American Journal of
Biomedical Science & Research

www.biomedgrid.com
ISSN: 2642-1747

Review Article

Cardiovascular Risks of Chemotherapy: Impacts on Cardio-Oncology and Targeted Therapies including HER2, Tyrosine Kinase Inhibitors, Immunotherapy, and Anthracyclines

Zahra Zahid Piracha[1,2,3]*, Muhammad Nouman Tariq[4], Syed Shayan Gilani[4], Hafiz Ahmad Bilal Akhtar Chughtai[1,6], Abdullah Basra[4], Muhammad Raza[4], Muhammad Shahmeer Fida Rana[4], Muhammad Saim Maqsood[4] Talha Ahmed[4], and Umar Saeed[5]*

[1]*International Center of Medical Sciences Research, Islamabad, Pakistan*

[2]*International Center of Medical Sciences Research, Austin, United States of America*

[3]*International Center of Medical Sciences Research, Chadwell Health, United Kingdom*

[4]*Akhtar Saeed Medical and Dental College, Lahore, Pakistan*

[5]*Clinical and Biomedical Research Center and Multidisciplinary Laboratories, Foundation University School of Health Sciences, Foundation University Islamabad, Pakistan*

[6]*Shaikh Khalifa Bin Zayed Al Nahyan Medical College Lahore*

***Corresponding author:** Zahra Zahid Piracha International Center of Medical Sciences Research, Islamabad, Pakistan, International Center of Medical Sciences Research Austin, United States of America, International Center of Medical Sciences Research, Chadwell Health, United Kingdom, and Umar Saeed, Clinical and Biomedical Research Center and Multidisciplinary Laboratories, Foundation University School of Health Sciences, Foundation University Islamabad, Pakistan.

To Cite This Article: *Zahra Zahid Piracha*, Muhammad Nouman Tariq, Syed Shayan Gilani, Abdullah Basra, Muhammad Raza, et al. Cardiovascular Risks of Chemotherapy: Impacts on Cardio-Oncology and Targeted Therapies including HER2, Tyrosine Kinase Inhibitors, Immunotherapy, and Anthracyclines. Am J Biomed Sci & Res. 2024 25(2) AJBSR.MS.ID.003307,* DOI: 10.34297/AJBSR.2024.25.003307

Received: October 21, 2024; **Published:** December 19, 2024

Abstract

Cardiovascular complications following chemotherapeutic management of cancer patients highlight a critical dimension of patient care, necessitating thorough cardio-oncology assessment. These complications, which encompass cardiomyopathy, arrhythmias, and vascular events, considerably affect patient morbidity and mortality. Addressing these adverse cardiovascular events is essential, not only for preserving the therapeutic efficacy of cancer treatments but also for ensuring long-term patient well-being. This review integrates insights from seminal studies and recent research to provide a comprehensive understanding of cardiovascular complications associated with specific chemotherapeutic agents, such as HER2 neu-targeting therapies, Tyrosine Kinase Inhibitors (TKIs), Immune Checkpoint Inhibitors (ICIs), and anthracyclines. The intricate interplay between cancer treatments and cardiovascular health is explored, underscoring the importance of multidisciplinary collaboration and proactive management to optimize treatment outcomes and minimize cardiovascular risks. The pivotal role of cardio-oncology assessment in modern oncology practice is highlighted to enhance patient care.

Keywords: HER2 neu, Tyrosine kinase inhibitors, Immune checkpoint inhibitors, Anthracyclines

Introduction

In the multifaceted landscape of oncology, managing cardiovascular complications that arise post-chemotherapy has become an essential aspect of patient care, demanding heightened attention. These complications, which include cardiomyopathy, arrhythmias, and vascular events, can significantly influence patient morbidity and mortality [1,2]. Understanding and addressing these adverse cardiovascular events is critical, not only for maintaining the therapeutic efficacy of cancer treatments but also for safeguarding patient well-being over the long term [3]. Thus, integrating comprehensive cardio-oncology assessments and intervention strategies into cancer care protocols is indispensable.

For instance, *Lipshultz, et al.,* (2019) conducted a meticulous analysis, revealing the significant impact of anthracycline-based regimens on cardiac function among pediatric cancer survivors. Their study underscored the prevalence of anthracycline-induced cardiomyopathy and highlighted the necessity for sustained cardiac monitoring in this vulnerable population [4]. Similarly, *Cardinale, et al.,* (2015) delineated the incidence and severity of myocardial damage associated with trastuzumab treatment in breast cancer patients, advocating for early detection and prompt intervention to mitigate cardiac dysfunction [5].

Recent research has expanded on these foundational studies, shedding light on the intricate relationship between cancer treatments and cardiovascular health. *Herrmann, et al.,* (2020) provided significant insights into the association between Immune Checkpoint Inhibitors (ICIs) and immune-related adverse events, including myocarditis and pericarditis, highlighting the imperative need for vigilant cardiovascular monitoring during treatment [6]. *Piotrowski, et al.,* (2019), in their research, emphasized the cardiotoxic effects of HER2 neu-targeting therapies, such as trastuzumab, stressing the urgency of early intervention to mitigate these effects [7]. Furthermore, *Moslehi's, et al.,* (2016) comprehensive review on Tyrosine Kinase Inhibitors (TKIs) underscored the cardiovascular risks posed by these agents, including hypertension and QT interval prolongation [8]. Despite advances in therapeutic modalities, the challenge of anthracycline-induced cardiotoxicity remains, as extensively documented by *Octavia, et al.,* (2012) [9].

This increasing prevalence of Cardio Vascular Disease (CVD) among cancer patients has driven the growth of cardio-oncology services designed to mitigate morbidity and mortality related to CVD. This development further underscores the vital role of interdisciplinary collaboration between oncologists and cardiologists within cardio-oncology, aimed at optimizing patient care [6,10].

Against this complex backdrop, this paper seeks to synthesize insights from the existing literature to provide a comprehensive understanding of the cardiovascular complications associated with specific chemotherapeutic agents. By elucidating these intricacies, this study aims to inform clinical practice and foster the implementation of proactive measures to safeguard cardiovascular health in cancer patients undergoing treatment.

Cardiovascular Complications Associated with Specific Chemotherapeutic Agents

Cardiovascular complications present a significant challenge in cancer patients undergoing chemotherapy, with specific chemotherapeutic agents being directly linked to various adverse cardiovascular effects. These complications, which can range from arrhythmias to cardiomyopathies and heart failure, necessitate a nuanced understanding of their pathophysiology, derived from both clinical studies and literature reviews.

HER2 neu Targeting Therapies

HER2 neu-targeting therapies, including trastuzumab and pertuzumab, have revolutionized the treatment paradigm for HER2-positive breast cancer. By targeting the human epidermal growth factor receptor 2 (HER2/neu), these therapies have demonstrated substantial efficacy in improving both overall survival and disease-free survival, particularly when used in conjunction with chemotherapy in adjuvant and metastatic settings [11,12].

However, despite their significant clinical benefits, HER2 neu-targeting therapies are associated with notable cardiovascular risks, especially cardiotoxicity. This concern has been well-documented across various landmark studies. For instance, the HERA trial demonstrated that adjuvant trastuzumab therapy substantially improved disease-free survival in HER2-positive breast cancer patients, but also revealed an increased incidence of cardiac dysfunction, reinforcing the need for vigilant cardiac monitoring during treatment [13-15].

Similarly, the CLEOPATRA trial assessed the efficacy and safety of pertuzumab in combination with trastuzumab and chemotherapy in metastatic HER2-positive breast cancer. While this combination significantly improved clinical outcomes, including overall survival, concerns about cardiac safety remained, necessitating ongoing cardiac assessments during treatment [16,17].

A study on heart failure incidence among HER2-positive breast cancer patients receiving trastuzumab-based regimens revealed a higher occurrence of heart failure compared to patients not receiving trastuzumab, further emphasizing the importance of continuous cardiac monitoring [18]. Additionally, a meta-analysis evaluating the cardiovascular safety profile of pertuzumab in combination with trastuzumab and chemotherapy confirmed its efficacy in improving clinical outcomes but highlighted the persistent need for cardiac assessments to mitigate the associated cardiovascular risks [19]. *Chien, et al.,* (2021) also investigated the long-term cardiovascular outcomes of patients receiving ado-trastuzumab emtansine (T-DM1) for HER2-positive metastatic breast cancer, reporting that while T-DM1 was generally well-tolerated, a subset of patients did experience cardiac events, underscoring the need for ongoing monitoring, particularly for those with pre-existing cardiovascular risk factors [20].

These findings collectively underscore the necessity for vigilant

cardiovascular monitoring and proactive management in patients receiving HER2 neu-targeting therapies. A multidisciplinary approach involving oncologists, cardiologists, and other healthcare professionals is essential to optimize treatment outcomes while effectively mitigating cardiac risks.

Tyrosine Kinase Inhibitors (TKIs)

Tyrosine Kinase Inhibitors (TKIs) represent a transformative class of targeted cancer therapies, significantly altering treatment paradigms across numerous malignancies. These agents function by selectively inhibiting tyrosine kinases, which are enzymes crucial for cellular signaling pathways responsible for regulating cell growth, proliferation, and survival. By targeting aberrant tyrosine kinases that drive oncogenic signaling in cancer cells, TKIs effectively disrupt these pathways, thereby inhibiting tumor growth and progression [21,22].

Despite their therapeutic success, TKIs are linked to a range of cardiovascular complications, necessitating vigilant monitoring and management. One of the most prevalent cardiovascular side effects of TKIs is hypertension, primarily induced by endothelial dysfunction and changes in renal sodium handling. Other cardiovascular toxicities associated with TKIs include myocardial ischemia, QT interval prolongation, and heart failure [23,24].

Several seminal studies have explored the cardiovascular risks posed by TKIs, highlighting the critical need for ongoing cardiovascular assessment during treatment. For instance, Moslehi's 2016 comprehensive review emphasized the array of cardiovascular complications caused by different TKIs and called for proactive risk management to mitigate these risks while maximizing treatment efficacy [8]. Similarly, *Leitner, et al.,* (2011) stressed the importance of early cardiovascular risk assessment and monitoring in patients undergoing TKI therapy, identifying timely intervention as essential for preventing treatment disruption [25]. Additionally, *Patel's, et al.,* (2020) research underscored the need for vigilant cardiovascular oversight to address the cardiotoxic effects of TKIs, further reinforcing the necessity of proactive management strategies to optimize patient outcomes [26]. TKIs have revolutionized cancer treatment, their potential for cardiovascular toxicity requires a multidisciplinary approach to patient care. Oncologists, cardiologists, and other healthcare professionals must collaborate to ensure that cardiovascular risks are minimized through thorough monitoring and timely intervention, thereby enhancing treatment outcomes for patients receiving TKI therapy.

Immune Checkpoint Inhibitors and Cardiovascular Complications

Immune Checkpoint Inhibitors (ICIs) have emerged as a groundbreaking cancer immunotherapy, showcasing remarkable success by enabling the immune system to recognize and eliminate cancer cells. These agents function by inhibiting key immune checkpoints, such as programmed cell death protein 1 (PD-1) and Cytotoxic T-Lymphocyte-Associated Protein 4 (CTLA-4), thus enhancing T-cell-mediated antitumor responses [27,28].

However, the increasing use of ICIs has revealed a spectrum of immune-related adverse events (irAEs), including those affecting the cardiovascular system. Cardiovascular complications related to ICIs can manifest as myocarditis, pericarditis, vasculitis, and arrhythmias, posing significant diagnostic and management challenges due to their often nonspecific presentation [29,30].

Research by *Herrmann, et al.,* has provided critical insights into ICI-related myocarditis and pericarditis, emphasizing the importance of cardiovascular monitoring to identify and manage these potentially fatal events. *Johnson, et al.,* (2016) contributed key findings on the incidence and clinical features of immune-related myocarditis, underscoring the necessity for early recognition and intervention to prevent fulminant cardiac complications [10]. Further studies by *Lyon, et al.,* (2018) and *Mahmood, et al.,* (2020) expanded the understanding of cardiovascular irAEs, highlighting the wide spectrum of cardiovascular issues linked to ICIs and reinforcing the need for cardiac function monitoring during treatment [29,31].

The development of clinical guidelines by organizations such as the Society for Immunotherapy of Cancer (SITC) and the European Society for Medical Oncology (ESMO) has provided valuable frameworks for managing cardiovascular complications in patients receiving ICIs. These guidelines advocate for baseline cardiac assessments, frequent biomarker monitoring, and prompt immunosuppressive therapy in suspected cases of immune-related cardiovascular toxicity [32]. While ICIs have transformed cancer care, their potential to cause serious cardiovascular complications necessitates vigilant monitoring and a multidisciplinary approach. Oncologists and cardiologists must work in concert to ensure that patients undergoing ICI therapy are closely monitored for cardiovascular events, facilitating early intervention and optimizing overall treatment safety.

Anthracyclines and Cardiotoxicity

Anthracyclines, including drugs like doxorubicin, daunorubicin, and epirubicin, are potent chemotherapeutic agents widely used in the treatment of cancers such as breast cancer, lymphomas, and leukemias. Despite their efficacy, anthracyclines are associated with dose-dependent cardiotoxicity, which remains a significant concern in clinical practice. These agents can cause both acute and chronic cardiovascular complications, ranging from arrhythmias to irreversible cardiomyopathy and heart failure [9].

Research has provided substantial insights into the mechanisms underlying anthracycline-induced cardiotoxicity. *Swain, et al.,* explored the role of oxidative stress and mitochondrial dysfunction in the pathogenesis of cardiotoxicity, offering potential targets for cardioprotective strategies [11]. Long-term studies, such as those by *Lipshultz, et al.,* have shown that anthracycline-induced cardiotoxicity can have lasting effects on cancer survivors, necessitating lifelong cardiac surveillance [33].

Efforts to mitigate anthracycline-induced cardiotoxicity include optimizing drug dosing, employing cardioprotective agents such as dexrazoxane, and utilizing alternative chemotherapy regimens.

The use of cardiac biomarkers, including troponins and natriuretic peptides, has also proven effective in detecting early cardiac injury, allowing for timely intervention [34,35].

In summary, anthracyclines remain critical to many cancer treatment regimens, but their cardiotoxic potential demands careful dose management and ongoing cardiac monitoring. Collaboration between oncologists and cardiologists is crucial to achieving a balance between maximizing anticancer efficacy and minimizing cardiovascular risks in patients receiving anthracycline-based therapies.

Discussion

This comprehensive review highlights the complex interplay between cancer treatment and cardiovascular health, emphasizing the need for robust cardiac monitoring and management strategies in oncology practice [36,37]. Cancer remains a global health burden, contributing to millions of deaths annually and representing a significant challenge in reducing mortality rates [36,38]. Through an extensive analysis of the literature, this review elucidates the diverse cardiovascular complications associated with key chemotherapeutic agents, including HER2 neu-targeting therapies, Tyrosine Kinase Inhibitors (TKIs), Immune Checkpoint Inhibitors (ICIs), and anthracyclines.

The cardiovascular risks posed by HER2 neu-targeting therapies, such as trastuzumab and pertuzumab, underscore the importance of vigilant cardiac surveillance throughout treatment. While these therapies have improved the prognosis of HER2-positive breast cancer, they carry a risk of cardiotoxicity, particularly left ventricular dysfunction and heart failure. Early detection of cardiac abnormalities through baseline and serial imaging is crucial for timely intervention and optimizing patient outcomes [11,13,36].

Similarly, the cardiovascular complications linked to TKIs, including hypertension and myocardial ischemia, highlight the necessity for close collaboration between oncologists and cardiologists. Studies examining the cardiovascular safety of TKIs underscore the importance of proactive risk assessment and management strategies to safeguard patient well-being [8,24].

The emergence of ICIs has introduced a new array of cardiovascular toxicities, such as myocarditis, pericarditis, and vasculitis, which can lead to severe morbidity if not promptly recognized and treated. Multidisciplinary collaboration is vital to ensure that immune-related cardiovascular events are promptly identified and managed, minimizing the risk of adverse outcomes [10,29].

Anthracyclines, despite their critical role in cancer therapy, are well-known for their dose-dependent cardiotoxicity, necessitating ongoing cardiac surveillance in cancer survivors. By employing cardioprotective measures and leveraging cardiac biomarkers, clinicians can reduce the risk of long-term cardiotoxic effects and optimize patient care [33-35].

Current study underscores the importance of a cardio-oncology approach to optimize treatment outcomes and minimize cardiovascular risks in cancer patients. By integrating insights from the literature, healthcare providers can develop tailored monitoring and management strategies to ensure the safe and effective use of chemotherapeutic agents while preserving cardiovascular health. Multidisciplinary collaboration and proactive interventions are essential to address the evolving landscape of cardiovascular complications in cancer care [39-46].

Acknowledgement

None.

Conflict of Interest

None.

References

1. Curigliano G, Cardinale D, Dent S, Criscitiello C, Aseyev O, et al. (2016) Cardiotoxicity of anticancer treatments: Epidemiology, detection, and management. CA Cancer J Clin 66(4): 309-325.
2. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, Aboyans V, Asteggiano R, et al. (2016) ESC Committee for Practice Guidelines; ESC Scientific Document Group. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Eur Heart J 37(36): 2768-2801.
3. Ewer MS, Ewer SM (2015) Cardiotoxicity of anticancer treatments. Nat Rev Cardiol 12(9): 547-558.
4. Lipshultz SE, Franco VI, Miller TL, Colan SD, Sallan SE, et al. (2019) Cardiovasculardisease in adult survivors of childhood cancer. Annu Rev Med 70: 169-184.
5. Cardinale D, Colombo A, Lamantia G, Colombo N, Civelli M, et al. (2015) Anthracycline-induced cardiomyopathy: Clinical relevance and response to pharmacologic therapy. J Am Coll Cardiol 66(21): 2424-2433.
6. Herrmann J, Lenihan D, Armenian S (2020) Defining cardiovascular toxicities of cancer therapies: An International Cardio-Oncology Society (IC-OS) consensus statement. Eur Heart J 41(22): 2041-2045.
7. Piotrowski G, Gawor R, Rygiel K (2019) Cardiotoxicity of trastuzumab in oncological treatment. Adv Clin Exp Med 28(9): 1217-1222.
8. Moslehi JJ (2016) Cardiovascular toxic effects of targeted cancer therapies. N Engl J Med 375(15): 1457-1467.
9. Octavia Y, Tocchetti CG, Gabrielson KL, Janssens S, Crijns HJ, et al. (2012) Doxorubicin-induced cardiomyopathy: From molecular mechanisms to therapeutic strategies. J Mol Cell Cardiol 52(6): 1213-1225.
10. Johnson CB, Davis MK, Law A, Sulpher J (2016) Shared care for cancer survivors: A healthcare improvement initiative to address cardio-oncology care. Can J Cardiol 32(8): 971-977.
11. Pai VB, Nahata MC (2000) Cardiotoxicity of chemotherapeutic agents: Incidence, treatment and prevention. Drug Saf 22(4): 263-302.
12. Swain SM, Baselga J, Kim SB, Ro J, Semiglazov V, et al. (2015) Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): Overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol 16(6): 603-615.
13. Piccart Gebhart MJ, Procter M, Leyland Jones B, Goldhirsch A, Untch M, et al. (2005) Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. N Engl J Med 353(16): 1659-1672.
14. Perez EA, Romond EH, Suman VJ, Jeong JH, Davidson NE, et al. (2008) Updated results of the combined analysis of NCCTG N9831 and NSABP

B-31 adjuvant chemotherapy with/without trastuzumab in patients with HER2-positive breast cancer. J Clin Oncol 26(15_suppl): 512.

15. Romond EH, Jeong JH, Rastogi P, Swain SM, Geyer CE Jr, et al. (2012) Seven-year follow-up assessment of cardiac function in NSABP B-31, a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel (ACP) with ACP plus trastuzumab as adjuvant therapy for patients with node-positive, human epidermal growth factor receptor 2–positive breast cancer. J Clin Oncol 30(31): 3792-3799.
16. Suter TM, Ewer MS (2013) Cancer drugs and the heart: Importance and management. Eur Heart J 34(15): 1102-1111.
17. Schoemaker MJ, Jones ME, Wright LB, Griffin J, McFadden E, et al. (2016) Cardiovascular disease risk in women with BRCA1 and BRCA2 mutations: Analysis of a UK prospective cohort study. Eur Heart J 37(14): 1122-1128.
18. Naaktgeboren WR, de Groot JAH, van der Windt DAWM, Verheij RA, de Wit NJ, et al. (2016) Diagnostic accuracy of non-invasive tests for coronary artery disease: A meta-analysis and meta-regression analysis of cohort studies. Eur Heart J 37(25): 1903-1915.
19. Ezaz G, Coviello JS, Matsouaka RA (2020) Incidence of heart failure in breast cancer patients receiving trastuzumab: A cohort study. J Clin Oncol 38(18_suppl): 507.
20. Minciullo PL, Calapai G, Parisi A, Gangemi S (2021) Cardiotoxicity of pertuzumab: A meta-analysis of randomized clinical trials. Eur J Clin Pharmacol 77: 243-251.
21. Chien AJ, Rugo HS, Lisano JK (2021) Long-term cardiovascular outcomes in HER2-positive breast cancer patients treated with ado-trastuzumab emtansine (T-DM1): A cohort study. J Clin Oncol 39(15_suppl): 1045.
22. Pao W, Chmielecki J (2010) Rational, biologically based treatment of EGFR-mutant non-small-cell lung cancer. Nat Rev Cancer 10(11): 760-774.
23. Sawyers C (2004) Targeted cancer therapy. Nature 432(7015): 294-297.
24. Force T, Kolaja KL (2011) Cardiotoxicity of kinase inhibitors: The prediction and translation of preclinical models to clinical outcomes. Nat Rev Drug Discov 10(2): 111-126.
25. Abdel Qadir H, Ethier JL, Lee DS, Thavendiranathan P, Amir E, et al. (2014) Cardiovascular toxicity of angiogenesis inhibitors in treatment of malignancy: A systematic review and meta-analysis. Cancer Treat Rev 40(9): 1177-1184.
26. Leitner M, Menzel J, Gielen GH (2011) Clinical aspects of cardio-oncology. Clin Res Cardiol 100(10): 771-782.
27. Patel VG, Ohn M, Pandey A (2020) Cardiovascular complications of targeted therapies for hematologic malignancies. Cardio Oncology 6(1): 1-15.
28. Ribas A, Wolchok JD (2018) Cancer immunotherapy using checkpoint blockade. Science 359(6382): 1350-1355.
29. Suzanne L Topalian, F Stephen Hodi, Julie R Brahmer, Scott N Gettinger, David C Smith, et al. (2012) Safety, activity, and immune correlates of anti–PD-1 antibody in cancer. N Engl J Med 366(26): 2443-2454.
30. Syed S Mahmood, Michael G Fradley, Justine V Cohen, Anju Nohria, Kerry L Reynolds, et al. (2018) Myocarditis in patients treated with immune checkpoint inhibitors. J Am Coll Cardiol 71(16): 1755-1764.
31. Salem JE, Manouchehri A, Moey M (2018) Cardiovascular toxicities associated with immune checkpoint inhibitors: An observational, retrospective, pharmacovigilance study. Lancet Oncol 19(12): 1579-1589.
32. Lyon AR, Yousaf N, Battisti NM, Moslehi J, Larkin J, et al. (2018) Immune checkpoint inhibitors and cardiovascular toxicity. Lancet Oncol 19(9): 447-e458
33. Haanen JBA, Carbonnel F, Robert C (2018) Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 29(Suppl_4).
34. Steven E Lipshultz, M Jacob Adams, Steven D Colan, Louis S Constine, Eugene H Herman, et al. (2013) Long-term cardiovascular toxicity in children, adolescents, and young adults who receive cancer therapy: pathophysiology, course, monitoring, management, prevention, and research directions: a scientific statement from the American Heart Association. Circulation 128(17): 1927-1995.
35. Daniela Cardinale, Alessandro Colombo, Giulia Bacchiani, Ines Tedeschi, Carlo A Meroni, et al. (2015) Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation 131(22): 1981-1988.
36. Saro H Armenian, Melissa M Hudson, Renee L Mulder, Ming Hui Chen, Louis S Constine, et al. (2015) Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 16(3): 123-136.
37. Piracha ZZ, Saeed U (2023) Leucine-rich repeats and immunoglobulin-like domains protein 1 (LRIG1) is downregulated in Invasive ductal carcinoma and potential prognostic marker of breast cancer. J Cancer Res Ther 19(7): 1870-1879.
38. REACCT Collaborative, Alexandra M Zaborowski, Ahmed Abdile, Michel Adamina, Felix Aigner, et al. (2021) Characteristics of early-onset vs late-onset colorectal cancer: a review. JAMA Surg 156(9): 865-874.
39. Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, et al. (2022) Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis. JAMA Oncology 8(3): 420-444.
40. Tran KB, Lang JJ, Compton K, Xu R, Acheson AR, et al. (2022) The global burden of cancer attributable to risk factors, 2010–19: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet 400(10352): 563-591.
41. Sharma R, Abbasi Kangevari M, Abd Rabu R, Abidi H, Abu Gharbieh E, et al. (2022) Global, regional, and national burden of colorectal cancer and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Gastroenterology & Hepatology 7(7): 627-647.
42. Alvarez EM, Force LM, Xu R, Compton K, Lu D, et al. (2022) The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Oncology 23(1): 27-52.
43. Da Cunha AR, Compton K, Xu R, Mishra R, Drangsholt MT, et al. (2023) 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. JAMA Oncology 9(10): 1401-1416.
44. Nejadghaderi SA, Moghaddam SS, Azadnajafabad S, Rezaei N (2022) Burden of thyroid cancer in North Africa and Middle East 1990–2019. Frontiers in Oncology 12: 955358.
45. Abbasi Kangevari M, Moghaddam SS, Ghamari SH (2022) The burden of prostate cancer in North Africa and Middle East, 1990–2019: Findings from the global burden of disease study. Frontiers in Oncology 12: 961086.
46. Azadnajafabad S, Moghaddam SS, Mohammadi E, Rezaei N (2023) Burden of breast cancer and attributable risk factors in the North Africa and Middle East region, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Frontiers in Oncology 13: 1132816.