

# Care Concordant With Guidelines Predicts Decreased Long-Term Mortality in Patients With Unstable Angina Pectoris and Non-ST-Elevation Myocardial Infarction

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Data are sparse regarding the long-term benefit of care concordant with clinical practice guidelines in patients presenting with unstable angina pectoris and non-ST-segment elevation myocardial infarction (UAP/NSTEMI), particularly in the general care setting. We extended follow-up in a preexisting cohort of 275 patients hospitalized with primary UAP/NSTEMI. Using Cox models, we compared long-term mortality between patients who received care concordant with  $\geq 80\%$  of 8 important guideline recommendations during the index hospitalization and patients who did not. Among all study patients, 68% received guideline-concordant care. During follow-up (median 9.4 years) 49% of patients died. Patients with UAP/NSTEMI who received guideline-concordant care had significantly decreased long-term mortality compared with those who received guideline-discordant care (hazards ratio [HR] 0.45, 95% confidence interval [CI] 0.32 to 0.64). Guideline-concordant care remained associated with decreased mortality

after adjusting for other predictors of long-term mortality (HR 0.57, 95% CI 0.39 to 0.84) and after adjustment for the propensity to receive guideline-concordant care (HR 0.61, 95% CI 0.43 to 0.88). The benefit of guideline-concordant care relative to discordant care was preserved in high-risk populations shown to be less likely to receive guideline-concordant care, including patients with advanced age, congestive heart failure, elevated serum creatinine, and prior myocardial infarction. Care concordant with UAP/NSTEMI clinical practice guidelines is associated with substantially improved long-term survival. Our findings endorse the approach adopted by authors of clinical practice guidelines in generalizing evidence-based medicine to usual clinical care. In firmly establishing the benefit of consensus guidelines, the foundation is set for efforts to improve practitioner compliance with these standards. ©2004 by Excerpta Medica, Inc.

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**D**espite the increasing promulgation of practice guidelines based on evidence from randomized-controlled trials, data are sparse regarding the association of care concordant with guideline recommendations and long-term outcomes in the general population. Initial research examining concordance of care with national practice standards has been conducted primarily in Medicare patients with ST-elevation myocardial infarction.<sup>1-3</sup> Less evidence is available for patients with unstable angina pectoris and non-ST-elevation myo-

cardial infarction (UAP/NSTEMI). We previously demonstrated improved 1-year survival among patients who received care concordant with the 1994 Agency for Health Care Policy and Research UAP/NSTEMI guidelines than among those who did not.<sup>4,5</sup> The association between guideline-recommended therapies and long-term survival in patients with UAP/NSTEMI has not been previously evaluated. Therefore, we extended follow-up out to 10 years for our preexisting cohort.

## METHODS

**Patient selection:** Details of patient selection have been described elsewhere.<sup>5-8</sup> Briefly, we screened the medical records of all adults admitted from the emergency department to the coronary or medical intensive care units or cardiac telemetry unit of a large, urban, teaching hospital between October 1, 1991 and September 30, 1992. The final cohort for this analysis consisted of 275 consecutive patients with a primary diagnosis of UAP or NSTEMI who survived to hospital discharge.

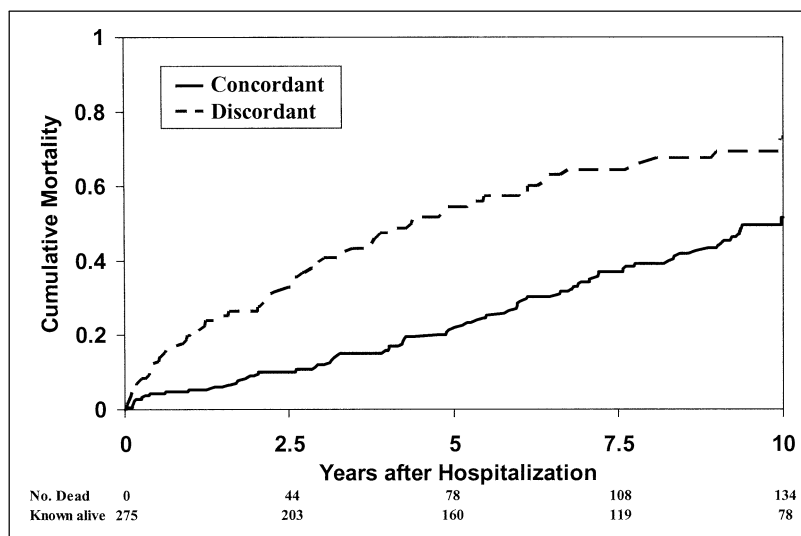
**Baseline characteristics and outcome data collection:** Data were collected on the study patients by trained physician abstractors through hospital chart

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**TABLE 1** Baseline Characteristics Stratified by Concordant and Discordant Care Groups

Characteristics	Guideline-concordant Group (n = 189)	Guideline-discordant Group (n = 86)	p Value
Mean age (yrs)	64	70	<0.001
Men	132 (70%)	53 (62%)	0.21
White race	174 (92%)	77 (90%)	0.50
Angina pectoris at rest	144 (76%)	68 (79%)	0.54
Typical angina pectoris	134 (71%)	51 (59%)	0.07
Prior myocardial infarction	85 (45%)	48 (56%)	0.12
Prior coronary revascularization	74 (39%)	33 (38%)	0.89
Prior congestive heart failure	38 (20%)	37 (43%)	<0.001
Current smoker	45 (24%)	14 (16%)	0.16
Total cholesterol $\geq$ 240 mg/dl or treated	112 (59%)	42 (49%)	0.15
Congestive heart failure at presentation	43 (23%)	44 (51%)	<0.001
Serum creatinine >1.5 mg/dl	23 (12%)	25 (29%)	0.001
Elevated serum cardiac markers	49 (26%)	16 (19%)	0.22



**FIGURE 1.** Kaplan-Meier mortality curve comparing long-term mortality in patients with UAP/NSTEMI, stratified by concordance versus discordance with the 1994 Agency for Health Care Policy and Research guideline recommendations at index hospitalization.

and computer database abstraction as previously described.<sup>5-8</sup> Congestive heart failure at presentation was defined by the presence of rales or S3 on recorded physical examination or chest x-ray consistent with pulmonary edema. Hypercholesterolemia was defined as total cholesterol  $\geq$ 240 mg/dl or taking a lipid-lowering medication at presentation. For this analysis, the primary outcome of interest was long-term mortality after index hospitalization. Vital status data were obtained from hospital records, discharge summaries, laboratory evaluations, and computerized clinic notes. A 1-year follow-up of mortality included contacting some patients by mail or telephone. When vital status remained uncertain through the end of the 10-year follow-up period, searches of the Social Security Death Index and Massachusetts Death Registry were performed. This research project was approved by the Subcommittee on Human Studies at our institution.

**Determination of guideline concordance:** From the 95 recommendations of the Agency for Health Care Policy and Research guidelines, we selected 8 that were supported by strong scientific evidence and that could be reliably assessed from the medical record.<sup>6</sup> Eligibility and concordance criteria for each were based on the language of the guideline. To determine whether a patient received guideline-concordant care overall, we calculated a concordance score for each patient, defined as the number of recommended therapies the patient received divided by the total number of recommended therapies for which the patient was eligible. Patients with a concordance score of  $\geq$ 80% were considered to have received “guideline-concordant care”; those with <80% were considered “guideline-discordant care.” To determine the association between each patient guideline recommendation and mortality, we performed 8 secondary analyses, examining the risk of mortality by concordance versus discordance separately for each of the 8 patient recommendations.

**Statistical analysis:** Baseline characteristics were compared between patients classified as receiving guideline-concordant versus guideline-discordant care using the *t* test or Wilcoxon rank-sum test for continuous variables and chi-squared or Fisher’s exact tests for categorical variables, as appropriate. Kaplan-Meier cumulative mortality curves were generated for patients with overall guideline-concordant and guideline-discordant care and were compared using the log-rank test. Cox proportional-hazards models were constructed to evaluate long-term mortality according to the presence or absence of guideline-concordant care. Proportional-hazards assumptions were tested and found to be appropriate.

Certain baseline characteristics were previously shown to predict whether patients in our sample received guideline-concordant care.<sup>6</sup> We therefore created a propensity score model to predict the likelihood of guideline-concordant care from baseline characteristics using stepwise logistic regression ( $p < 0.10$  for retention in model). From this analysis we generated a propensity score for each patient and used it in a Cox model to determine a propensity-adjusted hazards ratio for mortality.<sup>9,10</sup> To determine whether guideline-concordant care was associated with decreased long-term mortality after adjustment for other important confounders, we also adjusted for other predictors of

long-term mortality. From this analysis we generated a propensity score for each patient and used it in a Cox model to determine a propensity-adjusted hazards ratio for mortality.<sup>9,10</sup> To determine whether guideline-concordant care was associated with decreased long-term mortality after adjustment for other important confounders, we also adjusted for other predictors of

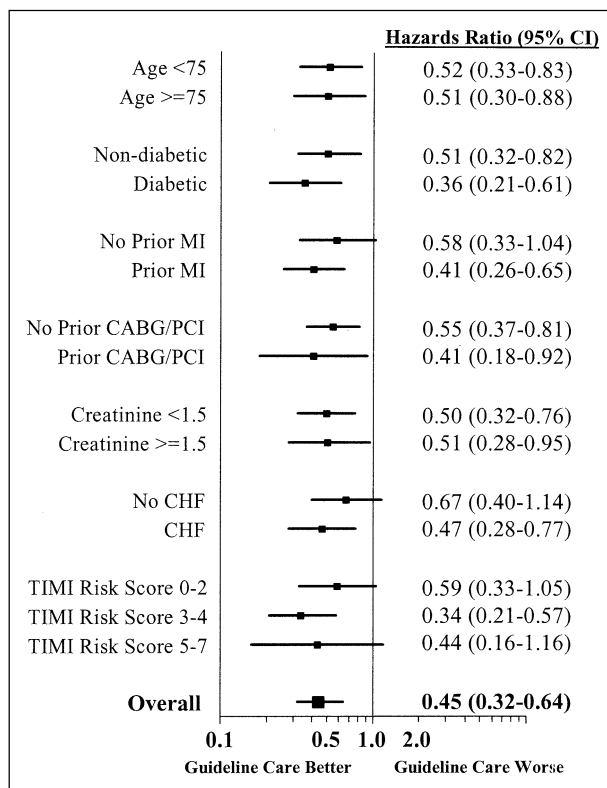
long-term mortality in these patients with UAP/NSTEMI in a multivariate Cox analysis.<sup>11</sup> To determine whether mortality hazards differed among patients in important clinical subgroups, we conducted stratified Cox analyses. All statistical analyses were performed using STATA version 6.0 (STATA Corp., College Station, Texas). A 2-tailed p value <0.05 was considered statistically significant. All hazards ratios (HRs) are reported with 95% confidence intervals (CIs).

## RESULTS

**Baseline characteristics:** Sixty-eight percent of patients received guideline-concordant care, and 41% had concordance scores of 100%. Baseline patient characteristics stratified by guideline-concordant and guideline-discordant care are listed in Table 1. Patients whose overall care was discordant with the guidelines were more likely to be older, have congestive heart failure, and have elevated serum creatinine than patients who received guideline-concordant care. Median follow-up was 9.4 years (interquartile range 3.7 to 9.9, mean 7.2). Follow-up between the concordant and discordant groups was not significantly different (p = 0.59). Ten years after hospitalization, death was documented in 134 subjects (49%).

**Overall guideline-concordant care and long-term mortality:** Patients who received guideline-concordant care had significantly decreased long-term mortality compared with those who received discordant care (univariate Cox HR 0.45, 95% CI 0.32 to 0.64; Figure 1). Adjustments for baseline differences between the 2 groups did not substantially attenuate the mortality benefit associated with guideline-concordant care. We found that 5 variables (age, congestive heart failure at presentation, elevated creatinine, prior myocardial infarction, and prehospital aspirin use) were independent predictors of the propensity to receive guideline-concordant care. After adjusting for the propensity score, guideline-concordant care remained associated with significantly decreased long-term mortality compared with discordant care (adjusted HR 0.61, 95% CI 0.43 to 0.88). Similarly, after multivariable adjustment for independent predictors of long-term mortality in our patients with UAP/NSTEMI (age, prior myocardial infarction, diabetes, congestive heart failure at presentation, elevated creatinine, systolic blood pressure, and leukocytosis),<sup>11</sup> the adjusted HR associated with guideline-concordant care compared with discordant care was 0.57 (95% CI 0.39 to 0.84). The mortality benefit associated with guideline-concordant care was present early and late (first year after hospitalization, HR 0.37, 95% CI 0.17 to 0.81; years 2 to 10, HR 0.53, 95% CI 0.35 to 0.78).

**Subgroup analysis:** The association of decreased mortality with guideline-concordant care was preserved across strata of important clinical subgroups (Figure 2), including patients aged  $\geq 75$  years, and those with diabetes, prior myocardial infarction, prior revascularization, elevated serum creatinine, and congestive heart failure at presentation. Stratification into 3 groups by the Thrombolysis In Myocardial Infarc-



**FIGURE 2.** HRs for long-term mortality for guideline-concordant care versus discordant care, stratified by baseline patient characteristics. CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; MI = myocardial infarction; PCI = percutaneous coronary intervention.

tion (TIMI) risk score<sup>12</sup> revealed similar mortality benefits associated with guideline-concordant care regardless of the TIMI risk score at presentation.

**Patient guideline recommendations and long-term mortality:** For the 8 guideline recommendations each considered individually, concordance ranged from 69% (for appropriate referral for coronary bypass surgery) to 99% (for no systemic thrombolysis). In separate analyses, concordance with each patient recommendation was associated with decreased long-term mortality, but only avoidance of calcium channel blockers achieved statistical significance (Table 2).

## DISCUSSION

These results demonstrate an association between care concordant with the 1994 UAP/NSTEMI clinical practice guidelines and decreased long-term mortality. Our findings endorse the approach adopted by authors of clinical practice guidelines and affirm the importance of generalizing evidence-based medicine to usual clinical care.

Association between guideline-concordant care and reduction in long-term mortality was preserved among high-risk patients, although these patients were less likely to receive guideline-concordant care. Therefore, future guideline updates should focus attention on the importance of applying the guideline broadly and include patients with comorbidities.

Guidelines	Mortality HR for Concordant Versus Discordant Care (95% CI)
1. No intravenous thrombolytic therapy	Unable to calculate
2. Initial aspirin therapy	0.67 (0.41–1.10)
3. Initial heparin therapy	0.75 (0.47–1.18)
4. Initial $\beta$ -blocker therapy	0.73 (0.41–1.30)
5. Avoidance of calcium channel blockers	0.42 (0.28–0.64)
6. Appropriate recommendation for cardiac catheterization	0.69 (0.46–1.06)
7. Appropriate recommendation for coronary artery bypass surgery	0.49 (0.21–1.20)
8. Discharge aspirin therapy	0.57 (0.31–1.06)

The major question arising from the results of this cohort study is whether the large difference in mortality between the concordant and discordant groups reflects a causal link between the delivery of guideline-concordant care and a durable survival benefit, or whether guideline concordance is merely a marker for healthier patients. To address the potential limitations of confounding biases, we used multiple approaches to adjust for baseline differences in prognosis between patients in the guideline-concordant and guideline-discordant groups. First, we used a propensity score analysis to control for the relation between prognostic baseline characteristics and assignment to treatment group. Second, we used multivariable Cox analysis to control for the relation between prognostic baseline characteristics and long-term outcomes. Third, we conducted stratified subgroup analyses to examine the effect of guideline concordance within patient clinical subgroups. In all 3 analyses, a significant improvement in long-term mortality was consistently noted in the guideline-concordant group versus the discordant group.

The association of guideline-concordant care during the index hospitalization with improved mortality was present both early as well as late after hospitalization. Given the paucity of contemporary data regarding long-term outcomes after UAP/NSTEMI, it is unclear whether differences in care during a single hospitalization alone could cause such a discrepancy in long-term mortality among patients. The guidelines are based on multiple therapies that have been shown to provide benefit individually. Applied cumulatively, implementation of guideline recommendations could avert substantial myocardial damage and prevent future cardiomyopathy and arrhythmia. Alternatively, concordant care during an index hospitalization may predict better medical care over the long term. We were unable to account for treatment differences beyond the index hospitalization.

In the decade since the cohort of patients we studied was hospitalized, updated guidelines for UAP/NSTEMI were published in 2000<sup>13</sup> and 2002<sup>14</sup> to reflect evolving diagnostic<sup>15,16</sup> and treatment strategies.<sup>17,18</sup> Nonetheless, the criteria for identifying patients with UAP/NSTEMI and the 8 guideline recommendations we examined remain largely unchanged.

This analysis of guideline concordance within a UAP/NSTEMI cohort comes at a time when national guidelines are becoming increasingly emphasized, particularly in the field of cardiology. The American Heart Association's "Get with the Guidelines" initiative<sup>19</sup> and the American College of Cardiology's "Guidelines Applied in Practice" project<sup>20</sup> are 2 examples. Given this direction, firmly establishing the generalizability of consensus guidelines into the usual-care setting lays the foundation for efforts to improve practitioner compliance with these standards.

Therefore, the positive association between guideline concordance and decreased mortality presented here is important, and it argues for further studies of the effectiveness of guideline-concordant care in diverse clinical settings.

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