292647.

Impact Factor: 0.5

Primary intrapulmonary thymoma a case report

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Abstract

Primary intrapulmonary thymoma (PIT), defined as the presence of thymoma tissue in the lung without an accompanying mediastinal component, is uncommon and so offers a diagnostic quandary. We describe the case of PIT in an 81-year-old man.

Keywords: oncology; primary intrapulmonary thymoma; respiratory medicine; thymoma.

Citation: Wasim Jamal SM, Hussein M, Albakri M, Rasheed I, Hameed M, Ul Haq I, Thomas M, Al Bozom I, Abdul Sattar H. Primary intrapulmonary thymoma a case report. Clin Case Rep. 2023 Sep 14;11(9):e6897. doi: 10.1002/ccr3.6897. PMID: 37720714; PMCID: PMC10502198.

Impact Factor: 0.285

Metastatic yolk sac tumor masquerading as multifocal hepatocellular carcinoma in a young adult: A case report.

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Abstract

Primary yolk sac tumor of the liver is very rare and can present as multifocal liver lesions. Multifocal nature may mimic other diagnoses such as hepatocellular carcinoma. Early recognition and therapeutic intervention are important as the prognosis of metastatic yolk sac tumors is poor. We present a case of a young adolescent who presented with bleeding per rectum abdominal pain and multiple liver lesions.

Keywords: germ cell tumor; metastasis; multifocal hepatocellular carcinoma; tumor in young adult; yolk sac tumor.

Citation: Mushtaq K, Khan MU, Al Soub D, Koshy SM, Petkar M, Al Ejji KM. Metastatic yolk sac tumor masquerading as multifocal hepatocellular carcinoma in a young adult: A case report. Clin Case Rep. 2023 Feb 3;11(2):e6861. doi: 10.1002/ccr3.6861. PMID: 36762145; PMCID: PMC9896153.

Impact Factor: 0.285

ONCOLOGY

REVIEW ARTICLES

CAR-cell therapy in the era of solid tumor treatment: current challenges and emerging therapeutic advances

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Abstract

In the last decade, Chimeric Antigen Receptor (CAR)-T cell therapy has emerged as a promising immunotherapeutic approach to fight cancers. This approach consists of genetically engineered immune cells expressing a surface receptor, called CAR, that specifically targets antigens expressed on the surface of tumor cells. In hematological malignancies like leukemias, myeloma, and non-

Hodgkin B-cell lymphomas, adoptive CAR-T cell therapy has shown efficacy in treating chemotherapy refractory patients. However, the value of this therapy remains inconclusive in the context of solid tumors and is restrained by several obstacles including limited tumor trafficking and infiltration, the presence of an immunosuppressive tumor microenvironment, as well as adverse events associated with such therapy. Recently, CAR-Natural Killer (CAR-NK) and CAR-macrophages (CAR-M) were introduced as a complement/alternative to CAR-T cell therapy for solid tumors. CAR-NK cells could be a favorable substitute for CAR-T cells since they do not require HLA compatibility and have limited toxicity. Additionally, CAR-NK cells might be generated in large scale from several sources which would suggest them as promising off-the-shelf product. CAR-M immunotherapy with its capabilities of phagocytosis, tumor-antigen presentation, and broad tumor infiltration, is currently being investigated. Here, we discuss the emerging role of CAR-T, CAR-NK, and CAR-M cells in solid tumors. We also highlight the advantages and drawbacks of CAR-NK and CAR-M cells compared to CAR-T cells. Finally, we suggest prospective solutions such as potential combination therapies to enhance the efficacy of CAR-cells immunotherapy.

Keywords: CAR-M; CAR-NK; CAR-T; Cellular immunotherapy; Combined therapies; Solid tumors.

Citation: Maalej KM, Merhi M, Inchakalody VP, Mestiri S, Alam M, Maccalli C, Cherif H, Uddin S, Steinhoff M, Marincola FM, Dermime S. CAR-cell therapy in the era of solid tumor treatment: current challenges and emerging therapeutic advances. Mol Cancer. 2023 Jan 30;22(1):20. doi: 10.1186/s12943-023-01723-z. PMID: 36717905; PMCID: PMC9885707.

Impact Factor: 37.3

The complex network of transcription factors, immune checkpoint inhibitors and stemness features in colorectal cancer: A recent update.

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Abstract

Cancer immunity is regulated by several mechanisms that include co-stimulatory and/or co-inhibitory molecules known as immune checkpoints expressed by the immune cells. In colorectal cancer (CRC), CTLA-4, LAG3, TIM-3 and PD-1 are the major co-inhibitory checkpoints involved in tumor development and progression. On the other hand, the deregulation of transcription factors and cancer stem cells activity plays a major role in the development of drug resistance and in the spread of metastatic disease in CRC. In this review, we describe how the modulation of such transcription factors affects the response of CRC to therapies. We also focus on the role of cancer stem cells in tumor metastasis and chemoresistance and discuss both preclinical and clinical approaches for targeting stem cells to prevent their tumorigenic effect. Finally, we provide an update on the clinical applications of immune checkpoint inhibitors in CRC and discuss the regulatory effects of transcription factors on the expression of the immune inhibitory checkpoints with specific focus on the PD-1 and PD-L1 molecules.

Keywords: Cancer stem cells; Colorectal cancer; Immune checkpoint inhibitors; Transcription factors.

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Epigenetic programing of cancer stemness by transcription factors-non-coding RNAs interactions

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Abstract

Cancer 'stemness' is fundamental to cancer existence. It defines the ability of cancer cells to indefinitely perpetuate as well as differentiate. Cancer stem cell populations within a growing tumor also help evade the inhibitory effects of chemo- as well as radiation-therapies, in addition to playing an important role in cancer metastases. NF-κB and STAT-3 are representative transcription factors

(TFs) that have long been associated with cancer stemness, thus presenting as attractive targets for cancer therapy. The growing interest in non-coding RNAs (ncRNAs) in the recent years has provided further insight into the mechanisms by which TFs influence cancer stem cell characteristics. There is evidence for a direct regulation of TFs by ncRNAs, such as, microRNAs (miRNAs), long non-coding RNAs (lncRNAs) as well as circular RNAs (circRNAs), and vice versa. Additionally, the TF-ncRNAs regulations are often indirect, involving ncRNA-target genes or the sponging of other ncRNA species by individual ncRNAs. The information is rapidly evolving and this review provides a comprehensive review of TF-ncRNAs interactions with implications on cancer stemness and in response to therapies. Such knowledge will help uncover the many levels of tight regulations that control cancer stemness, providing novel opportunities and targets for therapy in the process.

Keywords: Cancer stem cells; LncRNAs; MiRNAs; NF-κB; Non-coding RNAs; STAT-3.

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Uncertainties and controversies in axillary management of patients with breast cancer

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Abstract

The aims of this Oncoplastic Breast Consortium and European Breast Cancer Research Association of Surgical Trialists initiative were to identify uncertainties and controversies in axillary management of early breast cancer and to recommend appropriate strategies to address them. By use of Delphi methods, 15 questions were prioritized by more than 250 breast surgeons, patient advocates and radiation oncologists from 60 countries. Subsequently, a global virtual consensus panel considered available data, ongoing studies and resource utilization. It agreed that research should no longer be prioritized for standardization of axillary imaging, de-escalation of axillary surgery in node-positive cancer and risk evaluation of modern surgery and radiotherapy. Instead, expert consensus recommendations for clinical practice should be based on current evidence and updated once results from ongoing studies become available. Research on de-escalation of radiotherapy and identification of the most relevant endpoints in axillary management should encompass a meta-analysis to identify knowledge gaps, followed by a Delphi process to prioritize and a consensus conference to refine recommendations for specific trial designs. Finally, treatment of residual nodal disease after surgery was recommended to be assessed in a prospective register.

Keywords: Axillary dissection; Breast cancer; Breast surgery; Radiotherapy.

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Exosome nanovesicles as potential biomarkers and immune checkpoint signaling modulators in lung cancer microenvironment: recent advances and emerging concepts

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Abstract

Lung cancer remains the leading cause of cancer-related deaths globally, and the survival rate remains low despite advances in diagnosis and treatment. The progression of lung cancer is a multifaceted and dynamic phenomenon that encompasses interplays among cancerous cells and their microenvironment, which incorporates immune cells. Exosomes, which are small membrane-bound vesicles, are released by numerous cell types in normal and stressful situations to allow communication between cells. Tumor-derived exosomes (TEXs) possess diverse neo-antigens and cargoes such as proteins, RNA, and DNA and have a unique molecular makeup reflecting tumor genetic complexity. TEXs contain both immunosuppressive and immunostimulatory factors and may play a role in immunomodulation by influencing innate and adaptive immune components. Moreover, they transmit signals that contribute to the progression of lung cancer by promoting metastasis, epithelial-mesenchymal transition (EMT), angiogenesis, and immunosuppression. This makes them

a valuable resource for investigating the immune environment of tumors, which could pave the way for the development of non-invasive biomarkers that could aid in the prognosis, diagnosis, and immunotherapy of lung cancer. While immune checkpoint inhibitor (ICI) immunotherapy has shown promising results in treating initial-stage cancers, most patients eventually develop adaptive resistance over time. Emerging evidence demonstrates that TEXs could serve as a prognostic biomarker for immunotherapeutic response and have a significant impact on both systemic immune suppression and tumor advancement. Therefore, understanding TEXs and their role in lung cancer tumorigenesis and their response to immunotherapies is an exciting research area and needs further investigation. This review highlights the role of TEXs as key contributors to the advancement of lung cancer and their clinical significance in lung immune-oncology, including their possible use as biomarkers for monitoring disease progression and prognosis, as well as emerging shreds of evidence regarding the possibility of using exosomes as targets to improve lung cancer therapy.

Keywords: Biomarkers; Immune checkpoint signaling inhibitors; Immunotherapy; Lung cancer; Tumor micro-environment; Tumor-derived exosomes.

Citation: Khan NA, Asim M, Biswas KH, Alansari AN, Saman H, Sarwar MZ, Osmonaliev K, Uddin S. Exosome nanovesicles as potential biomarkers and immune checkpoint signaling modulators in lung cancer microenvironment: recent advances and emerging concepts. J Exp Clin Cancer Res. 2023 Aug 29;42(1):221. doi: 10.1186/s13046-023-02753-7. PMID: 37641132; PMCID: PMC10463467.

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Applications of polydopaminic nanomaterials in mucosal drug delivery

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Abstract

Polydopamine (PDA) is a biopolymer with unique physicochemical properties, including free-radical scavenging, high photothermal conversion efficiency, biocompatibility, biodegradability, excellent fluorescent and theranostic capacity due to their abundant surface chemistry. Thus, PDA is used for a myriad of applications including drug delivery, biosensing, imaging and cancer therapy. Recent reports present a new functionality of PDA as a coating nanomaterial, with major implications in mucosal drug delivery applications, particularly muco-adhesion and muco-penetration. However, this application has received minimal traction in the literature. In this review, we present the physicochemical and functional properties of PDA and highlight its key biomedical applications, especially in cancer therapy. A detailed presentation of the role of PDA as a promising coating material for nanoparticulate carriers intended for mucosal delivery forms the core aspect of the review. Finally, a reflection on key considerations and challenges in the utilizing PDA for mucosal drug delivery, along with the possibilities of translation to clinical studies is expounded.

Keywords: Cancer therapy; Muco-adhesion; Muco-penetration; Mucosal drug delivery; Polydopamine.

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Harnessing the potential of CAR-T cell therapy: progress, challenges, and future directions in hematological and solid tumor treatments

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Abstract

Traditional cancer treatments use nonspecific drugs and monoclonal antibodies to target tumor cells. Chimeric antigen receptor (CAR)-T cell therapy, however, leverages the immune system's T-cells to recognize and attack tumor cells. T-cells are isolated from patients and modified to target tumor-associated antigens. CAR-T therapy has achieved FDA approval for treating blood cancers like B-cell acute lymphoblastic leukemia, large B-cell lymphoma, and multiple myeloma by targeting CD-19 and B-cell maturation antigens. Bi-specific chimeric antigen receptors may contribute to mitigating tumor antigen escape, but their efficacy could be limited in cases where certain tumor cells do not express the targeted antigens. Despite success in blood cancers, CAR-T technology faces challenges in solid tumors, including lack of reliable tumor-associated antigens, hypoxic cores, immunosuppressive tumor environments, enhanced reactive oxygen species, and decreased T-cell infiltration. To overcome these challenges, current research aims to identify reliable tumor-associated antigens and develop cost-effective, tumor microenvironment-specific CAR-T cells. This review covers the evolution of CAR-T therapy against various tumors, including hematological and solid tumors, highlights challenges faced by CAR-T cell therapy, and suggests strategies to overcome these obstacles, such as utilizing single-cell RNA sequencing and artificial intelligence to optimize clinical-grade CAR-T cells.

Keywords: Antigen escape; CAR-T cell therapy; Cytokine release syndrome; Hematological malignancy; Immunotherapy; Solid tumor; Tumor antigens.

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Nano-vitamin C: A promising candidate for therapeutic applications

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Abstract

Vitamin C is an important nutrient implicated in different physiological functions in humans. Despite its important biological functions, therapeutic applications of vitamin C are rare and its use is further impacted by low chemical stability. Several nano-encapsulation techniques have been described in the literature and yet, there are only a handful of clinical investigations dedicated to unlocking the therapeutic applications of nano-encapsulated vitamin C. Clearly, further investigations are warranted in order to affirm the promising clinical potential of nano-encapsulated vitamin C. In this review, we describe the mechanisms of vitamin C activity as a modulator of crucial therapeutic uses in biological systems. We look at key factors affecting the chemical stability of vitamin C alone and in nano-encapsulated and explore pre-clinical and clinical evidence on current vitamin C nano-formulations along with their therapeutic applications. Finally, we critically appraise the gaps and opportunities prevailing in nano-vitamin C research and its potential translation towards relevant clinical outcomes.

Keywords: Clinical; Nano-vitamin C; Nanomedicine; Therapeutic; Vitamin C.

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Epigenetic inhibitors and their role in cancer therapy

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Abstract

Epigenetic modifications to DNA are crucial for normal cellular and biological functioning. DNA methylation, histone modifications, and chromatin remodeling are the most common epigenetic mechanisms. These changes are heritable but still reversible. The aberrant epigenetic alterations, such as DNA methylation, histone modification, and non-coding RNA (ncRNA)-mediated gene regulation, play an essential role in developing various human diseases, including cancer. Recent studies show that synthetic and dietary epigenetic inhibitors attenuate the abnormal epigenetic modifications in cancer cells and therefore have strong potential for cancer treatment. In this chapter, we have highlighted various types of epigenetic modifications, their mechanism, and as drug targets for epigenetic therapy.

Keywords: Acetylation; Cancer; Chromatin remodeling; Epigenetic modifications; HDAC inhibitors; Methylation.

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Tumour 63 protein (p63) in breast pathology: biology, immunohistochemistry, diagnostic applications, and pitfalls

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Abstract

Tumour protein 63 (p63) is a transcription factor of the p53 gene family, encoded by the TP63 gene located at chromosome 3q28, which regulates the activity of genes involved in growth and development of the ectoderm and derived tissues. p63 protein is normally expressed in the nuclei of the basal cell layer of glandular organs, including breast, in squamous epithelium and in urothelium. p63 immunohistochemical (IHC) staining has several applications in diagnostic breast pathology. It is commonly used to demonstrate myoepithelial cells at the epithelial stromal interface to differentiate benign and in situ lesions from invasive carcinoma and to characterize and classify papillary lesions including the distinction of breast intraduct papilloma from skin hidradenoma. p63 IHC is also used to identify and profile lesions showing myoepithelial cell and/or squamous differentiation, e.g. adenomyoepithelioma, salivary gland-like tumours including adenoid cystic carcinoma, and metaplastic breast carcinoma including low-grade adenosquamous carcinoma. This article reviews the applications of p63 IHC in diagnostic breast pathology and outlines a practical approach to the diagnosis and characterization of breast lesions through the identification of normal and abnormal p63 protein expression. The biology of p63, the range of available antibodies with emphasis on staining specificity and sensitivity, and pitfalls in interpretation are also discussed. The TP63 gene in humans, which shows a specific genomic structure, resulting in either TAp63 (p63) isoform or ΔNp63 (p40) isoform. As illustrated in the figure, both isoforms contain a DNA-binding domain (Orange box)

and an oligomerization domain (Grey box). TAp63 contains an N-terminal transactivation (TA) domain (Green box), while ΔNp63 has an alternative terminus (Yellow box). Antibodies against conventional pan-p63 (TP63) bind to the DNA binding domain common to both isoforms (TAp63 and p40) and does not distinguish between them. Antibodies against TAp63 bind to the N-terminal TA domain, while antibodies specific to ΔNp63 (p40) bind to the alternative terminus. Each isoform has variant isotypes (α, β, γ, δ, and ε).

Keywords: application; breast pathology; immunohistochemistry; p63; pitfalls.

Citation: Alkhayyat R, Abbas A, Quinn CM, Rakha EA. Tumour 63 protein (p63) in breast pathology: biology, immunohistochemistry, diagnostic applications, and pitfalls. Histopathology. 2024 Apr;84(5):723-741. doi: 10.1111/his.15101. Epub 2023 Nov 27. PMID: 38012539.

Impact Factor: 6.4

Organoboronic acids/esters as effective drug and prodrug candidates in cancer treatments: challenge and hope

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Abstract

Boronic acids/esters have recently emerged in the field of medicinal and pharmaceutical research due to their exceptional oxophilicity, low toxicity, and unique structure. They are known as potent enzyme inhibitors, cancer therapy capture agents, and can mimic certain types of antibodies to fight infections. They have been designed and developed into drugs, and this approach has emerged in the last 20 years. Five boronic acid drugs have been approved by the FDA and Health Canada, two of which are used to treat cancer, specifically multiple myeloma. The purpose of this review is to investigate boronic acid/ester derivatives as potential pharmaceutical agents as well as the mechanism of action. It will concentrate on six types of cancer: multiple myeloma, prostate cancer, breast cancer, lung cancer, cervical cancer, and colon cancer. Some newly developed boron-containing compounds have already demonstrated highly promising activities, but further investigation is required before final conclusions can be drawn.

Keywords: Boronic acid; cancer disease; drug; enzyme inhibitor; mechanism.

Citation: Al-Omari MK, Elaarag M, Al-Zoubi RM, Al-Qudimat AR, Zarour AA, Al-Hurani EA, Fares ZE, Alkharraz LM, Shkoor M, Bani-Yaseen AD, Aboumarzouk OM, Yassin A, Al-Ansari AA. Organoboronic acids/esters as effective drug and prodrug candidates in cancer treatments: challenge and hope. J Enzyme Inhib Med Chem. 2023 Dec;38(1):2220084. doi: 10.1080/14756366.2023.2220084. PMID: 37318308; PMCID: PMC10351539.

Impact Factor: 5.6

Current and emerging biomarkers in ovarian cancer diagnosis; CA125 and beyond

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Abstract

Ovarian cancer (OC) is one of the most common causes of cancer-related death in women worldwide. Its five-year survival rates are worse than the two most common gynecological cancers, cervical and endometrial. This is because it is asymptomatic in the early stages and usually detected in the advanced metastasized stage. Thus, survival is increasingly dependent on timely diagnosis. The delay in detection is contributed partly by the occurrence of non-specific clinical symptoms in the early stages and the lack of effective biomarkers and detection approaches. This underlines the need for biomarker identification and clinical validation, enabling earlier diagnosis, effective prognosis, and response to therapy. Apart from the traditional diagnostic biomarkers for OC, several new biomarkers have been delineated using advanced high-throughput molecular approaches in recent years. They are currently being clinically evaluated for their true diagnostic potential. In this chapter, we document

the commonly utilized traditional screening markers and recently identified emerging biomarkers in OC diagnosis, focusing on secretory and protein biomarkers. We also briefly reviewed the recent advances and prospects in OC diagnosis.

Keywords: Biomarkers; Cancer antigens; Cell-free DNA; Circulating tumor cells; Liquid biopsy; Multiplexed assays; Ovarian cancer; Secretory proteins.

Citation: Sharma T, Nisar S, Masoodi T, Macha MA, Uddin S, Akil AA, Pandita TK, Singh M, Bhat AA. Current and emerging biomarkers in ovarian cancer diagnosis; CA125 and beyond. Adv Protein Chem Struct Biol. 2023;133:85-114. doi: 10.1016/bs.apcsb.2022.08.003. Epub 2022 Sep 28. PMID: 36707207.

Impact Factor: 5.4

Cyclin-dependent kinases in cancer: Role, regulation, and therapeutic targeting

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Abstract

Regulated cell division is one of the fundamental phenomena which is the basis of all life on earth. Even a single base pair mutation in DNA leads to the production of the dysregulated protein that can have catastrophic consequences. Cell division is tightly controlled and orchestrated by proteins called cyclins and cyclin-dependent kinase (CDKs), which serve as licensing factors during different phases of cell division. Dysregulated cell division is one of the most important hallmarks of cancer and is commonly associated with a mutation in cyclins and CDKs along with tumor suppressor proteins. Therefore, targeting the component of the cell cycle which leads to these characteristics would be an effective strategy for treating cancers. Specifically, Cyclin-dependent kinases (CDKs) involved in cell cycle regulation have been identified to be overexpressed in many cancers. Many studies indicate

that oncogenesis occurs in cancerous cells by the overactivity of different CDKs, which impact cell cycle progression and checkpoint dysregulation which is responsible for development of tumor. The development of CDK inhibitors has emerged as a promising and novel approach for cancer treatment in both solid and hematological malignancies. Some of the novel CDK inhibitors have shown remarkable results in clinical trials, such as-Ribociclib®, Palbociclib® and Abemaciclib®, which are CDK4/6 inhibitors and have received FDA approval for the treatment of breast cancer. In this chapter, we discuss the molecular mechanism through which cyclins and CDKs regulate cell cycle progression and the emergence of cyclins and CDKs as rational targets in cancer. We also discuss recent advances in developing CDK inhibitors, which have emerged as a novel class of inhibitors, and their associated toxicities in recent years.

Keywords: Apoptosis; Cancer; Cell division; Cell proliferation; Cyclin-dependent kinases; Cyclins.

Citation: Gupta A, Dagar G, Chauhan R, Sadida HQ, Almarzooqi SK, Hashem S, Uddin S, Macha MA, Akil ASA, Pandita TK, Bhat AA, Singh M. Cyclin-dependent kinases in cancer: Role, regulation, and therapeutic targeting. Adv Protein Chem Struct Biol. 2023;135:21-55. doi: 10.1016/bs.apcsb.2023.02.001. Epub 2023 Mar 16. PMID: 37061333.

Impact Factor: 5.05

Shrinking the battlefield in cancer therapy: Nanotechnology against cancer stem cells

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Abstract

Cancer remains one of the leading causes of mortality worldwide, presenting a significant healthcare challenge owing to the limited efficacy of current treatments. The application of nanotechnology in cancer treatment leverages the unique optical, magnetic, and electrical attributes of nanomaterials to engineer innovative, targeted therapies. Specifically, manipulating nanomaterials allows for enhanced drug loading efficiency, improved bioavailability, and targeted delivery systems, reducing the non-specific cytotoxic effects characteristic of conventional chemotherapies. Furthermore, recent advances in nanotechnology have demonstrated encouraging results in specifically targeting CSCs, a key development considering the role of these cells in disease recurrence and resistance to treatment. Despite these breakthroughs, the clinical approval rates of nano-drugs have not kept pace with research advances, pointing to existing obstacles that must be addressed. In conclusion,

nanotechnology presents a novel, powerful tool in the fight against cancer, particularly in targeting the elusive and treatment-resistant CSCs. This comprehensive review delves into the intricacies of nanotherapy, explicitly targeting cancer stem cells, their markers, and associated signaling pathways.

Keywords: Cancer stem cells; Drug resistance; Nanotherapy; Pharmacokinetics; Signaling pathways.

Citation: Fernandes Q, Therachiyil L, Khan AQ, Bedhiafi T, Korashy HM, Bhat AA, Uddin S. Shrinking the battlefield in cancer therapy: Nanotechnology against cancer stem cells. Eur J Pharm Sci. 2023 Dec 1;191:106586. doi: 10.1016/j.ejps.2023.106586. Epub 2023 Sep 19. PMID: 37729956.

Impact Factor: 4.82

Signaling pathways governing glioma cancer stem cells behavior

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Abstract

Glioma is the most common malignant brain tumor that develops in the glial tissue. Several studies have identified that glioma cancer stem cells (GCSCs) play important roles in tumor-initiating features in malignant gliomas. GCSCs are a small population in the brain that presents an essential role in the metastasis of glioma cells to other organs. These cells can self-renew and differentiate, which are thought to be involved in the pathogenesis of glioma. Therefore, targeting GCSCs might be a novel strategy for the treatment of glioma. Accumulating evidence revealed that several signaling pathways, including Notch, TGF-β, Wnt, STAT3, AKT, and EGFR mediated GCSC growth, proliferation, migration, and invasion. Besides, non-coding RNAs (ncRNAs), including miRNAs, circular RNAs, and long ncRNAs have been found to play pivotal roles in the regulation of GCSC pathogenesis and drug

resistance. Therefore, targeting these pathways could open a new avenue for glioma management. In this review, we summarized critical signaling pathways involved in the stimulation or prevention of GCSCs tumorigenesis and invasiveness.

Keywords: Glioma; Glioma cancer stem cells; LncRNAs; Signaling pathways; circRNAs; miRNAs.

Citation: Nasrolahi A, Azizidoost S, Radoszkiewicz K, Najafi S, Ghaedrahmati F, Anbiyaee O, Khoshnam SE, Farzaneh M, Uddin S. Signaling pathways governing glioma cancer stem cells behavior. Cell Signal. 2023 Jan;101:110493. doi: 10.1016/j.cellsig.2022.110493. Epub 2022 Oct 10. PMID: 36228964.

Impact Factor: 4.8

Role of HMGB1 and its associated signaling pathways in human malignancies

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Abstract

The High-Mobility Group Box-1 (HMGB1), a non-histone chromatin-associated protein, plays a crucial role in cancer growth and response to therapy as it retains a pivotal role in promoting both cell death and survival. HMGB1 has been reported to regulate several signaling pathways engaged in inflammation, genome stability, immune function, cell proliferation, cell autophagy, metabolism, and apoptosis. However, the association between HMGB1 and cancer is complex and its mechanism in tumorigenesis needs to be further elucidated. This review aims to understand the role of HMGB1 in human malignancies and discuss the signaling pathways linked to this process to provide a

comprehensive understanding on the association of HMGB1 with carcinogenesis. Further, we will review the role of HMGB1 as a target/biomarker for cancer therapy, the therapeutic strategies used to target this protein, and its potential role in preventing or treating cancers. In light of the recent growing evidence linking HMGB1 to cancer progression, we think that it may be suggested as a novel and emergent therapeutic target for cancer therapy. Hence, HMGB1 warrants paramount investigation to comprehensively map its role in tumorigenesis.

Keywords: Clinical applications; HMGB1; Immune checkpoint blockade; Signaling pathways; cancer therapy.

Citation: Idoudi S, Bedhiafi T, Pedersen S, Elahtem M, Alremawi I, Akhtar S, Dermime S, Merhi M, Uddin S. Role of HMGB1 and its associated signaling pathways in human malignancies. Cell Signal. 2023 Dec;112:110904. doi: 10.1016/j.cellsig.2023.110904. Epub 2023 Sep 25. PMID: 37757902.

Impact Factor: 4.8

Current Understanding of Flavonoids in Cancer Therapy and Prevention

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Abstract

Cancer is a major cause of death worldwide, with multiple pathophysiological manifestations. In particular, genetic abnormalities, inflammation, bad eating habits, radiation exposure, work stress, and toxin consumption have been linked to cancer disease development and progression. Recently, natural bioactive chemicals known as polyphenols found in plants were shown to have anticancer capabilities, destroying altered or malignant cells without harming normal cells. Flavonoids have demonstrated antioxidant, antiviral, anticancer, and anti-inflammatory effects. Flavonoid type, bioavailability, and possible method of action determine these biological actions. These low-cost pharmaceutical components have significant biological activities and are beneficial for several chronic disorders, including cancer. Recent research has focused primarily on isolating, synthesizing, and studying the effects of flavonoids on human health. Here we have attempted to summarize our current knowledge of flavonoids, focusing on their mode of action to better understand their effects on cancer.

Keywords: anticancer; apoptosis; flavonoids; molecular mechanisms; polyphenols.

Citation: Farhan M, Rizvi A, Aatif M, Ahmad A. Current Understanding of Flavonoids in Cancer Therapy and Prevention. *Metabolites*. 2023 Mar 27;13(4):481. doi: 10.3390/metabo13040481. PMID: 37110140; PMCID: PMC10142845.

Impact factor: 4.1

Estrogens and the risk of breast cancer: A narrative review of literature

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Abstract

In female mammals, the development and regulation of the reproductive system and non-reproductive system are significantly influenced by estrogens (oestrogens). In addition, lipid metabolism is another physiological role of estrogens. Estrogens act through different types of receptors to introduce signals to the target cell by affecting many estrogen response elements. Breast cancer is considered mostly a hormone-dependent disease. Approximately 70% of breast cancers express progesterone receptors and/or estrogen receptors, and they are a good marker for cancer prognosis. This review will discuss estrogen metabolism and the interaction of estrogen metabolites with breast cancer. The carcinogenic role of estrogen is discussed in light of both conventional and atypical cancers susceptible to hormones, such as prostate, endometrial, and lung cancer, as we examine how estrogen contributes to the formation and activation of breast cancer. In addition, this review will discuss other factors that can be associated with estrogen-driven breast cancer.

Keywords: Breast cancer; ER; Estrogen; Oestrogen; Risk.

Citation: Al-Shami K, Awadi S, Khamees A, Alsheikh AM, Al-Sharif S, Ala' Bereshy R, Al-Eitan SF,

Banikhaled SH, Al-Qudimat AR, Al-Zoubi RM, Al Zoubi MS. Estrogens and the risk of breast cancer: A narrative review of literature. Heliyon. 2023 Sep 17;9(9):e20224. doi: 10.1016/j.heliyon.2023.e20224. PMID: 37809638; PMCID: PMC10559995.

Impact factor: 4.0

Efficacy of fusion imaging for immediate post-ablation assessment of malignant liver neoplasms: A systematic review

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Abstract

Background: Percutaneous thermal ablation has become the preferred therapeutic treatment option for liver cancers that cannot be resected. Since ablative zone tissue changes over time, it becomes challenging to determine therapy effectiveness over an extended period. Thus, an immediate post-procedural evaluation of the ablation zone is crucial, as it could influence the need for a second-look treatment or follow-up plan. Assessing treatment response immediately after ablation is essential to attain favorable outcomes. This study examines the efficacy of image fusion strategies immediately post-ablation in liver neoplasms to determine therapeutic response.

Methodology: A comprehensive systematic search using PRISMA methodology was conducted using EMBASE, MEDLINE (via PUBMED), and Cochrane Library Central Registry electronic databases to identify articles that assessed the immediate post-ablation response in malignant hepatic tumors with fusion imaging (FI) systems. The data were retrieved on relevant clinical characteristics, including population demographics, pre-intervention clinical history, lesion characteristics, and intervention type. For the outcome metrics, variables such as average fusion time, intervention metrics, technical success rate, ablative safety margin, supplementary ablation rate, technical efficacy rate, LTP rates, and reported complications were extracted.

Results: Twenty-two studies were included for review after fulfilling the study eligibility criteria. FI's immediate technical success rate ranged from 81.3% to 100% in 17/22 studies. In 16/22 studies, the ablative safety margin was assessed immediately after ablation. Supplementary ablation was performed in 9 studies following immediate evaluation by FI. In 15/22 studies, the technical effectiveness rates during the first follow-up varied from 89.3% to 100%.

Conclusion: Based on the studies included, we found that FI can accurately determine the immediate therapeutic response in liver cancer ablation image fusion and could be a feasible intraprocedural tool for determining short-term post-ablation outcomes in unresectable liver neoplasms. There are some technical challenges that limit the widespread adoption of FI techniques. Large-scale randomized trials are warranted to improve on existing protocols. Future research should emphasize improving FI's technological capabilities and clinical applicability to a broader range of tumor types and ablation procedures.

Keywords: ablation techniques; ablative margin; image fusion; liver neoplasms; treatment outcomes.

Citation: Rai P, Ansari MY, Warfa M, Al-Hamar H, Abinahed J, Barah A, Dakua SP, Balakrishnan S. Efficacy of fusion imaging for immediate post-ablation assessment of malignant liver neoplasms: A systematic review. Cancer Med. 2023 Jul;12(13):14225-14251. doi: 10.1002/cam4.6089. Epub 2023 May 16. PMID: 37191030; PMCID: PMC10358230.

Impact Factor: 4.0

Cancer stem cell-derived exosome-induced metastatic cancer: An orchestra within the tumor microenvironment

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Abstract

Although the mechanisms as well as pathways associated with cancer stem cell (CSC) maintenance, expansion, and tumorigenicity have been extensively studied and the role of tumor cell (TC)-derived exosomes in this process is well understood, there is a paucity of research focusing specifically on the functional mechanisms of CSC-derived exosomes (CSC-Exo)/-exosomal-ncRNAs and their impact on malignancy. This shortcoming needs to be addressed, given that these vesicular and molecular components of CSCs could have a great impact on the cancer initiation, progression, and recurrence through their interaction with other key tumor microenvironment (TME) components, such as MSCs/MSC-Exo and CAFs/CAF-Exo. In particular, understanding CSCs/CSC-Exo and its crosstalk with MSCs/MSC-Exo or CAFs/CAF-Exo that are associated with the proliferation, migration, differentiation, angiogenesis, and metastasis through an enhanced process of self-renewal, chemotherapy as well as radiotherapy resistance may aid cancer treatment. This review contributes to this endeavor by summarizing the characteristic features and functional mechanisms of CSC-Exo/MSC-Exo/CAF-Exo and their mutual impact on cancer progression and therapy resistance.

Keywords: CSC-Exos; CSC-Markers; Cancer stem cells; Chemoresistance; EMT; Metastasis; ncRNAs.

Citation: Rashid K, Ahmad A, Meerasa SS, Khan AQ, Wu X, Liang L, Cui Y, Liu T. Cancer stem cell-derived exosome-induced metastatic cancer: An orchestra within the tumor microenvironment. Biochimie. 2023 Sep;212:1-11. doi: 10.1016/j.biochi.2023.03.014. Epub 2023 Apr 1. PMID: 37011805.

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Gastric juice non-coding RNAs as potential biomarkers for gastric cancer

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Abstract

Gastric cancer (GC), being one of the most common malignant human tumors, occupies the second position in the structure of mortality in men and women. High rates of morbidity and mortality in this pathology determine its extremely high clinical and social significance. Diagnosis and timely treatment of precancerous pathology is the main way to reduce morbidity and mortality, and early detection of GC and its adequate treatment improve prognosis. The ability to accurately predict the development of GC and start treatment on time, as well as the ability to determine the stage of the disease if the diagnosis is confirmed - non-invasive biomarkers can become the key to solving these and many other problems of modern medicine. One of the promising biomarkers being studied are non-coding RNAs, namely, microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs). They are involved in a wide range of processes, including apoptosis, proliferation, differentiation, angiogenesis, which play a critical role in the development of GC oncogenesis. In addition, they are quite specific and stable due to their carriers (extracellular vesicles or Argonaute 2 protein) and can be detected in various human biological fluids, in particular gastric juice. Thus, miRNAs, lncRNAs, and circRNAs isolated from the gastric juice of GC patients are promising preventive, diagnostic and prognostic non-invasive biomarkers. This review article presents the characteristics of circulating or extracellular miRNAs, lncRNAs, and circRNAs in gastric juice, allowing their use in the GC preventive, diagnosis, prognosis and monitoring therapy.

Keywords: clinical perspectives; extracellular vesicles; gastric cancer; gastric juice; gastric juice ncRNAs and gastric cancer non-coding RNAs; liquid biopsy; non-invasive biomarkers; theories.

Citation: Gareev I, Ahmad A, Wang J, Beilerli A, Ilyasova T, Sufianov A, Beylerli O. Gastric juice non-coding RNAs as potential biomarkers for gastric cancer. Front Physiol. 2023 Apr 26;14:1179582. doi: 10.3389/fphys.2023.1179582. PMID: 37179825; PMCID: PMC10169709.

Impact Factor: 3.8

Current Understanding of Flavonoids in Cancer Therapy and Prevention

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Abstract

Cancer is a major cause of death worldwide, with multiple pathophysiological manifestations. In particular, genetic abnormalities, inflammation, bad eating habits, radiation exposure, work stress, and toxin consumption have been linked to cancer disease development and progression. Recently, natural bioactive chemicals known as polyphenols found in plants were shown to have anticancer capabilities, destroying altered or malignant cells without harming normal cells. Flavonoids have demonstrated antioxidant, antiviral, anticancer, and anti-inflammatory effects. Flavonoid type, bioavailability, and possible method of action determine these biological actions. These low-cost pharmaceutical components have significant biological activities and are beneficial for several chronic disorders, including cancer. Recent research has focused primarily on isolating, synthesizing, and studying the effects of flavonoids on human health. Here we have attempted to summarize our current knowledge of flavonoids, focusing on their mode of action to better understand their effects on cancer.

Keywords: anticancer; apoptosis; flavonoids; molecular mechanisms; polyphenols.

Citation: Farhan M, Rizvi A, Aatif M, Ahmad A. Current Understanding of Flavonoids in Cancer Therapy and Prevention. Metabolites. 2023 Mar 27;13(4):481. doi: 10.3390/metabo13040481. PMID: 37110140; PMCID: PMC10142845.

Impact Factor: 3.6

The role of LncRNA MCM3AP-AS1 in human cancer

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Abstract

Long noncoding RNAs (lncRNA) play pivotal roles in every level of gene and genome regulation. MCM3AP-AS1 is a lncRNA that has an oncogenic role in several kinds of cancers. Aberrant expression of MCM3AP-AS1 has been reported to be involved in the progression of diverse malignancies, including colorectal, cervical, prostate, lymphoma, lung, ovary, liver, bone, and breast cancers. It is generally believed that MCM3AP-AS1 expression is associated with cancer cell growth, proliferation, angiogenesis, and metastasis. MCM3AP-AS1 by targeting various signaling pathways and microRNAs (miRNAs) presents an important role in cancer pathogenesis. MCM3AP-AS1 as a competitive endogenous RNA has the ability to sponge miRNA, inhibit their expressions, and bind to different target mRNAs related to cancer development. Therefore, MCM3AP-AS1 by targeting several

signaling pathways, including the FOX family, Wnt, EGF, and VEGF can be a potent target for cancer prediction and diagnosis. In this review, we will summarize the role of MCM3AP-AS1 in various huma human cancers.

Keywords: Cancer; Long non-coding RNAs; MCM3AP-AS1; Signaling pathways; miRNAs.

Citation: Azizidoost S, Ghaedrahmati F, Sheykhi-Sabzehpoush M, Uddin S, Ghafourian M, Mousavi Salehi A, Keivan M, Cheraghzadeh M, Nazeri Z, Farzaneh M, Khoshnam SE. The role of LncRNA MCM3AP-AS1 in human cancer. Clin Transl Oncol. 2023 Jan;25(1):33-47. doi: 10.1007/s12094-022-02904-w. Epub 2022 Aug 24. PMID: 36002764.

Impact factor: 3.4

Expression, assessment and significance of Ki67 expression in breast cancer: an update

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Abstract

Ki67 expression is one of the most important and cost-effective surrogate markers to assess for tumour cell proliferation in breast cancer (BC). The Ki67 labelling index has prognostic and predictive value in patients with early-stage BC, particularly in the hormone receptor-positive, HER2 (human epidermal growth factor receptor 2)-negative (luminal) tumours. However, many challenges exist in using Ki67 in routine clinical practice and it is still not universally used in the clinical setting. Addressing these challenges can potentially improve the clinical utility of Ki67 in BC. In this article, we review the function, immunohistochemical (IHC) expression, methods for scoring and interpretation of results as well as address several challenges of Ki67 assessment in BC. The prodigious attention associated with use of Ki67 IHC as a prognostic marker in BC resulted in high expectation and overestimation of its performance. However, the realisation of some pitfalls and disadvantages, which are expected with any similar markers, resulted in an increasing criticism of its clinical use. It is time to consider a pragmatic approach and weigh the benefits against the weaknesses and identify factors to achieve

the best clinical utility. Here we highlight the strengths of its performance and provide some insights to overcome the existing challenges.

Keywords: breast; breast neoplasms; neoplasm metastasis.

Citation: Lashen AG, Toss MS, Ghannam SF, Makhlouf S, Green A, Mongan NP, Rakha E. Expression, assessment and significance of Ki67 expression in breast cancer: an update. J Clin Pathol. 2023 Jun;76(6):357-364. doi: 10.1136/jcp-2022-208731. Epub 2023 Feb 22. PMID: 36813558.

Impact Factor: 3.4

Potential roles of lncRNA-XIST/miRNAs/mRNAs in human cancer cells

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Abstract

Long non-coding RNAs (lncRNAs) are non-coding RNAs that contain more than 200 nucleotides but do not code for proteins. In tumorigenesis, lncRNAs can have both oncogenic and tumor-suppressive properties. X inactive-specific transcript (XIST) is a known lncRNA that has been implicated in X

chromosome silencing in female cells. Dysregulation of XIST is associated with an increased risk of various cancers. Therefore, XIST can be a beneficial prognostic biomarker for human malignancies. In this review, we attempt to summarize the emerging roles of XIST in human cancers.

Keywords: Cancer; LncRNAs; Pathogenesis; Tumorigenesis; XIST.

Citation: Farzaneh M, Nasrolahi A, Ghaedrahmati F, Masoodi T, Najafi S, Sheykhi-Sabzehpoush M, Dari MAG, Radoszkiewicz K, Uddin S, Azizidoost S, Khoshnam SE. Potential roles of lncRNA-XIST/miRNAs/mRNAs in human cancer cells. Clin Transl Oncol. 2023 Jul;25(7):2015-2042. doi: 10.1007/s12094-023-03110-y. Epub 2023 Feb 28. PMID: 36853400.

Impact Factor: 3.4

The first Middle East and North Africa expert consensus recommendations for management of advanced gastric cancer

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Abstract

Gastric cancer (GC) ranks as the fifth most prevalent cancer and the fourth deadliest cancer worldwide. In the Middle East and North Africa (MENA) region, GC represents about 4.8% of cancer cases with more than 35,000 new cases in 2020. To strengthen and improve the management of this cancer in the region, a group of MENA experts in the field of GC developed the first MENA consensus recommendations for the management of advanced GC. A total of 28 statements were drafted, discussed and voted on, using a modified Delphi process, during a virtual consensus meeting. The statements addressed the areas of epidemiology, biomarkers and treatment.

Keywords: MENA; clinical practice guidelines; consensus; gastric cancer.

Citation: Kourie HR, Mahrous M, Naim N, Zouein J, Benbrahim Z, Rasul K, Mokhtar M, Shehri AA,

Shakeeb M, Khatib S, Al-Shamsi H, Shamseddine A, Smyth E. The first Middle East and North Africa expert consensus recommendations for management of advanced gastric cancer. Future Oncol. 2023 Jul;19(21):1451-1459. doi: 10.2217/fon-2023-0219. Epub 2023 Aug 1. PMID: 37526151.

Impact Factor: 3.3

Efficacy of lycopene for management of oral potentially malignant disorders: A systematic review and meta-analysis

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Abstract

Objective: The aim of this study was to investigate the available evidence on the efficacy of lycopene in the management of oral potentially malignant disorders (OPMDs).

Study design: PubMed, Scopus, Web of Science, Google Scholar, China National Knowledge Infrastructure, and ProQuest databases were searched up to April 20, 2022. All clinical trials that assessed the efficacy of lycopene (I) on the signs/symptoms (O) of patients with OPMDs (P) in

comparison to either active control or placebo (C) were included. Meta-analysis was conducted using the RevMan software (Cochrane Collaboration, London, UK).

Results: A total of 27 clinical trials (20 on oral submucosa fibrosis [OSF], 5 on oral lichen planus [OLP], and 2 on leukoplakia) were included. Overall, lycopene was efficacious in reducing signs and symptoms of OSF, OLP, and leukoplakia. The pooled data revealed comparable efficacy of lycopene and prednisolone in reducing pain and promoting clinical resolution of OLP. Additionally, the pooled data reported comparable efficacy of lycopene and conventional controls in improving the mouth opening and tongue protrusion in patients with OSF.

Conclusions: The results reveal promising effects of lycopene in alleviating signs and symptoms of OSF, OLP, and leukoplakia. However, owing to the observed heterogeneity and short follow-up periods, further well-designed studies with long-term therapy and follow-up are highly recommended.

Citation: Al-Maweri SA, Halboub E, Al-Qadhi G, Al-Wesabi M, Al-Sharani HM, Parveen S, Alhashimi N, Almeslet A, Alhajj MN. Efficacy of lycopene for management of oral potentially malignant disorders: A systematic review and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2023 Jan;135(1):79-95. doi: 10.1016/j.oooo.2022.08.004. Epub 2022 Aug 23. PMID: 36167720.

Impact Factor: 2.9

Role of circulating-tumor DNA in the early-stage non-small cell lung carcinoma as a predictive biomarker

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Abstract

Lung cancer is one of the most common solid malignancies. Tissue biopsy is the standard method for accurately diagnosing lung and many other malignancies over decades. However, molecular profiling of tumors leads to establishing a new horizon in the field of precision medicine, which has now entered the mainstream in clinical practice. In this context, a minimally invasive complementary method has been proposed as a liquid biopsy (LB) which is a blood-based test that is gaining popularity as it provides the opportunity to test genotypes in a unique, less invasive manner. Circulating tumor cells (CTC) captivating the Circulating-tumor DNA (Ct-DNA) are often present in the blood of lung cancer patients and are the fundamental concept behind LB. There are multiple clinical uses of Ct-DNA, including its role in prognostic and therapeutic purposes. The treatment of lung cancer has drastically evolved over time. Therefore, this review article mainly focuses on the current literature on circulating tumor DNA and its clinical implications and future goals in non-small cell lung cancer.

Keywords: Biomarker; CtDNA; Lung cancer; Precision medicine; Treatment.

Citation: Khan SR, Scheffler M, Soomar SM, Rashid YA, Moosajee M, Ahmad A, Raza A, Uddin

S. Role of circulating-tumor DNA in the early-stage non-small cell lung carcinoma as a predictive biomarker. Pathol Res Pract. 2023 May;245:154455. doi: 10.1016/j.prp.2023.154455. Epub 2023 Apr 7. PMID: 37054576.

Impact Factor: 2.8

Insights into head and neck cancer research in Egypt: A scoping review

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Abstract

Background: Head and neck cancer (HNC) encompasses malignant tumors in areas like the oral cavity, pharynx, and larynx. This analysis identifies strengths and deficiencies in HNC research, aiming to improve published papers' quality, quantity, and diversity. It also encourages more participation from oncologists, particularly in Egypt, to bridge the gap with Western healthcare standards.

Methods: A systematic search was conducted in databases including PubMed, Scopus, Web of Science, and Embase. The goal was to gather research articles on HNC in Egypt published from January 1, 2000, to December 31, 2022.

Results: From 2150 articles, 1329 were screened by title and abstract, leading to 193 for full-text review. Finally, 174 articles were included in the final analysis. 2020 saw the highest number of publications. The majority were primary research articles, with randomized controlled trials

being prevalent. Most studies were clinical, focusing on radiotherapy, and involved adult patients, emphasizing service delivery. Publications were predominantly in non-Egyptian journals, with the Egyptian Journal of Radiology and Nuclear Medicine being the most frequent. Research was mainly conducted by Egyptian authors and at Cairo University.

Conclusion: The growing prevalence of HNC in Egypt underscores the need for more comprehensive research on its various aspects, including etiology, risk factors, and prevention. There's a call for increased research outputs at different Egyptian universities, multicenter studies, and international collaborations. This approach can improve the understanding and management of HNC, contributing to global discussions and advancing treatment and prevention strategies in Egypt.

Keywords: Cancer; Egypt; Head and Neck; Research output; Scoping review.

Citation: Moawad MHED, Shalaby MM, Sadeq MA, Al-Jafari M, A'amar JW, Alsayed O, Aissani MS, Serag I, Fayad T, Ghorab RMF, Ghoneim MMI, Nashwan AJ. Insights into head and neck cancer research in Egypt: A scoping review. Cancer Treat Res Commun. 2023;37:100782. doi: 10.1016/j.ctarc.2023.100782. Epub 2023 Dec 6. PMID: 38086296.

Impact Factor: 2.52

Comparing trimodal therapy with radical cystectomy in muscle-invasive bladder cancer: an updated meta-analysis

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Abstract

Background: We conducted this meta-analysis to compare the two muscle-invasive bladder cancer (MIBC) treatment modalities in terms of cancer-specific survival (CSS) and other outcome indicators.

Method: A systematic review and meta-analysis were performed in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. The search was conducted using various academic databases including Scopus, PubMed, Cochrane database, EMBASE, Chinese biomedical literature database, Wan fang databases, and China National Knowledge Internet databases between 1966 and December 2023. This review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) No. (CRD42023398977).

Result: This study included a total of 54,816 patients diagnosed with bladder cancer from 14 studies, of which 6,228 patients were assigned to the trimodal therapy (TMT) group and 48,588 patients were assigned to the radical cystectomy (RC) group. Based on the results, the RC group exhibited a higher rate of survival than the TMT group [pooled hazard ratio (HR) = 1.23, 95% CI: 1.18-1.28, Z = 1.46, P < 0.001]. In terms of CSS, patients in the RC group had a longer CSS compared with those in the TMT group (pooled HR = 1.47, 95% CI: 1.29-1.67, Z = 5.893, P < 0.001). Compared with RC,

TMT is significantly associated with an increased risk of both types of mortality (pooled HR: 1.30, P < 0.001).

Conclusion: Overall, the findings of this meta-analysis suggest that RC treatment may be associated with improved overall survival. Moreover, it was observed that cancer-specific survival was significantly prolonged among patients in the RC group as opposed to those who received TMT. In addition, it was shown that patients who received TMT exhibited a higher risk of all-cause mortality when compared with those who underwent RC.

Keywords: bladder preserving; cancer; muscle-invasive; radical cystectomy; trimodal.

Citation: Al-Qudimat AR, Singh K, Ojha LK, Moustafa DA, Elaarag M, Al-Zoubi RM, Aboumarzouk OM. Comparing trimodal therapy with radical cystectomy in muscle-invasive bladder cancer: an updated meta-analysis. Front Surg. 2023 Dec 7;10:1276746. doi: 10.3389/fsurg.2023.1276746. PMID: 38130884; PMCID: PMC10733497.

Impact Factor: 1.8

Genomic profiling for non-small cell lung cancer: Clinical relevance in staging and prognosis

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Abstract

Lung cancer is one of the most common cancers prevalent and around 80% of all cases are non-small cell lung cancer (NSCLC). Due to high recurrence rates, the mortality of NSCLC is high. Conventional staging systems allowed risk classification of patients in order to simplify the patient selection for adjuvant chemotherapy. Gene expression analysis has been shown to possess advantage over conventional staging systems in NSCLC in terms of patients risk classification. This article reviews the evidences on the genomic profiling of NSCLC patients into high and low-risk groups based on the expression of genes involved in various proliferative pathways.

Citation: Bhattarai A, Shah S, Abu Serhan H, Sah R, Sah S. Genomic profiling for non-small cell lung cancer: Clinical relevance in staging and prognosis. Medicine (Baltimore). 2023 Nov 24;102(47):e36003. doi: 10.1097/MD.0000000000036003. PMID: 38013359; PMCID: PMC10681555.

Impact factor: 1.6

Transforming cancer clinical trials: The integral role of artificial intelligence in electronic health records for efficient patient recruitment

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Abstract

Healthcare is one of the sectors where artificial intelligence (AI) is currently viewed as a crucial driving factor. Patient care, medical research, and clinical trial enrollment could all significantly improve due to AI's incorporation into electronic health records (EHRs). This short communication highlights how AI may improve the recruitment process regarding speed, accuracy, and overall cancer clinical trial efficiency. AI can automate this procedure by utilizing machine learning (ML) algorithms, identifying potential trial participants quickly and precisely. Many challenges could be addressed due to this integration, including data privacy and security that can be resolved through cutting-edge encryption techniques and differential privacy algorithms that ensure data anonymization. Another significant obstacle is the lack of common EHR formats and interoperability that can be addressed by creating a standardized structured layout. Automating and improving recruitment processes with AI may speed up research, increase the effectiveness of clinical trials, and open the door to more specialized cancer treatments.

Keywords: Artificial intelligence; Cancer; Clinical trials; Electronic health records; Subject recruitment.

Citation: Nashwan AJ, Hani SB. Transforming cancer clinical trials: The integral role of artificial intelligence in electronic health records for efficient patient recruitment. Contemp Clin Trials Commun. 2023 Nov 7;36:101223. doi: 10.1016/j.conctc.2023.101223. PMID: 38034843; PMCID: PMC10682526.

Impact Factor: 1.5

The role of Rezum in the management of refractory urinary retention due to benign prostate hyperplasia: A literature review

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Abstract

Background: Benign prostatic hyperplasia is the most common cause of urinary retention in men (BPH). The gold standard surgical treatment is transurethral resection of the prostate (TURP). However, due to the morbidity and mortality associated with TURP, more minimally invasive treatments, such as vaporizing the prostate with the Rezum system, have been introduced. We investigated the efficacy of Rezum in the treatment of refractory urinary retention due to BPH in this review.

Methodology and materials: To conduct this review, the Cochrane methodology for systematic reviews was used. All studies that used Rezum to treat catheter-dependent patients with enlarged prostates were included. The literature search showed 111 studies, 84 of which were excluded due to non-relevance based on titles and 18 due to lack of relevance based on abstract review. Full manuscripts were reviewed in nine studies, three of which were excluded because they did not meet the inclusion criteria.

Results: This review included 301 patients in total. The rate of a successful trial of voiding post

Rezum therapy was 85%. The complication rated between 3.8 and 4.3% all of which were mild and self-limited. As there was no major complication of Rezum (clavien dindo >2), the procedure-related morbidity is negligible.

Conclusion: In this review, Rezum was found to be an efficacious and safe alternative in the treatment of refractory retention with mild complications and minimal morbidity.

Keywords: Benign prostate hyperplasia; Rezum; TURP; refractory retention.

Citation: Khalil IA, Aldeeb M, Mohammed A, Awad K, Ibrahim T, Al-Zoubi RM, Aboumarzouk OM, Al-Rumaihi K. The role of Rezum in the management of refractory urinary retention due to benign prostate hyperplasia: A literature review. Arab J Urol. 2023 Feb 24;21(3):185-189. doi: 10.1080/2090598X.2023.2178104. PMID: 37521455; PMCID: PMC10373601.

Impact Factor: 1.36

Chronic kidney diseases and the risk of colorectal cancer: A systematic review and meta-analysis

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Abstract

Objective: We conducted this review to offer a comprehensive search and up-to-date overview of the currently available information about the probability risk of colorectal cancer among chronic kidney disease patients.

Method: We performed a systematic review and meta-analysis following Preferred Reporting Items for Systematic Reviews (PRISMA) and meta-analysis guidelines. We identified, reviewed, and extracted from Scopus, PubMed, EMBASE, and Komaki Databases for research publications on chronic kidney disease and colorectal cancer published between February 2016 and January 2023. We meta-analyzed the prevalence of colorectal cancer with chronic kidney disease. We ran a random effect meta-regression. Risk-of-bias assessment was evaluated using the Newcastle-Ottawa Scale. The systematic review was registered with PROSPERO (CRD42023400983).

Results: The risk of CRC in chronic kidney diseases was reported in 50 research studies, which included 4,337,966 people from 16 different countries. SIR of CRC was obtained from 14 studies and showed a significant relationship between CRC with CKD patients, with a pooled SIR of 1.33; 95% CI (1.30-1.36), with higher heterogeneity ($Q = 121.82$, $P < 0.001$, and $I2 = 86.9\%$). Metaregression showed that there was no significant correlation between the risk of CRC and the proportion of males or age.

Conclusion: Overall, this study shows that patients with chronic kidney disease have a significantly increased risk of colorectal cancer. More studies with larger sample sizes, and robust surveillance are needed.

Keywords: CKD; Chronic kidney disease; Risk; cancer; colorectal.

Citation: Al-Qudimat AR, Al Darwish MB, Altahtamouni SB, Singh K, Al-Zoubi RM, Aboumarzouk OM, Al-Ansari A. Chronic kidney diseases and the risk of colorectal cancer: A systematic review and meta-analysis. Arab J Urol. 2023 Jun 20;21(4):258-266. doi: 10.1080/2090598X.2023.2225315. PMID: 38178950; PMCID: PMC10763595.

Impact Factor: 1.36

A Double Battle: Fighting Cancer in the Shadows of Conflict in Gaza

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Abstract

The ongoing conflict in Gaza has intensified challenges for patients with cancer. Restrictions have limited essential medical supplies, and the recent Israeli airstrike severely damaged Gaza's primary cancer hospital, causing widespread panic. The blockade has caused shortages, and damaged infrastructure has reduced access to care. Many patients seeking treatment outside Gaza face permit delays, and the psychological and economic strains further burden patients and their families. This editorial highlights the broader humanitarian crisis, emphasizing the need for international collaboration to support Gaza's most vulnerable.

Keywords: cancer; conflict; gaza; humanitarian crisis; palestine.

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Impact Factor: 1.2

Extra neural metastasis of Glioblastoma Multiforme: A Literature Review

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Abstract

Extra-neural metastases of glioblastoma multiforme are uncommon with unidentified metastatic mechanism. There is no consensus over optimum treatment regimen. The current narrative review was planned to illuminate the presence criteria, sites of metastatic spread, incidence, mechanism, risk factors and management.

Keywords: Glioblastoma multiforme, Extra-neural metastases, Spread, Mechanism, Risk factors.

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MALIGNANT HEMATOLOGY

ORIGINAL ARTICLES

Other malignancies in the history of CLL: an international multicenter study conducted by ERIC, the European Research Initiative on CLL, in HARMONY

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Abstract

Background: Patients With Chronic Lymphocytic Leukemia (Cll) Have A Higher Risk Of Developing Other Malignancies (Oms) Compared To The General Population. However, The Impact Of Cll-Related Risk Factors And Cll-Directed Treatment Is Still Unclear And Represents The Focus Of This Work.

Methods: We Conducted A Retrospective International Multicenter Study To Assess The Incidence Of Oms And Detect Potential Risk Factors In 19,705 Patients With Cll, Small Lymphocytic Lymphoma, Or High-Count Cll-Like Monoclonal B-Cell Lymphocytosis, Diagnosed Between 2000 And 2016. Data Collection Took Place Between October 2020 And March 2022.

Findings: In 129,254 Years Of Follow-Up After Cll Diagnosis, 3513 Oms Were Diagnosed (27.2 Oms/1000 Person-Years). The Most Common Hematological Oms Were Richter Transformation, Myelodysplastic Syndrome (Mds) And Acute Myeloid Leukemia (Aml). Non-Melanoma Skin (Nmsc) And Prostate Cancers Were The Most Common Solid Tumors (Sts).The Only Predictor For Mds And

Aml Development Was Treatment With Fludarabine And Cyclophosphamide With/Without Rituximab (Fc ± R) (Or = 3.7; 95% Ci = 2.79-4.91; P < 0.001). Sts Were More Frequent In Males And Patients With Unmutated Immunoglobulin Heavy Variable Genes (Or = 1.77; 95% Ci = 1.49-2.11; P < 0.001/ Or = 1.89; 95% Ci = 1.6-2.24; P < 0.001).Cll-Directed Treatment Was Associated With Non-Melanoma Skin And Prostate Cancers (Or = 1.8; 95% Ci = 1.36-2.41; P < 0.001/Or = 2.11; 95% Ci = 1.12-3.97; P = 0.021). In Contrast, Breast Cancers Were More Frequent In Untreated Patients (Or = 0.17; 95% Ci = 0.08-0.33; P < 0.001).Patients With Cll And An Om Had Inferior Overall Survival (Os) Than Those Without. Aml And Mds Conferred The Worst Os (P < 0.001).

Interpretation: Oms In Cll Impact On Os. Treatment For Cll Increased The Risk For Aml/Mds, Prostate Cancer, And Nmsc. Fcr Was Associated With Increased Risk For Aml/Mds.

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Keywords: Chronic Lymphocytic Leukemia; Other Cancers; Other Malignancies; Second Primary Malignancies.

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The evolving landscape of COVID-19 and post-COVID condition in patients with chronic lymphocytic leukemia: A study by ERIC, the European research initiative on CLL

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Abstract

In this retrospective international multicenter study, we describe the clinical characteristics and outcomes of patients with chronic lymphocytic leukemia (CLL) and related disorders (small lymphocytic lymphoma and high-count monoclonal B lymphocytosis) infected by SARS-CoV-2, including the development of post-COVID condition. Data from 1540 patients with CLL infected by SARS-CoV-2 from January 2020 to May 2022 were included in the analysis and assigned to four phases based on cases disposition and SARS-CoV-2 variants emergence. Post-COVID condition was defined according to the WHO criteria. Patients infected during the most recent phases of the pandemic, though carrying a higher comorbidity burden, were less often hospitalized, rarely needed intensive care unit admission, or died compared to patients infected during the initial phases. The 4-month overall survival (OS) improved through the phases, from 68% to 83%, p = .0015. Age, comorbidity, CLL-directed treatment, but not vaccination status, emerged as risk factors for mortality. Among survivors, 6.65% patients had a reinfection, usually milder than the initial one, and 16.5% developed post-COVID condition. The latter was characterized by fatigue, dyspnea, lasting cough, and impaired concentration. Infection severity was the only risk factor for developing post-COVID. The median time to resolution of the post-COVID condition was 4.7 months. OS in patients with CLL improved during the different phases of the pandemic, likely due to the improvement of prophylactic and therapeutic measures against SARS-CoV-2 as well as the emergence of milder variants. However, mortality remained relevant and a significant number of patients developed post-COVID conditions, warranting further investigations.

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COVID-19 in adult acute myeloid leukemia patients: a long-term follow-up study from the European Hematology Association survey (EPICOVIDEHA)

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Abstract

Patients with acute myeloid leukemia (AML) are at high risk of dying from coronavirus disease 2019 (COVID-19). The optimal management of AML patients with COVID-19 has not been established. Our multicenter study included 388 adult AML patients diagnosed with COVID-19 between February 2020 and October 2021. The vast majority were receiving or had received AML treatment in the preceding 3 months. COVID-19 was severe in 41.2% and critical in 21.1% of cases. The chemotherapeutic schedule was modified in 174 patients (44.8%), delayed in 68 and permanently discontinued in 106. After a median follow-up of 325 days, 180 patients (46.4%) had died; death was attributed to COVID-19 (43.3%), AML (26.1%) or to a combination of both (26.7%), whereas in 3.9% of cases the reason was unknown. Active disease, older age, and treatment discontinuation were associated with death, whereas AML treatment delay was protective. Seventy-nine patients had a simultaneous AML and COVID-19 diagnosis, with better survival when AML treatment could be delayed (80%; P<0.001). Overall survival in patients with a diagnosis of COVID-19 between January 2020 and August 2020 was significantly lower than that in patients diagnosed between September

2020 and February 2021 and between March 2021 and September 2021 (39.8% vs. 60% vs. 61.9%, respectively; P=0.006). COVID-19 in AML patients was associated with a high mortality rate and modifications of therapeutic algorithms. The best approach to improve survival was to delay AML treatment, whenever possible.

Citation: Marchesi F, Salmanton-García J, Emarah Z, Piukovics K, Nucci M, López-García A, Ráčil Z, Farina F, Popova M, Zompi S, Audisio E, Ledoux MP, Verga L, Weinbergerová B, Szotkovski T, Da Silva MG, Fracchiolla N, De Jonge N, Collins G, Marchetti M, Magliano G, García-Vidal C, Biernat MM, Van Doesum J, Machado M, Demirkan F, Al-Khabori M, Žák P, Víšek B, Stoma I, Méndez GA, Maertens J, Khanna N, Espigado I, Dragonetti G, Fianchi L, Del Principe MI, Cabirta A, Ormazabal-Vélez I, Jaksic O, Buquicchio C, Bonuomo V, Batinić J, Omrani AS, Lamure S, Finizio O, Fernández N, Falces-Romero I, Blennow O, Bergantim R, Ali N, Win S, Van Praet J, Tisi MC, Shirinova A, Schönlein M, Prattes J, Piedimonte M, Petzer V, Navrátil M, Kulasekararaj A, Jindra P, Sramek J, Glenthøj A, Fazzi R, De Ramón-Sánchez C, Cattaneo C, Calbacho M, Bahr NC, El-Ashwah S, Cordoba R, Hanakova M, Zambrotta G, Sciumè M, Booth S, Rodrigues RN, Sacchi MV, García-Poutón N, Martín-González JA, Khostelidi S, Gräfe S, Rahimli L, Ammatuna E, Busca A, Corradini P, Hoenigl M, Klimko N, Koehler P, Pagliuca A, Passamonti F, Cornely OA, Pagano L; EPICOVIDEHA working group. COVID-19 in adult acute myeloid leukemia patients: a long-term follow-up study from the European Hematology Association survey (EPICOVIDEHA). Haematologica. 2023 Jan 1;108(1):22-33. doi: 10.3324/haematol.2022.280847. PMID: 35545919; PMCID: PMC9827164.

Impact Factor: 10.1

In vitro evaluation of Neosetophomone B inducing apoptosis in cutaneous T cell lymphoma by targeting the FOXM1 signaling pathway

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Abstract

Background: Cutaneous T cell lymphoma (CTCL) is a T cell-derived non-Hodgkin lymphoma primarily affecting the skin, with treatment posing a significant challenge and low survival rates.

Objective: In this study, we investigated the anti-cancer potential of Neosetophomone B (NSP-B), a fungal-derived secondary metabolite, on CTCL cell lines H9 and HH.

Methods: Cell viability was measured using Cell counting Kit-8 (CCK8) assays. Apoptosis was measured by annexin V/PI dual staining. Immunoblotting was performed to examine the expression of proteins. Applied Biosystems' high-resolution Human Transcriptome Array 2.0 was used to examine gene expression.

Results: NSP-B induced apoptosis in CTCL cells by activating mitochondrial signaling pathways and caspases. We observed downregulated expression of BUB1B, Aurora Kinases A and B, cyclin-dependent kinases (CDKs) 4 and 6, and polo-like kinase 1 (PLK1) in NSP-B treated cells, which was further corroborated by Western blot analysis. Notably, higher expression levels of these genes showed reduced overall and progression-free survival in the CTCL patient cohort. FOXM1 and BUB1B expression exhibited a dose-dependent reduction in NSP-B-treated CTCL cells.FOXM1 silencing decreased cell viability and increased apoptosis via BUB1B downregulation. Moreover, NSP-B suppressed FOXM1-regulated genes, such as Aurora Kinases A and B, CDKs 4 and 6, and PLK1. The combined treatment of Bortezomib and NSP-B showed greater efficacy in reducing CTCL cell viability and promoting apoptosis compared to either treatment alone.

Conclusion: Our findings suggest that targeting the FOXM1 pathway may provide a promising therapeutic strategy for CTCL management, with NSP-B offering significant potential as a novel treatment option.

Citation: Kuttikrishnan S, Masoodi T, Ahmad F, Sher G, Prabhu KS, Mateo JM, Buddenkotte J, El-Elimat T, Oberlies NH, Pearce CJ, Bhat AA, Alali FQ, Steinhoff M, Uddin S. In vitro evaluation of Neosetophomone B inducing apoptosis in cutaneous T cell lymphoma by targeting the FOXM1

signaling pathway. J Dermatol Sci. 2023 Nov;112(2):83-91. doi: 10.1016/j.jdermsci.2023.10.001. Epub 2023 Oct 6. PMID: 37865581.

Impact Factor: 4.6

Embelin inhibits viability of cutaneous T cell lymphoma cell lines HuT78 and H9 by targeting inhibitors of apoptosis

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Abstract

Cutaneous T cell lymphoma (CTCL) is a varied group of neoplasms that affects the skin. Acquired resistance against chemotherapeutic drugs and associated toxic side effects are limitations that warrant search for novel drugs against CTCL. Embelin (EMB) is a naturally occurring benzoquinone derivative that has gained attention owing to its anticancer pharmacological actions and nontoxic nature. We assessed the anticancer activity of EMB against CTCL cell lines, HuT78, and H9. EMB inhibited viability of CTCL cells in a dose-dependent manner. EMB activated extrinsic and intrinsic pathways of apoptosis as shown by the activation of initiator and executioner caspases. EMB-induced apoptosis also involved suppression of inhibitors of apoptosis, XIAP, cIAP1, and cIAP2. PARP cleavage and upregulation of pH2AX indicated DNA damage induced by EMB. In conclusion, we characterized a novel apoptosis-inducing activity of EMB against CTCL cells, implicating EMB as a potential therapeutic agent against CTCL.

Keywords: Cutaneous T cell lymphoma; apoptosis; caspases; embelin; inhibitors of apoptosis.

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of cutaneous T cell lymphoma cell lines HuT78 and H9 by targeting inhibitors of apoptosis. Leuk Lymphoma. 2023 Dec;64(14):2236-2248. doi: 10.1080/10428194.2023.2256909. Epub 2023 Sep 14. PMID: 37708450.

Impact Factor: 2.6

Evidence-Based Management of Chronic Lymphocytic Leukemia: Consensus Statements from the Gulf Region

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Abstract

Introduction: Despite recent advances in diagnosis, prognostication, and treatment options, chronic lymphocytic leukemia (CLL) is still a largely incurable disease. New concepts on diagnosis, staging, treatment, and follow-up on CLL have been incorporated throughout recent years. The lack of regional consensus guidelines has led to varying practices in the management of patients with CLL in the region. This manuscript aims to reach a consensus among expert hematologists regarding the definitions, classifications, and related practices of CLL. The experts developed a set of statements utilizing their personal experience together with the current literature on CLL management. This consensus aims to provide guidance for healthcare professionals involved in the management of CLL and serves as a step in developing regional guidelines. Methods: Eight experts responded to 50 statements regarding the diagnosis, staging, treatment, and prognosis of CLL with three potential answering alternatives ranging between agree, disagree, and abstain. This consensus adopted a modified Delphi consensus methodology. A consensus was reached when at least 75% of the agreement to the answer was reached. This manuscript presents the scientific insights of the participating attendees, panel discussions, and the supporting literature review. Results: Of the 50

statements, a consensus was reached on almost all statements. Statements covered CLL-related topics, including diagnostic evaluation, staging, risk assessment, different patient profiles, prognostic evaluation, treatment decisions, therapy sequences, response evaluation, complications, and CLL during the COVID-19 pandemic. Conclusion: In recent years, CLL management has progressed significantly, with many diagnostic tests and several novel treatments becoming available. This consensus gathers decades of consolidated principles, novel research, and promising prospects for the management of this disease.

Keywords: Chronic lymphocytic leukemia, Delphi, Gulf, GCC, Chemoimmunotherapy, Targeted therapy

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The utility of testing erythropoietin level in polycythemia diagnosis

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Abstract

Objectives: Polycythemia vera (PV) is classically thought to be associated with low erythropoietin (EPO) levels. Here, we present a review of the utility of using EPO levels in diagnosing polycythemia.

Methods: We conducted a systematic literature review of the Medline data through Pubmed and Google Scholar. We included the articles which described confirmed PV associated with elevated EPO level. Our search strategy included the following terms in Pubmed (((polycythemia vera[MeSH Terms]) OR (jak2 protein tyrosine kinase[MeSH Terms])) OR (Myeloproliferative Disorders[MeSH Terms])) AND (Erythropoietin[MeSH Terms]), and 'polycythemia vera with erythropoietin' in Google Scholar.

Results: Our research yielded four cases of PV with elevated EPO levels. The most common symptom was a headache. Thrombotic phenomena happened in a single case in the form of Budd-Chiari syndrome. The mean Hb level was 20.2 gm/dl, and the EPO level was 213 mlU/mL.

Discussion: Although PV is usually associated with low EPO levels, high levels do not exclude this diagnosis. Workup should include testing for JAK2 mutation and bone marrow biopsy in the presence of suggestive signs and symptoms. Novel biomarkers are also being proposed to aid in the diagnosis.

Conclusion: Although elevated EPO levels suggest secondary causes of polycythemia, cases where elevated EPO levels were associated with an underlying PV are reported in the literature, and we have summarized a review of them. Workup for polycythemia should include JAK2 mutation testing if signs and symptoms suggest PV even if EPO is elevated.

Keywords: EPO; JAK2 mutation; PV; Polycythemia vera; erythropoietin; myeloproliferative neoplasms.

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Impact Factor: 1.9

Cytogenetic profile of 1791 adult acute myeloid leukemia in India

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Abstract

Background: Cytogenetic analysis continues to have an important role in the management of acute myeloid leukemia (AML) because it is essential for prognostication. It is also necessary to diagnose specific categories of AML and to determine the most effective form of treatment. Reports from South Asia are few because the availability of cytogenetic services is relatively limited.

Methods: We performed a retrospective analysis of the cytogenetic findings in adults with AML seen consecutively in a single centre in India. The results were categorised according to the 2022 World Health Organisation (WHO), International Consensus Classification (ICC) and European LeukemiaNet (ELN) classifications.

Results: There were 1791 patients aged 18-85 years (median age 42, 1086 males). Normal karyotypes were seen in 646 (36%) patients. The 1145 (64%) abnormal karyotypes comprised 585 (32.7%) with recurrent genetic abnormalities (RGA), 403 (22.5%) with myelodysplasia-related

cytogenetic abnormalities (MRC), and 157 (8.8%) with other abnormalities. There were 567 (31.7%) patients with solitary abnormalities and 299 (16.7%) with two abnormalities. Among the 279 (15.6%) patients with ≥ 3 abnormalities, 200 (11.2%) had complex karyotypes (CK) as per the WHO/ICC and 184 (10.3%), as per the ELN definition. There were 158 (8.8%) monosomal karyotypes (MK). Patients with normal karyotypes had a higher median age (45 years) than those with abnormal karyotypes (40 years, $p < 0.001$), and those with ≥ 3 abnormalities (43 years), than those with fewer abnormalities (39 years, $p = 0.005$). Patients with CK (WHO/ICC) and monosomal karyotypes had a median age of 48 years. Those with RGA had a lower median age (35 years, $p < 0.001$) than MRC (46 years) or other abnormalities (44 years). The t(15;17) was the most common abnormality (16.7%),followed by trisomy 8 (11.6%), monosomy 7/del 7q (9.3%), t(8;21) (7.2%), monosomy 5/del 5q (6.7%) and monosomy 17/del 17p (5.2%).

Conclusion: Our findings confirm the lower age profile of AML in India and show similarities and differences with respect to the frequencies of individual abnormalities compared to the literature. The frequencies of the t(15;17), trisomy 8 and the high-risk abnormalities monosomy 7 and monosomy 5/del 5q were higher, and that of the inv(16), lower than in most reports.

Keywords: Acute myeloid leukemia; Age; Asia; Chromosomal; Complex karyotype; Cytogenetics; Frequency; Monosomal karyotype; Myelodysplasia-related; Translocation.

Citation: Srivastava VM, Nair SC, Sappani M, Manipadam MT, Kulkarni UP, Devasia AJ, Fouzia NA, Korula A, Lakshmi KM, Abraham A, Srivastava A. Cytogenetic profile of 1791 adult acute myeloid leukemia in India. Mol Cytogenet. 2023 Sep 16;16(1):24. doi: 10.1186/s13039-023-00653-1. PMID: 37716945; PMCID: PMC10504794.

Impact Factor: 1.3

The Impact of Tyrosine Kinase Inhibitors on Fatherhood in Patients With Chronic Myeloid Leukemia: A Mixed-Method Study

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Abstract

Introduction: Multiple studies have demonstrated that tyrosine kinase inhibitors (TKIs) exert a significant extent of control over chronic myeloid leukemia (CML), as evidenced by studies such as the population-based Swedish CML registry, which found that patients reaching age 70 had a relative survival rate close to one when compared to the general population. Consequently, new perspectives on the safety of treatments have emerged, particularly in the context of their impact on fatherhood in men. According to the authors, this is the first study to examine the effect of TKIs on fatherhood in CML patients. Methods: A single-center, mixed-design study (retrospective data review and phone interviews) was conducted with CML male patients in the chronic or accelerated phase, evaluating the effect of imatinib, dasatinib, and nilotinib on their fatherhood, irrespective of whether they were administered as a first, second, or third line of treatment.

Results: The study included interviews with 150 patients. Included were 27 patients. The average age was approximately 44.5 years. One hundred percent of the patients were in the chronic phase. The median age at first conception following TKI therapy was 36, and the median duration of TKI therapy was approximately seven years. The total number of offspring was 49; 98% were born at term and had a normal birth weight. No reports of stillbirths, fetal deaths, or congenital malformations were made. All the offspring grew and developed normally. No CML-related cancers were reported in any of the newborns.

Conclusion: Around 98% of male CML patients receiving imatinib, dasatinib, or nilotinib did not experience a negative impact on their fatherhood or the health of their children. However, improved education for patients beginning treatment with TKIs addresses the potential psychological worry of having an unfavorable effect on their fertility or offspring, which may increase medication adherence.

Keywords: chronic myeloid leukemia; cml; fatherhood; tkis; tyrosine kinase inhibitors.

Citation: Abu-Tineh M, Ali EA, Alshurafa A, Nashwan AJ, Albsheer K, Ahmed A, Hailan Y, Rozi W, Aljaloudi E, Yassin MA. The Impact of Tyrosine Kinase Inhibitors on Fatherhood in Patients With Chronic Myeloid Leukemia: A Mixed-Method Study. Cureus. 2023 Jan 5;15(1):e33407. doi: 10.7759/cureus.33407. PMID: 36751250; PMCID: PMC9899104.

Impact Factor: 1.2

An Artificial Intelligence-Based Diagnostic System for Acute Lymphoblastic Leukemia Detection

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Abstract

This study suggests a novel Acute Lymphoblastic Leukemia (ALL) diagnostic model, built solely on complete blood count (CBC) records. Using a dataset comprised of CBC records of 86 ALL and 86 control patients respectively, we identified the most ALL-specific parameters using a feature selection approach. Next, Grid Search-based hyperparameter tuning with a five-fold cross-validation scheme was adopted to build classifiers using Random Forest, XGBoost, and Decision Tree algorithms. A comparison between the performances of the three models demonstrates that Decision Tree classifier outperformed XGBoost and Random Forest algorithms in ALL detection using CBC-based records.

Keywords: ALL; CBC; Early detection; Machine learning.

Citation: El Alaoui Y, Padmanabhan R, Elomri A, Qaraqe MK, El Omri H, Yasin Taha R. An Artificial Intelligence-Based Diagnostic System for Acute Lymphoblastic Leukemia Detection. Stud Health Technol Inform. 2023 Jun 29;305:265-268. doi: 10.3233/SHTI230479. PMID: 37387013.

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MALIGNANT HEMATOLOGY

CASE REPORTS

Polatuzumab Vedotin in a Patient with Refractory Burkitt Lymphoma, a Case Report

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Abstract

Although Burkitt lymphoma is considered a curable disease due to the progress made in choosing the most effective first-line therapy, relapsed or refractory Burkitt lymphoma (BL) has a very poor outcome. There is a lack of data supporting the treatment regimens. We report a 48-year-old male with stage II Burkitt's lymphoma with no response to the first line of high-intensity chemotherapy. However, treatment with polatuzumab vedotin led to complete clinical remission for more than one year.

Keywords: Burkitt's lymphoma; Lymphoma; anti CD79b; polatuzumab; resistant lymphoma.

Citation: Alanzi M, Abu-Tineh M, Szabados L, Sharaf Eldean MZ, Alatasi S, Taha RY, Elkourashy SA. Polatuzumab Vedotin in a Patient with Refractory Burkitt Lymphoma, a Case Report. Onco Targets Ther. 2023 Feb 21;16:133-139. doi: 10.2147/OTT.S394193. PMID: 36852093; PMCID: PMC9961566.

Impact Factor: 4.0

Synchronous gnathic osteosarcoma and B-cell lymphoblastic lymphoma/leukemia: A rare case presentation

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Abstract

Multiple primary malignancies are a well-recognized entity, with increased recognition and detection alongside development of hybrid imagining. We present a rare case of a 16-year-old male with gnathic osteosarcoma and incidental finding of a second silent synchronous B-cell lymphoblastic lymphoma/leukemia in the lower limb. Treated successfully by chemotherapy, radiotherapy, and surgery.

Keywords: B cell lymphoma/leukemia; Double malignancy; Multiple primary malignancy; Osteosarcoma; Synchronous tumors.

Citation: Elawad MF, Sibira DM, Ammar A, Szabados L, Ibrahem RE. Synchronous gnathic osteosarcoma and B-cell lymphoblastic lymphoma/leukemia: A rare case presentation. Radiol Case Rep. 2023 Sep 6;18(11):4085-4090. doi: 10.1016/j.radcr.2023.08.028. PMID: 37705886; PMCID: PMC10495600.

Impact factor: 1.9

Central catheter-related Gordonia bronchialis bacteremia in an immunocompromised patient: A case report, and literature review

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Abstract

Gordonia is a rarely reported organism causing central line-associated bloodstream infection (CLABSI). This article reports an acute myeloid leukemia (AML) case in which the patient developed febrile neutropenia and was later found to have Gordonia bronchialis (G. bronchialis) CLABSI. The patient received a two-week ceftriaxone regimen, based on susceptibility. The microbiologic diagnosis of this organism is considered challenging due to its resemblance with other organisms; however, more sophisticated methods of diagnosis (such as gene sequencing) can aid in differentiation.

Keywords: AML; Bacteremia; Central line; Gordonia.

Citation: Alnajjar M, Mudawi D, Cherif H, Hashim SM, Zaqout A, Bougaila A, Jibril FI, Mohamed SF. Central catheter-related Gordonia bronchialis bacteremia in an immunocompromised patient: A case report, and literature review. IDCases. 2023 Mar 6;32:e01738. doi: 10.1016/j.idcr.2023.e01738. PMID: 36938335; PMCID: PMC10014288.

Impact Factor: 1.31

Carfilzomib-induced life-threatening lung injury in refractory multiple myeloma

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Abstract

Introduction: Carfilzomib is a second-generation selective proteasome inhibitor that is commonly used in the treatment of relapsed or refractory multiple myeloma. Carfilzomib is associated with respiratory side effects, such as cough, dyspnea, and upper respiratory tract infection. However, severe pulmonary toxicity is rare and is only reported in a few case reports.

Case report: Here, we present a case of a 65-year-old male with refractory multiple myeloma who developed a life-threatening lung injury during his third cycle of carfilzomib. The patient presented with a decreased level of consciousness and was found to have Type I respiratory failure. He was admitted to the intensive care unit, where he was intubated. Blood cultures and viral panel were negative. The patient received a prolonged course of antibiotics with 2 days of hydrocortisone.

Management and outcomes: After discharge, repeated myeloma workup showed disease progression and carfilzomib was reintroduced. The next day, he presented with fever, vomiting, and hypoxia. Chest x-ray showed congestive lung changes with patchy airspace opacities. Repeated echocardiography showed normal ejection fraction with moderate pulmonary hypertension (RVSP 46 mm Hg). The patient was transferred again to the ICU and kept on continuous positive airway pressure. Antibiotics were started, and blood cultures and respiratory viral panels were negative for any infectious organism. The patient improved in terms of inflammatory markers and oxygen requirements. Treatment with carfilzomib was stopped permanently.

Discussion: Pulmonary toxicity associated with carfilzomib in patients with multiple myeloma can be potentially life-threatening. The mechanism with which carfilzomib induces lung-related AEs is still not fully understood. In our patient, carfilzomib-induced lung injury was evident after rechallenging the patient with carfilzomib, in the radiographic x-ray changes and the new onset moderate pulmonary

hypertension. Healthcare providers should be encouraged to report rare adverse events in order to identify the risk factors that can predispose patients to the development of these adverse events.

Keywords: Carfilzomib; multiple myeloma; proteasome inhibitor; pulmonary toxicity.

Citation: Ghasoub R, Benkhadra M, Kassem N, Alshurafa A, Elsabah H. Carfilzomib-induced life-threatening lung injury in refractory multiple myeloma. J Oncol Pharm Pract. 2023 Dec;29(8):2041-2044. doi: 10.1177/10781552231190039. Epub 2023 Jul 24. PMID: 37489075.

Impact Factor: 1.3

DVT as the Initial Presentation of Multiple Myeloma: A Rare Case Report and Literature Review

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Abstract

Multiple myeloma patients are recognized to have a higher risk of venous thrombosis. The cause of this could be attributed to several risk factors, such as circulating prothrombotic microparticles, disease-specific variables, and alterations in coagulation and fibrinolysis factors. Recent research has revealed that these individuals also experience greater arterial thrombosis, including acute myocardial infarction and stroke. In this case report, we present the clinical profile and management of a 42-year-old patient who presented with signs and symptoms of deep venous thrombosis (DVT) and was diagnosed with multiple myeloma. The aim of this case report is to highlight a rare clinical presentation and diagnostic workup in a patient with multiple myeloma. Additionally, we discuss the possible factors provoking the development of DVT as a first presentation before treatment initiation and their possible mechanisms.

Keywords: deep venous thrombosis; diabetes mellitus (dm); multiple myeloma; pulmonary embolism (pe); smoking; venous thromboembolism (vte).

Citation: Khalil SK, Saeed L, Fadul A, Elawad MF, Ferih K. DVT as the Initial Presentation of Multiple Myeloma: A Rare Case Report and Literature Review. Cureus. 2023 Jul 28;15(7):e42600. doi: 10.7759/cureus.42600. PMID: 37644932; PMCID: PMC10461026.

Impact Factor: 1.2

The effectiveness of tyrosine kinase inhibitor for chronic myeloid leukemia in tuberous sclerosis. A case report and review of literature

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Abstract

The relationship between chronic myelogenous leukemia (CML) and tuberous sclerosis (TS) is unusual and uncommon. Here, we report a 24-year-old woman diagnosed with TS and later identified with CML, as the second case reported with such coexistence, treated with Nilotinib. This article proposes a hypothesis to explain the association. Therefore, we propose Nilotinib for the treatment of patients with such coexisting diseases. Further studies are warranted to reveal the dynamics between these conditions.

Keywords: CML; tuberous sclerosis; tyrosine kinase inhibitors.

Citation: Al-Abdulmalek A, Al-Suliman R, Abu-Tineh M, Ali M, Yassin MA. The effectiveness of tyrosine kinase inhibitor for chronic myeloid leukemia in tuberous sclerosis. A case report and review of literature. Clin Case Rep. 2023 Mar 17;11(3):e7087. doi: 10.1002/ccr3.7087. PMID: 36941833; PMCID: PMC10024035.

Impact factor: 1.089

A Rare Case of Lambert-Eaton Myasthenia Syndrome Associated with Non-Hodgkin's Lymphoma: A Case Report and Review of the Literature

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Abstract

Introduction: Lambert-Eaton myasthenia syndrome (LEMS) is a rare autoimmune disorder characterized by autoantibodies targeting presynaptic neuromuscular junctions. It results in muscle weakness and autonomic dysfunction. LEMS can be idiopathic or associated with neoplastic diseases, often small-cell lung cancer. This case report describes a rare instance of paraneoplastic LEMS in a man with non-Hodgkin lymphoma.

Case presentation: A 57-year-old male with non-Hodgkin lymphoma presented with progressive muscle weakness, diminished reflexes, and autonomic symptoms. Diagnosis revealed LEMS with autoantibodies against voltage-gated calcium channels. Immunosuppressive therapy and lymphoma treatment led to significant improvement in his condition.

Conclusion: This case highlights the rare occurrence of paraneoplastic LEMS in a patient with non-Hodgkin lymphoma. Recognition and timely management of LEMS alongside lymphoma treatment can lead to significant clinical improvement, emphasizing the need for increased awareness of such complex associations.

Keywords: Autoimmune disorders; Lambert-Eaton myasthenic syndrome; Non-Hodgkin lymphoma; Peripheral T-cell lymphoma.

Citation: Abu-Tineh M, Alamin MA, Aljaloudi E, Alshurafa A, Garcia-Cañibano B, Taha RY, Elkourashy SA. A Rare Case of Lambert-Eaton Myasthenia Syndrome Associated with Non-Hodgkin's Lymphoma: A Case Report and Review of the Literature. Case Rep Oncol. 2023 Nov 6;16(1):1300-1305. doi: 10.1159/000534557. PMID: 37942405; PMCID: PMC10629858.

Impact Factor: 0.75

Spontaneous Remission in a Patient with Chronic Myeloid Leukemia: A Case Report

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Abstract

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm in which granulocytic cells are the main proliferative component. At diagnosis, more than 90% of CML cases have the characteristic Philadelphia chromosome, containing the BCR::ABL1 fusion gene. The natural history of untreated CML is an initial indolent chronic phase which will be followed by an accelerated phase, blast phase, or both. Tyrosine kinase inhibitors (TKIs) have dramatically altered the natural history of CML. TKI discontinuation with the goal of treatment-free remission is currently part of current management recommendations. However, spontaneous remission without receiving any treatment is extraordinarily rare in CML patients. Herein, we report a 56-year-old male who presented with leukocytosis and was diagnosed as a case of CML in the chronic phase; however, treatment with TKIs was not initiated due to spontaneous hematological as well as molecular remission.

Keywords: Chronic myeloid leukemia; Philadelphia chromosome; Spontaneous remission; Tyrosine kinase inhibitors.

Citation: Alshurafa A, Ekeibed Y, Akiki S, Alzeyara M, Nawaz Z, Yassin MA. Spontaneous Remission in a Patient with Chronic Myeloid Leukemia: A Case Report. Case Rep Oncol. 2023 Oct 6;16(1):1073-1079. doi: 10.1159/000533660. PMID: 37900818; PMCID: PMC10601788.

Impact Factor: 0.75

Delayed Diagnosis of Indolent Systemic Mastocytosis as the Cause of Unexplained Skin Rash: A Case Report]

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Abstract

Mastocytosis is a heterogeneous group of disorders in which mast cells exhibit clonal proliferation that infiltrates one or more organs. In cutaneous mastocytosis, the mast cells infiltrate the skin only, whereas systemic mastocytosis is diagnosed when at least one extra-cutaneous site is involved, with or without the skin being affected. Given the rarity of mastocytosis and the fact that skin rash can be a manifestation of different conditions and many clinicians are not familiar with this disorder, an accurate diagnosis may be delayed. We report a delayed diagnosis of indolent systemic mastocytosis in a 40-year-old gentleman who had been complaining of an unexplained skin rash for 6 years.

Keywords: Indolent systemic mastocytosis; Mastocytosis; Skin rash; Urticaria pigmentosa.

Citation: Alshurafa A, Abu-Tineh M, Ibrahim FA, Petkar M, Yassin MA. Delayed Diagnosis of Indolent Systemic Mastocytosis as the Cause of Unexplained Skin Rash: A Case Report. Case Rep Oncol. 2023 Feb 10;16(1):62-68. doi: 10.1159/000529347. PMID: 36785740; PMCID: PMC9918867.

Impact Factor: 0.75

Acute Lymphoblastic Leukemia Presenting with Acute Decompensated Cardiac Failure

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Abstract

We report the case of acute lymphoblastic leukemia (ALL) in a 29-year-old male with no past medical history who presented with symptoms and signs of heart failure due to possible infiltrative cardiomyopathy as suggested by echocardiography. Workup including different imaging modalities confirmed the diagnosis of ALL. The patient completed his treatment course with a resolution of heart failure symptoms and normalization of cardiac function which was confirmed by different imaging modalities.

Keywords: Acute lymphoblastic leukemia; cardiac imaging; heart failure; restrictive cardiomyopathy.

Citation: Abdelghani MS, Altermanini M, El-Hassan M, Allam AG, Patel A. Acute Lymphoblastic Leukemia Presenting with Acute Decompensated Cardiac Failure. Heart Views. 2023 Apr-Jun;24(2):109-113. doi: 10.4103/heartviews.heartviews_85_22. Epub 2023 Mar 24. PMID: 37305334; PMCID: PMC10249640.

Impact Factor: 0.7

Mucosa-associated lymphoid tissue lymphoma (MALT lymphoma) in the thyroid mimicking a painless subacute (De Quervain's) thyroiditis on presentation, fine needle aspiration and cytology, and ultrasound findings: A rare case report

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Abstract

Introduction: We report a rare case of mucosa-associated lymphoid tissue lymphoma (MALT lymphoma) in the thyroid mimicking painless subacute (De Quervain's) thyroiditis.

Presentation of case: Patient with history of hypothyroidism presented with huge non-tender goiter, compression symptoms and choking, no lymphadenopathy. Ultrasound (US) showed large thyroid lobes. There was a small hypoechoic nodule, and nonspecific lymphadenopathy. Fine needle aspiration/cytology (FNAC) of right thyroid nodule showed scant follicular cells, abundant polymorphic lympocytes, epithelioid histiocytes, and tingible body macrophages, suggestive of De Quervain's (granulomatous) thyroiditis. Total thyroidectomy was decided due to compression symptoms and huge goiter.

Discussion: Intraoperative, thyroid was huge with no adhesions to the strap muscles/trachea. Total thyroidectomy with lymph node biopsy was undertaken. There were no complications. Postoperatively, the patient's condition was stable, breathing normally, and neck wound was clean. PTH was 11 pg/mL and calcium was 2.16 mmol/L, suggesting impending transient hypocalcemia. Histopathology showed lymphoepithelial lesions as clusters of lymphocytes within the thyroid follicles

epithelium (MALT Balls). Immunohistochemical staining showed that the neoplastic lymphocytes were B cells and stained positive with B-cell markers CD20 and PAX5, but were negative for Cyclin D1 and for T cell markers CD3, CD5 and CD43. The patient was discussed at the lymphoma MDT meeting and the decision was to start the patient on radiotherapy which the patient received.

Conclusion: Thyroid MALT lymphoma can mimic painless subacute thyroiditis. The triad of a large swelling of non-tender goiter with compression symptoms during a short period; FNAC findings suggestive of thyroiditis; and US showing enlarged thyroid lobes might cause confusion to the unsuspecting practitioner. Histopathology after excision provides definitive diagnosis.

Keywords: Lymphoma; Mucosa-associated lymphoid tissue (MALT) lymphoma; Non-hodgkin; Primary thyroid lymphoma; Thyroid.

Citation: Al Hassan MS, El Ansari W, Darweesh A, Sharaf Eldeen MZ, Obiedat S, Abdelaal A. Mucosa-associated lymphoid tissue lymphoma (MALT lymphoma) in the thyroid mimicking a painless subacute (De Quervain's) thyroiditis on presentation, fine needle aspiration and cytology, and ultrasound findings: A rare case report. Int J Surg Case Rep. 2023 May;106:108147. doi: 10.1016/j.ijscr.2023.108147. Epub 2023 Apr 11. PMID: 37080143; PMCID: PMC10140790.

Impact Factor: 0.6

Erythema nodosum following treatment with dasatinib plus chemotherapy in a patient with myeloid blast phase of chronic myeloid leukemia

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Abstract

Erythema nodosum (EN) is a type of panniculitis occurring due to various conditions. It can be associated with certain malignancies or manifest as a side effect of drugs. This article presents a unique case of EN in a patient with chronic myeloid leukemia (CML-blast phase) following dasatinib and chemotherapy. Timely recognition and appropriate management are crucial to alleviate symptoms and consider potential drug-induced etiology.

Keywords: chronic myeloid leukemia; cutaneous toxicity; dasatinib; erythema Nodosum.

Citation: Kassem N, Alshurafa A, Elsabah H, El Omri H. Erythema nodosum following treatment with dasatinib plus chemotherapy in a patient with myeloid blast phase of chronic myeloid leukemia. Clin Case Rep. 2023 Nov 22;11(11):e8223. doi: 10.1002/ccr3.8223. PMID: 38028081; PMCID: PMC10665579.

Impact Factor: 0.285

An interesting case of chronic myeloid leukemia (CML) with T315I mutation raising suspicion of de novo AML, a diagnostic conundrum

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Abstract

Chronic myeloid leukemia (CML) is a myeloproliferative disorder due to translocation between chromosomes (9, 22), known as the "Philadelphia chromosome." In 2016, the World health organization (WHO) introduced a new clinical entity of de novo acute myeloid leukemia (AML). Both diseases share some commonalities, therefore, create a challenge to diagnose.

Keywords: BCR-ABL1+ AML; Philadelphia chromosome; T315I; chronic myeloid leukemia; de Novo AML.

Citation: Iqbal P, Shahzad A, Shahid Z, Ghori F, Elomri H, Soliman D. An interesting case of chronic myeloid leukemia (CML) with T315I mutation raising suspicion of de novo AML, a diagnostic conundrum. Clin Case Rep. 2023 May 23;11(5):e5908. doi: 10.1002/ccr3.5908. PMID: 37234472; PMCID: PMC10206018.

Impact Factor: 0.285

Differentiation syndrome in patients with acute promyelocytic leukemia

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Abstract

A 48-year-old male diagnosed with acute promyelocytic leukemia (APL) started on all-trans-retinoic acid and arsenic trioxide, developed typical symptoms of differentiation syndrome, and improved dramatically on steroids. Hence, any APL patient started on chemotherapy, needs to be monitored closely for developing differentiation syndrome and to start steroid upon suspicion.

Keywords: ATRA syndrome; acute leukemia; steroids.

Citation: Elamin NH, Rashid F, Afana MS, Cherif H, Yassin MA. Differentiation syndrome in patients with acute promyelocytic leukemia. Clin Case Rep. 2023 Jan 26;11(1):e6697. doi: 10.1002/ccr3.6697. PMID: 36721680; PMCID: PMC9880381.

Impact factor: 0.258

MALIGNANT HEMATOLOGY

REVIEW ARTICLES

Extracorporeal membrane oxygenation in adults receiving haematopoietic cell transplantation: an international expert statement

Matteo Di Nardo [1], Graeme MacLaren [2], Peter Schellongowski [3], Elie Azoulay [4], Amy E DeZern [5], Cristina Gutierrez [6], Massimo Antonelli [7], Marta V Antonini [8], Gernot Beutel [9], Alain Combes [10], Rodrigo Diaz [11], Ibrahim Fawzy Hassan [12], Jo-Anne Fowles [13], In-Seok Jeong [14], Matthias Kochanek [15], Tobias Liebregts [16], Catherina Lueck [16], Karen Moody [17], Jessica A Moore [18], Laveena Munshi [19], Matthew Paden [20], Frédéric Pène [21], Kathryn Puxty [22], Matthieu Schmidt [10], Dawid Staudacher [23], Thomas Staudinger [3], Joachim Stemmler [24], R Scott Stephens [25], Lisa Vande Vusse [26], Philipp Wohlfarth [27], Roberto Lorusso [28], Antonio Amodeo [29], Kris M Mahadeo [30], Daniel Brodie [31];

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Abstract

Combined advances in haematopoietic cell transplantation (HCT) and intensive care management have improved the survival of patients with haematological malignancies admitted to the intensive care unit. In cases of refractory respiratory failure or refractory cardiac failure, these advances have led to a renewed interest in advanced life support therapies, such as extracorporeal membrane oxygenation (ECMO), previously considered inappropriate for these patients due to their poor prognosis. Given the scarcity of evidence-based guidelines on the use of ECMO in patients receiving HCT and the need to provide equitable and sustainable access to ECMO, the European Society of Intensive Care Medicine, the Extracorporeal Life Support Organization, and the International ECMO Network aimed to develop an expert consensus statement on the use of ECMO in adult patients receiving HCT. A steering committee with expertise in ECMO and HCT searched the literature for relevant articles on ECMO, HCT, and immune effector cell therapy, and developed opinion statements through discussions following a Quaker-based consensus approach. An international panel of experts was convened to vote on these expert opinion statements following the Research and Development/University of California, Los Angeles Appropriateness Method. The Appraisal of Guidelines for Research and Evaluation statement was followed to prepare this Position Paper. 36 statements were drafted by the steering committee, 33 of which reached strong agreement after the first voting round. The remaining three statements were discussed by all members of the steering committee and expert panel, and rephrased before an additional round of voting. At the conclusion of the process, 33 statements received strong agreement and three weak agreement. This Position Paper could help to guide intensivists and haematologists during the difficult decision-making process regarding ECMO candidacy in adult patients receiving HCT. The statements could also serve as a basis for future research focused on ECMO selection criteria and bedside management.

Citation: Di Nardo M, MacLaren G, Schellongowski P, Azoulay E, DeZern AE, Gutierrez C, Antonelli M, Antonini MV, Beutel G, Combes A, Diaz R, Fawzy Hassan I, Fowles JA, Jeong IS, Kochanek

M, Liebregts T, Lueck C, Moody K, Moore JA, Munshi L, Paden M, Pène F, Puxty K, Schmidt M, Staudacher D, Staudinger T, Stemmler J, Stephens RS, Vande Vusse L, Wohlfarth P, Lorusso R, Amodeo A, Mahadeo KM, Brodie D; European Society of Intensive Care Medicine, the International ECMO Network, and the Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation in adults receiving haematopoietic cell transplantation: an international expert statement. Lancet Respir Med. 2023 May;11(5):477-492. doi: 10.1016/S2213-2600(22)00535-5. Epub 2023 Mar 13. PMID: 36924784.

Impact factor: 76.2

Revolutionizing chronic lymphocytic leukemia diagnosis: A deep dive into the diverse applications of machine learning

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Abstract

Chronic lymphocytic leukemia (CLL) is a B cell neoplasm characterized by the accumulation of aberrant monoclonal B lymphocytes. CLL is the predominant type of leukemia in Western countries, accounting for 25% of cases. Although many patients remain asymptomatic, a subset may exhibit typical lymphoma symptoms, acquired immunodeficiency disorders, or autoimmune complications. Diagnosis involves blood tests showing increased lymphocytes and further examination using peripheral blood smear and flow cytometry to confirm the disease. With the significant advancements in machine learning (ML) and artificial intelligence (AI) in recent years, numerous models and algorithms have been proposed to support the diagnosis and classification of CLL. In this review, we discuss the benefits and drawbacks of recent applications of ML algorithms in the diagnosis and evaluation of patients diagnosed with CLL.

Keywords: Artificial intelligence; Chronic lymphocytic leukemia; Diagnosis; Machine learning.

Citation: Elhadary M, Elshoeibi AM, Badr A, Elsayed B, Metwally O, Elshoeibi AM, Mattar M, Alfarsi K, AlShammari S, Alshurafa A, Yassin M. Revolutionizing chronic lymphocytic leukemia diagnosis: A deep dive into the diverse applications of machine learning. Blood Rev. 2023 Nov;62:101134. doi: 10.1016/j.blre.2023.101134. Epub 2023 Sep 22. PMID: 37758527.

Impact factor: 10.626

Signaling pathways governing the behaviors of leukemia stem cells

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Abstract

Leukemia is a malignancy in the blood that develops from the lymphatic system and bone marrow. Although various treatment options have been used for different types of leukemia, understanding the molecular pathways involved in the development and progression of leukemia is necessary. Recent studies showed that leukemia stem cells (LSCs) play essential roles in the pathogenesis of leukemia by targeting several signaling pathways, including Notch, Wnt, Hedgehog, and STAT3. LSCs are highly proliferative cells that stimulate tumor initiation, migration, EMT, and drug resistance. This review summarizes cellular pathways that stimulate and prevent LSCs' self-renewal, metastasis, and tumorigenesis.

Keywords: Leukemia; Leukemia stem cells; Pathogenesis; Signaling pathways; Stem cells.

Citation: Azizidoost S, Nasrolahi A, Sheykhi-Sabzehpoush M, Anbiyaiee A, Khoshnam SE, Farzaneh M, Uddin S. Signaling pathways governing the behaviors of leukemia stem cells. Genes Dis. 2023 Mar 23;11(2):830-846. doi: 10.1016/j.gendis.2023.01.008. PMID: 37692500; PMCID: PMC10491880.

Impact Factor: 6.8

Non-coding RNAs in the epigenetic landscape of cutaneous T-cell lymphoma

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Abstract

Cutaneous T-cell lymphoma (CTCL) is a type of cancer that affects skin, and is characterized by abnormal T-cells in the skin. Epigenetic changes have been found to play a significant role in the development and progression of CTCL. Recently, non-coding RNAs (ncRNAs), such as microRNAs and long non-coding RNAs, have been identified as key players in the regulation of gene expression

in CTCL. These ncRNAs can alter the expression of genes involved in cell growth, differentiation, and apoptosis, leading to the development and progression of CTCL. In this review, we summarize the current understanding of the role of ncRNAs in CTCL, including their involvement in DNA methylation, and other biological processes. We also discuss the types of ncRNAs, their role as oncogenic or tumor suppressive, and their putative use as diagnostic and prognostic biomarkers, based on the emerging evidence from laboratory-based as well as patients-based studies. Moreover, we also present the potential targets and pathways affected by ncRNAs. A better understanding of the complex epigenetic landscape of CTCL, including the role of ncRNAs, has the potential to lead to the development of novel targeted therapies for this disease.

Keywords: Cutaneous T-cell lymphoma; Long non-coding RNAs; MicroRNAs; Mycosis fungoides; Non-coding RNAs; Sezary syndrome.

Citation: Adeeb M, Therachiyil L, Moton S, Buddenkotte J, Alam MA, Uddin S, Steinhoff M, Ahmad A. Non-coding RNAs in the epigenetic landscape of cutaneous T-cell lymphoma. Int Rev Cell Mol Biol. 2023;380:149-171. doi: 10.1016/bs.ircmb.2023.04.004. Epub 2023 Jul 21. PMID: 37657857.

Impact Factor: 6.8

The role of radiotherapy in newly diagnosed primary CNS lymphoma: A descriptive review and a pragmatic approach to clinical practice.

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Abstract

Earlier, prior to the development of effective systemic therapy, monotherapy with whole-brain radiotherapy (WBRT) was widely used to treat primary central nervous system lymphoma (PCNSL). Recently, chemotherapy, especially with high dose methotrexate (HDMTX), has largely replaced WBRT as upfront treatment, and the most accepted standard of care is induction with a combination drug therapy followed by consolidation therapy with either autologous stem-cell transplantation (ASCT) or radiation. Whilst WBRT is an effective component of treatment, it is occasionally associated with risk of permanent, irreversible neurotoxicity when doses of more than 30 Gy are used. Hence, there has been a strong focus on the optimization of radiotherapy (RT) which includes dose reduction in the consolidation phase. In this comprehensive review, we have summarized the progress on clinical results and evidence considering the role and use of radiation including combined treatment modalities, low-dose radiotherapy, and neurotoxicity. Finally, we present a practical approach to low-dose WBRT and boosting higher doses to the gross tumor that can be integrated into clinical practice.

Keywords: Chemotherapy; Low-dose radiotherapy; PCNSL; Radiotherapy; Stem cell transplantation.

Citation: Manickam Gurusamy V, Raveendran Divakar S, Halsnad Chandramouli S, Kunheri B, Hussain Al-Abdulla H, Shaikh G, Chaudary Apsani R, Riyaz Poolakundan M, Caparrotti P, Wafiq Hammoud R, Al-Hammadi N. The role of radiotherapy in newly diagnosed primary CNS lymphoma: A descriptive review and a pragmatic approach to clinical practice. Clin Transl Radiat Oncol. 2022 Dec 9;39:100559. doi: 10.1016/j.ctro.2022.12.002. PMID: 36590826; PMCID: PMC9800264.

Impact Factor: 6.7

Analysis of signaling cascades from myeloma cells treated with pristimerin

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Abstract

Multiple myeloma (MM) is the 2nd most frequently diagnosed blood cancer after non-Hodgkin's lymphoma. The present study aimed to identify the differentially expressed genes (DEGs) between the control and pristimerin-treated MM cell lines. We examined the GSE14011 microarray dataset and screened DEGs with GEO2R statistical tool using the inbuilt limma package. We used a bioinformatics pipeline to identify the differential networks, signaling cascades, and the survival of the hub genes. We implemented two different enrichment analysis including ClueGO and Metacore™, to get accurate annotation for most significant DEGs. We screened the most significant 408 DEGs from the dataset based on p-values and logFC values. Using protein network analysis, we found the genes UBC, HSP90AB1, HSPH1, HSPA1B, HSPA1L, HSPA6, HSPD1, DNAJB1, HSPE1, DNAJC10, BAG3, and DNAJC7 had higher node degree distribution. In contrast, the functional annotation provided that the DEGs were predominantly enriched in B-cell receptor signaling, unfolded protein response, positive regulation of phagocytosis, HSP70, and HSP40-dependent folding, and ubiquitin-proteasomal

proteolysis. Using network algorithms, and comparing enrichment analysis, we found the hub genes enriched were INHBE, UBC, HSPA1A, HSP90AB1, IKBKB, and BAG3. These DEGs were further validated with overall survival and gene expression analysis between the tumor and control groups. Finally, pristimerin effects were validated independently in a cell line model consisting of IM9 and U266 MM cells. Pristimerin induced in vitro cytotoxicity in MM cells in a dose-dependent manner. Pristimerin inhibited NF-κB, induced accumulation of ubiquitinated proteins and inhibited HSP60 in the validation of bioinformatics findings, while pristimerin-induced caspase-3 and PARP cleavage confirmed cell death. Taken together, we found that the identified DEGs were strongly associated with the apoptosis induced in MM cell lines due to pristimerin treatment, and combinatorial therapy derived from pristimerin could act as novel anti-myeloma multifunctional agents.

Keywords: Functional enrichment analysis; Heat shock proteins; Microarray; Multiple myeloma; Pristimerin; Protein-protein interaction.

Citation: Almaghrbi H, Elkardawy R, Udhaya Kumar S, Kuttikrishnan S, Abunada T, Kashyap MK, Ahmad A, Uddin S, George Priya Doss C, Zayed H. Analysis of signaling cascades from myeloma cells treated with pristimerin. Adv Protein Chem Struct Biol. 2023;134:147-174. doi: 10.1016/bs.apcsb.2022.10.006. Epub 2022 Nov 16. PMID: 36858733.

Impact Factor: 5.447

Integrating AI and ML in Myelodysplastic Syndrome Diagnosis: State-of-the-Art and Future Prospects

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Abstract

Myelodysplastic syndrome (MDS) is composed of diverse hematological malignancies caused by dysfunctional stem cells, leading to abnormal hematopoiesis and cytopenia. Approximately 30% of MDS cases progress to acute myeloid leukemia (AML), a more aggressive disease. Early detection is crucial to intervene before MDS progresses to AML. The current diagnostic process for MDS involves analyzing peripheral blood smear (PBS), bone marrow sample (BMS), and flow cytometry (FC) data, along with clinical patient information, which is labor-intensive and time-consuming. Recent advancements in machine learning offer an opportunity for faster, automated, and accurate diagnosis of MDS. In this review, we aim to provide an overview of the current applications of AI in the diagnosis of MDS and highlight their advantages, disadvantages, and performance metrics.

Keywords: artificial intelligence; bone marrow smears; flow cytometry; machine learning; myelodysplastic syndrome diagnosis; peripheral blood smears.

Citation: Elshoeibi AM, Badr A, Elsayed B, Metwally O, Elshoeibi R, Elhadary MR, Elshoeibi A, Attya MA, Khadadah F, Alshurafa A, Alhuraiji A, Yassin M. Integrating AI and ML in Myelodysplastic Syndrome Diagnosis: State-of-the-Art and Future Prospects. Cancers (Basel). 2023 Dec 22;16(1):65. doi: 10.3390/cancers16010065. PMID: 38201493; PMCID: PMC10778500.

Impact Factor: 5.2

Deep learning enhances acute lymphoblastic leukemia diagnosis and classification using bone marrow images

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Abstract

Acute lymphoblastic leukemia (ALL) poses a significant health challenge, particularly in pediatric cases, requiring precise and rapid diagnostic approaches. This comprehensive review explores the transformative capacity of deep learning (DL) in enhancing ALL diagnosis and classification, focusing on bone marrow image analysis. Examining ten studies conducted between 2013 and 2023 across various countries, including India, China, KSA, and Mexico, the synthesis underscores the adaptability and proficiency of DL methodologies in detecting leukemia. Innovative DL models, notably Convolutional Neural Networks (CNNs) with Cat-Boosting, XG-Boosting, and Transfer Learning techniques, demonstrate notable approaches. Some models achieve outstanding accuracy, with one CNN reaching 100% in cancer cell classification. The incorporation of novel algorithms like Cat-Swarm Optimization and specialized CNN architectures contributes to superior classification accuracy. Performance metrics highlight these achievements, with models consistently outperforming traditional diagnostic methods. For instance, a CNN with Cat-Boosting attains 100% accuracy, while others hover around 99%, showcasing DL models' robustness in ALL diagnosis. Despite acknowledged challenges, such as the need for larger and more diverse datasets, these findings underscore DL's transformative potential in reshaping leukemia diagnostics. The high numerical accuracies accentuate a promising trajectory toward more efficient and accurate ALL diagnosis in clinical settings, prompting ongoing research to address challenges and refine DL models for optimal clinical integration.

Keywords: acute lymphoblastic leukemia; bone marrow images; classification; convolutional neural networks; deep learning; diagnosis; medical image analysis.

Citation: Elsayed B, Elhadary M, Elshoeibi RM, Elshoeibi AM, Badr A, Metwally O, ElSherif RA, Salem ME, Khadadah F, Alshurafa A, Mudawi D, Yassin M. Deep learning enhances acute lymphoblastic leukemia diagnosis and classification using bone marrow images. Front Oncol. 2023 Dec 6;13:1330977. doi: 10.3389/fonc.2023.1330977. PMID: 38125946; PMCID: PMC10731043.

Impact factor: 4.7

Tyrosine Kinase Inhibitors in pediatric chronic myeloid leukemia: a focused review of clinical trials

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Abstract

Tyrosine Kinase Inhibitors (TKIs) is revolutionizing the management of pediatric Chronic Myeloid Leukemia (CML), offering alternatives to Allogeneic Hematopoietic Stem Cell Transplantation (AHSCT). We conducted a comprehensive review of 16 Randomized Controlled Trials (RCTs) encompassing 887 pediatric CML patients treated with TKIs including Imatinib, Dasatinib, and Nilotinib. The median patient age ranged from 6.5 to 14 years, with a median white blood cell count of 234 x 10^9/uL, median hemoglobin level of 9.05 g/dL, and median platelet count of 431.5 x 10^9/µL. Imatinib seems to be predominant first line TKI, with the most extensive safety and efficacy data. BCR::ABL response rates below 10% ranged from 60% to 78%, CCyR at 24 months ranged from 62% to 94%, and PFS showed variability from 56.8% to 100%, albeit with differing analysis timepoints. The Safety profile of TKIs was consistent with the known safety profile in adults. With the availability of three TKIs as first line options, multiple factors should be considered when selecting

first line TKI, including drug formulation, administration, comorbidities, and financial issues. Careful monitoring of adverse events, especially in growing children, should be considered in long term follow-up clinical trials.

Keywords: CML; Imatinib; TKI; Tyrosine Kinase Inhibitors; pediatric chronic myeloid leukemia.

Citation: Ata F, Benkhadra M, Ghasoub R, Fernyhough LJ, Omar NE, Nashwan AJ, Aldapt MB, Mushtaq K, Kassem NA, Yassin MA. Tyrosine Kinase Inhibitors in pediatric chronic myeloid leukemia: a focused review of clinical trials. Front Oncol. 2023 Dec 20;13:1285346. doi: 10.3389/fonc.2023.1285346. PMID: 38188307; PMCID: PMC10769570.

Impact Factor: 4.7

Distinct Clinical and Prognostic Features of Myelodysplastic Syndrome in Patients from the Middle East, North Africa, and Beyond: A Systemic Review

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Abstract

Myelodysplastic syndrome (MDS) describes a group of bone marrow malignancies with variable morphologies and heterogeneous clinical features. The aim of this study was to systematically appraise the published clinical, laboratory, and pathologic characteristics and identify distinct clinical features of MDS in the Middle East and North Africa (MENA) region. We conducted a comprehensive search of the PubMed, Web of Science, EMBASE, and Cochrane Library databases from 2000 to 2021 to identify population-based studies of MDS epidemiology in MENA countries. Of 1935 studies, 13 independent studies published between 2000 and 2021 representing 1306 patients with MDS in the MENA region were included. There was a median of 85 (range 20 to 243) patients per study. Seven studies were performed in Asian MENA countries (732 patients, 56%) and six in North African MENA countries (574 patients, 44%). The pooled mean age was 58.4 years (SD 13.14; 12 studies), and the male-to-female ratio was 1.4. The distribution of WHO MDS subtypes was significantly different between MENA, Western, and Far East populations (n = 978 patients, p <

0.001). More patients from MENA countries were at high/very high IPSS risk than in Western and Far East populations (730 patients, $p < 0.001$). There were 562 patients (62.2%) with normal karyotypes and 341 (37.8%) with abnormal karyotypes. Our findings establish that MDS is prevalent within the MENA region and is more severe than in Western populations. MDS appears to be more severe with an unfavorable prognosis in the Asian MENA population than the North African MENA population.

Keywords: Asia; MENA; North Africa; cytogenetics; epidemiology; myelodysplastic syndrome; prognosis.

Citation: Al-Haidose A, Yassin MA, Ahmed MN, Kunhipurayil HH, Al-Harbi AA, Aljaberi MA, Abbasi SA, Kordasti S, Abdallah AM. Distinct Clinical and Prognostic Features of Myelodysplastic Syndrome in Patients from the Middle East, North Africa, and Beyond: A Systemic Review. J Clin Med. 2023 Apr 12;12(8):2832. doi: 10.3390/jcm12082832. PMID: 37109168; PMCID: PMC10143809.

Impact Factor: 4.4

Long COVID treated successfully with antivirals in a rituximab-treated follicular lymphoma patient with persistent negative-antibodies to SARS-CoV2

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Abstract

Long COVID is a well-known complication to COVID-19 that affect millions of people worldwide and causes wide range of symptoms. We present a rare case of a previously diagnosed follicular lymphoma patient, who had a long COVID with persistent negative SARS-CoV-2 antibodies and required an aggressive antiviral treatment.

Keywords: Antivirals; COVID-19; Follicular lymphoma; Long COVID.

Citation: Tayar E, Isber R, Isber N. Long COVID treated successfully with antivirals in a rituximab-treated follicular lymphoma patient with persistent negative-antibodies to SARS-CoV2. Heliyon. 2023 Jun;9(6):e17149. doi: 10.1016/j.heliyon.2023.e17149. Epub 2023 Jun 21. PMID: 37378376; PMCID: PMC10284434.

Impact Factor: 4.0

SARS-CoV-2 and chronic myeloid leukemia: a systematic review

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Abstract

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus causing the coronavirus disease of 2019. The disease has caused millions of deaths since the first pandemic at the end of 2019. Immunocompromised individuals are more likely to develop severe infections. Numerous mutations had developed in SARS-CoV-2, resulting in strains (Alfa Beta Delta Omicron) with varying degrees of virulence disease severity. In CML (chronic myeloid leukemia) patients, there is a lot of controversy regarding the effect of the treatment on the patient outcome. Some reports suggested potential better outcomes among patients with CML, likely due to the use of TKI; other reports showed no significant effects. Additionally, it is unknown how much protection immunization provides for cancer patients.

Method: In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards, we conducted a systematic review. Retrospective, prospective studies, reviews, case series, and case reports of chronic myeloid leukemia patients aged above 18 years who had SARS-CoV-2 infection were included. English literature was screened using PubMed, SCOPUS, and Google Scholar. Search terms include chronic myeloid leukemia, chronic myelogenous leukemia, and SARS-CoV-2 and Coronavirus disease 2019 (COVID-19). We searched the reference lists of the included studies for any new articles. The search included all articles published up to April 20, 2023. The review is registered in PROSPERO (registration number CRD42022326674).

Results: We reviewed 33 articles of available published literature up to April 2023 and collected data from a total of 682 CML patients with COVID-19. Most patients were in the chronic phase,

seven were in the accelerated phase, and eight were in the blast phase. Disease severity was classified according to WHO criteria. Mortality was seen in 45 patients, and there were no reports of thrombotic events. Two hundred seventy-seven patients were in the era before vaccination; among them, eight were in the intensive care unit (ICU), and mortality was 30 (11%). There were 405 patients after the era of vaccination; among them, death was reported in 15 (4%) patients and ICU in 13 patients.

Limitations and conclusion: The major limitation of this review is the lack of details about the use or hold of TKIs during SARS-CoV-2 infection. Additionally, after the appearance of the different variants of the SARS-CoV-2 virus, few studies mentioned the variant of the virus, which makes it difficult to compare the outcome of the other variants of the SARS-CoV-2 virus in patients with CML. Despite the limitations of the study, CML patients with COVID-19 have no significant increase in mortality compared to other hematological malignancy. Hematological cancers are associated with an increased risk of thrombosis, which is expected to increase in patients with COVID-19. However, patient with CML has not been reported to have a significant increase in thrombosis risk. The available data indicates that COVID-19's effect on patients with chronic myeloid leukemia (CML) still needs to be better understood due to the limited data.

Keywords: COVID-19; SARS-CoV-2; SARS-CoV-2 variants; chronic myelocytic leukemia (CML); chronic myeloid leukemia.

Citation: Ali EA, Al-Sadi A, Al-Maharmeh Q, Subahi EA, Bellamkonda A, Kalavar M, Panigrahi K, Alshurafa A, Yassin MA. SARS-CoV-2 and chronic myeloid leukemia: a systematic review. Front Med (Lausanne). 2024 Jan 24;10:1280271. doi: 10.3389/fmed.2023.1280271. PMID: 38327268; PMCID: PMC10847560.

Impact Factor: 3.9

A practical guide to managing cardiopulmonary toxicities of tyrosine kinase inhibitors in chronic myeloid leukemia

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Abstract

Tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of chronic myeloid leukemia (CML) but their use was associated with a range of serious cardiopulmonary toxicities including vascular adverse events, QT prolongation, heart failure, pleural effusion, and pulmonary arterial hypertension. Dedicated clinical management guidelines for TKI-induced toxicities are not available. This review aims to discuss TKI-associated cardiopulmonary toxicities and proposes a practical guide for their management.

Keywords: QT prolongation; chronic myeloid leukemia; dasatinib; heart failure; pleural effusion; ponatinib; pulmonary arterial hypertension; tyrosine kinase.

Citation: Kaddoura R, Dabdoob WA, Ahmed K, Yassin MA. A practical guide to managing cardiopulmonary toxicities of tyrosine kinase inhibitors in chronic myeloid leukemia. Front Med (Lausanne). 2023 May 5;10:1163137. doi: 10.3389/fmed.2023.1163137. PMID: 37358999; PMCID: PMC10286131.

Impact Factor: 3.9

Pediatric Philadelphia-Negative Myeloproliferative Neoplasms in the Era of WHO Classification: A Systematic Review

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Abstract

Background: Philadelphia-negative myeloproliferative neoplasms (MPN) are most prevalent in the older population (median age at the diagnosis is above 60 years) and rarely diagnosed in pediatrics. Thus, our knowledge about the clinical presentation, mutational status, and complications of MPNs in pediatrics is limited.

Methods: The literature in English (PubMed, SCOPUS, and Google Scholar) was searched for studies, reviews, case series, and case reports of patients with Philadelphia-negative MPNs (including essential thrombocythemia, polycythemia vera, primary myelofibrosis, and profibrotic myelofibrosis) in the pediatrics age group (less than 18 years). Only studies that fulfilled WHO 2008 or 2016 criteria for MPNs were included. We aimed to describe the clinical characteristics, vascular and long-term complications, types of driver mutations, and treatment approaches in pediatric patients with MPNs.

Results: We reviewed 33 articles of available published literature from 2008 to 2022 and collected data from a total of 196 patients of the pediatric population. Among the cohort of patients, 139 had essential thrombocythemia (ET), 20 had polycythemia vera (PV), and 37 had primary myelofibrosis (PMF). The median age at the time of diagnosis for each disease varied, with 8.8 years for ET, 10

years for PV, and 3.6 years for MF. There was a slight difference in gender prevalence between both gender groups and all three diseases. The presenting symptoms were not mentioned in more than 50% of studies. We found that JAK2 was the most prevalent among all mutations. Both bleeding and thrombosis were present equally in ET, with 9% of cases complicated by bleeding and 9% complicated by thrombosis. Hemorrhagic events did not occur in patients with PV; thrombosis in children with MF was also not found. The progression into AML occurred in two patients with PV and one with ET.

Conclusion: Given the rarity of MPNs in pediatrics and their different characteristics compared with adults, we believe there is a need for unique diagnostic criteria to match the different molecular statuses in pediatrics. Based on our review, the incidence of MPN complications in pediatrics, including thrombotic events, hemorrhage, and leukemic transformation, differs from that in adults.

Keywords: MPN; essential thrombocythemia; myeloproliferative neoplasms; pediatrics; polycythemia vera; primary myelofibrosis.

Citation: Al-Mashdali AF, Aldapt MB, Rahhal A, Hailan YM, Elhakeem I, Ali EA, Rozi W, Yassin MA. Pediatric Philadelphia-Negative Myeloproliferative Neoplasms in the Era of WHO Classification: A Systematic Review. Diagnostics (Basel). 2023 Jan 19;13(3):377. doi: 10.3390/diagnostics13030377. PMID: 36766480; PMCID: PMC9914355.

Impact factor: 3.6

Applications of Machine Learning in Chronic Myeloid Leukemia

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Abstract

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by dysregulated growth and the proliferation of myeloid cells in the bone marrow caused by the BCR-ABL1 fusion gene. Clinically, CML demonstrates an increased production of mature and maturing granulocytes, mainly neutrophils. When a patient is suspected to have CML, peripheral blood smears and bone marrow biopsies may be manually examined by a hematologist. However, confirmatory testing for the BCR-ABL1 gene is still needed to confirm the diagnosis. Despite tyrosine kinase inhibitors (TKIs) being the mainstay of treatment for patients with CML, different agents should be used in different patients given their stage of disease and comorbidities. Moreover, some patients do not respond well to certain agents and some need more aggressive courses of therapy. Given the innovations and development that machine learning (ML) and artificial intelligence (AI) have undergone over the years, multiple models and algorithms have been put forward to help in the assessment and treatment of CML. In this review, we summarize the recent studies utilizing ML algorithms in patients with CML. The search was conducted on the PubMed/Medline and Embase databases and yielded 66 full-text articles and abstracts, out of which 11 studies were included after screening against the inclusion criteria. The studies included show potential for the clinical implementation of ML models in the diagnosis, risk assessment, and treatment processes of patients with CML.

Keywords: artificial intelligence; chronic myeloid leukemia; convolutional neural networks; hemoglobinopathies; machine learning.

Citation: Elhadary M, Elsabagh AA, Ferih K, Elsayed B, Elshoeibi AM, Kaddoura R, Akiki S, Ahmed K, Yassin M. Applications of Machine Learning in Chronic Myeloid Leukemia. Diagnostics (Basel). 2023 Apr 3;13(7):1330. doi: 10.3390/diagnostics13071330. PMID: 37046547; PMCID: PMC10093579.

Impact factor: 3.6

Applications of Artificial Intelligence in Philadelphia-Negative Myeloproliferative Neoplasms

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Abstract

Philadelphia-negative (Ph-) myeloproliferative neoplasms (MPNs) are a group of hematopoietic malignancies identified by clonal proliferation of blood cell lineages and encompasses polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). The clinical and laboratory features of Philadelphia-negative MPNs are similar, making them difficult to diagnose, especially in the preliminary stages. Because treatment goals and progression risk differ amongst MPNs, accurate classification and prognostication are critical for optimal management. Artificial intelligence (AI) and machine learning (ML) algorithms provide a plethora of possible tools to clinicians in general, and particularly in the field of malignant hematology, to better improve diagnosis, prognosis, therapy planning, and fundamental knowledge. In this review, we summarize the literature discussing the application of AI and ML algorithms in patients with diagnosed or suspected Philadelphia-negative MPNs. A literature search was conducted on PubMed/MEDLINE, Embase, Scopus, and Web of Science databases and yielded 125 studies, out of which 17 studies were included after screening. The included studies demonstrated the potential for the practical use of ML and AI in the diagnosis, prognosis, and genomic landscaping of patients with Philadelphia-negative MPNs.

Keywords: artificial intelligence; clinical decision support system; convolutional neural networks; deep learning; diagnosis; genomics; machine learning; myeloproliferative neoplasms; prognosis.

Citation: Elsayed B, Elshoeibi AM, Elhadary M, Ferih K, Elsabagh AA, Rahhal A, Abu-Tineh M, Afana MS, Abdulgayoom M, Yassin M. Applications of Artificial Intelligence in Philadelphia-Negative Myeloproliferative Neoplasms. Diagnostics (Basel). 2023 Mar 16;13(6):1123. doi: 10.3390/diagnostics13061123. PMID: 36980431; PMCID: PMC10047906.

Impact factor: 3.6

Multiple myeloma and its rare paraneoplastic manifestations simmering under the surface

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Abstract

Paraneoplastic syndromes are complex clinical manifestations that occur because of the underlying malignancy in which the malignant cells produce hormones, cytokines, peptides or antibodies that causes symptoms and may affect multiple organ systems. These paraneoplastic conditions may be associated with different solid and hematological malignancies. Multiple Myeloma (MM) accounts for 10-15 % of hematological malignancies and 1-2 % of all malignancies. It is associated with some atypical clinical and laboratory paraneoplastic manifestations. Although there is a low incidence of these paraneoplastic, significant knowledge of these manifestations may assist in making a differential diagnosis in cases of doubt. The clinical presentation may vary and be evident even before or after the diagnosis of malignancy. These include vascular, neurological, dermatological, physiological, and other atypical conditions. Furthermore, these rare paraneoplastic manifestations need more valid, relevant scientific information, as most information about these conditions is derived from case reports. After the literature search, we have reported the paraneoplastic manifestations associated with multiple myeloma, published in the English literature, and the cognate management in this review article. To our knowledge, this is the first review article discussing various paraneoplastic manifestations of multiple myeloma.

Keywords: Case reports; Multiple myeloma; Paraneoplastic symptoms; Polycythemia vera; Sweet syndrome.

Citation: Baloch SS, Khan SR, Tariq M, Wasio A, Ali AA, Shahzadi M, Moosajee M, Anwar S, Raza A, Uddin S. Multiple myeloma and its rare paraneoplastic manifestations simmering under the surface. Pathol Res Pract. 2023 Aug;248:154689. doi: 10.1016/j.prp.2023.154689. Epub 2023 Jul 15. PMID: 37478520.

Impact factor: 2.8

Management of chronic myeloid leukaemia: current treatment options, challenges, and future strategies

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Abstract

Small molecule therapy is a critical component of targeted anticancer treatment, with tyrosine kinase inhibitors (TKIs) being the first compounds to treat the clonal Chronic Myelogenous Leukaemia

(CML) translocation t (9;22) (q34; q11) effectively since 2001. TKIs, such as imatinib, have improved the 10-year survival rate of CML patients to 80%. They bind the BCR::ABL1 kinase and inhibit downstream signaling pathways. However, therapy failure may be seen in 20-25% of CML patients due to intolerance or inadequacy related to BCR::ABL1 dependent or independent mechanisms. This review aimed to summarize current treatment options involving TKIs, resistance mechanisms and the prospective approaches to overcome TKI resistance. We highlight BCR::ABL1-dependent mechanisms of TKI resistance by reviewing clinically-documented BCR::ABL1 mutations and their consequences for TKI binding. In addition, we summarize BCR::ABL1 independent pathways, including the relevance of drug efflux, dysregulation of microRNA, and the involvement of alternative signaling pathways. We also discuss future approaches, such as gene-editing techniques in the context of CML, as potential therapeutic strategies.

Keywords: BCR::ABL1;; Chronic Myeloid Leukaemia (CML); Tyrosine kinase inhibitors (TKIs); cancer; personalized medicine; precision medicine; resistance; therapeutic targets.

Citation: Younes S, Ismail MA, Al-Jurf R, Ziyada A, Nasrallah GK, Abdulrouf PV, Nagy M, Zayed H, Farrell T, Sorio C, Morsi H, Qoronfleh MW, Al-Dewik NI. Management of chronic myeloid leukaemia: current treatment options, challenges, and future strategies. Hematology. 2023 Dec;28(1):2196866. doi: 10.1080/16078454.2023.2196866. PMID: 37078896.

Impact Factor: 1.9

Strategic priorities for hematopoietic stem cell transplantation in the EMRO region

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Abstract

The World Health Organization-designated Eastern Mediterranean region (EMRO) consists of 22 countries in North Africa and Western Asia with a collective population of over 679 million. The area comprises some of the wealthiest countries per capita income and some of the poorest. The population structure is also unique and contrasts with western countries, with a much younger population. The region sits in the heart of the thalassemia belt. Many countries have a significant prevalence of sickle cell disease, and cancer is on the rise in the region. Therefore, the strategic priorities for the growth and development of hematopoietic stem cell transplantation (HSCT) differ from country to country based on resources, healthcare challenges, and prevalent infrastructure. Thirty-one reporting teams to the Eastern Mediterranean Blood and Marrow Transplantation Group have active HSCT programs in 12 countries; allogeneic transplants outnumber autologous transplants, and the proportion of allotransplants for non-malignant conditions is higher in the EMRO region than in Western Europe and North America. The vast majority (99%) of allotransplants are from matched related donors. Matched unrelated donors and other alternate donor transplants are underutilized. The chance of finding a matched related donor for allografts is higher, with a significant chance of finding matched donors among non-sibling related donors. Reasons for relatively lower rates of transplants compared with other countries are multifactorial. Capacity building, development of newer centers, innovative funding, and better utilization of information technology are required to make transplantation as an accessible modality to more patients. Cost-effectiveness and cost-containment, regulation, and ensuring quality will all be priorities in planning HSCT development in the region.

Citation: Ahmed SO, El Fakih R, Elhaddad A, Hamidieh AA, Altbakhi A, Chaudhry QU, Bazarbachi A, Adil S, Al-Khabori M, Ben Othman T, Gaziev J, Khalaf M, Alshammeri S, Alotaibi S, Alshahrani M, Bekadja MA, Ibrahim A, Al-Wahadneh AM, Altarshi M, Alsaeed A, Madani A, Abboud M, Abujazar H, Bakr M, Abosoudah I, El Cheikh J, Almasari A, Alfraih F, Baldomero H, Elsolh H, Niederwieser D, Chaudhri N, Aljurf M. Strategic priorities for hematopoietic stem cell transplantation in the EMRO region. Hematol Oncol Stem Cell Ther. 2023 Apr 4;16(3):162-169. doi: 10.1016/j.hemonc.2021.09.006. PMID: 34688625.

Impact Factor: 1.87

Osteolytic bone lesions as an initial presenting manifestation of adult acute lymphoblastic leukemia: a mini review

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Abstract

Hematological malignancies can lead to bone lesions, and the most common example is the osteolytic lesions found in multiple myeloma. Cases of osteolytic lesions have been rarely reported in acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma, Waldenström macroglobulinemia, chronic lymphocytic leukemia, acute myeloid leukemia, and myeloproliferative neoplasms. This review sheds light on the association between ALL and osteolytic bone lesions. To our knowledge, we found 15 cases of patients with ALL who developed osteolytic lesions. Most patients were males with a median age of 29 years. B-cell ALL was the most common type of ALL associated with osteolytic lesions. All patients presented with bone pain, and hypercalcemia was found in 80% of the reported cases. Osteolytic lesions were detected by plain radiography (X-ray) in approximately half of the patients; computed tomography, MRI, or PET scans confirmed the osteolytic lesions in the remaining patients. The axial skeleton was mainly affected. Based on our review, there was no association between osteolytic bone lesions and the Philadelphia chromosome. There are no case of spinal cord compression in adults ALL patients attributed to osteolytic lesions of the vertebra. The majority of patients received chemotherapy, and the outcomes among these patients were variable. Almost all of them achieved complete remission. However, two patients developed a disease relapse. Given that our review is solely based on case reports, we could not conclude if the presence of osteolytic bone lesions is a prognostic factor for adverse outcomes or indicates an 'aggressive' form of ALL.

Keywords: ALL; acute lymphoblastic leukemia; adult; complications; osteolytic bone lesions.

Citation: Al-Mashdali AF, Al-Dubai HN, Yassin MA. Osteolytic bone lesions as an initial presenting manifestation of adult acute lymphoblastic leukemia: a mini review. Ann Med Surg (Lond). 2023 Jul 20;85(9):4404-4409. doi: 10.1097/MS9.0000000000001065. PMID: 37663744; PMCID: PMC10473363.

Impact Factor: 1.752

Chronic Myeloid Leukemia following Exposure to Radioactive Iodine (I131): A Systematic Review

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Abstract

Background: Therapy-related leukemia is a term that describes the occurrence of leukemia following exposure to hematotoxins and radiation to emphasize the difference from leukemia that arises de novo. Many agents and host factors contribute to this entity of leukemias. Therapy-related acute myeloid leukemia has an extensive literature review in contrast to therapy-related chronic myeloid leukemia (t-CML). Radioactive iodine (RAI), an established agent in the management of differentiated thyroid carcinomas, has raised concern due to its possible carcinogenic effects.

Summary: In this article, we reviewed all the reports from the 1960s to date related to t-CML following RAI on Google Scholar and PubMed. We have identified 14 reports and found that most reports were for men under the age of 60 years with primary papillary thyroid carcinoma and mixed follicular-papillary thyroid carcinoma who developed t-CML mainly between 4 and 7 years after exposure to varying doses of I131. However, the mean dose was 287.78 millicuries (mCi). It was reported that a statistically significant increase in leukemia following RAI therapy (relative risk of 2.5 for I131 vs. no I131). Also, there was a linear relationship between the cumulative dose of I131 and the risk of leukemia. Doses higher than 100 mCi were associated with a greater risk of developing secondary leukemia, and most of the leukemias developed within the initial 10 years of exposure. The precise mechanism through which RAI provokes leukemia is largely unclear. A few mechanisms have been proposed.

Key messages: Although the risk for t-CML appears to be low based on current reports and does not represent a contraindication to RAI therapy, it should not be disregarded. We suggest including it in the risk-benefit discussion before initiating this therapy. Long-term follow-up for patients is advisable for those who received doses over 100 mCi with a complete blood count, possibly yearly, for the first 10 years. The new onset of significant leukocytosis post RAI exposure should raise the suspicion for

t-CML. Further studies are needed to establish or refute a causal relationship.

Keywords: Chronic myeloid leukemia; I131; Papillary thyroid cancer; Radioiodine; Secondary chronic myeloid leukemia; Therapy-related leukemia.

Citation: Ali Hailan YM, Al-Dubai HN, Yassin MA. Chronic Myeloid Leukemia following Exposure to Radioactive Iodine (I131): A Systematic Review. Oncology. 2023;101(6):362-368. doi: 10.1159/000530463. Epub 2023 May 9. PMID: 37231874.

Impact Factor: -

MALIGNANT HEMATOLOGY

ABSTRACTS

Clinically Significant CMV Infection in Allogeneic Stem-Cell Transplant Recipients: A Single Center Experience

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Abstract

Introduction: Cytomegalovirus (CMV) infection is one of the major causes of concern in allogeneic stem cell transplantation (allo-HSCT). Here we report the clinically significant CMV infections among allo-HSCT recipients at the National Center for Cancer Care and Research (NCCCR) in Qatar.

Methods: A retrospective review of the electronic health records of all malignant hematology patients who underwent allo-HSCT at NCCCR was performed from September 2017 to December 2022.

Results: Fifty-one malignant hematology patients have been transplanted during the data collection period. Patient characteristics are summarized in Table 1. The median age was 34 years (range 14-53 years). CMV-serostatus was positive in fifty recipients (98%) and all donors. Thirty-two patients (62.7%) have received matched-related grafts. The most frequent indication for HSCT was acute myeloid leukemia, followed by acute lymphoblastic leukemia. Forty-six patients (92%) underwent myeloablative conditioning therapy. Graft-versus-host disease (GvHD) prophylaxis used in the non-haploidentical group was cyclosporine and short-course methotrexate while haploidentical recipients received cyclosporine, mycophenolate mofetil, and post-transplant cyclophosphamide. Letermovir prophylaxis was accessible for use for high-risk patients from February 2022. CMV-PCR was monitored twice per week for all patients until day +100. The clinically significant CMV infection rate was 51%. The cumulative incidence of CMV infection in haploidentical and non-haploidentical groups was 70% and 30%, respectively (figure 1). The median CMV-PCR viral load was 1783.5 IU/mL (range 133- 9600 IU/mL), with the earliest CMV reactivation on day -1 of transplantation. The clinically significant CMV infection incidence was significantly higher in patients who did not receive letermovir prophylaxis. Preemptive antiviral therapy was initiated to prevent CMV disease in all indicated recipients. Foscarnet was the preferred first-line pre-emptive treatment option for patients during cytopenia. No CMV disease or CMV-related mortality occurred in our population.

Conclusion: This is the first report from Qatar to report CMV infection post-allogeneic stem cell transplantation. Future in-depth analysis of our population and treatment responses is needed.

Citation: Gulied A, Alasmar A, Bakr M, Shawayli H, Ghasoub R, Fadul A, Gameil A, Mudawi D, Hamad

A, Gaziev J. (2023) Clinically Significant CMV Infection in Allogeneic Stem-Cell Transplant Recipients: A Single Center Experience. Blood 2023; 142 (Supplement 1): 6986. doi: https://doi.org/10.1182/blood-2023-189903.

Impact Factor: 20.3

Pregnancy in Patents with CLL Systematic Review

Ahmed Abdelrehim Badr, Maria Benkhadra, Mohamed A Yassin

Abstract

Introduction: Chronic Lymphocytic Leukemia (CLL) is a hematologic malignancy characterized by the clonal expansion of non-functional, mature-appearing lymphocytes in the bone marrow, peripheral blood, and lymphoid tissues. While cases of CLL during pregnancy are rare,it is associated with many complications. It was reported that women with CLL are more susceptible to infections due to a weakened immune system; possibly leading to more complications. There is also 0increased risk of thrombocytopenia, which can increase the risk of bleeding during pregnancy and childbirth. This review aimed at identifying literature available on the complications in CLL and pregnancy as well as the data available on the potential therapeutic strategies.

Methods: A scoping review of case reports that discuss pregnant patients who were diagnosed with CLL were isolated. The effects of the disease on pregnancy outcomes regarding both mother and fetus were identified. Animal studies, reviews or non-original articles, and non-English articles were excluded from our study. FDA labels of medications in CLL were reviewed for data on pregnancy and animal outcomes. Information on those medications in pregnant patients were also identified where available.

Results: The search strategy across four databases yielded 448 articles. After eligibility assessment, 14 articles were included in the review. Cases were subdivided according to timing of pregnancy relative to CLL diagnosis (diagnosed before pregnancy or during pregnancy at early or late gestational periods). The pre-pregnancy reports were further subclassified based on the presence or absence of infection during pregnancy. None of the cases reported required immediate initiation of CLL therapy and only one case reported mortality post-delivery. This occurred in a patient with Richter transformation and no prior CLL treatments. There were no reported fetal malformations or severe adverse outcomes related to the infants in any of the reported pregnancies (Figure 2). The included studies provided insights into various aspects of CLL during pregnancy, including patient demographics, diagnosis timing and methods, acquired infections, changes in white blood cell count, treatment approaches, pregnancy outcomes, and complications for both mother and fetus.

From the marketed pharmacological alternatives for CLL, most were not studied in pregnant humans with CLL (Figure 1). However, venetoclax and rituximab have some data in pregnant patients with non-CLL indications. A case reported a pregnant refractory AML patient who received venetoclax with high dose cytarabine and mitoxantrone at 24 weeks of gestation. Bone marrow at 27 weeks

showed complete remission and labor was induced at 28 weeks + 5 days after corticosteroid-induced lung maturation. The infant had hyperbilirubinemia, transient B-cell depletion and required ventilation. The baby recovered from all complications, although possible long-term effects are still unclear. The mother underwent allogeneic hematopoietic stem cell transplant.

In a 30-year-old female (pregnant at 28 weeks) with primary CNS lymphoma, weekly rituximab was given for 4 weeks with dexamethasone. After delivery through C-section at 31 weeks, the patient started definitive treatment with chemotherapy and autologous transplant. The infant required brief mechanical ventilation and had transient B-cell depletion at delivery until 4 months post-delivery. The baby required a course of post-exposure acyclovir despite not developing an infection. Both mother and baby survived with good outcomes at last follow-up (4 years post-delivery)

Conclusion: Despite the rarity of CLL occurrence during pregnancy, there is evident need of further studies and management guidelines in this population. This review provides insights into the possible pregnancy-related concerns in women with CLL at different disease stages. While watchful waiting is generally recommended due to CLL's slow progression, individual evaluation is crucial. If treatment is necessary, delaying therapy until the second or third trimesters may help mitigate the risk of fetal malformations. The increased susceptibility to infections resulting from the combined immunosuppressive effects of CLL and pregnancy should be carefully considered

Citation: Badr A, Benkhadra M, Yassin M; Pregnancy in Patents with CLL Systematic Review. Blood 2023; 142 (Supplement 1): 6555. doi: https://doi.org/10.1182/blood-2023-178193

Impact factor: 20.3

The Applicability of Tyrosine Kinase Inhibitors in Pediatric Chronic Myeloid Leukemia

Fateen Ata, Rola Ghasoub, Maria Benkhadra, Liam Fernyhough, Mahmood Aldapt, Nabil E. Omar, Abdulqadir Nashwan, Kamran Mushtaq, Mohamed A Yassin

Abstract

Introduction: The advent of tyrosine kinase inhibitors (TKIs) has shifted the treatment paradigm of adult CML, limiting SCT to a last-resort option for TKI-ineligible or resistant cases. However, determination of the optimal dosing and duration, potential long-term side effects, and the viability of therapy discontinuation remain under-explored aspects of TKIs in pediatric CML. Emerging data supports administering novel TKIs as initial or second-line treatments in pediatric CML amid variable results. This review discusses the RCTs conducted on pediatric patients with CML who received TKIs, aiding in better understanding of the effectiveness and safety of TKIs in the pediatric CML population.

Methods: We searched Medline, OVID, and Web of Science for all RCTs reporting the efficacy and safety of TKI in pediatric CML (< 18 years). We compiled the individual efficacy and safety data into distinct tables, emphasizing demographics, treatment modalities, and outcomes pertaining to both the safety and efficacy of TKI.

Results:This review analyzed 17 Randomized Controlled Trials (RCTs) with 887 pediatric CML patients. Median age was 11.3 years (range 6.5-14 years). Efficacy studies had 718 patients, safety studies had 851.. The median white blood cell count was 234 x10 9/uL [range 19 to 378; reported in 9 RCTs], median hemoglobin level was 9 g/dL [range 5.6 to 10.8; from 7 RCTs], and the median platelet count was 431.5 x10 9/µL, [range 31 to 594; from 6 RCTs].

TKIs were first-line treatment in 65% of the studies, Imatinib being the commonest (61% of studies). Dasatinib and Nilotinib were used in 17% and 11% of studies, respectively, while 6% received a combination of imatinib and chemotherapy. Efficacy reporting in the RCTs was a major concern that challenged the accumulation of results (Table 1). BCR-ABL response of <10% ranged from 60 % to 78%, and the complete cytogenetic response (CCYR) at 24 months ranged from 62% to 94%. Progression free survival (PFS) ranged from 56.8% to 100%; however, the timepoint for PFS analysis was not standardized among studies (36 to 48 months).

Safety data from 16 studies (851 patients) included anemia (n=228), thrombocytopenia (n=161), neutropenia (n=257), hepatotoxicity (n=98), and cutaneous side-effects (n=156). Cardiovascular

complications with second generation TKIs included QTc prolongation with Nilotinib (n= 11) and heart failure with Dasatinib (n=4). Nausea/vomiting were reported in 119 patients on imatinib, vs. 64 and 37 patients on Dasatinib and Nilotinib, respectively. Diarrhea occurred in 40 patients on Imatinib ,and 20 and 2 patients in Dasatinib and Nilotinib cohorts, respectively. Other AEs included impaired bone growth (70 on Imatinib and 10 on Dasatinib), headache (44 on Imatinib, 38 on Nilotinib and 13 in Dasatinib), musculoskeletal pain (161 on Imatinib, 31 on Dasatinib and 8 on Nilotinib). Treatment AEs leading to drug discontinuation were reported in 22 patients (6 studies), however the exact AE leading to drug discontinuation were not reported.

Conclusion: There remains a limited experience in treating pediatric CML with TKIs. Hence, evidence from prospective clinical trials and real-life clinical practice are required to establish appropriate guidelines for the standard therapeutic management in this population. Imatinib has the most extensice efficacy and toxicity data in pediatric patients. The Safety profile of TKIs was consistent with the known safety profile in adults. With the availability of three TKIs as first line options, multiple factors should be considered when selecting first line TKI, including drug formulation, administration, comorbidities, and financial issues. Careful monitoring of adverse events, especially in growing children should be considered in long term follow-up clinical trials.

Citation: Ata F, Ghasoub R, Benkhadra M, Fernyhough L, Aldapt M, Omar NE, Nashwan A, Mushtaq K, Yassin M; The Applicability of Tyrosine Kinase Inhibitors in Pediatric Chronic Myeloid Leukemia. Blood 2023; 142 (Supplement 1): 6372. doi: https://doi.org/10.1182/blood-2023-179341

Impact Factor: 20.3

Permissibility of an Intermittent Fasting in Patients with Chronic Lymphocytic Leukemia in the Era of Novel Therapies :a Pharmacology Based Review

Maria Benkhadra, Nuha Fituri, Soha Aboukhalaf, Rola Ghasoub, Mervat Mattar, Khalil Al Farsi, Salem Alshemmari, Mohamed A Yassin

Abstract

Introduction: Chronic Lymphocytic Leukemia (CLL) is a mature neoplasm characterized by the proliferation of immunologically dysfunctional B cells. Inhibitors of BCL2 (venetoclax) and Bruton Tyrosine Kinase (BTK) (ibrutinib, acalabrutinib and zanubrutinib) are novel agents that have revolutionized outcomes in CLL patients in the newly diagnosed and relapsed/refractory settings. Nevertheless, tumor lysis syndrome (TLS) and gastrointestinal bleeding (GIB) remains concerning adverse events. In clinical trials, fasting has demonstrated reductions in chemotherapy-related side effects and improved treatment tolerability . However, with novel agents in CLL this can be challenging with the need for aggressive hydration in fluid-restricting fasting practices and the higher risk for GI bleeding and peptic ulcer disease complications with fasting. This review aims to explore the literature available to answer the permissibility of intermittent fasting (IF) in CLL patients who are being treated with first line novel agents (FLNAs).

Methods: Literature exploration was performed to identify IF practices and the effects of fasting conditions and fluid-restriction on the pharmacokinetics (PK) of FLNAs. Literature was also scoped for data on TLS and GIB risk associated with FLNAs in CLL patients as well as the effects of fasting and or fluid-restricted states on GIB and TLS risks. Lastly, the identified risks were accumulated to build a pathway for permissibility of IF in this patient population.

Results: Venetoclax has amplified the historical low risk of TLS in patients with CLL to a significant degree. Approaches to prevent TLS such as aggressive hydration and use of uric acid reducing drugs hinder patients wishing to practice fluid restricting IF (See Table 1 and Figure 1), especially during ramp-up phase. Moreover, venetoclax should be administered with food and on daily basis. Hence, only fluid liberal IF practices with daily food intake and medication administration may be possible in venetoclax CLL patients.

Furthermore, studies have indicated a possible increased baseline risk of GIB in patients who practice IF. Also, FDA reporting system for adverse events (AE) had higher GIB events among ibrutinib patients compared to other FLNAs. Overall, there was scarcity in the clinical data available on the effects of IF on treatment outcomes with FLNA in CLL patients. There was also evident variability in the number

of reported AE between the relatively older (ibrutinib and venetoclax) and newer medications (acalabrutinib and zanubrutinib), which may be causing an underestimation of treatment risks.

Conclusion: Until further data is available, patients on BTK inhibitors should refrain from practicing IF for GI bleeding risk. However, it may be possible for patients on venetoclax to practice fluid liberal IF conditionally and conservatively for TLS risk. This is on the condition that adequate hydration and daily administration with food are achieved.

Fasting's risks and benefits must be discussed with patients. Further prospective clinical trials, including exploration of different forms of IF, are needed to better elucidate the effect of IF on FLNAs treatment -related outcomes in CLL patients.

Citation: Benkhadra M, Fituri N, Aboukhalaf S, Ghasoub R, Mattar M, Al Farsi K, Alshemmari S, Yassin M; Permissibility of an Intermittent Fasting in Patients with Chronic Lymphocytic Leukemia in the Era of Novel Therapies :a Pharmacology Based Review. Blood 2023; 142 (Supplement 1): 6559. doi: https://doi.org/10.1182/blood-2023-178185

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Hematological Toxicity of Immune Checkpoint Inhibitors: Real-World Retrospective Outcomes from a Cohort Study in Qatar

Maria Benkhadra, Shereen Elazzazy, Anas Ahmad Hamad, Mohamed S. Elkhatim, Amaal Gulied, Arwa Osama Sahal , Aya Alasmar , Farah I. Jibril, Hebatalla Mahmoud Afifi, Sahar Nasser, Afnan Alnajjar, Rawan Dawoud P, Nabil E. Omar

Abstract

Introduction: The integration of immune checkpoint inhibitors (ICPIs) into cancer management has brought a paradigm shift in the outcome of cancer care. The incidence of hematological immune-related adverse events (Hem-irAEs) associated with ICIs is uncommon or exceedingly rare, particularly in comparison to chemotherapy (Johar, 2020). In this study, we provide an analysis of real-world experience with Hem-irAEs from the National Center of Cancer Care and Research (NCCCR) in Qatar.

Methods: Patient electronic medical records (EMR) were retrospectively analyzed for all patients who received ICPIs between 2015 and 2020. Collected data included patient demographics, Hem-irAEs-related incidence, characterization, management, and outcomes of Hem-irAEs.

Results: Over the five-year review period, a total of 165 irAEs were experienced among the 256 patients who received ICPIs in Qatar. The incidence of Hem-irAEs was 15 events (9.1% of all irAEs) among 14 patients (5.5% of all patients). Baseline characteristics of patients experiencing Hem-irAEs are described in Table 1. Majority of patients were diagnosed with solid malignancies (n=11; 78.6%) and were pre-treated with either chemotherapy or targeted therapies (n=12; 86%). Baseline hematological functions were also acceptable in most patients as shown in Table 1.

Nivolumab was the most used ICPI (n=8, 57%), followed by pembrolizumab (n=4, 29%), durvalumab (n=1, 7%) and avelumab (n=1, 7%). The most common Hem-irAE was thrombocytopenia (5/15); however, four of those events were worsening of baseline thrombocytopenia (Table 2). During this review period, two bleeding events have occurred; one was grade 1 gingival bleeding that spontaneously resolved, while the other event was grade 4 leading to severe anemia (hemoglobin 5.7 g/dL) requiring transfusion and ICPI discontinuation. Two grade 4 pancytopenia events were identified; one resolved with supportive transfusions and ICPI discontinuation, while the other resulted in fatal limbic encephalitis despite the use of intravenous immunoglobulins. There were no other fatal irAEs, but one more patient discontinued ICPI due to grade 3 anemia. Co-occurrence of non-HEM-irAEs were manifested in half of this population (n=7); majority of which were dermatitis (33.3%) and hepatitis (33.3%), followed by hypothyroidism (22.2%) and cardiac toxicity (11.2%).

Conclusion: Compared to the current literature describing Hem-irAEs, our center experience shows similar distribution of adverse events with thrombocytopenia and anemia. Thrombocytopenia was the most Hem-irAEs experienced followed by neutropenia and eosinophilia (1). On the other hand, our population is slightly different with the majority of cases described here being non-melanoma solid malignancies. Considering the rate of Hem-irAEs in the investigated population at NCCCR, there is a need for an integrated pathway for the diagnosis and management of these events.

Citation: Benkhadra M, Elazzazy S, Hamad A, Elkhatim M, Gulied A, Sahal A, Alasmar A, Jibril F, Afifi H, Nasser S, Alnajjar F, Dawoud R, Omar NE.; Hematological Toxicity of Immune Checkpoint Inhibitors: Real-World Retrospective Outcomes from a Cohort Study in Qatar. Blood 2023; 142 (Supplement 1): 5378.

Impact factor: 20.3

Deep Learning Models for the Diagnosis of Acute Lymphoblastic Leukemia from Bone Marrow Images : A Comprehensive Literature Review

Basel Elsayed, Amgad Elshoeibi, Mohamed Elhadary, Ahmed Badr, Omar Metwalli, Honar Cherif, Deena Mudawi, Awni Alshurafa, Mohamed A Yassin

Abstract

Introduction: Acute lymphoblastic leukemia (ALL) is an aggressive blood cancer that begins in the bone marrow. It is the most common childhood cancer and requires early and accurate diagnosis for optimal treatment outcomes. Through automated image analysis of peripheral blood smears and bone marrow biopsies, artificial intelligence (AI), particularly Deep Learning (DL), have opened new avenues for improving ALL diagnosis. While bone marrow testing is the gold standard for ALL confirmation, AI applications in diagnosing ALL from bone marrow images have received less attention in the literature than peripheral blood smears. This review aims to assess the current state of AI in ALL diagnosis using bone marrow aspirates and biopsies, with a focus on Deep Learning (DL) models such as Convolutional Neural Networks (CNNs).

Methods: A comprehensive literature search, conducted on June 11th, 2023, covered major medical databases, including PubMed/MEDLINE, Scopus, Embase, and Web of Science. Relevant keywords like "acute lymphoblastic leukemia," "deep learning," and "neural network" were employed, without time frame restrictions. Articles were included if they assessed the metrics of AI applications for ALL diagnosis in bone marrow aspirates. Articles were excluded if they: (1) had different outcomes, (2) were reviews, (3) were abstracts only, or (4) only reported peripheral blood smear metrics.

Results: The search yielded 496 articles. After eliminating duplicates (282), title and abstract screening on the Rayyan platform excluded 204 records, leaving 214 articles eligible for full-text screening. Ten relevant articles were ultimately included in the review. Diverse approaches were presented to enhance diagnostic accuracy and efficiency. One study achieved 100% accuracy in classifying leukemic cells using a unique Convolutional Leaky RELU with CatBoost and XGBoost (CLR-CXG) design. Another study employed transfer learning with CNNs, obtaining 95.3% accuracy for AML, ALL, and CML classification with DenseNet121. Furthermore, the novel "i-Net" model demonstrated 99.18% validation accuracy for white blood cancer segmentation and classification. Adaptive Multi-objective CAT algorithms achieved 99.45% accuracy in detecting bone marrow cancer cells. An AI-based system using deep learning exhibited 97.2% accuracy in diagnosing ALL, while a robust fuzzy logic algorithm combined with a radial basis function neural network achieved

82.93% accuracy in diagnosing ALL in developing countries. Additionally, AI technologies based on computer microscopy demonstrated 95% and 97.5% accuracy in diagnosing ALL and minimal residual disease, respectively. A computer-aided system achieved 97.78% accuracy in classifying ALL subtypes.

Conclusion: The potential of AI-driven approaches, particularly deep learning models like CNNs, in improving ALL diagnosis from bone marrow images is highlighted in this review. Because of their superior sensitivity and specificity over peripheral blood smears, bone marrow samples are the gold standard for ALL confirmation. The morphological and cellular properties of bone marrow samples provide important information for disease classification and monitoring. While DL and CNNs have shown promise in diagnosing ALL from peripheral blood smears, their use in bone marrow samples has yet to be investigated deeply. More research and external validation are required to fully realize AI's potential in ALL diagnosis from bone marrow specimens.

Citation: Basel Elsayed, Amgad Elshoeibi, Mohamed Elhadary, Ahmed Badr, Omar Metwalli, Honar Cherif, Deena Mudawi, Awni Alshurafa, Mohamed A Yassin; Deep Learning Models for the Diagnosis of Acute Lymphoblastic Leukemia from Bone Marrow Images : A Comprehensive Literature Review. Blood 2023; 142 (Supplement 1): 7184.

Impact Factor: 20.3

Establishment of a Clinical Pharmacist-Led Multiple Myeloma Clinic with Collaborative Prescribing Model at the National Center for Cancer Care and Research in Qatar

Rola Ghasoub, Shereen Elazzazy, Maria Benkhadra, Nancy Kassem, Honar Cherif, Javid Gaziev, Hesham Elsabah, Anas Ahmad Hamad

Abstract

Introduction: Multiple Myeloma (MM) is a chronic and incurable hematologic malignancy affecting the plasma cells, and is more prevalent among the elderly. Interprofessional patient care showed superiority over physician-only care in multiple settings, including MM. (Sweiss K et al.2019)In Qatar, real-world data analysis of MM patients treated in the ambulatory setting at the National Center for Cancer Care and Research (NCCCR) showed that clinical pharmacists (CPs) had an evident role in therapy optimization and ensuring adherence to treatment protocol schedule and supportive medications.(Elazzazy S et al.,2023) We aimed to provide a more structured and accessible link to MM patients considering the complexity of their treatment protocols and supportive care through the establishment of a clinical pharmacist-led clinic (CPLC). The most common challenges to optimum care of MM patients in the NCCCR before CPLC were identified and categorized (Figure 1) and then used to design the collaborative model for the MM CPLC (Figure 2).

Methods: The collaborative MM CPLC was initiated at NCCCR in February 2022. A collaborative practice agreement was established for this clinic, to allow clinical pharmacists -managing MM patients- to issue refills for supportive medications, and order any necessary laboratory tests. To investigate the quality of care provided by the clinic, data was retrospectively collected and analyzed for all MM patients managed in the clinic between February 2022 and February 2023. All patients who were newly diagnosed with MM were eligible for referral by the attending physician. Dedicated advanced hematology CPs provided consultation twice weekly for referred patients without additional fees. The provided services (in-person or virtual) included thorough medication profile review (prescribed antineoplastic and refills of supportive medications), and ordering follow-up laboratory tests. Services also included assessment and optimization of medication adherence, including immunomodulators and supportive medications (i.e., Venous Thromboembolism (VTE) prophylaxis, antimicrobial prophylaxis, bone modifying agents and vaccinations), providing comprehensive patient education, and communicating the recommended adjustments with physicians.

Results: During the 12-month period, there was a total of 22 patients referred to the clinic. The

average age for patients was 51 years (range 36-72). Patient characteristics are summarized in Table 1. The total number of documented encounters with the pharmacists was 73 visits, corresponding to a median of 4 visits per patient (range 1-11). The total amount of time spent with each patient over the course of their referral was 15 minutes. A total of 343 CPs interventions (average of 5 interventions per visit) were performed with an acceptance rate of 100%. The most common intervention was medication reconciliation (n=124), followed by monitoring for medication outcomes (n=72, safety and efficacy), addition of required medication (n=40), patient education (n=27), issuing refills (n=24), drug interactions review and management (n=19), suggesting referrals to relevant subspecialities (n=16), identification of adverse drug reactions (n=7), and required dose adjustments (n=12). Twenty-two medication refills for supportive medications and eight pre-chemotherapy laboratory investigations were issued and ordered by CPs, respectively. All newly diagnosed patients were started on the appropriate bisphosphonate therapy without the previously observed delay, with the median from diagnosis to initiation being 14 days [range from 1 to 117 days]. All clinic patients were maintained on the appropriate VTE prophylaxis (aspirin [n=14], rivaroxaban [n=7], warfarin [n=1]). All patients were adherent to antiviral and Pneumocystis jirovecii Pneumonia prophylaxis.

Conclusion: CPLC for MM patients treated in the ambulatory setting provided a robust and timely link to patients in alignment with the published literature. The newly implemented collaborative prescribing model in MM clinic encouraged the expansion of pharmacy services in other ambulatory clinics. Our collaborative model could be potentially applied to different cancer settings to optimize a safe and effective patient care. Further analysis is planned to compare the adherence to international MM care guidelines pre- and post-launch of our CPLC.

Citation: Rola Ghasoub, Shereen Elazzazy, Maria Benkhadra, Nancy Kassem, Honar Cherif, Javid Gaziev, Hesham Elsabah, Anas Ahmad Hamad; Establishment of a Clinical Pharmacist-Led Multiple Myeloma Clinic with Collaborative Prescribing Model at the National Center for Cancer Care and Research in Qatar. Blood 2023; 142 (Supplement 1): 5079.

Impact Factor: 20.3

Characteristics and Outcomes of Adolescent, Young Adults, and Adults 40-50 Years Old with Multiple Myeloma: A Single Center Experience

Shehab Mohamed, Hesham Elsabah, Hawra Shawayli, Feryal Abbas, Dina Sameh Soliman, Mohammad Afana, Deena Mudawi, Samah Ahmed Samy Kohla, Halima El Omri, Nancy Kessam, Anil Ellahie, Mohammed Abdulgayoom, Yahya Mulikandathil, Ibrahim Ganow, Awni Alshurafa, Kalpana Singh, Amna Gameil, Honar Cherif

Abstract

Background: Multiple myeloma (MM) is a malignant tumor with abnormal proliferation of plasma cells. Adolescent and Young Adult (AYA) patients are defined as patients between 15-39 years of age. Multiple myeloma is uncommon in non-elderly populations. Its prevalence is only 2% in AYA age group and only 10% in patients 40-50 years old.

The feature of MM is not well known or understood in those two age groups.

In this retrospective study we describe the clinical characteristics, cytogenetics, prognostic markers, treatments given and outcomes of MM in AYA and 40-50 years old patients.

Methods: We retrospectively analyzed data from the clinical database of our single tertiary hematology center, The National Center for Cancer Care and Research, Doha, Qatar. This center serves a country's population of about 2,8 million people. All patients diagnosed with MM between the age 50 or less during the period of January 2007 to December 2022 were included.

Results: Seventy-four patients were diagnosed at our centre with MM before the age of 50 years, total of all MM cases 222 (33%) Males was predominant 55/74 (74.3 %) with a median age of 41 years (range, 15-49). Most of the patients were from Asian 55%. At diagnosis patients had a median hemoglobin of 10.2 g/dl, creatinine 294 umol/L, total protein 90 gm/L, albumin 34.75 gm/L, calcium 2.7 mmol/L, LDH 255 U/L, IgG 2289.75 mg/dl, IgA 424.15 mg/dl, IgM 34.2 mg/dl, FLC-Kappa 1993 mg/L and FLC-Lambda 1177 mg/L. Median of bone marrow filtration by plasma cell was 51 %. Most of the patients presented at advance stages with 44 patient (59%) presented as IIIA Durie Salmon or stage III and IV by ISS 70 %. IgG Kappa most frequent type of MM 18 patients (24%), followed by Free light chain kappa (23%), IgG Lambda (18%) and others including two cases of plasmacytoma (Most recurrent cytogenetics were diploid cytogenetics in 42 patients (57%), while 7 patients (9%) had complex cytogenetics. Twenty-eight patients had spinal cord compression at single or multiple levels (thoracic were most common site 20%) while 3 patients had pathological fractures. Bortezomib based regimen is most one used to treat our patients. Daratumumab- Velcade, Revlimid,

and dexamethasone (D-VRD) was used for 35 patients (74%) and Velcade,Cyclophosphamide and Dexamethasone VCD in 20 patients (27%). The first response to treatment showed completed remission (CR) in 35 patients, very good partial remission in 10 patients, partial response in 9 patients, four patients either refractory or primary refractory disease and one patient with stable disease. Thirty -five patients (48%) underwent their first autologous bone marrow transplant ASCT. A total of 8 patients underwent second ASCT and one patient underwent third ASCT. After a median duration of follow up of 6.25 years and 72 % of the patients were still alive. We compared the characteristics and outcome for the AYA group (18-39) with patient age group 40 to 49 years. Although there was no statistical significance difference between the two groups regarding overall survival (p=0.21) , the older group had more cases of spinal cord compressions and more cases of refractory disease. Patient characteristics are described in Table 1.

Conclusion: One third of MM patients in our center are younger than 50 years. These patients tend to present with advanced stage and serious manifestation such as spinal cord compression. IgG kappa and free light chain are the most common myeloma type in this cohort. D-VRD is the most used protocol with a good response rate. Patient characteristics and treatment outcomes are the same for AYA patients compared with patients 40-49 years old (p=0.21). Patients who received first transplant had better OS compare the those who didn't (p0.01)

Citation: Shehab Mohamed, Hesham Elsabah, Hawra Shawayli, Feryal Abbas, Dina Sameh Soliman, Mohammad Afana, Deena Mudawi, Samah Ahmed Samy Kohla, Halima El Omri, Nancy Kessam, Anil Ellahie, Mohammed Abdulgayoom, Yahya Mulikandathil, Ibrahim Ganow, Awni Alshurafa, Kalpana Singh, Amna Gameil, Honar Cherif; Characteristics and Outcomes of Adolescent, Young Adults, and Adults 40-50 Years Old with Multiple Myeloma: A Single Center Experience. Blood 2023; 142 (Supplement 1): 6647

Impact Factor: 20.3

Hyperleukocytosis in Patients with Acute Myeloid Leukemia Characteristics and Outcome, a Single-Center Experience

Shehab Mohamed, Hawra Shawayli, Feryal Abbas, Dina Sameh Soliman, Mohammad Afana, Mohamed A Yassin, Deena Mudawi, Hesham Elsabah, Samah Ahmed Samy Kohla, Yahya Mulikandathil, Aliaa Amer, Awni Alshurafa Alshurafa, Kalpana Singh, Halima El Omri, Amna Gameil, Honar Cherif

Abstract

Background: Hyperleukocytosis is the condition where Acute myeloid leukemia (AML) is presented with white blood cell counts equal to or greater than 100,000. A small proportion of AML patients are presented with this condition which is associated with significant morbidity and mortality caused by related serious complications including leukostasis, tumor lysis syndrome (TLS) and disseminated intravascular coagulation. Hyperleukocytosis is a hematological emergency requiring immediate intervention.

In this retrospective study we describe the general characteristics, cytogenetics, mutational profile, treatment given, and outcome of AML patients having hyperleukocytosis at diagnosis.

Methods: Data were retrieved from the clinical data base of our tertiary cancer center (National Center for Cancer Care and Research, Doha, Qatar). All patients with AML diagnosed during the period January 2017 through December 2021 were included.

Results: A total of 186 AML patients were included. Twenty-one patients (11.5%) were presented with hyperleukocytosis. Males were more predominant 13/21 (62 %) and more than half of the patients had an Asian origin 52%. The median age for the group was 40.0 years (18-89). Complete blood count (CBC) showed median hemoglobin of 9.2g/dl, white blood cells of 176x10^3/uL and platelets 6x10^3/uL. the median percentage of the blast in the peripheral blood was 71 % and 72 % in bone marrow. Bone marrow cellularity was high in all the cases 100%. Bone marrow dysplasia was assessed with dysgranulopoiesis observed in 24%. All patients had de novo AML. In these patients the diploid KT was most common cytogenetic findings (57%), followed by CBF recurrent cytogenetics abnormalities in 4 patients (19%). FLT 3-ITD was positive in 7 patients (33%) and NPM1 mutation in 5 patients (28%). Hydroxyurea (HU) was used as cytoreductive therapy in 90% of patients. More than half of the patients 11/21 (52%) were admitted to intensive care unit (ICU). One patient had CNS relapse. Seven patients (33%) underwent allogenic bone marrow transplant. Progression occurred in 6 patients 28 (median1.4 years) and Overall survival in this cohort

was 76 % (median1.9 year) and the average duration of follow-up of 24.8 months. Early death within 30 days observed, with median time to death 4 days (1-12) among those who died.

Conclusion: One of ten AML patients are presented with hyperleukocytosis. Most of our AML patients with hyperleukocytosis were young males. This is most probably related to the young general population in our country. All patients had hypercellular marrow with high blast percentage. Diploid Karyotype, CBF rearrangements, FLT 3-ITD mutation and NPM1 mutation were frequent in this cohort. Most of the patients developed complications requiring intensive care admission. Hydroxyurea was the first choice for cytoreduction. Both disease progression and mortality were relatively high (28% and 24 % respectively) and occurred very early, within less than a week from presentation. Early diagnosis and immediate management are mandatory to tackle the complications of this hematological emergency and improve morbidity and mortality.

Citation: Shehab Mohamed, Hawra Shawayli, Feryal Abbas, Dina Sameh Soliman, Mohammad Afana, Mohamed A Yassin, Deena Mudawi, Hesham Elsabah, Samah Ahmed Samy Kohla, Yahya Mulikandathil, Aliaa Amer, Awni Alshurafa Alshurafa, Kalpana Singh, Halima El Omri, Amna Gameil, Honar Cherif; Hyperleukocytosis in Patients with Acute Myeloid Leukemia Characteristics and Outcome, a Single-Center Experience. Blood 2023; 142 (Supplement 1): 5836.

Impact Factor: 20.3

Real-World Use of Hypomethylating Agents (HMA)/Venetoclax Combinations in Patients with Myelodysplastic Neoplasms (MDS) in the Arabian Gulf Region

Fatima Khadadah, Honar Cherif, Halima El Omri, Ahmed Absi, Noor Merwass, Mohamed I. Abu Haleeqa, Waed Jaber, Ahmad Alhuraiji, Ramesh Pandita

Abstract

Context: Retrospective data thus far has supported improved responses with HMA/venetoclax combinations in both the frontline and relapsed settings. A Phase Ib trial of azacitidine and venetoclax for high-risk MDS patients demonstrated an overall response rate (ORR) of 80%. Retrospective data from the Moffitt Centre comparing HMA/venetoclax to patients who received HMA showed an ORR of 77% compared to 40% for patients who only received HMA.

Objectives: Our aim was to obtain real-world evidence for use of combination HMA/venetoclax to treat myelodysplastic patients in the Arabian Gulf region.

Methods: This is a retrospective study of patients with myelodysplastic neoplasm treated with a HMA/venetoclax in 4 different countries from Jan 2020 - May 2023. Cases were included if they were over the age of 18, and had a diagnosis of MDS or MDS/AML. Both frontline and relapsed/refractory patients were included. Patients were excluded if they had more than 20% blasts or received an additional agent with their treatment.

Results: Data on 16 patients was collected across 4 centres in the Arabian Gulf. The median age was 66 (range 51-84). All patients had high-risk MDS, MDS/AML including four patients with a TP53 mutation and/or complex cytogenetics. Median follow-up was 15 months (range 4-23). A median of 6 cycles were received (range 3-14). Azacitidine was the only HMA used at a starting dose of 75mg/m 2 for 7 days. Venetoclax starting dose was 400mg (or equivalent if given with an azole) and given for a median of 15 days (range 10-28). Thirteen patients received azole prophylaxis. Thirteen patients achieved a CR/CRi (81%), one patient who didn't had a TP53 mutation with complex cytogenetics, another had secondary MDS, and the third had stable disease and proceeded to transplant.

Overall survival (OS) at 12 months was 86.2% (95% CI 55.0-96.4). For patients with poor risk disease (TP53 or complex cytogenetics) OS was 66.7% (95% CI 5.4-94.5) vs 90.9% (95% CI 50.8-98.7) for non-poor risk patients; p=0.006. Median OS was 22 months (22-NR) for non-poor risk patients compared to 14 months (10-NR) for poor risk patients. Event-free survival (failure,

transformation or relapse) at 12 months was 84.6% (95% CI 51.2-95.9); it was 90.0% (95% CI 47.3-98.5) for those with no poor risk features and 66.7% (5.4-94.5) for those with poor-risk features; p=0.027. For those who stopped, 4/16 stopped due to failure and disease progression or transformation, 4/16 underwent stem cell transplantation, 3 stopped due to infectious complications, two from drug access issues, and one patient with secondary MDS had recurrence of their primary solid tumour. The most common toxicities were cytopenias and one patient died from cellulitis and COVID while on HMA/venetoclax.

Conclusion: The combination of HMA/ venetoclax is a feasible treatment for patients with high-risk MDS with significantly worse outcomes in patients with complex cytogenetics and/or TP53 mutations. This regimen seems to be adapted by many hematologists in our region. However, the long-term efficacy in comparison to standard of care for various subgroups of MDS needs to be explored in larger prospective studies

Citation: Fatima Khadadah, Honar Cherif, Halima El Omri, Ahmed Absi, Noor Merwass, Mohamed I. Abu Haleeqa, Waed Jaber, Ahmad Alhuraiji, Ramesh Pandita; Real-World Use of Hypomethylating Agents (HMA)/Venetoclax Combinations in Patients with Myelodysplastic Neoplasms (MDS) in the Arabian Gulf Region. Blood 2023; 142 (Supplement 1): 7428

Impact Factor: 20.3

EE45 Cost-Effectiveness of Venetoclax in Combination with Rituximab in Relapsed/Refractory Chroniclymphocytic Leukemia in Four Gulf Countries

A. Hamad, A. Abdaljalil, H.Y. Abdellatif, Q.T. Aladarbeh, K. Al Farsi, A. Alhuraiji, A.M. Gamaleldin, A. Hamadah, H.A. Ismail, H.Y. Osman, M. Siddiqui, R.Y. Taha, M. Tannira, R. Pandita

Abstract

Objectives: A cost-effectiveness analysis was performed to compare fixed duration venetoclax + rituximab with other treatments for the treatment of relapsed/refractory chronic lymphocytic leukemia in the public healthcare sector of four Gulf countries.

Methods: An existing model using a three-state partitioned survival framework was adapted to the public healthcare sector in Kuwait, Oman, Qatar and the United Arab Emirates (UAE). Inputs included disease epidemiology and local cost of treatment obtained via literature review and a two-round Delphi technique. Unit costs of medications, treatment administration, routine care and monitoring, and adverse event prophylaxis and management were considered. The time horizon for the cost-effectiveness model was 30 years (lifetime time horizon) and a discount rate of 3.5% was applied to costs and outcomes. Comparators included in the model were ibrutinib, fludarabine + cyclophosphamide + rituximab (FCR), bendamustine + rituximab (BR), ibrutinib + BR and acalabrutinib.

Results: In Kuwait, Qatar, Oman and United Arab Emirates, venetoclax + rituximab is a dominant strategy compared to acalabrutinib, ibrutinib and ibrutinib + BR due to the lower incremental cost (-$242,455, -$242,148, -$398,254 for Kuwait; -$292,609, -$134,051, -$243,747 for Qatar; -$46,921, -$47,892, -$194,793 for Oman; -$574,592, -$117,772, -$244,443 for UAE) and more QALYs gained (1.929, 1.928, 1.173 for Kuwait; 1.814, 1.813, 1.117 for Qatar; 1.473, 1.472, 0.921 for Oman; 1.851, 1.850, 1.129 for UAE), but not cost-effective compared to FCR or BR, due to the lower cost related to treatment with FCR and BR, despite the QALY gains for venetoclax + rituximab, at willingness-to-pay thresholds of 1 x GDP per capita ($32,373 for Kuwait, $50,806 for Qatar, $15,343 for Oman, $43,101 for UAE).

Conclusions: Venetoclax + rituximab as a fixed treatment duration regimen is a cost-effective treatment option compared to BTK inhibitors (acalabrutinib and ibrutinib) in the Gulf region.

Citation: Hamad A, Abdaljalil A, Abdellatif H, Aladarbeh Q, Al Farsi K, Alhuraiji A, Gamaleldin A, Hamadah A, Ismail H, Osman H, Siddiqui M, Taha R, Tannira M, Pandita R. (2023) Cost-Effectiveness of Venetoclax in Combination with Rituximab in Relapsed/Refractory Chronic Lymphocytic Leukemia in Four Gulf Countries. Value in Health, 26(6):S67-8.

Impact Factor: 4.5

The incidence of thrombotic events in hospitalized cancer patients despite the application of thromboprophylaxis in Qatar. A nationwide retrospective cohort study.

Arwa Sahal , Nabil Omar, Ali F, Sahar Nasser, Hebatallah Afifi H, Shereen Elazzazy

Abstract

Background: Haploidentical stem cell transplantation (Haplo-HSCT) using post-transplant cyclophosphamide (PTCy) is a readily available alternative option for patients who do not have HLA matched donors. This is an attractive approach in developing countries which usually do not have an unrelated donor registry and/or cannot afford the cost associated with the procurement of stem cells from an unrelated donor. Almost universal availability of haploidentical donor has made it possible for every patient in need of a transplant. Accumulated experience showed that outcomes of Haplo-HSCT in acute leukemias and lymphomas are similarto those obtained after matched related and unrelated transplants. We report our experience of Haplo-HSCT in hematologic malignancies.

Methods: 17 consecutive patients with median age of 34 years (range, 16-53), 9 with myeloid (AML, CMML, CML) and 8 with lymphoid (ALL, NHL) malignancies received Haplo-HSCT at our Center. Donors were sibling (n = 12), parent (n = 3) and child (n = 2). Only one patient had DSAs. At the time of transplantation 14 patients were in CR1/CR2 and 3 had relapsed/refractory disease.16 patients were intermediate-high risk. All patients received myeloablative conditioning regimen- 15 Fludarabine 160 mg/m2 total dose and TBI 1200 cGy (Flu160TBI1200), 1 Flu160TBI1200 and Thiotepa, and 1 patient Cy100TBI1200 due to shortage of fludarabine. GVHD prophylaxis consisted of PTCy on days +3 and +4, CSA starting from day -1 and MMF from day 0. Sixteen patients received PBSC and 1 patient bone marrow grafts. The median CD34 cell dose was 7.55 x 106/kg (range, 5.2-13), and CD3 cell dose was 157 x 106/kg (range, 46.5-257).

Results: All patients achieved sustained engraftment with complete donor chimerism. The median follow-up for surviving patients was 10 months (range, 3-30). 2-year OS and DFS were 88%, and GRFS was 74%. The cumulative incidence of grade 2-3 acute GVHD and mild chronic GVHD was 29% and 7%, respectively. None of the patients has developed moderate or severe chronic GVHD. None of the patients had relapse. One patient died 11 months after transplantation due to pneumonia (while in his home country). All but 2 patients are off immunosuppression therapy. Only one patient had grade 3 CRS requiring tocilizumab. The incidence of grade 1 or grade 3 CRS was 47% and 6%, respectively. One patient developed secondary poor graft function successfully treated with romiplostim and G-CSF. The incidence of clinically significant CMV infection was significantly

high in patients who did not receive letermovir prophylaxis (92%) compared with patients receiving letermovir (3%). Two patients developed grade 3 BK-virus associated hemorrhagic cystitis, 2 TA-TMA. Pneumonia occurred in 5 patients, one of them had successfully treated Covid-19 pneumonia. One patient developed tuberculosis.

Conclusions: Haplo-HSCT with PTCy leads excellent survival for patients with hematologic malignancies who lack matched donors. Myeloablative FluTBI regimen is safe, well tolerated and is associated with strong antileukemic effect leading to high relapse-free survival.

Citation: Sahal AO, Omar NE, Ali F, Nasser S, Afifi H, Elazzazy S. The incidence of thrombotic events in hospitalized cancer patients despite the application of thromboprophylaxis in Qatar. A nationwide retrospective cohort study. 2023 ACCP Virtual Poster Symposium. J Am Coll Clin Pharm.2023 May; 6: 759-835. https://doi.org/10.1002/jac5.1833. DOI: 10.1002/jac5.1833.

Impact factor: 1.6

NON-MALIGNANT HEMATOLOGY

ORIGINAL ARTICLES

Eltrombopag in patients with chronic immune thrombocytopenia in Asia-Pacific, the Middle East, and Turkey: final analysis of CITE

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Abstract

CITE was a prospective, noninterventional study in adult patients with chronic immune thrombocytopenia treated with eltrombopag under routine clinical care in Asia-Pacific, the Middle East, and Turkey. Data to assess eltrombopag usage, compliance, and outcomes were collected from May 2017 to December 2020. Platelet response was defined as platelet count ≥50 × 103/μL in the absence of rescue medications and splenectomy. Quality of life was evaluated using the

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire. Noncompliance was defined as the number of missed doses and number of days where the patient did not follow food instructions. A total of 231 patients were enrolled; the median (range) duration of eltrombopag treatment was 484.5 (1-642) days. Compliance to prescribed eltrombopag dose since the previous routine visit was high at ≥96.0%. Baseline median platelet count was 19.0 × 103/μL, which increased to ≥50 × 103/μL at month 2 and mostly fluctuated between 70 × 103/μL and 100 × 103/μL thereafter. The median time to first platelet response was 1.05 (95% confidence interval: 0.92-1.28) months, and the median (interquartile range) maximum duration of platelet response was 193 (57-456) days. FACIT-F scores improved from a mean (standard deviation) 34.4 (12.1) at baseline to 38.5 (9.1) at month 18. Adverse events occurred in 50.9% of patients (n = 116), the most common being upper respiratory tract infection (8.3%) and headache (6.6%). These findings confirmed the effectiveness of eltrombopag treatment in routine practice and reassured that real-world compliance to eltrombopag-prescribed doses and dietary instructions in Asia-Pacific, the Middle East, and Turkey were in line with current recommendations.

Citation: Wong RSM, Yavaşoğlu İ, Yassin MA, Tarkun P, Yoon SS, Wei X, Elghandour A, Angchaisuksiri P, Ozcan M, Yang R, Mattar M, Rahman M, Ingles S, Goldbrunner M, Frueh JA, Jang JH. Eltrombopag in patients with chronic immune thrombocytopenia in Asia-Pacific, the Middle East, and Turkey: final analysis of CITE. Blood Adv. 2023 Sep 12;7(17):4773-4781. doi: 10.1182/bloodadvances.2022008287. PMID: 36103340; PMCID: PMC10469381.

Impact Factor: 7.5

Persistence of spike-specific immune responses in BNT162b2-vaccinated donors and generation of rapid *ex-vivo* T cells expansion protocol for adoptive immunotherapy: A pilot study

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Abstract

Introduction: The BNT162b2 mRNA-based vaccine has shown high efficacy in preventing COVID-19 infection but there are limited data on the types and persistence of the humoral and T cell responses to such a vaccine.

Methods: Here, we dissect the vaccine-induced humoral and cellular responses in a cohort of six healthy recipients of two doses of this vaccine.

Results and discussion: Overall, there was heterogeneity in the spike-specific humoral and cellular responses among vaccinated individuals. Interestingly, we demonstrated that anti-spike antibody levels detected by a novel simple automated assay (Jess) were strongly correlated ($r=0.863$, $P<0.0001$) with neutralizing activity; thus, providing a potential surrogate for neutralizing cell-based assays. The spike-specific T cell response was measured with a newly modified T-spot assay in which the high-homology peptide-sequences cross-reactive with other coronaviruses were removed. This response was induced in 4/6 participants after the first dose, and all six participants after the second dose, and remained detectable in 4/6 participants five months post-vaccination. We have also shown for the first time, that BNT162b2 vaccine enhanced T cell responses also against known human common viruses. In addition, we demonstrated the efficacy of a rapid ex-vivo T cell expansion protocol for spike-specific T cell expansion to be potentially used for adoptive-cell therapy in severe COVID-19, immunocompromised individuals, and other high-risk groups. There was a 9 to 13.7-fold increase in the number of expanded T cells with a significant increase of anti-spike specific response showing higher frequencies of both activation and cytotoxic markers. Interestingly, effector memory T cells were dominant in all four participants' CD8+ expanded memory T cells; CD4+ T cells were dominated by effector memory in 2/4 participants and by central memory in the remaining two participants. Moreover, we found that high frequencies of CD4+ terminally differentiated memory T cells were associated with a greater reduction of spike-specific activated CD4+ T cells. Finally, we showed that participants who had a CD4+ central memory T cell dominance expressed a high CD69 activation marker in the CD4+ activated T cells.

Keywords: COVID-19 vaccine; SARS-CoV-2; spike-specific T cells expansion; spike-specific immune responses; surrogate neutralization.

Citation: Mestiri S, Merhi M, Inchakalody VP, Taib N, Smatti MK, Ahmad F, Raza A, Ali FH, Hydrose S, Fernandes Q, Ansari AW, Sahir F, Al-Zaidan L, Jalis M, Ghoul M, Allahverdi N, Al Homsi MU, Uddin S, Jeremijenko AM, Nimir M, Abu-Raddad LJ, Abid FB, Zaqout A, Alfheid SR, Saqr HMH, Omrani AS, Hssain AA, Al Maslamani M, Yassine HM, Dermime S. Persistence of spike-specific immune responses in BNT162b2-vaccinated donors and generation of rapid ex-vivo T cells expansion protocol for adoptive immunotherapy: A pilot study. Front Immunol. 2023 Feb 2;14:1061255. doi: 10.3389/fimmu.2023.1061255. PMID: 36817441; PMCID: PMC9933868.

Impact Factor: 7.3

Real-world observational study on the long-term effect of L-glutamine treatment on renal parameters of adult and pediatric patients with sickle cell disease

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Abstract

Background: Sickle cell disease (SCD) is a rare genetic blood condition affecting millions worldwide. Oxidative stress is a key player in the pathogenesis of SCD and its comorbid consequences. Renal function impairment is a common complication of SCD in both pediatric and adult patients with serious consequences leading to increased risk of mortality. In this observational real-world study, we are reporting the long-term (120 weeks) renal function in 10 patients treated with L-glutamine.

Methods: Ten patients (4 pediatric and 6 adults), with confirmed diagnoses of SCD (HbSS genotype), were enrolled, these included four patients from Qatar with Arab Indian haplotype and six patients from French Guiana with African haplotype. All patients were treated with L-glutamine oral powder (~0.3 g/kg body weight, Endari®) twice daily for 120 weeks. Clinical events and laboratory parameters (renal function, hemoglobin, reticulocytes, and lactate dehydrogenase [LDH]) were measured at baseline, 48, and 120 weeks.

Results: The study showed that with L-glutamine treatment there were improvements in renal and hematological parameters with no vaso-occlusive crisis at both 48-and 120-week follow-up time points in all 10 patients. Improvements were seen in the albumin creatinine ratio (ACR) from baseline to 48 weeks (mean [Standard deviation SD] ACR: -4.19 [9.81] mg/g) and 120 weeks (mean [SD] ACR: -12.31 [21.09] mg/g). Mean (SD) increase in hemoglobin concentrations from baseline to 48 weeks and 120 weeks was 0.72 (1) g/dL and 1.41 (0.79) g/dL, respectively. Mean (SD) reticulocyte counts and LDH levels decreased from baseline to 48 weeks (mean [SD] change from baseline to 48 weeks, reticulocyte counts: -40.30 [101.58] × 109 cells/L; LDH levels: -259 [154.93] U/L) and 120

weeks (mean [SD] change from baseline to 120 weeks, reticulocyte counts: -58.30 [128.38] × 109 cells/L; LDH levels: -344.80 [274.63] U/L).

Conclusion: This is one of the first studies that assessed the long-term renal outcomes in SCD using L-glutamine. L-glutamine improved the renal function in patients with SCD along with improvements in clinical outcomes and hemolysis, from 48 weeks and sustained through 120 weeks of treatment.

Keywords: L-glutamine; clinical outcomes; hemolysis parameters; renal parameters; sickle cell disease.

Citation: Elenga N, Yassin MA. Real-world observational study on the long-term effect of L-glutamine treatment on renal parameters of adult and pediatric patients with sickle cell disease. Front Med (Lausanne). 2023 Dec 6;10:1243870. doi: 10.3389/fmed.2023.1243870. PMID: 38131044; PMCID: PMC10735270.

Impact Factor: 5.2

Perception of consanguineous marriage among the qatari population

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Abstract

Background: Hereditary blood diseases are widespread among the Arab population due to the high rates of consanguineous marriages; research regarding the perception of consanguineous marriage in some countries, such as Qatar, is extremely scarce. Therefore, this study aimed to investigate the prevalence of consanguineous marriage and assess the perception of consanguineous marriage among the Qatari population.

Methods: A cross-sectional study used a self-administered questionnaire among 395 Qatari adults aged 18-35 who attended primary healthcare institutions in Qatar. A convenience sampling technique was used to select the study participants. An independent t-test was used to compare the significance of the mean between the two groups with positive and negative perceptions of consanguineous marriage. Categorical data were analyzed for association using the chi-square or Fisher's exact test. Finally, a multiple logistic regression analysis was conducted to determine the significant predictors of the positive perception of consanguineous marriage. A significant level was set at $p < 0.05$.

Results: Approximately 45% of the participants had a positive perception toward consanguineous marriage, and the most common reason stated by those participants was "habit and traditions." The prevalence of consanguineous marriage among married couples was 62.6%, and among those with consanguineous marriage, most were married to first cousins (81.7%). Moreover, compared to the participants with negative perceptions of consanguineous marriage, those with positive ones were significantly older, married, with lower educational levels and higher monthly income levels, did not hear about glucose-6-phosphate dehydrogenase (G6PD) deficiency, did not know what kinds of

diseases are being screened in the premarital test, and were married to a relative.

Conclusion: The prevalence of consanguineous marriage is high among the Qatari population, and this requires an immediate need for community-based campaigns to raise public awareness about the problem and its potential impact.

Keywords: consanguineous marriage; consanguinity; genetic blood diseases; genetic diseases; perception; premarital screening; sickle cell disease; thalassemia.

Citation: Abdu Y, Ahmed K, Ibrahim MIM, Abdou M, Ali A, Alsiddig H, Selim NA, Yassin MA. Perception of consanguineous marriage among the qatari population. Front Public Health. 2023 Aug 4;11:1228010. doi: 10.3389/fpubh.2023.1228010. PMID: 37601216; PMCID: PMC10436573.

Impact Factor: 5.2

Clinical and epidemiological features and therapeutic options of avascular necrosis in patients with sickle cell disease (SCD): a cross-sectional study

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Abstract

Background: Avascular necrosis (AVN) is a debilitating complication in sickle cell disease (SCD) patients, and its management is usually challenging. This study aims to evaluate the clinical and epidemiological features and therapeutic options of AVN in sickle cell patients in Qatar.

Patients and methods: A cross-sectional study was conducted on a 49 SCD patients who were diagnosed with AVN and attended the hematology clinic at the National Center for Cancer care & research, Hamad Medical Corporation, Qatar between Jan-2011 to Jan2021. Results: Forty-nine adult patients with SCD who were diagnosed with AVN were studied. The median age of the study population is 32 years, and the median age at the first AVN diagnosis was 26 years (range: 11-44 yr.). 37 (75.5%) patients suffered from multiple joints AVN while 12(24.5%) had single joint involvement. 31 (63.3%) patients had bilateral hip AVN and 18 (36.7%) had shoulder involvement. 30 patients (61%) were on Hydroxyurea treatment. Based on FICAT and Alert classification of AVN, 57 % of patients had stage III and above at first diagnosis. 20 (40.8%) were managed with a conservative approach, 11 (22.4%) received hyperbaric oxygen with good response, 6(12.2%) underwent hip core decompression and 12(24.5%) underwent hip replacement surgery.

Conclusion: In SCD patients, AVN occurred more during the 3rd and 4th decades of life. The majority of AVN represented with advanced stage and had multiple joint involvements. We recommend adopting a low threshold of joint imaging for early detection and prevention of further complications.

Citation: Alshurafa A, Soliman AT, De Sanctis V, Ismail O, Abu-Tineh M, Hemadneh MKE, Rashid FR, Yassin K, Qasim H, Nashwan AJ, Yassin MA. Clinical and epidemiological features and therapeutic options of avascular necrosis in patients with sickle cell disease (SCD): a cross-sectional study. Acta

Biomed. 2023 Oct 17;94(5):e2023198. doi: 10.23750/abm.v94i5.14603. PMID: 37850770; PMCID: PMC10644931.

Impact factor: 3.786

The effect of intermittent fasting on the clinical and hematological parameters of patients with sickle cell disease: A preliminary study

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Abstract

Introduction: Sickle cell disease is a genetic disorder that frequently presents with vaso-occlusive crisis (VOC). Most patients with sickle cell disease in Qatar are Muslims; hence, they practice intermittent fasting during the holy month of Ramadan. However, there is a paucity of literature describing the effect of intermittent fasting on the occurrence of severe VOC. As a result, there is a lack of guidelines or standardized protocols that can help physicians advise patients with sickle cell disease who wish to practice intermittent fasting. Therefore, this study's aim was to investigate the effect of intermittent fasting on the clinical and hematological parameters of individuals with sickle cell disease.

Methods: We conducted a retrospective study for 52 Muslim patients with sickle cell disease in Qatar aged ≥18 years who were confirmed to be fasting during the holy month of Ramadan during any of the years 2019-2021. The difference in the occurrence of severe VOC, hemolytic crisis, and other clinical, hematological, and metabolic parameters were studied one month before, during, and one month after the intermittent fasting of Ramadan using the patient's medical records. Mean (sd), median (IQR), and frequency (%) described the data. One-way with repeated measures ANOVA with a Greenhouse-Geisser correction and Friedman tests (*) were used at alpha level 0.05.

Results: The study participants' (mean±sd) age was (31.1±9.2) years, 51.9% were males, and 48.1% were females. Roughly seventy percent of the participants were of Arab ethnicity, while the rest were

either African or Asian. Most of the patients were homozygotes (SS) (90.4%). The median number of severe VOC (P = 0.7) and hemolytic crisis (P = 0.5) was not found to be significantly different before, during, or after Ramadan. Significant differences, however, were found in platelet count (P = 0.003), reticulocyte count (P < 0.001), and creatinine level (P = 0.038) with intermittent fasting.

Discussion: In this preliminary study, intermittent fasting does not seem to influence the rate of occurrence of severe vaso-occlusive crisis or hemolytic crisis in patients with sickle cell disease; however, it was found to be associated with differences in platelet count, reticulocytes count, and creatinine level. The statistical and clinical significance of these findings needs to be confirmed in studies with a larger sample size.

Keywords: cbc; hemolytic crisis; intermittent fasting; sickle cell disease; vaso-occlusive crisis.

Citation: Ahmed K, Abdu Y, Khasawneh S, Shukri A, Adam E, Mustafa S, Affas M, Mohamed Ibrahim MI, Al Zayed A, Yassin MA. The effect of intermittent fasting on the clinical and hematological parameters of patients with sickle cell disease: A preliminary study. Front Med (Lausanne). 2023 Feb 21;10:1097466. doi: 10.3389/fmed.2023.1097466. PMID: 36895718; PMCID: PMC9989014.

Impact Factor: 3.6

A retrospective study of glucose homeostasis, insulin secretion, sensitivity/resistance in non- transfusion-dependent beta-thalassemia patients (NTD- beta Thal): reduced beta-cell secretion rather than insulin resistance seems to be the dominant defect for glucose dysregulation (GD)

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Abstract

Aims: Non-transfusion - dependent β-thalassemias (NTD-βThal) can cause iron overload and serious iron-related organ complications as endocrine dysfunction, including glucose dysregulation (GD).

Patients and methods: We retrieved data of all NTD- β Thal patients referred consecutively to a single Outpatient Italian Clinic from October 2010 to April 2023. All patients underwent a standard 3-h oral glucose tolerance test (OGTT) for analysis of glucose homeostasis, insulin secretion and sensitivity/resistance (IR), using conventional surrogate indices derived from the OGTT. The collected data in NTD- β Thal patients were compared to 20 healthy subjects.

Results: Seventeen of 26 (65.3 %) NTD- β Thal patients (aged: 7.8 -35.1 years) had normal glucose tolerance, 1/26 (3.8 %) had impaired fasting glucose (IFG), 5/26 (19.2 %) impaired glucose tolerance

(IGT), 1/26 (3.8%) IFG plus IGT and 2/26 (7.6%) plasma glucose (PG) level ≥155 mg/dL 1-h after glucose load. GD was observed exclusively in young adult patients; none of them had diabetes mellitus (DM). These findings were associated with a low insulinogenic index (IGI) and oral disposition index. HOMA-IR and QUICKI were not significantly different compared to controls. Interestingly, in young adult patients, ISI-Matsuda index was statistically higher compared to the control group, suggesting an increased insulin sensitivity.

Conclusions: This study reported a high prevalence of GD in young adults with NTD- β Thal. The documented reduction of IGI rather than the presence of IR, indicates reduced insulin secretory capacity as the pathophysiological basis of dysglycemia that may represent a novel investigational path for future studies on the mechanism(s) responsible for GD in NTD- β Thal patients.

V. De Sanctis, S. Daar, A. Soliman, P. Tzoulis, M. Yassin and C. Kattamis

Citation: De Sanctis V, Daar S, Soliman A, Tzoulis P, Yassin M, Kattamis C. A retrospective study of glucose homeostasis, insulin secretion, sensitivity/resistance in non- transfusion-dependent β-thalassemia patients (NTD- β Thal): reduced β-cell secretion rather than insulin resistance seems to be the dominant defect for glucose dysregulation (GD). *Acta Biomed.* 2023 Dec 5;94(6):e2023262. doi: 10.23750/abm.v94i6.15001. PMID: 38054678; PMCID: PMC10734240.

Impact factor: 3.206

Immune Thrombocytopenia Relapse in Patients Who Received mRNA COVID-19 Vaccines

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Abstract

Background: Immune thrombocytopenia (ITP) is a blood disorder in which antibodies coating platelets cause platelet destruction in the spleen with a resultant low platelet count and an increased tendency for bleeding. Coronavirus disease 2019 (COVID-19) is an illness caused by SARS-CoV-2. Though pneumonia and respiratory failure are major causes of morbidity and mortality, multisystemic complications were identified, including hematological ones. Several ITP relapse cases post-mRNA SARS-CoV-2 vaccines have been reported, and different pathophysiological theories have been proposed.

Purpose: The objective of this study is to identify the causal relationship between mRNA COVID-19 vaccines and ITP relapse, to highlight the longer-term effect of these vaccines on the platelet count more than 6 months after receiving the vaccine, and to identify if there is a statistical difference between Comirnaty and Spikevax vaccines on ITP relapse rate.

Patients and methods: In this retrospective study, 67 patients with known ITP were followed before and after receiving the mRNA COVID-19 vaccine. The follow-up parameters included platelet counts when available and bleeding symptoms. All patients were adults over 18 years old, with no other identified causes of thrombocytopenia. Forty-seven patients received the Comirnaty vaccine, and 20

patients received the Spikevax vaccine.

Results: Data analysis showed 6% ITP relapse in the first 3 months, and a 10% relapse rate 3-6 months after receiving one of the mRNA COVID-19 vaccines, with no statically significant difference between the two vaccines.

Conclusion: mRNA COVID-19 vaccines increase the risk of ITP relapse and can lead to a prolonged reduction in platelet count in a proportion of ITP patients, with no statistically significant difference between Comirnaty and Spikevax vaccines.

Keywords: COVID-19; ITP; relapse; vaccine.

Citation: Qasim H, Rahhal A, Husain A, Alammora A, Alsa'ed K, Alsayed AAM, Faiyoumi B, Maen AbuAfifeh L, Abu-Tineh M, Alshurafa A, Yassin MA. Immune Thrombocytopenia Relapse in Patients Who Received mRNA COVID-19 Vaccines. J Blood Med. 2023 Apr 14;14:295-302. doi: 10.2147/JBM.S396026. PMID: 37082002; PMCID: PMC10112532.

Impact Factor: 1.6

The effects of thrombocytopenia, type 2 diabetes mellitus, and endothelial dysfunction on clinical outcomes in patients with COVID-19

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Abstract

Diabetes mellitus is a well-recognized contributor to increased COVID-19 severity. Endothelial dysfunction has been implicated in the pathogenesis of COVID-19, while thrombocytopenia has been identified as a potential risk factor for severe COVID-19. In this study, we evaluated the combined effect of thrombocytopenia and other markers of endothelial dysfunction on disease outcomes in patients with type 2 diabetes and active COVID-19 infection. Our aim was to risk stratify patients with COVID-19 and type 2 diabetes mellitus, which can help identify patients with high-risk features who will benefit the most from hospital admission and a high level of care. This cross-sectional study was performed after reviewing secondary data of 932 patients with COVID-19 and type 2 diabetes mellitus in the outpatient and inpatient settings across Qatar between March 1, 2020 and May 7, 2020. Univariate and multivariate analyses, with adjustment for low platelet counts, were performed for the following variables: age, hemoglobin, white blood cells (WBC), lymphocytes, monocytes, eosinophils, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, ferritin, D-dimer, and interleukin 6. Increasing age was associated with an increased risk for death and/or intensive care unit admission in diabetic patients with COVID-19 who have low platelet counts. These findings support the evidence found in the literature and give special attention to COVID-19 patients with low platelet counts and diabetes mellites. These results can guide physicians in making clinical decisions regarding hospital admission and escalation of care during follow-up in this population of patients.

Keywords: COVID-19; Diabetes Mellitus; Endothelial Dysfunction; thrombocytopenia.

Citation: Faisal M, Alzahraa Al-Hattab F, Mohammed Al-Boinin A, Mahmoud Al-Qudah B, Waheed MA, Danjuma M. The effects of thrombocytopenia, type 2 diabetes mellitus, and endothelial dysfunction on clinical outcomes in patients with COVID-19. Qatar Med J. 2022 Dec 27;2023(1):3. doi: 10.5339/qmj.2023.3. PMID: 36588776; PMCID: PMC9800283.

Impact Factor: 1.14

Effect of Hydroxyurea Therapy on Growth Parameters in Older Children (6-15 Year-Old) with Sickle Cell Disease: Low Dose Versus High Dose

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Abstract

Growth impairment is a known complication of sickle cell disease (SCD). Few studies explored the potential effects of hydroxyurea (HU) on growth in children with SCD in relation to HU dose and response. This is a prospective study conducted at Sultan Qaboos University Hospital, Oman, and included 91 SCD patients with age below 16 years when started on HU, aiming to explore the potential effect/s of HU on growth parameters of older children with SCD in relation to their clinical improvement and the dose required for this improvement. Weight, height, and body mass index (BMI) were collected at baseline, 6 and 18 months after initiation. Anthropometric data were compared to WHO standards. Initial height and BMI Z scores (HAZ and WAZ) were lower compared to WHO norms. HAZ and WAZ did not change significantly after 6 and 18 months on HU therapy. However, BMI Z-scores improved significantly after 6 and 18 months of follow-up (p value 0.044 and 0.028 respectively). No significant changes were observed in WAZ or HAZ among patients on low dose versus those on high dose. BMI Z score improved significantly after 18 months of low dose group ($p = 0.014$) but did not change in those on high dose HU. In conclusion, HU therapy did not adversely affect weight and height growth in older children with SCD. BMI Z scores improved at 18 months in patients on low dose but not in those on high dose ($p = 0.014$).

Keywords: Sickle cell disease; growth; hydroxyurea.

Citation: Khater D, Al-Mulaabed S, Alomairi A, Elshinawy M, Soliman A, Elshinawy N, Wali Y, Al Yaarubi S. Effect of Hydroxyurea Therapy on Growth Parameters in Older Children (6-15 Year-Old)

with Sickle Cell Disease: Low Dose Versus High Dose. Hemoglobin. 2023 Nov;47(4):157-162. doi: 10.1080/03630269.2023.2254238. Epub 2023 Sep 10. PMID: 37691435.

Impact Factor: 1.0

NON–MALIGNANT HEMATOLOGY

CASE REPORTS

Sickle cell leg ulcer successfully managed by hyperbaric oxygen: a case report

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Abstract

Sickle cell leg ulcers (SCLUs) are usually chronic, painful, and devastating complications of sickle cell disease. Skin vaso-occlusion with compromised blood flow, chronic inflammation, and endothelial dysfunction is thought to be the underlying mechanism. It is usually slow to heal, and it may become chronic and superinfected. The management of SCLUs is usually challenging and requires a multidisciplinary team. Multiple systemic and local therapies have been tried in SCLU treatment. However, the outcome is variable: currently, there are no official recommendations for the best effective treatment. Herein, we report a 34-year-old male patient with non-transfusion-dependent sickle cell disease who was suffering from a chronic left ankle ulcer and was successfully managed with hyperbaric oxygen therapy, resulting in a complete resolution of this devastating complication.

Keywords: hyperbaric oxygen; leg ulcer; sickle cell disease; wound care; wound healing.

Citation: Alshurafa A, Alkhatib M, Abu-Tineh M, Yassin MA. Sickle cell leg ulcer successfully managed by hyperbaric oxygen: a case report. Front Med (Lausanne). 2023 Jun 15;10:1171971. doi: 10.3389/fmed.2023.1171971. PMID: 37396892; PMCID: PMC10310543.

Impact factor: 3.9

Congenital Methemoglobinemia: First Confirmed Case in the Arab Population with a Novel Variant in the *CYB5R* Gene in the State of Qatar: A Case Report

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Abstract

Methemoglobinemia (MetHb) is a rare hematological condition characterized by high methemoglobin levels in the blood. It happens when hemoglobin is oxidized, resulting in hypoxia and cyanosis, which may occur in inherited or acquired forms. Inherited or congenital methemoglobinemia is a rare autosomal recessive condition and has never been reported in the Arab population. Here we report a case of a 22-year-old Arab man with a positive family history who presented with bluish discoloration of the fingers and lips and was found to have methemoglobinemia. Genetic study on the patient and his family revealed compound heterozygous variants in the CYB5R3 Exon 5 c.431G>A p.Gly144Asp likely pathogenic variant and CYB5R3 Exon 9 c.871G>A p.Val291Met variant of unknown significance. We suggest that the novel c.871G>A p.Val291Met variant could be causative for methemoglobinemia.

Keywords: Arab; Qatar; methemoglobinemia.

Citation: Al-Abdulmalek A, Al-Sulaiman R, Abu-Tineh M, Yassin MA. Congenital Methemoglobinemia: First Confirmed Case in the Arab Population with a Novel Variant in the CYB5R Gene in the State of Qatar: A Case Report. J Blood Med. 2023 Mar 31;14:247-251. doi: 10.2147/JBM.S395865. PMID: 37025988; PMCID: PMC10072335.

Impact factor: 2.0

Glanzmann Thrombasthenia Associated with Siderotic Synovitis and Arthropathy: A Case Report

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Abstract

Glanzmann thrombasthenia is a bleeding disorder with a low incidence. It typically manifests as superficial bleeding episodes, which tend to be mild. Deep organ involvement is not uncommon but remains rare due to the rarity of the disease itself and the unusual association between platelet disorders and deep organ implications. A 17-year-old boy with Glanzmann thrombasthenia since infancy developed ankle pain after a minor trauma. His initial workup was negative, but he continued to experience ankle pain. A magnetic resonance imaging (MRI) done after four weeks suggested siderotic synovitis. The patient was lost to follow-up after that and returned after two years with recurrent left ankle pain. Imaging and studies have shown evidence of chronic arthropathy. A specialized orthopedic team assessed the patient. The patient underwent intra-articular steroid injection for pain relief and was referred to continue physical therapy. In conclusion, hemarthrosis is more common in hemophilia than in platelet disorders and has potential morbidity and quality-of-life implications.

Keywords: Glanzmann thrombasthenia; hemarthrosis; synovitis.

Citation: Alawad MJ, Abu-Tineh M, Alshurafa A, Al-Taie A, Yousaf A, Yassin MA. Glanzmann Thrombasthenia Associated with Siderotic Synovitis and Arthropathy: A Case Report. J Blood Med. 2023 Nov 3;14:563-567. doi: 10.2147/JBM.S418937. PMID: 37941894; PMCID: PMC10629506.

Impact factor: 2.0

Recurrence of acute chest syndrome post stopping Crizanlizumab, the dilemma of stopping vs continuation in patient with sickle cell disease: case report

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Abstract

Sickle cell disease (SCD) is one of the most common hematological diseases, which results in variable complications. The treatment of SCD is evolving but limited options are available for now. Acute chest syndrome (ACS) is one of the serious complications observed in SCD and a challenging one in prevention. Crizanlizumab is a monoclonal antibody that binds to P-selectin and improves blood flow by preventing sickle cell adhesion to endothelium, resulting in improvement of vaso-oclusive crises (VOC). It is not well evaluated in terms of ACS prevention. Here we report a 23-year-old patient with SCD and recurrent ACS; she was started on Crizanlizumab and she had no more ACS, but once she was off Crizanlizumab she developed ACS again, later Crizanlizumab was re-started, and the patient has improved significantly.

Keywords: Crizanlizumab; Hydroxyurea; Voxelotor; acute chest syndrome; exchange transfusion; hemoglobinopathies; sickle cell disease; vaso-occlusive crisis.

Citation: Afana MS, Abu-Tineh M, Alshurafa A, Yasin AK, Ahmed K, Abdulgayoom M, Yassin MA. Recurrence of acute chest syndrome post stopping Crizanlizumab, the dilemma of stopping vs continuation in patient with sickle cell disease: case report. Hematology. 2023 Dec;28(1):2229115. doi: 10.1080/16078454.2023.2229115. PMID: 37519115.

Impact Factor: 1.9

Romiplostim use for thrombocytopenia following allogeneic hematopoietic stem cell transplantation: a case series from a single center in Qatar

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Abstract

Thrombocytopenia is a common and serious complication that can occur following hematopoietic stem cell transplantation (HSCT), and it contributes to increased morbidity and mortality. The mechanisms of post-HSCT thrombocytopenia are multifactorial and complex. There are no clear consensus and guidelines for managing thrombocytopenia post-HSCT. Recently, there has been promising use of thrombopoietin receptor agonists (TPO-RAs), particularly eltrombopag and romiplostim, as treatments for post-HSCT thrombocytopenia. Notably, that this indication is considered off-label, and data in this use are limited. Based on the existing body of evidence, romiplostim emerges as a safe and effective option for individuals with transfusion-dependent thrombocytopenia after HSCT. In this context, we present a summary of our experience at a single center, where romiplostim was used in the management of post-HSCT thrombocytopenia due to poor graft function. Notably, all four cases responded positively to romiplostim treatment, and no significant adverse events were observed.

Keywords: Hematopoietic stem cell transplantation; Romiplostim; Thrombocytopenia; Thrombopoietin receptor agonists.

Citation: Al-Mashdali AF, Gulied A, Bakr MM, Yassin MA. Romiplostim use for thrombocytopenia following allogeneic hematopoietic stem cell transplantation: a case series from a single center in Qatar. Hematology. 2023 Dec;28(1):2280872. doi: 10.1080/16078454.2023.2280872. Epub 2023 Nov 14. PMID: 37961987.

Impact factor: 1.9

Refractory cold agglutinin disease successfully treated with daratumumab. A case report and review of literature

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Abstract

Background: Cold agglutinin disease (CAD) is immune-mediated hemolytic anemia. The disease is caused by cold reactive autoantibodies that induce hemolysis through the activation of the complement pathway. Most patients with CAD are elderly, and half may have refractory CAD that may not respond to the first-line treatment option (i.e. rituximab). Some cases are refractory to multiple lines of therapy, including chemotherapeutic agents, which might be toxic, especially for elderly patients. Daratumumab is a human monoclonal antibody targeting CD 38 glycoprotein, a transmembrane protein highly expressed in lymphoid and plasma cells. Daratumumab is currently approved for treating multiple myeloma and is used mainly as a combination therapy with other agents.

Case presentation: Our patient is a 69-year-old female diagnosed with CAD after presenting with severe anemia and significant circulatory symptoms. Rituximab was not effective in controlling her disease, and she refused other available chemotherapeutic agents due to their side effects profile. We used daratumumab combined with erythropoietin, which led to a dramatic response measured by stabilizing her hemoglobin levels and transfusion independence.

Conclusion: Our case is the third reported case of refractory CAD successfully treated with daratumumab, which suggests that daratumumab might be a potential agent for the treatment and control of refractory Cold Agglutinin Disease.

Keywords: CD 38 protein; Cold agglutinin disease; autoimmune diseases; daratumumab; hemoglobin; hemolytic anemia; monoclonal antibodies; red blood cells.

Citation: Mohamed A, Alkhatib M, Alshurafa A, El Omri H. Refractory cold agglutinin disease successfully treated with daratumumab. A case report and review of literature. Hematology. 2023 Dec;28(1):2252651. doi: 10.1080/16078454.2023.2252651. PMID: 37664905.

Impact Factor: 1.9

Myocardial Infarction as an Initial Presentation of Essential Thrombocythemia With Calreticulin (CALR) Mutation (None Type 1, None Type 2)

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Abstract

Essential thrombocythemia (ET) is one of the classical Philadelphia-negative myeloproliferative neoplasms with different mutations that can be associated with it, like Janus kinase 2 (JAK2), myeloproliferative leukemia protein (MPL), and Calreticulin (CALR) (types 1 and 2). However, there is a lack in the literature concerning other types of CALR mutations and their clinical significance and prognosis. Here we report a 42-year-old male with type 2 diabetes who presented with an inferior ST-elevation myocardial infarction and thrombocytosis. The diagnosis of ET with CALR (neither type 1 nor type 2) was confirmed, which suggests the pathognomonic feature of this mutation.

Keywords: calreticulin; essential thrombocythemia; myeloproliferative neoplasm; myocardial infarction; thrombosis.

Citation: Afana M, Abu-Tineh M, Ellahie A, Ismail O, Sideeg D, Albattah A, Yassin MA. Myocardial Infarction as an Initial Presentation of Essential Thrombocythemia With Calreticulin (CALR) Mutation (None Type 1, None Type 2). Cureus. 2023 Jan 10;15(1):e33612. doi: 10.7759/cureus.33612. PMID: 36788855; PMCID: PMC9910808.

Impact Factor: 1.2

Congenital Methemoglobinemia in a 33-Year-Old Patient: A Case Report on a Rare Presentation and a Review of the Literature

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Abstract

Cyanosis and dyspnea are common complaints in adults and have broad differential diagnoses, of which rare ones such as congenital methemoglobinemia should always be considered in the differential diagnosis. Methemoglobinemia might be acquired or congenital. Patients' symptoms vary from severe shortness of breath, mental status changes, and cyanosis to none. The diagnosis of congenital methemoglobinemia is challenging and requires high index of suspension, especially in older patients. In addition, when diagnosed the treatment of congenital methemoglobinemia is oral ascorbic acid which is readily available. We present a rare case of a 33-year-old lady, who had a long history of recurrent episodes of cyanosis, headache, and fatigue. After excluding cardiopulmonary causes, methemoglobin levels were measured and found to be high, and the chart review revealed high levels of methemoglobin in all her previous episodes, without exposure to any offending agent. This raised the concern of a late diagnosis of congenital methemoglobinemia. The patient was treated with a high dose of ascorbic acid resulting in resolution of the symptoms. Congenital methemoglobinemia is a rare diagnosis that needs a high index of suspicion, especially in adults. A thorough history, physical examination, and multiple laboratory tests are needed to confirm the diagnosis and rule out other causes.

Keywords: asian; congenital; cyanosis; late diagnosis; methemoglobinemia.

Citation: Aldeeb M, Khalil IA, Yassin MA. Congenital Methemoglobinemia in a 33-Year-Old Patient: A Case Report on a Rare Presentation and a Review of the Literature. Cureus. 2023 Mar 10;15(3):e35974. doi: 10.7759/cureus.35974. PMID: 37041911; PMCID: PMC10082972.

Impact Factor: 1.2

Elderly Patient With Hematological and Neurological Manifestations of Undetermined Origin: A Diagnostic Dilemma of Pernicious Anemia

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Abstract

Pernicious anemia (PA) is a chronic inflammatory destructive disease of parietal cells of predominantly the gastric fundus. It leads to vitamin B12 (cobalamin) deficiency secondary to a deficiency of intrinsic factors. Despite the medical advances nowadays, diagnosing PA can be challenging. This report highlights a neglected case of PA with ongoing subacute combined degeneration of the cord (SCDS) in an elderly patient. An 86-year-old lady with multiple comorbidities was referred to the hematology outpatient clinic for refractory anemia for the last two months. At first, her general practitioner (GP) treated her as a case of anemia of chronic disease but without improvement. Her initial clinical assessment revealed hematological and neurological manifestations of undetermined origin, including global weakness, hypertonia, and hyperreflexia with sensory deficits, especially in the lower limbs. On investigation, the hemoglobin level was 9 g/dL with high indirect bilirubinemia and lactate dehydrogenase (LDH). Despite the normal mean corpuscular volume (MCV) and peripheral blood smear, positive anti-intrinsic factor and parietal cell antibodies tests were subsequently reported, suggesting the diagnosis of PA. As a result, she was commenced on lifelong parenteral cobalamin replacement therapy. On follow-up visits of three months, she illustrated a clinical recovery in fatigability and paranesthesia. As expected, the laboratory parameters revealed a rise in hemoglobin level (11 g/dL) and serum vitamin B12 (418 pg/mL). However, she remained bedridden with spastic limbs. Clinicians should have a high index of suspicion since PA is a rare disease with variable clinical presentations. The optimal management approach is by a multidisciplinary care team of internists, neurologists, gastroenterologists, and hematologists.

Keywords: diagnosis challenges; multidisciplinary care approach; pernicious anemia; subacute combined degeneration; vitamin b12 deficiency.

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Impact Factor: 1.2

Toe Gangrene as the First Presenting Symptom of Essential Thrombocythemia: A Case Report

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Abstract

Essential thrombocythemia is a myeloproliferative neoplasm. Thrombosis and bleeding complications are common with myeloproliferative neoplasms, particularly essential thrombocythemia and polycythemia vera. Here, we report the case of a 52-year-old female who presented initially with painful toe swelling and discoloration. Initial imaging showed a small abscess. An incision and drainage, and debridement of toe dry gangrene were performed twice in two months with no improvement in her complaint and worsening discoloration, ending in a toe amputation. Two years later, the patient was referred to a hematology clinic for a high platelet count. On review of her medical records, the patient had the same numbers during the initial presentation. The patient's condition was diagnosed retrogradely by a hematologist as essential thrombocythemia. This case sheds light on myeloproliferative neoplasm as a differential diagnosis in patients with atypical thrombosis. Thinking in such a way could have diagnosed our patient two years earlier.

Keywords: ischemia; lower limb; myeloproliferative neoplasm; thrombocythemia; thrombosis.

Citation: Altayyan MM, Abu-Tineh M, Alshurafa A, Abdulgayoom M, Afana M, Ahmed K, Toba HA, Yassin MA. Toe Gangrene as the First Presenting Symptom of Essential Thrombocythemia: A Case Report. Cureus. 2023 Jul 24;15(7):e42388. doi: 10.7759/cureus.42388. PMID: 37621813; PMCID: PMC10446243.

Impact Factor: 1.2

A Challenging Case of a Patient with Immune Thrombocytopenic Purpura on Eltrombopag Who Developed Atrial Fibrillation: An Anticoagulation Dilemma

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Abstract

A 61-year-old female, who was a known case of immune thrombocytopenic purpura (ITP) on eltrombopag, was admitted for atrial fibrillation (AF). Labs showed a platelet count of 116 × 103/µL. AF reverted to sinus rhythm by cardioversion. Therapeutic enoxaparin was started for two days. She was discharged on dabigatran for four weeks. The choice of anticoagulation in these cases (ITP and AF) is not straightforward and needs further research.

Keywords: anticoagulation; atrial fibrillation; cardiovascular disorders; hematology; immune thrombocytopenic purpura.

Citation: Yasin AK, Abu-Tineh M, Alshurafa A, Ahmed K, Abdulgayoom M, Afana M, Yassin MA. A Challenging Case of a Patient With Immune Thrombocytopenic Purpura on Eltrombopag Who Developed Atrial Fibrillation: An Anticoagulation Dilemma. Cureus. 2023 Feb 15;15(2):e35001. doi: 10.7759/cureus.35001. PMID: 36938285; PMCID: PMC10020874.

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Omicron-Induced Immune Thrombocytopenia: A Case Report

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Abstract

Coronavirus disease 2019 is a systemic infection that significantly impacts the hematopoietic system and hemostasis. Among the hematological manifestations described, severe and symptomatic thrombocytopenia is rare. Immune thrombocytopenia (ITP), also known as idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura, is an acquired thrombocytopenia caused by autoantibodies against platelet antigens. It is one of the more common causes of thrombocytopenia in otherwise asymptomatic adults. Here, we report the case of a patient who developed ITP after a severe acute respiratory syndrome coronavirus 2 infection to highlight the rarer hematological manifestations of the disease and the changes in treatment.

Keywords: covid-19; itp; ivig; steroids; thrombocytopenia.

Citation: Toba HA, Abu-Tineh M, Alshurafa A, Ahmed K, Mohammed B, Altayyan MM, Abdulgayoom M, Yassin MA. Omicron-Induced Immune Thrombocytopenia: A Case Report. Cureus. 2023 May 29;15(5):e39648. doi: 10.7759/cureus.39648. PMID: 37388604; PMCID: PMC10306311.

Impact Factor: 1.2

Co-infection of Cytomegalovirus and Epstein-Barr Virus in an Immunocompetent Patient: A Case Series and Literature Review

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Abstract

Cytomegalovirus (CMV) infection or Epstein-Barr virus (EBV) infection in immunocompetent patients usually resolves without treatment. However, it can cause severe symptoms that can last for several weeks, especially in immunocompromised patients. Indications for antiviral immunocompetent individuals with CMV disease are not well-established. Here, we report two cases who had concomitant CMV-EBV infection. The first patient ultimately received anti-CMV therapy with significant improvement in symptoms and labs. The second patient had a milder disease course and was treated conservatively.

Keywords: cmv ebv; cytomegalovirus-cmv; ebv-associated hepatitis; hepatitis; viruses.

Citation: AlAmeen O, Mohammed A, Faisal M, Kohla S, Abdulhadi A. Co-infection of Cytomegalovirus and Epstein-Barr Virus in an Immunocompetent Patient: A Case Series and Literature Review. Cureus. 2023 Oct 24;15(10):e47599. doi: 10.7759/cureus.47599. PMID: 38022095; PMCID: PMC10667022.

Impact Factor: 1.2

Rare congenital Dyserythropoietic anemia of childhood: A case report

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Abstract

Congenital dyserythropoietic anemias (CDA) is a heterogeneous class of anemia of varying degrees of ineffective erythropoiesis and secondary hemochromatosis. We reported a case of CDA and showed our approach to reaching a diagnosis, highlighting the importance of the typical morphological appearance of bone marrow erythroblasts to reach the diagnosis.

Keywords: CDA; anemia; bone marrow; case report; congenital dyserythropoietic anemia; erythropoiesis; pediatrics.

Citation: Al Hussien HF, Al-Ekeer BN, Serhan HA, Haddadin I, Nashwan AJ. Rare congenital Dyserythropoietic anemia of childhood: A case report. Clin Case Rep. 2023 Feb 15;11(2):e6975. doi: 10.1002/ccr3.6975. PMID: 36817311; PMCID: PMC9932249.

Impact factor: 1.089

NON-MALIGNANT HEMATOLOGY

REVIEW ARTICLES

Artificial intelligence in sickle disease

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Abstract

Artificial intelligence (AI) is rapidly becoming an established arm in medical sciences and clinical practice in numerous medical fields. Its implications have been rising and are being widely used in research, diagnostics, and treatment options for many pathologies, including sickle cell disease (SCD). AI has started new ways to improve risk stratification and diagnosing SCD complications early, allowing rapid intervention and reallocation of resources to high-risk patients. We reviewed the literature for established and new AI applications that may enhance management of SCD through advancements in diagnosing SCD and its complications, risk stratification, and the effect of AI in establishing an individualized approach in managing SCD patients in the future. Aim: to review the benefits and drawbacks of resources utilizing AI in clinical practice for improving the management for SCD cases.

Keywords: Artificial intelligence; Convolutional neural networks; Hemoglobinopathies; Machine learning; Sickle cell.

Citation: Elsabagh AA, Elhadary M, Elsayed B, Elshoeibi AM, Ferih K, Kaddoura R, Alkindi S, Alshurafa A, Alrasheed M, Alzayed A, Al-Abdulmalek A, Altooq JA, Yassin M. Artificial intelligence in sickle disease. Blood Rev. 2023 Sep;61:101102. doi: 10.1016/j.blre.2023.101102. Epub 2023 Jun 8. PMID: 37355428.

Impact factor: 10.626

Using artificial intelligence to improve body iron quantification: A scoping review

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Abstract

This scoping review explores the potential of artificial intelligence (AI) in enhancing the screening, diagnosis, and monitoring of disorders related to body iron levels. A systematic search was performed to identify studies that utilize machine learning in iron-related disorders. The search revealed a wide range of machine learning algorithms used by different studies. Notably, most studies used a single data type. The studies varied in terms of sample sizes, participant ages, and geographical locations. AI's role in quantifying iron concentration is still in its early stages, yet its potential is significant. The question is whether AI-based diagnostic biomarkers can offer innovative approaches for screening, diagnosing, and monitoring of iron overload and anemia.

Keywords: Anemia; Artificial intelligence; Deep learning; Hemochromatosis; Iron overload; Liver Iron concentration; Machine learning.

Citation: Nashwan AJ, Alkhawaldeh IM, Shaheen N, Albalkhi I, Serag I, Sarhan K, Abujaber AA, Abd-Alrazaq A, Yassin MA. Using artificial intelligence to improve body iron quantification: A scoping review. Blood Rev. 2023 Nov;62:101133. doi: 10.1016/j.blre.2023.101133. Epub 2023 Sep 18. PMID: 37748945.

Impact Factor: 7.5

Concurrent coronary artery disease and immune thrombocytopenia: a systematic review

Alaa Rahhal [1], Drew Provan [2], Khaled Shunnar [3], Mostafa Najim [4], Ashraf Omer Ahmed [5], Waail Rozi [5], Murtadha Al-Khabori [6], Mahmoud Marashi [7], Mona AlRasheed [8], Hani Osman [9], Mohamed Yassin [10]

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Abstract

Introduction: Coronary artery disease (CAD) management in the setting of immune thrombocytopenia (ITP) remains very challenging to clinicians as a reasonable balance between bleeding and thrombosis risks needs to be achieved, and the evidence guiding such management is scarce.

Methods: We conducted a systematic review following the PRISMA guidelines to summarize the available literature on the management and outcomes of CAD coexisting with ITP. We searched PubMed and Embase for studies published in English exploring CAD and ITP management until 05 October 2022. Two independent reviewers screened and assessed the articles for inclusion. Patients' characteristics, CAD treatment modalities, ITP treatment, and complications were reported.

Results: We identified 32 CAD cases, among which 18 cases were revascularized with percutaneous coronary intervention (PCI), 12 cases underwent coronary artery bypass graft surgery (CABG), and two cases were managed conservatively. More than 50% were men, with a mean age of 61 ± 13 years and a mean baseline platelet count of 52 ± 59 × 109/L. Irrespective of the revascularization modality, most patients were treated with either corticosteroids alone, intravenous immunoglobulins (IVIG) alone, or in combination. Among those who underwent PCI, two patients had bleeding events, and one patient died. Similarly, among those with CABG, one patient developed bleeding, and one patient died.

Conclusion: We found that revascularization with either PCI or CABG with the concurrent use of corticosteroids and/or IVIG for ITP was feasible, with an existing non-negligible risk of bleeding and mortality.

Keywords: acute coronary syndrome; coronary artery bypass graft surgery; coronary artery disease; immune thrombocytopenia; intravenous immunoglobulins; percutaneous coronary intervention.

Citation: Rahhal A, Provan D, Shunnar K, Najim M, Ahmed AO, Rozi W, Al-Khabori M, Marashi M, AlRasheed M, Osman H, Yassin M. Concurrent coronary artery disease and immune thrombocytopenia: a systematic review. Front Med (Lausanne). 2023 Oct 10;10:1213275. doi: 10.3389/fmed.2023.1213275. PMID: 37886354; PMCID: PMC10598342.

Impact Factor: 3.9

Applications of Artificial Intelligence in Thrombocytopenia

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Abstract

Thrombocytopenia is a medical condition where blood platelet count drops very low. This drop in platelet count can be attributed to many causes including medication, sepsis, viral infections, and autoimmunity. Clinically, the presence of thrombocytopenia might be very dangerous and is associated with poor outcomes of patients due to excessive bleeding if not addressed quickly enough. Hence, early detection and evaluation of thrombocytopenia is essential for rapid and appropriate intervention for these patients. Since artificial intelligence is able to combine and evaluate many linear and nonlinear variables simultaneously, it has shown great potential in its application in the early diagnosis, assessing the prognosis and predicting the distribution of patients with thrombocytopenia. In this review, we conducted a search across four databases and identified a total of 13 original articles that looked at the use of many machine learning algorithms in the diagnosis, prognosis, and distribution of various types of thrombocytopenia. We summarized the methods and findings of each article in this review. The included studies showed that artificial intelligence can potentially enhance the clinical approaches used in the diagnosis, prognosis, and treatment of thrombocytopenia.

Keywords: artificial intelligence; diagnosis; prediction; prognosis; thrombocytopenia; transmission.

Citation: Elshoeibi AM, Ferih K, Elsabagh AA, Elsayed B, Elhadary M, Marashi M, Wali Y, Al-Rasheed M, Al-Khabori M, Osman H, Yassin M. Applications of Artificial Intelligence in Thrombocytopenia. Diagnostics (Basel). 2023 Mar 10;13(6):1060. doi: 10.3390/diagnostics13061060. PMID: 36980370; PMCID: PMC10047875.

Impact factor: 3.6

Applications of Artificial Intelligence in Thalassemia: A Comprehensive Review

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Abstract

Thalassemia is an autosomal recessive genetic disorder that affects the beta or alpha subunits of the hemoglobin structure. Thalassemia is classified as a hypochromic microcytic anemia and a definitive diagnosis of thalassemia is made by genetic testing of the alpha and beta genes. Thalassemia carries similar features to the other diseases that lead to microcytic hypochromic anemia, particularly iron deficiency anemia (IDA). Therefore, distinguishing between thalassemia and other causes of microcytic anemia is important to help in the treatment of the patients. Different indices and algorithms are used based on the complete blood count (CBC) parameters to diagnose thalassemia. In this article, we review how effective artificial intelligence is in aiding in the diagnosis and classification of thalassemia.

Keywords: B-thalassemia; artificial intelligence; diagnosis; iron deficiency anemia; thalassemia.

Citation: Ferih K, Elsayed B, Elshoeibi AM, Elsabagh AA, Elhadary M, Soliman A, Abdalgayoom M, Yassin M. Applications of Artificial Intelligence in Thalassemia: A Comprehensive Review. *Diagnostics (Basel)*. 2023 Apr 26;13(9):1551. doi: 10.3390/diagnostics13091551. PMID: 37174943; PMCID: PMC10177591.

Impact factor: 3.6

Thrombopoietin-receptor agonists for adult patients with immune thrombocytopenia: a narrative review and an approach for managing patients fasting intermittently

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Abstract

Introduction: Thrombopoietin-receptor agonist (TPO-RAs) currently represent the state of art for treating immune thrombocytopenia. Their different molecular structures contribute to the difference in their pharmacodynamics and pharmacokinetics. This narrative review aims to provide an overview of the current TPO-RAs approved for primary immune thrombocytopenia (romiplostim, eltrombopag, avatrombopag) and the effect of intermittent fasting in adult patients receiving TPO-RAs.

Areas covered: Literature was searched with no limits on date or language, using various combinations of keywords. Data on the pharmacokinetics, pharmacodynamics, efficacy, and safety of TPO-RAs and the effect of intermittent fasting were summarized.

Expert opinion: Switching between TPO-RAs is a useful strategy to tackle some associated limitations. Romiplostim and avatrombopag have an advantage over eltrombopag as they do not require any dietary restrictions. In cases where romiplostim and avatrombopag are unavailable, patients should be educated on the appropriate administration, possible interactions, and dietary

restrictions before initiating eltrombopag.

Keywords: avatrombopag; eltrombopag; romiplostim; thrombocytopenia; thrombopoietin-receptor agonist.

Citation: Yassin MA, Al-Rasheed M, Al-Khaboori M, Marashi M, Osman H, Wali Y, Al Kindi S, Alsayegh F, Provan D. Thrombopoietin-receptor agonists for adult patients with immune thrombocytopenia: a narrative review and an approach for managing patients fasting intermittently. Front Cardiovasc Med. 2023 Dec 14;10:1260487. doi: 10.3389/fcvm.2023.1260487. PMID: 38162126; PMCID: PMC10755910.

Impact Factor: 3.6

The Role of p90 Ribosomal S6 Kinase (RSK) in Tyrosine Kinase Inhibitor (TKI)-Induced Cardiotoxicity

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Abstract

Targeted therapy, such as tyrosine kinase inhibitors (TKIs), has been approved to manage various cancer types. However, TKI-induced cardiotoxicity is a limiting factor for their use. This issue has raised the need for investigating potential cardioprotective techniques to be combined with TKIs. Ribosomal S6-kinases (RSKs) are a downstream effector of the mitogen-activated-protein-kinase (MAPK) pathway; specific RSK isoforms, such as RSK1 and RSK2, have been expressed in cancer cells, in which they increase tumour proliferation. Selective targeting of those isoforms would result in tumour suppression. Moreover, activation of RSKs expressed in the heart has resulted in cardiac hypertrophy and arrhythmia; thus, inhibiting RSKs would result in cardio-protection. This review article presents an overview of the usefulness of RSK inhibitors that can be novel agents to be assessed in future research for their effect in reducing cancer proliferation, as well as protecting the

heart from cardiotoxicity induced by TKIs.

Keywords: Anticancer; Cardiotoxicity; Tyrosine kinase inhibitors; p90 ribosomal S6 kinase.

Citation: Suleiman M, Al Najjar A, Zakaria ZZ, Ahmed R, Yalcin HC, Korashy HM, Uddin S, Riaz S, Abdulrahman N, Mraiche F. The Role of p90 Ribosomal S6 Kinase (RSK) in Tyrosine Kinase Inhibitor (TKI)-Induced Cardiotoxicity. J Cardiovasc Transl Res. 2023 Sep 19. doi: 10.1007/s12265-023-10431-4. Epub ahead of print. PMID: 37725271.

Impact Factor: 3.4

The effects of excess weight on glucose homeostasis in young adult females with beta-thalassemia major (beta-TM): a preliminary retrospective study

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Abstract

Background: With the rising prevalence of obesity worldwide, it is becoming imperative to detect disturbed glucose metabolism as early as possible in order to prevent type 2 diabetes (T2D) development.

Study design: The present retrospective observational study aimed to evaluate the relationship between BMI and glucose metabolism, insulin secretion and sensitivity indices, derived from glucose tolerance test (OGTT), in β -TM female patients who were overweight (BMI 25-29.9 kg/m2) and follow its outcome over time.

Subjects and methods: Eleven overweight and 11 females with ideal weight and β -TM, matched for age, were recruited. OGTT was undertaken and different indices for β-cell function, insulin sensitivity and insulin secretion were calculated.

Results: At first evaluation, 7 of 11 overweight β -TM patients (63.6%) and 3 of 11 normal weight β-TM patients (27.2%) had glucose dysregulation (GD) during OGTT. Overweight patients with β-TM

had increased HOMA-IR and QUICKI indices associated with decreased Matsuda WBISI index. The mean ± SD duration of follow-up was 4.5 ± 1.2 years. At last observation, 2/11 overweight patients had developed T2D (18.1%). In patients with normal weight, GD increased from 3/11 (27.2%) to 5/11 (45.4%), but none developed T2DM. The difference between SF at first and last observation (1,220 ± 702 vs.1,091 ± 454 ng/mL; P: 0.61) was not significant.

Conclusion: Overweight seems to be an additional risk factor for the development of GD in β-TM patients. This is particularly important in clinical practice, due to the lack of appropriate guidelines dedicated to this group of patients.

Citation: De Sanctis V, Daar S, Soliman AT, Tzoulis P, Yassin M, Kattamis C. The effects of excess weight on glucose homeostasis in young adult females with β-thalassemia major (β-TM): a preliminary retrospective study. *Acta Biomed*. 2023 Oct 17;94(5):e2023225. doi: 10.23750/abm.v94i6.14909. PMID: 37850764; PMCID: PMC10644933.

Impact factor: 3.206

Long-term efficacy and safety of L-glutamine in preventing sickle cell disease-related acute complications and hemolysis in pediatric and adult patients-Real-world, observational study

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abstract

Introduction: L-glutamine plays an important role in regulating oxidative stress, one of the key contributors to sickle cell disease pathophysiology. An earlier 48-week Phase 3 study conducted in the United States demonstrated significant reductions in acute complications associated with sickle cell disease, such as vaso-occlusive crises (VOCs) and acute chest syndrome (ACS) in patients on L-glutamine therapy compared to those on placebo (Niihara et al., 2018). This study also showed a significantly fewer number of hospitalizations and hospitalization days for those treated with L-glutamine. Our current real-world observational study is the first to report long term evaluation (120 weeks) of efficacy and safety of L-glutamine (Endari®) therapy in patients living with sickle cell disease in Qatar and French Guiana.

Methods: Nineteen patients (10 pediatric and 9 adults), 63% on hydroxyurea, with confirmed diagnosis of sickle cell disease (HbSS genotype) were treated with L-glutamine oral powder (~0.3 g/kg body weight) twice daily for 120 weeks. Of the enrolled patients, 4 patients were from Qatar with the Arab-Indian haplotype and 15 patients were from French Guiana with the African haplotype. The median age was 17 years (range 8 to 54 years) where 53% were <18 years of age. The median body weight of patients was 50 kilograms (range of 25 to 75 kilograms); 53% were males. Clinical events and laboratory parameters (hemoglobin, hematocrit, reticulocytes, and LDH) were collected

or measured at baseline, 24, 48, 72, 96, and at 120 weeks. Baseline measures for VOCs, number of hospitalizations, hospitalization days, ACS events, and blood transfusions were collected for the 12 months prior to L-glutamine initiation. Changes from baseline to 120 weeks (annualized) were analysed using MedCalc statistical software Version 20.015.

Results: Eighteen patients completed 120 weeks of the real-world L-glutamine treatment observation period. There were significantly fewer VOCs; median of 3 VOCs at baseline and median of 0 at 120 weeks. There were significantly fewer hospitalizations (median of 3 hospitalizations at baseline and 0 at 120 weeks), shorter hospitalization days (median of 15 days at baseline and 0 at end of the observation period), and fewer blood transfusions (median of 3 at baseline and 0 at 120 weeks). The change from baseline values to 120 weeks were significant ($p < .00001$) for VOCs, hospitalizations, days hospitalized, and the number of units transfused. The number of ACS events were also reduced from 11 at baseline to 0 at 120 weeks. Consistent with these findings, the mean increase in hemoglobin concentrations from baseline was 1.36 g/dL ± 0.17 SE and the mean percent increase in hematocrit from baseline was 5.85% ± 1.10 SE, both significantly improved at 120 weeks ($p < .001$) Figure 1A. Furthermore, mean reticulocyte counts decreased from baseline (-52.39 x 109/L ± 25.68 SE) and LDH levels decreased from baseline (-311.11 U/L ± 56.02 SE) both significantly changed at 120 weeks ($p < .001$) Figure 1B. Fewer number of patients were taking hydroxyurea at 120 weeks (8 patients) compared to baseline (12 patients). One patient died during the study (after the 72-week follow up visit) due to multiple deep vein thromboses resulting in a pulmonary embolism; this event was not related to L-glutamine treatment.

Conclusion: In this long-term observational study, oral L-glutamine therapy in pediatric and adults living with sickle cell disease resulted in sustained clinical efficacy with improvements in hematologic parameters. L-glutamine therapy was well-tolerated by all patients and there were no safety concerns.

Keywords: L-glutamine; acute chest syndrome; hemolysis; sickle cell disease; vaso-occlusive crisis.

Citation: Elenga N, Loko G, Etienne-Julan M, Al-Okka R, Adel AM, Yassin MA. "Long-term efficacy and safety of L-glutamine in preventing sickle cell disease-related acute complications and hemolysis in pediatric and adult patients-Real-world, observational study". Eur J Haematol. 2023 Jun;110(6):772-773. doi: 10.1111/ejh.13939. Epub 2023 Feb 20. PMID: 36732400.

Impact factor: 3.1

Genotypic and Phenotypic Composition of Sickle Cell Disease in the Arab Population - A Systematic Review

Fateen Ata [1], Alaa Rahhal [2], Lujain Malkawi [3], Phool Iqbal [4], Ibrahim Khamees [5], Mousa Alhiyari [5], Zohaib Yousaf [6], Hana Qasim [7], Awni Alshurafa [8], Sundus Sardar [9], Saad Javed [10], Liam Fernyhough [8 11], Mohamed Yassin [8]

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Abstract

Sickle cell disease (SCD) is a genetic disease influenced by ethnicity and regional differences in its clinical course. Recent advances in the management of SCD with newer therapies are being introduced to the Western population. However, many of these treatments are yet to be used in the Arabic SCD population. Understanding the genetic variations of SCD regionally is essential to anticipate the utilization of new treatments. This systematic review's main objective is to pool the available data on the genetic composition of SCD in the Arabic population. Data for 44,034 patients was extracted from 184 studies (11 case reports, 8 case series, 56 retrospectives, 107 prospective

observational studies, and 2 clinical trials) using PubMed, Scopus, and Google Scholar. Male (49%) and female (51%) patients were equally reported wherever gender was available (N=13105). Various SCD genotypes were reported in a total of 14,257 patients, including Hb SS (77%) Hb Sβ0 (9.9%), and Hb Sβ+ (7.2%), while the rest of the genotypes, including HbSC, HbSD, HbSE, HbSO Arab, Hb S/α-Thal, Hb Sβ0 + α-Thal, and HBS Oman were individually reported in <4% of the cases. Major SCD complications in the Arab population included pain crises (48.25%) followed by neurological complications (33.46%), hepatobiliary complications (25.53%), musculoskeletal complications (24.73%), and hemolytic anemia (23.57%). The treatments reported for SCD included hydroxyurea (20%), blood transfusion (14.32%), and Deferasirox (3.03%). We did not find the use of stem cell transplantation or newer treatments such as L-Glutamine, Voxelotor, Crizanlizumab, or gene therapy reported in any of the studies included in our review. This review highlights the genetic makeup of SCD in Arab countries and its common phenotypic manifestations and will help direct further research on SCD in this region, especially concerning genetic therapy.

Keywords: Arab; SCD; genotypes; sickle cell anemia; sickle cell disease.

Citation: Ata F, Rahhal A, Malkawi L, Iqbal P, Khamees I, Alhiyari M, Yousaf Z, Qasim H, Alshurafa A, Sardar S, Javed S, Fernyhough L, Yassin M. Genotypic and Phenotypic Composition of Sickle Cell Disease in the Arab Population - A Systematic Review. Pharmgenomics Pers Med. 2023 Feb 21;16:133-144. doi: 10.2147/PGPM.S391394. PMID: 36851992; PMCID: PMC9961577.

Impact Factor: 1.87

Low-Molecular-Weight Heparin Versus Warfarin in Adult Cancer Patients as a Precision Medicine for Thrombosis: A Systematic Review and Meta-Analysis

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Abstract

Venous thromboembolism (VTE) is a condition often seen in patients diagnosed with cancer and is recognized as a predictor of poor outcomes in these patients. The probability of VTE recurring is generally higher in people with cancer than in those without; hence, addressing this issue is essential when making healthcare decisions. Therefore, our systematic review was primarily designed to compare low-weight- molecular heparin (LMWH) to warfarin in reducing recurrent VTE among cancer patients. However, other outcomes were also evaluated, such as mortality and bleeding events observed more in cancer patients. The selection of relevant articles was carried out using a database search and a manual search, which involved reviewing reference lists of articles eligible for inclusion in the current review. The methodological quality of each included study was then assessed using Cochrane's risk of bias tool in the Review Manager software (RevMan 5.4.1). Additionally, pooled results were examined using the Review Manager software and presented as forest plots. Our search of electronic databases elicited a total of 2163 articles, of which only six were deemed eligible for inclusion and analysis. Data pooled from the six studies demonstrated the effectiveness of LMWH in minimizing the reoccurrence of VTE over warfarin [risk ratio (RR): 0.67; 95% CI: 0.47 - 0.95; p = 0.03]. However, LMWH had a similar effect statistically as warfarin on the major bleeding events (RR: 1.05; 95% CI: 0.62 - 1.77; p = 0.85), minor bleeding events (RR: 0.80; 95% CI: 0.54 - 1.20; p = 0.28), and all-cause mortality (RR: 1.00; 95% CI: 0.88 - 1.13; p = 0.99). While LMWH demonstrated its effectiveness in minimizing the incidence of VTE recurrence over warfarin in cancer patients, it had no statistical difference in terms of mortality or bleeding events when compared to warfarin. Based on our findings, we recommend that LMWH continues to be used as a first-line treatment regimen to mitigate recurrent VTE in cancer patients.

Keywords: dalteparin; enoxaparin; low-molecular weight heparin; malignancy; recurrent deep vein

thrombosis; recurrent venous thromboembolism; vitamin k antagonists; warfarin.

Citation: Zaki HA, Hamdi Alkahlout B, Basharat K, Elsayed WAE, Abdelrahim MG, Al-Marri NDR, Masood M, Shaban E. Low-Molecular-Weight Heparin Versus Warfarin in Adult Cancer Patients as a Precision Medicine for Thrombosis: A Systematic Review and Meta-Analysis. Cureus. 2023 Jul 1;15(7):e41268. doi: 10.7759/cureus.41268. PMID: 37533609; PMCID: PMC10390756.

Impact Factor: 1.2

COVID-19 and Anemia: What Do We Know So Far?

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Abstract

On 11 March 2020, the World Health Organization (WHO) declared the novel SARS-CoV-2 virus responsible for causing COVID-19, a global pandemic. The virus primarily targets the respiratory system but can also affect other systems, notably causing hematological pathologies. Anemia, a common hematologic disorder, is characterized by the reduced oxygen-carrying capacity of red blood cells. The existing literature has a suspected link between anemia and severe COVID-19 cases. Researchers are currently investigating the long-term complications of COVID-19 in anemic patients, as these complications may play a crucial role in predicting patient prognosis. Anemic individuals are at a higher risk of experiencing severe COVID-19 infections due to several contributing pathophysiological mechanisms, including thrombotic, hemorrhagic, and autoimmune etiologies. The primary effect of these mechanisms is a decrease in circulating hemoglobin levels, reducing oxygen availability for cells. This exacerbates the hypoxia caused by COVID-19-induced acute respiratory distress syndrome (ARDS). This review offers a comprehensive overview of the evidence regarding the long-term complications of COVID-19 in anemic patients.

Keywords: COVID-19; SARS-CoV-2; anemia; hematology; long COVID-19.

Citation: Abu-Ismail L, Taha MJJ, Abuawwad MT, Al-Bustanji Y, Al-Shami K, Nashwan A, Yassin M. COVID-19 and Anemia: What Do We Know So Far? Hemoglobin. 2023 May;47(3):122-129. doi: 10.1080/03630269.2023.2236546. Epub 2023 Jul 31. PMID: 37519257.

Impact Factor: 1.0

Chronic anemia complicated by cardiac failure, pulmonary hypertension, and pericardial effusion: a case report

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Abstract

Background: Worldwide, iron deficiency anaemia (IDA) is the most common cause of anaemia. Iron deficiency alone has an association with heart failure and pulmonary hypertension. Chronic iron deficiency anemia triggers various physiologic adjustments, leading to hyperdynamic circulation and enhanced hypoxic pulmonary vasoconstriction. Those mechanisms may result in the development of high output cardiac failure and pulmonary hypertension; however, pericardial effusion remains a rare association.

Case presentation: A 44-year-old Nepalese man presented with fatigability and swollen ankles. Except for a hemorrhoidectomy 4 years ago, he had no comorbidities. Labs confirmed severe iron deficiency anemia (hemoglobin 1.8 grams per deciliter) likely secondary to hemorrhoids. An echocardiogram revealed high output cardiac failure, pericardial effusion, and severe pulmonary hypertension. He responded well to the correction of anemia and diuretics with the resolution of vascular complications.

Conclusion: We report a unique presentation of chronic severe iron deficiency anemia complicated by heart failure, pulmonary hypertension, and pericardial effusion. We believe it to be the first-ever such case reported in the literature. These cardiovascular complications seem to result from internal homeostatic mechanisms against the chronic tissue hypoxemia observed in severe anemia. Furthermore, iron deficiency alone has an association with heart failure and pulmonary hypertension. After excluding other potential causes, we confirmed iron deficiency anaemia as the cause of those complications. The correction of anemia led to an excellent recovery without any sequelae. Our case

report highlights the fact that management of such a case should be focused on underlying etiology rather than the complications.

Keywords: Anemia; Cardiac failure; Heart failure; Iron deficiency; Pericardial effusion; Pulmonary hypertension.

Citation: Yousaf M, illahi M, Bibi A, Elhassan H, Sharif M, Abid AR, Omran MA, Hassan A, Haroon KH. Chronic anemia complicated by cardiac failure, pulmonary hypertension, and pericardial effusion: a case report. J Med Case Rep. 2023 Feb 7;17(1):44. doi: 10.1186/s13256-022-03686-z. PMID: 36750883; PMCID: PMC9906880.

Impact Factor: 1.0

Applications of Artificial Intelligence in Thalassemia: A Comprehensive Review

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Abstract

Thalassemia is an autosomal recessive genetic disorder that affects the beta or alpha subunits of the hemoglobin structure. Thalassemia is classified as a hypochromic microcytic anemia and a definitive diagnosis of thalassemia is made by genetic testing of the alpha and beta genes. Thalassemia carries similar features to the other diseases that lead to microcytic hypochromic anemia, particularly iron deficiency anemia (IDA). Therefore, distinguishing between thalassemia and other causes of microcytic anemia is important to help in the treatment of the patients. Different indices and algorithms are used based on the complete blood count (CBC) parameters to diagnose thalassemia. In this article, we review how effective artificial intelligence is in aiding in the diagnosis and classification of thalassemia.

Keywords: B-thalassemia; artificial intelligence; diagnosis; iron deficiency anemia; thalassemia.

Citation: Ferih K, Elsayed B, Elshoeibi AM, Elsabagh AA, Elhadary M, Soliman A, Abdalgayoom M, Yassin M. Applications of Artificial Intelligence in Thalassemia: A Comprehensive Review. Diagnostics (Basel). 2023 Apr 26;13(9):1551. doi: 10.3390/diagnostics13091551. PMID: 37174943; PMCID: PMC10177591.

Impact Factor: 0.33

Recurrent sideroblastic anemia during pregnancy

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Abstract

Sideroblastic anemia is a heterogeneous group of disorders typified by the presence of ring sideroblasts in the bone marrow and has congenital and acquired types. Sideroblastic anemia is a rare event in pregnancy. We report a case of a 32-year-old female patient, gravida 4 para 3, 27th weeks pregnant, who presented to the emergency department complaining of palpitation and generalized weakness for 2 weeks. She was found to have severe normochromic normocytic anemia, with hemoglobin of 4.2 g/dl, and low reticulocytes count of 13 × 103/μl. She gave a history of recurrent anemia, which had only occurred during pregnancy. Her bone marrow aspirate showed many ring sideroblasts concluding the diagnosis of sideroblastic anemia (SA). Further investigation revealed a significantly low pyridoxine level (vitamin B6) of (8 nmol/L). The Hb level improved with vitamin B6 replacement, without any transfusion support.

Keywords: acquired sideroblastic anemia; congenital sideroblastic anemia; heme biosynthesis; iron chelation; ring sideroblasts; vitamin B6.

Citation: Mohamed S, Ibrahim F, Alasafar MN, Alshurafa A, Akiki S, Soliman D, Kohla S, Amer A, Qasim H, Cherif H. Recurrent sideroblastic anemia during pregnancy. Clin Case Rep. 2023 Jan 11;11(1):e6814. doi: 10.1002/ccr3.6814. PMID: 36644616; PMCID: PMC9834147.

Impact Factor: 0.285

NON-MALIGNANT HEMATOLOGY

ABSTRACTS

Transplant Associated Thrombotic Microangiopathy: Acomprehensive Review and Local Experience

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Abstract

Introduction: Thrombotic Microangiopathy (TMA) is a rare, life-threatening severe condition characterized by microangiopathic hemolytic anemia, thrombocytopenia and microthrombi in the walls of small blood vessels leading to ischemic organ dysfunction. Transplant-associated TMA (TA-TMA) can occur as a complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT). The mechanism of TA-TMA is not fully understood, and conventional treatment options are based on targeting the identified risk factors and hypothesized pathophysiology. This review aimed to compile the information to date about TA-TMA and possible treatment strategies and report successful cases at the National Center for Cancer Care and Research (NCCCR).

Methods: Scientific databases were scoped for reviews on TA-TMA, its pathophysiology, risk factors and therapeutic strategies. Results were compiled to formulate an understanding of TA-TMA. Local cases of TA-TMA at NCCCR were also reported.

Results:TA-TMA pathophysiology and risk factors are described in Figure 1 and Table 1, respectively. Due to the complexity of the patient cases under investigation, TA-TMA diagnosis is clinical. Proposed diagnostic criteria include anemia, thrombocytopenia, elevated LDH, presence of schistocytes, hypertension, proteinuria, and elevated sC5b-9. Therapeutic approaches start the management of modifiable risk factors such as withdrawal or decreasing the dosage of calcineurin inhibitors (CNIs), control of hypertension and AKI, treatment of active infections and management of graft versus host disease (GvHD). Therapeutic plasma exchange (TPE) may benefit some patients who are positive for factor H autoantibodies. eculizumab, a humanized antibody against complement protein, can be highly effective in patients with TA-TMA. It is recommended for patients with high-risk features such as elevated sC5b-9 and proteinuria and can also be used for patients with organ damage or disseminated disease. Other available treatment options include rituximab and defibrotide. Other therapeutic agents are under clinical trials such as ravulizumab (C5 inhibitor), nomacopan (C5 and leukotriene B4 inhibitor) and narsoplimab (mannan-binding lectin-associated serine protease-2 [MASP-2] inhibitor). Four cases were diagnosed with TA-TMA at NCCCR between September 2017 and February 2023, as described in Figure 2. All cases recovered; however, the challenge remains in the choice of therapy. Thus far, the choice is to individualize therapy according to comorbidities, severity of clinical presentation and availability of the treatment options.

Conclusion: TA-TMA remains a significant clinical challenge for transplant physicians, and more research is needed to improve our understanding of its pathogenesis, diagnosis, and management, particularly in guiding the choice of therapy.

Citation: Benkhadra M, Gulied, A, Mohamed M, Mudawi D, Gaziev J, Al-khabori M, Yassin M. Transplant Associated Thrombotic Microangiopathy: A comprehensive Review and Local Experience. Blood 2023; 142 (Supplement 1): 7116. DOI: https://doi.org/10.1182/blood-2023-184374

Impact factor: 20.3

CONFERENCE ABSTRACTS AND POSTER PRESENTATIONS

Conference Abstracts and Poster Presentations

Title	Speaker
1st Qatar Stem Cell Transplantation Conference (QSCTC). Doha-Qatar 10-11 March 2023	
Implementation of BMT Pharmacist-Led Ambulatory Clinic at the National Center for Caner Care and Research	Amaal Gulied, Rola Ghasoub, Anas Hamad, Shereen Elazzazy.
Clinically Significant CMV Infection in Allogeneic Stem-Cell Transplant Recipients: A Single Center Experience.	Hawraa Shwaylia, Amaal Gulied, Aya Alasmar, Javid Gaziev
Cidofovir Use in Hematopoietic Stem-Cell Transplant Patients: A Retrospective Review	Maria Benkhadra, Farah Jibril, Hebatalla Afifi, Aya Alasmar, Amaal Gulied
MEF 2023.Doha-Qatar Mar-23	
Think Sepsis, Save lives: sustaining the gain amidst the COVID-19 pandemic.	Cicy Jacob, Farah Jibril , Emelita Ison , Mohammad Atieh , Priyadarshini Vatsyayan , Hiba ElTahir , Hatim El Derbhouhi, Dr Deena Mudawi, Sindhumole Nair, Jordana Delicana, Hannan Zadeh, Mutie Ahmed, Samar Hashim, Amir Nounou, Nayel Al Tarawneh, Awni AlShurafa, Mohammad Bakr.
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A Golden Step Towards Saving Lives: The Antibiotics Sepsis Kit.	Farah Jibril ,Anas Hamad, Elham Alsagga, Arwa Nasser.
Implementation of Pharmacist-Led Cancer Clinics (PLCCs) with Collaborative Prescribing Model at the National Cancer Center in Qatar.	Shereen Elazzazy, Rola Ghasoub, Amaal Gulied, Hebatallah Afifi, Maria Benkhadra, Nancy Kassem, Anas Hamad.

MASCC/JASCC/ISOO Annual Meeting 2023.NARA, JAPAN June 22-24 , 2023	
Safety and efficacy evaluation of Lenvatinib use in Qatar, a real-world data analysis.	Nabil Elhadi Omar, Shereen Elazzazy, Anas Hamad
Real-world pharmacovigilance analysis of the incidence and characteristics of fatal immune-related adverse events of immune checkpoint inhibitors.	Nabil Elhadi Omar, Anas Hamad, Mohamed S. Elkhatim, Afnan Alnajjar, Amaal Gulied, Arwa O. Sahal, Aya Alasmar, Farah I. Jibril, Hebtalla M. Afifi, Sahar M. Nasser, Maria Benkhadra, Rawan A. Dawoud, Shereen Elazzazy.
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Systematic mapping of gender disparities in oncology publications of north African countries: The Georgina study.	El Bairi, Khalid, Omar NE, Afifi, H.M and GEORGiNA study collaborators.
British Oncology Pharmacy Association 26th Annual Symposium 06-08 October 2023	
Real World Data effectiveness and Safety of TKIs in Metastatic Non-Small Cell Lung Cancer Patients in Qatar: Nationwide Retrospective Cohort Study.	Rawan Daowd, Kakil Rasul, Farah Jibril, Arwa Sahal, Randa Al-Okka, Yaser Mahfouz, Nabil E. Omar, Reyad Mohsen, Aladdin Kanbour Aladdin Kanbour ,Naim Battikh, Harman Saman, Prem Chandra ,Shereen Elazzazy
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Efficacy and safety of selinexor for patients with relapsed and refractory multiple myeloma: A meta-analysis.	Shaima Bashir, Esther W. Chan, Dina Abushanab, Anas Hamad, Daoud Al-Badriyeh.

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Her2 Low Non-Metastatic Breast Cancer in Qatar: A Nationwide Retrospective Cohort Study to Evaluate The Response To Neoadjuvant Chemotherapy: A Real- World Analysis.	Ahmed Kardousha, Ahmad Basha, Sahar Nasser, Wafa shehada, Salha Bu jassoum, Mufid, Anas hamad, Shereen Elazzazy.
The Association between DNA Repair Genes Polymorphisms and Cisplatin Induced Ototoxicity in Cancer Patients. A Systematic Review	Nabil Elhadi Omar, Anas Hamad, Rana Mekkawi, Fatima Hawasly, and Hazem Elewa.
An overview of Nasopharyngeal cancer patient demographics, staging, treatments, and outcomes over 5-year period. Retrospective Study.	Nabil Elhadi Omar, Anas Hamad, Mohamed S. Elkhatim, Afnan Alnajjar, Amaal Gulied, Arwa O. Sahal, Aya Alasmar, Farah I. Jibril, Hebtalla M. Afifi, Sahar M. Nasser, Maria Benkhadra, Rawan A. Dawoud, Shereen Elazzazy.
Signet Ring Cells outcome in gastric Adenocarcinoma in Qatar; upfront surgery and FLOT re-visited; A retrospective study.	M. S. Elkhatim, A. Abdalhadi, M. Abagla, Arwa O. Sahal, Aya Alasmar, Farah I. Jibril, Hebatalla Afifi, Maria Benkhadra, Shaima A. Abdelrahim, N.E. Omar, M. Gaber, Suha Abdo, Alhan Jama, Reni Anil, Wamda Abdalla, Aleem Akram, Arwa Isameldin, Mai Mostafa, A. Rehman Zar, Niloofar Allahverdi, A. Nafia, M. Petkar, K. Rasul, A. Al Bahrani, A. Shablak.
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Real- World Survival Data for Patients with Solid Tumors after Inpatient Chemotherapy Administration: A Retrospective Analysis on The National Level in Qatar.	Afnan Alnajjar, Maria Benkhadra, Ahmed Abdalhadi, Muhammed Hajmusa , Israa Elhakeem, Hassan Aakel , Shaima Abdelrahim, Amir Nounou , Salha Bujassoum, Mohammed Ussama Al Homsi , Alaaeldin Shablak
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Immune Checkpoint Inhibitors Related Adverse Events in Cancer Patients with Good versus Poor Performance Status: A Real-World Nationwide Retrospective Analysis	Afnan Alnajja , Shereen Elazzazy, Anas Hamad, Mohamed S. Elkhatim, Amaal Gulied, Arwa Sahal, Aya Alasmar, Farah Gebril , Hebatallah Afifi , Sahar Nasser, Maria Benkhadra , Rawan Dawoud , Mohamed Saad , Nabil E. Omar
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ESMO congress 2023. Madrid, Spain 20-24 October 2023	
Bridging the gender gap in oncology: GEORGiNA'S quest for equality in academic research.	El Bairi, Khalid, Omar NE, Afifi, H.M and GEORGiNA study collaborators.

6Th Qatar International Pharmacy Conference. Doha-Qatar 03-04 November 2023	
Use of Brentuximab Vedotin in Bone Marrow Transplant: A Safety Analysis at the National Centre for Cancer Care and Research (NCCCR).	Aya Alasmar, Amaal Gulied, Maria Benkadrah, Farah Jibril, Hebatallah Afifi, Shereen Elazzazy.
The Association between DNA Repair Genes Polymorphisms and Cisplatin Induced Ototoxicity in Cancer Patients. A Systematic Review	Nabil Elhadi Omar, Anas Hamad, Rana Mekkawi, Fatima Hawasly, and Hazem Elewa.
Immune checkpoint inhibitors related adverse events in cancer patients with good versus poor performance status: A real world nationwide retrospective analysis.	Nabil E. Omar, Afnan Alnajjar, Anas Hamad, Mohamed Saad, Mohamed S. Elkhatim, Amaal Gulied, Arwa Sahal, Aya Alasmar, Farah Gebril, Hebatallah Afifi, Sahar Nasser, Maria Benkhadra, Rawan Dawoud, Shereen Elazzazy.
Real-world pharmacovigilance analysis of the incidence and characteristics of fatal immune-related adverse events of immune checkpoint inhibitors.	Nabil Elhadi Omar, Anas Hamad, Mohamed S. Elkhatim, Afnan Alnajjar, Amaal Gulied, Arwa O. Sahal, Aya Alasmar, Farah I. Jibril, Hebtalla M. Afifi, Sahar M. Nasser, Maria Benkhadra, Rawan A. Dawoud, Shereen Elazzazy.
Real-World Efficacy and Safety of Off-Label Use of Immune Checkpoint Inhibitors (ICI) in Cancer in Qatar: A Nationwide Retrospective Cohort Study.	Seif Abaza, Mohamad Salman, Amir Nounou, Sahar Nasser, Kakil Rasul, Anas Hamad, Shereen Elazzazy.
Topotecan Safety and Efficacy Use Evaluation: A Real-World Data Analysis in a Tertiary Cancer Hospital in Qatar.	Hebatalla Afifi, Nabil Omar, Arwa Sahal, Sahar Nasser, Farah Jibril, Aya Alasmar, Anas Hamad, Asmaa Elhassan, Hind Elmalik , Shereen Elazzazy.
A pivotal Move to Preserving Lives: The Antibiotics Sepsis Kit	Farah Jibril, Anas Hamad, Elham Alsagga, Arwa Nasser.

Precision Medicine and Functional Genomics 2023.Doha-Qatar 11-14 November 2023	
The Association between DNA Repair Genes Polymorphisms and Cisplatin Induced Ototoxicity in Cancer Patients. A Systematic Review	Nabil Elhadi Omar, Anas Hamad, Rana Mekkawi, Fatima Hawasly, and Hazem Elewa.
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The Association between DNA Repair Genes Polymorphisms and Cisplatin Induced Ototoxicity in Cancer Patients. A Systematic Review	Nabil Elhadi Omar, Anas Hamad, Rana Mekkawi, Fatima Hawasly, and Hazem Elewa.
The European Society of Clinical Pharmacy (ESCP) annual Symposium, Aberdeen, Scotland October 31st to November 2nd, 2023	
Influences on health professionals' reporting of medication errors: a systematic review of qualitative evidence using the theoretical domains framework.	Neda J. Takhtinejad, Derek Stewart, Muhammad A. Hadi, Anas Hamad, Zachariah Nazar

The11th International Conference on Interprofessional Practice and Education. Nov-23Doha-Qatar	
Creating the Culture of Interprofessional Teamwork: All Together for Better Outcome of Sepsis in Cancer Patients.	Cicy Jacob, Farah Jibril, Emelita Ison , Mohammad Atieh , Priyadarshini Vatsyayan , Hiba ElTahir , Hatim El Derbhouhi, Dr Deena Mudawi, Sindhumole Nair, Jordana Delicana, Hannan Zadeh, Mutie Ahmed, Samar Hashim, Amir Nounou, Nayel Al Tarawneh, Awni AlShurafa, Mohammad Bakr.
All Together Better Health ATBH XI: The 11th International Conference on Interprofessional Practice and Education. Nov-23 Doha-Qatar	
Every Minute Counts: Improving Time to Antibiotics Administration in Sepsis at Qatar's National Cancer Center through a Multidisciplinary Approach.	Farah Jibril, Anas Hamad, Cicy Jacob, Elham Alsagga, Emelita Ison.
San Antonio Breast Cancer Symposium. 5-9 Dec 2023	
Her2 Low Non-Metastatic Breast Cancer in Qatar: A Nationwide Retrospective Cohort Study to Evaluate the Response To Neoadjuvant Chemotherapy: A Real- World Analysis.	Ahmed Kardousha, Ahmad Basha, Sahar Nasser, Wafa shehada, Salha Bu jassoum, Mufid, Anas hamad, Shereen Elazzaz
65th American Society of Hematology. San Diego-USA Dec 11th ,2023	
Establishment of a Clinical Pharmacist-Led (CPLC) Multiple Myeloma Clinic with Collaborative Prescribing Model at the National Center for Cancer Care and Research in Qatar.	Rola Ghasoub, Shereen Elazzazy, Maria Benkhadra, Nancy Kasse, Honar Cherif, Javid Gaziev, Hesham Elsabah, Anas Hamad.

Awards and Prizes

1. Second Place- Clinical Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha, Qatar. Title: Real- World Survival Data for Patients with Solid Tumors after Inpatient Chemotherapy Administration: A Retrospective Analysis on The National Level in Qatar. Authors: Afnan Alnajjar, Maria Benkhadra, Ahmed Abdalhadi, Muhammed Hajmusa , Israa Elhakeem, Hassan Aakel , Shaima Abdelrahim, Amir Nounou , Salha Bujassoum, Mohammed Ussama Al Homsi , Alaaeldin Shablak .

2. Best poster presentation at the 6th Qatar International Pharmacy Conference held from Nov 2nd to 5th, 2023 in Doha, Qatar. Title: Immune Checkpoint Inhibitors Related Adverse Events in Cancer Patients with Good versus Poor Performance Status: A Real-World Nationwide Retrospective Analysis. Authors: Afnan Alnajjar, Shereen Elazzazy, Anas Hamad, Mohamed S. Elkhatim, Amaal Gulied, Arwa Sahal, Aya Alasmar, Farah Jibril, Hebatallah Afifi, Sahar Nasse, Maria Benkhadra, Rawan Dawoud, Mohamed Saad, Nabil E. Omar.

3. Merit Travel Award to attend ASCO Breakthrough Conference; for our international project "Systematic mapping of gender disparities in oncology publications of north African countries: The Georgina study.31, Jul,2023.Japan.Authors: El Bairi K, Gihbid A, Benhima N., El Alami I , Omar N. Afifi H, Abdelhakam M, et al GEORGiNA collaborators.

4. Best poster presentation at the 6th Qatar International Pharmacy Conference held from Nov 2nd to 5th, 2023 in Doha, Qatar. Real-World Efficacy and Safety of Off-Label Use of Immune Checkpoint Inhibitors (ICI) in Cancer in Qatar: A Nationwide Retrospective Cohort Study. Authors: Saif Abaza , Sahar Nasser Mohamed Abu Younis ,Amir Nounou ,Kakil Rasul K, Anas Hamad ,Shereen Elazzazy .

5. First Place- Clinical Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha. Her2 Low Non-Metastatic Breast Cancer in Qatar: A Nationwide Retrospective Cohort Study To evaluate the response to neoadjuvant chemotherapy: A Real- World Analysis. Authors: Ahmed Kardousha, Wafa Shehada, Ahmed Basha, Sahar Nasser S, Mufid El Mistiri , Anas Hamad , Salha Bujassoum , Shereen Elazzazy.

6. Endorsed by Qatar National Commission for UNESCO for the UNESCO Equatorial Guinea International Prize for Research in the Life Sciences(2023). Name of applicant: Dr.Shereen Elazzazy.

7. Third Place- Clinical Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha. Serum biomarkers as predictors of treatment response in non-small cell lung cancer patients treated with immunotherapy Presented by Ms. Sheerena Hydrose Sherif

8. First Place- Quality/Applied Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha. Crosstalk in high-risk HPV16 and HPV18 coinfections in Colorectal cancer patients and in-Vitro cell Models Presented by Ms. Queenie Fernandez

9. Second Place- Quality/Applied Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha. Circulating exosomal immuno-oncological checkpoint and cytokines are potential biomarkers to monitor tumor response to anti-PD1/PD-L1 therapy in non-small cell lung cancer patients Presented by Ms. Shayista Akbar

10. Third Place- Quality/Applied Research Category at the concurrent poster session that accompany the BEST of ASCO 2023 on 13th-14th October 2023 in Doha. Bortezomib exerts its anti-cancer activity through the regulation of Skp2/p53 axis in non-melanoma skin cancer cells and C Elegans Presented by Dr. Kirti Prabhu

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