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Cardio-Oncology: Bridging Cancer Therapy and Cardiovascular Protection in the Era of Precision Medicine

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Abstract: The field of cardio-oncology is a service that is new and which integrates various disciplines to assist individuals with cardiac issues that may occur during the course of cancer development or during the administration of treatment. New cancer therapies have increased the chances of individuals living longer, though most of these therapies may result in heart disorders, such as cardiomyopathy, heart failure, arrhythmias, high blood pressure, and thromboembolic incidents. These issues can make both cancer outcomes and heart health worse. Cardio-oncology is the study of the hearts and blood vessels of people with cancer. Before treatment, it includes a full cardiovascular risk assessment. During treatment, it includes constant monitoring, quick detection of cardiotoxicity, and long-term cardiac care for cancer survivors. People who work in this field try to find a way to treat cancer while also keeping the heart safe. Some are oncologists, cardiologists, pharmacists, and other health care workers. Imaging tests are some of the most essential strategies, as they assist doctors in determining what is wrong, heart-protecting drugs as well as personalized treatment plans that are designed on a case-by-case basis. Pharmacists can help a lot, monitors of your medications, and ensures that they do not interact with other drugs and maximizes on therapy. The rules are increasing, yet much of the evidence remains grounded on what individuals concur on. This implies that we should have more good research that is forward looking. Cardio-oncology is quite crucial in ensuring that individuals with cancer live longer, safer, and better lives.

Keywords: *Cardio-Oncology, Cancer Therapy, Cardiotoxicity, Cardiovascular Complications, Chemotherapy, Targeted Therapy, Cancer Survivorship, Risk Stratification, Biomarkers, Cardiac Imaging, Pharmacologic Prevention, Heart Failure, Anthracyclines, Multidisciplinary Care, Personalized Medicine, Pharmacists' Role, Clinical Guidelines, Cardiovascular Monitoring, Cardioprotection, Long-Term Outcomes.*

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I. INTRODUCTION

Cardio-oncology is an emerging subspecialty of medicine that focuses on the treatment and prevention of cardiovascular issues related to cancer and its therapy. And it stresses a team-based model, in which cardiology partners closely and continuously with oncology, pharmacy, and other allied health professionals to maximize patient outcomes [1]. The advent of cancer therapy has led to great leaps in survival; however, many current anticancer therapies are also linked to high cardiovascular toxicity such as cardiomyopathy, heart failure, arrhythmias, hypertension and thromboembolic events. These therapy-associated complications could influence not only cardiac health but also the management of cancer. These pressing challenges are addressed by the emerging field of cardio-oncology, which optimizes patient-specific balance between effective cancer treatment and cardiovascular protection through integrated clinical decision-making [2]. The main goals of cardio-oncology are complete cardiovascular risk evaluation before the cancer therapy initiation, continuous monitoring during treatment, prevention and early management of cardiotoxicity and finally long-term cardiovascular outcomes while preserving oncologic benefit. Given that the number of cancer survivors is increasing and treatment plans are more sophisticated, cardio-oncology has emerged as an area of great clinical importance. Increasing peer-reviewed evidence supports the need for structured cardio-oncology programs to enhance patient safety and quality of life [3].

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➢ *Evolution of Cardio-Oncology as a Clinical Specialty*

The cardio-oncology is a subspecialty which has emerged quickly, as a niche, to a multidisciplinary area of critical medicine in response to cardiovascular issues of cancer therapies. Although its development began as a response to growing cancer survivorship and the awareness of the high cardiovascular risks of modern cancer treatments, cardio-oncology now provides comprehensive cardiovascular care to cancer patients. Its development has been tremendous: one UK service experienced a six-fold rise in referrals between 2011 and 2021, and outpatient consultations have increased ten-fold in the past five years [4]. More importantly, cardio-oncology is actively involved throughout the cancer treatment decision-making process, including risk assessment at pre-treatment stage, and post-therapy cardiac follow-up [5]. Importantly, cardio-oncology is now actively involved as the modern cancer therapies introduce complicated cardiovascular risks that cannot be effectively handled by a single physician.

➢ *Burden of Cardiovascular Complications in Cancer Survivors*

There is a high and significant burden of cardiovascular complications in cancer survivors with a maximum of 37 per cent greater cardiovascular disease (CVD) risk than non-cancer patients. The increased risk is greatly different to the specific cancer type, with the most prominent cardiovascular effects being reported with breast, lung, colorectal, and hematologic cancers [6]. The causes of cardiovascular effects are many: direct cardiotoxic effects of treatments, shared pathways of inflammation, or physiological changes of the treatments [7]. More importantly, the risk is still high in the long-term as certain effects of treatment still persist in cancer survivors up to 20 years of age, which is why it is crucial to implement active cardiovascular monitoring and management.

➢ *Role of Pharmacists in Cardio-Oncology Care*

The recent development of cardio-oncology is a subspecialty designed to help avert, diagnose, and treat the cardiovascular adverse effects of antineoplastic therapy. Close focus and a focus on optimal management of comorbidities are significant when providing cardio-oncologic care. Oncologists, cardiologists, and pharmacists working together across disciplines could help prevent and lessen the harmful effects of drugs used in treatments. The cytochrome P450 (CYP450) group of enzymes and the P-glycoprotein (P-g) carriers are very important for how drugs get broken down and how they become resistant to drugs. In this article, we talk about how CYP450 and P-g affect drug interactions in the field of cardio-oncology. We also give an overview of the cardiotoxicity of a range of cancer agents, stress the importance of precision medicine, and suggest that patients with cancer should be treated by a team of experts from different fields [9]. Pharmacists are part of the multidisciplinary team that cares for cancer patients with heart problems or who are at risk of cardiotoxicity. They help with prevention, detection, monitoring, and treatment [10].

➢ *Mechanisms of Chemotherapy-Induced Cardiotoxicity*

The cardiotoxicity of chemotherapy is the result of the multi-factorial molecular mechanisms, but the formation of reactive oxygen species (ROS) and mitochondrial dysfunction are the most important functions. Recent reports suggest that various chemotherapeutic agents especially anthracycline compounds cause cardiac injury by interfering with the mitochondrial homeostasis and cellular signaling pathways [11]. One of the leading causes is excessive ROS generation and occurs when the mitochondrial electron transport chain is perturbed. This brings about oxidative damage to lipids, proteins and DNA in cardiomyocytes [12]. Anthracyclines trigger cardiotoxicity by activating the topoisomerase **IIβ** that causes DNA double-strand breaks, which cause maladaptive responses to DNA damage and eventually cause cardiomyocyte apoptosis [13]. Also, anthracyclines induce inflammatory signaling and sustained oxidative stress, enhancing myocardial injury and resulting in progressive cardiac dysfunction [14]. Altogether, experimental and clinical data indicate that chemotherapy-induced cardiotoxicity is a highly complicated process, which requires sensitive detection methods and means of preventing its occurrence in the new science of cardio-oncology [15].

➢ *Classification of Cardiotoxicity*

Depending on the degree of myocardial damage and left ventricular (LV) dysfunction, cardiotoxicity may be categorized at a range of levels, and a variety of systems of classification with evolving systems including drug-specific pathogenic mechanisms. A broad and universal framework is suggested by the CARDIOTOX registry according to which cardiotoxicity is divided into four progressive clinical categories [16]. By this definition, patients who have normal cardiotoxicity have normal LV functions and normal cardiac biomarkers. Mild cardiotoxicity is marked by distorted biomarkers and/or minimal LV functional defect. Moderate cardiotoxicity- overt LV dysfunction with LVEF of 40-49%, severe cardiotoxicity- patients with LVEF ≤40% or those with symptomatic heart failure. Previously, mechanistic classifications were initiated where differentiated cardiotoxicity was defined as Type I and Type II. Type I cardiotoxicity, which is usually related to anthracyclines, is dose-related and usually irreversible, being caused by cumulative myocardial damage. Type II cardiotoxicity, which is typical of targeted therapies including trastuzumab, and is typically not dose-dependent and is believed to potentially be reversible after drug withdrawal. The epidemiology shows that severe cardiotoxicity is not very frequent (occurring in about 3.1 per cent of treated patients) yet carries a significant risk of morbidity and mortality risk and so there is a need to early stratify risks and closely monitor cardiac functions among patients undergoing cardiotoxic cancer treatment [17].

➢ *Anticancer Drugs Associated with Cardiotoxicity*

Strong links between cardiotoxicity of clinical significance and anthracyclines, targeted therapy like trastuzumab, and some classical chemotherapeutic agents are well linked. The anthracycline family as (doxorubicin, daunorubicin) is the best studied and proven to have cardiac toxicity that is dose-dependent. Other notable drugs that have the capability of damaging the heart include trastuzumab, 5-

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fluorouracil, bevacizumab, and certain tyrosine kinase inhibitors. Taking such kinds of drugs may cause numerous heart issues such as arrhythmias, high blood pressure, heart attacks, dysfunctional left ventricular functioning, and even cardiac failure [18]. It all depends on the mechanism and the timing of intervention, which can be reversible or irreversible [19]. Permanent myocardial injury, especially when used with anthracyclines, may be a major constraint to the further administration of effective cancer therapy and negatively influence the survival rate of the patient. However, the opposite scenario is that cardiotoxicity associated with some of the targeted therapies is potentially reversible with early intervention and proper management, at least in part [20].

II. RISK FACTORS FOR CARDIOTOXICITY

There are many cardiovascular and demographic factors that considerably increase chances of chemotherapy induced cardiotoxicity with hypertension, diabetes mellitus and obesity always being seen as the most important and consistent risk factors. Statistically significant high-risk factors of cardiotoxicity were found in patients with hypertension (OR 1.99), diabetes (OR 1.74), and obesity (OR 1.72), and the full meta-analysis included 7,488 patients, which is a large effect [21]. Very young or very old, heart disease history, and low baseline heart functioning are other patient-related risk factors. Treatment-related factors, including high combined drug dosage, mixed chemotherapy, and radiotherapy concurrently increase the risk of cardiotoxicity significantly. Recent research suggests that ethnic differences and pharmacogenomic variability might be the factors that affect the predisposition to cardiotoxic effects. This illustrates the increasing significance of personalized medicine in cardio-oncology [22]. These findings underscore the imperative for individualized cardiovascular risk assessment, preliminary cardiac evaluation, and intensified monitoring for patients with identified risk factors during treatment for cancer [23].

- *Biomarkers and Diagnostic Tools*

Cardiac biomarkers are essential in cardio-oncology for the reason that they help doctors figure out if cancer treatment is hurting the heart and keep an eye on the early signs of this. The most well-known biomarkers are troponins from the heart and natriuretic peptides. They have been shown to be very useful for finding subclinical myocardial injury and early cardiac dysfunction in people getting cancer treatment [24]. These biomarkers offer a cost-effective, minimally invasive, and easily reproducible method for evaluating the cardiovascular effects linked to anticancer therapies, rendering them especially appropriate for longitudinal monitoring in clinical settings [25]. Different biomarker classes have different levels of evidence, but cardiac troponins have shown to be very useful in the clinic, especially for finding and classifying the risk of anthracycline-induced cardiotoxicity early on [26]. Besides traditional biomarkers, new candidates like inflammatory markers (interleukin-6 (IL-6) and C-reactive protein (CRP)) and circulating microRNAs have shown promising links to cardiotoxicity. Nonetheless, these innovative biomarkers presently lack adequate validation for standard clinical application and necessitate additional extensive studies [27]. In the future, biomarker research is likely to include multiparametric omics-based methods along with advanced deep-learning and artificial intelligence techniques. This could greatly improve the accuracy of diagnoses, the ability to make predictions, and the ability to assess risk in a personalized way in cardio-oncology [28].

- *Pharmacologic Prevention Strategies*

Drug-based prevention strategies in cardio-oncology have produced encouraging yet inconsistent outcomes, with no single intervention demonstrating uniform cardiovascular protective effectiveness across diverse cancer patient cohorts. Various pharmacological agents have been investigated, which include neural hormone blockade therapies, statins, beta-blockers, and the drug angiotensin-converting enzyme (ACE) inhibitors. However, the overall evidence is still mixed because the studies used different designs, patient groups, and anticancer treatments [29]. Beta-blockers and ACE inhibitors have demonstrated notable efficacy among these interventions. Clinical studies have indicated their potential to mitigate left ventricular dysfunction, maintain ejection fraction, and enhance cardiac biomarker profiles, particularly in patients undergoing cardiotoxic chemotherapy [30]. Even though these results are promising, the benefits have not been consistently reproduced in all trials. The differences in results show how important it is to have personalized cardioprotective strategies [31]. They have stressed that the most effective prevention measures must work on the basis of the individual risks of each patient which may include his or her cardiovascular risk level, the nature of cancer therapy that he or she is getting and the cumulative number of drugs they have undergone. In line with this they advocated a complete evaluation of cardiovascular risk and a cardiac screening in routine cancer treatment plans. In general, the evidence we have now supports the idea that pharmacologic cardioprotection might help in cardio-oncology, but it is not certain. These results underscore the pressing necessity for meticulously designed, large-scale randomized controlled trials to formulate definitive guidelines and pinpoint patient populations that are most likely to gain from targeted preventive interventions [32].

- *Management of Established Cardiotoxicity*

Cardio-oncology requires a multidisciplinary approach that is comprehensive, i.e. it should prevent, diagnose, and reduce heart issues in cancer patients. This combined model emphasizes that oncologists, cardiologists, clinical pharmacists and other medical practitioners are required to work in harmony to enhance the level of cancer treatment as well as heart conditions [33]. The beginning of key management strategies is to determine the baseline cardiovascular risk of an individual prior to commencing treatment of cancer. After that, they should be checked on a regular basis with cardiac biomarkers and advanced imaging techniques to look for early signs of cardiotoxicity. The best way to avoid heart damage from treatment is to use cardioprotective interventions when they are needed. There is a lot of strong evidence that individualized patient care is important. The initial approach in key management strategies is to determine baseline cardiovascular risk in an individual

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before cancer treatment is commenced; this should be followed by the timely initiation of cardioprotective agents such as angiotensin-converting enzyme (ACE) inhibitors and beta-blockers in time, particularly in the high-risk patient group. Careful consideration of the advantages of the treatment of cancer and the cardiac risks is equally important. This will ensure that life-saving cancer treatments are not halted without any reason and that health of the heart is not compromised [34]. The long-term goal of cardio-oncology management is to preserve long-term cardiovascular performance and enable the successful treatment of cancer, with the awareness that cardiovascular complications may severely deteriorate the survival rates and quality of life of cancer patients and survivors.

➢ *Role of Pharmacists in Cardio-Oncology*

Pharmaceutical professionals are very important in cardio-oncology because they are medication experts. They provide specialized pharmacotherapeutic knowledge, oversee medication safety, and give personalized care to cancer patients who are at risk of cardiovascular problems. More and more evidence shows that pharmacists are playing a bigger role in the work that cardio-oncology teams do together. According to a specialized cardio-oncology clinic, pharmacy professionals were in charge of about 75% of the first cardiac medications interventions. This shows how important they are for making cancer treatment work better with cardiovascular drugs. It was also emphasized how important it is for pharmacists to do thorough medication safety evaluations, share their specialized knowledge of cardio-oncology, and give personalized patient education to encourage compliance and early detection of side effects. Even with these contributions, there are still some problems that need to be solved. For example, limited role recognition and fragmented continuity of care are two big problems that are keeping pharmacists from fully integrating into cardio-oncology services. In addition, it showed that there are still gaps in pharmacists' knowledge, with many saying they need more educational materials, structured training programmer, and specialized seminars in cardio-oncology practice. The general agreement is that pharmacists are very important for preventing, keeping an eye on, and managing the cardiovascular risks that come with cancer treatment. As the field of cardio-oncology continues to change, it will be important to improve pharmacist education, make their roles clearer, and encourage collaboration between different fields in order to get the most out of their work on patient outcomes [38].

➢ *Emerging and Novel Approaches*

Cardio-oncology has become an important and quickly growing field of medicine that deals with the complicated heart problems that can happen with modern cancer treatments. As chemotherapy has made great strides in helping people with cancer live longer, a greater emphasis has been paid to avoiding and curing heart disorders which are caused by treatment for cancer. The field emphasizes several critical strategies, including comprehensive cardiovascular risk assessment prior to the initiation of cancer treatment [39], the early detection and monitoring of cardiovascular issues during and post-treatment [40], and the management of therapy-related cardiovascular risks in collaboration with oncologists, cardiologists, and other healthcare professionals [41]. A lot of research on about 17 million cancer survivors shows that cardio-oncology is important. This is because modern cancer treatments are linked to a lot of cardiovascular problems [42]. Recent studies have demonstrated that targeted therapies and immune checkpoint inhibitors can induce various and occasionally unforeseen cardiovascular side effects. This makes it harder for doctors to manage patients' care [43]. The most compelling evidence suggests that early, interdisciplinary intervention within structured cardio-oncology programmed can significantly diminish cardiovascular risk, avert the advancement to overt cardiac disease, and enhance long-term outcomes for patients receiving cancer treatment.

➢ *Clinical Evidence and Guidelines*

Cardio-oncology is a growing field of medicine that looks at cardiac issues that can happen during cancer treatment. The 2022 European Society of Cardiology (ESC) instructions are a big step towards making cardio-oncology practice more consistent. They are a major step forward in this field. These guidelines seek to facilitate patients in undergoing potentially life-saving cancer treatments while reducing the risk of cardiotoxicity by establishing unified risk stratification frameworks and standardized definitions of cardiovascular toxicity [44]. Even though these guidelines are clinically important, there isn't a lot of evidence to back them up. A thorough assessment indicated that 209 of the 273 recommendations are substantiated by level of evidence C, indicating dependence on expert consensus, limited studies, or retrospective data, and highlighting a significant deficiency in high-quality prospective research [45]. Nonetheless, key recommendations stress the importance of checking the patient's baseline heart function before starting cancer treatment, as well as targeted preventive measures for high-risk patients and certain anticancer regimens [46]. Overall, this evidence presents cardio-oncology as an open playing field of clinical research. It implies that the potential to receive the robust evidence, enhance the clinical recommendation, and eventually advance the cardiovascular outcomes and quality of care of cancer patients are numerous.

➢ *Challenges and Future Perspectives*

There are many important issues that cardio-oncology needs to address. It should somehow prevent and manage cardiovascular toxicity as well as ensure that cancer treatment is also effective as possible. This involves a patient-centered interdisciplinary approach. As cancer treatments get harder and more people live through it, the heart health of both patients and survivors has become a big part of long-term outcomes. Some of the biggest problems in the field are the lack of standardized tools for cardiovascular risk stratification, the need to improve personalized medicine approaches, and the need to improve cooperation between oncologists, cardiologists, and other healthcare professionals [47]. Additionally, they identified several high-priority areas, such as the creation of strong predictors of cardiotoxicity, better ways to stop and treat cancer-related thromboembolism, and better long-term care for survivors[48].In the future, cardio-oncology will focus on

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figuring out the molecular and clinical causes of cardiovascular toxicity, coming up with effective ways to prevent it and protect the heart, and making personalized interventions based on each patient's risk profile. It is also very important to address healthcare disparities and make sure that everyone has equal access to cardio-oncology services. Cardio-oncology has become a significant aspect of the entire cancer care process, encompassing its prevention and detection prior to treatment and its monitoring during treatment as well as the treatment of survivors following treatment [49]. The discipline continues to expand due to improved cancer survival rates and increased use of new treatment. This demonstrates that it is necessary to continue with carrying out research and developing new concepts that can enhance heart health among cancer patients.

III. CONCLUSION

Cardiovascular oncology has emerged as a significant and required subspecialty which examines the complex nature of correlation between cancer therapy and cardiac well-being. As cancer survival rates improve and stronger anticancer drugs are used more often, heart problems have become a major cause of illness, death, and poor quality of life for cancer patients and survivors. This field focuses on early risk assessment, ongoing monitoring, and prompt management of cardiotoxicity using a patient-centered, multidisciplinary approach. Pharmacists, together with cardiologists and oncologists, are very important for making pharmacotherapy as effective as possible, stopping drug interactions, and making medications safer. Even though current guidelines give clinical practice a structured framework, a lot of the evidence is based on expert consensus. This shows how important it is to do more rigors prospective research. The interdisciplinary collaboration between cardio-oncology care and discovery of biomarkers as well as advancements in personalized medicine will improve cardio-oncology care in the future. It is only through the combination of cardiovascular protective measures and effective cancer therapy that one can ensure that cancer patients receive the best care and have more positive outcomes in the long term.

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