Editorial

Double Jeopardy: Cancer and Heart Failure

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Approximately 1.7 million new cases of cancer were diagnosed in the U.S. in 2018 and almost half were greater than 65 years of age at the time of diagnosis.[1] In the older cohort, approximately 40% suffer from one or more co-morbid conditions, with an estimated 10% having co-morbid heart failure (HF).[2] In general, co-morbid illness impacts survival in patients with cancer[2–4] and is associated with increased health care costs both in and outside the hospital.[3] However, few studies have assessed the influence of specific chronic conditions on outcomes. In this issue of the Journal of Cardiac Failure, Tuzovic and colleagues evaluated the impact of co-morbid HF on length of stay, in-hospital costs, and in-patient mortality among patients hospitalized with a primary diagnosis of cancer.[5]

Using National In-Patient Sample (NIS) data from 2014, Tuzovic et al. compared outcomes in 834,900 hospitalizations for cancer without co-morbid HF to 64,740 hospitalizations for cancer with HF.[5] Patients with HF were older and, as expected, had a greater burden of other co-morbidities including hypertension, diabetes, chronic kidney disease, coronary artery disease, atrial fibrillation, and chronic obstructive pulmonary disease. Patients with HF had higher age-standardized length of stay, in-patient costs, and in-patient mortality compared to those without HF. Importantly, this increased mortality risk persisted even after adjustment for potential confounders including age, race, Elixhauser co-morbidity score, insurance payer, and median household income (OR 1.12, 95% CI 1.04-1.20, p=0.002).

This study has major strengths[1]: it adds to the growing body of literature demonstrating an increased burden of cardiovascular disease (CVD) in patients with cancer, and[2] it highlights the prognostic implications of co-morbid HF in patients with active cancer, rather than survivors.

The burden of CV risk factors and CVD has increased substantially over the last decade in patients with active cancer.[6] This is partly due to the aging population and shared risk factors.[7] In the current study, almost half the patients with co-morbid HF were > 75 years old, compared to 21.5% without HF.[5] Furthermore, cancers such as lung and bladder cancer that are associated with tobacco use, a shared risk factor, represented a higher proportion of patients with HF.[5] Common genetic factors and signaling pathways, triggered by inflammation and oxidative stress, also play a pivotal role in the pathogenesis of cancer and HF.[7] Tuzovic et al. found that patients with hematologic cancers such as leukemia, non-Hodgkin lymphoma, and multiple myeloma were more likely to have co-morbid HF.[5] This observation is interesting given the recent discovery of clonal hematopoiesis as a driver of both hematologic malignancies and HF.[8] Lastly, cardiotoxic effects of various cancer therapies can lead to new-onset HF. The current study does not permit assessment of the contribution of cardiotoxicity since it does not differentiate between prevalent and incident HF.

Previous studies have shown decreased long-term survival in patients with HF and incident cancer compared to those without HF.[9,10] The analysis by Tuzovic et al. further emphasizes the added short-term risk that HF imposes on patients with cancer.[5] However, given the limitations of administrative database analyses, the reasons underlying this increased risk remain unexplained. First, because no specific cause of death is available, it remains unclear whether the increased in-patient mortality is related to cancer or HF. Second, the impact of co-morbidities on survival varies with type and stage of cancer.[3] Data regarding the interaction between cancer type, stage and HF could identify high-risk cohorts who might benefit from targeted intervention. Similarly, information on the type and severity of HF is also lacking. Third, previous studies suggest that patients with co-morbidities are less likely to receive standard cancer therapies due to concerns about toxicity and tolerability.[3,4] While the current analysis shows no influence of HF on the percentage of patients receiving chemotherapy,[5] details about chemotherapeutic regimens, surgery, or radiation in patients with or without HF are unavailable. Other unmeasured factors, such as drug-drug interactions, concerns over polypharmacy, and hemodynamic/electrolyte disturbances during cancer therapy, may also lead to withdrawal/under-treatment of HF that may impact survival negatively.

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Clinical trials can provide insight into the mechanisms contributing to adverse outcomes in patients with co-existent cancer and HF. However, one-third of cancer treatment trials exclude patients with HF, and the odds are higher in trials involving drugs with cardiotoxic potential.[11] Similarly, most HF trials exclude patients with active cancer. Future efforts should focus on encouraging greater enrollment of patients with CVD in cancer trials, and vice-versa, or on the creation of a prospective registry involving these patients, as suggested in the current paper.[5]

Additional steps needed to improve outcomes in patients with cancer and HF include[1]: better assessment and management of baseline CV co-morbidities,[2] improved monitoring of at-risk patients to prevent the development of incident HF and to limit exacerbation of co-morbid HF,[3] greater integration and coordination of care between oncologists and cardiologists, and[4] efforts to increase inter-disciplinary research that addresses common pathways linking cancer and HF.

In conclusion, the study by Tuzovic et al. demonstrates the detrimental impact of co-morbid HF on in-patient outcomes among patients hospitalized with cancer.[5] The findings of this study emphasize the need for physicians to move beyond the single disease model of cancer and embrace the complexities of managing patients with co-morbid medical conditions, including HF.

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