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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)

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OBJECTIVES The purpose of this study was to examine treatment and outcomes in patients admitted to the hospital with acute myocardial infarction (AMI) complicated by congestive heart failure (CHF).

BACKGROUND Although cardiogenic shock complicating AMI has been studied extensively, the hospital course of patients presenting with CHF is less well established.

METHODS The Second National Registry of Myocardial Infarction (NRMI-2) was analyzed to determine hospital outcomes for patients with ST-elevation AMI admitted with CHF (Killip classes II or III).

RESULTS Of 190,518 patients with AMI, 36,303 (19.1%) had CHF on admission. Patients presenting with CHF were older (72.6 ± 12.5 vs. 63.2 ± 13.5 years), more often female (46.8% vs. 32.1%), had longer time to hospital presentation (2.80 ± 2.6 vs. 2.50 ± 2.4 h), and had higher prevalence of anterior/septal AMI (38.8% vs. 33.3%), diabetes (33.1% vs. 19.5%), and hypertension (54.6% vs. 46.1%) (all $p < 0.0005$). Also, they had longer lengths of stay (8.1 ± 7.1 vs. 6.8 ± 5.3 days, $p < 0.00005$) and greater risk for in-hospital death (21.4% vs. 7.2%; $p < 0.0005$). Patients with CHF were less likely to receive aspirin (75.7% vs. 89.0%), heparin (74.6% vs. 91.1%), oral beta-blockers (27.0% vs. 41.7%), fibrinolytics (33.4% vs. 58.0%), or primary angioplasty (8.6% vs. 14.6%), and more likely to receive angiotensin-converting enzyme inhibitors (25.4% vs. 13.0%). Congestive heart failure on admission was one of the strongest predictors of in-hospital death (adjusted odds ratio 1.68; 95% confidence interval 1.62, 1.75).

CONCLUSIONS Patients with AMI presenting with CHF are at higher risk for adverse in-hospital outcomes. Despite this, they are less likely to be treated with reperfusion therapy and medications with proven mortality benefit. (J Am Coll Cardiol 2002;40:1389–94) © 2002 by the American College of Cardiology Foundation

Left ventricular decompensation complicating acute myocardial infarction (AMI) results in the clinical syndromes of congestive heart failure (CHF) and cardiogenic shock. Although cardiogenic shock has been the focus of several studies (1,2), little attention has been paid to CHF. This complication occurs in approximately 15% to 25% of patients with AMI (3–7) and is associated with an in-hospital mortality rate of 15% to 40% (3–6) and a one-year mortality rate of 25% to 55% (3,6,8). Several studies have described the occurrence of CHF developing after AMI (8–12), particularly in relation to treatment with fibrinolytics (11,12), whereas others have investigated the utility of using the Killip classification (13) as a prognostic indicator of survival after AMI (14–16). However, only a few studies have specifically examined the clinical outcome of patients with AMI presenting with CHF on admission (6,7,13).

The Second National Registry of Myocardial Infarction (NRMI-2) is a multicenter, community-based database of patients presenting with AMI. In this report, we analyzed the NRMI-2 population to determine the incidence and characteristics of CHF complicating AMI and to identify the predictors of hospital outcome.

METHODS

Data collection. The NRMI-2 is a prospective, observational database of consecutive patients admitted to 1,674 participating hospitals throughout the U.S. A total of 772,586 patients were enrolled from June 1994 to March 1998. All treatment decisions were made at the discretion of the treating physicians.

The data collection process used in the study and quality control features have been previously described (17). Patients were included in the registry if they had documented

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Abbreviations and Acronyms

ACE	= angiotensin-converting enzyme
AMI	= acute myocardial infarction
CCP	= Cooperative Cardiovascular Project
CHF	= congestive heart failure
CI	= confidence interval
IV	= intravenous
NRMI-2	= Second National Registry of Myocardial Infarction
OR	= odds ratio
PO	= oral
PTCA	= percutaneous transluminal coronary angioplasty

AMI by clinical, electrocardiographic, or serial enzyme level criteria before hospital discharge. Patients transferred out to a non-NRMI hospital were excluded to avoid incomplete or inconsistent data. Patients were included in the present analysis if they: 1) presented within 12 h of symptom onset; 2) had electrocardiographic evidence of AMI including ST-segment elevation or left bundle-branch block; and 3) were admitted in Killip class I, II, or III (i.e., Killip class IV excluded). Congestive heart failure was defined as Killip class II or III. In order to analyze as uniform a population of AMI patients presenting with CHF as possible, we did not include patients with non–ST-segment elevation AMI in this study.

Statistical analysis. Differences in selected characteristics between patients presenting with CHF and those without were analyzed using chi-square tests for discrete variables and two-tailed *t* tests for continuous variables. A p value <0.05 indicated statistical significance. The simultaneous effects of CHF and several potential confounding factors on hospital mortality were examined using logistic regression analysis. Using stepwise selection, we entered variables into the multivariate logistic regression model in the following order: 1) presence of CHF on admission and demographic data (age, gender, race); 2) medical history (smoking, diabetes, hypertension, history of angina, history of AMI, history of CHF, prior stroke, prior percutaneous transluminal coronary angioplasty [PTCA], and prior coronary artery bypass graft surgery); 3) presentation characteristics (anterior or septal AMI, posterior or lateral AMI, chest pain at presentation, transferred in); 4) medications within 24 h (aspirin, subcutaneous heparin, intravenous [IV] heparin, angiotensin-converting enzyme [ACE] inhibitor, oral [PO] beta-blocker, IV beta-blocker, calcium-channel blocker, fibrinolytics); and 5) primary reperfusion strategies (fibrinolysis, PTCA). Because so many variables were entered into the multivariate logistic regression model, tests for multicollinearity between variables were performed. A covariance matrix did not demonstrate significant multicollinearity, and tolerance values of all variables in a linear regression model were high, also indicating low multicollinearity. Statistical analyses were performed with SAS software, version 8.02 (SAS Institute, Cary, North Carolina).

RESULTS

Baseline characteristics. A total of 190,518 patients met inclusion criteria; 36,303 (19.1%) had CHF. Baseline patient characteristics are shown in Table 1. Of the patients with CHF, 70.6% were Killip class II and 29.4% were Killip class III. Patients with CHF were more likely to be older and female, and to have a higher prevalence of diabetes, hypertension, prior AMI, and history of CHF. They more often had an anterior or septal AMI and presented later to the hospital than those without CHF. Although there were no clinically significant differences in systolic or diastolic blood pressure, patients with CHF had higher heart rates than those without CHF.

Treatment. Patients presenting with CHF were less likely to receive aspirin, heparin, beta-blockers, and fibrinolytics but were more likely to receive ACE inhibitors and calcium-channel blockers (Table 2). Procedures performed during hospitalization are shown in Table 3. A greater proportion of patients with CHF required supportive interventions, including mechanical ventilation, pacemaker placement, and intra-aortic balloon counterpulsation. Fewer patients with CHF were treated with primary or elective PTCA or surgical revascularization.

Hospital events. As shown in Table 4, patients presenting with CHF experienced more adverse clinical outcomes, including recurrent AMI, stroke, second- or third-degree atrioventricular block, ventricular arrhythmias, cardiac rupture, and unexpected cardiac arrest. In-hospital mortality was three times higher for patients with CHF than those without CHF (21.4% vs. 7.2%; $p < 0.0005$). In addition, length of hospital stay was longer.

Multivariate analysis. The logistic regression analysis performed to assess the effect of CHF while adjusting for potential confounding factors is shown in Table 5. Congestive heart failure on admission with AMI was one of the strongest predictors of in-hospital death (adjusted odds ratio [OR] 1.68; 95% confidence interval [CI] 1.62, 1.75), in addition to anterior AMI (adjusted OR 1.85; 95% CI 1.78, 1.92) and older age (adjusted OR 1.58; 95% CI 1.55, 1.61). Treatment with aspirin, PO (but not IV) beta-blockers, and ACE inhibitors were negatively associated with in-hospital death, as was chest pain at presentation. Although risk of in-hospital death was reduced with both fibrinolytics (adjusted OR 0.91; 95% CI 0.87, 0.95) and primary PTCA (adjusted OR 0.67; 95% CI 0.63, 0.72), the latter appeared to impart a stronger survival benefit.

DISCUSSION

CHF complicating AMI. Drawn from over 1,600 hospitals nationwide, our large study population was a representative sample of patients presenting with CHF complicating AMI in the U.S. in the mid-1990s. Both the incidence of CHF (19%) and distribution of Killip class II (13.5%) and III (5.6%) were similar to those found in older randomized studies of fibrinolytic therapy (3–5). Interestingly, these

Table 1. Baseline Characteristics

Characteristic	No CHF (N = 154,215) N (%)	CHF (N = 36,303) N (%)	p Value
Age (yrs, mean ±SD)	63.2 ± 13.5	72.6 ± 12.5	*
Male	104,637 (67.9%)	19,308 (53.2%)	*
White	132,311 (89.4%)	31,287 (89.3%)	0.6
Medical history			
Smoking	56,202 (36.4%)	8,228 (22.7%)	*
Diabetes	30,134 (19.5%)	12,012 (33.1%)	*
Hypertension	71,107 (46.1%)	19,837 (54.6%)	*
Family history of CAD	52,775 (34.2%)	8,535 (23.5%)	*
History of angina	20,967 (13.6%)	7,432 (20.5%)	*
History of MI	30,488 (19.8%)	11,989 (33.0%)	*
History of CHF	7,308 (4.7%)	10,649 (29.3%)	*
Prior stroke	8,312 (5.4%)	4,253 (11.7%)	*
Prior PTCA	13,012 (8.5%)	2,716 (7.5%)	*
Prior CABG	12,659 (8.2%)	4,360 (12.0%)	*
Clinical characteristics			
Anterior or septal AMI	51,373 (33.3%)	14,099 (38.8%)	*
Posterior or lateral AMI	34,678 (22.5%)	7,601 (20.9%)	*
Killip class			
I (No CHF)	154,215 (80.9%)	—	—
II (Rales, JVD)	—	25,644 (13.5%)	
III (Pulmonary edema)	—	10,659 (5.6%)	
Chest pain at presentation	138,823 (92.4%)	26,201 (74.8%)	*
Symptom onset to 1st hospital arrival (h, mean ± SD)	2.50 ± 2.4	2.80 ± 2.6	*
Systolic blood pressure (mm Hg, mean ± SD)	141.1 ± 30.9	140.9 ± 35.0	0.3
Diastolic blood pressure (mm Hg, mean ± SD)	82.6 ± 18.0	81.4 ± 19.5	*
Heart rate (beats/min, mean ± SD)	78.7 ± 20.3	94.0 ± 27.0	*

*p values < 0.001, unless otherwise noted.

AMI = acute myocardial infarction; CABG coronary artery bypass graft surgery; CAD = coronary artery disease; CHF = congestive heart failure; JVD = jugular venous distention; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty.

rates have decreased in more recent trials (18,19), probably reflecting recruitment bias. Patients with CHF were more likely to be older and female, and have a prior history of cardiovascular and comorbid disease (6–9). Furthermore, this patient subgroup was more likely to present with high-risk AMI characteristics including anterior location (20), tachycardia (21), absence of chest pain (22), and longer period from symptom onset to hospital presentation (3).

In their landmark 1967 publication, Killip and Kimball (13) demonstrated increasing hospital mortality with greater degree of CHF severity (i.e., higher Killip class), and their classification has endured as a simple and accurate tool for early risk assessment of patients with AMI (23). Although survival for patients with CHF has improved since 1975 (9), the association between higher Killip class and poorer outcomes has not changed. In our study, Killip class II or III patients were at higher risk for adverse outcomes, including death. Furthermore, CHF on admission was one of the most powerful predictors of in-hospital mortality. In a secondary analysis of the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) trial, Lee et al. (15) found that higher Killip class, in addition to older age, lower systolic blood pressure, tachycardia, and anterior AMI accounted for 90% of the prognostic value found in baseline data.

Table 2. Medications Within 24 h

Medication	No CHF	CHF	p Value
Aspirin	137,203 (89.0%)	27,492 (75.7%)	*
Heparin			
SQ	2,168 (1.4%)	1,336 (3.7%)	*
IV	140,458 (91.1%)	27,093 (74.6%)	*
ACE inhibitors	19,982 (13.0%)	9,231 (25.4%)	*
Beta-blockers			
PO	64,271 (41.7%)	9,809 (27.0%)	*
IV	36,859 (23.9%)	5,558 (15.3%)	*
Calcium-channel blockers	16,292 (10.6%)	4,914 (13.5%)	*
Fibrinolytics	89,453 (58.0%)	12,128 (33.4%)	*

*All p values < 0.001.

ACE = angiotensin-converting enzyme; CHF = congestive heart failure; IV = intravenous; PO = oral; SQ = subcutaneous.

Table 3. Procedures

Procedure	No CHF	CHF	p Value
Echocardiography	67,260 (43.6%)	19,933 (54.9%)	*
Stress test	21,581 (14.0%)	3,398 (9.4)	*
Mechanical ventilation	22,999 (14.9%)	8,876 (24.4)	*
Pacemaker	8,211 (5.3%)	2,297 (6.3)	*
IABP	10,449 (6.8%)	3,313 (9.1)	*
Primary PTCA	22,491 (14.6%)	3,105 (8.6)	*
Elective PTCA	37,098 (24.1%)	4,070 (11.2)	*
CABG	21,010 (13.6%)	3,633 (10.0)	*

*All p values <0.001.

CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; IABP = intra-aortic balloon counterpulsation; PTCA = percutaneous transluminal coronary angioplasty.

Table 4. Hospital events

Event	No CHF	CHF	p Value
Recurrent MI	4,107 (2.7%)	1,075 (3.0%)	0.002
Stroke	2,213 (1.4%)	795 (2.2%)	*
2nd or 3rd degree AV block	7,103 (4.6%)	2,055 (5.7)	*
Sustained VT or VF	13,900 (9.0%)	4,335 (11.9%)	*
Cardiac rupture/EMD	1,584 (1.0%)	646 (1.8%)	*
Unexpected cardiac arrest	6,785 (4.4%)	2,998 (8.3%)	*
Death	11,078 (7.2%)	7,761 (21.4%)	*
Length of stay (days, mean ± SD)	6.8 ± 5.3	8.1 ± 7.1	*

*p values < 0.001, unless otherwise noted.
AV = atrioventricular; CHF = congestive heart failure; EMD = electrical-mechanical dissociation; MI = myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

Adjunctive drug therapy. Aspirin and beta-blockers have been demonstrated in randomized trials to improve survival in patients with AMI (24,25), as has ACE inhibitor therapy for patients with CHF complicating AMI (26,27). We found that AMI patients presenting with CHF are at high risk for adverse hospital outcomes, but despite their poor prognosis, they are less aggressively treated with potentially life-saving medications. In multivariate analysis, treatment with ACE inhibitor, aspirin, and PO beta-blocker therapy provided the strongest protection against in-hospital death in this high-risk population. Despite this marked benefit, 25% of these high-risk patients did not receive aspirin, and three-quarters did not receive beta-blockers or ACE inhibitors. Additionally, patients presenting with CHF were more likely to receive calcium-channel blockers, which do not have proven clinical benefit for patients with AMI and are an American College of Cardiology/American Heart Association (ACC/AHA) class III indication for patients with CHF (28). In our analysis, treatment with calcium-channel blockers had a neutral effect on hospital mortality.

Table 5. Multivariate Logistic Regression Analysis of Predictors of Hospital Death

Variable	Adjusted OR	95% CI
Anterior MI	1.85	1.78, 1.92
CHF on admission	1.68	1.62, 1.75
Age (decade)	1.58	1.55, 1.61
Posterior MI	1.57	1.46, 1.68
Transferred in	1.40	1.34, 1.47
History of stroke	1.36	1.29, 1.44
History of CABG	1.25	1.18, 1.32
Diabetes	1.21	1.17, 1.26
History of angina	1.06	1.01, 1.11
Previous MI	1.04	1.00, 1.09
History of CHF	0.92	0.88, 0.97
IV fibrinolytics	0.91	0.87, 0.95
Male	0.84	0.81, 0.87
History of PTCA	0.82	0.76, 0.88
Current smoking	0.80	0.77, 0.84
SQ heparin	0.75	0.67, 0.83
IV heparin	0.73	0.69, 0.76
Primary PTCA	0.67	0.63, 0.72
Chest pain at presentation	0.53	0.50, 0.55
ACE inhibitor	0.51	0.48, 0.53
Aspirin	0.42	0.41, 0.44
PO beta blocker	0.42	0.41, 0.44

CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; CI = confidence interval; MI = myocardial infarction; OR = odds ratio; PTCA = percutaneous transluminal coronary angioplasty; other abbreviation as in Table 2.

Easily administered medications such as aspirin, beta-blockers, and ACE inhibitors have always been underused in the treatment of patients with AMI. In 1992, only 38% of hospitalized patients with AMI were treated with beta-blockers (29). In hospitalized Medicare patients with AMI, approximately 80% received aspirin, 45% received beta-blockers, and less than 60% received ACE inhibitors, even when contraindications were absent (30). Other large studies have found similar suboptimal usage rates of these medications for patients with AMI (31,32).

The reasons behind underuse of potentially life-saving medications in our patient population are not entirely clear and are probably multifactorial. Possible contributors include care providers' overestimation of potential side effects (such as hypotension) or unawareness of current standards of care, lack of hospital protocols to ensure that treatment is consistent with evidence-based guidelines, or non-clinical factors such as patient gender and race or geographic variation that may influence treatment decisions (29,31). Although the presence of transient CHF, pulmonary edema, reduced left ventricular ejection fraction, or higher Killip class is associated with lack of beta-blocker therapy (33,34), the risk of worsening heart failure with initiation of beta-blocker therapy may be overstated. Among AMI patients with a known history of CHF, clinical heart failure was precipitated in only 15% (35), and these patients benefited from treatment with a greater reduction in absolute mortality (36,37). Even patients with severe left ventricular dysfunction demonstrate long-term mortality benefit from beta-blocker treatment (34). More recently, a large multicenter trial demonstrated a 29% risk reduction for the combined end point of all-cause mortality and non-fatal AMI in patients with left ventricular dysfunction randomized to treatment with the beta-blocker carvedilol after AMI (38). The ACE inhibitors have been an ACC/AHA class I indication for patients with CHF since 1996 (28). Further investigation of potential barriers to optimal care of patients with CHF complicating AMI is warranted.

Reperfusion therapy. This study confirmed the previous observation that patients with AMI presenting with CHF are less likely to undergo primary reperfusion, either with fibrinolysis or PTCA, than Killip class I patients (6,7). Although one small randomized study showed survival benefit after fibrinolysis in patients presenting with CHF (39), others have not (5), and it has not conclusively been shown that this subgroup of patients benefits from fibrinolysis (40). In this study, the largest report on patients with CHF complicating AMI, there was a small (9%) reduction in relative risk of mortality that was statistically significant. The failure of fibrinolytic therapy to dramatically decrease mortality in patients who present with CHF could be explained by physiologically more significant left ventricular dysfunction, lower reperfusion rates, associated mechanical

complications (such as mitral regurgitation), or completed infarction (40). We found that the risk of in-hospital mortality was reduced more by primary PTCA than by fibrinolysis. Similar favorable results have been observed with primary PTCA in cardiogenic shock (1,2,40) and in Killip class II or III patients (41), presumably due to improved infarct artery patency. DeGeare and co-workers (42) reported lower than expected in-hospital mortality rates of 2.4%, 7.0%, and 19.2% for 2,654 patients undergoing primary percutaneous coronary intervention in Killip class I, II, and III, respectively. However, further investigation is needed to clarify whether primary PTCA is superior to fibrinolytic therapy for patients with AMI complicated by CHF.

Study limitations. Although the NRMI-2 registry includes more than 1,600 hospitals throughout the U.S., participating hospitals may not be entirely representative of all hospitals in the country. Registry hospitals have been shown to be larger, more likely to be affiliated with a medical school, more likely to be certified by the Joint Commission on Accreditation of Health Care Organizations, and more likely to have facilities for cardiac catheterization and cardiac surgery than non-registry hospitals (17). However, a recent analysis found that the NRMI-2 registry compared favorably with the Cooperative Cardiovascular Project (CCP), a large national registry which employs very rigorous data collection methods, with regard to demographic, past medical, procedural, and medication use data (43).

A second limitation of our analysis is that NRMI-2 is an observational registry rather than a randomized treatment trial, and thus CHF was defined by chart-abstracted Killip class. Killip class in NRMI-2 has not been externally validated. In the recent comparison with the CCP, CHF complicating AMI during hospitalization was under-reported in NRMI-2 (43). However, if NRMI-2 also under-reported CHF on admission, any differences between patients presenting with CHF versus those without would be attenuated rather than falsely exaggerated. Also, NRMI-2 did not include data on the different mechanisms of CHF in patients with AMI, so their impact on management and outcomes cannot be determined.

Conclusion. Our study demonstrates that patients presenting with AMI complicated by CHF are at high risk for hospital mortality and adverse outcomes. Despite their increased risk, these patients are less frequently treated with medications with proven mortality benefit or with primary reperfusion strategies. Further study to determine and overcome barriers to treatment with aspirin, beta-blockers, and ACE inhibitors in this high-risk group of patients is warranted. In addition, primary PTCA appears to be associated with greater mortality benefit than fibrinolytics, a finding that merits further investigation with prospective clinical trials. Early identification of patients with CHF and aggressive targeting of this patient population for medical treatment and reperfusion therapy may reduce hospital mortality and adverse events.

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