Cardiovascular Risk Assessment and Prevention in Cardio-Oncology

Beyond Traditional Risk Factors

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KEYWORDS

• Cardio-oncology • Precision medicine • Multi-omics • Wearable technology • Real-time data • Social determinants • Gut microbiome • Machine learning

KEY POINTS

- Cardio-oncology care extends beyond traditional risk factors, encompassing social determinants, environment, and even gut microbiome.
- Multi-omics approaches, wearable technology, and big data analytics offer deeper insights into real-world patient experiences beyond controlled settings.
- Seamless integration of novel tools with established practices is crucial for personalized care strategies.
- Continuous real-time data-driven updates to treatment plans empower true precision medicine. This holistic approach holds great potential for improved patient outcomes and a future of precision cardio-oncology.

INTRODUCTION

Cardio-oncology has emerged as a vital interdisciplinary field addressing cardiovascular complications from cancer treatments, such as chemotherapies, radiotherapy, immunotherapy, and targeted therapies, which may cause adverse effects like cardiomyopathies, heart failure, and hypertension.[1–8] This field has evolved from treating overt cardiotoxicities to focusing on prevention and early detection of these complications, integrating preventive cardiology into cancer patient care.[9–11] Moreover, cardiovascular diseases (CVDs) and cancer share common risk factors, including lifestyle behaviors and genetic predispositions, but broader social, commercial, and environmental determinants impacting patient health are often overlooked in cardio-oncology clinical studies.[12–15]

Emerging risk factors such as the social determinants of health (SDOH), environmental factors, and microbiome disturbances play a critical role in the risk for both CVDs and cancer (**Fig. 1**). These factors not only disproportionately affect patients with cancer compared with the general population but also create a complex interplay

Funding: None.

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Cardiol Clin 43 (2025) 1–11
https://doi.org/10.1016/j.ccl.2024.08.003

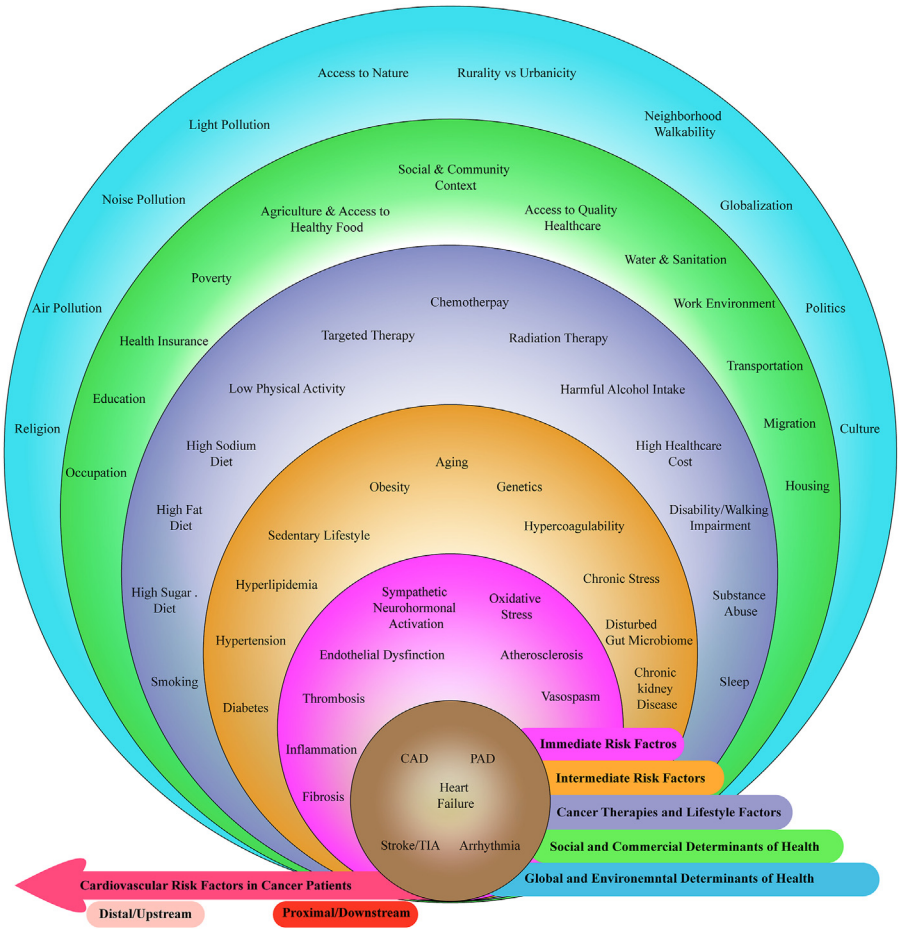

Fig. 1. The web causation of cardiovascular diseases (CVD) in cardio-oncology population. Distal/Upstream risk factors are the factors that have indirect impact on health and are usually more remote, broader, and systemic and have long-term influence; Proximal/Downstream risk factors are the factors that have direct impact on health and usually occur closer in time to the health outcome, specific, and have more immediate effect; Intermediate risk factors are those factors that act as independent cardiovascular risk factors and also as mediating factors for the more distal factors.

of risks that significantly impact these individuals' health. This vignette-based review aims to enhance cardio-oncology care by examining these factors, understanding their interactions, and exploring strategies to manage and mitigate their impact on patient outcomes.

EMERGING RISK FACTORS

Social Determinants of Health

A 63-year-old male prostate cancer survivor from a rural community who relies on public transportation is facing delays in accessing cardiac care post cancer treatment because of missed appointments and inconsistent follow-up. His low income, educational background, having no health insurance, and limited access to health care further complicate the situation and exacerbate his cardiovascular risk.

ACCESS TO CARE

SDOH significantly impact cardiovascular health in patients with cancer, with access to care being a critical factor. Economic stability and education level influence disparities in CVD outcomes,[16–18] where unemployment and low income restrict access to quality health care,[19–21] essential medications, and nutritious food, exacerbating CVD risk.[22] These disparities extend to life-saving procedures such as percutaneous coronary interventions,[23–26] with affordability and provider discrimination limiting access for low-income and rural individuals, further complicating the cardiovascular health landscape for patients with

cancer.[12,13,27,28] Similarly, educational attainment is closely related to the risk of CVD, especially in patients with cancer.[27,29] By recognizing the individual circumstance and providing tailored support, health care providers can empower patients to navigate these challenges and improve their overall health, particularly cardiovascular health.[30,31]

Coordination between specialists and primary care physicians (PCPs) is also vital in providing comprehensive care for the growing number of cardio-oncology patients, especially in remote and disadvantaged areas.[32] With that growth and the shortage of dedicated cardio-oncologists, PCPs and general cardiologists are becoming crucial to bridge that access gap. PCPs especially emerge as central figures in coordinating cardio-oncology care in survivorship owing to their established patient relationships, holistic approach, and the frequent patient interactions allowing closer monitoring.[33]

NEIGHBORHOOD

The neighborhood environment plays a significant role in cardiovascular health outcomes. Areas with lower socioeconomic status (SES) often lack healthy food options ("food deserts") and are saturated with unhealthy alternatives ("food swamps"), contributing to risk factors such as diabetes and obesity.[34–36] Additionally, neighborhood factors, including limited access to nature and transportation, poor walkability, and high crime rates, can increase CVD risks and negatively impact mental health through stress and depression, highlighting the need for interventions tailored to these environmental challenges.[37–44] Community-based education programs and counseling can empower individuals with the knowledge of health ownership and encourage the adoption of healthy habits like physical activity, with outreach programs such as Walk Your Heart to Health program in Michigan and Houston Bayou Greenways program in Texas.[45,46]

FINANCIAL TOXICITY

Financial toxicity arises from the adverse economic impacts of cancer treatment costs, leading to cost-cutting behaviors that can affect medication adherence and increase mental health burdens.[47,48] Key risk factors include demographic characteristics, cancer-related factors, treatment type, and insurance coverage.[49] The high costs of health care contribute to significant financial hardship, with many patients with cancer depleting their assets or incurring debt.[50] Another study revealed that cost concerns led around 20% of patients to underuse prescribed medications, 18% to partially fill prescriptions, and 24% to skip medications entirely.[51] Furthermore, the psychological impact is substantial, with more studies suggesting that 20% to 50% of patients with cancer report financial stress.[52,53] Multifaceted solutions, including societal and clinic-level strategies, are proposed to mitigate these effects, emphasizing the importance of addressing financial toxicity in cancer care. At the national policy level, broader interventions, such as government price negotiations, aim to align drug prices with evidence-based effectiveness and support clinical trials for more affordable alternatives.[48,49]

HEALTH INSURANCE COVERAGE

Health insurance coverage is crucial in mitigating financial toxicity and ensuring access to necessary care. The lack of adequate coverage can delay cardiovascular screenings and contribute to higher mortality rates among cancer survivors, particularly those uninsured or on Medicaid.[54,55] Multidisciplinary teams and initiatives, such as the administration of questionnaires (eg, Comprehensive Score for Financial Toxicity questionnaire) to understand patients' SDOH challenges, are essential in tailoring support and alleviating financial burdens.[47] At our cardio-oncology clinic at the Medical College of Georgia and Georgia Cancer Center, we have launched an initiative where all our patients are administered the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences questionnaire. This tool allows us to gain a deeper understanding of each patient SDOH challenges and tailor the support accordingly.[13]

ENVIRONMENTAL FACTORS AND AIR QUALITY

A 48-year-old colon cancer survivor, who reports living in an urban area with high pollution levels, shows increased heart palpitations during days with poor air quality. Despite completing his cancer treatment, he remains attentive about his health, but the environmental conditions significantly impact his ability to exercise and spend more time in nature and green spaces.

Environmental factors, particularly pollution, play a critical role in cardiovascular health, contributing significantly to morbidity and mortality worldwide.[56] Notably, pollution is responsible for 21% of CVD deaths globally, with contaminants like lead, arsenic, and cadmium being significant

contributors.[57,58] The World Health Organization has identified air pollution as the largest environmental health risk, attributing 37% of deaths from ischemic heart disease and stroke to air pollution.[59]

This impact is further compounded by the exacerbation of existing cardiovascular risk factors such as hypertension, diabetes, and atherosclerosis, even below regulatory standards, affecting an estimated 94% of the global population living in areas with unsafe air quality levels.[14,60–62] Furthermore, the disproportionate impact on lower SES groups and communities of color highlights the inequities in the global impact of air pollution, emphasizing the need for policy changes to reduce exposure.[14,15,63]

In response to the growing concern over the health risks associated with air pollution, initiatives like the Environmental Protection Agency's Air Quality Index (AQI) have been developed.[64] The AQI provides daily air quality reports and activity recommendations based on pollution levels, empowering individuals with heart disease to make informed decisions regarding their exposure.[65] Additionally, technological advancements, such as wearable devices, offer real-time environmental data, revealing significant associations between environmental factors and adverse patient responses, including increased blood pressure due to noise pollution and higher heart rate variability with air pollution exposure.[66–69] These insights underscore the importance of understanding the impact of environmental factors on cardiovascular health and the potential of policy changes and innovative technologies to mitigate risks and improve cardiovascular outcomes.[70]

MICROBIOME

A 45-year-old lymphoma survivor experiences persistent unexplained digestive issues and cardiovascular symptoms including higher blood pressure and palpitations. On further examination, he is found to have a gut microbiota dysbiosis with elevated levels of trimethylamine N-oxide (TMAO), a metabolite associated with higher risk for CVD and risk factors.

The gut microbiota, a complex community of microbes residing in the human gut, plays a significant role in health and disease, extending its influence beyond mere digestion to act as a secondary endocrine organ.[71] Its composition and function are intricately linked to CVD development and progression, with gut-derived metabolites like TMAO emerging as potent predictors of CVD risk.[71–77] Factors such as diet, gut age, and renal functions significantly influence TMAO levels, underscoring the impact of dietary choices, particularly red meat and animal products, on cardiovascular health.[78–81] Moreover, the interplay between cancer treatments and gut microbiota highlights the complex relationships affecting cardiovascular health.[82] Promising therapeutic interventions include dietary modifications, such as the Mediterranean diet, and the use of metformin, intermittent fasting, prebiotics, and probiotics to modulate gut microbiota composition, alongside the potential of nanomedicine for targeted interventions.[76,83–87] With advancements in sequencing technologies and bioinformatics, there is an increasing emphasis on personalized therapies targeting the gut microbiota, offering new avenues for CVD prevention and management.[88–90]

NOVEL METHODS OF RISK FACTOR DETECTION AND PREVENTION

Wearable Technologies

A 58-year-old lung cancer survivor experiences challenges with frequent palpitations and in maintaining physical activity levels. Despite regular follow-ups, his PCP is struggling with detecting and characterizing these palpitations. Upon using a smartwatch, both the physician and the patient were able to identify the blood pressure, heart rate fluctuation patterns, and irregular sleep patterns. They were also able to associate it with different environmental factors such as air quality, pollution, and noise.

Wearable technologies, exemplified by devices such as the Apple Watch, have transformed cardiovascular care by enabling self-monitoring and early disease detection (**Fig. 2**). Equipped with advanced sensors for accelerometers, electrocardiography, and photoplethysmography, these devices facilitate continuous health monitoring, improving pulse checks, and enhancing the detection of arrhythmias like atrial fibrillation with notable accuracy.[91–95] Their adoption has democratized access to health monitoring, bypassing the need for extensive outreach or training programs. Furthermore, they play a pivotal role in managing chronic conditions by promoting physical activity and adherence to medical advice, thus significantly benefiting patients with heart failure and those with complex care needs by monitoring vital signs and activity levels, enhancing rehabilitation, and medication adherence.[96–98]

In the context of cardio-oncology, wearable devices offer the ability to not only monitor the shared traditional risk factors but also continuously track the various environmental factors

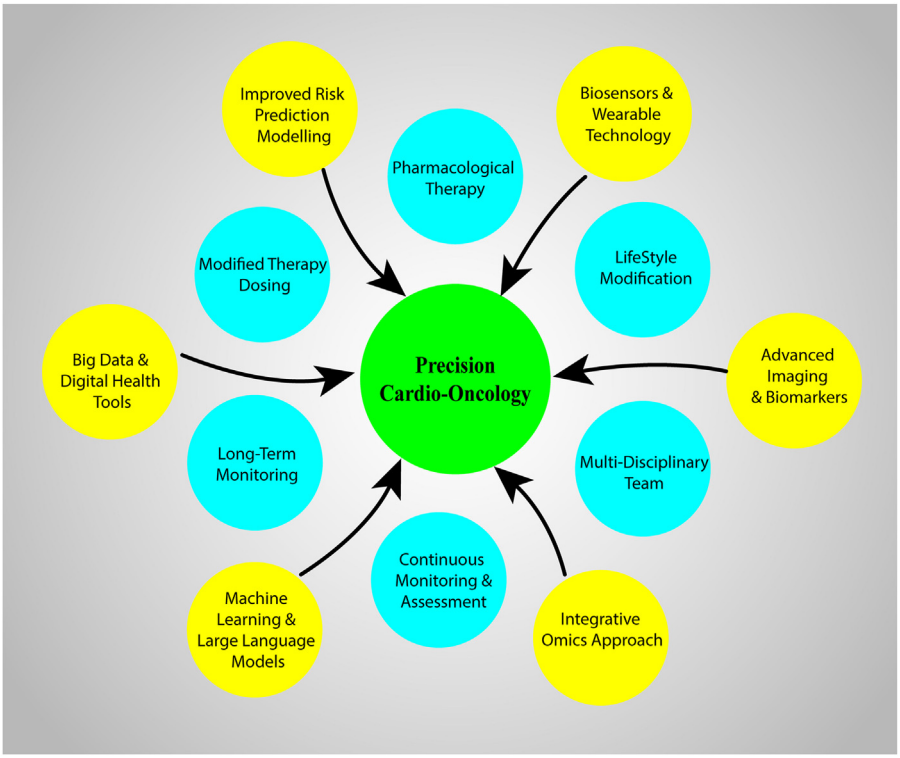

Fig. 2. The toolbox for achieving precision cardio-oncology care. Yellow circles represent the emerging methods to identify risk factors. Blue circles represent the preventative strategies taken to mitigate the risk factors impact.

such as pollution and noise and lifestyle factors like sleep patterns and physical activity levels. These devices can also measure vital signs including blood pressure and heart rate and detect arrhythmias, facilitating earlier detection of cardiotoxicities. This continuous monitoring increases the patients' awareness of their health and environment, encouraging healthier lifestyles and enabling earlier behavioral and lifestyle interventions. When combined with artificial intelligence and telehealth, wearable technology would promote healthy lifestyles and personalized care, marking a shift toward precision health care by analyzing real-time data to provide tailored health recommendations.[99–101]

MULTI-OMICS APPROACH

A 42-year-old lymphoma patient with a strong family history of heart disease presented with complex medical history that includes several comorbidities. During the cancer treatment, he showed fluctuating biomarkers and varying responses to cancer therapies which further complicated his cardiovascular risk assessment. Utilizing the multi-omics approach, the team was able to integrate the genomic, radiomic, proteomic, and metabolomic data to construct a detailed cardiovascular health profile, develop a personalized treatment strategy, and monitor for potential cardiotoxicities.

The multi-omics approach represents a systemic strategy to understand the complex interplay between various biological layers (genome, epigenome, transcriptome, proteome, and metabolome) in CVD.[102,103] This approach transcends traditional single-target investigations, employing tools for disease states such as familial congenital heart diseases,[104] pulmonary arterial hypertension,[105] and coronary artery disease,[106] while enabling novel biomarker discovery. The integration of multi-omics data, utilizing network science tools, offers a holistic understanding of disease mechanisms at multiple levels.[107–111] This systemic perspective is essential for identifying key pathways, differentiating between disease phenotypes, and guiding personalized treatment strategies, thereby unlocking immense potential for drug discovery and precision medicine in cardio-oncology.[112,113]

ADVANCED IMAGING STUDIES AND RADIOMICS

A 55-year-old multiple myeloma survivor presents with unexplained shortness of breath on exertion.

Traditional risk factors appear within the normal range. A comprehensive cardiac evaluation, including coronary artery calcium scoring, reveals the presence of subclinical atherosclerosis, and further cardiac MRI suggested cardiac amyloidosis.

Advanced cardiac imaging and radiomics have significantly expanded beyond their traditional diagnostic roles, becoming instrumental in prognostication, risk stratification, and the early detection of cancer therapy–related cardiac dysfunction.[114]

Techniques such as echocardiography and cardiac magnetic resonance offer detailed assessments of cardiac function and structure (eg, myocardial strain).[114–118] Recent advancements in deep learning have further enhanced the capabilities of these imaging modalities, enabling accurate detection and risk stratification of various cardiac conditions (eg, point-of-care screening for aortic stenosis).[119] Additionally, computed tomography calcium scoring has emerged as a valuable tool for assessing coronary atherosclerosis and predicting major adverse cardiovascular events.[120–123]

MACHINE LEARNING AND LARGE LANGUAGE MODELS

Machine learning (ML) and large language models (LLMs) are reshaping the landscape of cardiovascular care and research by enabling the analysis and interpretation of vast amounts of medical data. These technologies have demonstrated their potential in improving cardiovascular risk stratification, particularly in patients with cancer undergoing treatment.[124] By analyzing clinical notes, electronic health records, and leveraging cancer-specific ML algorithms, these models have shown superiority over conventional risk scores in predicting CVD in patients with cancer.[125,126] In our lab, we were able to leverage ML models to improve risk prediction models for CVD in patients with cancer, for example, breast[127,128] and prostate cancers.[129] The application of ML and LLMs in cardio-oncology holds promise for enhancing diagnostic accuracy, personalizing treatment plans, and ultimately improving patient outcomes in the intersection of CVD and cancer.

SUMMARY AND CONCLUDING REMARKS

This review delves into the often-overlooked factors impacting cardio-oncology patient care, highlighting existing tools and emerging approaches to navigate these challenges. In an increasingly complex world, SDOH, environmental influences, access to health care, financial toxicity, and microbiome disruptions pose significant burdens on patient well-being.

The use of multi-omics approach offers a powerful lens to delve deeper into the intricate relationships between diseases and the interplay of contributing factors. Combining real-time data from wearable technologies with machine learning and big data analytics allows for deeper understanding of daily life experiences beyond controlled research settings.

Besides the advancements in pharmacologic therapies and multidisciplinary teams, our ultimate goal lies in seamlessly integrating innovative approaches with established practices. This synergy will unlock the secrets of complex and heterogenous CVD in patients with cancer, ushering in an era of precision cardio-oncology. This vision translates to tailored therapies and comprehensive management plans, continuously updated for each patient based on real-world data, empowering us to provide truly personalized care.

CLINICS CARE POINTS

- Comprehensive Risk Stratification: Utilize cancer-specific cardiovascular risk assessment tools that integrate traditional risk factors with cancer- and tratment-related characteristics, including cancer type and types of therapies.
- SDOH and Personalized Risk: Incorportae social detrminants of health (eg, access to care and financial stress) into cardiovascualr risk assessments to better tailor management strategies for vulnerable patients.
- Wearable Technology and Remote Monitoring: Leverage the real-time data from wearbale devices and telehealth to detect early cardiovascular anomalies and adjust care accordingly.
- Tailored Lifestyle Modifications: Provide personalized recommendations for exercise, dietary interventions, and stress management based on each patient's cardiovascular risk profile, cancer treatment plan, and gut microbiome health to improve long-term outcomes.

ACKNOWLEDGMENTS

The authors would like to acknowledge the valuable contributions of Lakshya Seth, BS, Vraj Patel, BS, Akanksha Samyal, BA, Rana Rashwan, MBBCh, and Zeyad Kholeif, MBBCh in collecting data and drafting sections on social determinants of health, environmental factors,

wearable technology, advanced imaging, and omics approaches. Their assistance was greatly appreciated.

DISCLOSURE

A. Guha and N.L. Weintraub are supported by the American Heart Association-Strategically Focused Research Network Grant in Disparities in Cardio-Oncology (#847740, #863620). A. Guha is also supported by the Department of Defense Prostate Cancer Research Program's Physician Research Award (#HT94252310158).

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