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EDITORIAL COMMENT

Adding a Rock to a Hard Place

Mechanical Circulatory Support, Active Cancer, Proceed With Caution*

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In isolation, medical decision-making and management for advanced heart failure and active malignancy are complicated (1); when they overlap, complexity increases exponentially (2). At the extreme is the intersection of left ventricular assist devices (LVADs) and active cancer therapy. LVADs and cancer therapy both involve significant risks, side effects, and burdens, and these are usually cumulative. LVADs and cancer therapy often stabilize rather than cure disease, and both tend to occur in older patients with overlapping risk factors, leaving patients to contend with multiple chronic conditions. LVADs and cancer therapy can have detrimental interactions that include bleeding, infection, and hemodynamic stability. Thus, embarking on cancer therapy in the setting of LVADs is, at best, worrisome. Conversely, committing to LVAD implantation in the setting of active cancer is, at the very least, brazen.

Unfortunately, there is a paucity of data to guide clinicians and patients faced with the need for both LVAD support and cancer therapy. Only isolated reports and case series exist and give a fragmented and incomplete picture of LVAD support in the setting of active malignancy (3,4). Per guideline recommendations from the International Society for Heart and Lung Transplantation, "mechanical circulatory support is not recommended for patients with an active malignancy and a life expectancy of <2 years" (5). However, population-based survival models function poorly when applied to individual patients, making such guidance impractical, leaving clinicians to grapple with high degrees of uncertainty (6). As the population ages, and malignancies and incident heart failure become more prevalent, these scenarios will become increasingly common. When should LVAD implantation be considered for patients with active cancer who are experiencing progressive heart failure? How should aggressive chemotherapies, radiation, and surgery be optimally combined in the setting of LVAD support?

In this issue of *JACC: CardioOncology*, Schlam et al. (7) attempt to provide answers to these questions. They reviewed all 1,123 patients implanted with an LVAD between 2005 and 2019 at either the University of Washington in Seattle or MedStar in Washington, DC. Electronic medical records of all patients, from implant through death or end of follow-up (April 2020), were queried for evidence of cancer diagnosis or treatment. Non-melanoma skin cancers and premalignancies were excluded. The investigators then created a 3:1 match of patients with LVADs without cancer, controlling for age, sex, and implant criteria at time of LVAD placement. A number of important findings emerged from this systematic approach.

First, active malignancy while on LVAD support was quite rare. Despite the high prevalence of cancer, only 22 cases of malignancy were identified from more than 1,000 patients (<2% of all LVAD implants). Of these, 6 patients had active malignancy at the time of LVAD implantation, the so-called "bridge to cancer treatment." The other 16 patients were diagnosed with malignancy while already living on durable mechanical circulatory support. Time from LVAD implant to cancer diagnosis was 371 days (range: 42 to 1,436 days). Prostate cancer was the most common

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malignancy (n = 5), which was not surprising because of the strong propensity for LVAD support used in men (73% in this cohort). Four patients had LVAD implantation for chemotherapy-induced cardiomyopathies following presumed cancer cure, 1 of whom had recurrent malignancy; 2 developed a secondary malignancy (multiple myeloma, acute myelogenous leukemia), and 1 had a separate primary malignancy.

Second, LVAD as a bridge to cancer treatment had heterogenous outcomes. Of the 6 patients with active malignancy at the time of LVAD implant, 5 died. However, the deaths were not clearly related to either malignancy treatment or LVAD complications, and the time to death for these 5 patients varied widely, from 2 to 1,644 days (median: 451 days). The investigators did not say whether this group was younger than the median age of 62 years, but presumably these patients were highly selected. It should also be noted that median survival was less than the LVAD guideline recommendations for more than 2 years (5), but a significant minority of patients exceeded this somewhat arbitrary threshold.

Third, cancer treatments seemed to be reasonably well-tolerated. Early stage cancer was present in 14 patients, 13 of whom underwent chemotherapy with curative intent; for the other 8 patients with more advanced cancer, 6 received palliative regimens. Surgery was used in 12 patients and radiation therapy in 5 patients. Compared with LVAD control subjects without cancer, the patients with LVADs with cancer had similar rates of stroke, pump thrombosis (50% had a HeartMate II device [Abbott Laboratories, Abbott Park, Illinois]), and infection (2 patients had septic shock within 20 days of their first cycle of chemotherapy). Gastrointestinal bleeding was statistically less common in the patients with cancer, although these were small numbers without statistical adjustment for multiple comparisons, and no mechanistic explanation was provided.

Fourth, mortality among the patients with LVADs was high and increased with co-occurrence of cancer. The unadjusted median survival estimate of the 22 patients with LVADs with cancer was 3.53 years compared with the matched control subjects at 3.03 years; however, after adjustment for additional variables, cancer was associated with a doubling of the hazard of death. Although there were limitations in matching and multivariable modeling—with particularly strong treatment selection biases in the bridge to cancer treatment group—these findings did suggest that most patients with LVADs could reasonably undergo thoughtfully designed regimens for cancer treatment.

This 2-center, 2-decade review of LVADs suggested we should occasionally proceed with caution when mixing LVADs and cancer treatment. Most convincingly, these results supported the feasibility of oncologic treatment applied to patients with preexisting LVAD, because feared complications were not markedly increased. In contrast, the mortality data were sobering, with median survival in all patients of <4 years and in the subset with LVAD implantation at the time of active cancer living for <2 years. Another review of 37 patients implanted with LVADs after a history of malignancy showed median survival of more than 2 years; among the 5 patients with active cancer at the time of implant, only 2 lived past 18 months (3). Another report of 8 patients treated with LVADs as bridge to cancer treatment found that 3 died of progression of their cancer, whereas 5 were alive at a median follow-up of 45 months (4). Although patients wish to be "given a chance" and uncertainty allows for hope of long life, the reality is that patients with contemporary LVADs—on average, and especially with cancer—do not tend to live a long time. And the patient, caregiver, and societal burdens are significant.

Overall, we should continue to be highly judicious in the application of LVADs as a bridge to cancer treatment. Multidisciplinary teams should oversee decisions about LVAD implantation—leveraging the infrastructure put into place by heart transplantation—to help parse out what is "medically reasonable." Only in the rare patient—who has managed to thread the unusual needle of active cancer and advanced heart failure at a relatively young age without major predisposing comorbidities or unfavorable social determinants of health—should an LVAD be considered. Even then, high-quality shared decision-making is essential, bringing together the medical team with the patients and caregivers. This process can be facilitated by formal patient decision aids (8), which are shown to improve decision quality (9), but obviously inform rather than replace dynamic discussions that tailor shared decision-making to the coexistence of cancer. The same type of multidisciplinary approach, integrated with patient health goals and treatment preferences, should be used to create medically optimal and patient-centered cancer care. Meanwhile, the cardiovascular community must catch up with the pace of discovery and innovation seen in the cancer space. Only with improved options for advanced heart failure will most patients simultaneously struggling with cancer have a fighting chance of getting out from between a rock and a hard place.

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