Consensus Statement

Acute Decompensated Heart Failure: Update on New and Emerging Evidence and Directions for Future Research

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ABSTRACT

Acute decompensated heart failure (ADHF) is a complex clinical event associated with excess morbidity and mortality. Managing ADHF patients is challenging because of the lack of effective treatments that both reduce symptoms and improve clinical outcomes. Existing guideline recommendations are largely based on expert opinion, but several recently published trials have yielded important data to inform both current clinical practice and future research directions. New insight has been gained regarding volume management, including dosing strategies for intravenous loop diuretics and the role of ultrafiltration in patients with heart failure and renal dysfunction. Although the largest ADHF trial to date (ASCEND-HF, using nesiritide) was neutral, promising results with other investigational agents have been reported. If these findings are confirmed in phase III trials, novel compounds, such as relaxin, omecamtiv mecarbil, and ularitide, among others, may become therapeutic options. Translation of research findings into quality clinical care can not be overemphasized. Although many gaps in knowledge exist, ongoing studies will address issues around delivery of evidence-based care to achieve the goal of improving the health status and clinical outcomes of patients with ADHF. (*J Cardiac Fail 2013;19:371−389*)

Key Words: Heart failure, clinical trials, diuretics, vasodilators, biomarkers, quality of care, ultrafiltration.

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Heart failure is a complex syndrome that involves both acute and chronic processes. Acute heart failure has various presentations. It can be characterized by rapidly developing symptoms of new-onset or de novo heart failure, or it can be a gradual worsening of chronic heart failure culminating in acute decompensated heart failure (ADHF), sometimes referred to as ''acute on chronic'' heart failure. Many different terms have been used in the literature to describe this syndrome, including acute heart failure, acute heart failure syndromes, and ADHF.[1] The latter term will be used for this report.

Despite ongoing and intense efforts, clinical trials have not yielded therapeutic strategies that improve outcomes in the ADHF population. Many factors may contribute to inadequate trial results, including the heterogeneity of the condition, the likelihood that multiple triggers or pathophysiologic processes exist and differ among individual patients, the timing of patient enrollment, and inherent challenges such as obtaining informed consent and conducting clinical trials in patients who are acutely symptomatic and may have high adverse event rates. As a result, there are limited data to guide patient management. Of the 44 recommendations relevant to ADHF in the 2010 Heart Failure Society of America (HFSA) heart failure guidelines, 3 were supported by strength of evidence A, 8 by strength of evidence B, and 33 by strength of evidence C.[2] Similarly, in the American College of Cardiology/American Heart Association 2009 heart failure guidelines, only 1 of 25 recommendations related to ADHF was a class I, level of evidence A recommendation.[3]

Despite the paucity of evidence, practicing clinicians routinely seek guidance on the management of patients with ADHF. Since the publication of the 2010 HFSA heart failure guidelines, several trials in ADHF have yielded new data. Although these studies advance knowledge and inform clinical decision making, their results do not warrant a complete revision of the guidelines. The purpose of the present paper is to review new data generated in the broad ADHF population involving therapeutic drugs or strategies, biomarkers, and quality of care initiatives. This paper also highlights gaps in the current evidence base for the diagnosis, prognosis, risk stratification, management and monitoring of ADHF. Future research efforts should focus on these high-priority areas of unmet needs. This paper does not address the management of heart failure in the setting of shock, specific precipitants (eg, acute myocardial infarction or atrial fibrillation), early management with bilevel positive airway pressure, or other agents not approved for use in the United States (eg, levosimendan). Readers interested in these topics should refer to the 2010 HFSA guidelines for further information.[2]

Epidemiology

More than 1 million hospitalizations for heart failure occur annually in the USA.[4,5] Heart failure remains a primary cause of hospitalization among older Americans. An analysis from the Centers for Medicare and Medicaid Services (CMS) revealed a risk-adjusted heart failure hospitalization rate of ~2,000 per 100,000 person-years among Medicare beneficiaries based on 2008 data.[6] A decline in the relative rate of hospitalization from 1998 to 2008 was detected in that study, which the authors primarily attributed to a reduction in the number of unique individuals hospitalized for heart failure rather than to a reduction in repeated hospitalizations. Unfortunately, heart failure is a progressive disease in most patients, and although some therapies slow or reverse progression, only cardiac transplantation is curative for patients with irreversible causes. The prevalence of heart failure is expected to increase in the USA over the next 20 years.[7] Moreover, the risk of hospitalization tends to increase as heart failure progresses, and ADHF admissions increase the risk of subsequent readmission and death.

If the expected increase actually occurs, the burden of heart failure hospitalization will continue to place a major strain on health care resources. Clinicians, hospital administrators, and patients now have access to CMS publicly reported ''quality metrics'' for ADHF, including 30-day mortality and readmission rates (www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/HospitalQualityInits/OutcomeMeasures.html). It remains hotly debated whether the ideal end points have been defined for ADHF clinical trials and quality metrics.[8] Event rates were lower than predicted in the Acute Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial,[9] revealing that emerging therapies must have large treatment effects for an ADHF trial to have the power to detect a mortality benefit (even with >5,000 patients enrolled). Therefore, the process to develop new therapies from small mechanistic trials to large outcome trials will be prolonged and expensive.

Patient Characteristics

In general, patients hospitalized for ADHF are elderly, approximately one-half are women, and 25% are nonwhite.[10] The majority (88% in the OPTIMIZE [Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure] registry)[11] have a history of chronic heart failure rather than a de novo presentation. These patients typically have multiple comorbidities and moderately elevated systolic blood pressure, and approximately one-half have heart failure with preserved ejection fraction (HF-PEF).[10] The majority of patients present with evidence of congestion or volume overload.[10,12] Increases in body weight are associated with heart failure hospitalization and begin at least a week before presentation.[13] Cardiogenic shock during the initial presentation to the emergency department (ED) is very rare.[14,15] ADHF is a heterogeneous syndrome, and more focus on presenting characteristics may allow for better-targeted therapies. Clinical characteristics have been proposed to subcategorize patients with ADHF based on parameters such as blood pressure, degree of congestion, time course