Predicting 6-Month Mortality for Older Adults Hospitalized With Acute Myocardial Infarction
A Cohort Study

John A. Dodson, MD, MPH; Alexandra M. Hajduk, PhD, MPH; Mary Geda, RN, MSN; Harlan M. Krumholz, MD; Terrence E. Murphy, PhD; Sui Tsang, MS; Mary E. Tinetti, MD; Michael G. Nanna, MD; Richard McNamara, MD; Thomas M. Gill, MD; and Sarwat I. Chaudhry, MD

Background: Older adults with acute myocardial infarction (AMI) have higher prevalence of functional impairments, including deficits in cognition, strength, and sensory domains, than their younger counterparts.

Objective: To develop and evaluate the prognostic utility of a risk model for 6-month post-AMI mortality in older adults that incorporates information about functional impairments.

Design: Prospective cohort study. (ClinicalTrials.gov: NCT01755052).

Setting: 94 hospitals throughout the United States.

Participants: 3006 persons aged 75 years or older who were hospitalized with AMI and discharged alive.

Measurements: Functional impairments were assessed during hospitalization via direct measurement (cognition, mobility, muscle strength) or self-report (vision, hearing). Clinical variables associated with mortality in prior risk models were ascertained by chart review. Seventy-two candidate variables were selected for inclusion, and backward selection and Bayesian model averaging were used to derive (n = 2004 participants) and validate (n = 1002 participants) a model for 6-month mortality.

Results: Participants' mean age was 81.5 years, 44.4% were women, and 10.5% were nonwhite. There were 266 deaths (8.8%) within 6 months. The final risk model included 15 variables, 4 of which were not included in prior risk models: hearing impairment, mobility impairment, weight loss, and lower patient-reported health status. The model was well calibrated (Hosmer–Lemeshow P > 0.05) and showed good discrimination (area under the curve for the validation cohort = 0.84). Adding functional impairments significantly improved model performance, as evidenced by category-free net reclassification improvement indices of 0.21 (P = 0.008) for hearing impairment and 0.26 (P < 0.001) for mobility impairment.

Limitation: The model was not externally validated.

Conclusion: A newly developed model for 6-month post-AMI mortality in older adults was well calibrated and had good discriminatory ability. This model may be useful in decision making at hospital discharge.

Primary Funding Source: National Heart, Lung, and Blood Institute of the National Institutes of Health.

One third of patients hospitalized for acute myocardial infarction (AMI) in the United States are older adults (aged ≥75 years) (1), and the number of incident AMI cases among older adults is projected to double over the next several decades (2). Advanced age is a strong determinant of post-AMI mortality in the 6 months after hospital discharge (3–5). Compared with their younger counterparts, older adults have more comorbid diseases, lower physiologic reserve, and more functional impairments (including physical capabilities and cognition), which may contribute to their higher risk for post-AMI mortality. However, there is considerable heterogeneity among older adults, and some have exceptional outcomes (6, 7).

Although clinical practice guidelines endorse routine use of AMI mortality risk models to assist with de-

cision making (8), current models were derived from younger cohorts and may have limited discrimination (9) and calibration (10) in older adults. Physiologic changes with aging may have important prognostic value, and several small studies have shown that functional impairments related to these changes may be independently associated with post-AMI mortality (11, 12). Although a recent joint scientific statement from several cardiology and geriatrics professional societies emphasized "a need for risk-stratification tools relevant to older adults" (13), no AMI mortality risk models that consider these impairments have been developed specifically for the older adult population.

Our primary objective was to develop and validate a 6-month mortality risk model for use in older adults at the time of discharge from hospitalization for AMI. Our model selection process considered functional impairments as well as traditional demographic and clinical variables to assess whether functional impairments would have sufficiently high prognostic utility to be retained in the final model. We evaluated the incremental prognostic utility of adding information about functional impairments to traditional cardiovascular risk factors and compared the model's performance with that

of the existing Global Registry of Acute Coronary Events (GRACE) 6-month mortality risk score (4).

METHODS

This article follows the guidelines in the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) consensus document (14).

Data Source

We used data from the SILVER-AMI (Comprehensive Evaluation of Risk in Older Adults with AMI) study. This prospective observational cohort study involved 3041 patients aged 75 years or older who were hospitalized with AMI at 94 U.S. hospitals. Participants were enrolled from 11 January 2013 to 28 October 2016. Institutional review board approval was obtained at all centers, and informed consent was obtained from participants or their designated proxies.

Participants

The design of SILVER-AMI has been described previously (15). Patients aged 75 years or older were enrolled if they met the criteria in the Third Universal Definition of MI (16). Patients were excluded if they were transferred to the study hospital from another hospital after more than 24 hours. We did not exclude participants with cognitive impairment, but we did screen for capacity (17) and used proxy respondents when necessary. Because our objective was to model risk for postdischarge death, we excluded those who died in the hospital ($n = 35$), retaining a final sample of 3006 participants for analysis.

Study Procedures

At the time of hospitalization, participants underwent a baseline assessment, including demographic characteristics, symptoms, health status (12-Item Short Form Health Survey), functional impairments (including cognition, vision, hearing, muscle strength, and mobility), and other conditions common with aging (such as unintentional weight loss). Fifty-two percent of assessments occurred within the first 2 days of hospitalization. Medical record review included details of initial presentation, comorbidities, medications, cardiac procedures, and laboratory results.

Outcome

The primary outcome was death within 6 months of hospital discharge, which was ascertained via medical records (in-hospital death), death certificates (out-of-hospital death), or obituaries (out-of-hospital death). When these were not available (<5% of cases), mortality information was obtained through secondary report, such as from a family member. All deaths were double-adjudicated by physician investigators who reviewed source documents to determine the cause, which was classified as cardiovascular (attributable to coronary disease, heart failure, AMI, valvular heart disease, arrhythmia, venous thrombosis, peripheral artery disease, stroke, or complications of a cardiac procedure), non-

cardiovascular, or unknown. Mortality status was definitively obtained for 99.9% of participants.

Predictors at Baseline

Functional impairments and other conditions common with aging were selected on the basis of the geriatrics literature and feasibility of measurement in the hospital setting and are defined in **Table 1** of **Supplement 1** (available at Annals.org). The following impairments and conditions were performance-based: general cognitive function (Telephone Interview for Cognitive Status) (18), verbal fluency (Controlled Oral Word Association Test) (19), upper-extremity strength (handheld dynamometer [B&L Engineering]) (20, 21), and functional mobility (Timed Up and Go [TUG]) (22). The TUG was measured according to a standard protocol that involved the participant standing from a chair, walking 10 feet at his or her usual pace, turning around, walking back to the chair, and sitting. The following impairments and conditions were assessed via self-report: vision impairment (Visual Function Questionnaire) (23), hearing impairment (global question about impairments imposed by hearing) (24), unintentional weight loss (>10 lb in the prior year), activities of daily living disability (bathing, dressing, rising from chair, or ambulating) (25), depressive symptoms (Patient Health Questionnaire 8) (26), and fall history in the prior year. Cut points were selected on the basis of previously validated thresholds; if the definitive threshold was ambiguous, consensus was reached among study team members on the basis of the best available evidence.

Statistical Analysis

The 3006 participants were randomly assigned using simple random sampling, as implemented in the SAS SURVEYSELECT procedure, such that two thirds ($n = 2004$) were chosen for derivation and one third ($n = 1002$) were assigned to validation. This allowed sufficient power to develop and validate the risk prediction model, and the random nature of the process protected against selection bias.

We initially selected 72 candidate variables for inclusion (**Table 2** of **Supplement 1**) based on existing risk models for adverse clinical events after AMI hospitalization (4, 27–29), the study's objective of evaluating functional impairments and other conditions common with aging that could influence mortality risk, and clinical judgment of the study investigators with regard to other variables that might influence postdischarge mortality.

We generated descriptive statistics for all participants (that is, for the derivation and validation cohorts combined, using means for continuous variables and percentages for categorical variables (**Table 1**). We also assessed baseline characteristics of the derivation and validation cohorts separately (**Table 3** of **Supplement 1**). When feasible, we used continuous variables to retain statistical power, although some were converted into categorical variables for clinical interpretability. Thresholds were chosen on the basis of clinical relevance and distributions. From our initial list, we omitted variables with missingness greater than 20% and those with extremely low (<5%) or high (>95%) prevalence

Table 1. Participant Characteristics at Baseline

Characteristic	Deceased at 180 Days (n = 266)		Alive at 180 Days (n = 2740)	
	Mean (SD) or Number (Percentage)	Missing Data, n (%)	Mean (SD) or Number (Percentage)	Missing Data, n (%)
Demographic characteristics				
Mean age (SD), y	83.7 (5.8)	0 (0.0)	81.3 (4.9)	0 (0.0)
Male, n (%)	140 (52.6)	0 (0.0)	1531 (55.9)	0 (0.0)
Nonwhite race, n (%)	43 (16.4)	3 (1.1)	274 (10.2)	45 (1.6)
Married/living with partner, n (%)	107 (40.4)	1 (0.4)	1407 (51.4)	4 (0.1)
Education ≤12 y, n (%)	170 (64.6)	3 (1.1)	1537 (56.6)	23 (0.8)
Medical history, n (%)				
Hypertension	247 (92.9)	0 (0.0)	2319 (84.6)	0 (0.0)
Dyslipidemia	165 (62.0)	0 (0.0)	1733 (63.3)	0 (0.0)
Current or ever-smoker	160 (61.3)	5 (1.9)	1506 (55.4)	19 (0.7)
Arrhythmia	86 (32.3)	0 (0.0)	663 (24.2)	0 (0.0)
Heart failure	96 (36.1)	0 (0.0)	467 (17.0)	0 (0.0)
Peripheral artery disease	58 (21.8)	0 (0.0)	305 (11.1)	0 (0.0)
Valvular disease	50 (18.8)	0 (0.0)	299 (10.9)	0 (0.0)
Stroke	64 (24.1)	0 (0.0)	404 (14.7)	0 (0.0)
Diabetes mellitus	112 (42.1)	0 (0.0)	1004 (36.7)	0 (0.0)
Chronic obstructive pulmonary disease	59 (22.2)	0 (0.0)	367 (13.4)	0 (0.0)
Sleep apnea	36 (13.5)	0 (0.0)	213 (7.8)	0 (0.0)
Prior myocardial infarction	84 (31.6)	0 (0.0)	735 (26.8)	0 (0.0)
Prior revascularization procedure	113 (42.5)	0 (0.0)	1107 (40.4)	0 (0.0)
Presentation characteristics				
STEMI, n (%)	53 (19.9)	0 (0.0)	738 (26.9)	0 (0.0)
Chest pain as presenting symptom, n (%)	102 (40)	13 (4.9)	1109 (41.8)	86 (3.1)
≥6 h from symptoms to presentation, n (%)	131 (49.6)	2 (0.8)	1140 (41.8)	14 (0.5)
Mean body mass index (SD), kg/m²	26.5 (5.8)	0 (0.0)	27.6 (5.3)	0 (0.0)
Killip class II to IV, n (%)	70 (26.3)	0 (0.0)	322 (11.8)	0 (0.0)
Mean initial systolic BP (SD), mm Hg	136.3 (28.8)	0 (0.0)	146.8 (30.8)	0 (0.0)
Mean initial diastolic BP (SD), mm Hg	74.1 (17.0)	0 (0.0)	78.5 (17.7)	0 (0.0)
Mean initial heart rate (SD), beats/min	89.3 (21.9)	0 (0.0)	83.0 (22.7)	0 (0.0)
Atrial fibrillation, n (%)	68 (25.6)	0 (0.0)	478 (17.5)	0 (0.0)
Mean initial hemoglobin level (SD), g/L	118 (21)	0 (0.0)	129 (20)	8 (0.3)
Mean initial leukocyte count (SD), × 10⁹ cells/L	10.7 (6.7)	0 (0.0)	9.5 (4.7)	11 (0.4)
Mean eGFR (SD), mL/min/1.73 m²	44.1 (21.6)	0 (0.0)	55.7 (19.5)	2 (0.1)
Mean TIMI score (SD)				
NSTEMI	4.3 (1.2)	0 (0.0)	4.6 (1.2)	0 (0.0)
STEMI	6.8 (1.8)	0 (0.0)	6.0 (1.6)	14 (1.9)
Mean GRACE ACS score (SD)	162.4 (22.9)	0 (0.0)	143.8 (21.8)	2 (0.1)
In-hospital diagnostics, therapies, and complications, n (%)				
Left ventricular ejection fraction		30 (11.3)		247 (9.0)
Normal (>50%)	90 (38.1)		1437 (57.6)	
Mildly reduced (40%–50%)	56 (23.7)		541 (21.7)	
Moderately reduced (30%–40%)	54 (22.9)		339 (13.6)	
Severely reduced (<30%)	36 (15.3)		176 (7.1)	
Medications within first 24 h				
Aspirin	249 (93.6)	0 (0.0)	2627 (95.9)	1 (0.0)
Antiplatelet agent (P2Y12 inhibitor)	147 (55.3)	0 (0.0)	1726 (63.0)	1 (0.0)
β-Blocker	206 (77.4)	0 (0.0)	2159 (78.8)	1 (0.0)
Statin	182 (68.4)	0 (0.0)	2090 (76.3)	1 (0.0)
Intravenous antithrombotic agent		0 (0.0)		1 (0.0)
None	62 (23.3)		453 (16.5)	
Heparin or bivalirudin	194 (72.9)		2004 (73.2)	
Heparin or bivalirudin plus glycoprotein IIb/IIIa	10 (3.8)		282 (10.3)	
Revascularization status		0 (0.0)		0 (0.0)
No cardiac catheterization	97 (36.5)		361 (13.2)	
Cardiac catheterization only	56 (21.1)		438 (16.0)	
Cardiac catheterization with PCI	101 (38.0)		1599 (58.4)	
Coronary artery bypass graft surgery	12 (4.5)		342 (12.5)	
In-hospital complications				
Bleeding	71 (26.7)	0 (0.0)	702 (25.6)	0 (0.0)
Acute kidney injury	99 (37.2)	0 (0.0)	593 (21.7)	2 (0.1)
Heart failure	63 (23.7)	0 (0.0)	351 (12.8)	0 (0.0)

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Table 1–Continued

Characteristic	Deceased at 180 Days (*n* = 266)		Alive at 180 Days (*n* = 2740)	
	Mean (SD) or Number (Percentage)	Missing Data, *n* (%)	Mean (SD) or Number (Percentage)	Missing Data, *n* (%)
Functional impairments and conditions common with aging				
Cognitive impairment, *n* (%)		7 (2.6)		42 (1.5)
None (TICS score ≥27)	173 (66.8)		2278 (84.4)	
Mild (TICS score 23–26)	44 (17.0)		270 (10.0)	
Moderate or severe (TICS score ≤22)	42 (16.2)		150 (5.6)	
Mean total "S" words (SD) (COWAT)	8.2 (4.8)	15 (5.6)	9.8 (4.7)	44 (1.6)
Clinically significant vision impairment, *n* (%)	40 (15.1)	1 (0.4)	216 (7.9)	4 (0.1)
Clinically significant hearing impairment, *n* (%)	52 (19.8)	3 (1.1)	352 (13.0)	35 (1.3)
Unintentional weight loss >10 lb in past year, *n* (%)	102 (38.8)	3 (1.1)	569 (20.9)	14 (0.5)
Any ADL disability, *n* (%)	75 (28.3)	1 (0.4)	337 (12.3)	0 (0.0)
>1 fall in past year, *n* (%)	70 (26.9)	6 (2.3)	523 (19.1)	6 (0.2)
Weak grip, *n* (%)	192 (78.4)	21 (7.9)	1615 (61.3)	107 (3.9)
Functional mobility (based on Timed Up and Go), *n* (%)		39 (14.7)		440 (16.1)
Completed in ≤15 s	37 (16.3)		828 (36.0)	
Completed in >15 and ≤25 s	30 (13.2)		589 (25.6)	
Completed in >25 s	46 (20.3)		437 (19.0)	
Unable to complete	114 (50.2)		446 (19.4)	
SF-12: general health question (4 categories), *n* (%)		4 (1.5)		2 (0.1)
Excellent or very good	38 (14.5)		804 (29.4)	
Good	72 (27.5)		1034 (37.8)	
Fair	91 (34.7)		669 (24.4)	
Poor	61 (23.3)		231 (8.4)	
Depressive symptoms (PHQ-8 score ≥10), *n* (%)	56 (22.7)	19 (7.1)	366 (13.8)	80 (2.9)

ACS = acute coronary syndrome; ADL = activity of daily living; BP = blood pressure; COWAT = Controlled Oral Word Association Test; eGFR = estimated glomerular filtration rate; GRACE = Global Registry of Acute Coronary Events; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PHQ-8 = Patient Health Questionnaire 8; SF-12 = 12-Item Short Form Health Survey; STEMI = ST-segment elevation myocardial infarction; TICS = Telephone Interview for Cognitive Status; TIMI = Thrombolysis In Myocardial Infarction.

(the full rationale is described in the Statistical Methods section of **Supplement 1**). All variables except ejection fraction (9.2%) and functional mobility (15.9%) had missingness less than 5%. After confirming the absence of collinearity between variables and assuming that missing values were missing at random, we multiply imputed the data 20 times. All variables were imputed using fully conditional specification (30), drawing from the 72 candidates eligible for model selection. Details of the imputation process are provided in the Statistical Methods section of **Supplement 1**.

Our process for model selection and estimation used imputed derivation data and was previously described in a methods paper using an outcome of death within 30 days of discharge in the SILVER-AMI cohort (31). We first reduced the number of candidate variables by applying multivariable logistic regression with backward selection to an aggregate data set of the 20 imputations, retaining the 30 variables with the strongest adjusted associations with the outcome. We subsequently applied Bayesian model averaging with multivariable logistic regression to these final candidates in each of the multiply imputed data sets. We previously demonstrated the utility of Bayesian model averaging to inform retention of variables differentially selected across imputed data sets in the SILVER-AMI cohort (31). We prespecified that the final predictors would be those exhibiting a positive posterior probability in at least half of the imputations. These predictors were subsequently examined for linearity and used in a multivariable model fit separately to each imputation using generalized estimating equations to adjust for clustering of patients within hospitals, with the coefficients estimated from the separate imputations combined using Rubin rules to yield final coefficients (32). Because Bayesian model averaging was used to select variables rather than *P* values, some model terms did not have *P* values below 0.05 (33).

Discrimination and calibration of the final model were evaluated in the derivation and validation cohorts using the c-statistic and the Hosmer–Lemeshow goodness-of-fit statistic, respectively. Observed and predicted probabilities of the outcome were calculated for deciles of risk obtained by applying the final model to the validation data. We evaluated the incremental value of separately adding functional impairments to the model using category-free (continuous) net reclassification improvement (NRI) indices (34).

The GRACE score, which was developed for 6-month post-AMI mortality, includes the following factors: age, history of AMI, heart failure, increased heart rate at presentation, low systolic blood pressure at presentation, elevated initial serum creatinine level, elevated initial levels of serum cardiac biomarkers, ST-segment depression on presenting electrocardiogram, and not undergoing percutaneous coronary intervention in the hospital (4). Predictive performance of the SILVER-AMI and GRACE risk scores was compared in several ways. The difference in area under the curve (AUC) for the SILVER-AMI and GRACE risk scores (evaluated in the SILVER-AMI validation cohort) was tested using the methods of DeLong and colleagues (35). We also compared specificity, positive predictive value, and negative predictive value of the GRACE and

SILVER-AMI models as applied to the SILVER-AMI validation data for selected values of sensitivity. Kaplan–Meier curves were generated based on quartiles of predicted probability of death from the GRACE and SILVER-AMI models as applied to the SILVER-AMI derivation and validation data sets and compared using log-rank statistics. Finally, integrated predictiveness curves from application of both models to the SILVER-AMI validation data were compared (36).

Analyses were performed using SAS, version 9.4 (SAS Institute), except for the Bayesian model averaging, for which the BMA package in R (R Foundation for Statistical Computing) was used (37). We developed a Web-based calculator derived from model effect estimates for bedside prognostication.

Role of the Funding Source

The National Heart, Lung, and Blood Institute of the National Institutes of Health supported this study but had no role in its design, conduct, or reporting.

RESULTS

Baseline Characteristics

Baseline characteristics of the study participants are shown in **Table 1**. Mean age was 81.5 years (SD,

Figure 1. Receiver-operating characteristic curves for the SILVER-AMI and GRACE mortality risk models.

In our validation cohort, we compared the AUCs for the SILVER-AMI 6-month mortality risk model and the GRACE risk model (which was previously developed for post–acute myocardial infarction 6-month mortality). The GRACE risk model includes the following factors: age, development (or history) of heart failure, peripheral vascular disease, systolic blood pressure, Killip class, initial serum creatinine concentration, elevated initial cardiac markers, cardiac arrest on admission, and ST-segment deviation. The diagonal line indicates 50% discrimination and is provided to show how much each model improves on purely random assignment of risk. As shown, the SILVER-AMI mortality risk model showed superior discrimination compared with the GRACE model (AUC = 0.84 vs. 0.76; *P* < 0.001). AUC = area under the curve; GRACE = Global Registry of Acute Coronary Events; SILVER-AMI = Comprehensive Evaluation of Risk in Older Adults with Acute Myocardial Infarction.

5.0; range, 75 to 101 years) (**Figure 1** of **Supplement 1**), 44.4% were women, 10.5% were nonwhite, and 2.8% had proxy consent. The most common chronic medical conditions were hypertension (85.3%), dyslipidemia (63.2%), and diabetes (37.2%). Most participants (73.7%) presented with non–ST-segment elevation AMI, and most underwent invasive coronary angiography (84.6% in the overall sample, 97.0% in the ST-segment elevation AMI subgroup, and 80.2% in the non–ST-segment elevation AMI subgroup). The most common functional impairments were weak grip (62.8%) and impaired mobility based on a TUG greater than 15 seconds (65.7%). Baseline characteristics are shown separately for the derivation and validation cohorts in **Table 3** of **Supplement 1**.
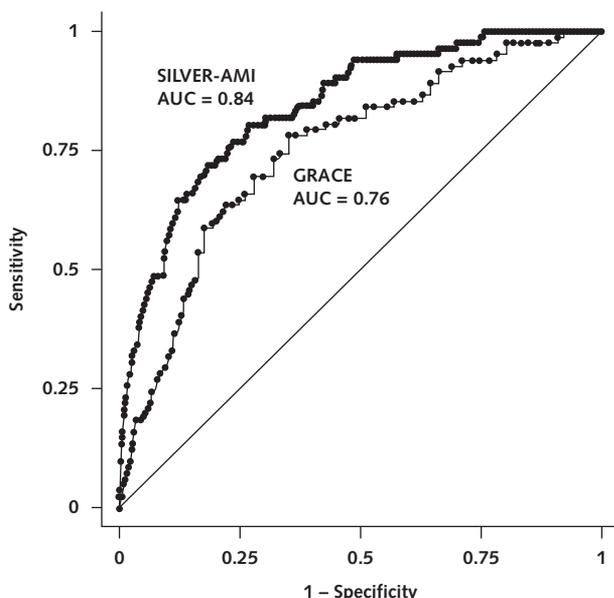
Mortality at 6 Months

Overall, 266 participants (8.8%) who were alive at hospital discharge died within 6 months (184 [9.2%] in the derivation cohort and 82 [8.2%] in the validation cohort). Cause of death was adjudicated as cardiovascular in 41.7% of these participants, noncardiovascular in 24.4%, and unknown in 33.8%. Participants who died were older (83.7 vs. 81.3 years), more likely to be nonwhite (16.4% vs. 10.2%), and more likely to present with non–ST-segment elevation AMI (80.1% vs. 73.1%). They also had a higher burden of comorbid disease, including history of heart failure (36.1% vs. 17.0%), peripheral artery disease (21.8% vs. 11.1%), and stroke (24.1% vs. 14.7%) (**Table 1**). They were also more likely to have in-hospital acute kidney injury (37.2% vs. 21.7%) and heart failure (23.7% vs. 12.8%). Several functional impairments and other conditions common with aging were more common among decedents, including cognitive impairment (33.2% vs. 15.6%), unintentional weight loss (38.8% vs. 20.9%), and impaired mobility based on a TUG greater than 15 seconds (83.7% vs. 64.0%).
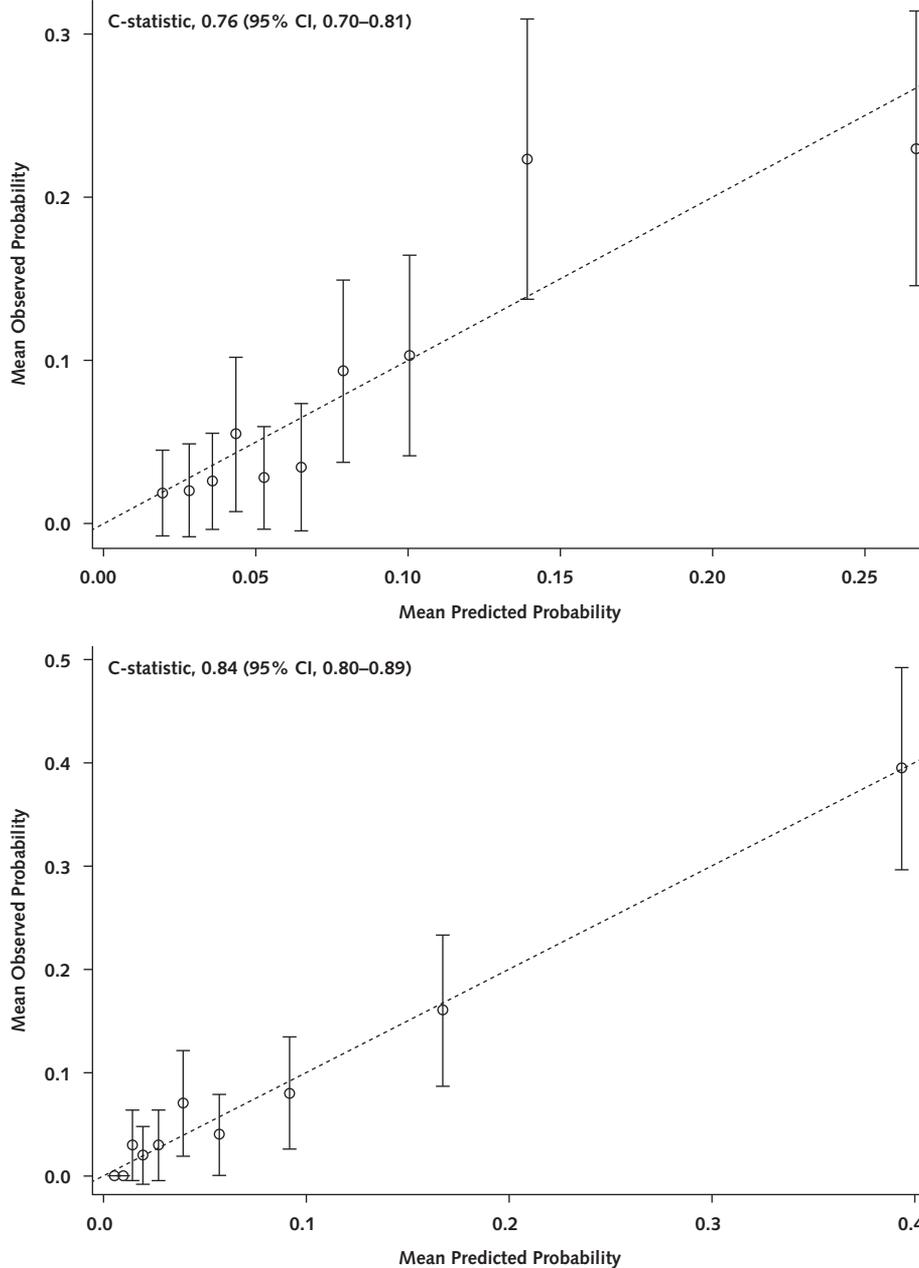
Multivariable Results

In the multivariable model, 15 factors were associated with 6-month mortality (**Table 4** of **Supplement 1**). The strongest factors (based on standardized β-coefficients) included receipt of in-hospital coronary artery bypass graft (CABG), age, length of stay, self-reported health status, and unintentional weight loss. Among these, CABG was protective (odds ratio [OR], 0.15 [95% CI, 0.07 to 0.31]), whereas the others were associated with increased risk (OR for age [per year], 1.06 [CI, 1.02 to 1.11]; OR for length of stay [per day], 1.05 [CI, 1.02 to 1.08]; OR for self-reported health status [per level of worsening], 1.34 [CI, 1.11 to 1.61]; OR for unintentional weight loss, 1.69 [CI, 1.19 to 2.39]). Model discrimination was good (AUC = 0.82 in the derivation cohort and 0.84 in the validation cohort). Compared with the GRACE mortality risk score (4) (evaluated in the SILVER cohort), discrimination was improved (AUC = 0.84 vs. 0.76; *P* < 0.001) (**Figure 1**). The model was also well calibrated (**Figure 2**). Standard operating characteristics from application of the SILVER-AMI and GRACE models to the SILVER-AMI validation co-

Figure 2. Calibration plot for the SILVER-AMI mortality risk model.

Shown are deciles of observed 6-month risk versus predicted 6-month mortality, with the GRACE model applied to the SILVER-AMI validation cohort (*top*) and the SILVER-AMI model applied to the SILVER-AMI validation cohort (*bottom*). Error bars represent 95% CIs. GRACE = Global Registry of Acute Coronary Events; SILVER-AMI = Comprehensive Evaluation of Risk in Older Adults with Acute Myocardial Infarction.

hort are shown in **Tables 2** and **3**. Specificity and positive predictive values were higher, although still modest, for the SILVER-AMI model across selected values of sensitivity (details are provided in the Statistical Methods section of **Supplement 1**).

Kaplan–Meier curves for time to death by quartiles of predicted probabilities from the GRACE and SILVER-AMI scores in both the derivation and validation cohorts are provided in **Figure 2** of **Supplement 1**. In both cohorts, there was larger separation between the third

and fourth quartiles in SILVER-AMI relative to GRACE, indicating that SILVER-AMI assigns higher probabilities to persons most likely to die. Integrated predictiveness curves for SILVER-AMI and GRACE (**Figure 3** of **Supplement 1**) show that for predicted probabilities below the observed outcome incidence (8.2%), SILVER-AMI consistently yields lower risk, and for values above the observed outcome incidence, SILVER-AMI consistently yields higher risk, reflecting its ability to better identify patients at either risk level.

Table 2. Standard Operating Characteristics From Application of the GRACE Model to the SILVER-AMI Validation Cohort for Death Within 180 Days (*n* = 1002)

Characteristic	Sensitivity (95% CI)*				
	0.70 (0.67–0.72)	0.74 (0.71–0.77)	0.81 (0.78–0.83)	0.85 (0.83–0.88)	0.92 (0.90–0.93)
Specificity (95% CI)	0.72 (0.70–0.75)	0.67 (0.64–0.70)	0.57 (0.54–0.60)	0.43 (0.40–0.46)	0.34 (0.31–0.37)
Positive predictive value (95% CI)	0.18 (0.16–0.21)	0.17 (0.14–0.20)	0.14 (0.12–0.17)	0.12 (0.10–0.14)	0.11 (0.10–0.13)
Negative predictive value (95% CI)	0.96 (0.95–0.98)	0.97 (0.96–0.98)	0.97 (0.96–0.98)	0.97 (0.96–0.98)	0.98 (0.97–0.99)

GRACE = Global Registry of Acute Coronary Events; SILVER-AMI = Comprehensive Evaluation of Risk in Older Adults with Acute Myocardial Infarction.
* Due to risk model differences, sensitivity values in Tables 2 and 3 are statistically equivalent rather than numerically identical.

The addition of functional impairments significantly improved the predictive ability of the model, as measured by category-free NRI indices (38). The TUG yielded an event NRI of 16% (CI, 11% to 22%) and a nonevent NRI of 10% (CI, 9% to 12%) for a combined NRI of 0.26 (*P* < 0.001), and hearing impairment yielded an event NRI of −4% (CI, −7% to −1%) and a nonevent NRI of 25% (CI, 23% to 27%) for a combined NRI of 0.21 (*P* = 0.008).

We used the results from our multivariable model to develop a Web-based calculator for 6-month mortality after discharge, which is available at www.silverscore.org (**Figure 4** of **Supplement 1**). To illustrate, consider 2 hypothetical patients, both aged 85 years, who undergo percutaneous coronary intervention and have an admission heart rate of 90 beats/min, estimated glomerular filtration rate of 60 mL/min/1.73 m^2, hemoglobin level of 120 g/L, mildly decreased ejection fraction, length of stay of 5 days, no peripheral artery disease, and no sleep apnea (**Figure 5** of **Supplement 1**). If the first patient reports that hearing interferes with activities "a lot," has fair health status, has a TUG greater than 25 seconds, and reports unintentional weight loss of more than 10 pounds in the past year, the predicted risk for death within 6 months is 22% using the SILVER-AMI model. Conversely, if the second patient reports that hearing interferes with activities "a little," has good health status, has a TUG of 15 seconds or less, and denies unintentional weight loss of more than 10 pounds in the past year, the predicted risk for death within 6 months is 5% using the SILVER-AMI model.

DISCUSSION

In our sample of patients aged 75 years or older, 15 risk factors were selected for inclusion in the prediction model of death within 6 months of hospitalization for AMI. These included comorbid diseases, laboratory values, in-hospital procedures, and functional impairments. Our model had good discrimination and was well calibrated. Functional impairments enhanced the predictive ability of the model, as demonstrated by their retention in the final model and by the NRI indices. We are unaware of any other postdischarge AMI mortality risk models specifically developed for older adults.

Risk prediction is critical to informed decision making for older adults with AMI and, in the context of discharge planning, can help identify high-risk patients who may benefit from closer outpatient monitoring and potentially more aggressive secondary preventive measures, including multidrug lipid-lowering therapy and cardiac rehabilitation. In addition, for patients at the highest risk, setting expectations for patients and family members and early involvement of palliative care may be appropriate.

The GRACE 6-month mortality risk score is the most commonly cited model for prediction of mortality after hospital discharge in the setting of AMI (4, 10, 29). It was developed from a registry of patients with acute coronary syndrome (AMI and unstable angina) at a mean age of 65 years (4). Like the SILVER-AMI model, the GRACE model excluded patients who died in the hospital. Several variables in the GRACE model (age, heart rate, serum creatinine level, and revascularization status) were also retained in the final SILVER-AMI model, reflecting shared risk factors that are clinically plausible predictors of mortality. When we applied the GRACE risk score in the SILVER-AMI validation cohort, we found discrimination similar to that in the original GRACE validation cohort (AUC = 0.76), indicating that the score performs reasonably well in our cohort and suggesting that many factors identified by GRACE de-

Table 3. Standard Operating Characteristics From Application of the SILVER-AMI Model to the SILVER-AMI Validation Cohort for Death Within 180 Days (*n* = 1002)

Characteristic	Sensitivity (95% CI)*				
	0.71 (0.68–0.74)	0.76 (0.73–0.78)	0.80 (0.78–0.83)	0.85 (0.83–0.88)	0.90 (0.88–0.92)
Specificity (95% CI)	0.82 (0.80–0.85)	0.77 (0.75–0.80)	0.73 (0.71–0.76)	0.60 (0.57–0.63)	0.55 (0.52–0.58)
Positive predictive value (95% CI)	0.26 (0.24–0.29)	0.23 (0.20–0.26)	0.21 (0.19–0.24)	0.16 (0.14–0.18)	0.15 (0.13–0.17)
Negative predictive value (95% CI)	0.97 (0.96–0.98)	0.97 (0.96–0.98)	0.98 (0.97–0.99)	0.98 (0.97–0.99)	0.98 (0.98–0.99)

SILVER-AMI = Comprehensive Evaluation of Risk in Older Adults with Acute Myocardial Infarction.
* Due to risk model differences, sensitivity values in Tables 2 and 3 are statistically equivalent rather than numerically identical.

note risk across the age spectrum. Although the SILVER-AMI risk score showed better predictive accuracy than the GRACE model in our validation cohort, some degradation of performance is expected when a risk score is applied to an external data set. Applying the SILVER-AMI score to a different population (that is, external validation) may yield less favorable estimates of performance. The GRACE and SILVER-AMI scores may also give different estimates of risk for some patients. As illustrated by the hypothetical examples, patients with functional impairments have substantially higher mortality risk according to the SILVER-AMI risk score, and these are not considered in the GRACE score. Although the importance of functional impairment is supported by their retention in the final SILVER-AMI model and their NRIs, the SILVER-AMI score has not been externally validated. It is therefore important that estimates be used judiciously and incorporated into the totality of clinical information, including response to and tolerance of therapies and goals of care.

Our study was designed to explicitly consider functional impairments and other conditions common with aging given that these factors are independently associated with adverse post-AMI outcomes (11, 12). Two impairments were retained in our final risk model: hearing and mobility. The association between hearing impairment and mortality may be mediated by patients' difficulty in comprehending complex medication and follow-up instructions at the time of hospital discharge, which may interfere with subsequent care (39, 40). We selected a mobility measure (TUG) that is a key indicator of frailty (41). Frail patients are at increased risk for death, likely due to an inability to maintain homeostasis in the settings of acute events (such as infection or injury) and chronic functional decline (42, 43). Weight loss, another factor retained in our model, is also a common frailty indicator and may be a marker of underlying advanced disease.

Of note, CABG was protective in our model. Although this may seem counterintuitive given that patients undergoing CABG typically have more severe atherosclerosis and a higher incidence of in-hospital complications, similar findings have been reported in other cohorts (44). The most likely explanation is selection bias given that patients referred for CABG were judged by surgeons as robust enough to withstand a major operation. We captured a broad range of comorbidities and functional impairments, but this selection process may not have been fully accounted for in our multivariable model.

Several limitations of our study deserve consideration. First, although we internally validated our prediction model, we did not evaluate its performance in an external data set. Second, rates of vision and hearing impairment in our sample were lower than in other published studies (45, 46), perhaps because these impairments posed a barrier to study participation. Furthermore, the mortality rate in SILVER-AMI was lower than in some cohort studies of older adults (47, 48), which may reflect lower mortality with improvements in AMI care over time (49, 50) or possibly a healthy en-

rollee effect. Third, our model requires information on functional impairments, which are not typically assessed as part of routine inpatient care. Collectively, the assessments required for our model should take less than 10 minutes to complete. Fourth, we were unable to distinguish between cardiovascular and noncardiovascular causes of death in about a third of participants. Inaccuracies in cause-of-death reporting are common (51), and assigning a single primary cause may be even more challenging in older populations. Fifth, the SILVER-AMI model is characterized by a modest positive predictive value, an inherent limitation of population-based models of low-incidence outcomes (52, 53). Finally, we recognize that there is a potential for misuse of risk models by health systems (for example, to justify withholding care). However, we are unaware of any such misuse with other risk models, and we believe it is important to provide patients and clinicians with information about their predicted outcomes based on the highest-quality data.

In conclusion, we developed a novel risk model for mortality within 6 months of hospitalization for AMI in patients aged 75 years or older that considered traditional risk factors, functional impairments, and other conditions common with aging. We found that several factors relevant to older adults and not considered in prior AMI risk models were independently associated with mortality. Our model was well calibrated; had good discrimination; and, with use of a Web-based calculator, can be used to inform prognostication at the time of hospital discharge.

From New York University School of Medicine, New York, New York (J.A.D.); Yale School of Medicine, New Haven, Connecticut (A.M.H., M.G., T.E.M., S.T., M.E.T., T.M.G., S.I.C.); Yale New Haven Hospital, Yale School of Medicine, and Yale School of Public Health, New Haven, Connecticut (H.M.K.); Duke University School of Medicine, Durham, North Carolina (M.G.N.); and Spectrum Health, Grand Rapids, Michigan (R.M.).

Corresponding Author: Sarwat I. Chaudhry, MD, Yale University School of Medicine, 367 Cedar Street, Room 416, New Haven, CT 06510; e-mail, Sarwat.chaudhry@yale.edu.

Current author addresses and author contributions are available at Annals.org.

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Current Author Addresses: Dr. Dodson: New York University School of Medicine, 227 East 30th Street, TRB 851, New York, NY 10016.

Drs. Hajduk, Murphy, Tinetti, Gill, and Chaudhry; Ms. Geda; and Ms. Tsang: Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510.

Dr. Krumholz: Yale University – Center for Outcomes Research & Evaluation, 1 Church Street, Suite 200, New Haven, CT 06510.

Dr. McNamara: SHMG Cardiovascular Medicine, 2900 Bradford Street NE, MC229, Grand Rapids, MI 49525-6427.

Dr. Nanna: Duke Clinical Research Institute, 200 Morris Street, Durham, NC 27701.

Author Contributions: Conception and design: J.A. Dodson, T.E. Murphy, M.G. Nanna, T.M. Gill, S.I. Chaudhry.

Analysis and interpretation of the data: J.A. Dodson, A.M. Hajduk, H.M. Krumholz, T.E. Murphy, S. Tsang, M.G. Nanna, S.I. Chaudhry.

Drafting of the article: J.A. Dodson, A.M. Hajduk, T.E. Murphy, M.G. Nanna, S.I. Chaudhry.

Critical revision of the article for important intellectual content: J.A. Dodson, A.M. Hajduk, M. Geda, H.M. Krumholz, T.E. Murphy, M.E. Tinetti, M.G. Nanna, T.M. Gill, S.I. Chaudhry.

Final approval of the article: J.A. Dodson, A.M. Hajduk, M. Geda, H.M. Krumholz, T.E. Murphy, S. Tsang, M.E. Tinetti, M.G. Nanna, R. McNamara, T.M. Gill, S.I. Chaudhry.

Provision of study materials or patients: S.I. Chaudhry.

Statistical expertise: A.M. Hajduk, T.E. Murphy.

Obtaining of funding: T.M. Gill, S.I. Chaudhry.

Administrative, technical, or logistic support: M. Geda, S. Tsang, R. McNamara, S.I. Chaudhry.

Collection and assembly of data: M. Geda, S. Tsang, M.G. Nanna, R. McNamara, S.I. Chaudhry.