

# The Impact of Worsening Heart Failure in the United States



Lauren B. Cooper, MD\*, Adam D. DeVore, MD,  
G. Michael Felker, MD, MHS

## KEYWORDS

• Worsening heart failure • Clinical trials • Outcomes • Medications

## KEY POINTS

- In-hospital worsening heart failure is an increasingly important endpoint in trials of acute heart failure.
- In-hospital worsening heart failure is associated with increased short- and long-term mortality, re-hospitalization, and health care costs.
- Renal dysfunction and cardiac dysfunction predict worsening heart failure in patients hospitalized with acute heart failure.
- A standardized definition of worsening heart failure should be established for use in future clinical trials.

## INTRODUCTION AND DEFINITIONS

Heart failure is a common condition in the United States. More than 5 million Americans have heart failure, with more than 800,000 new cases diagnosed annually.<sup>1</sup> This chronic condition is marked by episodes of acute decompensation, often requiring hospitalization. In the United States alone, there are greater than 1 million hospitalizations annually for acute heart failure.<sup>1</sup> Unfortunately, patient outcomes remain poor with a 5-year survival rate of approximately 50% and there is an urgent public health need to improve

our understanding and treatment options for patients suffering with acute heart failure.<sup>1</sup> Acute heart failure therapeutics remain largely homogenous and unchanged over the past 40 years in the United States.<sup>2,3</sup>

The term “worsening heart failure” has been used to indicate worsening of chronic heart failure, also termed “acute heart failure” or “acute decompensated heart failure.” This acute worsening of chronic heart failure often results in adjustment of chronic therapy or requires in-patient hospitalization and is associated with worse prognosis.<sup>4,5</sup> Worsening heart failure has also been used to

---

Disclosures: Dr L.B. Cooper reports receiving research support from Novartis. Dr A.D. DeVore reports receiving research support from Amgen, the American Heart Association, Novartis, Maquet, and Thoratec, and serving as a consultant for Maquet. Dr G.M. Felker reports receiving grant support from the National Heart, Lung, and Blood Institute, Novartis, Roche Diagnostics, Otsuka, and Amgen, and serving as a consulting for Trevena, Amgen, Novartis, Celladon, Sorbent, Bristol-Myers Squibb, Singlulex, St. Jude Medical, and Medtronic. Funding Source: Dr L.B. Cooper was supported by grant T32HL069749-11A1 from the National Institutes of Health.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute, or the National Institutes of Health.

Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715, USA

\* Corresponding author.

E-mail address: [lauren.b.cooper@duke.edu](mailto:lauren.b.cooper@duke.edu)

Heart Failure Clin 11 (2015) 603–614

<http://dx.doi.org/10.1016/j.hfc.2015.07.004>

1551-7136/15/\$ – see front matter © 2015 Elsevier Inc. All rights reserved.

describe worsening of acute heart failure that occurs during a hospitalization for acute heart failure. For the purposes of this review, we focus on the latter condition, namely, in-hospital worsening heart failure.

In-hospital worsening heart failure represents a clinical scenario in which a patient hospitalized for treatment of acute heart failure experiences a worsening of their condition while in the hospital, requiring escalation of therapy. This can occur in patients who do not respond to initial therapy or in those who do respond to initial therapy but subsequently stop responding or worsen. Worsening heart failure can occur at any point throughout the hospitalization.<sup>6,7</sup> There is a growing body of evidence that in-hospital worsening heart failure is also associated with a worse prognosis and signals an important change in the heart failure patient's clinical course (Fig. 1). These data suggest therapeutic strategies designed to reduce the incidence of in-hospital worsening heart failure could improve patient outcomes.

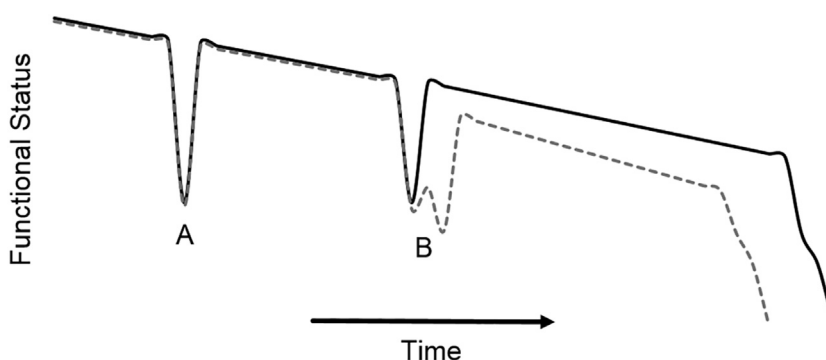
#### ESTABLISHING A DEFINITION FOR WORSENING HEART FAILURE AS A CLINICAL TRIAL ENDPOINT

Several clinical trials in acute heart failure have examined worsening heart failure as an endpoint. The first trial to define and examine worsening heart failure was published in 2004 and compared different doses of tezosentan, an endothelin receptor antagonist with vasodilating properties.<sup>8</sup> This study included patients from centers in Europe, Israel, and the United States. Investigators examined both hemodynamic and clinical endpoints, including worsening heart failure, defined as "either failure to improve (persistent symptoms

and signs of acute heart failure during the first 24 h of treatment) or recurrent symptoms and signs of acute heart failure, pulmonary edema, or cardiogenic shock after initial stabilization within 30 days after randomization, either of which required the initiation or increase of appropriate intravenous therapy or the implementation of mechanical circulatory or ventilatory support to treat the event."<sup>8</sup>

The rationale for using worsening heart failure as an endpoint in acute heart failure trials was summarized in subsequent publications.<sup>9</sup> Worsening heart failure during a hospitalization for acute heart failure was analogous to reinfarction after an episode of acute coronary syndrome—a failure of the initial treatment strategy. This endpoint was a departure from traditional acute heart failure studies that focused on acute symptoms—primarily dyspnea—or postdischarge outcomes. Neither acute symptoms nor postdischarge outcomes capture the inpatient clinical course, a critical time for heart failure patients. The purpose of worsening heart failure as an endpoint is to represent the inpatient course in a way that can be measured in a clinical trial. Furthermore, in-hospital worsening heart failure is unique to episodes of acute heart failure. Recognizing the different physiology of acute and chronic heart failure underscores the need for different outcomes in clinical trials of these disease states.<sup>10</sup>

Despite the value of identifying worsening heart failure, there are also some challenges with using worsening heart failure as a clinical trial endpoint. Most notably, it may be difficult to ascertain whether escalation of care is due to true worsening of a patient's condition or due to initial undertreatment. This determination is particularly challenging for patients who are deemed



**Fig. 1.** Patient's clinical trajectory after an episode of in-hospital worsening heart failure (*dotted gray line*) compared with clinical trajectory without worsening heart failure (*solid black line*). The heart failure syndrome is characterized by acute changes in status typically requiring a hospitalization (A). In-hospital worsening heart failure (B, *dotted gray line*) represents a more complicated and costly hospitalization associated with worse long-term outcomes.

Download English Version:

<https://daneshyari.com/en/article/3473253>

Download Persian Version:

<https://daneshyari.com/article/3473253>

[Daneshyari.com](https://daneshyari.com)