Management of Heart Failure in Cancer Patients and Cancer Survivors

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KEYWORDS

• Heart failure • Cancer • Cardiotoxicity • Cardioprotection • Anthracyclines • Trastuzumab • Cardio-oncology • Myocardial dysfunction

KEY POINTS

- Patients at high risk of cancer therapeutics–related cardiac dysfunction (either high-risk patients because of their inherent cardiovascular risk factor burden, or planned cardiotoxic cancer therapeutics) should be referred to a cardio-oncology specialist for prevention, surveillance, early management, and recovery of cardiomyopathy.
- Baseline and serial echocardiographic evaluation of systolic and diastolic left ventricular function should be performed in all patients undergoing anthracyclines and/or ERBB2 inhibitors, irrespective of baseline cardiovascular risk, with the exception of asymptomatic patients with metastatic disease.
- If left ventricular ejection fraction declines to less than 40%, cardiotoxic chemotherapy should be stopped; alternative cancer therapies should be discussed, standard heart failure therapies should be implemented, and other causes of left ventricular dysfunction should be excluded.
- Patients with cancer who develop left ventricular dysfunction should be aggressively treated with standard heart failure guideline–directed medical therapies, just as any other patient with heart failure, especially if the neoplasia allows a long-term survival.
- Cancer survivors exposed to high cumulative anthracycline doses and/or chest radiotherapy should be offered lifelong cardiac surveillance.

DEFINITION, CLASSIFICATION, AND EPIDEMIOLOGY OF HEART FAILURE

Heart failure (HF) is currently defined as a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.[1] This condition can be classified by stages of disease progression (A–D), severity of symptoms (New York Heart Association [NYHA] class I–IV), degree of left ventricular (LV) systolic dysfunction (HF with preserved ejection fraction [HFpEF] or HF with reduced ejection fraction [HFrEF]), and need for either standard or advanced HF therapies (**Table 1**).[1–3]

This syndrome is characterized by pulmonary and/or splanchnic congestion, and/or peripheral edema; impaired end-organ perfusion is the hallmark of advanced HF.[1] A list of typical clinical features of this syndrome is provided in **Table 2**. It is most commonly caused by LV diastolic or systolic dysfunction; however, disorders of the other cardiac chambers, pericardium, heart valves, and great vessels can also elicit an HF syndrome.

It is estimated that 20% of the US population greater than or equal to 40 years of age will develop HF in their lifetime.[4] As with cancer, the

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Table 1
American College of Cardiology Foundation/American Heart Association heart failure classifications

Stages		Definition	LVEF	NYHA Class
A: At Risk of HF				
B: Asymptomatic LV dysfunction				I: No physical activity limitation
C: Prior or current symptomatic HF	HFpEF	Diastolic HF	LVEF ≥50%	I: No physical activity limitation
		Borderline HF	LVEF 41%–49%	
		Improved HF	LVEF >40%	II: Slight physical activity limitation
	HFrEF	Systolic HF	LVEF ≤40%	III: Marked physical activity limitation IV: Unable to perform physical activity
D: Refractory HF		Advanced HF	LVEF <30%	III: Marked physical activity limitation IV: Unable to perform physical activity

INTERMACS Profile[2]	UNOS Status[3]
7: Advanced NYHA III 6: Exertion limited 5: Exertion intolerant 4: Resting symptoms on home oral therapy	2
3: Stable but inotrope dependent	1B
2: Progressive decline on inotropes 1: Critical cardiogenic shock	1A

Abbreviations: AHA, American Heart Association; INTERMACS, Interagency Registry for Mechanically Assisted Circulator Support; LVEF, left ventricular ejection fraction; UNOS, United Network of Organ Sharing.
Data from Refs.[1–3]

incidence of HF proportionally increases with age[5]; 5.7 million adults have HF currently in the United States, and it is projected to affect 46% of the population by 2030,[6] and cost $69.7 billion.[7]

HF is involved in 1 every 9 deaths in the United States.[6] Although stable in recent years,[8] the mortality in the HF population has progressively declined since 1979[9] because of the implementation of evidence-based approaches to prevent and treat this condition.[10] Nonetheless, the 5-year mortality risk of the overall HF population is still more than 50%, increasing proportionally with age.[8,9]

In the general population, LV diastolic dysfunction has a prevalence of 21%, whereas 6% of the population has systolic dysfunction.[11] Even when asymptomatic, both systolic and diastolic LV dysfunction have an increased risk of developing HF and all-cause death.[12] Approximately half of patients who seek attention for HF symptoms have a normal or near-normal LV ejection fraction (LVEF)[13]; the prevalence of HFpEF is higher in older patients, especially in women with hypertension, obesity, and anemia.[6,14] The long-term survival of patients with HFpEF in the community is lower than that of patients with HFrEF,[15] mostly driven by noncardiovascular causes[16]; however, in most clinical studies, HFrEF carries a worse prognosis.[17]

Coronary artery disease, hypertension, diabetes mellitus, age, tobacco smoking, and obesity continue to be the leading risk factors for HF.[6] Age, tobacco smoking, diabetes mellitus, and obesity are also cancer risk factors.[18,19] Recently identified shared pathophysiologic mechanisms,[20] and similar long-term survival and prognosis,[21] seem to relate both conditions more than was previously thought. In addition, certain cancer therapies have been recognized to cause or exacerbate HF; among these, anthracycline agents have historically been the most notorious.[22–24]

HEART FAILURE IN CANCER PATIENTS AND CANCER SURVIVORS

The number of cancer survivors continues to increase annually, because of both advances in early detection and treatment, and the aging and growth of the population.[25] It is projected that there will be more than 20 million cancer survivors by 2026.[25] This increase in cancer survivorship has brought forth a concomitant increase in morbidity and mortality from other conditions related to the adverse effects of cancer treatments.[26] Cardiovascular diseases, and