



EDITORIAL COMMENT

The bidirectional association between cardiovascular disease and cancer: Is there an increased risk of cancer among heart failure patients?



A relação bidirecional entre doenças cardiovasculares e cancro: existe risco aumentado de cancro em doentes com Insuficiência Cardíaca?

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Cancer and cardiovascular diseases (CVDs) share many of the same risk factors.¹ Some studies have shown that patients with lung and hematologic malignancies had the highest prevalence of all types of CVDs. Their prevalence is unexpectedly high and sub-optimally managed in patients with cancer. This could be an opportunity for onco-cardiologists to fulfill this unmet need and to help improve outcomes in patients with cancer and coexisting heart disease.¹

Heart failure (HF) is one of the most severe complications of many CVDs, and over the past decades we have witnessed an exponential growth in its incidence.²

Cancer patients may develop HF due to the well-known cardiotoxic effects of antineoplastic treatments. In order to provide better care to subjects experiencing cardiotoxicity, cardio-oncology was born and has gained a relevant role in cardiology settings.² Whereas HF risk from cancer drugs has been actively investigated in numerous clinical trials, there are very little data available in the setting of reverse cardio-

oncology, which looks at cancer incidence in patients with pre-existing HF.²

An emerging concept of reverse cardio-oncology focuses on the heightened risk of cancer in patients with cardiovascular disease. Common mechanistic characteristics of cancer and HF, such as chronic inflammation and clonal hematopoiesis, as well as common predisposing factors such as obesity and diabetes underline the relation between both cardiovascular disease and various cancers.³

Shared biological mechanisms and risk factors may explain the link between cardiovascular disease and cancer. Among others, pathways related to inflammation, clonal hematopoiesis, and hypoxia, as well as circulating microRNAs, extracellular vesicles, and mediators of cardiac origin are of interest in this regard. Advancements in our scientific understanding behind the interactions between cardiovascular disease and cancer and the exact role of all the factors in this cross talk could potentially lead to mechanistic insights that can guide future therapeutic research and clinical decision making.⁴

In recent years, studies have been conducted of community-based cohorts suggesting a higher prevalence of

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cancer in subjects with HF compared with those without HF, even when the influence of shared risk factors, surveillance biases and cardiovascular medications were taken into due consideration. The association between cancer and HF may have important implications, fostering research on common pathophysiological mechanisms and setting the stage for preventive cancer screening in HF patients and the identification of new targets for pharmacological interventions.²

The association between HF and cancer has gained increasing attention in recent years. The coexistence of these two entities is increasingly common; it is caused by the progressive aging of the population and the growth in risk factors predisposing patients to both conditions and poses a substantial clinical and economic burden to society.⁵

The complex and bidirectional nature of the interaction between HF and cancer has been recently addressed in epidemiological and preclinical studies.⁵

Barbosa et al. in "The association between pre-existing heart failure and cancer incidence: a systematic review and meta-analysis" present us with a very well conducted systematic review and meta-analysis, where they summarize all cohort studies presently available and suggest that there is a significantly increased risk of incident cancer among HF patients. The pooled hazard ratio across the 9 studies was 1.30 (95% CI: 1.04–1.62, $p=0.02$), showing that HF patients are at 30% greater risk of being diagnosed with a new malignancy.⁶

The authors provided tables presenting adequate details and clear figures, illustrating the association between HF and site-specific cancer risk with statistical significance for lung, gastrointestinal, hematologic, and female reproductive system cancers. The cancer types associated with major risk were those of the lung and female reproductive system, followed by hematologic cancer.⁶

The authors propose potential explanations for the observed association between increased incidence of cancer in patients with pre-existing chronic HF⁶:

- (1) HF and cancer share common risk factors (smoking, aging, genetic predisposition, obesity, and diabetes mellitus) that can explain, at least in part, the co-occurrence of these two conditions.
- (2) Some common pathophysiological mechanisms are involved in both diseases; inflammation plays an important role in these two conditions, angiogenesis adaptations are another common mechanism favoring this linkage and the hypothesis that neurohormonal activation may also account for the increased risk of cancer observed in HF.

- (3) HF may promote oncogenesis through the release of cardiac circulating factors.
- (4) Mutual pathogenic gene variants may also predispose individuals to both cancer and HF.

This review draws our attention to the screening of our patients and also to the translational research that is justified in these cases, both to understand the mechanisms underlying this association and to treat these patients better.

Cardio-oncology emerged to evaluate and treat the cardiovascular repercussions of therapies used in oncology, and to prevent progression to HF.

With this presentation of reverse cardio-oncology and the increasingly clear bidirectionality and sharing of risk factors and promoters of both cardiovascular diseases and cancer, we are facing a new paradigm with the need to investigate oncological disease in cardiovascular patients, particularly in patients with HF.

Conflicts of interest

The author has no conflicts of interest to declare.

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