ORIGINAL RESEARCH

American Heart Association | American Stroke Association

Predicting Outcomes Over Time in Patients With Heart Failure, Left Ventricular Systolic Dysfunction, or Both Following Acute Myocardial Infarction

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***Background*—**Most studies of risk assessment or stratification in patients with myocardial infarction (MI) have been static and fail to account for the evolving nature of clinical events and care processes. We sought to identify predictors of mortality, cardiovascular death or nonfatal MI, and cardiovascular death or nonfatal heart failure (HF) over time in patients with HF, left ventricular systolic dysfunction, or both post-MI.

***Methods and Results*—**Using data from the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial, we developed models to estimate the association between patient characteristics and the likelihood of experiencing an event from the time of a follow-up visit until the next visit. The intervals are: hospital arrival to discharge or 14 days, whichever occurs first; hospital discharge to 30 days; 30 days to 6 months; and 6 months to 3 years. Models were also developed to predict the entire 3-year follow-up period using baseline information. Multivariable Cox proportional hazards modeling was used throughout with Wald chi-squares as the comparator of strength for each predictor. For the baseline model of overall mortality, the 3 strongest predictors were age (adjusted hazard ratio [HR], 1.35; 95% CI, 1.28–1.42; $P<0.0001$), baseline heart rate (adjusted HR, 1.17; 95% CI, 1.14–1.21; $P<0.0001$), and creatinine clearance (≤100 mL/min; adjusted HR, 0.86; 95% CI, 0.84–0.89; $P<0.0001$). According to the integrated discrimination improvement (IDI) and net reclassification improvement (NRI) indices, the updated model had significant improvement over the model with baseline covariates only in all follow-up periods and with all outcomes.

***Conclusions*—**Patient information assessed closest to the time of the outcome was more valuable in predicting death when compared with information obtained at the time of the index hospitalization. Using updated patient information improves prognosis over using only the information available at the time of the index event. **(*J Am Heart Assoc*. 2016;5:e003045 doi: 10.1161/JAHA.115.003045)**

Key Words: heart failure • left ventricular systolic dysfunction • myocardial infarction • risk factor

Patients with myocardial infarction (MI) complicated by heart failure (HF), left ventricular (LV) systolic dysfunction (LVSD), or both face a higher risk of in-hospital and postdischarge fatal and nonfatal ischemic and arrhythmic events than patients without these complications.[1–5] Although the management of patients with MI is dynamic, most studies of risk assessment or stratification in these patients have been static, derived only from data collected at admission[6–9] or discharge,[10] and have failed to account for the evolving nature of clinical measures and care processes. Updated stratification of risk at follow-up visits may allow clinicians to target those more likely to experience adverse events. This would allow clinicians to tailor intensity of treatment to severity of illness and may result in cost savings by avoiding unnecessary treatments in lower-risk patients.

Using data from the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial, we sought to identify predictors of in-hospital, 30-day, 6-month, and 3-year mortality; and cardiovascular death or MI, and cardiovascular death or HF in patients with HF, LVSD, or both post-MI. In particular, we examined whether baseline risk markers lost relevance over time with current physical findings supplanting these factors as the most potent predictors of risk in the next time interval.

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Methods

A detailed description of the VALIANT trial has been published.[11] In brief, 14 703 patents with MI complicated by HF, LVSD, or both were randomized a median of 4.9 days post-MI. VALIANT was a double-blind, randomized, controlled trial of treatment with valsartan, captopril, or both in patients with acute MI complicated by HF, LVSD, or both. Patients were enrolled at 931 hospitals in 24 countries between December 1998 and June 2001. Median duration of follow-up was 24.7 months. We analyzed data collected at discharge (or at 14 days if the patient was still hospitalized), 30 days±15, and 180 days±15.

An institutional review board or ethics committee at each participating site approved the VALIANT trial protocol, and all patients provided informed consent.

Statistical Analysis

Baseline data were nearly complete. There were very few missing observations for any one variable. Across the baseline parameters used, this ranged from 0% to 3%. In the postbaseline factors, no variable exhibited more than 10% missingness. Markov chain Monte Carlo imputation was used to complete the data set for modeling. Multiple imputation methodology was applied to the mortality model as well as single imputation, and changes in estimates were negligible when comparing the 2 methods; therefore, only single imputation was used in the analyses presented. A series of models were developed to predict outcomes as follows: data collected before randomization into the VALIANT study (baseline data) were used to predict to 3 years; baseline data were used to predict outcomes to discharge from the index hospitalization; baseline through hospital discharge data were used to predict outcomes to 30 days; baseline through 30 days data were used to predict outcomes to 6 months; and baseline through 6 months data were used to predict outcomes to 3 years. These prediction intervals approximate the information a physician has at the time of a follow-up visit. The models were developed to see how well this information can predict status post-visit until the patient returns for a subsequent visit. Three endpoints were considered in this modeling process—all-cause mortality, cardiovascular death or HF resulting in hospitalization, and cardiovascular death or MI. Cardiovascular death was defined as any death adjudicated as cardiovascular, including the following categories: sudden death; presumed cardiovascular death; fatal heart failure; fatal reinfarction; cardiovascular-procedure–related death; fatal stroke; and death from other cardiovascular death.[11,12]

Forty-six baseline candidate variables, chosen based on clinical input, were considered. These variables included medical history, events post-qualifying MI and before randomization, geographical region, vital signs, randomized treatment, and creatinine levels at randomization. For the models starting after hospital discharge, the following additional variables were considered during follow-up visits: heart rate; blood pressure; hospitalization for HF; cardiac arrest; MI; unstable angina; stroke; New York Heart Association (NYHA) class; use of an automatic implantable cardioverter defibrillator; percutaneous coronary intervention (PCI); coronary artery bypass graft (CABG) surgery; and nonrandomized use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. If a nonfatal event or treatment occurred during any previous follow-up period, it was included as a covariate in subsequent models. For heart rate, blood pressure, and NYHA classification, only measures from the visits preceding the follow-up period of interest and at baseline were used.

Multivariable Cox proportional hazards modeling was used throughout. The assumptions of linearity for each model were assessed for continuously distributed candidate variables using restricted cubic splines. In all cases, either contiguous linear splines or truncation of the variable were deemed adequate to meet assumptions of linearity. When possible, the same knot point for linear splines and truncations was used across all models to make interpretation easier. Backward, forward, and step-wise variable selections were performed using a P value of 0.05 for inclusion and retention. If a difference existed between the resulting models, the likelihood ratio tests and Akaike's information criterion were compared to determine the final model. All models were regenerated using the baseline characteristics only to examine improvement in discrimination and calibration with the inclusion of time-sensitive variables. The relative importance of variables within each model was ranked according to the model Wald chi-squares.

Discrimination was described with the c-index, integrated discrimination improvement (IDI) index, and net reclassification improvement (NRI) index.[13,14] The horizon of follow-up for all measures was the length of the follow-up period. Events occurring after the follow-up period were considered non-events for the period of interest. Probability curves were created for the last 3 follow-up periods.[15] These curves illustrate the distribution of predicted probabilities for models with and without the time-sensitive factors. They also include deciles of actual versus predicted risk as a measure of the calibration of each model. These curves allow the reader to note the distribution of risk across the population, if and where the distribution is different for the 2 models, and how well the models agree with the actual distribution of risk.

The NRI index evaluates the movement between risk categories based on the predicted probabilities of 2 models. Four risk categories were chosen approximately at the quartiles. The better of 2 models would predict higher event rates for those with the event and lower event rates for those

Table 1. Predictors of Death Over Time

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Age, y*	1	129.41	1.35 (1.28, 1.42)	9	7.41	1.19 (1.05, 1.35)	3	33.96	1.58 (1.36, 1.85)	9	13.38	1.21 (1.09, 1.34)	1	193.58	—
Age (≤60†)*	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.25 (1.07, 1.47)
Age (>60†)*	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.59 (1.47, 1.72)
Region (North America is reference)	6	50.63	—	—	—	—	12	11.78	—	7	27.25	—	16	17.26	—
South America	—	—	1.51 (1.28, 1.78)	—	—	—	—	—	2.05 (1.25, 3.34)	—	—	1.75 (1.28, 2.38)	—	—	1.37 (1.06, 1.77)
East Europe	—	—	1.40 (1.25, 1.56)	—	—	—	—	—	1.61 (1.11, 2.34)	—	—	1.01 (0.80, 1.29)	—	—	1.13 (0.95, 1.33)
West Europe	—	—	1.06 (0.96, 1.17)	—	—	—	—	—	1.19 (0.86, 1.63)	—	—	0.78 (0.63, 0.97)	—	—	0.87 (0.75, 1.01)
Female	—	—	—	—	—	—	17	3.82	0.78 (0.61, 1.00)	—	—	—	34	1.92	0.92 (0.81, 1.04)
Time to randomization‡	—	—	—	5	25.93	—	—	—	—	—	—	—	21	8.32	1.03 (1.01, 1.05)
0 to 72 hours†	—	—	—	—	—	0.76 (0.64, 0.91)	—	—	—	—	—	—	—	—	—
72 to 216 hours†	—	—	—	—	—	1.00 (0.94, 1.06)	—	—	—	—	—	—	—	—	—
>216 hours†	—	—	—	—	—	0.14 (0.04, 0.45)	—	—	—	—	—	—	—	—	—
Baseline HR*	2	126.34	1.17 (1.14, 1.21)	1	92.97	1.37 (1.28, 1.46)	—	—	—	—	—	—	—	—	—
Baseline SBP*	10	28.71	0.93 (0.90, 0.95)	—	—	—	—	—	—	—	—	—	—	—	—
DBP	15	16.34	—	—	—	—	—	—	—	—	—	—	—	—	—
DBP (≤70†)*	—	—	0.96 (0.90, 1.03)	—	—	—	—	—	—	—	—	—	—	—	—
DBP (>70†)*	—	—	1.14 (1.07, 1.21)	—	—	—	—	—	—	—	—	—	—	—	—

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Table 1. Continued

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Height, cm*	—	—	—	—	—	—	—	—	—	26	2.51	1.08 (0.98, 1.19)	—	—	—
Weight, kg*	16	15.88	—	4	19.78	1.17 (1.09, 1.25)	—	—	—	27	2.74	—	—	—	—
Weight (≤100†)*	—	—	1.03 (0.99, 1.06)	—	—	—	—	—	—	—	—	0.94 (0.87, 1.02)	—	—	—
Weight (>100†)*	—	—	1.13 (1.05, 1.22)	—	—	—	—	—	—	—	—	1.06 (0.91, 1.24)	—	—	—
Baseline CrCl	3	110.49	—	2	44.71	—	11	8.09	0.92 (0.87, 0.97)	8	22.05	—	—	—	—
CrCl (≤100†)*	—	—	0.86 (0.84, 0.89)	—	—	0.79 (0.74, 0.85)	—	—	—	—	—	0.89 (0.84, 0.94)	—	—	—
CrCl (>100†)*	—	—	1.01 (0.99, 1.03)	—	—	1.02 (0.99, 1.06)	—	—	—	—	—	1.03 (1.00, 1.06)	—	—	—
Pulse pressure index§	—	—	—	6	11.25	0.79 (0.69, 0.91)	—	—	—	—	—	—	—	—	—
MAP	—	—	—	3	36.33	—	—	—	—	28	2.74	—	—	—	—
MAP (≤85†)*	—	—	—	—	—	0.58 (0.46, 0.73)	—	—	—	—	—	0.89 (0.74, 1.07)	—	—	—
MAP (>85†)*	—	—	—	—	—	0.92 (0.81, 1.04)	—	—	—	—	—	1.07 (0.98, 1.17)	—	—	—
Killip class 3 or 4 at baseline (1 or 2 is the reference)	8	35.26	1.28 (1.18, 1.39)	8	7.98	1.35 (1.10, 1.66)	—	—	—	6	21.26	1.47 (1.25, 1.74)	22	7.91	1.18 (1.05, 1.32)
ECG site: anterior	18	9.69	1.13 (1.05, 1.22)	—	—	—	—	—	—	—	—	—	—	—	—
ECG type: new LBBB	14	15.45	1.34 (1.16, 1.55)	—	—	—	—	—	—	17	6.58	1.45 (1.09, 1.93)	31	4.87	1.27 (1.03, 1.56)
ECG type: Q-wave	24	6.86	0.90 (0.82, 0.97)	—	—	—	—	—	—	—	—	—	24	6.97	0.86 (0.76, 0.96)
Current smoking at baseline	7	37.27	1.35 (1.23, 1.49)	—	—	—	—	—	—	10	12.66	1.42 (1.17, 1.72)	7	28.96	1.54 (1.31, 1.80)

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Table 1. Continued

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Previous smoking at baseline	—	—	—	—	—	—	—	—	—	—	—	—	15	12.30	1.27 (1.11, 1.46)
History of alcohol abuse	21	8.49	1.47 (1.14, 1.91)	12	6.59	2.21 (1.21, 4.04)	—	—	—	—	—	—	—	—	—
History of angina	12	22.50	1.23 (1.13, 1.33)	—	—	—	19	3.53	1.27 (0.99, 1.64)	20	6.03	1.24 (1.04, 1.48)	18	11.45	1.23 (1.09, 1.39)
History of HF	9	31.35	1.31 (1.19, 1.44)	—	—	—	—	—	—	21	5.20	1.25 (1.03, 1.51)	13	19.03	1.33 (1.17, 1.52)
History of COPD	23	7.22	1.17 (1.04, 1.31)	—	—	—	—	—	—	—	—	—	—	—	—
History of diabetes	—	—	—	—	—	—	10	11.01	1.52 (1.19, 1.95)	2	24.04	1.53 (1.29, 1.81)	9	25.93	1.36 (1.21, 1.54)
New diabetes	—	—	—	—	—	—	16	4.83	1.68 (1.06, 2.68)	15	6.99	1.60 (1.13, 2.26)	20	8.66	1.46 (1.13, 1.88)
History of hypertension	—	—	—	—	—	—	—	—	—	—	—	—	26	6.36	1.17 (1.04, 1.32)
History of dyslipidemia	—	—	—	—	—	—	18	3.69	0.77 (0.59, 1.01)	—	—	—	29	5.16	0.87 (0.76, 0.98)
History of MI	5	57.68	1.40 (1.28, 1.52)	—	—	—	7	12.12	1.55 (1.21, 1.98)	19	6.33	1.25 (1.05, 1.50)	3	49.42	1.55 (1.37, 1.75)
History of PCI	—	—	—	—	—	—	—	—	—	—	—	—	27	5.92	0.77 (0.62, 0.95)
History of primary PTCR	—	—	—	14	3.86	0.69 (0.48, 1.00)	—	—	—	22	4.89	0.71 (0.53, 0.96)	25	6.59	0.75 (0.61, 0.94)
History of PAD	22	7.95	1.17 (1.05, 1.31)	—	—	—	—	—	—	—	—	—	—	—	—
History of stroke	19	9.58	1.22 (1.07, 1.38)	—	—	—	—	—	—	23	4.63	1.31 (1.02, 1.66)	—	—	—
History of TIA	—	—	—	11	6.74	0.31 (0.13, 0.75)	—	—	—	—	—	—	19	10.25	1.47 (1.16, 1.85)
History of unstable angina	—	—	—	15	3.51	1.24 (0.99, 1.55)	—	—	—	—	—	—	—	—	—
AF post-qualifying MI	11	25.94	1.28 (1.16, 1.41)	—	—	—	15	5.23	1.36 (1.05, 1.78)	—	—	—	8	26.37	1.42 (1.24, 1.62)

Continued

Table 1. Continued

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
AICD post-qualifying MI	—	—	—	—	—	—	—	—	—	—	—	—	28	5.89	2.11 (1.16, 3.87)
Angina post-qualifying MI	—	—	—	13	4.11	1.26 (1.01, 1.58)	—	—	—	—	—	—	33	2.37	0.90 (0.79, 1.03)
CABG post-qualifying MI	—	—	—	—	—	—	—	—	—	24	4.36	0.35 (0.13, 0.94)	23	7.22	0.56 (0.36, 0.85)
HF post-qualifying MI	13	18.06	1.20 (1.10, 1.31)	7	9.89	1.44 (1.15, 1.80)	—	—	—	—	—	—	—	—	—
Diabetes mellitus post-qualifying MI	4	66.84	1.41 (1.30, 1.52)	—	—	—	—	—	—	—	—	—	—	—	—
PCI post-qualifying MI	—	—	—	—	—	—	—	—	—	—	—	—	12	19.18	0.66 (0.55, 0.79)
VFIB post-qualifying MI	—	—	—	—	—	—	—	—	—	—	—	—	30	4.95	0.66 (0.46, 0.95)
Previous hospitalization	20	8.63	1.15 (1.05, 1.27)	—	—	—	—	—	—	18	6.51	1.28 (1.06, 1.55)	—	—	—
NYHA class 3 or 4 at start of given time period (reference is 1 or 2)	—	—	—	—	—	—	5	18.86	1.75 (1.36, 2.26)	1	24.48	1.57 (1.31, 1.88)	6	31.38	1.46 (1.28, 1.66)
HR change from baseline to start of given time period*	—	—	—	—	—	—	8	11.47	1.16 (1.06, 1.26)	29	0.10	1.01 (0.95, 1.07)	32	4.78	1.05 (1.00, 1.09)
HR at start of given time period*	—	—	—	—	—	—	1	72.99	—	3	23.90	1.15 (1.09, 1.22)	2	63.64	1.20 (1.15, 1.25)
HR at start of given time period (≤70†)*	—	—	—	—	—	—	—	—	0.88 (0.70, 1.12)	—	—	—	—	—	—
HR at start of given time period (>70†)*	—	—	—	—	—	—	—	—	1.65 (1.47, 1.85)	—	—	—	—	—	—
MAP at start of given time period*	—	—	—	—	—	—	6	13.15	0.63 (0.49, 0.81)	—	—	—	10	23.77	0.90 (0.86, 0.94)
HF (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	2	62.65	3.29 (2.45, 4.42)	4	23.74	1.75 (1.40, 2.19)	4	39.37	1.58 (1.37, 1.83)

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Table 1. Continued

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
MI (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	4	27.83	3.45 (2.18, 5.46)	13	7.70	1.57 (1.14, 2.16)	14	14.53	1.42 (1.18, 1.70)
Clinical evidence of HF	—	—	—	—	—	—	—	—	—	11	9.49	1.42 (1.14, 1.78)	—	—	—
Imaging evidence of LVSD	—	—	—	—	—	—	—	—	—	14	7.32	1.25 (1.06, 1.47)	—	—	—
AICD (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	16	6.83	2.34 (1.24, 4.43)	—	—	—
CABG (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	9	11.32	2.45 (1.45, 4.12)	—	—	—	5	38.90	0.40 (0.30, 0.53)
Catheterization (any time from qualifying MI to start of given time period)	—	—	—	10	6.91	0.70 (0.53, 0.91)	20	2.65	0.76 (0.54, 1.06)	25	3.76	0.80 (0.64, 1.00)	—	—	—
Renal insufficiency (any time from qualifying MI to start of given time period)	17	12.51	1.28 (1.12, 1.47)	—	—	—	—	—	—	—	—	—	—	—	—
PTCA (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	—	—	—	17	11.56	0.69 (0.55, 0.85)
Rehospitalization (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	12	8.05	1.33 (1.09, 1.61)	11	19.66	1.33 (1.17, 1.50)

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Table 1. Continued

Parameter	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 282)			30 Days to 6 Months (N=13 955)			6 Months to 3 Years (N=13 247)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Stroke (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	14	5.54	2.48 (1.16, 5.29)	5	21.63	2.93 (1.86, 4.60)	—	—	—
DBP at start of given time period*	—	—	—	—	—	—	13	6.55	1.44 (1.09, 1.90)	—	—	—	—	—	—

AF indicates atrial fibrillation; AICD, automatic implantable cardioverter defibrillator; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; DBP, diastolic blood pressure; ECG, electrocardiogram; HF, heart failure; HR, heart rate; LBBB, left bundle branch block; LVSD, left ventricular systolic dysfunction; MAP, mean arterial pressure; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PTCR, percutaneous transluminal coronary revascularization; SBP, systolic blood pressure; TIA, transient ischemic attack; VFIB, ventricular fibrillation.

*Hazard ratio is for an increase in 10 units (eg, for age, 1.35 implies a 35% increase in risk for every additional 10 years of age).

†Variable is a linear spline for values in the listed range.

‡Hazard ratio is for an increase of 24 hours.

§Pulse pressure index=pulse pressure/systolic blood pressure; where pulse pressure=systolic−diastolic blood pressures.

without. Therefore, movement of events into a higher-risk category and nonevents into a lower-risk category is considered improvement. Likewise, movement of events into a lower-risk category and nonevents into a higher-risk category is considered worsening of classification. The NRI index is the sum of the percent improvement, for events and nonevents, achieved by using the model with time-updated variables versus the model with baseline covariates only. Those lost to follow-up before the specified time horizon were handled using Kaplan–Meier estimates of the expected number of events and nonevents ("prospective NRI").[13]

$$\mathrm{NRI} = (a + b)_{\mathrm{events}} + (b - a)_{\mathrm{nonevents}}$$

a = proportion in higher-risk category based on predicted values from a model using time-updated variables rather than a model using baseline variables only. b = proportion in lower-risk category based on predicted values from a model using time-updated variables rather than a model using baseline variables only.

The IDI index is the difference in discrimination slopes under 2 models where the discrimination slope is the difference in the average predicted probabilities for events and nonevents. It can be interpreted as the percent improvement in discrimination attained by using the time-updated model over the model with baseline covariates only.

$$\mathrm{IDI} = c - d$$

c = (mean predicted probability in patients with events−mean predicted probability in patients without events) in the time-updated model. d = (mean predicted probability in patients with events−mean predicted probability in patients without events) in the baseline model.

All models were developed using SAS software (versions 8.2 and 9.1; SAS Institute Inc., Cary, NC).

Results

Mortality Model

The main predictors of mortality at the different time points are shown in Table 1. For overall mortality, the 5 strongest predictors were age (adjusted hazard ratio [HR], 1.35 per 10 years; 95% CI, 1.28–1.42; $P<0.0001$), baseline heart rate (adjusted HR, 1.17 per 10 beats/min; 95% CI, 1.14–1.21; $P<0.0001$), creatinine clearance (≤100 mL/min; adjusted HR, 0.86 per 10 units; 95% CI, 0.84–0.89; $P<0.0001$), new onset diabetes (adjusted HR, 1.41; 95% CI, 1.30–1.52; $P<0.0001$), and MI before the qualifying MI (adjusted HR, 1.40; 95% CI, 1.28–1.52; $P<0.0001$). The same factors were the 5 most significant for the composite outcome of cardiovascular death or MI to 3 years (Table 2). For cardiovascular death or HF,

Table 2. Predictors of Cardiovascular Death or MI Over Time

	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 178)			30 Days to 6 Months (N=13 784)			6 Months to 3 Years (N=12 969)		
Variable	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Age, y*	3	80.06	—	12	7.07	1.15 (1.04, 1.28)	10	9.45	1.20 (1.07, 1.34)	12	12.95	—	3	53.14	—
Age (≤60†)*	—	—	1.01 (0.92, 1.11)	—	—	—	—	—	—	—	—	0.97 (0.82, 1.15)	—	—	0.91 (0.80, 1.05)
Age (>60†)*	—	—	1.30 (1.23, 1.38)	—	—	—	—	—	—	—	—	1.21 (1.09, 1.35)	—	—	1.37 (1.26, 1.49)
Region (North America is reference)	—	—	—	15	6.27	—	—	—	—	26	5.54	—	35	4.21	—
South America	—	—	—	—	—	1.19 (0.82, 1.72)	—	—	—	—	—	1.19 (0.91, 1.56)	—	—	1.01 (0.79, 1.30)
East Europe	—	—	—	—	—	1.00 (0.78, 1.28)	—	—	—	—	—	0.96 (0.81, 1.13)	—	—	1.03 (0.89, 1.19)
West Europe	—	—	—	—	—	1.25 (1.02, 1.54)	—	—	—	—	—	0.88 (0.75, 1.03)	—	—	0.90 (0.79, 1.03)
Female	—	—	—	—	—	—	—	—	—	—	—	—	26	7.11	0.85 (0.75, 0.96)
Black	25	5.38	1.25 (1.04, 1.51)	—	—	—	—	—	—	—	—	—	21	8.68	1.46 (1.14, 1.88)
Time to randomization‡	—	—	—	3	21.56	0.92 (0.89, 0.95)	12	7.24	0.95 (0.92, 0.99)	—	—	—	—	—	—
Baseline HR*	1	108.16	—	1	76.68	—	6	14.69	—	20	6.67	1.07 (1.02, 1.12)	—	—	—
HR (≤70†)*	—	—	1.00 (0.91, 1.09)	—	—	1.09 (0.86, 1.37)	—	—	0.92 (0.72, 1.17)	—	—	—	—	—	—
HR (>70†)*	—	—	1.18 (1.14, 1.22)	—	—	1.31 (1.22, 1.40)	—	—	1.17 (1.08, 1.27)	—	—	—	—	—	—
Baseline SBP*	—	—	—	6	9.06	0.86 (0.78, 0.95)	—	—	—	—	—	—	24	8.04	1.04 (1.01, 1.07)
Weight, kg*	12	22.85	—	5	10.65	1.10 (1.04, 1.17)	—	—	—	—	—	—	34	4.91	—
Weight (≤100†)*	—	—	1.10 (1.05, 1.15)	—	—	—	—	—	—	—	—	—	—	—	1.03 (0.98, 1.08)
Weight (>100†)*	—	—	1.13 (1.04, 1.23)	—	—	—	—	—	—	—	—	—	—	—	1.08 (0.99, 1.18)

Continued

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Table 2. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 178)			30 Days to 6 Months (N=13 784)			6 Months to 3 Years (N=12 969)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Baseline CrCl	2	95.29	—	2	35.68	—	4	25.13	—	2	33.74	—	11	28.37	—
CrCl (≤100†)*	—	—	0.88 (0.86, 0.91)	—	—	0.84 (0.79, 0.89)	—	—	0.87 (0.83, 0.92)	—	—	0.90 (0.86, 0.93)	—	—	0.91 (0.88, 0.94)
CrCl (>100†)*	—	—	1.01 (1.00, 1.03)	—	—	1.02 (0.98, 1.05)	—	—	0.98 (0.91, 1.06)	—	—	1.02 (1.00, 1.05)	—	—	1.00 (0.97, 1.03)
MAP	29	5.94	—	13	8.58	—	—	—	—	—	—	—	—	—	—
MAP (≤85†)*	—	—	0.90 (0.83, 0.98)	—	—	0.83 (0.68, 1.01)	—	—	—	—	—	—	—	—	—
MAP (>85†)*	—	—	1.01 (0.96, 1.06)	—	—	1.21 (1.01, 1.45)	—	—	—	—	—	—	—	—	—
PP	18	12.27	—	—	—	—	—	—	—	—	—	—	—	—	—
PP (≤42†)*	—	—	0.86 (0.78, 0.95)	—	—	—	—	—	—	—	—	—	—	—	—
PP (>42†)*	—	—	0.99 (0.96, 1.02)	—	—	—	—	—	—	—	—	—	—	—	—
Killip class 3 or 4 at baseline (1 or 2 is the reference)	7	33.02	1.26 (1.16, 1.36)	7	8.89	1.31 (1.10, 1.57)	—	—	—	7	20.38	1.36 (1.19, 1.56)	17	11.07	1.20 (1.08, 1.34)
ECG site: anterior	30	3.72	1.07 (1.00, 1.15)	—	—	—	—	—	—	—	—	—	—	—	—
ECG type: new LBBB	9	27.50	1.44 (1.25, 1.64)	—	—	—	—	—	—	10	16.26	1.61 (1.28, 2.02)	25	7.74	1.32 (1.08, 1.60)
Current smoking at baseline	8	27.97	1.27 (1.16, 1.39)	—	—	—	—	—	—	3	27.34	1.51 (1.29, 1.76)	15	15.45	1.34 (1.16, 1.55)
Previous smoking at baseline	—	—	—	—	—	—	—	—	—	—	—	—	20	9.17	1.21 (1.07, 1.37)
History of AF	—	—	—	—	—	—	13	7.08	1.44 (1.10, 1.88)	—	—	—	—	—	—
History of alcohol abuse	22	5.98	1.36 (1.06, 1.75)	—	—	—	—	—	—	—	—	—	—	—	—
History of angina	6	39.99	1.29 (1.19, 1.40)	—	—	—	11	9.10	1.35 (1.11, 1.63)	9	16.98	1.34 (1.17, 1.55)	9	25.46	1.33 (1.19, 1.48)
History of HF	11	20.84	1.23 (1.13, 1.35)	—	—	—	—	—	—	24	4.74	1.19 (1.02, 1.39)	12	20.15	1.32 (1.17, 1.49)

Continued

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Table 2. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 178)			30 Days to 6 Months (N=13 784)			6 Months to 3 Years (N=12 969)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
History of diabetes	—	—	—	—	—	—	—	—	—	1	30.25	1.47 (1.28, 1.69)	7	37.77	1.42 (1.27, 1.58)
New diabetes	—	—	—	—	—	—	—	—	—	17	7.32	1.51 (1.12, 2.03)	23	8.13	1.41 (1.11, 1.78)
History of hypertension	19	8.04	1.12 (1.04, 1.21)	—	—	—	—	—	—	—	—	—	31	4.32	1.13 (1.01, 1.26)
History of dyslipidemia	27	5.04	0.91 (0.84, 0.99)	—	—	—	—	—	—	—	—	—	—	—	—
History of MI	4	72.41	1.42 (1.31, 1.55)	—	—	—	9	9.63	1.36 (1.12, 1.65)	5	23.86	1.43 (1.24, 1.65)	4	44.99	1.46 (1.31, 1.63)
History of primary PTCR	14	11.23	0.80 (0.70, 0.91)	9	8.38	0.65 (0.48, 0.87)	—	—	—	—	—	—	—	—	—
History of PAD	16	10.62	1.19 (1.07, 1.32)	—	—	—	—	—	—	18	7.19	1.28 (1.07, 1.53)	30	4.66	1.17 (1.01, 1.35)
History of stroke	17	9.65	1.21 (1.07, 1.36)	—	—	—	—	—	—	—	—	—	—	—	—
History of TIA	28	4.46	1.19 (1.01, 1.41)	14	5.32	0.49 (0.27, 0.90)	—	—	—	—	—	—	18	10.83	1.44 (1.16, 1.79)
History of unstable angina	20	6.90	1.12 (1.03, 1.22)	4	18.32	1.51 (1.25, 1.82)	—	—	—	—	—	—	—	—	—
AF post-qualifying MI	21	6.58	1.13 (1.03, 1.24)	—	—	—	—	—	—	—	—	—	22	8.61	1.22 (1.07, 1.39)
AICD post-qualifying MI	—	—	—	—	—	—	—	—	—	—	—	—	29	5.05	1.94 (1.09, 3.46)
Angina post-qualifying MI	—	—	—	11	7.38	1.29 (1.07, 1.56)	—	—	—	—	—	—	—	—	—
CABG post-qualifying MI	10	25.21	0.42 (0.30, 0.59)	—	—	—	—	—	—	14	9.18	0.29 (0.13, 0.64)	19	9.81	0.50 (0.33, 0.77)
HF post-qualifying MI	24	5.77	1.10 (1.02, 1.19)	10	7.51	1.30 (1.08, 1.56)	—	—	—	16	7.50	1.22 (1.06, 1.40)	—	—	—
Diabetes mellitus post-qualifying MI	5	71.96	1.40 (1.29, 1.51)	—	—	—	—	—	—	—	—	—	—	—	—
PCI post-qualifying MI	13	17.23	0.78 (0.70, 0.88)	—	—	—	—	—	—	—	—	—	6	40.08	0.60 (0.51, 0.70)

Continued

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Table 2. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 178)			30 Days to 6 Months (N=13 784)			6 Months to 3 Years (N=12 969)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
VFIB post-qualifying MI	—	—	—	8	8.53	1.69 (1.19, 2.40)	—	—	—	—	—	—	—	—	—
Sustained VTACH post-qualifying MI	—	—	—	—	—	—	—	—	—	25	4.51	0.63 (0.41, 0.97)	—	—	—
Previous hospitalization	15	10.68	1.16 (1.06, 1.27)	—	—	—	—	—	—	11	11.87	1.31 (1.12, 1.53)	—	—	—
NYHA class 3 or 4 at start of given time period (reference is 1 or 2)	—	—	—	—	—	—	5	17.03	1.55 (1.26, 1.90)	4	27.32	1.49 (1.28, 1.73)	10	25.44	1.37 (1.21, 1.56)
HR at start of given time period*	—	—	—	—	—	—	3	28.01	—	—	—	—	5	40.88	1.15 (1.10, 1.20)
HR at start of given time period (≤70†)*	—	—	—	—	—	—	—	—	0.91 (0.74, 1.11)	—	—	—	—	—	—
HR at start of given time period (>70†)*	—	—	—	—	—	—	—	—	1.28 (1.17, 1.40)	—	—	—	—	—	—
SBP at start of given time period*	—	—	—	—	—	—	8	9.96	0.93 (0.88, 0.97)	—	—	—	—	—	—
HF (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	1	45.80	2.49 (1.91, 3.24)	6	20.99	1.58 (1.30, 1.91)	8	31.46	1.45 (1.27, 1.65)
MI (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	2	35.08	3.24 (2.20, 4.78)	8	17.81	1.79 (1.36, 2.34)	2	49.53	1.78 (1.51, 2.09)
Clinical evidence of HF	23	5.84	1.12 (1.02, 1.23)	—	—	—	14	5.51	1.31 (1.05, 1.64)	—	—	—	—	—	—
Radiologic evidence of LV failure	—	—	—	—	—	—	—	—	—	—	—	—	33	3.52	1.10 (1.00, 1.22)
AICD (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	21	6.41	2.07 (1.18, 3.62)	32	3.99	0.57 (0.33, 0.99)
BMI	26	7.70	—	—	—	—	—	—	—	—	—	—	—	—	—
BMI (≤30†)	—	—	0.98 (0.96, 0.99)	—	—	—	—	—	—	—	—	—	—	—	—

Continued

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Table 2. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 178)			30 Days to 6 Months (N=13 784)			6 Months to 3 Years (N=12 969)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
BMI (>30†)	—	—	0.99 (0.97, 1.01)	—	—	—	—	—	—	—	—	—	—	—	—
CABG (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	15	7.79	0.56 (0.38, 0.84)	1	68.90	0.26 (0.19, 0.36)
Cardiac arrest with resuscitation (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	—	—	—	27	6.80	1.78 (1.15, 2.74)
PTCA (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	22	5.07	0.72 (0.54, 0.96)	13	17.14	0.67 (0.55, 0.81)
Rehospitalization (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	23	4.95	1.21 (1.02, 1.43)	—	—	—
Stroke (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	13	9.29	2.04 (1.29, 3.23)	28	6.57	1.59 (1.11, 2.26)
DBP at start of given time period*	—	—	—	—	—	—	—	—	—	—	—	—	16	13.19	0.92 (0.88, 0.96)
Unstable angina (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	7	9.96	1.63 (1.20, 2.20)	19	6.95	1.33 (1.08, 1.65)	14	16.07	1.33 (1.16, 1.53)

Values presented as hazard ratios (95% CIs). AICD indicates automatic implantable cardioverter defibrillator; AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft surgery; CrCl, creatinine clearance; DBP, diastolic blood pressure; ECG, electrocardiogram; HF, heart failure; HR, heart rate; LBBB, left bundle branch block; LV, left ventricular; MAP, mean arterial pressure; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PP, pulse pressure; PTCA, percutaneous transluminal coronary angioplasty; PTCR, percutaneous transluminal coronary revascularization; SBP, systolic blood pressure; TIA, transient ischemic attack; VFIB, ventricular fibrillation; VTACH, ventricular tachycardia.

*Hazard ratio is for an increase in 10 units (eg, for age, 1.20 implies a 20% increase in risk for every additional 10 years of age).

†Variable is a linear spline for values in the listed range.

‡Hazard ratio is for an increase of 24 hours.

Table 3. Predictors of Cardiovascular Death or HF Over Time

	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 163)			30 Days to 6 Months (N=13 757)			6 Months to 3 Years (N=12 934)		
Variable	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Age, y*	2	137.67	1.29 (1.24, 1.35)	3	30.03	1.26 (1.16, 1.37)	6	19.08	1.23 (1.12, 1.35)	6	27.85	1.21 (1.13, 1.30)	2	90.68	—
Age (≤60†)*	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.06 (0.92, 1.21)
Age (>60†)*	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1.40 (1.30, 1.51)
Region (North America is reference)	28	11.57	—	—	—	—	24	4.55	—	11	22.01	—	28	14.72	—
South America	—	—	1.16 (1.00, 1.34)	—	—	—	—	—	1.33 (0.98, 1.80)	—	—	1.33 (1.06, 1.67)	—	—	1.09 (0.88, 1.35)
East Europe	—	—	1.09 (0.99, 1.20)	—	—	—	—	—	1.11 (0.91, 1.35)	—	—	0.86 (0.73, 1.01)	—	—	0.91 (0.79, 1.04)
West Europe	—	—	0.96 (0.88, 1.05)	—	—	—	—	—	0.99 (0.82, 1.19)	—	—	0.81 (0.70, 0.94)	—	—	0.81 (0.71, 0.91)
Female	34	1.30	1.05 (0.96, 1.15)	—	—	—	—	—	—	32	1.51	1.08 (0.96, 1.21)	—	—	—
Black	—	—	—	—	—	—	—	—	—	—	—	—	13	21.63	1.66 (1.34, 2.05)
Time to randomization‡	—	—	—	10	9.90	0.96 (0.93, 0.98)	—	—	—	—	—	—	—	—	—
Baseline HR*	1	181.97	—	1	136.10	—	8	17.03	1.13 (1.06, 1.19)	9	18.57	1.10 (1.05, 1.15)	—	—	—
HR (≤70†)*	—	—	1.05 (0.97, 1.15)	—	—	1.14 (0.94, 1.39)	—	—	—	—	—	—	—	—	—
HR (>70†)*	—	—	1.20 (1.16, 1.24)	—	—	1.32 (1.25, 1.39)	—	—	—	—	—	—	—	—	—
Baseline SBP*	13	26.20	0.95 (0.93, 0.97)	2	43.18	0.87 (0.83, 0.91)	16	6.47	0.94 (0.89, 0.99)	—	—	—	—	—	—
Weight, kg*	9	41.68	—	—	—	—	22	4.37	1.06 (1.00, 1.12)	—	—	—	—	—	—
Weight (≤100†)*	—	—	1.03 (1.00, 1.06)	—	—	—	—	—	—	—	—	—	—	—	—
Weight (>100†)*	—	—	1.19 (1.13, 1.26)	—	—	—	—	—	—	—	—	—	—	—	—

Continued

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Table 3. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 163)			30 Days to 6 Months (N=13 757)			6 Months to 3 Years (N=12 934)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Baseline CrCl	7	48.94	0.94 (0.92, 0.96)	4	19.60	0.92 (0.89, 0.96)	4	19.31	0.91 (0.88, 0.95)	15	11.85	0.96 (0.94, 0.98)	25	12.03	0.97 (0.95, 0.98)
Killip class 3 or 4 at baseline (1 or 2 is the reference)	5	56.37	1.31 (1.22, 1.41)	6	17.84	1.35 (1.18, 1.56)	—	—	—	3	39.02	1.45 (1.29, 1.63)	11	25.04	1.28 (1.16, 1.41)
ECG site: anterior	19	18.07	1.15 (1.08, 1.23)	14	7.01	1.20 (1.05, 1.37)	—	—	—	23	6.54	1.16 (1.03, 1.29)	—	—	—
ECG type: new LBBB	14	25.92	1.38 (1.22, 1.56)	—	—	—	17	6.37	1.42 (1.08, 1.87)	27	5.39	1.29 (1.04, 1.60)	14	17.58	1.44 (1.22, 1.71)
ECG type: Q-wave	—	—	—	—	—	—	—	—	—	25	6.09	0.86 (0.77, 0.97)	—	—	—
Current smoking at baseline	8	47.81	1.34 (1.23, 1.45)	—	—	—	—	—	—	7	20.93	1.38 (1.20, 1.58)	8	33.37	1.46 (1.28, 1.66)
Previous smoking at baseline	—	—	—	—	—	—	—	—	—	—	—	—	20	15.20	1.24 (1.11, 1.38)
History of AF	29	6.67	1.16 (1.04, 1.30)	—	—	—	—	—	—	—	—	—	33	4.48	1.18 (1.01, 1.38)
History of alcohol abuse	—	—	—	9	9.94	1.96 (1.29, 2.97)	—	—	—	—	—	—	—	—	—
History of angina	22	14.37	1.15 (1.07, 1.24)	—	—	—	—	—	—	26	6.03	1.17 (1.03, 1.32)	18	15.90	1.23 (1.11, 1.36)
History of HF	6	55.32	1.37 (1.26, 1.48)	—	—	—	20	5.58	1.25 (1.04, 1.50)	4	35.57	1.51 (1.32, 1.72)	9	32.60	1.38 (1.24, 1.54)
History of COPD	31	4.91	1.12 (1.01, 1.23)	—	—	—	—	—	—	—	—	—	—	—	—
History of diabetes	3	112.59	1.48 (1.37, 1.59)	—	—	—	7	18.52	1.41 (1.21, 1.66)	2	40.04	1.47 (1.30, 1.66)	4	68.48	1.52 (1.37, 1.67)
New diabetes	18	18.14	1.39 (1.20, 1.62)	—	—	—	23	4.30	1.42 (1.02, 1.98)	22	6.76	1.42 (1.09, 1.84)	23	12.54	1.48 (1.19, 1.84)
History of hypertension	10	28.15	1.22 (1.13, 1.31)	17	5.20	1.18 (1.02, 1.36)	14	8.39	1.27 (1.08, 1.50)	13	13.68	1.29 (1.13, 1.48)	24	12.32	1.20 (1.08, 1.33)
History of dyslipidemia	30	5.32	0.91 (0.84, 0.99)	—	—	—	—	—	—	—	—	—	—	—	—
History of MI	4	67.03	1.38 (1.28, 1.49)	—	—	—	21	5.53	1.21 (1.03, 1.43)	12	14.38	1.27 (1.12, 1.44)	6	52.35	1.46 (1.32, 1.62)

Continued

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Table 3. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 163)			30 Days to 6 Months (N=13 757)			6 Months to 3 Years (N=12 934)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
History of PCI	35	0.24	0.97 (0.86, 1.10)	—	—	—	—	—	—	—	—	—	—	—	—
History of primary PTCR	15	24.14	0.75 (0.67, 0.84)	—	—	—	—	—	—	—	—	—	30	6.50	0.80 (0.68, 0.95)
History of PAD	23	13.11	1.19 (1.08, 1.31)	—	—	—	—	—	—	31	3.49	1.16 (0.99, 1.36)	27	10.58	1.24 (1.09, 1.40)
History of stroke	26	10.42	1.19 (1.07, 1.33)	16	6.37	1.32 (1.06, 1.65)	—	—	—	20	8.84	1.30 (1.09, 1.54)	—	—	—
History of TIA	—	—	—	—	—	—	—	—	—	—	—	—	26	10.95	1.39 (1.14, 1.69)
History of unstable angina	—	—	—	8	10.33	1.28 (1.10, 1.48)	—	—	—	—	—	—	—	—	—
AF post-qualifying MI	20	16.40	1.21 (1.10, 1.33)	12	8.15	1.27 (1.08, 1.50)	10	13.62	1.39 (1.17, 1.66)	24	6.14	1.20 (1.04, 1.38)	21	14.60	1.29 (1.13, 1.47)
Angina post-qualifying MI	—	—	—	11	8.56	1.25 (1.08, 1.45)	—	—	—	—	—	—	—	—	—
CABG post-qualifying MI	24	12.81	0.62 (0.48, 0.81)	—	—	—	15	7.70	0.28 (0.12, 0.69)	—	—	—	—	—	—
HF post-qualifying MI	16	22.07	1.20 (1.11, 1.29)	7	16.11	1.36 (1.17, 1.58)	—	—	—	29	4.72	1.15 (1.01, 1.31)	—	—	—
PCI post-qualifying MI	—	—	—	5	18.14	0.65 (0.54, 0.79)	—	—	—	—	—	—	10	27.35	0.67 (0.58, 0.78)
Previous hospitalization	17	20.80	1.21 (1.11, 1.31)	—	—	—	19	6.16	1.26 (1.05, 1.51)	17	10.21	1.24 (1.09, 1.42)	32	4.73	1.13 (1.01, 1.27)
NYHA class 3 or 4 at start of given time period (reference is 1 or 2)	—	—	—	—	—	—	3	35.73	1.65 (1.40, 1.95)	5	28.00	1.42 (1.25, 1.61)	7	50.95	1.49 (1.34, 1.67)
HR at start of given time period*	—	—	—	—	—	—	2	56.35	—	8	18.60	1.10 (1.05, 1.15)	3	72.55	1.18 (1.14, 1.23)
HR at start of given time period (≤70†)*	—	—	—	—	—	—	—	—	0.95 (0.80, 1.11)	—	—	—	—	—	—

Continued

Table 3. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 163)			30 Days to 6 Months (N=13 757)			6 Months to 3 Years (N=12 934)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
HR at start of given time period (>70†)*	—	—	—	—	—	—	—	—	1.30 (1.21, 1.40)	—	—	—	—	—	—
HF (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	1	101.28	2.82 (2.30, 3.45)	1	79.08	2.06 (1.75, 2.41)	1	104.48	1.86 (1.65, 2.09)
MI (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	5	19.15	2.23 (1.56, 3.20)	16	10.72	1.48 (1.17, 1.87)	12	24.26	1.45 (1.25, 1.69)
Clinical evidence of HF	27	7.08	1.13 (1.03, 1.24)	—	—	—	11	12.27	1.43 (1.17, 1.74)	14	12.70	1.34 (1.14, 1.57)	—	—	—
Imaging evidence of LVSD	21	14.97	1.15 (1.07, 1.23)	—	—	—	—	—	—	18	9.42	1.20 (1.07, 1.34)	—	—	—
Radiologic evidence of LV failure	11	27.64	1.20 (1.12, 1.28)	—	—	—	18	6.20	1.21 (1.04, 1.40)	—	—	—	17	16.68	1.21 (1.10, 1.33)
Height	32	4.86	0.99 (0.99, 1.00)	—	—	—	—	—	—	—	—	—	—	—	—
BMI*	—	—	—	13	7.95	1.25 (1.07, 1.46)	—	—	—	—	—	—	—	—	—
CABG (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	—	—	—	5	60.25	0.40 (0.32, 0.50)
Cardiac arrest with resuscitation (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	—	—	—	22	12.67	1.86 (1.32, 2.62)
History of AICD	—	—	—	—	—	—	12	11.59	2.91 (1.57, 5.39)	—	—	—	—	—	—
History of CABG	25	11.24	1.22 (1.08, 1.36)	—	—	—	—	—	—	—	—	—	31	5.64	1.19 (1.03, 1.38)
Catheterization post-qualifying MI	—	—	—	—	—	—	—	—	—	21	8.42	0.81 (0.70, 0.93)	—	—	—

Continued

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Table 3. Continued

Variable	Overall: 3 Years (N=14 703)			In-Hospital (N=14 703)			Discharge to 30 Days (N=14 163)			30 Days to 6 Months (N=13 757)			6 Months to 3 Years (N=12 934)		
	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)	Rank	Chi-square	Hazard Ratio (95% CI)
Hypertension post-qualifying MI	—	—	—	—	—	—	—	—	—	28	5.05	0.87 (0.76, 0.98)	—	—	—
Dyslipidemia post-qualifying MI	33	4.85	0.92 (0.85, 0.99)	—	—	—	—	—	—	—	—	—	—	—	—
Renal insufficiency post-qualifying MI	12	26.26	1.37 (1.21, 1.54)	15	6.98	1.38 (1.09, 1.74)	—	—	—	—	—	—	—	—	—
PTCA (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	—	—	—	15	17.54	0.69 (0.58, 0.82)
Rehospitalization (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	19	8.84	1.24 (1.08, 1.42)	16	17.53	1.26 (1.13, 1.40)
SBP at start of given time period*	—	—	—	—	—	—	13	12.46	—	—	—	—	—	—	—
SBP (≤125†)*	—	—	—	—	—	—	—	—	0.89 (0.83, 0.95)	—	—	—	—	—	—
SBP (>125†)*	—	—	—	—	—	—	—	—	1.01 (0.94, 1.08)	—	—	—	—	—	—
Stroke (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	—	—	—	10	16.33	2.15 (1.48, 3.12)	19	15.45	1.80 (1.34, 2.41)
DBP at start of given time period*	—	—	—	—	—	—	—	—	—	—	—	—	29	7.16	0.95 (0.91, 0.99)
Unstable angina (any time from qualifying MI to start of given time period)	—	—	—	—	—	—	9	14.11	1.62 (1.26, 2.08)	30	3.74	1.20 (1.00, 1.44)	—	—	—

Values presented as hazard ratios (95% CIs). AF indicates atrial fibrillation; AICD, automatic implantable cardioverter defibrillator; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance; DBP, diastolic blood pressure; ECG, electrocardiogram; HF, heart failure; HR, heart rate; LBBB, left bundle branch block; LVSD, left ventricular systolic dysfunction; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PTCR, percutaneous transluminal coronary revascularization; SBP, systolic blood pressure; TIA, transient ischemic attack.

*Hazard ratio is for an increase in 10 units (eg, for age, 1.29 implies a 29% increase in risk for every additional 10 years of age).

†Variable is a linear spline for values in the listed range.

‡Hazard ratio is for an increase of 24 hours.

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Killip class was ranked among the highest 5 and creatinine clearance was not (Table 3). When evaluating predictors of survival from events occurring during the index hospitalization only, more baseline measurements become important and the history variables less so. Weight and blood pressure now join the ranks of heart rate and creatinine clearance as top 5 predictors. The 3 sets of models for events occurring after discharge from the index hospitalization now include updated events, such as new occurrence of HF, MI, stroke, or CABG surgery in the top 5 predictors list. Table 4 shows all factors chosen for the models as well as their relative ranks.

Comparison of Baseline With Time-Sensitive Models

Inclusion of time-sensitive factors in mortality models had the greatest effect on the acute model (c-index=0.77–0.81; IDI index=4.9%; NRI index=22.3% for hospital discharge to 30 days; Table 5). Overall risk of dying between discharge and 30 days was 2.2%. Models of 30-day to 6-month and 6-month to 3-year mortality showed improvements in c-indices of 0.02 and 0.02, IDI indices of 2.2% and 3.2%, and NRI indices of 7.3% and 6.8% (Table 5).

When comparing 2 models, one would prefer to have a lower prediction in the patients without the event and a higher prediction in those with the event. As illustrated in the Figure, one would expect the values for those without the event to go down (ie, lower predicted values with the updated information) and the values for those with the event to go up (ie, higher predicted values with the updated information). Between the 25th and 75th percentiles of the change in predicted values, the 2 models were comparable in their predictions of patients who survived during each time interval (Figure). However, more change was observed in predictions in the patients who subsequently died, with the updated models assigning those who subsequently died a higher probability of the event than that assigned by the baseline model.

Changes in c-indices were less pronounced for the models of composite outcomes (Table 5). According to the IDI and NRI indices, the updated model had significant improvement over the model with baseline covariates only in all follow-up periods and with all outcomes (Table 5).

Discussion

Although assessment of risk at the time of an acute event is interesting and important, the approach seems insensitive when more information on clinical status is collected in the hospital and during subsequent outpatient clinic visits. The dynamic, time-updated approach more closely simulates clinical practice in which providers assess patient status and adjust treatment and expectations as a function of the trajectory of the disease process.

Our findings demonstrate the need to move from risk modeling based on a fixed time point to more-dynamic risk modeling in which future outcomes are predicted with the most relevant and time-updated data, including intervening changes in clinical status between the initial and current evaluations. Many of the baseline factors associated with outcomes to 3 years are also found to be important during the follow-up periods. However, the relationship of these factors at baseline weakens as time passes, and intervening events and current clinical findings become much stronger predictors of outcomes in the subsequent intervals. The period from discharge to 30 days is short, and thus the overall risk is low (FigureA). Most patients had predicted risks around that for the overall group (2.2% for mortality). The information updated at hospital discharge mainly changed the distribution of risk for those at high risk of an event. By 6 months of follow-up, updating the clinical risk factors was associated with changes in risk to 3 years across the entire spectrum of risk.

It has been over 40 years since Killip first described the importance of the hemodynamic status after acute MI as a predictor of mortality.[16] Since then, numerous studies have identified clinical signs of HF in the setting of MI as important predictors of prognosis.[3–5,8,17] However, the majority of these predictors are baseline characteristics and infarct severity,[18] and previous statistical approaches have not taken into account the changes that occur in a patient's health over time. In addition, it has been shown that in patients with chronic HF, risk of death is highest in the early phase after hospital discharge (attributed to a hospitalization for an HF event) and related to the duration and frequency of HF hospitalizations.[19]

Chang et al.[20] showed that risk stratification for patients with non-ST-segment elevation (NSTE)-acute coronary syndromes (ACS) should be updated over time to better estimate the patient's risk and provide information that might lead to improved decision making. In that study, it was shown that the methodological process of assessing risk at different time points during the hospital stay was a feasible and reliable strategy to guide the management of patients with NSTE-ACS.

Dynamic risk assessment models were also tested in over 6000 patients with ST-segment elevation MI.[12] In that study, factors not available at baseline, such as ST-segment evolution and in-hospital complications, added prognostic information. These results were applicable not only for patients who received thrombolytic therapy, but also for those who underwent primary PCI.

We were able to assess patient characteristics at different time points, including in-hospital, short-, and long-term periods, using almost 15 000 patients enrolled in the VALIANT study, and we used the data from each time point to obtain better predictions of risk.[21] We demonstrated that

Table 4. Top 5 Predictors of All-Cause Mortality, Cardiovascular Death or Nonfatal MI, or Cardiovascular Death or Nonfatal HF Over Time (Wald chi-squares)*

	All-Cause Mortality					CV Death or Nonfatal MI					CV Death or Nonfatal HF				
Parameter	Overall	IH	D/C-30D	30D-6M	6M-3Y	Overall	IH	D/C-30D	30D-6M	6M-3Y	Overall	IH	D/C-30D	30D-6M	6M to 3Y
Baseline characteristics															
Age	129.41	—	33.96	—	193.58	80.06	—	—	—	53.14	137.67	30.03	—	—	90.68
Time to randomization	—	25.93	—	—	—	—	21.56	—	—	—	—	—	—	—	—
Baseline HR	126.34	92.97	—	—	—	108.16	76.68	—	—	—	181.97	136.10	—	—	—
Weight, kg	—	19.78	—	—	—	—	10.65	—	—	—	—	—	—	—	—
Baseline CrCl	110.49	44.71	—	—	—	95.29	35.68	25.13	33.74	—	—	19.60	19.31	—	—
Baseline SBP	—	—	—	—	—	—	—	—	—	—	—	43.18	—	—	—
MAP	—	36.33	—		—	—	—	—	—	—	—	—	—		—
Current smoker	—	—	—	—	—	—	—	—	27.34	—	—	—	—	—	—
History of diabetes mellitus	—	—	—	24.04	—	—	—	—	30.25	—	112.59	—	—	40.04	68.48
PCI post-qualifying MI	—	—	—	—	—	—	—	—	—	—	—	18.14	—	—	—
History of MI	57.68	—	—	—	49.42	72.41	—	—	23.86	44.99	67.03	—	—	—	—
History of HF	—	—	—	—	—	—	—	—	—	—	—	—	—	35.57	—
History of unstable angina	—	—	—	—	—	—	18.32	—	—	—	—	—	—	—	—
Diabetes mellitus post-qualifying MI	66.84	—	—	—	—	71.96	—	—	—	—	—	—	—	—	—
Killip class	—	—	—	—	—	—	—	—	—	—	56.37	—	—	39.02	—
Factors updated with values from follow-up visits															
NYHA†	—	—	18.86	24.48	—	—	—	17.03	27.32	—	—	—	35.73	28.00	—
HR†	—	—	72.99	23.90	63.64	—	—	28.01	—	40.88	—	—	56.35	—	72.55
HF‡	—	—	62.65	23.74	39.37	—	—	45.80	—	—	—	—	101.28	79.08	104.48
MI‡	—	—	27.83	—		—	—	35.08	—	49.53	—	—	19.15	—	—
CABG‡	—	—	—	—	38.90	—	—	—	—	68.90	—	—	—	—	60.25
Stroke‡	—	—	—	21.63	—	—	—	—	—	—	—	—	—	—	—

CABG indicates coronary artery bypass graft surgery; CrCl, creatinine clearance; CV, cardiovascular; HF, heart failure; HR, heart rate; MAP, mean arterial pressure; MI, myocardial infarction; NYHA, New York Heart Association; SBP, systolic blood pressure.

*Overall refers to baseline predictors of 3 outcomes to 3 years. IH is baseline predictors of index hospitalization outcomes. D/C-30D is baseline to index hospitalization predictors of outcomes from discharge to 30 days. 30D-6M is baseline to 30-day predictors of outcomes from 30 days to 6 months. 6M-3Y is baseline to 6-month predictors of outcomes from 6 months to 3 years.

†The value collected at the start of the follow-up interval.

‡Any occurrence from index hospitalization through the beginning of the follow-up interval.

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Table 5. Comparison of Models Using Baseline Data Only and Models Using Updated Variables

	Mortality				CV Death or HF				CV Death or MI			
	C Index (Baseline)	C Index (Updated)	IDI*	NRI*	C Index (Baseline)	C Index (Updated)	IDI*	NRI*	C Index (Baseline)	C Index (Updated)	IDI*	NRI*
Overall	0.73 (0.72–0.74)	—	—	—	0.73 (0.72–0.74)	—	—	—	0.71 (0.70–0.72)	—	—	—
In-hospital	0.76 (0.73–0.78)	—	—	—	0.72 (0.70–0.73)	—	—	—	0.71 (0.69–0.73)	—	—	—
Discharge to 30 days	0.77 (0.74–0.79)	0.81 (0.79–0.83)	0.049 (0.038–0.061)	0.223 (0.159–0.283)	0.74 (0.72–0.75)	0.77 (0.76–0.79)	0.042 (0.034–0.050)	0.127 (0.089–0.171)	0.72 (0.70–0.74)	0.74 (0.71–0.76)	0.027 (0.021–0.035)	0.073 (0.026–0.130)
30 days to 6 months	0.75 (0.73–0.76)	0.77 (0.75–0.78)	0.022 (0.016–0.028)	0.073 (0.031–0.112)	0.74 (0.73–0.75)	0.76 (0.75–0.78)	0.030 (0.023–0.036)	0.101 (0.075–0.127)	0.71 (0.70–0.73)	0.73 (0.71–0.74)	0.020 (0.016–0.024)	0.072 (0.040–0.103)
6 months to 3 years	0.75 (0.74–0.76)	0.77 (0.76–0.78)	0.032 (0.025–0.038)	0.068 (0.028–0.107)	0.76 (0.75–0.77)	0.79 (0.78–0.80)	0.040 (0.034–0.047)	0.164 (0.134–0.197)	0.73 (0.72–0.74)	0.76 (0.75–0.77)	0.035 (0.030–0.040)	0.088 (0.056–0.117)

CV indicates cardiovascular; HF, heart failure; IDI, integrated discrimination improvement; MI, myocardial infarction; NRI, net reclassification improvement.
*All *P* values for the IDI and NRI are <0.0001, except the NRI for CV death or MI from discharge to 30 days (*P*=0.0011).

Figure. Box plots of the change in predicted risk of mortality (predicted risk from the updated model—predicted risk from baseline characteristics only model). Distributions of change in prediction are illustrated separately for those who died and those who did not within each of the last 3 follow-up intervals: (A) hospital discharge to 30 days; (B) 30 days to 6 months; and (C) 6 months to 3 years.

baseline characteristics were not strongly associated with 30-day, 6-month, and 3-year mortality after adjusting for these same values measured closer to the latest time period. For example, the most important predictive factors in the model of mortality between hospital discharge and the 30-day follow-up visit were variables captured at discharge and not at baseline. Similarly, the most important factors for the model of mortality from 30 days to the 6-month follow-up visit were

variables assessed at the 30-day visit and not baseline or discharge characteristics. Finally, the most important variables in the model of mortality from 6 months to the 3-year follow-up visit were those measured at the 6-month visit, such as heart rate and NYHA class.

This was true not only for mortality, but also for the cardiovascular death or HF and cardiovascular death or MI models. This is the first time that a dynamic assessment with 4 different time points including short- and long-term (3-year) outcomes has been performed to better understand the predictors of these clinical outcomes in patients with HF after acute MI.

Analyses from the Worcester Heart Attack study showed a decline in the incidence rates of HF complicating acute MI and significant improvements in in-hospital survival after acute MI complicated by HF.[1] These decreased rates of HF after acute MI are likely attributed to the increasing use of preventive and appropriate therapeutic strategies directed at patients at high risk for developing HF. However, this trend was not observed in the postdischarge 1-year survival. These findings highlight the prognostic influence of HF after acute MI. The lack of improvement over time in the long-term outcomes of these patients may reflect the underuse or underdosing of effective cardiac therapies available; poor patient compliance; or less focus on characteristics that might predict worse outcomes, other than baseline variables, that were important for the in-hospital period. Therefore, there is a need to identify modifiable long-term predictors for physicians to focus on in order to intensify treatment and improve clinical outcomes. Our study showed that there are several strong predictors of outcomes that can be potentially modified or better controlled, such as NYHA class, heart rate, creatinine clearance, weight, and diabetes mellitus, that might inform future targets for interventions. These risk markers might be modified in beneficial or detrimental ways; therefore, randomized trials are needed to test further interventions in this population. All available evidence indicates that the greatest absolute benefit for proven therapies is for those at the highest risk, and identification of a high-risk patient at a clinic visit may merit special allocation of time to ensure that the best evidence-based therapies are available and used. Time-updated risk models may be used to identify populations in need of further research in follow-up from acute events, to use in adjusting for risk when comparing outcomes between centers in quality exercises, or to create an opportunity for providers and health systems to focus on the highest-risk populations to ensure that they are treated with the highest standards.

Limitations

Not all of the clinical measures were available at both baseline and follow-up. NYHA class could not be included in the baseline models, creatinine clearance was measured only when changes in the study drug titration occurred during the follow-up period, and LV function was not measured in a uniform manner at baseline and not at all during the follow-up periods. Thus, assessing changes over time in these measures was not possible. We did not have information about the extent of coronary disease in all patients, which may have been an important contributor to patient status. It is also possible that other important factors were not captured in our database. For example, biomarkers were not available for us to model and our results may have been different had they been known.

We did not examine all of the possible follow-up periods; however, we felt that the time points evaluated were representative of important clinic visits.

We used imputed data instead of complete case analyses. If complete case results had been performed and different results found, we cannot be sure that the imputed results were less biased. The proportional hazards assumption may have been violated in some models. Thus, the predictions are averaged within each time interval rather than allowing for changing risk within a time interval.

We also evaluated changes in patient status from one visit to the next. We could have examined the changes from the visit of interest to the last known follow-up and differing results may have been noted. We were more interested in how the information obtained at a clinic visit helps physicians predict how the patient will do until the next important milestone; therefore, the process chosen better fits our goals.

Conclusions

We found that although baseline characteristics at the time of MI are important in determining outcome, patient information assessed over time provides a clearer view of patient status and is a better predictor of long-term outcomes. In these mortality models, it appears that the use of updated information does more to upgrade predictions of events than to downgrade predictions of nonevents. In addition, we identified important predictors that are modifiable and could be better controlled. Clinical care should focus on these to improve the care of patients with HF after acute MI. Further exploration of the dynamic process of evaluating factors associated with outcomes over long periods of time is needed.

Author Contributions

Lopes had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis; he contributed to the conception and design

of the study, data acquisition, data analysis, data interpretation, manuscript drafting, and critical revision of the manuscript. Pieper and Stevens performed the statistical analyses. Leimberger was the statistician for the original study. Solomon, McMurray, Pfeffer, Leimberger, and Velazquez were involved with original study conduct and have reviewed the results of the current study, contributed to its interpretation, and helped revise the manuscript.

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Predicting Outcomes Over Time in Patients With Heart Failure, Left Ventricular Systolic Dysfunction, or Both Following Acute Myocardial Infarction

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