The Year in Heart Failure

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With health care reform and pay-for-performance measures in the near future, the heart failure (HF) community must critically appraise our practice patterns and processes of care. Ideally, our efforts begin with strategies to prevent HF, followed by therapies to treat HF and approaches to improving the cost-effectiveness of care. It is increasingly apparent that our current model is not sustainable, and we look to the scientists and clinicians in our field to provide innovative yet practical solutions. Herein, we discuss the major published clinical advances in HF over the past academic year (July 2010 to June 2011), including guidelines and scientific statements in Table 1 (1–9), state-of-the-art reviews in Table 2 (10–20), and key clinical trials in Table 3 (21–28).

Epidemiology, Risk Profiling, and Prevention

In the United States, HF incidence approaches 10 per 1,000 population after 65 years of age (29). Efforts to prevent HF focus on the treatment of established risk factors and the development of risk scores to predict incident HF. One risk prediction score, the Health ABC Heart Failure Model, was validated externally in Cardiovascular Health Study participants, confirming the utility of 9 variables to predict incident HF. The strength of the model is its applicability to real-world practice, in which all of the variables are readily available (30). A separate study suggested that including only common cardiovascular risk factors (coronary disease, hypertension, diabetes, atrial fibrillation, valvular disease, and age) can predict incident HF in men and women during 1,015,794 person-years of follow-up (31). Lam et al. (32) showed that after adjustment for cardiac dysfunction, subclinical dysfunction in each noncardiac organ system was associated with a 30% increased risk for HF.

Nevertheless, there is an unmet need to predict risk earlier. A small study by Yan et al. (33) reported the use of cardiac magnetic resonance imaging to detect subclinical, regional left ventricular (LV) dysfunction, as an independent predictor for incident HF and cardiovascular events in the asymptomatic, lower risk MESA (Multi-Ethnic Study of Atherosclerosis) cohort. Another investigation of an elderly cohort revealed an increased risk for LV diastolic dysfunction, independent of LV mass and traditional risk factors, that occurred with increased body mass index (34). These studies suggest that lifestyle counts in HF prevention efforts. Indeed, an analysis of almost 60,000 Finnish subjects free of HF at baseline showed that moderate and high levels of occupational and leisure-time physical activity were associated with a reduced risk for HF (35).

Biomarkers

This year saw no new evidence that serial biomarker-guided management of HF could reduce morbidity or mortality. In both the STARBRITE (Strategies for Tailoring Advanced HF Regimens in the Outpatient Setting) and PRIMA (Can Pro-Brain-Natriuretic Peptide Guided Therapy of Chronic HF Improve HF Morbidity and Mortality) trials, the use of natriuretic peptide–guided therapy was associated with increased use of evidence-based medications but no improvement in days alive or decrease in HF hospitalizations (36,37).

Several biomarker studies focused on predicting HF incidence in the community. Elevated cardiac troponin T measured using a highly sensitive assay was associated with increased risk for coronary heart disease, mortality, and incident HF (hazard ratio [HR] for HF: 5.95; 95% confidence interval [CI]: 4.47 to 7.92) after adjustment for traditional risk factors, kidney function, C-reactive protein, and N-terminal pro–brain natriuretic peptide. Surprisingly, measurable cardiac troponin T levels were detected in 66.5% of the 9,698 subjects in this study, all of whom were general participants in the ARIC (Atherosclerosis Risk in Communities) study, age 54 to 74 years (38). A similar study investigated the association between the highly sensitive cardiac troponin T assay and incident HF in adults from the CHS (Cardiovascular Health Study) age >65 years, finding a strikingly similar percent of patients with detectable levels of troponin (66.2%). Furthermore, they found that >50% increases in troponin T in subjects who had undetectable levels at baseline were associated with an increased risk for incident HF (39). Multimarker strategies for predicting risk for HF were studied in 2 cohorts. In the Framingham...
cohort, brain natriuretic peptide and urinary albumin/creatinine ratio provided incremental risk prediction to classic risk factors (40). In the Malmo Diet and Cancer Study cohort, only the natriuretic peptides improved risk prediction over standard factors (41). These publications, reflecting a limitation of many biomarker studies, beg the question of what therapeutic strategy could be implemented early, in a pre-clinical stage, to mitigate risk for HF.

**Pathophysiology**

The link between iron deficiency and HF continued to be a much investigated topic. In a prospective, observational cohort of patients with chronic systolic HF, iron deficiency was more prevalent in women and in those with advanced New York Heart Association (NYHA) functional class and higher biomarker levels. In multivariate models, iron deficiency was significantly associated with increased risk for death or transplantation (adjusted HR: 1.58; 95% CI: 1.14 to 2.17; p < 0.01) (42). In a separate study, Maeder et al. (43) investigated the link between anemia and HF severity, reporting reduced myocardial iron content in patients with HF compared with controls. Additionally, catecholamines and aldosterone both down-regulated the myocardial messenger ribonucleic acid expression of the type 1 transferrin receptor, suggesting a mechanistic link (43).

**Genetics and genomics.** A thorough review of inherited cardiomyopathies was published by Watkins et al. (44), highlighting our growing knowledge of the overlap between genes that cause structurally distinct inherited cardiomyopathies. An additional study from the German Competence Network Heart Failure (45) was likewise contributory. Given the genetic basis of some cardiomyopathies, it is imperative for clinicians to perform screening protocols for at-risk family members, with adjunctive genetic counseling and testing. To this end, guidelines from the European Society of Cardiology (3), as well as a consensus statement from the Heart Rhythm Society in conjunction with the European Heart Rhythm Association (9), were published.

**Management of HF**

**Acute decompensated HF.** There are 3 million hospitalizations for acute HF annually in the United States, 80% of which arrive through emergency departments. Accordingly, the National Heart, Lung, and Blood Institute published the findings of a working group on emergency department management of acute HF, which outlines the existing opportunities and challenges (46). The search for pharmacological strategies to relieve acute HF continues, including publication of the phase 3 PROTECT (Placebo-Controlled Randomized Study of the Selective A1 Adenosine Receptor Antagonist Rolofylline for Patients Hospitalized With Acute Decompensated Heart Failure and Volume Overload to Assess Treatment Effect on Congestion and Renal Function) trial. In this randomized study of more than 2,000 patients, rolofylline was not found beneficial in reducing symptoms or improving survival or renal function (47,48). Disappointment continued with publication of the randomized controlled ASCEND–HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure). In this study of 7,000 patients, nesiritide was not associated with a change in the rate of rehospitalization or rehospitalizations.
Table 3  Key Clinical Trials in Heart Failure From Academic Year 2010–2011

<table>
<thead>
<tr>
<th>Trial</th>
<th>n</th>
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<tbody>
<tr>
<td>Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (21)</td>
<td>7,141</td>
</tr>
<tr>
<td>CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (22)</td>
<td>550</td>
</tr>
<tr>
<td>Diuretic Optimization Strategies Evaluation (23)</td>
<td>308</td>
</tr>
<tr>
<td>Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (24)</td>
<td>2,737</td>
</tr>
<tr>
<td>Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multiple-Dose Study to Evaluate the Effects of RLY5016 in Heart Failure Patients (25)</td>
<td>120</td>
</tr>
<tr>
<td>Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (26)</td>
<td>1,798</td>
</tr>
<tr>
<td>Systolic Heart Failure Treatment With the I, Inhibitor Ibradivine Trial (27)</td>
<td>6,558</td>
</tr>
<tr>
<td>SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in CRT (28)</td>
<td>980</td>
</tr>
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AV = atrioventricular; CRT = cardiac resynchronization therapy; NYHA = New York Heart Association.

death and had a nonsignificant effect on dyspnea (21). Moreover, the DOSE (Diuretic Optimization Strategies Evaluation) trial showed no significant difference in symptoms or renal function when loop diuretic therapy was administered by continuous infusion or bolus and no significant difference in outcomes at low versus high dose (23).

The combination of loop diuretic therapy and inotropes was investigated in 60 patients in the DAD–HF (Dopamine in Acute Decompensated Heart Failure) trial, which demonstrated that the combination of a low-dose infusion of furosemide with 5 μg/kg/min of dopamine was as effective as high-dose furosemide infusion on symptoms, length of stay, rehospitalization, and 60-day mortality. Furthermore, the combination of dopamine and low-dose furosemide was associated with improved renal function (49).

Pharmacological therapy. There were a number of randomized controlled trials investigating pharmacological therapy for chronic systolic HF. The first, EMPHASIS-HF (Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure), was stopped prematurely, after showing that eplerenone reduced the risk for death and hospitalization in patients with systolic HF and NYHA functional class II symptoms. Serum potassium levels >5.5 mmol/l were found in 11.8% of patients on eplerenone versus 7.2% on placebo (p < 0.001) (24), suggesting that patient selection and monitoring are still critical when prescribing aldosterone antagonists. A future strategy to mitigate hyperkalemia might include the use of RLY5016, an oral potassium-binding polymer, the efficacy and safety of which were suggested in a recent randomized trial (25).

The SHIFT (Systolic Heart Failure Treatment With the I, Inhibitor Ivabradine) trial investigators reported a reduction in hospital admissions for HF (21% placebo vs. 16% drug; HR: 0.74; 95% CI: 0.66 to 0.83; p < 0.0001) and a reduction in deaths due to HF (5% placebo vs. 3% drug; HR: 0.74; 95% CI: 0.58 to 0.94; p = 0.14). It is important to note that although approximately 90% of patients in the study were treated with beta-blockers, they were not maximally beta-blocked. A statistically significant number of subjects treated with ivabradine experienced symptomatic bradycardia and visual side effects compared with the placebo group (27). A follow-up study revealed that patients with heart rates lower than 60 beats/min in the drug-treated group had fewer events at 28 days than did those with higher heart rates. After adjustment for change in heart rate, the treatment effect was neutralized, suggesting that it is the selective reduction in heart rate that may underlie the beneficial effect of ivabradine (50). In a smaller, randomized trial, Guazzi et al. (51) found a beneficial effect of sildenafil on functional capacity and clinical status in patients with NYHA functional class II or III systolic HF. Moreover, parameters of diastolic function also improved, with no serious adverse events (51).

Two small studies suggested a potential role for n-3 polyunsaturated fatty acids in nonischemic cardiomyopathy (52) and testosterone in elderly women with advanced HF (53). Coenzyme Q10, a cofactor in mitochondrial oxidative phosphorylation and generation of adenosine triphosphate, was not found to be an independent prognostic variable in HF, according to a pre-specified substudy of the CORONA (Controlled Rosuvastatin Multinational Study in Heart Failure) (54).

Chemotherapy-induced cardiomyopathy. The concerning finding that many patients with chemotherapy-associated cardiotoxicity are not receiving guideline-based pharmacological treatment for LV dysfunction was reported by Yoon et al. (55). Of patients with ejection fractions <55% after receiving chemotherapy, only 40% were treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and 51% were treated with beta-blockers. The investigators noted an opportunity for collaboration with oncologists to optimally manage these patients (55). Strategies for detecting subclinical signs of LV dysfunction are actively being investigated, including a study demonstrating that longitudinal strain and high-sensitivity troponin I can predict subsequent development of cardiotoxicity in patients who were treated with anthracyclines and trastuzumab (56).

Surgical interventions. The STITCH (Surgical Treatment for Ischemic Heart Failure) trial results were reported by Velazquez et al. (57), demonstrating that coronary artery bypass grafting (CABG) in addition to medical therapy did not reduce mortality compared with medical therapy alone in patients with LV dysfunction and coronary artery disease amenable to CABG (HR with CABG: 0.86; 95% CI: 0.72 to 1.04; p = 0.12). However, patients in the CABG arm were less likely to die of cardiovascular causes (57).

Imaging. A substudy of the STITCH trial demonstrated that the presence of myocardial viability using single-photon emission computed tomography or dobutamine echocardiography did not influence the likelihood of survival benefit from CABG plus medical therapy versus medical therapy alone. This substudy included 601 patients with LV dys-
function (left ventricular ejection fraction ≤35%) and coronary artery disease amenable to CABG who underwent viability testing at the discretion of the recruiting investigator (58). Publication of these results fueled the ongoing controversy of when and how to use myocardial viability testing. The use of late gadolinium enhancement in cardiac magnetic resonance imaging for prognostication and risk assessment in almost all types of cardiomyopathy was reviewed by Mewton et al. (59).

Remote Patient Monitoring

Several studies added to our knowledge regarding remote management and monitoring. A report of the long-term follow-up from the DIAL (Randomized Trial of Phone Intervention in Chronic Heart Failure) trial observed a reduction in the rate of death or hospitalization for HF in the intervention group at both 1 and 3 years, driven by a reduction in hospitalizations. Interestingly, these positive results may be attributed to the educational piece of the intervention; patients who increased their adherence had lower event rates (60). In contrast, 2 groups reported no benefit of telemonitoring in patients with HF (61,62). In the larger study, 1,653 patients with recent hospitalizations were randomized to telemonitoring or usual care. The intervention consisted of an interactive voice response system that collected data but did not provide education. There was no significant difference between the 2 groups with respect to readmission for any cause, death, or any secondary end point. One acknowledged limitation of this trial was that 14% of patients randomized to the intervention never used the telemonitoring system (61). Additionally, the information gathered by telemonitoring did not result in a uniformly prescribed change in management strategy. In the smaller trial, again no benefit was observed with a telemonitoring strategy that did not include education (62).

Data gathered in the COMPASS–HF (Chronicle Offers Management to Patients With Advanced Signs and Symptoms of Heart Failure) study, which used implantable hemodynamic monitors, demonstrated chronically elevated filling pressures in many patients. Furthermore, patients enrolled had a progressive increase in risk for HF events with higher chronic 24-h estimated pulmonary artery pressure (event risk 20% at 18 mm Hg, 34% at 25 mm Hg, and 56% at 30 mm Hg) (63). Abraham et al. (22) used an invasive, implantable hemodynamic monitoring device in the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial and showed a 39% reduction in HF-related hospitalizations compared with the control group over 15 months (153 vs. 253; HR: 0.64; 95% CI: 0.55 to 0.75; p < 0.0001), with an acceptable safety profile (22).

Transplantation

Important reports in the area of heart transplantation focused on patient selection for transplantation, strategies to bridge patients with mechanical circulatory support, and optimization of outcomes after transplantation by sex matching and immunosuppression. Gorodeski et al. (64) found that the Seattle Heart Failure Model provided modest discrimination of risk for mortality or need for ventricular assist device (VAD) implantation or urgent transplantation. However, risk was underestimated in patients who were ultimately listed as United Network of Organ Sharing status 2 (64). Another risk model, the Heart Failure Survival Score, was found to outperform peak oxygen consumption in patients who had implantable cardioverter-defibrillators (ICDs) and/or cardiac resynchronization therapy (CRT). They postulated that perhaps a peak oxygen consumption ≤10 ml/kg/min rather than ≤14 ml/kg/min may be a more useful discriminator in the device era. It was surprising to note, however, that in this single-center study of 715 patients referred for transplantation evaluation, 46.6% had no device therapy in place (65).

Two studies reported outcomes after transplantation in patients who were bridged with mechanical circulatory support. John et al. (66) found no difference in survival between patients who were bridged with continuous-flow VADs versus no VADs and no difference in survival on the basis of the duration of VAD support. Nativi et al. (67) analyzed data for 8,557 patients from the International Society for Heart and Lung Transplantation Registry, finding no significant difference in post-transplant survival between patients bridged with pulsatile versus continuous-flow VADs between 2004 and 2008. Graft rejection and survival rates were similar between both VAD groups and non-VAD patients who underwent transplantation. In another study, renal outcomes after heart transplantation in patients who were bridged with VADs were dependent on the level of renal function obtained during the time of mechanical support, not on the level of renal function before VAD implantation (68).

A retrospective single-center study confirmed that heart transplantation patients with donor-recipient sex mismatch have statistically significantly lower rates of survival (69), a finding that has yet to change practice. Finally, the TICTAC (Tacrolimus in Combination, Tacrolimus Alone Compared) trial was published, which demonstrated equivalent composite biopsy scores, allograft vasculopathy, and 3-year survival between patients treated with tacrolimus alone versus tacrolimus plus mycophenolate (70). If confirmed in a larger trial with longer follow-up, chronic immunosuppressive strategies may change.

Mechanical Circulatory Support

The year saw an important report focusing on health-related quality of life and exercise tolerance in patients after heart
transplantation compared with those during VAD support (71). Quality of life and exercise capacity increased in both groups over the time course of the study, but after adjustment, transplantation patients showed higher exercise tolerance compared with the VAD group. Nevertheless, these data, coupled with those of Starling et al. (72), who prospectively examined the outcome of patients bridged to transplantation with the commercially available HeartMate II device (Thoratec Corporation, Pleasanton, California), demonstrated the utility of VADs in the advanced HF population. The percent of patients reaching transplantation, cardiac recovery, or ongoing VAD support by 6 months was 91% for the commercial device, and the Kaplan-Meier survival for patients remaining on support at 1 year was 85% (72). Quality of life was significantly improved at 3 months of support and sustained through 12 months compared with baseline.

The improved outcomes with continuous-flow VADs have been tempered by a growing body of research on adverse effects, including multiple reports of acquired von Willebrand syndrome after VAD placement, manifested by severe impairment of platelet aggregation as well as a loss of large von Willebrand multimers (73,74). Although it appears that these hematologic changes occur in the majority of patients, not all patients have clinical bleeding and a controversial report by Schaffer et al. (75) argued that although patients with continuous-flow VADs have shown decreases in infectious complications, this was likely related to increased provider experience, not the newer technology. Cowger et al. (76) produced 1 in a series of reports showing that aortic insufficiency progresses over time in continuous-flow VAD-supported patients, and Goda et al. (77) described their further attention to the aortic valve, proposing that additional procedures to the aortic valve at the time of VAD placement are feasible. Finally, Piacentino et al. (78) focused on the tricuspid valve, demonstrating that tricuspid regurgitation is not reduced immediately after VAD implantation; significant tricuspid regurgitation was associated with longer post-implantation inotropic support and length of hospital stay.

Strategies to improve outcomes include a careful scrutiny of patient selection for continuous-flow VAD therapy. Boyle et al. (79) analyzed data from the Interagency Registry for Mechanically Assisted Circulatory Support and demonstrated that less acutely ill but functionally impaired patients with HF receiving continuous-flow VADs had longer survival and shorter lengths of stay compared with patients who were more acutely ill, as stratified by the registry’s patient profile schema. This finding, which was not entirely surprising, is nonetheless important to remember as we consider the optimal timing of VAD therapy with respect to progression of HF symptoms. Adamson et al. (80) argued that properly selected patients over 70 years of age had good functional recovery, survival, and quality of life at 2 years with current VAD technology. Even perioperative strategies paled in comparison with proper patient selection.

In a randomized controlled trial evaluating the effect of inhaled nitric oxide in patients undergoing VAD implantation, the use of nitric oxide at 40 ppm in the perioperative phase did not achieve significance for the primary end point of reduction in right ventricular dysfunction (81). Similarly, secondary end points of time on mechanical ventilation, hospital or intensive care unit stay, and the need for right ventricular VAD support were not significantly improved.

Efforts to recover the failing heart are ongoing, given the mixed news about long-term mechanical circulatory support. Birks et al. (82) repeated their studies in myocardial recovery, showing that reversal of end-stage HF secondary to nonischemic cardiomyopathy could be achieved in a substantial proportion of patients with nonpulsatile flow through the use of a combination of mechanical and pharmacological therapy. A less sustained approach to patients in shock has been facilitated by the use of percutaneous, nondurable circulatory support, reviewed in 2 reports (83,84).

**Novel Therapeutics**

There were several studies investigating new therapeutic strategies. The Rheos phase III trial evaluated the effect of baroreflex activation therapy on systolic blood pressure in patients with resistant hypertension, demonstrating sustained efficacy and safety of the device (85). Another emerging therapy for resistant hypertension targeted renal sympathetic denervation (86). A smaller phase II study evaluated chronic vagus nerve stimulation in systolic HF and showed significant improvements in quality of life, 6-min walking distance, and LV size and function. However, a fairly high rate of adverse events was noted, suggesting the need for a larger, controlled trial (87). In the phase II CUPID (Calcium Upregulation by Percutaneous Administration of Gene Therapy in Cardiac Disease) study, the investigators suggested safety and potential efficacy of percutaneous administration of gene therapy in patients with advanced HF, providing rationale to continue with a larger investigation (88).

**Cardiorenal Syndrome**

As investigations continue into the often observed link between worsening renal function and adverse prognosis, several studies explored the role of renal biomarkers in predicting cardiorenal syndrome. Cystatin C was found to be a marker of acute kidney injury in the first 48 h after hospitalization for HF. Furthermore, a rise in cystatin C by >0.3 mg/l was an independent predictor of 90-day mortality (adjusted odds ratio: 2.8; 95% CI: 1.2 to 6.7; p = 0.02) (89). In a second, small biomarker study, both urinary kidney injury molecule-1 (p < 0.001) and urinary N-acetyl-beta-D-glucosaminidase (p = 0.01) concentrations rose significantly after diuretic agents were withdrawn temporarily from patients with stable HF, whereas serum and urinary neutrophil gelatinase–associated lipocalin levels and serum creatinine were not significantly affected. After restarting diuretic therapy, both urinary kidney injury molecule-1 and
N-acetyl-beta-D-glucosaminidase concentrations returned to baseline (both p values <0.05), suggesting that these renal biomarkers may be sensitive to subclinical changes in volume status (90). It is not yet clear how these biomarkers can be used to alter clinical practice or outcomes.

Arrhythmias and Device Therapy for Heart Failure

The year witnessed many investigations into the benefits of and appropriate patient selection for ICD and CRT. The National Cardiovascular Data Registry revealed that in patients with ICDs, 22.5% did not meet evidence-based criteria for implantation (91), while nearly 1 in 4 patients receiving CRT devices did not fulfill guideline-based indications (92). These sobering statistics have often been coupled with the concern that as many as 40% to 80% of patients eligible for ICDs fail to receive them, especially among women and minorities. On a more optimistic note, LaPointe et al. (93) reported that after a detailed chart review, the true rate of ICD underuse may be substantially lower than previous estimates, and adjusting for ICD eligibility criteria virtually abolished patient sex and age disparities in ICD therapy. Fewer vascular complications with ICD implantation may be a reality with entirely subcutaneous ICDs, which consistently detected and converted ventricular fibrillation induced during electrophysiological testing (94).

The theme of appropriate patient selection to optimize outcomes after CRT implantation was reiterated in many studies. Tang et al. and the RAFT (Resynchronization-Defibrillation for Ambulatory Heart Failure) trial investigators (26) confirmed the efficacy of CRT in patients with milder HF; subsequent meta-analyses underscored the lessons learned from the available CRT trials (95,96). Additional studies from the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) trial emphasized the greater effectiveness of CRT in women (97) and the strong association between CRT-induced reverse LV remodeling and the beneficial outcomes of fewer HF hospitalizations (98) as well as the decreased risk for ventricular tachyarrhythmias (99). A series of reports examined predictors of CRT success or failure: Bilchick et al. (100) noted that right bundle branch block, ischemic cardiomyopathy, NYHA functional class IV status, and advanced age were powerful adjusted predictors of poor outcomes; a related study from the Netherlands showed that larger baseline LV dysynchrony predicted superior long-term survival, whereas discordant LV lead position and myocardial scar predicted worse outcome (101). Two additional investigations emphasized the importance of LV lead position on clinical outcomes (102) and prognosis (103).

Heart Failure With Normal Ejection Fraction

Our understanding of the pathophysiology of HF with normal ejection fraction (HFNEF) was advanced by 2 exercise studies with concomitant invasive hemodynamic monitoring (104,105). Although the 2 studies did not agree on all findings, they suggest that exercise testing with simultaneous right-heart catheterization may be useful in exploring the diverse pathophysiologic mechanisms in HFNEF.

Despite a better understanding of the hemodynamic derangements in HFNEF, an efficacious pharmacologic treatment has not been identified. A small study showed that patients with HFNEF had elevations in specific parameters of collagen content that correlated with impaired tissue Doppler (106), but the RAAM-PEF (Randomized Aldosterone Antagonism in Heart Failure With Preserved Ejection Fraction) trial was not associated with symptomatic reduction, although significant reductions in markers of collagen turnover and improvement in diastolic function were observed (107). Enalapril also proved unhelpful in HFNEF in a randomized double-blind trial (108). Although patients with HFNEF commonly have symptoms with exercise, exercise training improved peak and submaximal exercise capacity in older patients with HFNEF (109).

Processes and Quality of Care

Debate continues regarding the best measure of quality of care, including whether or not readmission is an accurate measure of the quality of care delivered (110). Several publications addressed process of care in HF (111–114), beginning with a study that showed the association between increased experience in managing HF, measured by an institution’s volume, and higher quality of care and outcomes, albeit at a higher cost (115). Lee et al. (112) demonstrated that collaborative care, with a cardiologist and primary care physician, was associated with reduced mortality compared with primary care alone (HR: 0.79; 95% CI: 0.63 to 1.00; p = 0.45) after discharge from the emergency department. A staffing survey revealed that most HF practices (43%) have <4 staff members, with 4 to 10 staff members in 34% of practices and only 23% of practices having >11 staff members (116). The care of complicated patients with HF is time intensive, and optimal resource utilization of caregivers has not yet been defined.

Three reports from the IMPROVE-HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting) provided insight into strategies for increasing evidence-based care. Seven quality measures were assessed in 34,810 participants, and interventions included decision support tools, structured improvement strategies, and audits with feedback, resulting in statistically significant improvements in beta-blocker use, aldosterone antagonist use, CRT, ICD implantation, and HF education (117). Furthermore, HF measures (angiotensin-converting enzyme inhibitor and beta-blocker use, anticoagulation for atrial fibrillation, CRT and ICD use, and HF education) were found to be independently associated with 24-month survival, with each 10% improvement in composite care...
associated with 13% lower odds of 24-month mortality (113). The sobering, but not surprising, finding that doses of all evidence-based therapies remain lower in real-world practice than in clinical trials was also confirmed (114).

Conclusions
Another year concludes without a paradigm-changing advance in the treatment or prevention of HF. In the absence of new therapies, it is apparent that clinicians must focus on improving the continuity of care that patients with HF receive, beginning in the emergency department, through the hospitalization, and to the discharge process, using a multidisciplinary group of care givers. The transition of our patients outside the hospital is even more important, so that communication and plans of care are optimized. We need to identify the critical components of this care at every juncture; best practices should be celebrated and adopted.

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