# Improved Survival after Acute Myocardial Infarction in Patients with Advanced Killip Class

WAYNE L. MILLER, M.D., PH.D., R. SCOTT WRIGHT, M.D., JOSEPH P. GRILL, M.S., STEPHEN L. KOPECKY, M.D.

Coronary Care Unit Group, Mayo Clinic and Mayo Foundation, Division of Cardiovascular Diseases, Department of Internal Medicine, and Mayo Clinic Physician Alliance for Clinical Trials (MPACT), Rochester, Minnesota, USA

#### Summary

*Background:* The continuing applicability of the Killip classification system to the effective stratification of long-term and short-term outcome in patients with acute myocardial infarction (MI) and its influence on treatment strategy calls for reanalysis in the setting of today's primary reperfusion treatments.

*Hypothesis:* Our study sought to test the hypothesis that Killip classification, established on admission in patients with acute MI, is an effective tool for early prediction of in-hospital mortality and long-term survival.

*Methods:* A series of 909 consecutive Olmsted County patients admitted with acute MI to St. Marys Hospital, Mayo Clinic, between January 1988 and March 1998 was analyzed. Killip classification was the primary variable. Endpoints were in-hospital death, major in-hospital complications, and posthospital death.

*Results:* Patients analyzed included 714 classified as Killip I, 170 classified as Killip II/III, and 25 classified as Killip IV. Increases in in-hospital mortality and prevalence of in-hospital complications correspond significantly with advanced Killip class (p < 0.01), with in-hospital mortality 7% in class I, 17.6% in classes II/III, and 36% in class IV patients (p < 0.001). Killip classification was strongly associated with mode of therapy administered within 24 h of admission (p < 0.01). Killip IV pa-

Address for reprints:

Wayne L. Miller, M.D., Ph.D. CCU Group Division of Cardiovascular Diseases Mayo Clinic and Foundation Mayo Building, East 16 B 200 First Street SW Rochester, MN 55905, USA

Received: August 31, 1999 Accepted with revision: January 10, 2000 tients underwent primary angioplasty most commonly and were less likely to receive medical therapy.

*Conclusions:* Killip classification remains a strong independent predictor of in-hospital mortality and complications, and of long-term survival. Early primary angioplasty has contributed to a decrease in mortality in Killip IV patients, but effective adjunctive medical therapy is underutilized.

Key words: acute myocardial infarction, Killip class, reperfusion therapy, in-hospital mortality, long-term mortality

## Introduction

The Killip classification system, introduced in 1967 for clinical assessment of patients with acute myocardial infarction (MI),<sup>1</sup> stratifies individuals according to the severity of their post-MI congestive heart failure (CHF). The original report by Killip and Kimball<sup>1</sup> demonstrated an increase in in-hospital mortality corresponding with increased severity of post-MI CHF. A patient's Killip classification is defined by the following parameters: Killip class I, no CHF; Killip class II, third heart sound, rales; Killip class III, pulmonary edema; and Killip class IV, cardiogenic shock. While the observed in-hospital mortality rate in patients without CHF (Killip class I) was 6% in the Killip and Kimball study, the rate of in-hospital mortality in patients with pulmonary edema (Killip class III) was 38%, and in patients with cardiogenic shock (Killip class IV) it was 81%. The Killip classification, demonstrated in past decades to be effective in the risk stratification and prognostic evaluation of patients with acute MI,<sup>1</sup> is still used widely in the era of primary reperfusion,2-5 despite the more recent identification of other predictive indices for evaluation of acute MI.<sup>6–12</sup>

A recent report by Rott *et al.* from the Secondary Prevention Reinfarction Israeli Nifedipine Trial (SPRINT) examined the prognostic utility of Killip classification among 1,873 patients with acute MI.<sup>2</sup> The SPRINT investigators reported an in-hospital mortality rate of 3% in patients without post-MI CHF, 21% in patients with mild CHF, 35% in patients with pulmonary edema, and 60% in patients with cardiogenic shock. Although the overall mortality rate associated with acute MI is lower today than during the era of the Killip report, the observed mortality for patients with advanced Killip class, particularly class III (pulmonary edema) and class IV (cardiogenic shock), remains high.

Cardiogenic shock (Killip class IV) occurs in 5 to 15% of patients with acute MI, and reports of mortality in these patients range from 50 to 80%.<sup>13, 14</sup> Several recent reports have suggested that aggressive revascularization may reduce the mortality rate in cardiogenic shock to < 40%, <sup>15–22</sup> and this hypothesis is the subject of a randomized trial.<sup>23, 24</sup> Treatment of acute MI has improved significantly over the past three decades with the introduction of revascularization therapy,<sup>25, 26</sup> superior antiplatelet and antithrombotic agents, 27-30 and improved adjunctive medical therapy,<sup>31-34</sup> all of which have contributed to a significant reduction in observed mortality. The continuing value of the Killip classification system in providing important prognostic information in an era of aggressive revascularization and medical therapy is uncertain, since large clinical trial databases often fail to record a patient's Killip classification at the time of admission, or may exclude certain subsets of patients (such as those with cardiogenic shock). Because recent reevaluation of more complex scoring systems, including the Norris score, 12 has demonstrated the inapplicability of some scoring systems in this era because of their tendency to predict excessive mortality, the relevance in today's treatment environment of the Killip classification system needs to be evaluated. Our study was designed to test the hypothesis that a patient's Killip classification, determined at the time of admission for management of acute MI, still serves as an effective tool for early risk stratification and prediction of in-hospital and long-term mortality. A second hypothesis was that improved outcome in patients with acute MI in the era of thrombolysis and angioplasty would be reflected in changes in Killip class-related mortality.

## Methods

## **Study Group**

Included in this analysis was a series of 909 consecutive patients admitted with acute MI to St. Marys Hospital Coronary Care Unit (CCU), Mayo Medical Center from January 1, 1988, to March 31, 1998. The Mayo Clinic CCU database has prospectively collected data on patients admitted with acute MI since January 1988. Our study includes only those patient who were residents of Olmsted County, Minn., at the time of presentation and who gave informed consent for research analysis as required by Minnesota statute 144.335. Most (~95%) Olmsted County patients with acute MI are ultimately admitted to St. Marys Hospital in Rochester, where they are treated by a coronary care team. This investigation was approved by the Mayo Foundation Institutional Review Board. Each patient's diagnosis of acute MI was based upon fulfillment of World Health Organization criteria.35 Killip classification was determined and recorded at admission for each patient, as described by Killip and Kimball.1

## Endpoints

In-hospital survival was the primary endpoint. Secondary endpoints included in-hospital reinfarction, occurrence of a new complication (all patients with Killip class IV were classified as presenting with cardiogenic shock, and all Killip class II/III patients were classified as presenting with CHF), and posthospital survival. Important complications analyzed included ischemic (reinfarction, recurrent angina, development of CHF), mechanical (cardiac tamponade, ventricular freewall rupture, development of a ventricular septal defect, or rupture of a papillary muscle with severe mitral regurgitation), and electrical (cardiac arrest, electromechanical dissociation, asystole, ventricular fibrillation, ventricular tachycardia).

The cause of each in-hospital death was determined by review of the patient's chart and recorded as having resulted from sudden cardiac arrest, cardiogenic shock, reinfarction, cardiac rupture, and/or electromechanical dissociation. Patient followup data were derived from the Mayo Clinic CCU database and from administrative files (ongoing data registration) or notification of death.

## Definitions

Each patient's Killip classification was assigned on the basis of the severity of signs of heart failure at the time of hospital admission: Killip class I was defined by the absence of rales in the lung fields and the absence of an S3 heart sound; Killip class II was defined by the presence of rales in < 50% of the lung fields, or by the presence of an S3 gallop, accompanied by elevated jugular venous pressure; Killip class III was defined by the presence of rales in > 50% of the lung fields; and Killip class IV was defined as cardiogenic shock (i.e., the presence of pulmonary edema with hypotension-systolic blood pressure < 90 mmHg with or without signs of inadequate peripheral perfusion). Primary reperfusion therapy was defined as the first therapy used to restore blood flow through a coronary artery suspected or known to be occluded by means of intravenous (IV) fibrinolytic therapy, percutaneous transluminal coronary angioplasty (PTCA), or immediate coronary artery bypass graft surgery (CABG). The use of concomitant medications (IV heparin, inotropic agents, IV or oral beta blocker, aspirin, calcium-channel blocker, IV/oral/topical/sublingual nitroglycerin, or angiotensin-converting enzyme inhibitor), invasive procedures, and adverse events were recorded at the time of implementation or occurrence during hospitalization.

### Statistical Methods

Demographic and clinical characteristics of the patients studied were compared by Killip class using Pearson's chisquare test on the categorical variable and then applying the nonparametric Kruskal-Wallis test to the continuous variables. For selected dichotomous variables (in-hospital mortality and complications), the Armitage linear-trend test was used to determine positive or negative correlation (via linear trend) with Killip class. The degree of association between Killip class and each of the demographic and clinical factors included in

753

the study was assessed by log-rank test. A multivariate proportional-hazards model was fitted to the study data to assess the effect of Killip class after adjustment of demographic and clinical factors that remained significantly independent ( $p \le 0.01$ ). The Wald chi-square test by Cox proportional-hazard model and logistics-regression model were employed. All analyses were carried out using the SAS statistical package (version 6.12; Cary, N.C.).

## Results

## **Demographic/Clinical Characteristics**

A comparison of demographic and clinical characteristics by Killip classification on admission (class I vs. class II-III vs. class IV) is presented in Table I. The majority of patients (78%) were identified as Killip class I on admission, and only a minority (5% of all patients) were categorized as Killip class IV (cardiogenic shock). Killip classes II/III (CHF or pulmonary edema) included 18% of admitted patients. Gender and age showed variation between the Killip classifications, and female gender, prior MI, anterior MI location, and lower ejection fraction correlated with advanced Killip class, as shown in Table I. Left ventricular ejection fraction < 35% was significantly more prevalent in patients in Killip class IV (60% of this class) than in patients in the other classes. Mean ejection fraction was also lowest (29%) among patients in Killip class IV. Preserved left ventricular systolic function with ejection fraction > 50% was most common in Killip class I patients (64% of this class).

## **Characteristics of Patient Management**

Table II shows the primary treatment modality and medications administered within the first 24 h of admission. Statistically significant associations between Killip class and modes of primary treatment were demonstrated, including CABG, thrombolytic therapy, PTCA, and medical therapy. Primary reperfusion by CABG, thrombolysis, or PTCA was carried out in 46% of the patients studied, most commonly in Killip class IV patients (76% of this group). Coronary bypass surgery as primary treatment, although used in only 2% of the patients studied, was most common in Killip class II/III patients. Only 1% of all patients studied underwent CABG surgery as a primary means of reperfusion. Coronary artery angioplasty was used most commonly in Killip class IV (56% of patients in this class) and least commonly in Killip class II/III patients (12% of patients in this class). Of all patients studied, 23% underwent primary PTCA. Thrombolytic therapy was used in 25% of class I patients and in 20% of class IV patients, but in only 12% of patients in Killip classes II/III. Overall, approximately 22% of patients admitted with MI received thrombolytic therapy.

Higher Killip classification was significantly associated with decreased use of medical therapy. Adjuvant medical ther-

Demographic/ clinical characteristics	Killip class I $(n = 714)$		Killip class II/III (n = 170)		Killip class IV (n = 25)		р
	n	%	n	%	n	%	Value <sup><i>a</i></sup>
Gender (female)	254	35.6	87	51.2	10	40.0	0.001
Age							
<65	325	45.5	36	21.2	11	44.0	0.001
65-75	169	23.7	42	24.7	9	36.0	
>75	220	30.8	92	54.1	5	20.0	
Age							
Mean	66.2		74.8		64.7		0.001
Median	66.8		76.0		69.1		
Range							
25–75th percentile	55.4-77.3		68.7-83.0		53.4-72.4		
Hypertension	292	40.9	104	61.2	8	32.0	0.001
Diabetes mellitus	92	12.9	46	27.1	8	32.0	0.001
Smoking history	443	62.0	99	58.2	15	60.0	0.651
Family history of CAD	133	18.6	23	13.5	5	20.0	0.281
Prior MI	134	18.8	57	33.5	6	24.0	0.001
Anterior MI location	257	36.0	76	44.7	10	40.0	0.106
EF							
<35	58	11.6	43	35.2	9	60.0	0.001
35–49	124	24.8	46	37.7	5	33.3	
≥50	318	63.6	33	27.1	1	6.7	

TABLE I Comparison of demographic/clinical characteristics by Killip class (I vs. II/III vs. IV) at admission

<sup>a</sup> Testing for equal distributions using Pearson's chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables. *Abbreviations:* n = number of patients, CAD = coronary artery disease, MI = myocardial infarction, EF = ejection fraction.

Demographic/ clinical characteristics	Killip class I (n = 714)		Killip class II/III $(n = 170)$		Killip class IV $(n=25)$		р
	n	%	n	%	n	%	Value <sup><i>a</i></sup>
Primary treatment		A					
CABG	4	0.6	3	1.8	0	0.0	0.001
Lytics	178	24.9	20	11.8	5	20.0	
PTCA	174	24.4	21	12.4	14	56.0	
Meds	358	50.1	126	74.1	6	24.0	
Primary reperfusion	356	49.9	44	25.9	19	76.1	0.001
Beta blocker	500	70.0	90	52.9	11	44.0	0.001
Aspirin	586	82.1	118	69.4	14	56.0	0.001
Nitrates	617	86.4	140	82.4	14	56.0	0.001
Heparin	667	93.4	145	85.3	20	80.0	0.001
ACE inhibitor	64	9.0	45	26.5	1	4.0	0.001

TABLE II Comparison of demographic/clinical characteristics by Killip class (I vs. II/III vs. IV) at admission

<sup>a</sup> Testing for equal distribution using Pearson's chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables.

*Abbreviations:* n = number of patients, CABG = coronary artery bypass graft, PTCA = percutaneous transluminal coronary angioplasty, ACE = angiotensin-converting enzyme.

apy was used least commonly in Killip class IV patients (24%) and most commonly in class II/III patients (74%) (Fig. 1), specifically demonstrated by decreased use of beta blockers, aspirin, nitrate, and IV heparin therapy during the first 24 h of hospitalization. Intravenous heparin was the mode of medical therapy used most commonly in all three Killip groups. Nitrate use was lowest in class IV patients (56%) relative to patients in classes I and II/III, reflecting utilization rates of 80 to 85%. Only 44% of patients in Killip class IV were treated with a beta blocker, compared with 70% of patients in Killip class I. Converting enzyme inhibitors comprised the mode of medical therapy used least in all patient classes (12%); 26% of patients in Killip class I Were given this treatment. Of the Killip class I patients, 36% had presented with anterior wall MI.

#### **Endpoint Analysis**

Rates of in-hospital mortality (Fig. 2) and incidence of inhospital complications, both of which increased significantly with advanced Killip class, are presented in Table III. An inhospital mortality rate of 36% was seen in Killip class IV patients, and in-hospital complications were also significantly more prevalent in this group. A significant between-groups survival rate difference was seen in the 820 patients who lived to be discharged, but median survival between class II/III and class IV group patients was not significantly different.

Several independent variables were initially considered as possible confounding or biasing factors in the observed significant association between Killip class and each endpoint. Table IV outlines the relationship between patient Killip class groups and their in-hospital survival stratified by initial treatment. Killip class remained a powerful predictor of in-hospital survival independent of the use of primary reperfusion therapy. Indeed, the predictive value of Killip class was greatest in patients who received primary lytic therapy or primary PCTA. Age was demonstrated to be the most significant factor for inhospital mortality, and age and MI location were independent predictors of in-hospital complications. Significant predictors (requiring adjustment) of long-term survival were age, hypertension, prior infarction, and location of MI. Diabetes mellitus was not found to be an independent predictor that would re-



FIG. 1 Treatment decisions associated with Killip class. Primary reperfusion (thrombolysis and angioplasty) and medical therapy (Med Rx) significantly associated with Killip class (p < 0.001).  $\square =$  Primary reperfusion,  $\square =$  Med. Rx.

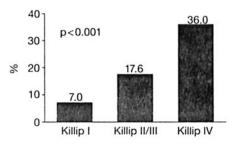


Fig. 2 In-hospital mortality associated with Killip class (p < 0.001).

	Killip class I (n=714)		Killip class II/III (n = 170)		Killip class IV (n=25)		р
Endpoints	n	%	n	%	n	%	Value <sup><i>a</i></sup>
In-hospital death	50	7.0	30	17.6	9	36.0	0.001
In-hospital complications b	189	26.5	65	38.2	18	72.0	0.001
Death following discharge	,						
N discharged alive	664		140		16		
N died as of August 1998	146		61		7		
Median survival	Not attained		4.0 years		4.5 years		
Est. % survival and 95% CI at:							0.001
1 year	93.5% (91.6, 95.4)		78.7% (72.1, 85.9)		85.9% (69.5, 100.0)		
3 years	87.1% (84.3, 89.9)		60.0% (51.5, 70.0)		75.2% (53.7, 100,0)		
5 years	78.7% (75.0, 82.6)		45.7% (3	6.0, 58.1)	45.1% (20.5, 99.5)		

TABLE III Comparisons of endpoints by Killip class (I vs. II/III vs. IV) at admission

<sup>a</sup> Armitage test for linear trend of the percentages of in-hospital deaths (complications) by Killip class and the log-rank test for comparing survival following discharge by Killip class.

<sup>b</sup> Including in-hospital death and the following in-hospital complications: mechanical (tamponade, acute VSD, papillary muscle rupture, and free wall rupture), ischemic (recurrent MI, cardiogenic shock, and CHF), electrical (cardiac arrest, EMD, and ventricular arrhythmia), and stroke. *Abbreviations:* CI = confidence interval, n = number of patients, VSD = ventricular septal defect, MI = myocardial infarction, CHF = congestive heart failure, EMD = electromechanical dissociation.

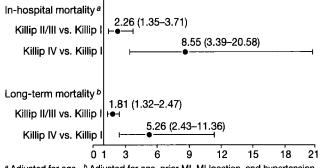
TABLE IV Comparison of Killip class (I vs. II/III vs. IV) by treatment strategy and in-hospital survival

Killip	Number of		ied ospital	Chi- square	n	
class	patients	n %		statistic <sup>a</sup>	p Value	
All patients						
I	710	50	7.0	35.28	0.001	
11/111	167	29	17.4			
IV	25	9	36.0			
Lytics patients						
Ī	178	10	5.6	20.54	0.001	
11/111	20	4	20.0			
IV	5	3	60.0			
Meds patients						
I	358	32	8.9	4.67	0.031	
II/III	126	20	15.9			
IV	6	1	16.7			
PTCA patients						
I	174	8	4.6	22.54	0.001	
П/ПІ	21	5	23.8			
IV	14	5	35.7			
Adjusting for p	rimary treatr	nent usi	ing the log	gistic model:	•	

Model -2 Log (likelihood) Primary treatment (lytics, meds, PTCA) 575.333 Primary treatment+Killip class (I,II/III,IV) 547.607 27.726 with 2 DF (p value = 0.001)

<sup>a</sup> Using the Armitage test for linear trend.

*Abbreviations:* PTCA = percutaneous transluminal coronary angioplasty, DF = degrees of freedom. quire adjustment in measuring the effect of Killip class on mortality and complication endpoints. Figure 3 illustrates the measure of relative risks after adjustment for those variables on analysis of Killip class and endpoints of in-hospital and longterm mortality. After adjustment for variables, a patient's Killip classification at admission continued to be a significant predictor of risk of both short-term and long-term survival after hospital discharge. Adjustment for long-term survival based on age, hypertension, prior MI, and MI location showed the most significant effect in Killip class IV patients relative to those in Killip class I, increasing the odds ratio from 3.4 (confidence in-



<sup>a</sup> Adjusted for age. <sup>b</sup> Adjusted for age, prior MI, MI location, and hypertension.

FIG. 3 Relative risk of short-term and long-term mortality. Adjusted variables estimating the effect of Killip class on in-hospital mortality and long-term mortality (multivariate analysis). In-hospital mortality adjusted for age and long-term mortality adjusted for age, hypertension, prior myocardial infarction (MI), and location of MI. Estimates of relative risk significant at p < 0.001.

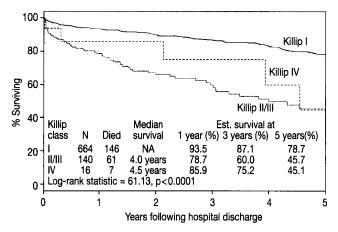


Fig. 4 Kaplan-Meier survival curves for all patients according to Killip class designation at time of admission for acute myocardial infarction. NA = not available.

terval [CI] 1.57–7.20) to 5.3 (CI 2.43–11.36). Figure 4 depicts the postdischarge survival curve analysis by Killip class. Differences in 5-year survival among patients in Killip classes I, II/III, and IV are significant (p < 0.0001). Patients in Killip class I who lived to hospital discharge demonstrated the highest long-term survival. The survival curves suggest slightly better survival in Killip class IV patients than in patients in classes II/III until Year 5. Admission in Killip class IV, however, is a significant predictor of in-hospital mortality and in-hospital complications. Hospital length of stay (LOS) also varied significantly with Killip classification (p < 0.001). Median LOS was 6 days for patients in Killip class I, 9 days for patients in Killip class II/III, and 11 days for patients in Killip class IV.

#### Discussion

From a clinical perspective, reassessment of the relevance and value of simple bedside prognostic indices such as the Killip classification is important in this era strongly influenced by advanced technology in patient assessment and management. Comparison of the prognostic utility of clinical assessment with that of technology-driven patient assessment is also important, particularly when cost containment is a consideration.<sup>12, 36, 37</sup> The Killip classification system remains attractive because of the relative simplicity of its application; it is based upon clinical findings of increasing severity of CHF in the post-MI hospital period, and it does not require the use of imaging technology or the derivation of a mathematical score.1 While Killip classification was reported during the prethrombolytic era to be a strong independent predictor of in-hospital mortality,1 its relevance in the current milieu of thrombolysis/angioplasty and improved medical therapies and patient outcomes has been questioned.<sup>2-5, 36</sup>

Accurate prediction of in-hospital mortality continues to be important for patient stratification and to ensure optimal use of therapeutic strategies.<sup>37, 38</sup> Projection of long-term outcomes and identification of patient subgroups requiring close followup are also vital in light of the demonstrated improvement in short-term outcome in patients with MI and the need for costeffective, long-term patient management.<sup>38</sup> Although the outcomes of patients with advanced Killip classification (CHF and cardiogenic shock) in the era of primary thrombolysis and angioplasty might also be expected to show improvement over patient outcomes documented at the time of the original formulation of the Killip classification,<sup>15–22</sup> such a conclusion cannot be made without appropriate trial data support.<sup>23</sup>

The results of our study indicate that Killip classification of patients at admission for acute MI continues to be a significant tool for early risk stratification and prediction of in-hospital and long-term survival. The initial report by Killip and Kimball<sup>1</sup> in 1967 describes a study of approximately 250 patients in which Killip class IV patients demonstrated a high 30-day mortality (81% in their study). Our study in the era of primary thrombolytic and angioplasty therapies reports an in-hospital mortality of 36%, which is still high but considerably lower than that reported in earlier studies. Mortality in Killip class IV patients in our study is also lower than that reported in recent studies.<sup>3,4</sup> An explanation for this improvement in early mortality is not entirely evident from this outcomes analysis, but is related in part to the relatively younger age of the Killip class IV patients (mean age 65 years) compared with Killip class II/III patients (mean age 75 years) and modes of initial therapy. Our findings would suggest that primary reperfusion by PTCA, used most extensively in Killip class IV patients, made a significant contribution to improved outcomes in these severely ill patients. Among the groups studied, Killip class IV patients were least likely to undergo aggressive adjunctive medical therapy and most likely to be treated with primary angioplasty. Hochman et al.24 reported a survival benefit at 6 months after early revascularization in acute MI complicated by cardiogenic shock when compared with medical therapy. Of the patients undergoing revascularization, 54.6% (of 152 patients) were treated by PTCA and 37.5% by CABG surgery. Age was also a factor in their study results, with early revascularization demonstrating a significant benefit in those patients <75 years of age but medical therapy shown to be better in patients > 75 years. Our findings in Killip class IV patients with a mean age of 65 years also support an improved outcome with primary revascularization therapy.

Advanced Killip class was associated with reduced use of beta blockers, converting enzyme inhibitors, and nitrate therapy, which suggests underutilization of effective medical therapy in high-risk patients with acute MI. While our results indicate a lower short-term mortality than previously reported for Killip class IV patients, the underutilization of adjunctive medical therapy in this group of patients, even with their improved outcomes, may have contributed to an excessive mortality.<sup>27-34</sup> The question therefore arises whether more aggressive adjunctive medical therapy in conjunction with primary reperfusion therapy could result in further reductions in mortality.

An additional observation in our community-based study population relates to survival after hospital discharge, where the median survival and 5-year survival rates were similar between Killip class IV and Killip classes II/III patients. Most patients in Killip class IV were male, and with a mean age of 65 years it was the youngest of the groups studied. Patients in Killip class IV, however, also had the highest incidence of diabetes mellitus (32%) and the lowest left ventricular ejection fractions (29%) among patients studied. Thus, specific factors contributing to their improved in-hospital and 5-year survival include younger age and early revascularization. However, the smaller number of patients designated as Killip class IV at admission (25) and the number surviving to follow-up also suggest a cautious approach to the interpretation of survival curve comparisons.

Patients in Killip classes II/III were more likely than Killip class IV patients to undergo primary medical therapy (74 vs. 24%) but less likely to undergo primary reperfusion therapy (26 vs. 76%), which may have contributed to a limitation in their long-term outcomes. If patients in Killip classes II/III had received more aggressive reperfusion therapy, their in-hospital and long-term mortality rates could conceivably have been improved. Five-year survival rates were comparable between Killip class II/III and class IV patients, but significantly lower than those of Killip class I patients (p = 0.001).

Four variables—age, hypertension, prior MI, and anterior versus nonanterior MI location—were shown to be significant independent predictors and were used to adjust the effect of Killip class on in-hospital mortality and long-term survival. Age proved to be the most significant variable for predicting in-hospital mortality, a finding in agreement with data from the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO)-1 trial. GUSTO-1 data showed age to be the strongest independent variable in association with 30-day mortality,<sup>3, 38</sup> as did other reports of clinically derived indices of prognosis in patients with acute MI.<sup>7, 11, 12</sup>

## Conclusion

The results of our study document the most substantial reduction reported to date in Killip class IV in-hospital and longterm mortality. As discussed here, several factors may contribute to the improvement in outcome observed despite the presence among these patients of the highest incidence of inhospital complications. Our data are derived from a community-based population, which may reflect different patient characteristics from a more selected referral or clinical trial based population, and the Killip class IV patients in our study were relatively young. Also, our data and those of other investigators<sup>24</sup> suggest that early reperfusion therapy, principally angioplasty, contributes to improved short- and long-term outcomes.

The Killip classification system continues to be a risk stratification tool of great value to the clinician treating patients with acute MI. Assessment of Killip class at the time of admission is an effective predictor of in-hospital mortality and longterm outcome and maintains its place as one of the most useful and economical clinical tools in the management of patients with acute MI. Our findings support early stratification by Killip class as a means of contributing to cost-effective management and mortality reduction in patients with acute MI, even in the era of advancing technologic resources of primary reperfusion therapy.

## Acknowledgments

The authors wish to thank Darlene Albrecht and Amy Oeltjen for their expertise in manuscript preparation; the physicians, cardiology fellows, medical residents, nursing staff, and cardiac rehabilitation staff for their expert care of Mayo Clinic patients admitted to the coronary care unit; and Mary Peterson for her meticulous work as the CCU Database Collection Specialist. CCU Physician Staff: M.R. Bell, P.B. Berger, I.P. Clements, R.L. Click, W.K. Freeman, B.J. Gersh, D.L. Johnston, S.L. Kopecky, A.C. Lapeyre, W.L. Miller, T.M. Munger, J.G. Murphy, J.K. Oh, P.A. Pellikka, G.S. Reeder, C. Rihal, J.A. Rumberger, R.D. Simari, L.J. Sinak, R.T. Tilbury, R.S. Wright.

### References

- Killip T, Kimball JT: Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol 1967;20:457–464
- Rott D, Behar S, Gottlieb S, Boyko V, Hod H: Usefulness of the classification for early risk stratification of patients with acute myocardial infarction in the 1990s compared with those treated in the 1980s. Am J Cardiol 1997;80:859–864
- Lee KL, Woodlief LH, Topol EJ, Weaver WD, Betriu A, Col J, Simoons M, Aylward P, Van de Werf F, Califf RM: Predictors of 30day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. *Circulation* 1995;91:1659–1668
- Becker RC, Burns M, Gore JM, Spencer FA, Ball SP, French W, Lambrew C, Bowlby L, Hilbe J, Rogers WJ: Early assessment and in-hospital management of patients with acute myocardial infarction at increased risk for adverse outcomes: A nationwide perspective of current clinical practice. *Am Heart J* 1998 May 135:5 Pt 1 786–796
- Launbjerg J, Berning J, Fruergaard P, Eliasen P, Borch-Johnsen K, Eiken P, Appleyard M: Risk stratification after acute myocardial infarction by means of echocardiographic wall motion scoring and Killip classification. *Cardiology* 1992;80:375–381
- Norris RM, Brandt PWT, Caughey DE, Lee A: A new coronary prognostic index. *Lancet* 1969;1:274–278
- Norris RM, Lee AJ, Brandt PWT: Mortality in a coronary care unit analysed by a new coronary prognostic index. *Lancet* 1969;1: 278–281
- Funk M, Pooley-Richards RL: Predicting hospital mortality in patients with acute myocardial infarction. Am J Crit Care 1994;3: 168–176
- Chapman BL, Gray CH: Prognostic index for myocardial infarction treated in a coronary care unit. *Br Heart J* 1973;35:135–141
- Dubois C, Piérard LA, Albert A, Smeets J-P, Demoulin J-C, Boland J, Kulbertus HE: Short-term risk stratification at admission based on simple clinical data in acute myocardial infarction. *Am J Cardiol* 1988;61:216–219
- Piérard LA, Albert A, Chapelle J-P, Carlier J, Kulbertus HE: Relative prognostic value of clinical, biochemical, echocardiographic and haemodynamic variables in predicting in-hospital and one-year cardiac mortality after acute myocardial infarction. *Eur Heart J* 1989;10:24–31

- Christiansen JP, Liang C-S: Reappraisal of the Norris score and the prognostic value of left ventricular ejection fraction measurement for in-hospital mortality after acute myocardial infarction. *Am J Cardiol* 1999;83:589–591
- Scheidt S, Ascheim R, Killip T: Shock after acute myocardial infarction. Am J Cardiol 1970;26:556–564
- Leor J, Goldbourt U, Reicher-Reiss H, Kaplinsky E, Behar S, and the Sprint Study Group: Cardiogenic shock complicating acute myocardial infarction in patients without heart failure on admission: Incidence, risk factors and outcome. *Am J Med* 1993;94:265–273
- Holmes DR, Bates ER, Kleiman NS, Sadowski Z, Horgan JHS, Morris DC, Califf RM, Berger PB, Topol EJ: Contemporary reperfusion therapy for cardiogenic shock: The GUSTO-1 Trial experience. J Am Coll Cardiol 1995;26:668–674
- Berger PB, Holmes DR, Stebbins AL, Bates ER, Califf RM, Topol EJ, for the GUSTO-1 Investigators: Impact of an aggressive invasive catheterization and revascularization strategy on mortality in patients with cardiogenic shock in the Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded Coronary Arteries (GUSTO-1) Trial. An observational study. *Circulation* 1997;96:122–127
- Lee L, Erbel R, Brown TM, Laufer N, Meyer J, O'Neill W: Multicenter registry of angioplasty therapy of cardiogenic shock: Initial and long-term survival. J Am Coll Cardiol 1991;17:559–603
- Lee L, Bates ER, Pitt B, Walton JA, Laufer N, O'Neill WW: Percutaneous transluminal coronary angioplasty improves survival in acute myocardial infarction complicated by cardiogenic shock. *Circulation* 1988;78:1345–1351
- Disler L, Haitas B, Steingo BJ, McKibbon J: Cardiogenic shock in evolving myocardial infarction: Treatment by angioplasty and streptokinase. *Heart Lung* 1987;16:649–652
- Verna E, Repetto S, Boscarini M, Ghezzi I, Binaghi G: Emergency coronary angioplasty in patients with severe left ventricular dysfunction or cardiogenic shock after acute myocardial infarction. *Eur Heart J* 1989;10:58–66
- Hibbard M, Holmes DR, Bailey KR, Reeder GS, Bresnahan JF, Gersh BJ: Percutaneous transluminal coronary angioplasty in patients with cardiogenic shock. J Am Coll Cardiol 1992;19:636–649
- Itoh T, Fukami K, Oriso S, Umemura J, Nakajima J, Obonai H, Hiramori K: Survival following cardiogenic shock caused by left main coronary artery total occlusion: A case report and review of the literature. *Angiology* 1997;48:163–171
- Hochman JS, Boland J, Sleeper JA, Porway M, Brinker J, Col J, Jacobs A, Slater J, Miller D, Wasserman H, Menegus MA, Talley JD, McKinlay S, Sandborn T, LeJemtel T, and the SHOCK registry investigators: Current spectrum of cardiogenic shock and the effect of early revascularization on mortality. *Circulation* 1995;91: 873–881
- Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, LeJemtel TH, for the SHOCK Investigators: Early revascularization in acute myocardial infarction complicated by cardiogenic shock. N Engl J Med 1999;341:625–634
- 25. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group: Indications for fibrinolytic therapy in suspected acute myocardial infarction: Collaborative overview of early mortality and major morbidi-

ty results from all randomised trials of more than 1000 patients. Lancet 1994;343:311-322

- Weaver WD, Simes J, Betriu A, Grines CL, Zijstra F, Garcia E, Grinfeld L, Gibbons RJ: Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction. A quantitative review. J Am Med Assoc 1997;278: 2093–2098
- ISIS-2 (Second International Study of Infarct Survival) Collaborative Group: Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction. *Lancet* 1988;2:349–360
- Antiplatelet Trialists' Collaboration: Collaborative overview of randomized trials of antiplatelet therapy. I. Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *Br Med J* 1994;308:81–106
- 29. The Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-Plus) study investigators: Inhibition of the platelet glycoprotein IIB/IIIA receptor with tirofiban in unstable angina and non-Q wave myocardial infarction. N Engl J Med 1998;338:1488–1497
- Cohen M, Demers C, Gurfinkel EP, Turpie AG, Fromell GJ, Goodman S, Langer A, Califf RM, Fox KA, Premmereur J, Bigonzi F: A comparison of low-molecular-weight heparin with unfractionated heparin for unstable coronary artery disease. Efficacy and safety of subcutaneous enoxaparin in non-Q-wave coronary events study group. N Engl J Med 1997;337:447–452
- Gottlieb SS, McCarter RJ, Vogel RA: Effect of beta-blocker on mortality among high risk and low risk patients after myocardial infarction. *N Engl J Med* 1998;339:489–497
- 32. ISIS-4 Collaborative Group. ISIS-4: A randomized factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulfate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 1995;345:669–685
- The GISSI-3 Study Group: GISSI-3: Effects of lisinopril and transdermal glycerol trinitrate singly and together on 6 week mortality and ventricular function after acute myocardial infarction. *Lancet* 1994;343:1115–1122
- Dries DL, Solomon AJ, Gersh BJ: Adjunctive therapy after reperfusion therapy in acute myocardial infarction. *Clin Cardiol* 1998; 21:379–386
- Gillum RF, Fortmann SP, Prineas RJ, Kottke TE: WHO criteria for diagnosis of acute myocardial infarction. Am Heart J 1984;108: 150–158
- Rott D, Behar S, Gottlieb S, Boyko V, Hod H: Does Killip classification still work in the thrombolytic era? *Cardiol Rev* 1998;8:22–25
- 37. Rollag A, Mangschau A, Jonsbu J, Aase O, Nerdrum HF, Erikssen J: Do x-ray determined cardiac volume and signs of congestive heart failure provide additional prognostic information after my-ocardial infarction if the left ventricular ejection fraction is known? J Intern Med 1989;225:267–272
- Newby LK, Califf RM, Guerci A, Weaver WD, Col J, Horgan JH: Early discharge in the thrombolytic era: An analysis of criteria for uncomplicated infarction from the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial. J Am Coll Cardiol 1996;27:625–632