

VIEWPOINT

Cardio-Oncology and the Intersection of Cancer and Cardiotoxicity

The Role of Palliative Care



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Over the last several decades, palliative care has evolved from a subspecialty focusing on end-stage disease to one that provides comprehensive care for patients with complex illness. It has been well established for many years in oncology. More recently, palliative care has been recognized as a valuable tool in the arsenal of heart failure (HF) cardiologists. The burden of disease and its associated impact on the patient and caregiver in cancer and HF are exceedingly high and compounded when both diseases coexist. A systematic review and meta-analysis on a diverse spectrum of patients found that palliative care was associated with improvement in quality of life and symptom burden (1). The PAL-HF (Palliative Care in HF) trial confirmed that an interdisciplinary palliative care intervention improves quality of life, anxiety, depression, and spiritual well-being in HF patients (2).

The conceptual framework underlying palliative care in oncology and cardiology is similar (i.e., acute treatment, chronic management, psychosocial issues, and existential or spiritual concerns), as is the focus of supportive care in addressing patient symptoms and the complications of treatment. Palliative care also involves discussions on decision making related to goals of care and advance care planning, focusing on the balance of benefits and burdens of treatment.

Advance care planning, caregiver support, and facilitated decision making in HF are different because the disease trajectory in HF is more unpredictable (3). For example, the role of palliative care is unclear for a patient who returns to New York Heart Association functional class II status after an acute HF decompensation; yet, advanced care planning remains crucial in light of the persisting high readmission and mortality risk. Although cancer may have a steady decline in many instances, cancer patients with cardiotoxicity have highly unpredictable courses because of competing risk. Furthermore, there are important differences in palliative care needs between patients with cancer at risk for cardiotoxicity and patients with HF who develop cancer. It is vitally important that cardio-oncologists leverage their perspective to meet the unique and diverse needs of patients with an uncertain prognostic trajectory from cardiotoxicity.

GROWTH OF CARDIO-ONCOLOGY AND THE NEED FOR PALLIATIVE CARE

The field of cardio-oncology has grown in recent years due to a combination of complex cancer treatment regimens with cardiotoxic risk, increased awareness, and evidence for potential mitigation of cardiovascular complications. Competing concerns constitute an important challenge in patients with cardiotoxicity from cancer therapy and with pre-existing and/or emerging cardiovascular conditions. Although the progression of cancer may be ominous, the specter of cardiovascular complications adds layers of complexity and uncertainty. The interaction of cardiovascular and oncologic disease processes makes the role of the cardio-oncologist in the delivery of palliative care, alongside palliative care specialists, particularly salient.

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TABLE 1 Specific Population in Cardio-Oncology That Could Benefit From Focused Palliative Care

Specific Population	Specific Cardio-Oncology and Palliative Care Concerns
Before treatment: high-risk subgroups (e.g., history of LV dysfunction, high doses of anthracyclines, dual ICI, etc.)	<ul style="list-style-type: none"> • Patients without LV dysfunction: care planning (“primary supportive care”) with cardiology or oncology regarding risks, side effects, and benefits of cancer treatment • Patients with pre-existing HF: involvement of palliative care specialists regarding need to balance HF with cancer treatment • Example: HF patient referred for advanced therapies found to have colon cancer during work-up. Are they eligible for transplant? What is the risk of mechanical circulatory support with increased risk of bleeding, thrombosis, and infection?
During treatment: acute cardiac complications (e.g., clinical heart failure, arrhythmias, myocarditis during immunotherapy, etc.)	<ul style="list-style-type: none"> • Facilitate decision making for balancing risk of complications versus ongoing treatment • Decrease psychological stress related to uncertainty from variability of cardiotoxicity and fear of recurrent cardiotoxicity if resuming treatment • Example: Metastatic breast cancer patient with angina while on capecitabine but no clinical evidence of ischemia. How do you balance risks and benefits of ongoing 5-FU based therapy and manage anxiety due to risk of a coronary event?
During treatment: high-risk subgroups with competing mortality risk (e.g., AL amyloid)	<ul style="list-style-type: none"> • Early referral to specialist palliative care due to high morbidity and mortality • Assist with symptom management for both HF and cancer; advance care planning • Example: AL amyloid patient with substantial cardiac involvement who presents with syncope. What is the prognosis? Should one proceed with cancer treatment?
During treatment: cancer patients on chronic therapy (e.g., CML patients on TKIs, long-term ICI use, etc.)	<ul style="list-style-type: none"> • Guide decision making to balance patient wishes with treatment risk and side effects • Attenuate anxiety over potential for decreased efficacy of cancer treatment and increased CV side effects over time • Example: CML patient on ponatinib who develops severe peripheral vascular disease with ischemia. Should treatment with ponatinib be continued if this is the only effective option for CML?
After treatment: long-term childhood cancer survivors and adult cancer survivors (e.g., post-chemotherapy, post-radiation therapy, bone marrow transplant)	<ul style="list-style-type: none"> • Frame long-term CV risk and importance of lifelong risk factor reduction • Increase understanding of potential lifelong side effects including risk for secondary malignancy, neuropathy, decreased functional capacity, and high cardiometabolic risk • Example: Childhood survivor of Hodgkin lymphoma with mild LV dysfunction (48%) who is intolerant of beta-blockers and ACE inhibitors due to fatigue. What are long-term implications and trade-offs of continuing HF medications?
5-FU = fluorouracil; AL = amyloid light chain; AML = acute myelogenous leukemia; CML = chronic myelogenous leukemia; CV = cardiovascular; HF = heart failure; ICI = immune checkpoint inhibitor; LV = left ventricular; TKI = tyrosine kinase inhibitor.	

Patients may benefit from assistance with decision making, particularly regarding the clarification of values, goals, and preferences. These constitute crucial foundations for making informed decisions about high-stakes interventions. Patients and oncology clinicians may focus on cancer-specific goals, overlooking risks for cardiotoxicity and its implications, or may react to cardiovascular events without putting cancer treatment options in perspective. The inherent global orientation of palliative care considers both diagnoses and integrates patient values, goals, and preferences with a holistic perspective on prognosis and symptom burden. Applied early in the disease process, palliative care can assist with the coordination of care to avoid low value and ineffective therapies and interventions that are discordant with patient wishes.

A PubMed search yielded no studies of palliative care interventions specific to cardio-oncology; yet,

there are multiple groups of patients in the sphere of cardio-oncology with a need for palliative care (Table 1).

HF PATIENTS WITH CANCER

A challenging subset involves patients with advanced cardiac disease diagnosed with cancer. There are limited data to guide cancer treatment in end-stage HF patients under consideration for advanced therapies or home inotropes. Patients with cancer and left ventricular assist devices are prone to thrombosis or bleeding, and chemotherapy may escalate infection risk. In post-heart transplant patients, the risk of solid organ malignancy is increased due to chronic immunosuppression, regardless of whether there is a history of malignancy. Difficult decisions surrounding home inotropes (symptom palliation in the setting of increased mortality risk) are similar to those

involving cancer therapy (extension of survival and control of disease to mitigate symptoms) and need to be framed in the context of overall prognosis.

Implantable cardioverter-defibrillator (ICD) deactivation raises complex questions in cardio-oncology. With progressive HF, there is a transition from sudden cardiac death to pump failure. By nature, sudden cardiac death is unpredictable but may be preferable to having end-stage cancer. On the other hand, ICD discharges save lives, giving a chance for cancer therapies to have an effect. Patients/families (and clinicians) may be willing to discontinue cancer therapy and embrace hospice but may be unwilling to forego ICD therapy. Even though shocks would not modify the eventual outcome, they may be willing to endure them for life prolongation or less uncertainty about the time of death.

INTEGRATING PALLIATIVE CARE INTO CARDIO-ONCOLOGY PRACTICE

Palliative care needs to be continuous and ongoing, whether or not specialty palliative care providers are involved. So-called “primary palliative care” is delivered by generalist, cardiologist, or oncologist clinicians and includes basic symptom management, identification of decision makers, and elucidation of goals of care. Given that a subspecialty of cardio-oncology palliative care is unlikely to be feasible from either a systems or financial standpoint, the unique palliative care needs of the cardio-oncology population should be addressed by primary palliative care with referral to specialist palliative care as needed.

In both oncology and cardiology, there have been numerous proposed models for how to integrate palliative care into the framework of standard treatment. The incorporation of palliative care into cardio-oncology can lean heavily on work previously done in the oncology and HF realms and leverage current resources and programs.

Oncology has the most established frameworks for the integration of palliative care into specialty service models. Cardio-oncology palliative care may fit into these existing frameworks (Table 1). For example, auto-referrals for cancer patients to palliative care based on prespecified criteria may increase the yield and appropriateness of referrals (4). In cancer cohorts, screening tools have been developed to estimate palliative care need, similar to risk models. Cardiovascular issues could be integrated into the existing risk models as an additional trigger for referral.

Although less well developed than in oncology, palliative care integration into HF care is increasing.

The Centers for Medicare and Medicaid Services encourages the participation of a palliative care specialist on mechanical circulatory support clinical teams, and cardio-oncology palliative care could leverage the experience of these specialists, particularly for patients with advanced HF. Regardless of the model, there is a need for high-level expertise in the field and for equipping palliative care, cardiovascular, oncology, and cardio-oncology clinicians.

Patients’ palliative needs may be primarily cardiology driven, oncology driven, or a combination. An optimal process embodies true team-based care, requiring palliative care specialists to play a recognized role. Depending on individual institutions, multi-disciplinary expertise can be developed under the auspices of general palliative care, oncology, or cardiology; however, close collaboration among all 3 specialties is critical to successfully meet the existing needs.

BARRIERS, GAPS, AND OPPORTUNITIES

Despite recognition of the need for palliative care in cardio-oncology and the potential to build on existing models, many questions remain as to how to effectively incorporate sustainable palliative care interventions into the cardio-oncology framework. Potential barriers include the following:

- A projected shortage of palliative care-trained physicians is imminent. In the next 2 decades, the absolute growth in palliative care physicians is estimated at 1%, whereas the need will increase by 20%, resulting in a supply-demand mismatch (5).
- Palliative care specialists who partner with oncology programs may be unfamiliar with the unique issues faced by patients with cardiovascular conditions.
- The Centers for Medicare and Medicaid Services now reimburses time spent for advance care planning under *Current Procedural Terminology* billing codes 99497 and 99498 (6), and there are no limitations on place of service. Cardiovascular and oncology clinicians may both conduct and bill for advance care planning for an individual patient, and many patients may end up receiving separate and potentially conflicting input. At present, there are no established models for how to coordinate this care.
- The optimal timing and mechanisms for referral need to be studied. Many oncology programs have established triggers for referral, but most institutions are not as formalized when referring patients for cardiac symptoms. Should patients with cardiotoxicity rely on referral within the

oncology infrastructure, or should cardiovascular concerns provide increased urgency and impetus for referral? The availability and prompt access to subspecialized cardio-oncology care for different types of cardiovascular morbidity need to be a feature of the referral pathway.

- Cardio-oncology patients may have heterogeneity of symptoms, stemming from cancer and/or cardiovascular or unrelated diagnoses requiring the identification of individual needs.
- Novel telephone and video-based palliative care delivery methods offer an attractive opportunity to address some of the challenges described previously; however, their effectiveness needs to be proven.

WHAT CAN BE DONE TODAY?

The 2017 expert consensus decision pathway for HF highlights how to integrate palliative care into the full spectrum of disease severity in HF, the management of symptoms, and assistance with decision making (7). Modifying this approach for cardio-oncology may be an option until more specific, evidence-based strategies become available. Oncology, cardiovascular, and primary care clinicians and trainees in all of these fields who work within cardio-oncology should incorporate advance care planning into routine care. The Palliative Care and Hospice Education and Training Act seeks to address the projected shortage of specialist clinicians by fostering additional training. The act will establish centers to educate physicians, nurses, and allied health professionals on the core knowledge and skill sets of palliative care.

There is an emphasis to train all clinicians, not just dedicated specialists, to learn the basics of essential palliative care skills (8).

The American College of Cardiology offers resources for palliative care education such as webinars on ACC.org (9), which curate resources and links to palliative care and state-specific advance directives, as well as a PINNACLE work group that developed an advance care planning tool kit (10). These resources are not specific to cardio-oncology, but many of the principles are easily applied.

In summary, with rapidly emerging therapies for cancer treatment, the field of cardio-oncology is anticipated to grow. With increasing numbers of vulnerable cancer patients and survivors with cardiovascular disease, there is a need for a comprehensive approach to symptom control and improved, patient-centered understanding of the risks and benefits of oncology and cardiovascular treatment options. Palliative care will have an essential role, although the specifics for models of care, patient subgroups, delivery methods, and treatment strategies need further exploration. Reassuringly, much has already been accomplished with palliative care in the fields of oncology and HF, and we anticipate that these lessons can be adopted and implemented for the cardio-oncology population.

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REFERENCES

1. Kavalieratos D, Corbelli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA* 2016;316:2104-14.
2. Rogers JG, Patel CB, Mentz RJ, et al. Palliative care in heart failure: the PAL-HF randomized, controlled clinical trial. *J Am Coll Cardiol* 2017;70:331-41.
3. Kavalieratos D, Gelfman LP, Tycon LE, et al. Palliative care in heart failure: rationale, evidence, and future priorities. *J Am Coll Cardiol* 2017;70:1919-30.
4. Adelson K, Paris J, Horton JR, et al. Standardized criteria for palliative care consultation on a solid tumor oncology service reduces downstream health care use. *J Oncol Pract* 2017;13:e431-40.
5. Kamal AH, Bull JH, Swetz KM, Wolf SP, Shanafelt TD, Myers ER. Future of the Palliative Care Workforce: preview to an impending crisis. *Am J Med* 2017;130:113-4.
6. Advanced Care Planning Services. Available at: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/FAQ-Advance-Care-Planning.pdf>. Accessed June 15, 2019.
7. Yancy CW, Januzzi JL Jr., Allen LA, et al. 2017 ACC Expert Consensus Decision Pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. *J Am Coll Cardiol* 2018;71:201-30.
8. Palliative Care and Hospice Education and Training Act. Available at: <https://www.congress.gov/bills/115/congress-house-bill/1676>. Accessed June 15, 2019.
9. CardioSmart. Available at: <https://www.cardiosmart.org/Palliative-Care>. Accessed September 6, 2019.
10. Advanced Care Planning Toolkit. Available at: <https://cvquality.acc.org/login?rurl=http://cvquality.acc.org/clinical-toolkits/advance-care-planning-toolkit>. Accessed September 6, 2019.

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