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CHEMOTHERAPY-INDUCED CARDIAC TOXICITY AND HEART FAILURE

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Over the past 20 years, advancements in cancer treatments have contributed to a consistent decline in cancer-related mortality, paralleled by an increase in cancer survivorship. As survivorship rises, treatment-related side effects, particularly cardiovascular toxicities associated with cancer therapies, have gained prominence due to their significant impact on patient outcomes. Effective management of cardiovascular toxicities is critical, as it influences the choice of anticancer therapies and affects long-term morbidity and mortality among cancer patients. Despite significant advancements in anti-cancer therapies that have improved patient survival, these treatments are often accompanied by an increased risk of treatment-related morbidity and mortality, particularly from cardiovascular diseases. Cardio-oncology, the multidisciplinary field, has gained considerable attention in recent years. However, further research is required to explore the complex mechanisms of chemotherapy-induced cardiovascular toxicity. This review includes recent information and evidence related to assessing the cardiotoxicity of chemotherapy and the ways of managing this problem.

Key words: chemotherapy, cardiotoxicity, myocardial dysfunction.

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КАРДІОТОКСИЧНІСТЬ І СЕРЦЕВА НЕДОСТАТНІСТЬ, СПРИЧИНЕНІ ХІМІОТЕРАПІЄЮ

За останні 20 років досягнення в лікуванні раку сприяли послідовному зниженню смертності, пов'язаної з раком, паралельно зі зростанням виживання при раку. У міру зростання виживання побічні ефекти, пов'язані з лікуванням, особливо серцево-судинна токсичність, пов'язана з терапією раку, набули популярності через їх значний вплив на результати лікування пацієнтів. Ефективне управління серцево-судинною токсичністю має вирішальне значення, оскільки воно впливає на вибір протиракової терапії та на довгострокову захворюваність та смертність серед онкологічних хворих. Незважаючи на значні досягнення у протираковій терапії, які покращили виживання пацієнтів, ці методи лікування часто супроводжуються підвищеним ризиком захворюваності та смертності, пов'язаної з лікуванням, особливо від серцево-судинних ускладнень. Кардіоонкологія, міждисциплінарна область, останніми роками привертає значну увагу. Однак необхідні подальші дослідження для вивчення складних механізмів серцево-судинної токсичності, спричиненої хіміотерапією. Цей огляд включає останні відомості та докази, пов'язані з оцінкою кардіотоксичності хіміотерапії та способами керування цією проблемою.

Ключові слова: хіміотерапія, кардіотоксичність, дисфункція міокарда.

The growing need to address these challenges has fostered the development of cardio-oncology, a multidisciplinary field dedicated to managing the intersection of cancer and cardiovascular disease. However, the inconsistent terminology and definitions for cardiovascular toxicities associated with cancer therapies (CTR-CVT) have historically impeded accurate diagnosis, standardized management, and research efforts [27, 30].

With the continued increase in the number of cancer survivors due to remarkable and continuous advances in cancer treatment, a paradigm shift is occurring from cancer as a "fatal disease" to a "chronic condition" with cardiovascular risks. This also impacts the practice of cardiology with the increase in cardiovascular morbidity and mortality among patients with cancer due to direct and/or indirect side effects of cancer treatment. Thus, cardio-oncology has emerged as a new cardiac subspecialty that focuses on risk stratification, prevention, diagnosis, treatment and follow-up of cardiovascular disease associated with cancer treatment [23].

To encapsulate the diverse presentations and etiological links between cancer therapies and cardiac dysfunction, the term cancer therapy-related cardiac dysfunction (CTRCD) is recommended. This term encompasses a wide spectrum of cardiovascular complications associated with chemotherapy, targeted agents, immunotherapies, and radiation therapy [13, 20].

In the course of our work, we used international databases such as Scopus, Web of Science, Elsevier for the period 2019–2024. We used the following keywords for the search: chemotherapy, cardio-oncology, cardiotoxicity biomarkers.

Cardiovascular complications arising from cancer treatments encompass a range of conditions, including myocardial dysfunction and heart failure (HF), valvular heart disease, coronary artery disease (CAD), hypertension, pulmonary hypertension, arrhythmias, thromboembolic events, peripheral vascular disease, stroke, and pericardial complications [2].

Given that cancer patients often receive combination chemotherapy, cardiotoxicity may increase due to interactions between various treatment regimens, making it challenging to predict long-term cardiovascular outcomes [13].

Cardiotoxicity may accompany with toxicity of other organs (e.g., liver, pancreas etc.) [28]. Among these complications, myocardial dysfunction and HF are significant contributors to morbidity and mortality, collectively referred to as cardiotoxicity. The multidisciplinary collaboration of healthcare specialists is crucial in managing cardiotoxicity while ensuring the continuation of cancer therapy [3, 4].

Although cardiotoxicity can manifest immediately following treatment, it may also present years later, particularly with anthracycline-based therapies, and can cause transient myocardial dysfunction in some cases [5].

Pediatric patients and older adults with pre-existing cardiovascular risks who are treated with anthracycline-containing regimens have a 15–fold increased lifetime risk of developing HF compared to matched controls [29]. Additionally, myocardial dysfunction and HF are more common in patients receiving tyrosine kinase inhibitors, especially those with pre-existing cardiovascular risk factors [32].

Anthracycline drugs, frequently used in the treatment of breast cancer and hematological malignancies, are highly effective but their use is limited by their cardiotoxic effects, which can result in irreversible damage to the heart. This can negatively affect patient prognosis [14, 31]. Notably, while many patients tolerate standard doses of anthracyclines without developing long-term complications, others may experience cardiotoxicity after the first dose. Anthracycline-induced cardiotoxicity may present acutely, early (within one year), or late (several years after treatment). The incidence of HF is particularly high among patients under 65 years of age who receive high doses of anthracyclines [2, 3]. Characterized by a progressive decline in left ventricular ejection fraction (LVEF), anthracycline-related cardiotoxicity may remain asymptomatic initially, but symptoms often emerge years later [14]. Early detection and treatment of cardiac dysfunction generally leads to better functional recovery, whereas delayed diagnosis makes heart failure management more challenging [23].

Numerous risk factors contribute to anthracycline-related cardiotoxicity, including the chemotherapy infusion regimen, the use of other chemotherapeutic agents, cumulative lifetime doses, pre-existing heart disease, and age (>65 years). In addition, chemotherapy agents such as cisplatin and taxanes (e.g., paclitaxel and docetaxel) are also associated with myocardial dysfunction and HF. Some protocols recommend avoiding anthracyclines in patients with pre-existing left ventricular dysfunction, suggesting taxane-based therapies as a safer alternative [19, 24].

Immunotherapy and targeted therapies have significantly advanced cancer treatment, yielding promising results in various malignancies. Human epidermal growth factor receptor 2 (HER-2) inhibitors, such as trastuzumab, pertuzumab, and trastuzumab emtansine (T-DM1), in combination with tyrosine kinase inhibitors (e.g., lapatinib), have shown substantial improvements in the treatment of HER-2 positive breast cancer [9].

Long-term follow-up of patients treated with trastuzumab, particularly those with low pre-treatment cardiovascular risk, has revealed a risk for late-onset HF. However, trastuzumab-induced HF is typically reversible upon discontinuation of the drug or treatment for HF. Risk factors for anti-HER2-induced cardiotoxicity include prior anthracycline treatment, short intervals between anthracycline and anti-HER2 therapies, low LVEF at baseline, a history of hypertension, and older age [9, 13].

In clinical practice, treatment with trastuzumab is often discontinued when LVEF falls below 45 % or when patients develop symptoms of HF. The risk of cardiotoxicity with other agents, such as lapatinib, pertuzumab, and T-DM1, is comparable to that of trastuzumab [32].

Inhibition of the vascular endothelial growth factor (VEGF) signaling pathway can be beneficial in the treatment of solid tumors but may lead to reversible or persistent myocardial dysfunction when combined with chemotherapy. A prospective study of bevacizumab, an anti-VEGF antibody, used after chemotherapy in breast cancer patients, revealed that 1 % of patients developed symptomatic HF and 2 % exhibited left ventricular dysfunction [31]. Similarly, tyrosine kinase inhibitors such as sunitinib, pazopanib, and axitinib have been shown to cause cardiotoxicity, with cardiac dysfunction developing in 3–15 % of patients and symptomatic HF in 1–10 % of cases [4].

Management of Diagnosis and Treatment.

The first step in identifying patients at high risk for cardiotoxicity is a comprehensive assessment of cardiovascular risk factors. For patients undergoing treatment with anthracyclines, initial evaluation of cardiac function is essential. If systolic dysfunction or severe valvular heart disease is detected, consideration should be given to switching to non-anthracycline chemotherapy or implementing cardiac protective strategies. Patients at high risk for cardiotoxicity should undergo regular re-assessment of cardiac function during and after treatment [5, 7].

It is recommended that cardiac biomarkers, such as high-sensitivity troponin I, troponin T, or natriuretic peptides, be measured at the initiation of chemotherapy. A baseline measurement of at least one of these biomarkers is advised, with a high-sensitivity troponin I test recommended at each subsequent cycle of anthracycline chemotherapy [26].

For patients receiving anti-HER2 treatment, cardiac monitoring is crucial, particularly as they are often pre-treated with anthracyclines. These patients should undergo follow-up evaluations every three months during treatment, and once after treatment completion [9].

Left ventricular function, as part of overall cardiac assessment, should be monitored in all patients immediately following the completion of cardiotoxic chemotherapy. However, there is limited data on the optimal approach and frequency of follow-up for asymptomatic adults receiving cardiotoxic cancer therapies, and randomized studies are lacking in this area.

A retrospective study indicated that older patients with lung cancer who received adjuvant anthracyclines had an elevated risk of developing heart failure over a 10-year follow-up period. Cancer survivors should be informed of their increased risk of cardiovascular diseases at the outset of their chemotherapy and should be advised and supported to make appropriate lifestyle modifications. Both paediatric and adult survivors of anthracycline-based chemotherapy have a lifelong risk for development of LV dysfunction and HF [33].

Evaluating Myocardial Toxicity: Methods and Tools.

Electrocardiography (ECG).

Electrocardiography is a cornerstone in monitoring cardiovascular status during cancer therapy. A 12-lead ECG is recommended for all patients before initiating treatment, especially therapies known to cause corrected QT interval (QTc) prolongation. One of the most common side effects of chemotherapy that can be detected on the ECG in 12 leads is sinus bradycardia [22, 29].

Spinu Ș. et al, noted that some medicines (e.g., paclitaxel) can affect the infrahisian conduction system (after the bifurcation of the His) and lead to the appearance of the right or left branch block. If the lesion is located at the suprahisan level, atrioventricular blocks of varying degrees, from 1 to 3, may occur. The mechanism by which paclitaxel affects the conduction system is either directly by affecting the sinus node, atrioventricular node, and His-Purkinje system or indirectly by affecting the parasympathetic nervous system, which induces bradycardia or conduction disorders, which can be found out with ECG [29].

Another mechanism promoting cardiac arrhythmias is through myocardial ischemia or even necrosis if myocardial ischemia persists for a long time. Thus, alkylating agents lead to atrial and ventricular arrhythmias within the first 24 hours-3 days of initiating treatment, that made important the role of ECG in diagnosis of cardiovascular toxicity [11, 18, 25].

Madanat L, et al emphasized that potential cardiovascular toxicities linked to these anticancer agents include arrhythmias, QT prolongation, myocardial ischemia and infarction should be assessed by ECG to create the effective management strategies [20].

One of the studies analyzed by us demonstrates the effectiveness and the possibility of oncological patients remote monitoring using I single-lead ECG with machine learning algorithms to detect rhythm and conductivity disorders, also demonstrates the high effectiveness of early detection of diastolic dysfunction, and this has enables timely care and treatment [21].

An approach to the American and European Cardio-Oncology Guidelines (American Society of Clinical Oncology (ASCO–2017 and ASCO–2018) European Society for Medical Oncology (ESMO–2017 and ESMO–2020), and the European Society of Cardiology (ESC–2016) provides detailed information regarding the cardiovascular toxicities. According to some recommendations in evaluation of QTc Fridericia correction should be preferred to Bazett correction and cancer treatment can be continued as long as QTc interval is ≤500 ms and a change in QTc is <60 ms and there is no occurrence of any ventricular arrhythmias or syncope [1, 2, 3].

Thus, baseline ECG findings, such as chamber enlargement, conduction abnormalities, arrhythmias, ischemia, evidence of prior myocardial infarction (MI), and low voltage, should be evaluated

in their clinical context. Regular ECG monitoring aids in detecting QTc prolongation, arrhythmias, tachycardia, and ST-T segment changes, all of which may influence therapeutic decisions [11].

It should be emphasized that the cardiologist must know the limits that are acceptable for subclinical cardiac toxicity such as a mild but reasonably prolonged QT interval below 480 ms, the presence of benign arrhythmias such as atrial or ventricular premature beats, the presence of insignificant ST segment and T-wave changes, and changes in the heart axis [18].

It is believed that all these ECG changes should not stop a child or adult from receiving potentially life-saving therapy. However, in situations where a cardiac oncologist is not available, close collaboration with a cardiology clinic or outpatient cardiology clinic with experienced physicians in monitoring the toxic effects of chemotherapy is necessary.

Echocardiography.

Echocardiography is among the primary diagnostic tools for assessing myocardial dysfunction at all stages of cancer therapy. The two-dimensional biplane Simpson method is recommended for calculating left ventricular (LV) volumes and ejection fraction (EF) when endocardial boundaries are clearly visualized. A reduction of >10 % in LVEF below the lower limit of normal is indicative of cardiac dysfunction, which is commonly associated with certain chemotherapies [24].

In one of recent studies Negishi T, et al summarized echocardiographic evaluation of cardiac dysfunction and heart failure as they are the most concerning cardiovascular complications of cancer therapy and worsen its morbidity and mortality. Their review covered cardiac function assessment and proposed cut-off values before/during/after cancer chemotherapy [23].

According to recommendations from basic guidelines LVEF of 50–55 % is considered borderline low LVEF and considered as a high risk for potential cardiotoxic effects of chemotherapy. If the baseline LVEF is less than 50 %, cardio-protection therapy with an angiotensin converting enzyme inhibitor/angiotensin receptor blocker and a beta blocker can improve the LVEF. If LVEF-recovered, the patients even may be able to tolerate a chemotherapy regimen with potential cardiotoxic effect ESMO Guidelines also used EF 50 % as the cut-off, at which point cardio-protection should be considered [26].

It should be taken into account that even though withholding a certain cancer therapy is a last resort in cardio-oncology, it has been suggested to withhold chemotherapy when the LVEF becomes <45 % during anthracyclines use or LVEF becomes <40 % with trastuzumab. So, LVEF has been used for cardio-oncology decision making. However, some evidence has revealed that LVEF is an imperfect marker because it is insensitive to early changes in cardiac function during a potentially cardiotoxic treatment [23].

Emerging imaging techniques, such as strain imaging, have shown promise in early detection of subclinical myocardial dysfunction. A relative decrease of ≥15 % in global longitudinal strain (GLS) from baseline may precede reductions in LVEF, signaling early myocardial impairment [6, 16, 34].

Expert commentary related to assessment of cardiotoxic effects of chemotherapy suggested that while traditional imaging-based assessment of left ventricular ejection fraction still has its place in cardiac monitoring, more advanced echocardiographic modalities, in particular, myocardial deformation imaging with speckle tracking strain analysis, show great potential for detecting early signs of cardiotoxicity. According to their opinion, larger studies are needed to determine both the clinical role of strain measurement in influencing initiation of cardioprotective agents and its prognostic value in long term outcome [33].

Some researchers noted that abnormalities in systolic deformation parameters have been identified as early manifestation but left ventricular diastolic properties remain less well defined. The authors hypothesize that onset as well as progression of cardiotoxicity not only should disturb deformation curves of myocardial contraction, but also relaxation. Thus, the parameters of diastolic function should be taken into account [33].

Transthoracic echocardiography (TTE) remains the preferred modality for baseline risk stratification, offering comprehensive assessments of LV and right ventricular function, chamber dilation, LV hypertrophy, regional wall motion abnormalities, diastolic function, valvular heart disease, pulmonary arterial pressure, and pericardial disease [5].

Cardiac Magnetic Resonance (CMR).

Cardiac magnetic resonance imaging provides detailed structural and functional cardiac assessments, supplementing echocardiography when more precise data are required. CMR is particularly

useful for evaluating LV and RV function, detecting myocardial scarring or fibrosis, and assessing pericardial involvement in patients undergoing thoracic radiotherapy. Scar and fibrosis detected via CMR also offer prognostic insights [15].

The accuracy of CMR in measuring dynamic changes in ventricular volumes and ventricular mass make it an important tool to monitor and identify early subtle cardiac changes associated with cancer therapy used by a number of prospective studies. From a clinical standpoint, it is particularly helpful in determining biventricular function in challenging cases (e.g., patients who have undergone left sided breast surgery or with LVEF results that are borderline or conflicting) or in determining the etiology of the cardiomyopathy [12, 35].

Cardiac Biomarkers.

Biomarkers play a pivotal role in detecting and managing cancer therapy-related cardiovascular toxicity. Natriuretic peptides, such as B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP), are well-established in the identification of heart failure, even at low levels, helping stratify high-risk patients and guide therapy [26].

Novel biomarkers, including myeloperoxidase, C-reactive protein, galectin-3, arginine–nitric oxide metabolites, growth differentiation factor-15, placental growth factor, fms-like tyrosine kinase-1, micro-ribonucleic acids, and immunoglobulin E, have been investigated for their potential in CTR-CVT risk stratification. However, evidence supporting their clinical utility remains limited, necessitating further research [4].

In order for a biomarker to be useful, it should be accurate, be easy to measure, and provide important information relative to treatment outcome. A prognostic biomarker forecasts the likely course of a disease irrespective of treatment, whereas a predictive biomarker forecasts the likely response to a specific treatment.

B-type natriuretic peptide and troponins can help identify the development of a CV adverse event during cancer therapy. In general, an elevated natriuretic peptide level represents hemodynamic congestion, whereas an abnormal troponin is a marker of myocardial injury. Although the specific CV conditions a patient may experience with contemporary cancer therapy are broad, cardiac biomarkers can indicate ongoing stress and injury [36].

Thus, serum biomarkers are a reproducible, sensitive, minimally invasive and inexpensive method for investigating potential adverse cardiovascular effects of cancer treatments. They are useful tools for risk stratification, early detection of cardiotoxicity and follow-up and prognostic evaluation of cancer patients. The interrelationship of cardiovascular biomarkers in patients with cancer (especially in HF) allows their use in risk stratification and detection of chemotherapy-induced cardiotoxicity [36].

Throughout the cancer treatment pathway, maintaining consistency in the imaging modality and biomarker assay used for screening is essential for accurate monitoring. Switching between modalities or assays is strongly discouraged, as it may compromise diagnostic accuracy. Preference should be given to imaging modalities with high reproducibility and the ability to provide additional clinically relevant information, such as right ventricular function, pulmonary pressures, valvular function, and pericardial evaluation. Where available, radiation-free imaging modalities of high quality are preferred to minimize cumulative radiation exposure [12, 35].

Patients undergoing potentially cardiotoxic therapies are at an elevated risk of developing heart failure (HF) and should receive comprehensive medical care focused on stringent control of cardiovascular risk factors. For such patients, left ventricular ejection fraction (LVEF) should be assessed prior to initiating treatment and monitored periodically during therapy. Consistency in the imaging method used is crucial to ensure accurate detection of cardiac dysfunction. A significant decline in LVEF (e.g.,>10 %) that remains above the lower limit of normal warrants immediate re-evaluation of cardiac function during the course of treatment [32, 33].

If LVEF decreases by >10 % to a value below the lower limit of normal (defined as LVEF <50 %), early intervention is necessary to mitigate further cardiac deterioration. In such cases, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) are recommended, combined with beta-blockers, unless contraindicated. These therapies have demonstrated efficacy in preventing the progression of left ventricular dysfunction and the onset of symptomatic HF. The same treatment approach is advised for patients presenting with symptomatic HF or asymptomatic cardiac dysfunction to reduce cardiovascular risk and improve outcomes [8, 10].

Continued research and implementation of standardized screening protocols are critical to optimizing the management of cardiotoxicity in cancer patients. Early detection and prompt intervention remain key to minimizing long-term cardiovascular complications associated with chemotherapy [17].

Conclusion

Survivors of anthracycline-based chemotherapy, both pediatric and adult, face a lifelong risk of developing left ventricular (LV) dysfunction and heart failure (HF). Notably, the onset of HF may occur years or even decades after treatment, underscoring the importance of long-term vigilance.

LV dysfunction and HF can manifest even in asymptomatic patients, particularly those who have received cardiotoxic therapies, such as high cumulative doses of anthracyclines or who experienced reversible LV dysfunction during treatment. The time lapse between treatment and the development of HF can be very long (>10 years). Thus, periodic surveillance is recommended.

Periodic screening with cardiac imaging and biomarkers, such as B-type natriuretic peptide (BNP), should be prioritized for these high-risk groups to facilitate early detection and management. Furthermore, as intercurrent illnesses may unmask reduced cardiac reserve in individuals with prior anthracycline exposure, any symptoms suggestive of HF warrant thorough investigation.

Although robust clinical trial data are currently lacking, it is recommended that HF therapy be continued indefinitely unless stable systolic LV function is achieved and maintained after cessation of HF treatment, provided no additional cardiotoxic cancer therapies are planned. This approach emphasizes the need for proactive and personalized management strategies in this population.

Cardio-oncology remains a developing field with significant unmet needs and gaps in evidence. Further research is essential to establish comprehensive guidelines and optimize outcomes for cancer survivors at risk of cardiovascular complications.

References

1. Abdul-Rahman T, Dunham A, Huang H, Bukhari SMA, Mehta A, Awuah WA, et al; American College of Cardiology Medical Student Member Community (ACC:MSMC) – Cardiovascular Research Initiative (CVRI) group. Chemotherapy Induced Cardiotoxicity: A State of the Art Review on General Mechanisms, Prevention, Treatment and Recent Advances in Novel Therapeutics. Curr Probl Cardiol. 2023 Apr;48(4):101591. doi: 10.1016/j.cpcardiol.2023.101591.

2. Alexandre J, Cautela J, Ederhy S, Damaj GL, Salem JE, Barlesi F, et al. Cardiovascular Toxicity Related to Cancer Treatment: A Pragmatic Approach to the American and European Cardio-Oncology Guidelines. J Am Heart Assoc. 2020 Sep 15;9(18):e018403. doi: 10.1161/JAHA.120.018403.

3. Beavers CJ, Rodgers JE, Bagnola AJ, Beckie TM, Campia U, Di Palo KE, et al; American Heart Association Clinical Pharmacology Committee and Cardio-Oncology Committee of the Council on Clinical Cardiology and Council on Genomic and Precision Medicine; and the Council on Peripheral Vascular Disease. Cardio-Oncology Drug Interactions: A Scientific Statement From the American Heart Association. Circulation. 2022 Apr 12;145(15):811–838. doi: 10.1161/CIR.0000000000001056.

4. Brown SA, Ray JC and Herrmann J. Precision cardio-oncology: a systems-based perspective on cardiotoxicity of tyrosine kinase inhibitors and immune checkpoint inhibitors. J. Cardiovasc. Transl. Res 2020; 13, 402–416, 10.1007/s12265-020-09992-5.

5. Bychowski J, Sobiczewski W. Current perspectives of cardio-oncology: Epidemiology, adverse effects, pre-treatment screening and prevention strategies. Cancer Med. 2023 Jul;12(13):14545–14555. doi: 10.1002/cam4.5980.

6. Chaganti BT, Negishi K, Okajima K. Role of Myocardial Strain Imaging in Cancer Therapy-Related Cardiac Dysfunction. Curr Cardiol Rep. 2022 Jun;24(6):739–748. doi: 10.1007/s11886-022-01692-7.

7. Couch LS, Lyon AR, López-Fernández T. Cardio-oncology: a new field requiring guidance. Eur Heart J Cardiovasc Imaging. 2023 Feb 17;24(3): 47. doi: 10.1093/ehjci/jeac250.

8. Curigliano G, Lenihan D, Fradley M, Ganatra S, Barac A, Blaes A, et al. Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations. Ann Oncol 2020; 31:171–190.

9. Dent SF, Morse A, Burnette S, Guha A, Moore H. Cardiovascular toxicity of novel HER2-targeted therapies in the treatment of breast cancer. Curr Oncol Rep. 2021; 23:128. doi: 10.1007/s11912-021-01114-x.

10. Fanola CL, Ruff CT, Murphy SA, Jin J, Duggal A, Babilonia NA et al. Efficacy and safety of edoxaban in patients with active malignancy and atrial fibrillation: analysis of the ENGAGE AF – TIMI 48 trial. J. Am. Heart Assoc. 2018. 7, e008987, 10.1161/JAHA.118.008987.

11. Gioffré S, Chiesa M, Cardinale DM, Ricci V, Vavassori C, Cipolla CM, et al. Circulating microRNAs as potential predictors of anthracycline-induced troponin elevation in breast cancer patients: diverging effects of doxorubicin and epirubicin. J Clin Med 2020; 9:1418.

12. Harries I, Liang K, Williams M, Berlot B, Biglino G, Lancellotti P, et al. Magnetic Resonance Imaging to Detect Cardiovascular Effects of Cancer Therapy: JACC CardioOncology State-of-the-Art Review. JACC CardioOncol. 2020 Jun 16;2(2):270–292. doi: 0.1016/j.jaccao.2020.04.011.

13. Hauwanga WN, McBenedict B, Amadi ES, Dohadwala TK, Johnny C, Asaju F, et al. A Systematic Review of the Cardiotoxic Effects of Targeted Therapies in Oncology. Cureus. 2024 Aug 6;16(8):e66258. doi: 10.7759/cureus.66258.

14. Kamaraju S, Mohan M, Zaharova S, Wallace B, McGraw J, Lokken J, et al. Interactions between cardiology and oncology drugs in precision cardio-oncology. Clin Sci (Lond). 2021 Jun 11;135(11):1333–1351. doi: 10.1042/CS20200309.

15. Kersten J, Fink V, Kersten M, May L, Nunn S, Tadic M, et al. CMR reveals myocardial damage from cardiotoxic oncologic therapies in breast cancer patients. Int J Cardiovasc Imaging. 2024 Feb;40(2):225-235. doi: 10.1007/s10554-023-02996-7.

16. Laksono S, Yuniadi Y, Soesanto AM, Raharjo SB, Lisnawati, Bardosono S, et al. Comparison of Global Longitudinal Strain in Dual-chamber versus Ventricular Pacemaker in Complete Heart Block. J Cardiovasc Echogr. 2024 Jan-Mar;34(1):14–18. doi: 10.4103/jcecho.jcecho_78_23.
17. Lancellotti P, Suter TM, López-Fernández T, Galderisi M, Lyon AR, Van Der Meer P, et al. Cardio-oncology services: rationale, organization, and implementation. Eur Heart J 2019; 40:1756–1763.
18. López-Fernández T, Martín-García A, Roldán Rabadán I, Mitroi C, Mazón Ramos P, Díez-Villanueva P, et al. Atrial fibrillation in active cancer patients: expert position paper and recommendations. Rev Esp Cardiol (Engl Ed). 2019; 72:749–759.
19. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al; ESC Scientific Document Group. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J. 2022 Nov 1;43(41):4229–4361. doi: 10.1093/eurheartj/ehac244.
20. Madanat L, Gupta R, Weber P, Kumar N, Chandra R, Ahaneku H, et al. Cardiotoxicity of Biological Therapies in Cancer Patients: An In-depth Review. Curr Cardiol Rev. 2023; 19(3):e310522205428. doi: 10.2174/1573403X18666220531094800.
21. Mesitskaya DF, Zaki ZAF, Poltavskaya MG, Andreev DA, Levshina AR, Sultygova EA, et al. A single-lead ECG based cardiotoxicity detection in patients on polychemotherapy, IJC Heart & Vasculature, Volume 50, 2024, 101336, ISSN 2352–9067. https://doi.org/10.1016/j.ijcha.2024.101336.
22. Muresan L, Cismaru G, Martins RP, Bataglia A, Rosu R, Puiu M, et al. Recommendations for the use of electrophysiological study: Update 2018. Hellenic J Cardiol. 2019 Mar-Apr;60(2):82–100. doi: 10.1016/j.hjc.2018.09.002.
23. Negishi T, Miyazaki S, Negishi K. Echocardiography and Cardio-Oncology. Heart Lung Circ. 2019 Sep;28(9):1331–1338. doi: 10.1016/j.hlc.2019.04.023.
24. Nolan MT, Creati L, Koczwara B, Kritharides L, Lynam J, Lyon AR, et al. First European Society of Cardiology Cardio-Oncology Guidelines: A Big Leap Forward for an Emerging Specialty. Heart Lung Circ. 2022 Dec;31(12):1563–1567. doi: 10.1016/j.hlc.2022.11.003.
25. Salem J-E, Nguyen LS, Moslehi JJ, Ederhy S, Lebrun-Vignes B, Roden DM, et al. Anticancer drug-induced life-threatening ventricular arrhythmias: a World Health Organization pharmacovigilance study. Eur Heart J 2021; 42:3915–3928.
26. Shaaban NH, Abayazeed RM, Sobhy MA, Elsharkawy EM, Hammad BA. Role of Global Left Ventricle Longitudinal Strain and Cardiac Biomarkers in the Early Detection of Cancer Therapy-Related Dysfunction in Patients Treated with Cardiotoxic Chemotherapeutic Drugs in a Cardio-Oncology Clinic. Cureus. 2024 Oct 18;16(10): 71766. doi: 10.7759/cureus.71766.
27. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024 Jan-Feb;74(1):12–49. doi: 10.3322/caac.21820.
28. Skrypnyk IM, Maslova GS, Lymanets TV. Overweight and obesity as risk factors for chemotherapy-induced hepatotoxicity in patients with acute lymphoblastic leukemia. World of medicine and biology. 2022; 2 (80): 146–150. doi: 10.26724/2079-8334-2022-2-80-146-150.
29.Spînu Ș, Cismaru G, Boarescu PM, Istratoaie S, Negru AG, Lazea C, et al. ECG Markers of Cardiovascular Toxicity in Adult and Pediatric Cancer Treatment. Dis Markers. 2021 Jan 19; 2021:6653971. doi: 10.1155/2021/6653971.
30.Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71:209–249.
31. Tandia M, Abbara C, Noel-Hudson M-S, Amor D, Polrot M, Gonin P et al. Bevacizumab and sorafenib modulate p-glycoprotein function in vitro and bevacizumab increases in vivo sorafenib plasma concentrations in mice. Int. J. Innov. Res. Med. Sci 2020; 5, 261–267, 10.23958/ijirms/vol05-i08/396.
32. Teske AJ. The ESC cardio-oncology 2022 guidelines; the ball is in our court. Eur Heart J Cardiovasc Imaging. 2023 Feb 17;24(3):45–46. doi: 10.1093/ehjci/jeac219.
33. Venneri L, Zoppellaro G, Khattar RS. Cardio-oncology: the role of advanced echocardiography in cancer patients. Expert Rev Cardiovasc Ther. 2019 Apr;16(4):249–258. doi: 10.1080/14779072.2018.1443394.
34. Watanabe M, Yakushijin K, Tanaka H, Chijiki R, Saeki M, Hirakawa Y, et al. Global longitudinal strain is superior to ejection fraction for long-term follow-up after allogeneic hematopoietic stem cell transplantation. EJHaem. 2022 Nov 7;4(1):192–198. doi: 10.1002/jha2.586.
35. Zhang L, Awadalla M, Mahmood SS, Nohria A, Hassan MZ, Thuny F, et al. Cardiovascular magnetic resonance in immune checkpoint inhibitor-associated myocarditis. Eur Heart J. 2020;41:1733–1743.
36. Zhang X, Sun Y, Zhang Y, Fang F, Liu J, Xia Y, et al. Cardiac Biomarkers for the Detection and Management of Cancer Therapy-Related Cardiovascular Toxicity. J Cardiovasc Dev Dis. 2022 Oct 29;9(11):372. doi: 10.3390/jcdd9110372.

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