Heart Failure

Acute Heart Failure Syndromes in Patients With Coronary Artery Disease
Early Assessment and Treatment

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Acute heart failure syndromes (AHFS) have emerged as a leading public health problem worldwide, accounting for a substantial number of hospitalizations and a high utilization of resources. Although in-hospital mortality rates are relatively low, patients with AHFS have very high early after-discharge mortality and rehospitalization rates. The majority of patients admitted with AHFS have coronary artery disease (CAD), which independently has an adverse impact on prognosis. The initial in-hospital and after-discharge management of AHFS may be dependent on clinical presentation: AHFS in patients with underlying CAD or acute coronary syndromes (ACS) complicated by heart failure. In addition, the extent and severity of CAD and the presence of ischemia and/or stunned/hibernating myocardium should be assessed for optimal management. Although the overall management of AHFS with CAD may be similar to that in patients with ACS complicated by heart failure, for which specific guidelines exist, management of the former is less well defined. Prospective studies of the assessment and treatment of CAD in patients with AHFS are urgently needed. (J Am Coll Cardiol 2009;53:254–63) © 2009 by the American College of Cardiology Foundation

Acute heart failure syndromes (AHFS) can be defined as a rapid or gradual change in signs and symptoms in patients with chronic heart failure (HF) or new-onset HF that necessitates urgent therapy (1). Acute HF syndromes are a leading and increasingly common cause of hospitalization worldwide. Despite considerable expenditures and intensive investigational efforts, hospitalization for AHFS continues to be associated with a poor prognosis (2–5). The mortality rate after hospitalization for AHFS has been reported to be

as high as 15% and 35% at 30 days and 1 year, respectively, in patients already receiving pharmacologic therapy (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and beta-blockers) (4,5).

AHFS represent a heterogeneous group of patients in terms of their clinical presentation, pathophysiology, prognosis, and therapeutic options (1). The majority of patients presenting with AHFS have coronary artery disease (CAD). These patients may present in 1 of 2 ways: acute coronary syndromes (ACS) complicated by HF or AHFS with underlying CAD. The role of CAD in AHFS has not been well studied in clinical trials. Therapies that have shown to significantly improve morbidity and mortality, including pharmacologic and device therapies, have been studied in patients with chronic ambulatory HF with or without CAD. Given the severity of hemodynamic and neurohormonal activation in acute versus chronic HF, assessing for the presence, extent, and severity of CAD in patients with AHFS may have important therapeutic implications for the initial (emergency department), in-hospital, and after-discharge management.

The cornerstone of the evaluation of CAD in ACS is coronary angiography. The evaluation of CAD in AHFS with coronary angiography, often in conjunction with noninvasive functional imaging to detect ischemic or dysfunctional but viable myocardium, may represent an emerging approach to the assessment and management of AHFS patients. Current practice guidelines (6–11) have considerable overlap with respect to patients with HF. Although these guidelines provide recommendations on the use of coronary angiography for more appropriate use of pharmacological and/or myocardial revascularization in patients with chronic HF, they do not specifically address the timing and selection for these measures in patients with AHFS and CAD (6–11).

This document represents a consensus summary of discussions that occurred during the fourth International Acute Heart Failure Syndromes Working Group meeting in Chicago, Illinois, in April 2007.

AHFS

Epidemiology. AHFS account for more than 1 million hospitalizations per year in the U.S. and a similar number in Europe (12). They are the most common cardiovascular cause of hospitalization in the U.S., with a median stay of 3 to 4 days (1). AHFS is also the most common overall cause of hospitalization in adults 65 years and older, accounting for more than 5% to 10% of all admissions (13). Approximately 80% of patients hospitalized with AHFS carry a previous diagnosis of HF. In 15% of patients the diagnosis of HF is new, and the remaining 5% are admitted with advanced or refractory HF (1). The highest relative risk for mortality occurs within 30 to 60 days after discharge (1,2). The total direct and indirect health care costs of HF in the U.S. for 2006 have been estimated to be $29.6 billion, with

the great majority of costs attributable to hospitalization (14). As the burden of AHFS increases with the aging population, the importance of evidence-based strategies to prevent HF exacerbations, decrease hospitalizations, contain costs, and improve outcomes has become an urgent public health issue.

Prognosis. The long-term prognosis for chronic HF patients with left ventricular (LV) systolic dysfunction has improved over the past 10 to 20 years, largely because of improved pharmacological therapy, advanced cardiovascular surgical and interventional techniques, and the use of implantable cardiac-defibrillators and cardiac resynchronization therapy (15,16). Despite these advances, hospitalization for HF is one of the most important predictors for rehospitalization and mortality (2–5). In several recent large registries (17–19), AHFS had a 4% to 7% in-hospital mortality rate. Survivors of hospitalization with AHFS have an early after-discharge mortality as high as 10% to 15% and rehospitalization rates of 30% at 60 to 90 days. One-year mortality rates in community cohorts and registries have ranged from 30% to 40% (4,5). Randomized controlled trials investigating the role of novel intravenous vasoactive compounds and the routine use of pulmonary artery catheters in the management of AHFS have failed to demonstrate improved survival or decreased length of hospitalization (20–25). In addition, serious concerns regarding the safety of intravenous vasoactive compounds in the setting of AHFS, especially in those patients with pre-existing CAD, have been raised (22,23,26). The traditional targets for therapy in AHFS are congestion and/or low cardiac output. Although interventions that improve hemodynamics are important for the alleviation of the signs and symptoms of HF, they may not prevent myocardial or renal injuries, which are often present in AHFS. As a consequence, these interventions may not only be ineffective in improving clinical outcomes but may even be deleterious (26–28).

Ventricular function. Although the majority of trials in AHFS conducted to date (19,29–35) studied patients with reduced systolic function, relatively preserved systolic function is present in approximately one-half of all patients hospitalized with AHFS. Approximately 60% of these patients have documented CAD (32). Over the past 20 years, the relative proportion of patients with AHFS and preserved systolic function has steadily risen relative to those with LV systolic dysfunction (29). This rise has corresponded with increased rates of CAD, hypertension, diabetes, and atrial fibrillation among patients with AHFS (36). Multiple registries have

Abbreviations and Acronyms

ACS = acute coronary syndrome(s)

AHFS = acute heart failure syndrome(s)

CABG = coronary artery bypass graft

CAD = coronary artery disease

CTA = computed tomography angiography

HF = heart failure

LV = left ventricular

MI = myocardial infarction

MRI = magnetic resonance imaging

demonstrated that the risk of early death and long-term risk of death or rehospitalization in AHFS is similar for patients with preserved systolic function and LV systolic dysfunction (29,32–34). In the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry (30), the risk of in-hospital death in patients with AHFS and preserved systolic function was slightly lower than in those with AHFS and LV systolic dysfunction (2.9% vs. 3.9%). However, among survivors of the index hospitalization, the risk of death (~10%) and rehospitalization (~30%) in the first 60 to 90 days after hospital discharge was the same in the 2 groups (30). These patients, however, are more likely to die from other cardiac comorbidities, including CAD, rather than HF (37,38).

AHFS and CAD

Hospitalization. Coronary artery disease has emerged as the dominant etiologic factor in patients with HF. Pooling data from 24 multicenter trials of chronic HF over the past 20 years with >43,000 patients (1,36) revealed that 62% carried a diagnosis of CAD. This number is an underestimation of the prevalence of CAD in this population, as in clinical practice and in most studies there is no systemic assessment of coronary artery anatomy. Patients hospitalized with AHFS have a worse prognosis when they also carry a diagnosis of CAD (39). Long-term survival in patients with HF is directly related to the angiographic burden of CAD, although this observation may reflect only the extent of CAD in the epicardial vessels (40,41). Survivors of acute myocardial infarction (MI) not complicated by HF have a relatively high incidence of subsequent HF hospitalization, which is associated with significantly increased mortality (42).

In a study of 136 patients younger than 75 years of age hospitalized with incident HF, Fox et al. (43) combined clinical, angiographic, and myocardial perfusion imaging data to determine that CAD was the primary etiology in at least 52% of cases. Of note, in this study, 67% of patients who underwent angiography had anatomically significant CAD (defined as ≥50% luminal stenosis), identifying CAD as a therapeutic target in AHFS even when it was not the primary etiologic factor. From the OPTIMIZE-HF registry of AHFS patients, in which less than one-half had known CAD, Fonarow et al. (44) identified ischemia as the primary precipitant for hospitalization in 15% of patients. These patients had significantly worse in-hospital and 60- to 90-day after-discharge mortality. Although these data indicate that CAD may cause or precipitate AHFS, the contribution of CAD to clinical decompensation can be difficult to determine when multiple comorbid conditions are present.

After-discharge events. There is no single explanation for the high mortality and rehospitalization rates in patients who survive hospitalization for AHFS. It is possible that CAD is an important contributor to this high after-discharge event rate. An autopsy study of 180 patients with

Table 1	Characteristics of Patients With AHFS and CAD Versus Patients With ACS Complicated by HF	
	AHFS and CAD	**ACS Complicated by HF**
Dyspnea	Common	Common
Chest discomfort	Uncommon	Common
Prior HF	Common	Uncommon
BNP/N-terminal proBNP	Elevated	Elevated
Troponin	Normal or elevated*	Usually elevated
Left ventricular systolic function	Normal or depressed	Normal or depressed
Diagnostic testing for CAD† (ischemia/viability/ angiography)	Uncommon	Standard (per guidelines)
Myocardial revascularization	Uncommon†	Standard (per guidelines)
Secondary prevention for CAD	Underused	Standard (per guidelines)
In-hospital mortality	Relatively low	Relatively high
Early after-discharge death or rehospitalization	High	High

*Typically low-level elevation. †During index hospitalization.

ACS = acute coronary syndrome; AHFS = acute heart failure syndrome; BNP = B-type natriuretic peptide; CAD = coronary artery disease; HF = heart failure.

known ischemic cardiomyopathy (45) revealed that acute MI was responsible for 57% of the deaths. This study revealed that many deaths due to acute MI in patients with HF were misclassified as due to progressive HF or arrhythmias. In the ATLAS (Assessment of Treatment with Lisinopril and Survival) study (46), 54% of patients with chronic HF and CAD who died suddenly had autopsy evidence of acute MI.

In a group of patients with HF and LV systolic dysfunction, 25% of repeat hospitalizations were attributed to ACS (47). Approximately 10% of patients subsequently hospitalized for ACS were originally classified as nonischemic. The in-hospital mortality rate in this group was 36%. These data suggest that patients with AHFS can be mislabeled as nonischemic or that CAD may either develop or progress in patients with nonischemic cardiomyopathies (48).

Pathophysiology: AHFS and CAD

The majority of patients with AHFS and CAD are not hospitalized or diagnosed with ACS. There are, however, considerable similarities between non-ACS AHFS patients and ACS patients complicated by HF (Table 1). In contrast with ACS complicated by HF, where myocardial injury is the principal cause for HF, the myocardial injury in AHFS in patients with underlying CAD may be related to worsening HF. The injury may be the result of marked hemodynamic and neurohormonal abnormalities known to occur in the setting of AHFS but less likely to be present in chronic HF. In AHFS, the high LV diastolic pressure often results in subendocardial ischemia, which is associated with further activation of neurohormones. This activation can increase cardiac contractility and reduce coronary perfusion through endothelial dysfunction. In addition, patients with AHFS and CAD often have hibernating or stunned myo-

cardium (28). Together, all of these factors may result in myocardial injury (1).

Hypotension in AHFS patients is associated with increased mortality (49). Coronary perfusion may be further impaired in AHFS in the setting of low systemic blood pressure. In this setting, the autoregulation between coronary artery perfusion pressure and coronary vasoactive tone may be lost or impaired in patients with obstructive epicardial CAD (28). This may explain why patients with AHFS and CAD frequently have troponin elevation. These troponin elevations most likely represent myocardial injury and are associated with worse outcomes (50–55). In the PRESERVED-HF (Pilot Randomized Study of Nesiritide Versus Dobutamine in Heart Failure) trial, 74% of non-ACS patients with AHFS and known CAD had low-level troponin elevation at the time of hospital admission (54). Of the 26% who did not initially have troponin elevation, 42% had troponin elevation within 72 h (for a total of 85% of all patients within 72 h of admission). Data from ADHERE (Acute Decompensated Heart Failure National Registry) (55) indicate that patients admitted with AHFS not thought to have ACS but with troponin elevations that exceed the laboratory threshold for acute MI have significantly higher in-hospital mortality (8.0% vs. 2.7%, $p < 0.001$).

It appears that a history of myocardial revascularization in patients with AHFS is associated with improved outcomes (53,56). The lack of typical angina despite myocardial injury in AHFS patients may be due to the predominance of respiratory symptoms; the high incidence of diabetes; and the use of medications, including nitrates and beta-blockers, that may blunt angina. When it does occur, chest pain in AHFS patients is often a sign of myocardial injury. In one study (57), 32% of patients with chronic HF presenting to the emergency department with chest pain were diagnosed with ACS.

Pathophysiology: ACS Complicated by HF

Approximately 10% to 20% of patients with ACS have concomitant HF, and up to 10% of ACS patients develop HF during hospitalization (58–63). In the EuroHeart Survey II on HF (64), 37% of patients had de novo HF, 42% of which was attributable to ACS. Patients with ACS and ST-segment elevation typically have high levels of cardiac biomarker elevation, corresponding to high levels of myocardial injury. Of ACS patients with HF but without ST-segment elevation, more than two-thirds have significant cardiac enzyme elevation (troponin >3 times the upper limit of normal), a proportion similar to those presenting without HF (52). The majority of these patients do not have a history of HF and have preserved systolic function (58,60). The short-term risk of adverse clinical outcomes in patients with ACS complicated by HF is directly proportional to the level of troponin elevation (65).

Patients with ACS complicated by HF have markedly increased short- and long-term mortality rates compared with those without HF (58–60,66–73). Patients who develop HF after presentation have even higher mortality than those presenting with ACS and HF (59,63). The prognosis of ACS complicated by HF is directly related to the degree of HF as measured by the Killip classification (59,61,63). Compared with those with Killip class I HF, patients with an ACS in Killip class II or III HF are 4 times more likely to die during the index hospitalization, whereas those with cardiogenic shock (class IV) have a 10-fold higher mortality (60,63). Furthermore, among ACS patients who recover from transient HF, the majority develop recurrent HF (42).

Assessment of CAD in AHFS

Currently, there are no consensus statements or practice guidelines on the most appropriate timing and methods to detect or reassess CAD in patients with AHFS. Most studies have used clinical criteria, including a history of MI, angina, or myocardial revascularization, or the results of exercise testing and/or noninvasive imaging to determine which patients with AHFS have CAD. This approach may contribute to the underdiagnosis of CAD and its severity in this population.

Electrocardiography and echocardiography are the most common cardiac diagnostic tests obtained in patients with AHFS (19). Patients with LV systolic dysfunction and electrocardiographic Q waves usually have significant CAD (74). However, most patients with HF and CAD do not have Q waves, whereas those with nonischemic cardiomyopathies can have Q waves (74). Similarly, segmental wall motions identified by echocardiography are predictive of CAD, but not its extent and severity (74,75).

Coronary Angiography

Coronary angiography is the gold standard for the diagnosis and reassessment of CAD against which all other modalities are compared (41). In patients with HF, the long-term prognosis is directly related to the angiographic extent and severity of CAD (40,41). This has been demonstrated in HF patients with LV systolic dysfunction and preserved systolic function (76). A clinical strategy in the evaluation of AHFS that does not assess for the presence, extent, and severity of CAD may grossly underestimate its prevalence. Despite the existing guidelines and the high incidence of CAD in patients with AHFS, angiography is used infrequently for the assessment or reassessment of CAD (6). In 3 large AHFS registries, coronary angiography was performed in only 9% to 16% of patients during the index hospitalization (1,19). Similarly low rates of angiography have been observed in a community-practice setting for patients with newly diagnosed AHFS (77). Patients with ACS complicated by HF are less likely to undergo coronary angiography and revascularization and to receive pharmacological therapy for CAD than ACS patients without HF (62,63,73,78,79). In the OPTIMIZE-HF registry, it has been preliminarily reported (80) that performance of coro-

nary angiography during the index hospitalization for AHFS was associated with an increased utilization of aspirin, statins, and myocardial revascularization and a reduced risk of death at 60 to 90 days after discharge. This raises the hypothesis that the knowledge of the extent and severity of CAD in AHFS patients will have an important role in treatment decisions.

Multidetector coronary computed tomography angiography (CTA) has been shown to be highly accurate to determine the presence or absence of CAD in patients with HF (81). However, when CAD is present, the ability of CTA to define its extent and severity is hampered by unseen segments and artifacts caused by motion and calcium (82). This role of coronary CTA in this population may be an important focus of future investigations, but currently cannot be recommended in lieu of coronary angiography at this time.

Myocardial Ischemia

In patients with AHFS and evidence of ischemia, the diagnosis of obstructive CAD by angiography should lead to the consideration of early myocardial revascularization and aggressive medical therapy with antiplatelet agents and statins in addition to beta-blockers and ACE inhibitors/angiotensin receptor blockers. In the absence of clinical signs of ischemia, additional testing may be needed to guide therapeutic choices (83). Dobutamine stress echocardiography detects ischemia through the induction of new or exaggerated LV wall motion abnormalities during stepwise infusion of dobutamine. Nuclear perfusion imaging with single-photon emission computed tomography uses intravenously delivered radioisotopes (thallium-201 chloride or technetium-99m labeled tracers); regions with defects following stress that normalize at rest are indicative of ischemia. More recently, positron emission tomography has also been used to assess ischemia, employing tracers such as rubidium-82, N13-ammonia, or O15-labeled water. Vasodilator stress magnetic resonance imaging (MRI) is a newer noninvasive stress imaging modality that has not yet been studied in HF patients for the assessment of ischemia (84).

Myocardial Viability

The presence of viable but dysfunctional myocardium can be used to predict a favorable response to myocardial revascularization and pharmacological therapy (85–87). Left ventricular systolic dysfunction can be secondary to repetitive stunning or hibernation. In this setting, stunning is defined as reversible LV dysfunction attributable to repetitive episodes of ischemia, whereas hibernating myocardium is defined as reversible LV dysfunction caused by chronic hypoperfusion (88). Up to 50% of patients with CAD and chronic LV dysfunction have significant areas of dysfunctional but viable myocardium (89). Hibernating myocardium is associated with global alterations in LV volumes and shape, not just impairment of underperfused ventricular segments (88). This explains why myocardial revasculariza-

tion of hibernating territories can promote reverse remodeling globally (90).

The identification of viable myocardium is based on detection of its characteristics, which include intact perfusion, cell membrane integrity, intact mitochondria, preserved glucose metabolism and contractile reserve (85,88,91,92). Intact perfusion, cell membrane integrity, and intact mitochondria can be evaluated with single-photon emission computed tomography imaging using thallium-201 chloride and/or technetium-99m labeled tracers. Preserved glucose metabolism can be assessed by positron emission tomography using F18-fluorodeoxyglucose. Contractile reserve can be unmasked by infusion of low-dose dobutamine during echocardiography. The use of these techniques has been associated with improved survival in patients with chronic HF and significant viability who underwent myocardial revascularization (85,88,91,92).

Cardiac MRI is another technique to assess myocardial viability (93,94). Resting cine MRI can be used to assess LV end-diastolic wall thickness. It has been shown that an end-diastolic wall thickness <5 to 6 mm is a marker of transmural MI and virtually excludes the presence of viable myocardium. In dysfunctional myocardium with preserved end-diastolic wall thickness (≥6 mm), detection of contractile reserve during low-dose dobutamine infusion confirms the presence of viable myocardium. Gadolinium-based contrast agents have been used to detect nonviable myocardium, as these agents accumulate selectively in areas of scar tissue. It should be noted that this technique is extremely sensitive to detect scar tissue (with very high spatial resolution), but the absence of scar tissue does not permit discrimination between normal tissue and hibernating or stunned myocardium (93).

Treatment of CAD in AHFS

Pharmacologic therapy. The presence of CAD in patients with AHFS may have a profound impact on treatment. Considering the overlap in pathophysiology, including increased platelet reactivity, myocardial ischemia and injury,

Table 2	Therapies for AHFS and CAD Versus ACS Complicated by HF	
	AHFS and CAD	**ACS Complicated by HF**
Immediate therapies		
Nitrates	Yes	Yes
Antiplatelet agents	Yes	Yes
Anticoagulation	No	Yes
Inotropes	Avoid if possible	Avoid if possible
Statins	Yes	Yes
Renin-angiotensin system modulation		
ACE-I or ARB	Yes	Yes
Aldosterone blockade (if LVSD)	Yes	Yes
Beta-blockers	Yes	Yes
Early angiography/revascularization	Yes*	Yes*

*If jeopardized myocardium present (ischemia or viability).

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; LVSD = left ventricular systolic dysfunction; other abbreviations as in Table 1.

impaired coronary perfusion, and elevated LV filling pressure, the treatment approach for AHFS with CAD can be modeled after the standard approach for ACS (Tables 1 and 2). This may include the early administration of antiplatelet therapy in AHFS patients with known CAD or suspected ischemia (95).

The immediate management of AHFS usually occurs in the emergency department. In patients with underlying CAD who are not hypotensive, nitrates may be the ideal initial agents. Nitrates provide rapid reduction of myocardial ischemia and can improve coronary perfusion. In patients with severe pulmonary edema, the combination of high-dose nitrates and low-dose diuretics (vs. low-dose nitrates and high-dose diuretics) led to a decreased need for mechanical ventilation and significantly lower rates of MI (96). A regimen consisting of lower doses of diuretics has been proposed as a method of preserving renal function in AHFS. In a large AHFS registry, the use of intravenous nitroglycerin or nesiritide was associated with lower in-hospital mortality compared with treatment with dobutamine or milrinone (97). However, compared to intravenous nesiritide in AHFS patients (>60% with documented CAD), intravenous nitroglycerin has been associated with less deterioration of renal function and a trend toward less mortality at 30 days (23,98,99).

Inotropes may be particularly harmful when used in patients with AHFS and CAD. Experimentally, the use of dobutamine in a model of HF with hibernating myocardium led to increased myocardial necrosis (27). Patients with AHFS and troponin elevation have significantly higher in-hospital mortality when inotropes are used (55). In the OPTIME-CHF (Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure) trial (26), the phosphodiesterase inhibitor milrinone was assessed during AHFS. In patients with CAD, milrinone was associated with increased after-discharge mortality compared with placebo. In general, a decrease in coronary perfusion as a result of a decrease in blood pressure and/or an increase in heart rate, often resulting from inotropes with vasodilator properties or inotropes used in conjunction with vasodilators, may be particularly deleterious in patients with AHFS and CAD (26,100).

The pre-discharge initiation of optimal medical therapy for HF, including beta-blockers and ACE inhibitors or angiotensin receptor blockers, is associated with improved medication adherence and an early survival advantage (80,101–103). The continuation of beta-blocker therapy in patients hospitalized with AHFS is associated with lower after-discharge mortality risk (104). Also, the addition of the aldosterone blocker eplerenone to optimal medical therapy in ACS patients complicated by HF and LV systolic dysfunction was shown (105) to significantly reduce overall mortality, sudden cardiac death, and rehospitalization.

Medical regimens for CAD can differ according to HF status. Acute coronary syndrome patients complicated by HF are less likely to receive antiplatelet agents, beta-blockers, ACE inhibitors, or statins than are ACS patients without HF (42,58,60,62,63). In the OPTIMIZE-HF registry (106), only 14,904 of 38,066 (39.2%) AHFS patients with documented CAD, hyperlipidemia, diabetes, or other atherosclerotic vascular disease were treated with statins.

Myocardial revascularization. The American College of Cardiology/American Heart Association and European Society of Cardiology practice guidelines for coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention do not specifically address patients with CAD and AHFS (9–11). Revascularization may improve outcomes in patient with HF and dysfunctional but viable myocardium. In a meta-analysis of >3,000 patients with LV systolic dysfunction, revascularization was associated with markedly decreased yearly mortality (3.2% vs. 16.0%, p < 0.0001) if viability was present (85). In patients without hibernating myocardium, revascularization did not improve survival. Recently, a retrospective observational study (107) examined the role of myocardial revascularization in ~4,000 patients with chronic HF. At 1 year, patients who underwent revascularization had substantially reduced mortality (11.8% vs. 21.6%, hazard ratio: 0.52, 95% confidence interval: 0.47 to 0.58). The survival curves continued to diverge through 7 years of follow-up. This data is limited by its restrospective nature. However, the ongoing prospective randomized STICH (Surgical Treatment for Ischemic Heart Failure) trial may help elucidate the role of revascularization in chronic heart failure patients with CAD and LV systolic dysfunction (36).

Revascularization is rarely performed during hospitalization for AHFS. In 3 large AHFS registries that included approximately 170,000 patients, only 2% to 4% of patients underwent coronary artery bypass graft surgery or percutaneous coronary intervention (1,14,108). Outcomes in patients with AHFS in the setting of ACS are improved by a strategy of early revascularization (109). Patients hospitalized with AHFS have improved early survival if they have a history of myocardial revascularization, although this is a retrospective finding (53,56). These data generate the hypothesis that early revascularization will be beneficial in AHFS patients with ischemia due to CAD. This hypothesis remains to be tested in a prospective randomized study of early myocardial revascularization in non-ACS patients with AHFS and CAD.

A strategy of early angiography and revascularization, where appropriate, in AHFS must take into account the potential risks and costs. The risk of vascular complications and contrast-induced nephropathy has steadily declined in recent years owing to technical and preventative advancements (110,111). The cost-effectiveness of such a strategy will probably depend most on its impact, if any, on rehospitalization rates. The use of coronary angiography during hospitalization for AHFS is associated with a decreased risk of early rehospitalization (80), but this also needs to be prospectively studied. A formal strategy to detect or reassess the extent and severity of CAD in patients
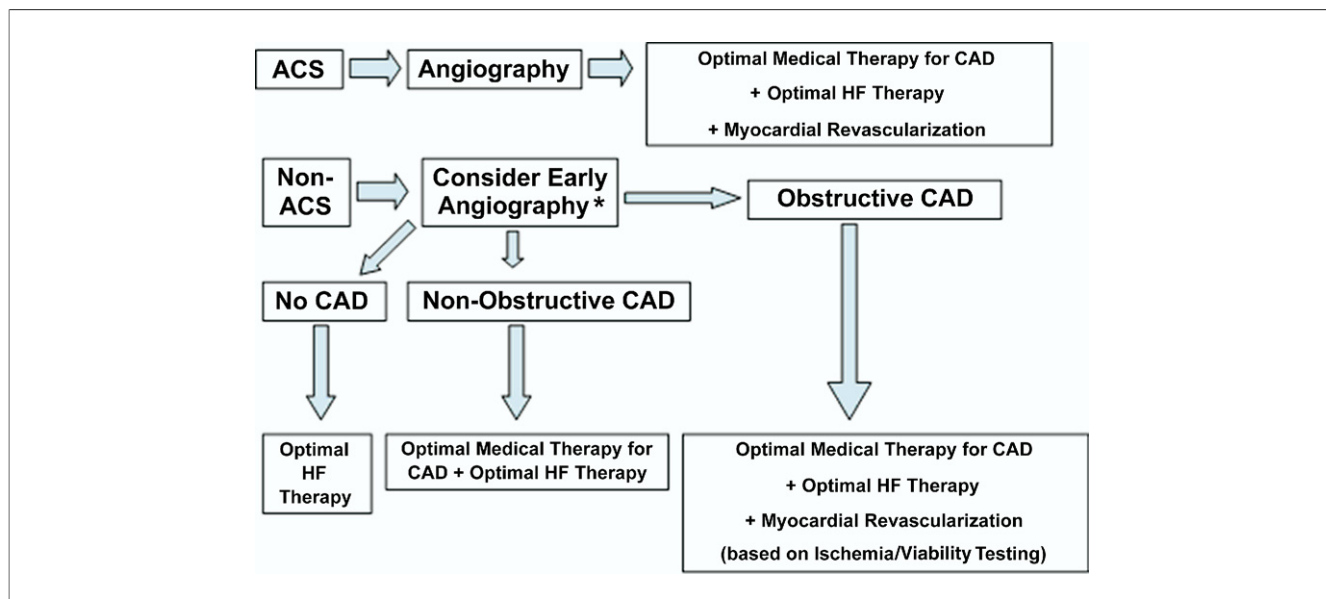
Figure 1   **Therapeutic Strategies in Patients With AHFS**

*For those patients with remote or no history of coronary angiography. ACS = acute coronary syndrome; CAD = coronary artery disease; HF = heart failure.

with AHFS may improve the implementation of evidence-based therapies that can improve clinical outcomes (Fig. 1).

Conclusions

AHFS have emerged as a leading public health problem worldwide, accounting for a substantial number of hospitalizations and a high utilization of resources. A significant number of patients admitted with AHFS have CAD and can be divided into those who present with or without ACS. Both groups have high early after-discharge mortality and rehospitalization rates. Knowledge of the extent and severity of CAD and the presence of ischemic and/or stunned/hibernating myocardium may influence the initial and in-hospital management of these patients. Although specific guidelines exist for patients with ACS complicated by HF, prospective studies of the assessment and treatment of CAD in the setting of acute HF are urgently needed.

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REFERENCES

1. Gheorghiade M, Zannad F, Sopko G, et al. Acute heart failure syndromes: current state and framework for future research. Circulation 2005;112:3958–68.
2. Solomon SD, Dobson J, Pocock S, et al. Influence of nonfatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. Circulation 2007;116:1482–7.
3. Ahmed A, Allman RM, Fonarow GC, et al. Incident heart failure hospitalization and subsequent mortality in chronic heart failure: a propensity-matched study. J Cardiac Fail 2008;14:211–8.
4. Jong P, Vowinckel E, Liu PP, et al. Prognosis and determinants of survival in patients newly hospitalized for heart failure: a population-based study. Arch Intern Med 2002;162:1689–94.
5. Goldberg RJ, Ciampa J, Lessard D, et al. Long-term survival after heart failure: a contemporary population-based perspective. Arch Intern Med 2007;167:490–6.
6. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2005;46:e1–82.
7. Guidelines on the diagnosis and treatment of acute heart failure. Available at: http://www.escardio.org/. Accessed May 1, 2008.
8. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction. J Am Coll Cardiol 2007;50:e1–157.
9. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery. Summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2004;44:e213–310.
10. Smith SC Jr., Feldman TE, Hirshfeld JW, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2005;47:216–35.
11. Silber S, Albertsson P, Aviles FF, et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 2005;26:804–7.
12. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics—2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2007;115:e69–171.
13. DeFrances CJ, Podgornik MN. 2004 National Hospital Discharge Survey. Atlanta, GA: CDC, 2006.
14. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2006;113:e85–151.
15. Bardy GH, Lee KL, Mark DB, et al., for the SCD-HeFT Investigators. Amiodarone or an implantable cardiac-defibrillator for congestive heart failure. N Engl J Med 2005;352:225–37.

16. McAlister FA, Ezekowitz J, Hooton N, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction. JAMA 2007;297:2502–14.
17. Fonarow GC, Abraham WT, Albert NM, et al. Association between performance measures and clinical outcomes for patients hospitalized with heart failure. JAMA 2007;297:61–70.
18. Adams JKF, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 2005;149:209–16.
19. Cleland JGF, Swedberg K, Follath F, et al. The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe: Part 1: patient characteristics and diagnosis. Eur Heart J 2003;24:442–63.
20. The ESCAPE Investigators. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. JAMA 2005;294:1625–33.
21. Gheorghiade M, Gattis WA, O'Connor CM, et al. Effects of tolvaptan, a vasopressin antagonist, in patients hospitalized with worsening heart failure: a randomized controlled trial. JAMA 2004;291:1963–71.
22. Cuffe MS, Califf RM, Adams KF Jr., et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. JAMA 2002;287:1541–7.
23. Sackner-Bernstein J, Kowalski M, Fox M, et al. Short-term risk of death after treatment with nesiritide for decompensated heart failure. JAMA 2005;293:1900–5.
24. Konstam MA, Gheorghiade M, Burnett JC, Jr., et al. Effects of oral tolvaptan in patients hospitalized for worsening heart failure: the EVEREST outcome trial. JAMA 2007;297:1319–31.
25. Mebazaa A, Nieminen MS, Packer M, et al. Levosimendan vs. dobutamine for patients with acute decompensated heart failure: the SURVIVE randomized trial. JAMA 2007;297:1883–91.
26. Felker GM, Benza RL, Chandler AB, et al. Heart failure etiology and response to milrinone in decompensated heart failure: results from the OPTIME-CHF study. J Am Coll Cardiol 2003;41:997–1003.
27. Schultz R, Rose J, Martin C, Brodde OE, Heusch G. Development of short-term myocardial hibernation. Circulation 1993;88:684–95.
28. Beohar N, Erdogan AK, Lee DC, et al. Acute heart failure syndromes and coronary perfusion. J Am Coll Cardiol 2008;52:13–6.
29. Owan TE, Hodge DO, Herges RM, et al. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355:251–9.
30. Fonarow GC, Gattis Stough W, Abraham WT, et al. Characteristics, treatments and outcomes of patients with preserved systolic function hospitalized with heart failure: a report from OPTIMIZE-HF. J Am Coll Cardiol 2007;50:768–77.
31. Judge KW, Pawitan Y, Caldwell J, et al. Congestive heart failure symptoms in patients with preserved left ventricular systolic function: analysis of the CASS registry. J Am Coll Cardiol 1991;18:377–82.
32. Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population based study. N Engl J Med 2007;355:260–9.
33. Lenzen MJ, Scholte op Reimer WJM, Boersma E, et al. Differences between patients with preserved and a depressed left ventricular function: a report from the EuroHeart Failure Survey. Eur Heart J 2004;25:1214–20.
34. Tribouilloy C, Rusinaru D, Mahjoub H, et al. Prognosis of heart failure with preserved ejection fraction: a 5 year prospective population-based study. Eur Heart J 2008;29:339–47.
35. Siirilä-Waris K, Lassus J, Melin J, et al. Characteristics, outcomes, and predictors of 1-year mortality in patients hospitalized for acute heart failure. Eur Heart J 2006;27:3011–7.
36. Gheorghiade M, Sopko G, De Luca L, et al. Navigating the crossroads of coronary artery disease and heart failure. Circulation 2006;114:1202–13.
37. Shah SJ, Gheorghiade M. Heart failure with preserved ejection fraction. JAMA 2008;300:431–3.
38. Ahmed A, Rich MW, Fleg JL, et al. Effects of digoxin on morbidity and mortality in diastolic heart failure. Circulation 2006;114:397–403.
39. Purek L, Laule-Kilian K, Christ A, et al. Coronary artery disease and outcome in acute congestive heart failure. Heart 2006;92:598–602.

40. Felker GM, Shaw LK, O'Connor CM. A standardized definition of ischemic cardiomyopathy for use in clinical research. Circulation 2002;39:210–8.
41. Bart BA, Shaw LK, McCants BSCB Jr., et al. Clinical determinants of mortality in patients with angiographically diagnosed ischemic or nonischemic cardiomyopathy. J Am Coll Cardiol 1997;30:1002–8.
42. Torabi A, Cleland JGF, Khan NK, et al. The timing of development and subsequent clinical course of heart failure after a myocardial infarction. Eur Heart J 2008;29:859–70.
43. Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as the cause of incident heart failure in the population. Eur Heart J 2001;22:228–36.
44. Fonarow GC, Abraham WT, Albert NM, et al. Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: findings from OPTIMIZE-HF. Arch Intern Med 2008;168:847–54.
45. Orn S, Cleland JGF, Romo M, et al. Recurrent infarction causes the most deaths following myocardial infarction with left ventricular dysfunction. Am J Med 2005;118:752–8.
46. Uretsky BF, Thygesen K, Armstrong PW, et al. Acute coronary findings at autopsy in heart failure patients with sudden death: results from the Assessment of Treatment with Lisinopril and Survival (ATLAS) trial. Circulation 2000;102:611–6.
47. Cleland JGF, Thygesen K, Uretsky BF, et al. Cardiovascular critical event pathways for the progression of heart failure: a report from the ATLAS study. Eur Heart J 2001;22:1601–12.
48. Hedrich O, Jacob M, Hauptman P. Progression of coronary artery disease in non-ischemic dilated cardiomyopathy. Cor Art Dis 2004;15:291–7.
49. Gheorghiade M, Abraham WT, Albert NM, et al. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. JAMA 2006;296:2217–26.
50. Horwich TB, Patel J, MacLellan WR, et al. Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. Circulation 2003;108:833–8.
51. You JJ, Austin PC, Alter DA, et al. Relation between cardiac troponin I and mortality in acute decompensated heart failure. Am Heart J 2007;153:462–70.
52. Metra M, Nodari S, Parrinello G, et al. The role of plasma biomarkers in acute heart failure: serial changes and independent prognostic value of NT-proBNP and cardiac troponin-T. Eur J Heart Fail 2007;9:776–86.
53. Tavazzi L, Maggioni AP, Lucci D, et al. Nationwide survey on acute heart failure in cardiology ward services in Italy. Eur Heart J 2006;27:1207–15.
54. Gheorghiade M, Gattis Stough W, Adams KF Jr., et al. The Pilot Randomized Study of Nesiritide Versus Dobutamine in Heart Failure (PRESERVD-HF). Am J Cardiol 2005;96:18G–25.
55. Peacock WF, De Marco T, Fonarow GC, et al. Cardiac troponin and outcome in acute heart failure. N Engl J Med 2008;358:2117–26.
56. Rossi JS, Flaherty JD, Fonorow GC, et al. Influence of coronary artery disease and coronary revascularization status on outcomes in patients with acute heart failure syndromes: a report from OPTIMIZE-HF. Eur J Heart Fail 2008;10:1215–23.
57. Lettman NA, Sites FD, Shofer FS, Hollander JE. Congestive heart failure patients with chest pain: incidence and predictors of acute coronary syndrome. Acad Emerg Med 2002;9:903–9.
58. Roe MT, Chen AY, Riba AL, et al. Impact of congestive heart failure in patients with non–ST-segment elevation acute coronary syndromes. Am J Cardiol 2006;97:1707–12.
59. Khot UN, Jia G, Moliterno DJ, et al. Prognostic Importance of physical examination for heart failure in non–ST-elevation acute coronary syndromes: the enduring value of Killip classification. JAMA 2003;290:2174–81.
60. Steg PG, Dabbous OH, Feldman LJ, et al. Determinants and prognostic impact of heart failure complicating acute coronary syndromes: observations from the Global Registry of Acute Coronary Events (GRACE). Circulation 2004;109:494–9.
61. Di Chiara A, Fresco C, Savonitto S, et al. Epidemiology of non–ST elevation acute coronary syndromes in the Italian cardiology network: the BLITZ-2 study. Eur Heart J 2006;27:393–405.

62. Shibata MC, Collinson J, Taneja AK, et al. Long term prognosis of heart failure after acute coronary syndromes without ST elevation. Postgrad Med J 2006;82:55–9.
63. Spencer FA, Meyer TE, Gore JM, et al. Heterogeneity in the management and outcomes of patients with acute myocardial infarction complicated by heart failure: the national registry of myocardial infarction. Circulation 2002;105:2605–10.
64. Nieminen MS, Brutsaert K, Dickstein K, et al. Euroheart failure survey II: a survey on hospitalized acute heart failure patients: description of population. Eur Heart J 2006;27:2725–36.
65. Gattis WA, O'Connor CM, Hasselblad V, Adams KF, Kobrin I, Gheorghiade M. Usefulness of an elevated troponin-I in predicting clinical events in patients for acute heart failure and acute coronary syndrome (from the RITZ-4 trial). Am J Cardiol 2004;93:1436–7.
66. Emanuelsson H, Karlson BW, Herlitz J. Characteristics and prognosis of patients with acute myocardial infarction in relation to occurrence of congestive heart failure. Eur Heart J 1994;15:761–8.
67. O'Connor CM, Hathaway WR, Bates ER, et al. Clinical characteristics and long-term outcome of patients in whom congestive heart failure develops after thrombolytic therapy for acute myocardial infarction: development of a predictive model. Am Heart J 1997;133:663–73.
68. Hasdai D, Topol EJ, Kilaru R, et al. Frequency, patient characteristics, and outcomes of mild-to-moderate heart failure complicating ST-segment elevation acute myocardial infarction: lessons from 4 international fibrinolytic therapy trials. Am Heart J 2003;145:73–9.
69. Ali AS, Rybicki BA, Alam M, et al. Clinical predictors of heart failure in patients with first acute myocardial infarction. Am Heart J 1999;138:1133–9.
70. Spencer FA, Meyer TE, Goldberg RJ, et al. Twenty-year trends (1975–1995) in the incidence, in-hospital and long-term death rates associated with heart failure complicating acute myocardial infarction: a community-wide perspective. J Am Coll Cardiol 1999;34:1378–87.
71. Wu AH, Parsons L, Every NR, Bates ER, Second National Registry of Myocardial Infarction. Hospital outcomes in patients presenting with congestive heart failure complicating acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMI-2). J Am Coll Cardiol 2002;40:1389–94.
72. Segev A, Strauss BH, Tan M, et al., for the Canadian Acute Coronary Syndrome Registries Investigators. Prognostic significance of admission heart failure in patients with non–ST-elevation acute coronary syndromes. Am J Cardiol 2006;98:470–3.
73. Haim M, Battler A, Behar S, et al. Acute coronary syndromes complicated by symptomatic and asymptomatic heart failure: does current treatment comply with guidelines? Am Heart J 2004;147:859–64.
74. Whellan DJ, Tuttle RH, Velazquez EJ, et al. Predicting significant coronary artery disease in patients with left ventricular dysfunction. Am Heart J 2006;152:340–7.
75. Sawada SG, Ryan T, Segar D, et al. Distinguishing ischemic cardiomyopathy from nonischemic dilated cardiomyopathy with coronary echocardiography. J Am Coll Cardiol 1992;19:1223–8.
76. O'Connor CM, Gattis WA, Shaw L, Cuffe MS, Califf RM. Clinical characteristics and long-term outcomes of patients with heart failure and preserved systolic function. Am J Cardiol 2000;86:863–7.
77. Kurtz CE, Gerber Y, Weston SA, et al. Use of ejection fraction tests and coronary angiography in patients with heart failure. Mayo Clinic Proc 2006;81:906–13.
78. Srichai MB, Jaber WA, Prior DL, et al. Evaluating the benefits of glycoprotein IIb/IIIa inhibitors in heart failure at baseline in acute coronary syndromes. Am Heart J 2004;147:84–90.
79. Lewis EF, Velazquez EJ, Solomon SD, et al. Predictors of the first heart failure hospitalization in patients who are stable survivors of myocardial infarction complicated by pulmonary congestion and/or left ventricular dysfunction: a VALIANT study. Eur Heart J 2008;29:748–56.
80. Flaherty JD, Rossi JS, Davidson CJ, et al., for the OPTIMIZE-HF Investigators. Influence of coronary angiography on therapy utilization and survival in acute heart failure: a report from the OPTIMIZE-HF registry (abstr). Am J Cardiol 2008;102 Suppl 1:25I.
81. Andreini D, Pontone G, Pepi M, et al. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. J Am Coll Cardiol 2007;49:2044–50.
82. Shapiro MD, Butler J, Rieber J, et al. Analytic approaches to establish the diagnostic accuracy of coronary computed tomography angiography as a tool for clinical decision making. Am J Cardiol 2007;99:1122–7.
83. Schuijf JD, Shaw LJ, Wijns W, et al. Cardiac imaging in coronary artery disease: differing modalities. Heart 2005;91:1110–7.
84. Bodi V, Sanchis J, Lopez-Lereu MP, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007;50:1174–9.
85. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol 2002;39:1151–8.
86. Bello D, Shah DJ, Farah GM. Gadolinium cardiovascular magnetic resonance predicts reversible myocardial dysfunction and remodeling in patients with heart failure undergoing beta-blocker therapy. Circulation 2003;108:1945–53.
87. Seghatol FF, Shah DJ, Deluzio S, et al. Relation between contractile reserve and improvement in left ventricular function with beta-blocker therapy in patients with heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol 2004;93:854–9.
88. Bonow RO. Identification of viable myocardium. Circulation 1996;94:2674–80.
89. Al-Mohammad A, Mahy IR, Norton MY, et al. Prevalence of hibernating myocardium in patients with severely impaired ischaemic left ventricles. Heart 1998;80:559–64.
90. Carluccio E, Biagioli P, Alumni G, et al. Patients with hibernating myocardium show altered left ventricular volumes and shape, which revert after revascularization. J Am Coll Cardiol 2006;47:969–77.
91. Schinkel AF, Bax JJ, Poldermans D, et al. Hibernating myocardium: diagnosis and patient outcomes. Curr Prob Cardiol 2007;32:375–410.
92. Camici PG, Prasad SK, Rimoldi OE. Stunning, hibernation, and assessment of myocardial viability. Circulation 2008;117:103–14.
93. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.
94. Soriano CJ, Ridocci F, Estornell J, et al. Noninvasive diagnosis of coronary artery disease in patients with heart failure and systolic dysfunction of uncertain etiology using late gadolinium-enhanced cardiovascular magnetic resonance. J Am Coll Cardiol 2005;45:743–8.
95. Al-Khadra AS, Salem FDN, Rand WM, et al. Antiplatelet agents and survival: a cohort analysis from the Studies of Left Ventricular Dysfunction (SOLVD) trial. J Am Coll Cardiol 1998;31:419–25.
96. Cotter G, Metzkor E, Kaluski E, et al. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. Lancet 1998;351:389–93.
97. Abraham WT, Adams KF, Fonarow GC, et al. In-hospital mortality in patients with acute compensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure Registry (ADHERE). J Am Coll Cardiol 2005;46:57–64.
98. The VMAC Investigators. Intravenous nesiritide vs. nitroglycerin for treatment of decompensated congestive heart failure. JAMA 2002;287:1531–40.
99. Sackner-Bernstein JD, Skopicki HA, Aaronson KD. Risk of worsening renal function with nesiritide in patients with acutely decompensated heart failure. Circulation 2005;111:1487–91.
100. Elkayam U, Tasissa G, Binanay C, et al. Use and impact of inotropes and vasodilator therapy in hospitalized patients with severe heart failure. Am Heart J 2007;153:98–104.
101. Gattis WA, O'Connor CM, Gallup DS, Hasselblad V, Gheorghiade M, on behalf of the IMPACT-HF Investigators and Coordinators. Predischarge initiation of carvedilol in patients hospitalized for decompensated heart failure. J Am Coll Cardiol 2004;43:1534–41.
102. Fonarow GC, Abraham WT, Albert NM, et al., on behalf of the OPTIMIZE-HF Investigators and Coordinators. Carvedilol use at discharge in patients hospitalized for heart failure is associated with improved survival. Am Heart J 2007;153:82.e1–11.

103. Butler J, Arbogast PG, Daugherty J, Jain MK, Ray WA, Griffin MR. Outpatient utilization of angiotensin-converting enzyme inhibitors among heart failure patients after hospital discharge. J Am Coll Cardiol 2004;43:2036–43.

104. Fonarow GC, Abraham WT, Albert NM, et al., on behalf of the OPTIMIZE-HF Investigators and Coordinators. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure. J Am Coll Cardiol 2008;52:190–9.

105. Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 2003;348:1309–21.

106. Gheorghiade M, Abraham WT, Albert NM, et al. Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry. Eur Heart J 2007;28:980–8.

107. Tsuyuki RT, Shrive FM, Galbraith D, et al. Revascularization in patients with heart failure. Can Medical Assn J 2006;175:361–73.

108. Fonarow GC, Abraham WT, Albert NM, et al. Organized program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF): rationale and design. Am Heart J 2004; 148:43–51.

109. Rott D, Behar S, Leor J, et al. Effect on survival of acute myocardial infarction in Killip classes II or III patients undergoing invasive coronary procedures. Am J Cardiol 2001;88:618–23.

110. Applegate RJ, Sacrinty MT, Kutcher MA, et al. Trends in vascular complications after diagnostic cardiac catheterization and percutaneous coronary intervention via the femoral artery, 1998 to 2007. J Am Coll Cardiol Intv 2008;1:317–26.

111. McCullough PA, Adam A, Becker CR, et al., on behalf of the CIN Consensus Working Panel. Epidemiology and prognostic implications of contrast-induced nephropathy. Am J Cardiol 2006;98S:5K–13.

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