Team-Based Care for Managing Noncardiac Conditions in Patients with Heart Failure

Justin M. Vader, MD, Michael W. Rich, MD*

KEYWORDS

• Heart failure • Noncardiac comorbidity • Team-based care • Multimorbidity • Geriatric

KEY POINTS

- Noncardiac comorbidity is present in most patients with heart failure (HF), and more than 50% have 4 or greater noncardiac conditions.
- Noncardiac comorbidities are associated with adverse outcomes in HF, particularly chronic kidney disease, chronic obstructive pulmonary disease, dementia, malignancy, and depression.
- Team-based care strategies improve process measures and outcomes in noncardiac conditions, but the efficacy of these interventions in the setting of coexisting HF requires further study.

INTRODUCTION

Heart failure (HF) affects 5.1 million Americans, with a mortality rate approaching 50% at 5 years, a major burden of morbidity and hospitalization,[1] and total costs estimated at $32 billion per year.[2] Although there are no proven therapies for reducing morbidity and mortality in HF with preserved ejection fraction (HFpEF), patients with HF with reduced ejection fraction (HFrEF) treated with guideline-recommended drug and device therapies experience greatly improved quality of life and reduced mortality and hospitalization.[3] Such a prevalent, mortal, morbid, expensive but modifiable disease state with care administered across multiple environments is a natural fit for highly integrated team-based care strategies. Moreover, HF rarely stands alone. Cardiovascular comorbidities contribute to the development of and progression of HF; guideline recommendations exist for these conditions, including coronary artery disease, atrial and ventricular arrhythmias, valvular heart disease, peripheral vascular disease, and cerebrovascular disease. However, guidance on the comanagement of noncardiac comorbidities, equally if not more prevalent than cardiac comorbidities, is largely absent from practice guidelines; key knowledge gaps exist in the interplay of noncardiac comorbidity and HF.

NONCARDIAC COMORBIDITY IN PATIENTS WITH HEART FAILURE

Prevalence

HF prevalence increases with age; thus, Medicare represents the major payer for HF in the United States. The 14% of Medicare beneficiaries with HF account for 43% of Medicare Part A and Part B expenditures.[4] HF in the absence of noncardiovascular comorbidity among Medicare beneficiaries is *very rare*, occurring in only 4% of patients with HF. More than 50% of Medicare patients with HF have 4 or more noncardiovascular comorbidities and more than 25% have 6 or more.[5] The most prevalent noncardiac comorbidities include hypertension, hyperlipidemia, anemia,

Disclosures: Research support NHLBI Heart Failure Network (J.M. Vader); none (M.W. Rich).
Division of Cardiology, Washington University School of Medicine, 660 South Euclid Avenue, Campus Box 8086, St Louis, MO 63110, USA
* Corresponding author.
E-mail address: mrich@wustl.edu

Heart Failure Clin 11 (2015) 419–429
http://dx.doi.org/10.1016/j.hfc.2015.03.006
1551-7136/15/$ – see front matter

diabetes, arthritis, chronic kidney disease (CKD), chronic respiratory conditions, depression, and dementia (Table 1). Furthermore, data from the National Health and Nutrition Examination Survey (NHANES) indicate that the burden of comorbidity is growing, with the prevalence of 5 or more comorbidities in HF increasing from 42% in 1988 to 1994 to 58% in 2003 to 2008 (Fig. 1) and the mean number of prescriptions increasing from 4.1 to 6.4 per patient.[6] Noncardiac comorbidities particularly increase as a function of age, though in the oldest old the greater prevalence of conditions such as dementia is offset by a lower prevalence of diabetes.[7] In European patients with HF, comorbidities may be less prevalent (or less frequently diagnosed); but 43% of patients in a large European HF cohort had 2 or more comorbidities.[8]

Outcomes

Braunstein and colleagues[5] analyzed the risk ratio of various noncardiovascular comorbidities in relation to ambulatory-care sensitive HF hospitalizations (ie, potentially preventable through optimal primary care delivery) in Medicare patients with HF and found that the highest risks for such hospitalizations were in those with renal failure, hypertension, obstructive lung disease, lower respiratory illness, and diabetes. Meanwhile, risk of death was greatest for lower respiratory illness, renal failure, dementia, cerebrovascular disease, and depression. The risks posed by specific comorbidities for hospitalization and overall mortality were not necessarily concordant (eg, dementia was associated with greater mortality but less hospitalization). In a separate multivariate analysis of mortality among Medicare/Medicaid beneficiaries with HF, the conditions contributing the highest hazard for death were lung and colorectal cancer, CKD, dementia, and chronic obstructive pulmonary disease (COPD), whereas the effect of diabetes was modest. In comparing hospitalized versus nonhospitalized patients with HF, noncardiovascular comorbidity contributed a relatively greater hazard of death among nonhospitalized patients with HF, suggesting that in those with less advanced HF, attention to noncardiac comorbidity might be relatively more important (Table 2).[9]

Table 1
Prevalence of selected noncardiac comorbidities in HF

	Age <65 y
COPD	33%
Arthritis	35%
Depression	36%
CKD	45%
Diabetes	59%
Hypertension	81%
	Age ≥65 y
Dementia	28%
COPD	30%
CKD	42%
Arthritis	44%
Diabetes	46%
Hypertension	84%

Medicare data, 2011.

Abbreviation: COPD, chronic obstructive pulmonary disease.

From Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;128(16):e294; with permission.

Noncardiac Comorbidity in Heart Failure with Preserved Versus Reduced Ejection Fraction

Noncardiac comorbidities in HFpEF and HFrEF differ in terms of prevalence and influence on outcomes.[10] A systematic review of studies comparing HFpEF with HFrEF showed higher prevalence of certain noncardiovascular comorbidities in HFpEF, particularly hypertension, renal impairment, chronic lung diseases, anemia, cancer, liver disease, peptic ulcer disease, and hypothyroidism.[11] Overall, all-cause mortality in patients with HFpEF is minimally if at all better than in patients with HFrEF.[12–14] Although some data suggest noncardiovascular causes of death are relatively more common in HFpEF compared with HFrEF,[15] reported rates of noncardiovascular death in HFpEF vary widely, ranging from 20% to 49%, perhaps because of the variability in cause-specific death reporting or definition of HFpEF.[11] In a largely male cohort, HFpEF compared with HFrEF was associated with more noncardiovascular comorbidities, particularly diabetes, anemia, COPD, obesity, cancer, and psychiatric disorders. In this study, HFpEF subjects had lower overall mortality and HF hospitalization but higher non-HF hospitalization. The contribution of various comorbidities to the hazard of death was similar between HFrEF and HFpEF, except for COPD, which was associated with a greater hazard for death in HFpEF.[16]

THE ROLE OF TEAM-BASED CARE IN NONCARDIAC COMORBID CONDITIONS

As described elsewhere in this edition of *Heart Failure Clinics*, and as adopted by the Institute of

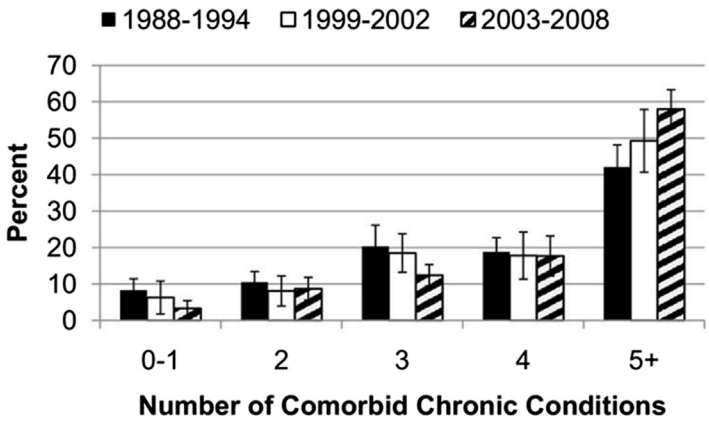

Fig. 1. Trends in number of comorbid conditions in patients with HF from NHANES. (*From* Wong CY, Chaudhry SI, Desai MM, et al. Trends in comorbidity, disability, and polypharmacy in heart failure. Am J Med 2011;124(2):140; with permission.)

Medicine in their *Core Principles & Values of Effective Team-Based Health Care*,[17] team-based health care is the provision of health services to individuals, families, and/or their communities by at least 2 health providers who work collaboratively with patients and their caregivers, to the extent preferred by each patient, to accomplish shared goals within and across settings to achieve coordinated high-quality care.[18] The role of team-based care in managing noncardiac comorbidities prevalent in the HF population is reviewed later.

Hypertension

Hypertension is well suited to team-based intervention. Contemporary hypertension guidelines[19] endorse the "2013 (American College of Cardiology/American Heart Association) ACC/AHA Guideline on Lifestyle Management to Reduce Cardiovascular Risk,"[20] creating an opportunity for dieticians, trainers, physical therapists, and exercise physiologists to contribute to favorable outcomes. Pharmacotherapy is goal directed, requiring dose titration and attention to pharmacodynamics and pharmacokinetics as well as intraindividual and interindividual variability of drug effects, creating a need for office and home-based nursing, pharmacist consultation, patient education, patient self-monitoring, and potentially remote monitoring strategies. Quality-improvement strategies that include adoption of multidisciplinary care teams result in the greatest improvements in blood pressure (BP).[21] In clinical trials using team-based care, greater likelihood of controlled BP was seen in studies involving nurses, clinic-based pharmacists, and community pharmacists (in order of increasing benefit).[22] Strategies using pharmacist recommendations to physicians, counseling on lifestyle modification, pharmacist-led interventions, and algorithm use were associated with the greatest benefits. Finally, regular review of patient charts with an associated stepped-care approach to pharmacotherapy is effective for lowering BP; interventions using nurse or pharmacist-based care seem to be particularly effective.[23]

Although these trials in hypertension were in the setting of the prevention of heart disease as

Table 2
Effect of burden of comorbidity on mortality among beneficiaries with HF

	Adjusted Hazard Ratio (95% CI)		Interaction Between Hospitalization Status & Comorbidity Burden
Burden of Comorbidity	Hospitalized Beneficiaries	Nonhospitalized Beneficiaries	*P* Value
Low (≤2 conditions)	1.0 (Reference)	1.0 (Reference)	—
Medium (3–4 conditions)	1.22 (1.13, 1.31)	1.49 (1.39,1.59)	.0003
High (≥5 conditions)	1.57 (1.44, 1.68)	2.35 (2.17, 2.54)	<.0001

Adjusted for age, sex, and race.

Abbreviation: CI, confidence interval.

From Ahluwalia SC, Gross CP, Chaudhry SI, et al. Impact of comorbidity on mortality among older persons with advanced heart failure. J Gen Intern Med 2012;27(5):516; with permission.

opposed to the therapy for HF, the principles of organized or protocol-driven patient review with stepped pharmacotherapy using the assistance of nurses and pharmacists has a direct application to the titration of HF pharmacotherapy. Pharmacist-led titration has been shown to increase the percentage of patients receiving optimal HF drug dosing,[24] and nurse-led phone-based intervention may increase both the proportion of patients achieving the trial-defined optimal dose and may improve left ventricular ejection fraction and reduce the need for device therapy in HF.[25]

Diabetes

Diabetes is present in more than one-third of Medicare recipients with HF.[5] The literature supports a role for poor diabetes control in the development of worsening HF in both patients with type I diabetes and patients with type II diabetes.[26–28] Although diabetes is a risk factor for HF hospitalization, its contribution to overall mortality is modest compared with other comorbidities.[5,9] In general, team-based care in diabetes is firmly rooted. The quality-improvement interventions with the greatest effect on improving glycemic control include adoption of multidisciplinary teams with expanded professional roles, non–medical record relay of information to physicians, and promotion of patient self-management.[28] Diabetes care teams involve primary care physicians, nurses, nurse educators, dietitians, and pharmacists but may expand to include endocrinologists, ophthalmologists, nephrologists, podiatrists, cardiologists, and vascular surgeons. Communication between care providers is an essential part of diabetes care.

Optimal glycemic control in patients with co-occurring HF and diabetes is unclear. Tighter glycemic control (A1c <6% vs 7%–8%) may increase mortality,[29] and this effect has also been observed in patients with HF.[30] The diabetes guidelines address the use of specific hypoglycemic agents in diabetic patients with HF.[31] Thiazolidinediones are contraindicated in symptomatic HF because of the associated peripheral edema and weight gain and should be used with caution in asymptomatic HF. US guidelines recommend that metformin be avoided in symptomatic HF or in the setting of renal insufficiency. However, based on observational data showing superior overall clinical outcomes in patients treated with metformin,[32,33] the European HF guidelines recommend metformin as the first-line therapy for the management of diabetes in patients with HF.[34] Limited data are available on the use of insulin and sulfonylureas in patients with HF. Meanwhile, there are mechanistic reasons to think that the newer glucagon-like-peptide agents have intrinsic benefits in HF, though clinical trial data are not yet available. A clinical pharmacist can play a pivotal role in navigating the options for glycemic control in HF, considering drug-specific effects and side effects. In patients with more advanced HF, a dietitian may also be needed for the purpose of reconciling the protein-calorie nutritional needs of patients and their glycemic control.

Chronic Obstructive Pulmonary Disease

COPD is present in nearly one-third of patients with HF, with greater prevalence in HFpEF compared with HFrEF.[35] Treating HF in patients with COPD may be challenging, both because of the difficulty in distinguishing between cardiac and pulmonary causes of dyspnea and because of the need to balance beta-blockers in HF with beta-agonists in COPD. Although cardioselective beta-blockers (eg, metoprolol) have theoretic benefits over noncardioselective beta-blockers (eg, carvedilol) with regard to bronchoconstriction in patients with COPD, data are limited by the lack of enrollment of patients with known cardiovascular comorbidity in clinical trials of bronchodilators. In retrospective analysis, there was no evidence that beta-blocker cardioselectivity was associated with differences in outcomes for patients with HF with COPD versus those without.[36] For the long-term prevention of COPD exacerbations, the inhaled anticholinergic agent tiotropium is superior to the long-acting beta-2 agonist salmeterol[37]; however, a meta-analysis of inhaled anticholinergic trials demonstrated an increased risk of cardiovascular death, myocardial infarction, or stroke among patients with COPD using these agents.[38]

A team-based approach with pharmacist input and integration of pulmonary and cardiac diagnostic testing has much to offer in balancing the benefits and harms of pharmacotherapy in COPD and HF, but to date no such studies have been published. Limited literature on team-based care in COPD (using self-management, delivery system design, decision support, and clinical information systems) demonstrates lower rates of hospitalizations and emergency visits as well as shorter lengths of stay.[39] For patients with HF with COPD, an expanded care team including respiratory therapists, physical therapists, and exercise physiologists along with physiologic testing, such as ambulatory oxygen testing, pulmonary function testing, and cardiopulmonary stress testing, may help determine which condition is dominant in limiting exertion and causing dyspnea. Regardless of the dominant cause, many centers offer

combined pulmonary and cardiac rehabilitation programs targeted at improvement of overall disability rather than a specific disease state; a combined approach has been demonstrated to be effective.[40]

Chronic Kidney Disease

HF and CKD interact bidirectionally to exacerbate one another in the cardiorenal syndrome.[41] CKD progression causes unfavorable changes in preload, afterload, inflammatory response, and hormonal systems, such as the renin-angiotensin-aldosterone system (RAAS) leading to worsening HF. Meanwhile, in patients with chronically or intermittently decompensated HF, the cycle of arterial hypoperfusion and especially venous congestion can lead to renal injury and progressive deterioration of renal function. Often the root cause of both HF and CKD are systemic illnesses: diabetes, hypertension, and other proinflammatory disease states. In these cases, team-based coordinated care across disciplines to manage diabetes, hypertension, lipids, and modify lifestyle is imperative. In patients with CKD, a multidisciplinary care team consisting of a nephrology nurse educator, renal dietitian, social worker, and pharmacy specialist, in addition to a nephrologist and vascular surgeon, can improve guideline adherence, slow the progression of renal disease, and improve overall survival.[42] In elderly patients with CKD, multidisciplinary care teams have been associated with reduced all-cause mortality and trends toward reduced hospitalization.[43]

The management of CKD in the setting of HF presents particular challenges regarding the use of diuretics. Worsening HF may result in diminished diuretic effectiveness, with diuretic braking and postdiuretic sodium retention, leading to a need for greater doses of diuretics.[44] Meanwhile, worsening renal function (WRF) is common in acute HF, occurring in 20% to 40% of patients.[45] However, even in advanced HF, it is the degree of venous congestion rather than the cardiac output that mediates worsening renal function[46]; congested patients with WRF often need more, not less, diuresis. Such decisions require knowledge of patient symptoms, volume status, and present renal function, achievable in hospitalized patients but challenging in nonhospitalized patients. In these instances, outpatient team-based care may preempt hospital admission and define the trajectory of cardiac and renal dysfunction. These teams may include nephrologists, HF cardiologists, HF nurses, primary care physicians, home care nurses, and dieticians. Discussions with patients with the severe HF and CKD may include consideration of advanced HF therapies, such as single-organ or combined-organ transplant and mechanical circulatory support.

RAAS blockers are fundamental in the therapy for HFrEF; but in moderate to advanced CKD, attention to serum potassium and creatinine clearance is required. Although prospective clinical trials to address the safety and effectiveness of RAAS blockade in patients with HF with CKD are lacking, propensity-matched analysis suggests that even in older patients with more advanced CKD (estimated glomerular filtration rate [eGFR] <45 mL/min/1.73 m^2), the prescription of RAAS blockade at discharge is associated with less hazard of death.[47] Guideline-based recommendations regarding renal dysfunction, potassium, and RAAS blockade are shown in **Table 3**. Navigating the changes in renal function and potassium with the use of RAAS blockers in HF and CKD requires care coordination between physician, nurse, pharmacist, and often home-care resources with iterative assessment of renal function, BP, and medication dosage.

Other Noncardiac Comorbidities

Osteoarthritis (OA) occurs in approximately 40% of patients with HF and may result in significant impairment in quality of life. Nonsteroidal antiinflammatory drugs (NSAIDs) are a foundation of therapy for OA, and those that preferentially inhibit cyclooxygenase-2 (COX-2) are less likely to cause gastrointestinal bleeding. However, COX-2–mediated increases in BP, sodium retention, and thrombosis worsen HF.[48] NSAID use is associated with the development of clinical HF[49–51] and increased mortality among those with a previous HF diagnosis.[52] Therapy for OA in HF is most safely achieved through avoidance of NSAIDs and specifically avoidance of COX-2–specific NSAIDs,[48] with a role for topical and nonpharmacologic (eg, physical therapy) approaches to pain relief.[53] A team approach with a primary care physician, nursing, pharmacy, physical and occupational therapy, and occasionally pain management specialists seems justified, though no literature currently exists to support such an intervention.

Cognitive impairment is present in up to 50% of patients with HF, and dementia occurs in about 25% of elderly patients with HF.[3] The co-occurrence of dementia and HF more than doubles hospital and home care costs compared with either condition alone.[54] In general, pharmacotherapy for HF may improve cognitive impairment in patients with HF[55]; exercise may also have salutary effects on cognition.[56] Multisource disease management programs for dementia

Table 3
Guideline-based recommendations regarding renal dysfunction, potassium, and RAAS blockade

Noncardiac Comorbidity	Therapeutic Considerations in Combined HF and Comorbidity	Team-Based Care Considerations	Pertinent Guidelines
CKD	ACE-inhibitor/angiotensin receptor blocker: caution if very low BPs (SBP <80 mm Hg), increased serum creatinine (>3 mg/dL), bilateral renal artery stenosis, elevated levels of serum potassium (>5.0 mEq/L) Aldosterone antagonists: serum creatinine <2.5 mg/dL (or eGFR >30 mL/min/1.73 m^2) and serum potassium <5.0 mEq/L without history of severe hyperkalemia	PCP, nephrologist, pharmacist, nurse coordinator, nutritionist	3,80
COPD	Cardioselective beta-blockers may cause less bronchoconstriction Inhaled anticholinergic agents may be superior to beta-agonists but associated with adverse cardiac events	PCP, pulmonologist, pharmacist, nurse coordinator Physical therapy, respiratory therapy	3,81
Diabetes Mellitus	Thiazolidinediones: predispose to edema, avoid in symptomatic HF Metformin: avoid in decompensated HF, renal failure; evidence overall in HF of improved outcomes GLP-1 receptor agonists: mechanistic rationale for benefit in HF, ongoing studies, limited guidance Dipeptidyl dipeptidase 4 inhibitors: associated with increased risk of HF, limited guidance Insulin: limited data on influence on HF outcomes Sulfonylureas: limited data on influence on HF outcomes	PCP, endocrinologist, pharmacist, nurse coordinator Diabetes educator, nutritionist, podiatrist, ophthalmologist	3,31,34
Hypertension	Consider class-specific effects In HFrEF prioritize ACE-inhibitor/angiotensin receptor blocker, beta-blocker, spironolactone; add hydralazine/nitrate in African Americans In HFpEF no agent proven to reduce mortality, major adverse cardiac events	PCP, pharmacist, nurse coordinator	3,19,20
Geriatrics	Avoid polypharmacy	PCP, geriatrician, pharmacist, nurse coordinator, home care, physical therapy	3,63
Osteoarthritis	Avoid NSAIDs (especially COX-2 specific)	PCP, rheumatologist, pharmacist, nurse coordinator, pain management	3,48,53
Dementia	Cholinesterase inhibitors modestly associated with bradycardia and hypotension	PCP, neurologist psychiatrist, psychologist, pharmacist, nurse coordinator	3,82
Depression	Uncertain effectiveness of SSRI in HF Role for regular exercise	PCP, psychiatrist, psychologist, pharmacist, nurse coordinator	3,83

Abbreviations: ACE, angiotensin-converting enzyme; COX-2, cyclooxygenase-2; GLP-1, glucagonlike peptide-1; NSAIDs, nonsteroidal antiinflammatory drugs; PCP, primary care physician; SBP, systolic BP; SSRI, selective serotonin reuptake inhibitor.

improve outcomes for both patients[57] and caregivers.[58] Whether team-based care strategies emphasizing effective pharmacologic and nonpharmacologic therapies in co-occurring HF and dementia can improve health care delivery and outcomes is not known.

Depression affects approximately 20% of patients with HF and is associated with increased mortality, hospitalization, and resource utilization.[59] Unfortunately, the largest trial of pharmacotherapy of depression in HF showed no improvement in either depression or cardiovascular status with the use of sertraline.[60] Structured aerobic exercise, however, may modestly improve depressive symptoms in HF.[61] Cognitive therapy may also be promising, but methodological variability limits the ability to apply existing evidence to real-world practice.[62] Whether multidisciplinary team-based approaches to HF and depression could synergize various therapeutic modalities for benefit remains to be seen.

Geriatric Care

The confluence of multiple comorbidities and the need to consider therapeutic trade-offs increases the need for flexibility and multidisciplinary approaches in geriatric patients.[63] Polypharmacy is a major issue in geriatrics, with studies showing that 44% of elderly patients discharged from an acute hospitalization are prescribed an inappropriate medication[64]; more than half of patients older than 65 years are receiving 5 or more medications[65]; and nearly 1 in 25 individuals are potentially at risk for a major drug-drug interaction.[66] Pharmacist-led interventions can have favorable effects on therapeutic, safety, hospitalization, and adherence outcomes in older adults[67]; inpatient geriatric specialty consultation to reduce errors in prescription or care transitions may have intermediate-term favorable effects on postdischarge outcomes.[68]

Although patients with HF with complex care needs are often in the geriatric age group, guidelines do not specify age-related contraindications to the use of medical or device-based therapies for HF. However, guidelines do recommend attention to eGFR as opposed to serum creatinine when considering angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers caution regarding digoxin toxicity, and more frequent monitoring with more gradual changes during dose titration of guideline-directed medications in older patients.[3] As described elsewhere in this issue of *Heart Failure Clinics*, in patients with limited expected survival, the continued use of certain life-prolonging therapies, such as implantable cardioverter-defibrillators, should be revisited periodically as a patient ages or severity of illness progresses.

HEART FAILURE REHOSPITALIZATION AND THE ROLE OF NONCARDIAC COMORBIDITY

In the midst of an "epidemic of heart failure hospitalization,"[69] the impact of team-based care of noncardiac comorbidities on HF readmission rates is of great importance. Currently, readmission to the hospital within 30 days of HF hospital discharge occurs in 20% to 25% of patients and the associated costs are large, with Medicare shouldering approximately 45% of the burden.[70] Measures from Medicare penalizing hospitals with 30-day HF readmission rates in excess of a risk-standardized estimate have prompted the proliferation of programs geared toward readmission prevention, but preventing readmission after HF hospitalization is about more than HF. More than half of Medicare readmissions within 30 days of hospital discharge for HF are for non-HF diagnoses,[71] and such hospitalizations for noncardiovascular causes portend unfavorable long-term prognosis. In an analysis of the CHARM trial (Candesartan in Heart failure - Assessment of moRtality and Morbidity), though mortality within 30 days was greater after cardiovascular (CV) compared with non-CV hospitalization, subsequent rates of mortality were similar between CV and non-CV groups, a finding seen in both patients with HFrEF and patients with HFpEF.[72] Attention to comorbidity is a key to overall improvements in both survival and readmission, reflected in a recent transitional care trial involving an advanced practice nurse-directed discharge planning and home follow-up protocol. Readmissions and costs at 1 year were reduced, but the reduction in readmissions was primarily attributable to comorbidity-related readmissions, not HF-related readmissions, suggesting that multilevel interventions may improve care of comorbidities that drive readmissions.[73]

MULTIMORBIDITY

As described throughout this review, the management of comorbidities influences the delivery of care in HF. The presence of multiple comorbidities in HF can decrease patient self-efficacy and challenge self-care,[74] and chronic disease management of multiple comorbidities may exceed physician time available for patient care.[75] The impact of multiple interacting comorbidities may not be purely summative, particularly with the coexistence of 2 or more chronic conditions

whereby neither condition is clearly dominant; this state has been termed *multimorbidity*.[76] A patient-centered approach focused on the overall multimorbidity state in patients with HF may be most effective. As outlined by the American Geriatrics Society, this approach includes the following[77,78]:

- Elicitation or patient preferences
- Recognition of the limitations of applying the evidence base to a given individual
- Assessing prognosis and framing of risks and benefits with an emphasis on tradeoffs
- Recognizing therapeutic complexity and assessing feasibility
- Continual optimization of therapies to account for these factors and changes over time.

Multimorbidity interventions are emerging in the literature and tend to be complex and multifaceted with reorganization of care delivery and team-based approaches, resulting in modest improvements in prescribing and medication adherence with uncertain financial implications.[79] A large multisite intervention trial focusing on multimorbidity in HF is currently in development.

SUMMARY

HF is a condition in which the prognosis and treatment are often defined by comorbidities, many of which are noncardiac. Knowledge of the interactions between HF and specific comorbidities is essential, yet to date the clinical trial evidence base for managing comorbidity in patients with HF is limited; further investigations are clearly needed. Perhaps the most pressing need is a focus on the overall multimorbidity state and its relationship to HF—a need that should be addressed in forthcoming trials. Successful navigation between HF and common interacting comorbidities requires coordination of care and team-based approaches that continually evolve to meet patient needs.

REFERENCES

1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics–2014 update: a report from the American Heart Association. Circulation 2014;129(3):e28–292.
2. Heidenreich PA, Trogdon JG, Khavjou OA, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. Circulation 2011;123(8):933–44.
3. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2013;128(16):e240–327.
4. Dall T, Blanchard T, Gallo P, et al. The economic impact of Medicare Part D on congestive heart failure. Am J Manag Care 2013;19:S97–100.
5. Braunstein JB, Anderson GF, Gerstenblith G, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. J Am Coll Cardiol 2003;42(7):1226–33.
6. Wong CY, Chaudhry SI, Desai MM, et al. Trends in comorbidity, disability, and polypharmacy in heart failure. Am J Med 2011;124(2):136–43.
7. Ahluwalia SC, Gross CP, Chaudhry SI, et al. Change in comorbidity prevalence with advancing age among persons with heart failure. J Gen Intern Med 2011;26(10):1145–51.
8. van Deursen VM, Urso R, Laroche C, et al. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. Eur J Heart Fail 2014;16:103–11.
9. Ahluwalia SC, Gross CP, Chaudhry SI, et al. Impact of comorbidity on mortality among older persons with advanced heart failure. J Gen Intern Med 2012;27(5):513–9.
10. Mentz RJ, Kelly JP, von Lueder TG, et al. Noncardiac comorbidities in heart failure with reduced versus preserved ejection fraction. J Am Coll Cardiol 2014;64(21):2281–93.
11. Lam CS, Donal E, Kraigher-Krainer E, et al. Epidemiology and clinical course of heart failure with preserved ejection fraction. Eur J Heart Fail 2011;13(1):18–28.
12. Bursi F, Weston S, Redfield M. Systolic and diastolic heart failure in the community. JAMA 2006;296(18):2209–16.
13. Bhatia R, Tu J, Lee D. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355(3):260–9.
14. Lenzen MJ, Scholte op Reimer WJ, Boersma E, et al. Differences between patients with a preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey. Eur Heart J 2004;25(14):1214–20.
15. Henkel DM, Redfield MM, Weston SA, et al. Death in heart failure: a community perspective. Circ Heart Fail 2008;1(2):91–7.
16. Ather S, Chan W, Bozkurt B, et al. Impact of noncardiac comorbidities on morbidity and mortality in a predominantly male population with heart failure and preserved versus reduced ejection fraction. J Am Coll Cardiol 2012;59(11):998–1005.
17. Mitchell P, Wynia M, Golden R, et al. Core principles & values of effective team-based health care. Discussion Paper, Institute of Medicine, Washington, DC. Available at: http://www.iom.edu/tbc.

18. Naylor M. Translational care: moving patients from one care setting to another. Am J Nurs 2009; 108(9 Suppl):58–63.
19. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014;311(5):507–20.
20. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 63(25 Pt B):2960–84.
21. Walsh J, McDonald K, Shojania K, et al. Quality improvement strategies for hypertension management: a systematic review. Med Care 2006;44(7): 646–57.
22. Carter BL, Rogers M, Daly J, et al. The potency of team-based care interventions for hypertension. Arch Intern Med 2009;169(19):1748–55.
23. Glynn LG, Murphy AW, Smith SM, et al. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database Syst Rev 2010;(3):CD005182.
24. Martinez AS, Saef J, Paszczuk A, et al. Implementation of a pharmacist-managed heart failure medication titration clinic. Am J Health Syst Pharm 2013; 70(12):1070–6.
25. Steckler AE, Bishu K, Wassif H, et al. Telephone titration of heart failure medications. J Cardiovasc Nurs 2011;26(1):29–36.
26. Boudina S, Abel ED. Diabetic cardiomyopathy revisited. Circulation 2007;115(25):3213–23.
27. Iribarren C, Karter AJ, Go AS, et al. Clinical investigation and reports glycemic control and heart failure among adult patients with diabetes. Circulation 2001;103:2668–73.
28. Tricco AC, Ivers NM, Grimshaw JM, et al. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. Lancet 2012;379(9833):2252–61.
29. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein H, Miller ME, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008;358(24):2545–59.
30. Calles-Escandón J. Effect of intensive compared with standard glycemia treatment strategies on mortality by baseline subgroup characteristics the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. Diabetes Care 2010;33(4): 721–7.
31. American Diabetes Association. Standards of medical care in diabetes–2014. Diabetes Care 2014; 37(Suppl 1):S14–80.
32. Masoudi FA, Inzucchi SE, Wang Y, et al. Thiazolidinediones, metformin, and outcomes in older patients with diabetes and heart failure: an observational study. Circulation 2005;111(5):583–90.
33. Eurich D, Majumdar S, McAlister FA, et al. Improved clinical outcomes associated with metformin in patients with diabetes and heart failure. Diabetes Care 2005;28(21):2345–51.
34. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; 33(14):1787–847.
35. Hawkins NM, Petrie MC, Jhund PS, et al. Heart failure and chronic obstructive pulmonary disease: diagnostic pitfalls and epidemiology. Eur J Heart Fail 2009;11(2):130–9.
36. Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of beta-blocker use and selectivity with outcomes in patients with heart failure and chronic obstructive pulmonary disease (from OPTIMIZE-HF). Am J Cardiol 2013;111(4):582–7.
37. Vogelmeier C, Hederer B, Glaab T, et al. Tiotropium versus salmeterol for the prevention of exacerbations of COPD. N Engl J Med 2011;364(12): 1093–103.
38. Singh S, Loke Y, Furberg C. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. JAMA 2014;300(12):1439–50.
39. Adams S, Smith P. Systematic review of the chronic care model in chronic obstructive pulmonary disease prevention and management. Arch Intern Med 2007;167:551–61.
40. Evans RA, Singh SJ, Collier R, et al. Generic, symptom based, exercise rehabilitation; integrating patients with COPD and heart failure. Respir Med 2010;104(10):1473–81.
41. Ronco C, Haapio M, House AA, et al. Cardiorenal syndrome. J Am Coll Cardiol 2008;52(19):1527–39.
42. Chen Y-R, Yang Y, Wang S-C, et al. Effectiveness of multidisciplinary care for chronic kidney disease in Taiwan: a 3-year prospective cohort study. Nephrol Dial Transplant 2013;28(3):671–82.
43. Hemmelgarn BR, Manns BJ, Zhang J, et al. Association between multidisciplinary care and survival for elderly patients with chronic kidney disease. J Am Soc Nephrol 2007;18(3):993–9.
44. Ronco C, Cicoira M, McCullough PA. Cardiorenal syndrome type 1: pathophysiological crosstalk leading to combined heart and kidney dysfunction in the setting of acutely decompensated heart failure. J Am Coll Cardiol 2012;60(12):1031–42.
45. Butler J, Chirovsky D, Phatak H, et al. Renal function, health outcomes, and resource utilization in acute

heart failure: a systematic review. Circ Heart Fail 2010;3(6):726–45.
46. Mullens W, Abrahams Z, Francis GS, et al. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. J Am Coll Cardiol 2009;53(7):589–96.
47. Ahmed A, Fonarow GC, Zhang Y, et al. Renin-angiotensin inhibition in systolic heart failure and chronic kidney disease. Am J Med 2012;125(4):399–410.
48. Antman EM, Bennett JS, Daugherty A, et al. Use of nonsteroidal antiinflammatory drugs: an update for clinicians: a scientific statement from the American Heart Association. Circulation 2007;115(12):1634–42.
49. Feenstra J, Heerdink E, Grobbee D, et al. Association of nonsteroidal anti-inflammatory drugs with first occurrence of heart failure and with relapsing heart failure. Arch Intern Med 2014;162:265–70.
50. John P, David H. Consumption of NSAIDs and the development of congestive heart failure in elderly patients: an underrecognized public health problem. Arch Intern Med 2000;160:777–84.
51. Rodríguez L, Hernández-Díaz S. Nonsteroidal antiinflammatory drugs as a trigger of clinical heart failure. Epidemiology 2003;14:240–6.
52. Gislason G, Rasmussen J, Abildstrom S, et al. Increased mortality and cardiovascular morbidity associated with use of nonsteroidal anti-inflammatory drugs in chronic heart failure. Arch Intern Med 2009;169(2):141–9.
53. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken) 2012; 64(4):465–74.
54. Maslow K. Dementia and serious coexisting medical conditions: a double whammy. Nurs Clin North Am 2004;39:561–79.
55. Dardiotis E, Giamouzis G, Mastrogiannis D, et al. Cognitive impairment in heart failure. Cardiol Res Pract 2012;2012:595821.
56. Gary RA, Brunn K. Aerobic exercise as an adjunct therapy for improving cognitive function in heart failure. Cardiol Res Pract 2014;2014:157508.
57. Vickrey B, Mittman B, Connor K, et al. The effect of a disease management intervention on quality and outcomes in dementia care. Ann Intern Med 2006; 145(10):727.
58. Belle S, Burgio L, Burns R, et al. Enhancing the quality of life of dementia caregivers from different ethnic or racial groups. Ann Intern Med 2006;145:727–38.
59. Rutledge T, Reis VA, Linke SE, et al. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48(8):1527–37.
60. O'Connor CM, Jiang W, Kuchibhatla M, et al. Safety and efficacy of sertraline for depression in patients with heart failure: results of the SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) trial. J Am Coll Cardiol 2010; 56(9):692–9.
61. Blumenthal JA, Babyak MA, Connor CO, et al. Effects of exercise training on depressive symptoms in patients with chronic heart failure. JAMA 2014; 308(5):465–74.
62. Dekker R. Cognitive therapy for depression in patients with heart failure: a critical review. Heart Fail Clin 2012;43(1):127–41.
63. Partnership for Health in Aging Workgroup on Interdisciplinary Team Training in Geriatrics. Position statement on interdisciplinary team training in geriatrics: an essential component of quality health care for older adults. J Am Geriatr Soc 2014;62(5):961–5.
64. Hajjar E, Cafiero A, Hanlon J. Polypharmacy in elderly patients. Am J Geriatr Pharmacother 2007; 5(4):345–51.
65. Kaufman DW, Kelly JP, Rosenberg L, et al. Recent patterns of medication use in the ambulatory adult population of the United States. JAMA 2014; 287(3):337–44.
66. Qato D, Alexander G, Conti R. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. JAMA 2008;300(24):2867–78.
67. Lee JK, Slack MK, Martin J, et al. Geriatric patient care by U.S. pharmacists in healthcare teams: systematic review and meta-analyses. J Am Geriatr Soc 2013;61(7):1119–27.
68. Deschodt M, Flamaing J, Haentjens P, et al. Impact of geriatric consultation teams on clinical outcome in acute hospitals: a systematic review and meta-analysis. BMC Med 2013;11(1):48.
69. Giamouzis G, Kalogeropoulos A, Georgiopoulou V, et al. Hospitalization epidemic in patients with heart failure: risk factors, risk prediction, knowledge gaps, and future directions. J Card Fail 2011; 17(1):54–75.
70. Pfuntner A, Wier LM, Steiner C. Costs for Hospital Stays in the United States, 2010. HCUP Statistical brief # 146. 2013. Agency for Healthcare Research and Quality, Rockville, MD. Available at: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb146.pdf.
71. Dharmarajan K, Hsieh A, Lin Z, et al. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. JAMA 2013;309(4):355–63.
72. Desai AS, Claggett B, Pfeffer MA, et al. Influence of hospitalization for cardiovascular versus noncardiovascular reasons on subsequent mortality in patients with chronic heart failure across the spectrum of ejection fraction. Circ Heart Fail 2014; 7(6):895–902.
73. Naylor M, Brooten D, Campbell RL, et al. Transitional care of older adults hospitalized with heart failure: a

randomized, controlled trial. J Am Geriatr Soc 2004; 52:675–84.
74. Dickson VV, Buck H, Riegel B. Multiple comorbid conditions challenge heart failure self-care by decreasing self-efficacy. Nurs Res 2013;62(1):2–9.
75. Østbye T, Yarnall K, Krause K, et al. Is there time for management of patients with chronic diseases in primary care? Ann Fam Med 2005;3:209–14.
76. Boyd CM, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design. Public Health Rev 2011;32(2):451–74.
77. American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. Patient-centered care for older adults with multiple chronic conditions: a stepwise approach from the American Geriatrics Society: American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. J Am Geriatr Soc 2012;60(10):1957–68.
78. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians. Guiding principles for the care of older adults with multimorbidity: an approach for clinicians: American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. J Am Geriatr Soc 2012; 60(10):E1–25.
79. Sm S, Soubhi H, Fortin M, et al. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings [review]. Cochrane Database Syst Rev 2013;(4):CD006560.
80. Drüeke TB, Parfrey PS. Summary of the KDIGO guideline on anemia and comment: reading between the guidelines. Kidney Int 2012;82(9):952–60. Available at: http://kdigo.org/home/guidelines/.
81. Qaseem A, Wilt TJ, Weinberger SE, et al. Clinical guideline diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011;155:179–92.
82. Qaseem A, Snow V, Cross JT Jr, et al. Current pharmacologic treatment of dementia: a clinical practice guideline. Ann Intern Med 2007;148:370–8.
83. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder. 3rd edition. Arlington, VA: American Psychiatric Association; 2010.