Mortality rates for patients with acute myocardial infarction (MI) continue to decline as evidence-based therapies are implemented on a broader scale, invasive management and revascularization are more widely used, and reperfusion times for patients with acute ST-segment elevation myocardial infarction (STEMI) are shortened. Recent data from the Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines (ACTION Registry-GWTG) in the United States demonstrated that, by 2009, risk-adjusted in-hospital mortality had decreased to 5.5% among STEMI patients treated in routine practice. In addition, mortality rates through and beyond 1 year among STEMI patients treated with primary percutaneous coronary intervention (PCI) enrolled in recent clinical trials have declined by 3% to 6%. Yet, improvements in survival demonstrated with STEMI patients may be tempered by the consequent morbidity of postinfarction heart failure (HF), which, unfortunately remains a common clinical event. Acute STEMI is an independent predictor of HF at admission, and the development of HF among STEMI patients is associated with a much higher long-term mortality rate compared with patients who do not develop HF. Because mortality rates for STEMI patients have declined and reinfarction rates have been shown to be low with the widespread use of primary PCI, attention has shifted toward reducing postinfarction HF in patients who do not develop HF.7 Because mortality rates for STEMI patients have declined and reinfarction rates have been shown to be low with the widespread use of primary PCI, attention has shifted toward reducing postinfarction HF because this outcome is thought to reflect the downstream impact of acute therapies for STEMI.

There are multiple convergent trends that could contribute to the rising prevalence of HF after STEMI, including an aging population and a decrease in sudden cardiac death because of defibrillator therapy. Fortunately, though, HF hospitalizations are declining nationwide, partially because of a declining risk of postinfarction HF. Given that ischemic heart disease is the most common cause of HF, the relationship of improvements in upstream treatment of acute MI should be evaluated in terms of its impact on postinfarction HF. Unfortunately, the timing and scope of HF after presentation with STEMI have not been well defined. Unlike de novo MI and reinfarction, there is no universally agreed-upon definition of HF as a clinical outcome in the post-MI population. Consequently, there has been limited adoption of postinfarction HF as a clinical end point in trials or registries. Following the progress in reducing mortality from STEMI over the past 2 decades, reducing postinfarction HF events remains an important clinical need. In this review, we will explore the incidence of HF across previous STEMI trials, examine earlier experiences with the use and definition of HF end points for STEMI trials, and discuss options for developing a universal definition of post-STEMI HF that can be considered by regulatory bodies and clinical investigators to better delineate the impact of novel therapies for STEMI on myocardial salvage and subsequent downstream HF events.

**Rationale for Collecting Heart Failure End Points in STEMI Trials**

Since Braunwald and Maroko first described the time-sensitive nature of limiting infarct size, therapies that have targeted the early restoration of myocardial perfusion. Contemporary treatment strategies have moved beyond epicardial artery patency toward the restoration of microvascular flow and myocardial tissue perfusion to better preserve left ventricular function and reduce mortality. Heart failure on admission may reflect the extent of myocardial damage or decompensation already present in the setting of ongoing STEMI and often portends a worse prognosis proportional to the severity of HF as assessed by Killip class. In the Global Registry of Acute Coronary Events, for example, in-hospital mortality for Killip classes I, II, and III present on admission was 2.9%, 9.9%, and 20.4%, respectively (P<0.001). The degree of HF after presentation anticipates a similar prognosis. Contemporary trials of acute coronary syndromes largely use thrombosis-related end points such as cardiovascular death, MI, and stroke, but treatments that are specifically designed for STEMI care also need to be evaluated in the context of left ventricular dysfunction.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Department of Medicine, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC (Z.J.E., G.M.F., A.F.H., K.W.M., M.T.R.); and Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH (W.H.W.T., A.M.L.)

The online-only Data Supplement is available at http://circoutcomes.ahajournals.org/lookup/suppl/doi:10.1161/CIRCOUTCOMES.112.966150/-/DC1.

Correspondence to Matthew T. Roe, MD, MHS, 2400 Pratt St, Durham, NC 27710. E-mail roe00001@mc.duke.edu

(Circ Cardiovasc Imaging. 2012;5:594-600.)

© 2012 American Heart Association, Inc.

*Circ Cardiovasc Qual Outcomes* is available at http://circoutcomes.ahajournals.org

DOI: 10.1161/CIRCOUTCOMES.112.966150
Several studies have explored the impact of post-STEMI HF. For example, an analysis of the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries-I (GUSTO-I) trial found that cardiogenic shock occurred in 7.2% of patients with STEMI but was responsible for 58% of deaths at 30 days. Mild-to-moderate HF (similar to Killip classes II and III at presentation) was a more common complication of STEMI in the early lytic trials. Among the patients enrolled in GUSTO-I, GUSTO-IIb, GUSTO-III, and the Assessment of the Safety of a New Thrombolytic-IC (ASSENT-II) trials, 57.6% developed mild-to-moderate HF after STEMI. In a post hoc analysis, the incidence of death at 30 days was four times higher in patients with even mild-to-moderate HF compared with patients without HF (8% versus 2%). Therefore, the morbidity and mortality associated with developing HF after STEMI suggest that HF is an appropriate end point for the evaluation of novel treatments and reperfusion strategies for STEMI patients. With 30-day mortality rates decreasing in clinical trials to as low as 2.1% in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial, it is increasingly difficult to show a mortality benefit that can be directly attributed to therapeutic impact on the index event of STEMI. Similarly, reinfarction rates have diminished considerably with broader use of PCI. Reinfarction within 30 days occurred in 4.2% of patients in GUSTO-III, whereas it occurred in 1.8% of patients in HORIZONS-AMI. It is a natural extension to consider composite end points for future STEMI trials that include HF as one of the key components of a composite primary end point.

The use of HF end points also makes sense from an economic standpoint, particularly in the contemporary era of unsustainable growth in healthcare spending. Prospective economic evaluations are increasingly used to justify the cost-effectiveness of novel therapies. To encourage the broad-scale addition of a new treatment, cost-effectiveness studies can show that a new therapy not only improves patient outcomes but also decreases downstream costs. In 2009, overall HF costs in the United States were an estimated $37.2 billion, of which $20.1 billion was attributable to inpatient care. As the use of device therapies (such as defibrillators and cardiac resynchronization therapy) for left ventricular dysfunction and HF grows, costs may continue to increase. Therefore, reducing the incidence of a resource-intensive complication such as HF after STEMI could justify the cost of a novel therapeutic agent for STEMI patients.

Past Experience With HF End Points in STEMI Trials

Despite the importance of HF as a consequence of STEMI, HF end points have not been consistently defined or systematically collected in previous STEMI trials. Several previous trials that have informed current treatment approaches for STEMI—Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto miocardico (GISSI) trial, many of the GUSTO trials, Trandolapril Cardiac Evaluation (TRACE) study, Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT), and Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)–Thrombolysis in Myocardial Infarction (TIMI) 28 trial, among others—demonstrated little consensus regarding the definition of HF end points and the optimal duration for the ascertainment of HF end points. As a result, recent STEMI trials that have captured and reported HF end points use different definitions (Table 1) and ascertainment time periods (Table 2), making it difficult to compare HF event rates across trials.

Early Lytic Trials and Contemporary Primary/Facilitated PCI Trials

Early lytic trials focused on HF as a dichotomous baseline covariate (either present or absent at the time of presentation with STEMI), rather than as a time-dependent clinical end point whose incidence could potentially be modified by the studied treatment. Analyses of these trials have defined HF as a sign or symptom of pulmonary congestion in the absence of a noncardiac cause. Although the criteria for HF as an end point are similar in more contemporary STEMI trials, there are several permutations of these criteria. The Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial, which found that the monoclonal antibody pexelizumab had no effect on mortality as an adjunctive therapy to STEMI patients undergoing primary PCI, exemplifies the subtle changes in the HF end point over time. Congestive HF was included in a composite secondary end point of death, cardiogenic shock, or congestive HF through 90 days. Similar to the early lytic trials, HF was defined on the basis of the physician’s decision to treat HF with an intravenous diuretic, inotropic agent, or vasodilator; yet fewer additional clinical criteria were needed to establish a diagnosis of HF, and the determination was not made at the time of STEMI presentation.

Issues Confounding the Definition and Ascertainment of HF End Points in STEMI Trials

Defining a temporal causal relationship between the incidence of postinfarction HF and the index STEMI event is particularly important, given the presence of many confounding factors. For example, the administration of intravenous contrast and fluids during primary PCI procedures may contribute to the development of early acute HF events, mostly because of volume overload or contrast nephropathy. To avoid such confounding and identify preventable events independent of the index event, trials such as APEX-AMI have only adjudicated HF events occurring >24 hours after randomization. Using a proper adjudication process to exclude clinical events that occur outside the timeframe for ascertainment is important to fully characterize treatment effect. Similar to distinguishing between the index acute MI and subsequent reinfarction by trends in cardiac biomarkers, new-onset HF must be separated from periprocedural circumstances that surround the index STEMI event. Beyond properly ascertaining HF events, an HF end point in STEMI trials must also minimize confounding from comorbidities and practice patterns. Both qualitative (dyspnea scales) and quantitative (measured hemodynamics with a pulmonary artery catheter) components of an HF definition are confounded by concomitant pulmonary disease (in the case of dyspnea scales) and large differences in the use of pulmonary artery catheters among post-MI patients across practices and regions.
Assessing the Downstream Impact of HF Events in STEMI Trials

The clinical outcomes that occur after HF events involve more than a simple assessment of mortality. Indeed, reductions in mortality increase the likelihood of competing events, such as recurrent hospitalizations, longer lengths of stay, and the need for prophylactic defibrillator placement or cardiac resynchronization therapy. To adequately capture a novel treatment’s effect on these metrics, the ascertainment period for HF events should be long enough to provide continued surveillance over an extended time period after the index STEMI event (Figure). Capturing a treatment’s effect on the morbidity of downstream HF will be further complicated in international trials by variations from country to country in practice patterns for HF events, leading to differences in the length of stay and readmission rates for HF.\textsuperscript{33} Given the global scale of STEMI trials, a standardized definition for HF must be logistically feasible and broadly ascertainable across different systems of care.

Proposing a Standardized Definition of HF in STEMI Trials

A standardized definition of HF as an end point is needed to guide the conduct and interpretation of future STEMI trials. A common HF end point that is universally applied across STEMI trials would facilitate comparisons of treatments and identification of safety signals. To facilitate broad adoption, a standardized definition should be as simple as possible in an effort to facilitate ascertainment and allow the requisite data to be captured as part of routine clinical care. In addition, with increasing use of electronic data capture in clinical trial operations, a standardized definition in STEMI trials could streamline the clinical event classification process by using computer algorithmic adjudication, thereby improving efficiency and reducing costs.\textsuperscript{33}

For the past decade, there has been a universal definition of MI that has been used to construct the reinfarction end point definition for non-ST-segment elevation acute coronary syndrome trials.\textsuperscript{37-40} Although the importance of using a similar approach for standardization of the HF end point across clinical trials is evident, several challenges exist, including generating consensus and implementing common end point definitions on a broad scale. Whether a standardized definition of HF could be properly integrated into trials for a single precursor disease state such as STEMI raises additional questions such as the following: (1) Will a standardized definition clarify the relationship between acute treatments administered for STEMI patients and downstream morbidity?; and (2) What would be the optimal duration of ascertainment for HF end points?

Many relevant efforts are already underway, which can inform the development of a tailored definition to describe the incidence of post-STEMI HF, both in-hospital and after discharge.

---

### Table 1. Definitions of HF End Points Used in Prior STEMI Trials*  

<table>
<thead>
<tr>
<th>Study Acronym</th>
<th>Year</th>
<th>Signs or Symptoms of Heart Failure</th>
<th>Ascertainment Time Period for End Points</th>
</tr>
</thead>
</table>
| GUSTO III\textsuperscript{25} | 1997 | • Radiographic evidence of pulmonary edema  
  • Rales >1/3 of lung fields  
  • PCWP >18 mm Hg with cardiac index <2.4 L/min per m\textsuperscript{2}  
  • Dyspnea, with documented PO\textsubscript{2} <80 mm Hg or O\textsubscript{2} saturation <90%, without known preexisting lung disease | • Reinfarction at 30 days  
  • Mortality at 30 days |
| ADVANCE MI\textsuperscript{24} | 2005 | • Radiographic evidence of pulmonary edema  
  • Rales >1/3 of lung fields  
  • PCWP >18 mm Hg | • Reinfarction at 30 days  
  • All-cause mortality or severe HF at 30 days |
| ASSENT-4\textsuperscript{27} | 2006 | • Radiographic evidence of pulmonary edema  
  • Rales >1/3 of lung fields  
  • PCWP >25 mm Hg  
  • Dyspnea with PO\textsubscript{2} <80 mm Hg or oxygen saturation <90% without known lung disease | • Reinfarction at 90 days  
  • All-cause mortality, HF, or cardiogenic shock at 90 days  
  • HF at 90 days  
  • Cardiogenic shock at 90 days  
  • HF rehospitalization at 90 days  
  • Rehospitalization for cardiogenic shock at 90 days |
| APEX-AMI\textsuperscript{26} | 2007 | • Radiographic evidence of pulmonary edema  
  • Rales >1/3 of the lung fields  
  • PCWP or LVEDP >18 mm Hg  
  • Dyspnea, with documented PO\textsubscript{2} <80 mm Hg on room air or oxygen saturation <90% on room air, without significant lung disease | • Reinfarction at 90 days  
  • All-cause mortality, cardiogenic shock, or HF at 90 days  
  • Cardiogenic shock at 90 days  
  • HF at 90 days |
| FINESSE\textsuperscript{29} | 2008 | No signs or symptoms included in HF definition | • Reinfarction at 90 days  
  • All-cause mortality, ventricular fibrillation >48 hours after randomization, cardiogenic shock, and HF requiring ED visit or rehospitalization at 90 days  
  • Hospitalization for HF at 90 days |

*Trial definitions of heart failure are included in the online-only Data Supplement Appendix. HF indicates heart failure; STEMI, ST-segment elevation myocardial infarction; ED, emergency department; LVEDP, left ventricular end diastolic pressure; PCWP, pulmonary capillary wedge pressure; GUSTO III, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries III; ADVANCE MI, Addressing the Value of Facilitated Angioplasty After Combination Therapy or Eptifibatide Monotherapy in Acute Myocardial Infarction; ASSENT-4, Assessment of the Safety of a New Thrombolytic-4; APEX-AMI, Assessment of Pexelizumab in Acute Myocardial Infarction; and FINESSE, Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events.
The Standardized Data Collection for Cardiovascular Trials Initiative is in the process of creating a standardized, multiple-component definition for HF events—an important step toward establishing a common framework for novel treatments in HF. The definition, which was posted for public review and is now being finalized, may serve as a template for a tailored multiple-component HF end point that can also reflect downstream morbidity. Such a multiple-component HF end point, which evaluates events beyond the index hospitalization, has been proposed for acute HF syndrome trials and could also be adapted for STEMI trials. A multiple-component HF end point, built using elements of these existing efforts, could provide a common platform upon which the efficacy of STEMI treatments could be compared based on overall rankings. In addition to the overall results from the multiple-component end point definition, the outcomes associated with each of the individual components of the end point definition used to form the overall definition could be reported in a consumer fashion, which has been done previously in non–ST-segment elevation acute coronary syndrome trials when reporting the different subclassifications of MI for reinfarction end points.

We propose that a composite end point of HF for STEMI trials meet these issues of generalizability by broadly capturing events during the initial hospitalization and beyond. At the same time, a standardized HF end point definition must define HF narrowly enough to capture clinically meaningful events while excluding confounding circumstances such as periprocedural intravenous fluid administration and contrast-induced nephropathy. We propose a standardized multiple-component HF end point that adapts elements of the definition of HF requiring hospitalization from the Standardized Data Collection for Cardiovascular Trials Initiative while accounting for postdischarge events (Table 3).

### Table 2. Incidence of Heart Failure in Selected STEMI Trials*

<table>
<thead>
<tr>
<th>Study Acronym</th>
<th>Date</th>
<th>Intervention</th>
<th>Ascertainment Time Period for HF Events</th>
<th>Incidence of HF Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lytic trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GUSTO III</td>
<td>1997</td>
<td>Reteplase vs accelerated alteplase</td>
<td>30 days</td>
<td>17.2% in reteplase arm, 17.5% in alteplase arm</td>
</tr>
<tr>
<td>PCI trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADVANCE MI</td>
<td>2005</td>
<td>Facilitated PCI with eptifibatide-half-dose tenecteplase vs facilitated PCI with eptifibatide-placebo</td>
<td>30 days</td>
<td>6% in the eptifibatide-half-dose TNK group vs 3% in the facilitated PCI with eptifibatide-placebo group</td>
</tr>
<tr>
<td>ASSENT-4 PCI</td>
<td>2006</td>
<td>Facilitated PCI with full-dose tenecteplase vs standard PCI</td>
<td>90 days</td>
<td>12% in the TNK+PCI group vs 9% in the standard PCI group</td>
</tr>
<tr>
<td>APEX-AMI</td>
<td>2007</td>
<td>Pexelizumab vs placebo as adjunct to PCI</td>
<td>30 and 90 days</td>
<td>At 30 days: 4% in placebo group vs 4% in pexelizumab group At 90 days: 5% in placebo group vs 5% in pexelizumab group</td>
</tr>
<tr>
<td>FINESSE</td>
<td>2008</td>
<td>Combination-facilitated PCI vs abciximab-facilitated PCI vs primary PCI</td>
<td>In-hospital</td>
<td>HF during index hospitalization: 6.5% in combination-facilitated PCI group vs 5.5% in abciximab-facilitated PCI group vs 6.5% in placebo group</td>
</tr>
</tbody>
</table>

ADVANCE MI indicates Angioplasty After Combination Therapy or Eptifibatide Monotherapy in Acute Myocardial Infarction; ASSENT-4 PCI, Assessment of the Safety and Efficacy of a New Treatment Strategy for Acute Myocardial Infarction; APEX-AMI, Assessment of Pexelizumab in Acute Myocardial Infarction; FINESSE, Facilitated Intervention With Enhanced Reperfusion Speed to Stop Events; GUSTO III, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; HF, heart failure; PCI, percutaneous coronary intervention; and TNK, tenecteplase.

*Key STEMI trials that did not use HF in an end point: Harmonizing Outcomes With Revascularization and Stents (HORIZONS), Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment-Thrombolysis in Myocardial Infarction 25 (EXTRACT), Hirulog and Early Reperfusion or Occlusion-2 (HERO-2), Organization for the Assessment of Strategies for Ischemic Syndromes (OASIS-6), Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT), Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY), Assessment of the Safety of a New Thrombolytic-3 (ASSENT-3), Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico (GISSI), Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO)-I, GUSTO-IIb, GUSTO-V, Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC), Fibrinolytic and Aggrastat for ST Elevation Resolution (FASTER-TIMI 24) and Time to Integri

[Figure](http://circoutcomes.ahajournals.org/). Progression of HF post-STEMI. This figure displays the pathophysiological progression of heart failure following STEMI. HF indicates heart failure; LV, left ventricular; and STEMI, ST-segment elevation myocardial infarction.
Table 3. Proposed Standardized Definition for HF in STEMI Trials

<table>
<thead>
<tr>
<th>HF during the index hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea, beginning or persisting &gt;24 hours after hospital admission, accompanied by both of the following criteria:</td>
</tr>
<tr>
<td>Criterion 1: Physical signs of HF, including at least 2 of the following:</td>
</tr>
<tr>
<td>Edema (&gt;2+ lower extremity)</td>
</tr>
<tr>
<td>Pulmonary crackles/rales greater than basilar</td>
</tr>
<tr>
<td>Jugular venous distention</td>
</tr>
<tr>
<td>Tachypnea (respiratory rate &gt;20 bpm)</td>
</tr>
<tr>
<td>Rapid weight gain</td>
</tr>
<tr>
<td>S3 gallop</td>
</tr>
<tr>
<td>Increasing abdominal distension or ascites</td>
</tr>
<tr>
<td>Hepatocutaneous reflex</td>
</tr>
<tr>
<td>Radiological evidence of worsening HF</td>
</tr>
<tr>
<td>A right heart catheterization showing a pulmonary capillary wedge pressure &gt;18 mm Hg or a cardiac output &lt;2.2 L/min per m²</td>
</tr>
</tbody>
</table>

| Criterion 2: Need for additional/increased HF therapy, including at least 1 of the following: |
| Therapy initiation or significant augmentation in oral therapies for HF, including diuretics, ACE-I/ARB, vasodilators, or ARBs |
| Initiation of intravenous diuretic, inotrope, or vasodilator therapy |
| Uptitration of intravenous therapies (diuretics, inotropes, vasodilators), if already treated with these therapies |
| Initiation of mechanical or surgical intervention, or the use of ultrafiltration, hemofiltration, or dialysis that is specifically directed at treatment of HF |

<table>
<thead>
<tr>
<th>HF after hospital discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>New-onset dyspnea, persisting &gt; 24 hours, accompanied by at least 1 of the following criteria:</td>
</tr>
<tr>
<td>Criterion 1: Outpatient need for additional/increased therapy for HF at 30 days</td>
</tr>
<tr>
<td>Initiation or significant upward dose titration of oral therapies for HF, including diuretics, ACE-I/ARB, vasodilators, or ARBs</td>
</tr>
<tr>
<td>Initiation of intravenous diuretic, inotrope, or vasodilator therapy</td>
</tr>
<tr>
<td>Initiation of mechanical or surgical intervention, or the use of ultrafiltration, hemofiltration, or dialysis that is specifically directed for the treatment of HF</td>
</tr>
</tbody>
</table>

| Criterion 2: Physical signs of HF within 30 days, including at least 2 of the following: |
| Edema (> 2+ lower extremity) |
| Pulmonary crackles/rales greater than basilar |
| Jugular venous distention |
| Tachypnea (respiratory rate >20 bpm) |
| Rapid weight gain |
| S3 gallop |
| Increasing abdominal distension or ascites |
| Hepatocutaneous reflex |
| Radiological evidence of worsening HF |
| A right heart catheterization showing a pulmonary capillary wedge pressure >18 mm Hg or a cardiac output <2.2 L/min per m² |

STEMI indicates ST-segment elevation myocardial infarction; ACE-I, angiotensin-converting enzyme inhibitor; HF, heart failure; and ARB, angiotensin receptor blocker.

Drawing from previous STEMI trials, such as APEX-AMI, we propose that HF events be ascertained only after the first 24 hours during the index STEMI hospitalization to minimize confounding from other treatment strategies specific to STEMI care. We propose that ascertainment for HF events extend well beyond the index hospitalization to reflect the full extent of the downstream morbidity post-STEMI. Ascertainment of HF events should extend to at least 30 days after discharge from the index event, allowing trials to assess the impact of a novel STEMI therapy on the hospital metric of 30-day readmission rates.

Such a composite definition could be integrated into a composite end point that accurately reflects competing risks. Comprehensively capturing morbidity and mortality will also align the objectives of a trial with outcomes important to patients. To do so, more reliable ascertainment of subjective components, such as in-hospital physical signs of HF, is needed.

In addition, consensus among various stakeholders, such as academia, industry, and patients, is needed on other components, such as what constitutes significant titration of HF therapies.

**Conclusions**

The mortality rates for STEMI patients will likely continue to decline through more widespread and timely use of primary PCI and through the broad use of evidence-based secondary prevention therapies. Thus, a new approach needs to be developed, with particular attention paid to reducing the incidence of postinfarction HF, a typical complication seen among STEMI patients. As an initial step, we propose the development of a consistent, multiple-component HF end point definition that is relevant for post-STEMI patients and that can be used in future STEMI trials. A standardized HF end point for STEMI trials
should include both in-hospital events and postdischarge events to fully assess the impact of HF as a time-dependent covariate. To chart a path forward, stakeholders must generate consensus on how to define and how to ascertain individual components within a composite definition of HF. Through ongoing collaborative efforts, a relevant, consistent, and uniform HF end point definition can be refined to contribute to the comprehensive evaluation of promising new treatments for STEMI patients.

Acknowledgments
We thank Erin LoFrese for editorial contributions. She did not receive compensation for her assistance, apart from her employment at the institution where the study was conducted.

Sources of Funding
This work was supported by an award from the American Heart Association Pharmaceutical Roundtable and David and Stevie Spina. Dr Eapen received funding from an American Heart Association Pharmaceutical Roundtable outcomes training grant (0875142N).

Disclosures
Dr Tang reports research funding from Abbott Laboratories, and consulting or honoraria from Medtronic, St. Jude Medical. Dr Felker reports research funding from NHLBI, Amgen, Otsuka, and consulting or honoraria from NHLBI, Amgen, Otsuka, BG Medicine, Critical Diagnostics, Roche Diagnostics, Johnson & Johnson; and consulting or honoraria from NHLBI, Amgen, Otsuka, BG Medicine, Critical Diagnostics, Roche Diagnostics, Johnson & Johnson, Medpace, Novartis, Geron. Dr Hernandez reports research funding from Johnson & Johnson, Proventys, Amylin; and consulting or honoraria from NHLBI, Amgen, Otsuka, BG Medicine, Critical Diagnostics, Roche Diagnostics, Johnson & Johnson, Medpace, Novartis, Geron. Dr Eapen received funding from an American Heart Association Pharmaceutical Roundtable and David and Stevie Spina. Dr Tang reports research funding from Abbott Laboratories, and consulting or honoraria from Medtronic, St. Jude Medical. Dr Eapen received funding from an American Heart Association Pharmaceutical Roundtable outcomes training grant (0875142N).

References


Defining Heart Failure End Points in ST-Segment Elevation Myocardial Infarction Trials: Integrating Past Experiences to Chart a Path Forward

Circ Cardiovasc Qual Outcomes. 2012;5:594-600
doi: 10.1161/CIRCOUTCOMES.112.966150
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/5/4/594

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/