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Heart Failure in Older Adults

Hoda Butrous, MD[1] and **Scott L. Hummel, MD, MS**[2,3]

[1]Oakland University William Beaumont School of Medicine, Beaumont Dearborn-Oakwood Hospital, Dearborn, MI, USA

[2]Frankel Cardiovascular Center, University of Michigan, Ann Arbor, MI, USA

[3]Ann Arbor Veterans Affairs Health System, Ann Arbor, MI, USA

Abstract

Heart failure (HF) is a leading cause of morbidity, hospitalization, and mortality in older adults, and a growing public health problem placing a huge financial burden on the health care system. Many challenges exist in the assessment and management of HF in geriatric patients, who often have co-existing multi-morbid illness, polypharmacy, cognitive impairment, and frailty. These complex 'geriatric domains' greatly affect physical and functional status as well as long-term clinical outcomes. Geriatric patients have been under-represented in major HF clinical trials. Nonetheless, available data suggest that guideline-based medical and device therapies improve morbidity and mortality. Non-pharmacological strategies, such as exercise training and dietary interventions, are an active area of research. Targeted geriatric evaluation including functional and cognitive assessment can improve risk stratification and guide management in older HF patients. Clinical trials that enroll multi-morbid older HF patients and evaluate functional status and quality of life in addition to mortality and cardiovascular morbidity should be encouraged to guide management of this age group.

Keywords

Heart failure; geriatrics; co-morbidities; frailty; polypharmacy; cognitive impairment; quality of life

Introduction

Heart failure (HF) is a growing public health problem affecting an estimated 600,000 Canadians, with 50,000 new diagnoses annually (1). The incidence of HF is strongly dependent on age, with an estimated incidence of 1% at age 65 that approximately doubles with each decade of age thereafter. The lifetime risk of developing HF for both men and women at age 80 is 20%, which is the same risk as those 40 years old despite a much shorter

Address for correspondence: Scott L. Hummel, MD MS, University of Michigan Frankel Cardiovascular Center, 1500 East Medical Center Dr., SPC 5853, Ann Arbor, MI 48109-5853, scothumm@med.umich.edu, (T) 734-998-7991; (F) 734-232-4132.

life expectancy (2). HF is a leading cause of mortality, morbidity, and hospitalization in elderly persons. The cardinal HF symptoms of fatigue, dyspnea and reduced exercise tolerance are common among older adults and are frequently attributed to advanced age or comorbid conditions. The diagnosis and management of HF are often more challenging in elderly patients due to multi-morbid illness, polypharmacy, cognitive impairment, and frailty. Comprehensive assessment of these “geriatric domains” is key for prognosis determination, patient-centered management, and improvement of overall clinical outcomes in older adults with HF.

The Cardiovascular Health Study, a U.S. longitudinal cohort of community-dwelling older adults, reported 1-, 5-, and 10-year mortality rates of 19%, 56%, and 83% following the onset of HF (3). Administrative data from the Canadian Chronic Disease Surveillance System confirm that once HF develops, mortality increases exponentially with age (4). The proportion of hospitalizations that are related to decompensated HF also sharply increases after the age of 65, with 1 in 7 HF hospitalizations occurring in patients ≥ 80 years of age (5). Mortality and hospitalization rates in Canadian HF patients have declined over the past 20 years (6), but much work remains to be done. The large societal burden of HF presents substantial financial challenge to the health care system, with estimated annual direct costs of $2.8 billion (1). In the U.S., estimated yearly expenditures of $30.7 billion are expected to rise to $69 billion/year by 2030 (7), with proportional increases forecast in Canada over this time frame as well.

The average age of enrollment in HF randomized clinical trials is nearly 20 years younger than the average age in epidemiological cohorts. This under-representation of elderly patients in clinical trials has led to uncertainty about the efficacy of guideline-recommended therapies in heart failure with reduced ejection fraction (HFrEF) in this population. Moreover, heart failure with preserved ejection fraction (HFpEF), the most common type of HF in older adults, remains without definitive treatment. Adding to the challenge, the complexity and effectiveness of HF management in the elderly are often influenced by the presence of multi-morbid illness, polypharmacy, and declines in cognitive and/or physical functioning. The presence of one or several of these factors strongly and independently predicts hospital admission as well as in-hospital and post-discharge mortality in elderly HF patients (8–10) This observation highlights the importance of these so-called ‘geriatric domains,’ which are presented in more detail below.

Multi-morbid illness

Advanced management of cardiovascular disease and improved survival has resulted in a more elderly HF population overall. More than a quarter of community-living HF patients are ≥ 80 years of age; such patients often have multiple comorbid illnesses that complicate HF management (11). One recent study reported that 60% of elderly with incident HF had three or more comorbidities and only 2.5% had no associated comorbid illnesses. Hypertension was the most common associated comorbidity at 82%, followed by coronary heart disease with 60% prevalence. Other cardiovascular comorbidities include arrhythmias, peripheral vascular disease, and cardiac valvular disease. Frequent non-cardiac comorbidities include diabetes mellitus, chronic kidney disease, sleep apnea, anemia, malnutrition, depression, arthritis, and cognitive dysfunction. Not surprisingly, some comorbid conditions independently increase mortality in older HF patients, in particular diabetes mellitus, cerebrovascular disease, depression, and chronic kidney disease, which confers the highest risk (3). Patients with HFpEF have a higher burden of non-cardiovascular comorbid diagnoses when compared to those with HFrEF, resulting in a higher non-cardiovascular hospitalization rate in HFpEF patients [(3)].

Polypharmacy

Polypharmacy is defined as the chronic use of five or more medications, and presents an underestimated challenge in the management of geriatric HF patients. Leaving aside medications for symptom management such as diuretics or treatment directed at other chronic illnesses, guideline-recommended medical therapy for HFrEF includes beta blockers (BB), angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), and mineralocorticoid antagonists. In selected patients, isosorbide dinitrate and hydralazine, ivabradine, and/or valsartan/sacubitril are guideline-recommended in HFrEF management (12), but add yet another layer of complexity for providers and patients. Therapy for HFpEF, while not evidence-based per se, frequently includes multiple medications directed at hypertension, atrial arrhythmias, or vascular disease plus associated non-cardiovascular comorbidities.

As HF pharmacotherapy has become more complex and the number of comorbid illnesses in older HF patients has risen, polypharmacy has become the rule rather than the exception. U.S. national survey data indicate that the average older adult with HF now takes more than 6 chronic prescription medications, an increase of more than 50% over the past 2 decades (11). At the time of hospitalization for decompensated HF, 85% of U.S. patients require at least one additional medication to achieve the full complement of HF guideline-recommended pharmacotherapies (13). Polypharmacy negatively impacts HF management by increasing risk of drug non-adherence, drug interactions and adverse effects (14).

Older HF patients commonly use prescription drugs, over-the-counter medications, and herbal supplements that can negatively interact with the HF syndrome itself or the prescription medications used to treat it (15,16). Potentially inappropriate medications in multi-morbid elderly have been defined using Beers criteria and Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP), a list of medications associated with higher rates of adverse drug events in older hospitalized adults (17). Non-steroidal anti-inflammatory agents (NSAIDs) are of particular concern, as these drugs increase mortality and cardiovascular morbidity in HF and are frequently used for acute and/or chronic pain by older adults (18). Recently developed HF-specific lists of potentially inappropriate medications through expert consensus may be more effective in predicting adverse events than the more general STOPP criteria, but further validation is needed (19).

Cognitive impairment

Cognitive impairment (CI) is defined as "having trouble remembering or learning new things, concentrating, or making decisions." Given the prevalence of complex multi-morbid illness and polypharmacy in elderly HF patients, the potential impact of CI on management and outcomes is clear. Age is the greatest unavoidable risk factor for CI, which can range from mild impairment to severe advanced dementia. At least 25% of elderly HF patients have some degree of CI (20), although the prevalence is likely higher and depends on characteristics of the patient population measured and the cognitive test used. Elderly HF patients with CI have poorer self-care abilities and medication adherence, and accordingly an increased risk of mortality and hospital admission (3,21,22). Despite this prognostic importance, treating providers often do not investigate for or document the presence of CI in elderly HF patients (23).

The Mini Mental Status Evaluation (MMSE) is the most widely used tool for evaluation of dementia (3,23), but is time-consuming and not highly sensitive for evaluating milder forms of CI. The Montreal Cognitive Assessment (MOCA) is a 10 minute, 30-point cognitive screening tool with higher sensitivity and reasonable specificity for detecting mild CI when compared to MMSE (24). The MOCA evaluates 6 domains: memory, visuospatial, executive function, attention and concentration, language and orientation. A cut off score of < 26 is the accepted threshold for mild CI; in one cross-sectional study, >70% of elderly HF outpatients scored < 26 on the MOCA even in the absence of previous suspicion or history of CI (25). Further work suggests that a cutoff score of < 24 provides the best balance of sensitivity and specificity to detect CI in patients with cardiovascular disease (26). Low scores on both the MMSE and MOCA have been associated with adverse events in HF patients (23,25), but the length and complexity of administration has limited the uptake of these instruments in HF clinical practice.

The National Institute for Neurological Disorders and Stroke/Canadian Stroke Network (NINDS-CSN) Protocol consists of three MOCA items that assess delayed memory recalling, orientation and fluency/executive functioning. A cut-off score of ≤9 on the NINDS-CSN Protocol has adequate sensitivity and specificity for mild CI when validated against the full MOCA tool in elderly HF patients (27). This five-minute screen can be performed at bedside, clinic or even via telephone. An even shorter instrument is the Mini-Cog test, which consists of three-word recall and clock-face drawing. The Mini-Cog is scored on a scale 0–5, with score ≤ 2 indicating the presence of CI. The test provides excellent accuracy in identifying moderate to severe dementia, but only modest accuracy for mild CI. Despite this limitation, in hospitalized HF patients, a Mini-Cog score ≤ 2 at discharge doubles the hazard for death or hospital readmission independent of other predictors (28). Some advocate that a brief CI screening instrument should serve as a “fifth vital sign” that could guide more intensive self-care support and frequent outpatient follow up, although evidence for these approaches is as yet limited (29).

Decreased functional capacity

Decreased functional capacity is common in elderly HF patients, especially post hospitalization. An objective evaluation of functional capacity can provide prognostic value in geriatric HF patients. Symptom-limited cardiopulmonary exercise testing (CPET) is the gold-standard modality, as it identifies the underlying mechanisms of exercise intolerance and provides several independent predictors of survival in HF patients (e.g. peak oxygen

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consumption, ventilatory equivalent ratio for carbon dioxide)(30). However, CPET is expensive, not universally available, time consuming, and can be challenging for elderly adults to perform.

A 6-minute walk test (6MWT) measures the distance that a patient can walk on a hard flat surface over a period of 6 minutes. The 6MWT is simple, inexpensive, and reproducible after an initial learning effect between the 1st and 2nd tests. However, the correlation of 6MWT with peak oxygen consumption is variable and dependent on the severity of HF and the distance walked. The 6MWT may better reflect activities of daily living than CPET, and increases in 6MWT distance tend to track with improvements in HF symptoms (31). The prognostic value of 6MWT in HF is uncertain, as some studies have reported a marked inverse relationship between 6MWT distance and mortality while others reported no prognostic implications (32,33).

The short physical performance battery (SPPB) is a standardized measure of lower extremity performance focused on three skills; walking, muscle strength, and balance. Up to 4 points are awarded for each of five-meter gait speed, timed chair rises, and standing balance tests, with higher score representing better performance. The SPPB predicts functional disability, rehospitalization, and death in acutely ill elderly patients following hospital discharge for various diagnoses (34). In elderly HF patients, a lower SPPB score is a strong and independent predictor of mortality following hospital discharge for acute decompensation (35).

Disability and frailty

In older patients, HF is associated with progressive decline in function and high rates of institutionalization. Over half of HF patients ≥ 60 years of age report some degree of mobility limitation, and many have difficulty with basic activities of daily living such as bathing, eating, and dressing (11). Even at the time of HF diagnosis, 22% and 44% of older adults describe at least one impairment in basic and independent activities of daily living, respectively. Mobility and functional disability are associated with comorbidity burden and cognitive impairment, an association that is likely bidirectional. An important additional contributor is frailty, a multi-systemic, aging-associated syndrome that encompasses fatigue, weakness, and decreased tolerance to physiological stressors.

Frailty is classically defined as a constellation of three or more of the following criteria: unintentional weight loss (more than 4.5 kg in one year), slow gait speed, weak grip strength, and physical exhaustion by self-report or measured low physical activity (36). Other scales evaluate up to 70 clinical deficits based on signs, symptoms, and laboratory tests, but this information is time-consuming to collect and analyze. Recognizing this limitation, the Clinical Frailty Scale was prospectively created and analyzed within the Canadian Study of Health and Aging. Rather than following specific rules or thresholds, this measure is based on the clinical judgment of the treating provider and represents a ‘gestalt’ summary of the information contained in deficit-based scales. Clinical Frailty Scale scores range from 1 (very fit) to 7 (severely frail), with higher scores predicting increased risk of death or institutionalization as effectively as more complex scales in community-dwelling elderly (37).

Regardless of how it is defined, frailty is extremely common in elderly HF patients. Prospective observational cohorts in Spain and the U.S. document up to 75% prevalence. The presence of frailty in turn is associated with mortality and increased healthcare utilization including emergency department visits and hospitalizations (38,39). Frailty negatively affects HF management in elderly patients through impacting their self-care and indirectly by decreasing their enrollment in clinical trials. Despite the substantial overlap with typical HF symptoms such as exhaustion and reduced exertional capacity, formally assessed frailty predicts mortality and all-cause hospitalizations even in advanced HF patients who receive ventricular assist devices (40–42). The proposed mechanisms of frailty that intersect with findings in HF include chronic systemic inflammation with elevated levels of inflammatory markers (TNFα, IL-6, and C-reactive protein), hormonal and metabolic derangement resulting in anabolic-catabolic imbalance, and skeletal muscle weakness (43). Clinical distinction between primary and HF-specific frailty is at present challenging. There may be subtle differences in the pathophysiology and reversibility between them (44), and these distinctions are important topics for future research.

Guideline-based medical therapy in elderly HF patients

"Guideline-directed medical therapy (GDMT)," as defined by the American College of Cardiology-American Heart Association and the Canadian Cardiovascular Society guidelines, refers to therapies with strong evidence from randomized trials to improve morbidity and/or mortality in patients with HF (12,45). However, some uncertainty exists regarding the applicability of these guidelines to elderly HF patients. While there have been recent exceptions (46), few HF clinical trials have focused on functional capacity or quality of life. The mean age of HF diagnosis in community-dwelling U.S. elderly adults is 79 years (3), but the mean age of participation in large HF randomized controlled trials was slightly greater than 60 years. Fewer than 30% of participants were older than 70 years; octogenarians were rarely included and were overtly excluded in some studies. Most commonly, elderly potential participants have been excluded from HF clinical trials due to medical comorbidities or preserved left ventricular ejection fraction. One study evaluated U.S. Medicare beneficiaries who survived hospitalization for HF and found that 25% or fewer would have met inclusion criteria for landmark studies of ACEI, BB, and mineralocorticoid antagonists; women and the 'oldest old' (above 85 years of age) were particularly under-represented (47). Subsequent studies focused on patients with HFpEF have eliminated some of this disparity, but have not produced definitive treatment for this increasingly common and age-related syndrome (45).

Available subgroup analyses and the few HF clinical trials that have specifically enrolled large numbers of elderly suggest similar long-term benefits of GDMT in older HFrEF patients (48–54). However, under-prescription of GDMT has been noted in older HF patients across a broad range of clinical settings, even after adjustment for comorbidities and potential contraindications. Many elderly HF patients are principally managed by primary care providers or geriatricians, and HF patients > 75 years of age are less likely to have an attending cardiologist during hospitalization for acute decompensation (55). Co-management with a cardiologist tends to increase the prescription and doses of GDMT, but possibly also drug-drug interactions and side effects (56–59).

Elderly HF patients are undoubtedly at higher risk of adverse effects during standard HF management than younger patients. For example, older patients are more vulnerable to problems during diuresis including intravascular depletion and overt dehydration, electrolyte imbalance, blood pressure lability, and renal impairment. Frail elderly patients often have additional challenges with diuretics including nocturia, urinary incontinence, and increased risk of falls. Inhibitors of the renin-angiotensin-aldosterone system are more likely to cause renal insufficiency, and hyperkalemia in elderly HF patients, particularly when used in combination (60). Beta-blockers carry concerns of bradycardia, fatigue, erectile dysfunction, and cognitive effects. Despite these legitimate concerns, real-world use of GDMT strongly and additively reduces mortality and hospitalizations in elderly inpatients and outpatients with HFrEF (61–63). The Trial of Intensified vs Standard Medical Therapy in Elderly Patients With Congestive Heart Failure (TIME-CHF) study examined GDMT titration guided by serial natriuretic peptide levels in HFrEF patients aged ≥ 60 years. While this strategy improved outcomes in patients 60–74 years of age, it was equivalent to clinical judgment in patients ≥75 years old (64). General recommendations for GDMT in elderly HF patients include slow and gradual dose titration with more frequent clinical visits and laboratory monitoring than younger patients (45). Practical guidance and support for this endeavor is available from the Canadian Cardiovascular Society in a recently published “Heart Failure Companion” manuscript (12) and the Med-HF mobile application (http://www.ccs.ca/index.php/en/resources/mobile-apps).

Defibrillators and cardiac resynchronization in elderly HF patients

Implantable cardiac defibrillators (ICD) effectively prevent sudden cardiac death in symptomatic HFrEF patients. However, multi-morbid elderly HFrEF patients have higher risk of non-arrhythmic death compared to their younger counterparts. In a large retrospective study from Spain, 15% of ICD recipients for primary prevention were ≥ 75 years of age, and had attenuated mortality reduction due to competing risks of death at the time of ICD implantation (65). A propensity-adjusted analysis of previously hospitalized U.S. Medicare HF patients demonstrated similar findings, with ICD implantation conferring lower all-cause mortality over 3 years. While the interaction with age was not statistically significant, the benefit was numerically attenuated in patients 75–84 years of age compared to those 65–74 years of age (HR 0.80 [0.62–1.03] vs. 0.65 [0.47–0.89]) (66).

One study including over 200,000 U.S. Medicare HF patients confirmed mortality reduction for secondary prevention ICDs, but suggested no benefit for primary prevention (67). However, subsequent analysis of the U.S. National Cardiovascular Data Registry by the same group found that elderly registry patients who met major ICD trial enrollment criteria derived mortality benefit from primary prevention ICD implantation, and had similar survival when propensity-matched with the original ICD trial participants (68). The decision to implant an ICD in an older HF patient should incorporate evaluation of the patient’s functional status, burden of co-morbidities, goals of care, expected survival, risk of ventricular arrhythmia, and competing risk of non-arrhythmic death. Other issues to discuss prior to implantation are the possible risks, such as inappropriate shocks and/or infection, as well as the possibility of not replacing the device battery or device deactivation based on the patient's wishes.

Cardiac Resynchronization Therapy (CRT) increases survival, improves quality of life, and reduces HF symptoms in selected patients with symptomatic HFrEF and prolonged electrocardiogram QRS duration. Registry data indicate that CRT is frequently used in elderly patients, with 39% of the CRT with defibrillators implanted in patients older than 75 years and 38% of pacing-only CRT devices implanted in patients older than 80 years. Post-hoc analyses of CRT clinical trials and large device registries suggest that CRT benefits are largely independent of age, and that eligible older HF patients derive additional benefit from CRT use when compared to defibrillator-only implantation (69).

Non-pharmacological treatment in elderly HF patients

As discussed above, physical limitations and frailty are emblematic features of HF in elderly patients. Exercise training interventions consistently improve measures of physical performance in frail older adults and hold promise for stabilizing or even partially reversing the frailty phenotype (70). A 2005 U.K. study of 200 stable HFrEF patients demonstrated that a 24-week multidisciplinary cardiac rehabilitation program improved functional capacity and quality of life while reducing overall hospital days (71). The much larger (2,331 participants), multinational Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study confirmed that aerobic exercise training in stable HFrEF was safe, improved exertional capacity and health-related quality of life, and reduced cardiovascular event rates after adjustment for prognostic factors. Only 19% of HF-ACTION participants were ≥ 70 years of age (72), but benefits appeared similar in elderly and younger HFrEF patients. In small randomized trials enrolling HFpEF patients, supervised exercise training also consistently increases oxygen consumption and exercise capacity (73–75).

Current guidelines strongly recommend supervised rehabilitation in all HFrEF patients with New York Heart Association class I–III symptoms, and in frail elderly patients multi-component exercise focused on endurance, resistance, and balance is suggested. While the effects on overall quality of life are variable and the impact on hospitalization and mortality rates is unknown, a similar approach is reasonable in patients with HFpEF (76). Suggestions for patient selection, exercise prescription, and self-care counseling related to exercise training have recently been reviewed (77). The effects of early physical training following hospital discharge for HF exacerbation are unknown, but the ongoing Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF; NCT 02196038) should provide answers in this population.

Malnutrition is a strong and independent risk factor for poor quality of life, hospitalization, and death in elderly HF patients (78,79). Low body mass index (BMI) is a well-known risk factor for death in HF, but many older adults in Western countries have sarcopenic obesity, or muscle wasting despite increased BMI (80). The relationships between sarcopenic obesity, frailty, quality of life, and nutritional status in elderly HF patients are an active area of research (73). Current HF dietary guidelines are not evidence-based (81), and standard recommendations for low sodium intake may inadvertently deprive older HF patients of important calories and nutrients (82). Moreover, one recent study linked dietary sodium restriction with increased risk of adverse outcomes in symptomatic HF patients (83). The Study of Dietary Intervention Under 100 MMOL in Heart Failure (SODIUM-HF; NCT02012179) study is further evaluating the impact of sodium restriction on clinical events in stable outpatients with HF, and the Geriatric Out of Hospital Randomized Meal Trial in Heart Failure (GOURMET-HF; NCT 02148679) is currently evaluating the effects of home-delivered, nutritionally complete meals on quality of life in elderly HF patients immediately following hospital discharge (84). These studies will add to the current knowledge base and guide future dietary studies in older HF patients.

Additional comments

Decision-making in HF management begins with open discussion of the disease prognosis, the goals of care, and the available treatment options, and should take into account geriatric domains that affect the complexity and efficacy of care. The conventional viewpoint that elderly HF patients value symptom control and quality of life over longevity is not always true. In one large study three-quarters of elderly HF outpatients were unwilling to trade any survival time for improved quality of life (85), and preferences can change over the course of illness in HF (86). Palliative care consultations are often not obtained until the last month of life in HF patients (87). Earlier involvement of multidisciplinary palliative care specialists can improve symptom control, functional status, and quality of life, while also helping patients and caregivers cope with uncertainty and make patient-centered medical decisions as HF progresses (88).

Summary

The evaluation and treatment of the growing number of elderly HF patients is often complicated by multi-morbid illness, polypharmacy, cognitive impairment, and functional deficits. Assessment of these geriatric domains can improve determination of prognosis and facilitate patient-centered management. Clinical trials with broader enrollment criteria and more efforts to specifically include elderly HF patients, focusing on quality of life and functional measures in addition to mortality and hospitalization, are needed to improve the quality of evidence guiding the care of complex elderly HF patients.

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Summary

Heart failure (HF) is a leading cause of morbidity, hospitalization, and mortality in older adults, Geriatric HF patients often have co-existing multi-morbid illness, polypharmacy, cognitive impairment, and frailty. These complex 'geriatric domains' strongly affect physical and functional status and long-term clinical outcomes. Targeted geriatric evaluation can improve risk stratification and direct management in older HF patients. Clinical trials that enroll complex, multi-morbid elderly patients should be encouraged to guide management of HF in older adults.