Original Article
Predictive models for short- and long-term adverse outcomes following discharge in a contemporary population with acute coronary syndromes

Dharam J Kumbhani[1], Brian J Wells[2], A Michael Lincoff[1], Anil Jain[3], Susana Arrigain[2], Changhong Yu[2], Marlene Goormastic[1], Stephen G Ellis[1], Eugene Blackstone[1], Michael W Kattan[2]

[1]Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH; [2]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; [3]Information Technology, Cleveland Clinic, Cleveland, OH

Abstract: Although numerous risk-prediction models exist in patients presenting with acute coronary syndromes (ACS), they are subject to important short-comings, including lack of contemporary information. Short-term models are frequently biased by in-hospital events. Accordingly, we sought to create contemporary risk-prediction models for clinical outcomes following ACS up to 1 year following discharge. Models were constructed for death at 30 days and 1 year, death/myocardial infarction (MI)/revascularization at 30 days and death/MI at 1 year in consecutive patients presenting with ACS at our institution between 2006 and 2008, and discharged alive. Logistic regression was used to model the 30 day outcomes and Cox proportional hazards were used to model the 1 year outcomes. No linearity assumptions were made for continuous variables. The final model coefficients were used to create a prediction nomogram, which was incorporated into an online risk calculator. A total of 2,681 patients were included, of which about 9.5% presented with ST-elevation MI. All-cause mortality was 2.6% at 30 days and 13% at 1 year. Demographic, past medical history, laboratory, pharmacological and angiographic parameters were identified as being predictive of adverse ischemic outcomes at 30 days and 1 year. The c-indices for these models ranged from 0.73 to 0.82. Our study thus identified risk factors that are predictive of short- and long-term ischemic and revascularization outcomes in contemporary patients with ACS, and incorporated them into an easy-to-use online calculator, with equal or better discriminatory power than currently available models.

Keywords: Mortality, myocardial infarction, predictors, registry, revascularization
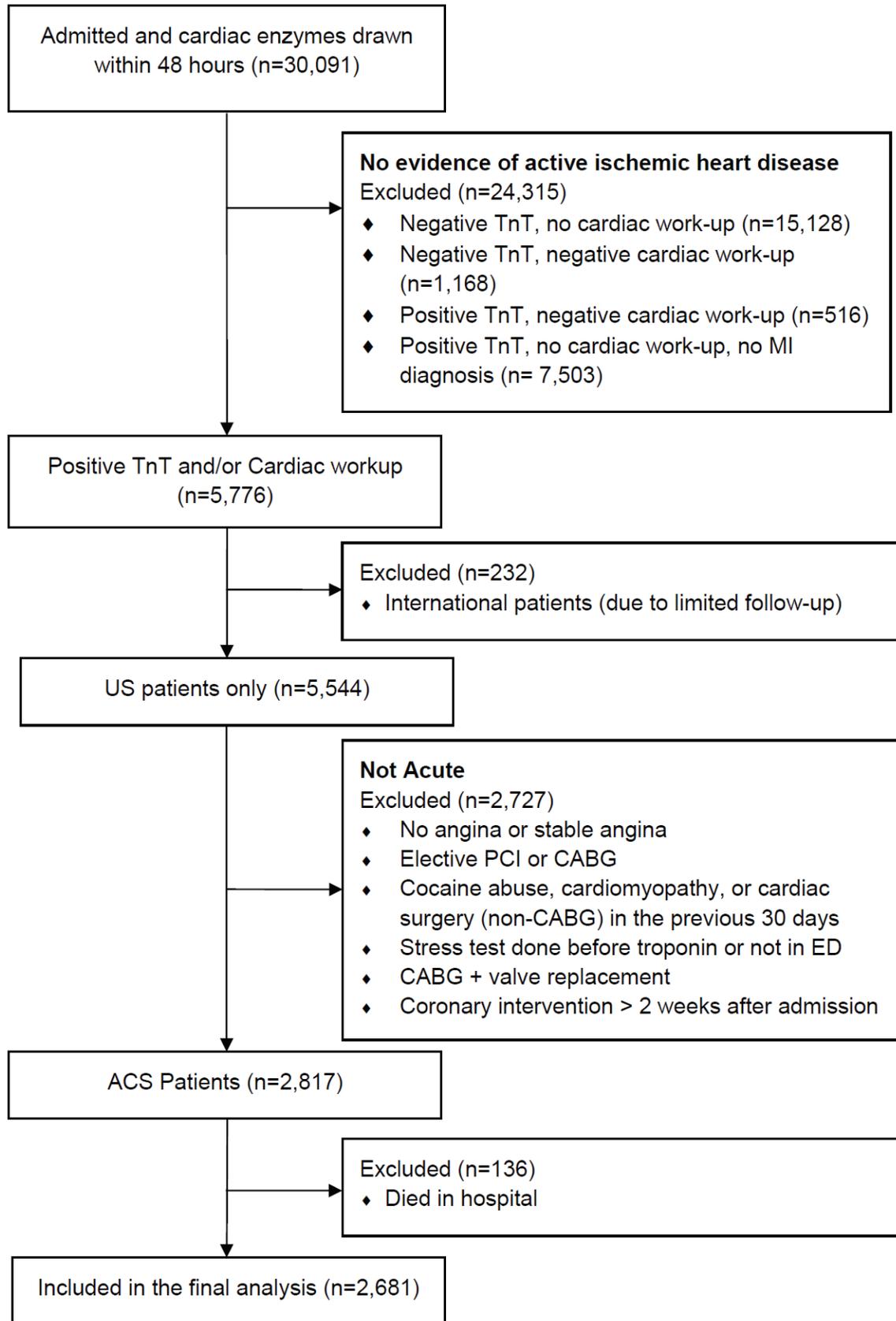
Introduction

The management of acute coronary syndromes (ACS), defined as unstable angina, non ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), has made considerable progress in the past few years. This has been possible due to a number of factors, including procedural advances in coronary reperfusion techniques, a greater proportion of patients receiving timely mechanical reperfusion, newer additions to the pharmaco-invasive armamentarium, and increased adherence to evidence-based therapies, both acutely and at discharge [1-4].

Numerous models have been developed to identify patients at highest risk for short- and intermediate-term adverse outcomes after ACS [5-8]. However, these models have substantial disadvantages, including the lack of information on the use of current pharmacological agents and angiographic severity of disease, which have been shown to be significantly associated with outcomes in these patients [9-12]. Moreover, two of the commonly used models: the Thrombolysis in Myocardial Infarction (TIMI) models for STEMI and NSTE-ACS, and the Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (eptifibatide) Therapy (PURSUIT) model predict short-term mortality (up to 30 days) only; the Global Registry of Acute Coronary Events (GRACE) model predicts 6 month mortality following hospital discharge [5]. Clinical decision models pre-

Admitted and cardiac enzymes drawn within 48 hours (n=30,091)

No evidence of active ischemic heart disease
Excluded (n=24,315)
- Negative TnT, no cardiac work-up (n=15,128)
- Negative TnT, negative cardiac work-up (n=1,168)
- Positive TnT, negative cardiac work-up (n=516)
- Positive TnT, no cardiac work-up, no MI diagnosis (n= 7,503)

Positive TnT and/or Cardiac workup (n=5,776)

Excluded (n=232)
- International patients (due to limited follow-up)

US patients only (n=5,544)

Not Acute
Excluded (n=2,727)
- No angina or stable angina
- Elective PCI or CABG
- Cocaine abuse, cardiomyopathy, or cardiac surgery (non-CABG) in the previous 30 days
- Stress test done before troponin or not in ED
- CABG + valve replacement
- Coronary intervention > 2 weeks after admission

ACS Patients (n=2,817)

Excluded (n=136)
- Died in hospital

Included in the final analysis (n=2,681)

Figure 1. CONSORT flow diagram of study participants. ACS represents acute coronary syndromes; CABG, coronary artery bypass graft surgery; ED, emergency department; MI, myocardial infarction; PCI, percutaneous coronary intervention; TnT, troponin T.

Table 1. Baseline characteristics of the study population[*]

Characteristic	NSTEMI (n =1187)	STEMI (n = 253)	Unstable Angina (n =1,222)
Demographic characteristics			
Age (years)	69.6 (59.5,78.2)	62.3 (53.3,71.9)	65.5 (57.1,75.2)
Female	419 (35.3)	86 (34)	402 (32.9)
Race			
White	847 (72.4)	160 (64)	969 (80.1)
Black	296 (25.3)	83 (33.2)	211 (17.4)
Other	27 (2.3)	7 (2.8)	30 (2.5)
Body mass index (kg/m^2)	27.2 (23.7,31.4)	27.3 (24.7,31.1)	28.1 (24.9,32.7)
Past medical history			
Diabetes	561 (47.3)	84 (33.2)	603 (49.3)
Peripheral vascular disease	301 (25.4)	31 (12.3)	270 (22.1)
History of prior stroke	241 (20.3)	20 (7.9)	258 (21.1)
History of prior CHF	333 (28.1)	27 (10.7)	290 (23.7)
On lipid medication prior to hospitalization	875 (73.7)	214 (84.6)	1101 (90.1)
Chronic kidney disease	466 (39.3)	40 (15.8)	336 (27.5)
Chronic obstructive lung disease	260 (21.9)	36 (14.2)	217 (17.8)
Admission characteristics			
Pulse at presentation (bpm)	97 (95,98)	96 (95,98)	97 (95,98)
Serum ALT (IU/L)	25 (16,42.2)	30 (20.5,50)	20 (14,31)
HDL cholesterol (mg/dl)	43 (35,53)	44 (37,54)	42 (35,52)
Ejection fraction (%)	50 (35,55)	45 (35,55)	55 (45,55)
Maximum troponin T (mcg/L)	0.4 (0.2,1.1)	3.5 (1.8,7.5)	0 (0,0)
Serum creatinine (mg/dl)	1.1 (0.9,1.7)	0.9 (0.8,1.2)	1 (0.8,1.3)
Serum albumin (g/dl)	3.5 (3,3.9)	3.6 (3.3,3.9)	3.9 (3.6,4.2)
Serum hematocrit (%)	33.1 (30,37.4)	36.2 (33,40.4)	37.4 (33.1,40.8)
Events during hospitalization			
Number of vessels with ≥50% stenoses			
0	76 (10.5)	21 (8.3)	155 (12.7)
1	341 (47)	232 (91.7)	735 (60.3)
2	73 (10.1)	0 (0)	128 (10.5)
3	213 (29.4)	0 (0)	174 (14.3)
4	22 (3)	0 (0)	26 (2.1)
Treatment			
CABG	197 (16.6)	0 (0)	92 (7.5)
Medical Management	638 (53.7)	0 (0)	386 (31.6)
PCI-BMS	149 (12.6)	155 (61.3)	216 (17.7)
PCI-DES	175 (14.7)	62 (24.5)	456 (37.3)
PCI-Other	28 (2.4)	36 (14.2)	72 (5.9)
Number of Vessels Treated			
0	641 (56.9)	0 (0)	386 (32.6)
1	285 (25.3)	230 (93.1)	586 (49.5)
2	84 (7.5)	16 (6.5)	144 (12.2)
3	116 (10.3)	1 (0.4)	68 (5.7)
4	0 (0)	0 (0)	1 (0.1)
Stroke during hospitalization	33 (2.8)	2 (0.8)	23 (1.9)

New CHF in hospital	137 (11.5)	59 (23.3)	60 (4.9)
Discharged to home	967 (81.5)	241 (95.3)	1187 (97.1)
	Medication utilization		
Beta blocker in hospital	1002 (84.4)	213 (84.2)	1091 (89.3)
Gp IIb/IIIa inhibitor for PCI	255 (23.7)	158 (86.8)	135 (12.8)
Clopidogrel pre-procedure	481 (44.2)	248 (99.2)	965 (81)
Clopidogrel at discharge	753 (63.4)	250 (98.8)	1037 (84.9)

*There were 19 patients that had missing ACS type prior to imputation. Values represent numbers (%) for dichotomous/categorical variables, and median (interquartile range) for continuous variables. ALT represents alanine aminotransferase; BMS, bare-metal stent; bpm, beats per minute; CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; DES, drug-eluting stent; Gp, glycoprotein; HDL, high density lipoprotein; PCI, percutaneous coronary intervention.

dicting longer-term mortality in these patients are scant. Moreover, short-term models can be heavily influenced by in-hospital mortality [13]. Accordingly, we sought to create prediction models for death, death/ recurrent myocardial infarction, and death/recurrent MI/ repeat revascularization in a contemporary cohort of patients presenting with acute coronary syndromes, who were discharged alive from the hospital. Since predictors of short- and long-term mortality are likely to be different, we constructed models for these 3 outcomes at 2 separate time-points: 30 days and 1 year.

Methods

Data source

Successive patients presenting to the Cleveland Clinic, Cleveland, OH between January 1, 2006 and December 31, 2008 were included. A detailed review of their baseline demographics, past medical history, clinical presentation, laboratory values, medications given, procedures performed, complications and outcomes was conducted using our electronic health record (EHR) system, which includes the eResearch Data Repository, the diagnostic catheterization registry, the percutaneous coronary intervention (PCI) registry, the coronary artery bypass graft (CABG) registry, the nuclear perfusion imaging stress test registry, procedure billing data, and inpatient pharmacy data.

Study population

Patients with acute coronary syndromes were identified from the PCI registry and from encounters in the Cleveland Clinic main campus hospital or emergency department (ED). PCI patients undergoing elective procedures were excluded. ED and hospital patients were included only if they underwent serial serum troponin measurements and these values were either elevated, further cardiac testing (e.g. cardiac catheterization or stress nuclear imaging) revealed ischemic heart disease, or they underwent a coronary revascularization procedure during the index admission. We excluded patients undergoing coronary artery bypass graft (CABG) surgery if they also underwent concomitant coronary valve replacement surgery, since the vast majority of these patients appeared to be having elective procedures. **Figure 1** demonstrates the CONSORT flow diagram used to identify patients for this study.
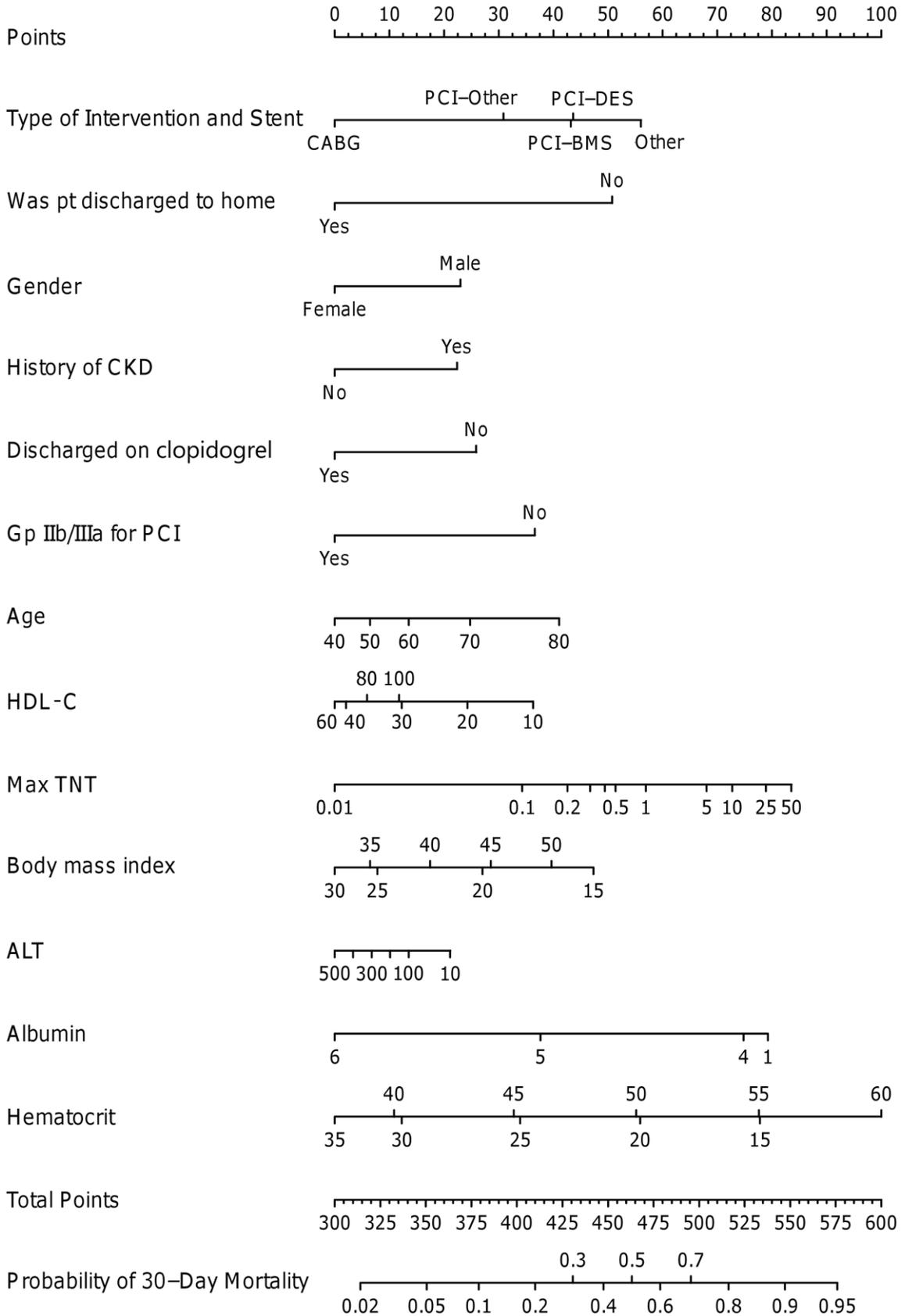
Assessment of outcomes

All outcomes were assessed only in patients discharged alive from the hospital after their index ACS hospitalization. Mortality was assessed from the EHR and from the Social Security Death Index. Reinfarction (or new infarction, if the index event was not acute MI) was defined as a serum troponin T ≥ 0.08mcg/L on any occasion after the index hospitalization. A patient was considered to undergo repeat revascularization (or new revascularization, if the index event did not result in revascularization) if he/she was identified in either the CABG or PCI database or if one of the relevant Current Procedural Terminology (CPT) codes were identified in the EHR. All events except mortality were censored on the date of the patient's last encounter.

Predictor variables

Table 1 shows the predictor variables that were considered for inclusion in the final models due to their known association with the outcomes of interest. Admission, inpatient and discharge medications were separately considered. The same high sensitivity troponin assay was utilized throughout the duration of the study.

Kumbhani - predictors of ACS

| Points | 0 10 20 30 40 50 60 70 80 90 100 |

Type of Intervention and Stent: PCI–Other, PCI–DES, CABG, PCI–BMS, Other

Was pt discharged to home: No / Yes

Gender: Male / Female

History of CKD: Yes / No

Discharged on clopidogrel: No / Yes

Gp IIb/IIIa for PCI: No / Yes

Age: 40 50 60 70 80

HDL-C: 80 100 / 60 40 30 20 10

Max TNT: 0.01 0.1 0.2 0.5 1 5 10 25 50

Body mass index: 35 40 45 50 / 30 25 20 15

ALT: 500 300 100 10

Albumin: 6 5 4 1

Hematocrit: 40 45 50 55 60 / 35 30 25 20 15

Total Points: 300 325 350 375 400 425 450 475 500 525 550 575 600

Probability of 30–Day Mortality: 0.3 0.5 0.7 / 0.02 0.05 0.1 0.2 0.4 0.6 0.8 0.9 0.95

Figure 2. Nomogram for 30-day mortality. ALT represents alanine aminotransferase; BMS, bare-metal stents; CABG, coronary artery bypass graft surgery; CKD, chronic kidney disease; DES, drug-eluting stent; Gp, glycoprotein; HDL, high density lipoprotein; PCI, percutaneous coronary intervention; TNT, troponin T.

Statistical analysis

Prediction models were constructed for death at 30 days and 1 year, death/recurrent MI/ revascularization at 30 days, and death/recurrent MI at 1 year. As no censoring was done prior to 30 days, logistic regression was used to model the 30 day outcomes. Multivariate Cox proportional hazards were used to model the 1 year outcomes. For each of the Cox models besides mortality, patients were followed until the time of event or until the date of the last contact in our EHR. Time zero was the time of discharge from the hospital. Variable selection was performed using the "stepdown" method suggested by Harrell [14], and the models were reduced until achieving the best model discrimination according to the bias-corrected c-statistic using tenfold cross-validation. A calibration curve was created by plotting the quintiles of the predicted probabilities on the observed estimates for the entire cohort. The final model coefficients were used to create a Web-based risk calculator that calculated the predictions automatically (prediction nomogram), and is available free of charge at http://rcalc.ccf.org.

Missing values were imputed using Multiple Imputation by Chained Equations package, version 2.3, for R. (Van Burren, 2010) Imputation was performed to maximize the available information and to reduce the potential bias introduced by deleting incomplete records. Imputation was performed using regression techniques that include all baseline patients and all baseline variables as predictors, including the outcome [15]. All statistical analyses were performed using SAS software (version 9.1, SAS Institute, Cary, North Carolina) and R version 2.10. All p- values were two-tailed, with statistical significance set at 0.05. All confidence intervals (CI) were calculated at the 95 percent level.

Results

A total of 2,681 patients met our study criteria (44.6% with unstable angina, 45.9% with NSTEMI and 9.5% with STEMI on presentation). Baseline characteristics of the study popula-

tion are listed in **Table 1**. About 51% of the patients received PCI, while 38.2% were medically managed, and 10.8% underwent CABG. Overall in-hospital mortality was 4.8%. Of all the patients discharged alive, 90% were discharged to home.
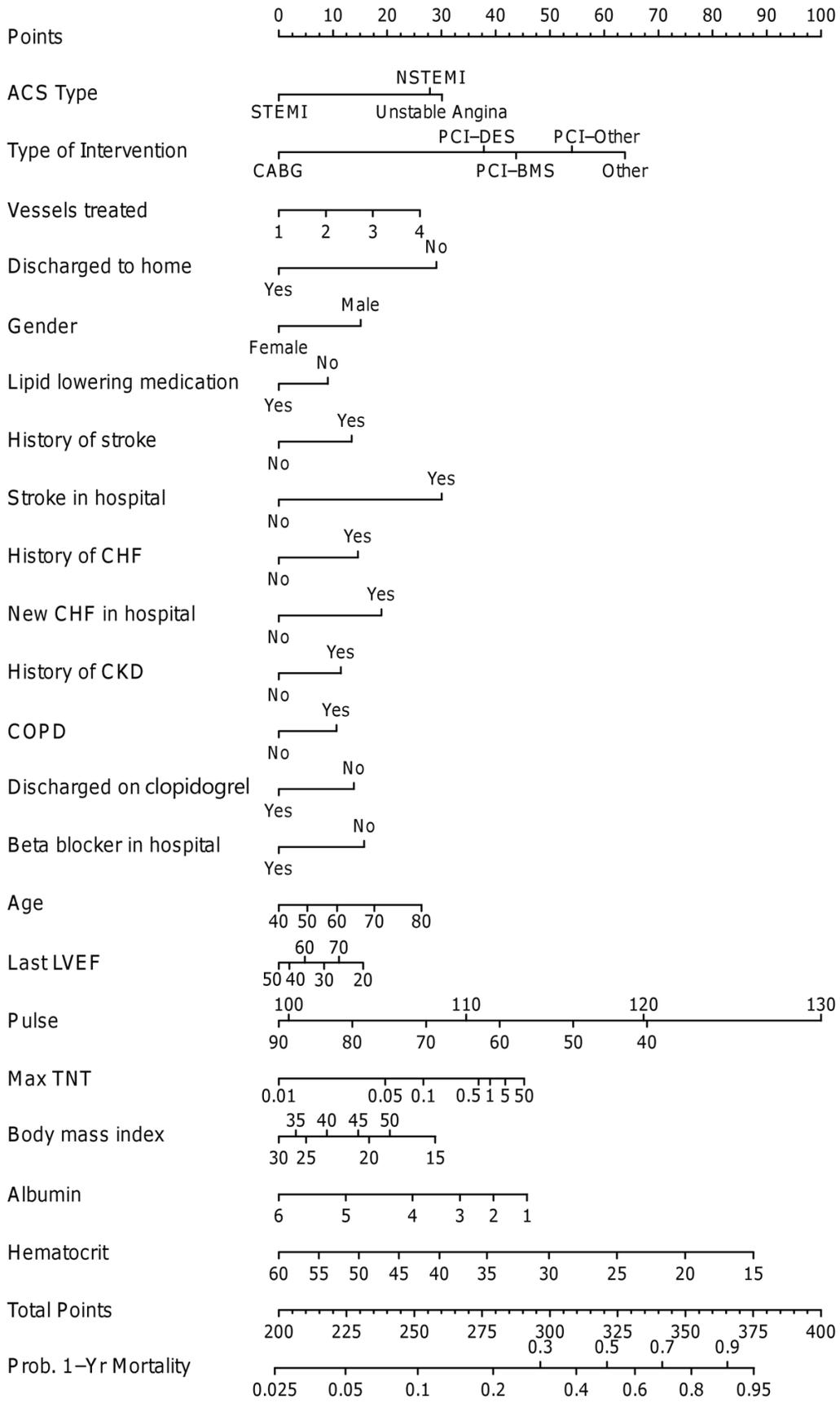
30-day mortality

Of the patients discharged alive from the hospital, a total of 69 deaths (2.6%) occurred within 30 days. The nomogram for 30-day mortality is demonstrated in **Figure 2**. Significant risk factors of 30-day mortality included medical management, male gender, history of CKD, lack of use of a glycoprotein IIb/IIIa inhibitor in the hospital in patients undergoing PCI, lack of discharge on clopidogrel, older age, lower serum alanine transaminase (ALT) at admission, lower high density lipoprotein (HDL) cholesterol at admission, higher maximal troponin T, lower serum albumin at admission, and discharge to facility other than home; BMI and hematocrit demonstrated a U-shaped relationship. The c-index was 0.82.

1-year mortality

Of the patients discharged alive from the hospital, a total of 348 deaths (13.0%) were noted within 1 year. The nomogram for 1-year mortality is demonstrated in **Figure 3**. Significant risk factors for 1-year mortality included presentation with NSTEMI/unstable angina (as compared with STEMI), medical management, multi-vessel revascularization, male gender, history of stroke, stroke during hospitalization, history of CHF, new onset CHF during hospitalization, history of CKD, history of COPD, absence of the use of beta-blocker in the hospital and lipid lowering medications and clopidogrel at discharge, older age, lower ejection fraction, higher troponin T, lower albumin at admission, lower hematocrit on admission and discharge to a facility other than home. BMI and pulse on presentation demonstrated a U-shaped relationship, with very low and high values being associated with a higher risk of mortality. The c-index was 0.80.

Kumbhani - predictors of ACS

Points	0 10 20 30 40 50 60 70 80 90 100
ACS Type	NSTEMI / STEMI / Unstable Angina
Type of Intervention	PCI–DES / PCI–Other / CABG / PCI–BMS / Other
Vessels treated	1 2 3 4
Discharged to home	No / Yes
Gender	Male / Female
Lipid lowering medication	No / Yes
History of stroke	Yes / No
Stroke in hospital	Yes / No
History of CHF	Yes / No
New CHF in hospital	Yes / No
History of CKD	Yes / No
COPD	Yes / No
Discharged on clopidogrel	No / Yes
Beta blocker in hospital	No / Yes
Age	40 50 60 70 80
Last LVEF	60 70 / 50 40 30 20
Pulse	100 110 120 130 / 90 80 70 60 50 40
Max TNT	0.01 0.05 0.1 0.5 1 5 50
Body mass index	35 40 45 50 / 30 25 20 15
Albumin	6 5 4 3 2 1
Hematocrit	60 55 50 45 40 35 30 25 20 15
Total Points	200 225 250 275 300 325 350 375 400
Prob. 1–Yr Mortality	0.3 0.5 0.7 0.9 / 0.025 0.05 0.1 0.2 0.4 0.6 0.8 0.95

Figure 3. Nomogram for 1-year mortality. ACS represents acute coronary syndrome; BMS, bare-metal stents; CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DES, drug-eluting stent; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TNT, troponin T.

30-day composite of mortality/recurrent MI/ revascularization

Of the patients discharged alive from the hospital, a total of 326 composite events (13.8%) were noted within 30 days. The nomogram for 30-day events is demonstrated in **Figure 4**. Significant risk factors included medical management, smoking, diabetes mellitus, presence of peripheral vascular disease, stroke during hospitalization, lower ejection fraction, higher serum low density lipoprotein (LDL) cholesterol, higher maximum troponin T, higher serum creatinine, lower ALT, higher pulse rate on admission, no clopidogrel loading in patients undergoing PCI, absence of use of angiotensin converting enzyme inhibiting agents or angiotensin receptor blocking agents in-hospital/at discharge, and discharge to a facility other than home. The c-index was 0.73.

1-year composite of mortality/recurrent MI

Of the patients discharged alive from the hospital, a total of 723 composite events (30.1%) were noted within 1 year. The nomogram for 1-year events is demonstrated in **Figure 5**. Significant risk factors included presentation with NSTEMI/unstable angina (as compared with STEMI), medical management, multivessel disease, African American race, smoking, diabetes mellitus, history of stroke, history of CHF, history of CKD, history of COPD, absence of the use of beta-blocker in the hospital and lipid lowering medications, lower ejection fraction, higher maximum troponin T, higher serum creatinine at admission, higher serum LDL cholesterol at admission, lower serum albumin at admission, lower serum hematocrit at admission, and discharge to a facility other than home. BMI on presentation seemed to have a U-shaped relationship, with very low and high values being associated with a higher risk of mortality/re-infarction. The c-index was 0.74.

Discussion

In our analysis of a contemporary population of 2,681 presenting with entire spectrum of ACS to a large quarternary care institution, we confirm the prognostic importance of several baseline characteristics reported from previous models developed from other databases [5-8, 16]. In addition, we report on the prognostic significance of several pharmacological and angiographic characteristics, which although routinely encountered in clinical practice, are not incorporated into most of the currently available risk stratification models.
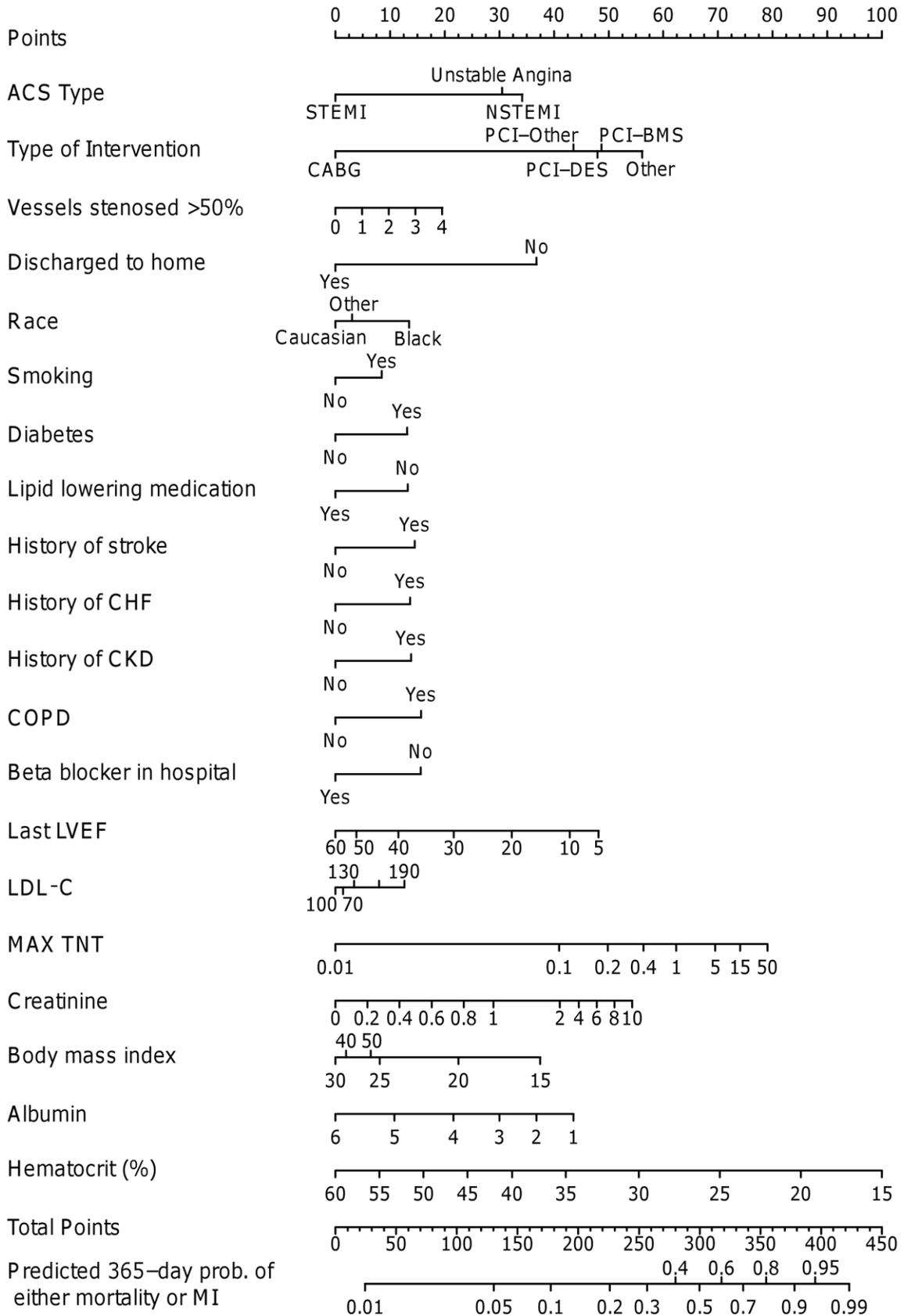
The prognosis of patients presenting with ACS is heterogeneous, with high-risk patients having a significant risk of progression to MI and death. Although risk stratification models such as the TIMI and PURSUIT models are well validated, they are often underutilized and have a number of shortcomings [17]. For one, although some factors such as age, gender, past medical history, and hemodynamic measurements are relatively easy to characterize, others factors such as those based on clinical examination findings (for example, the presence of a summation gallop) or symptoms (for example, angina class) can be quite subjective, and are often difficult to characterize. Continuous variables such as age and pulse rate are also included in most models and are either included as linear (age in 10-year increments, for example) [5], or dichotomous (age $\geq$ 65 years, for example) [6], although these relationships are not linear [18, 19]. Further, the hazard of an adverse ischemic outcome within 30 days after an ACS event is non-linear, with the majority of the risk concentrated in the initial hours and days following presentation [13]. Thus, by including in-hospital events, the majority of the currently available 30-day risk prediction models are likely unduly influenced by factors predictive of in-hospital events rather than those after discharge. A number of these limitations were addressed by the GRACE 6 months post-discharge model, and it remains one of the most widely cited ACS risk scores in clinical practice today [5]. Despite this, most of ACS models including GRACE cannot be considered to be totally relevant in today's ACS population, since they were constructed at least a decade ago. Information on
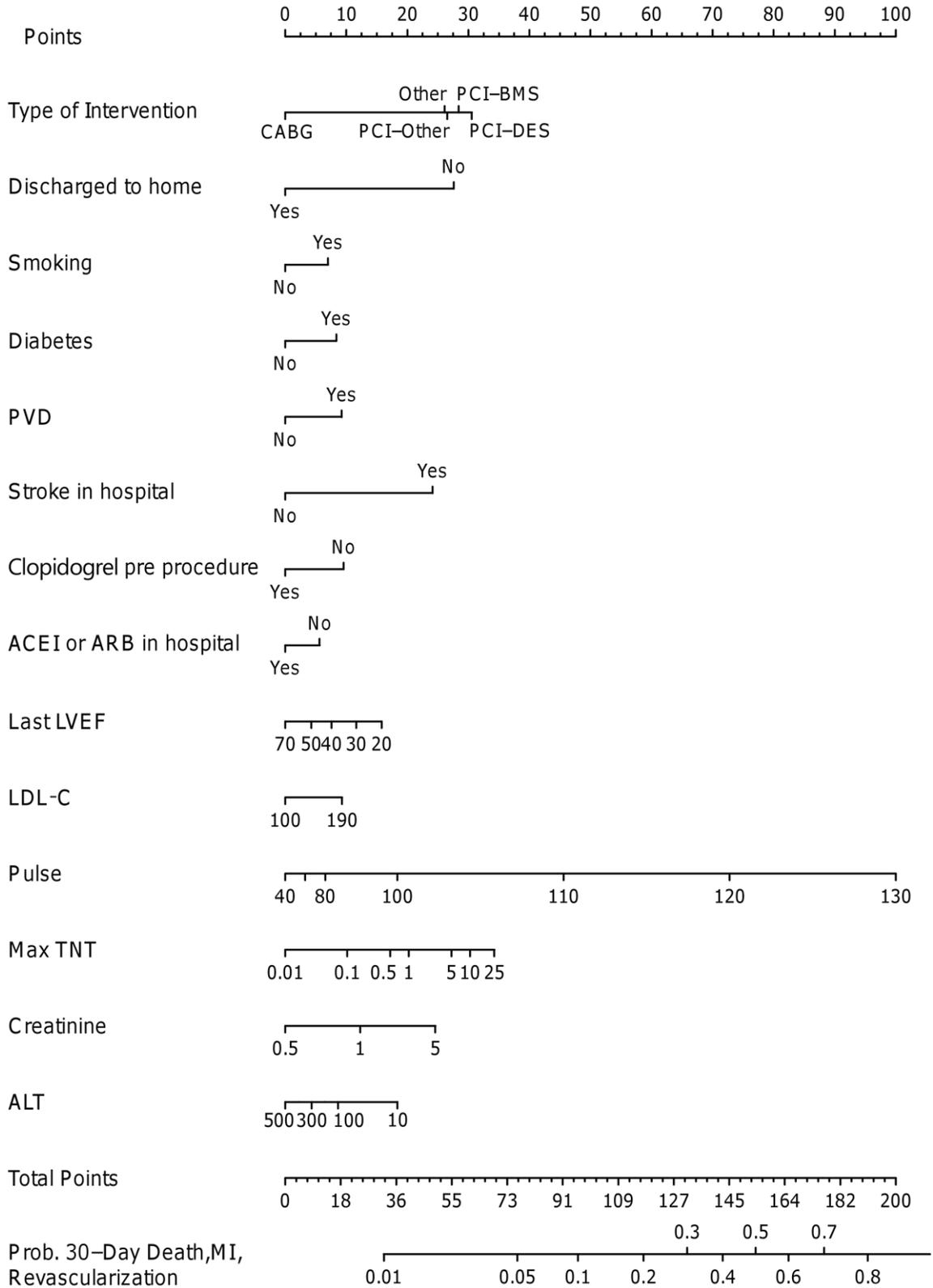
Figure 4. Nomogram for 30-day death/repeat myocardial infarction/revascularization. ACEI represents angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker, ALT, alanine aminotransferase; BMS, bare-metal stents; CABG, coronary artery bypass graft surgery; DES, drug-eluting stent; LDL-C, low density lipoprotein cholesterol, LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TNT, troponin T.

Kumbhani - predictors of ACS

Points 0 10 20 30 40 50 60 70 80 90 100

ACS Type
Unstable Angina
STEMI NSTEMI

Type of Intervention
PCI–Other PCI–BMS
CABG PCI–DES Other

Vessels stenosed >50% 0 1 2 3 4

Discharged to home
No
Yes

Race
Other
Caucasian Black

Smoking
Yes
No

Diabetes
Yes
No

Lipid lowering medication
No
Yes

History of stroke
Yes
No

History of CHF
Yes
No

History of CKD
Yes
No

COPD
Yes
No

Beta blocker in hospital
No
Yes

Last LVEF 60 50 40 30 20 10 5

LDL-C 130 190 100 70

MAX TNT 0.01 0.1 0.2 0.4 1 5 15 50

Creatinine 0 0.2 0.4 0.6 0.8 1 2 4 6 8 10

Body mass index 40 50 30 25 20 15

Albumin 6 5 4 3 2 1

Hematocrit (%) 60 55 50 45 40 35 30 25 20 15

Total Points 0 50 100 150 200 250 300 350 400 450

Predicted 365–day prob. of either mortality or MI 0.4 0.6 0.8 0.95 0.01 0.05 0.1 0.2 0.3 0.5 0.7 0.9 0.99

Figure 5. Nomogram for 1-year death/repeat myocardial infarction. ACS represents acute coronary syndrome; ALT, alanine aminotransferase; BMS, bare-metal stents; CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DES, drug-eluting stent; LDL-C, low density lipoprotein cholesterol, LVEF, left ventricular ejection fraction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TNT, troponin T.

adjunctive pharmacotherapy (example, dual antiplatelet therapy) and angiographic severity were not incorporated into these models. When included, these models only studied a subset of the ACS population (for example, patients undergoing PCI only in the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) sub-analysis [12]). Our current models attempts to address all the above issues. We only included variables that can be reliably measured and reproduced. We also made no assumptions regarding the linearity of the associations between continuous variables and outcomes. We think that this significantly improves the prognostic utility of our models over other existing models. As is evident from the nomograms, none of the continuous predictors tested including age, BMI, pulse, hematocrit, LDL/HDL cholesterol, creatinine, troponin or LVEF had a true linear relationship with the endpoints; BMI, pulse and hematocrit in fact demonstrated a U-shaped relationship. We also did not attempt to reduce the model using variable selection techniques (example, stepwise regression) because the omission of insignificant predictors tends to harm predictive accuracy [14]. This is evidenced by the fact that the c-indices in our models are at least as high as or higher than those reported for currently available models, especially for composite endpoints [19]. Further, by excluding peri-procedural and in-hospital events, our 30-day and 1 year models are likely predictive of only those factors that influence adverse outcomes in patients being discharged alive. This is thus more likely to be meaningful to physicians taking care of these patients after an ACS hospitalization. Finally, we included data on the angiographic severity of coronary artery disease, and also on pharmacological agents utilized during the index admission and at discharge in all patients, including in patients who were medically managed only. We believe that our model is thus very contemporary, and highly representative of "all-comers" ACS patients.

Several of the identified predictors deserve special comment. Firstly, we note that 1-year

death and death/ MI are both higher in patients presenting with NSTEMI or unstable angina versus those presenting with STEMI. Earlier analyses have suggested similar 1-year ischemic outcomes in patients presenting with STEMI or NSTEMI [20]. Since we included patients discharged alive only, this is likely a reflection that STEMI patients have higher "up-front" mortality (not captured in this analysis), while NSTE-ACS patients may be at higher risk for recurrent ischemic events due to "non-completion" of the event. They are also more likely to be older with more advanced and complex CAD, and less likely to be completely revascularized and receive evidence-based secondary prevention therapies at discharge [21-23]. Secondly, our models suggest that in patients undergoing PCI, lack of pretreatment with clopidogrel and lack of use of glycoprotein IIb/IIIa inhibitors are detrimental, which corroborates with current literature [10, 24]. Similarly, we confirm the prognostic significance of the use of evidence-based therapies such as beta-blockers and clopidogrel at discharge on ischemic outcomes in these patients [25]. Improving adherence to these measures is critically important. Quality improvement national initiatives such as the American Heart Association's Get With the Guidelines program and the American College of Cardiology's Guidelines Applied in Practice (GAP) program have been launched to improve adherence in patients with CAD, and have resulted in significant improvements [26-28]. However certain subgroups remain vulnerable [17, 28]. Thirdly, the type of management was associated with each of the 4 models, with medically managed patients having the highest risk of adverse outcomes and patients undergoing CABG the lowest. Although the distribution of patients undergoing various management strategies is similar to that reported from large national registries and clinical trials [29, 30], the choice of management strategy was not randomized, and could be influenced by patient characteristics [31]. A propensity matched analysis might thus be more instructive. Nonetheless, our findings support data from randomized controlled trials that suggest

that patients with NSTE-ACS who are medically managed have worse outcomes when compared with those who undergo an invasive strategy [4]. As far as the comparison between CABG and PCI is concerned, the completeness of revascularization with CABG over PCI may play a role, especially in reducing the need for repeat revascularization [32]; factors influencing perceived suitability for CABG may also independently influence outcome.

Limitations of our study include the relatively modest sample size, and that this represents a single quaternary referral center experience. Data on pharmacological agents used was abstracted from inpatient and outpatient pharmacy data. Data on outcomes such as reinfarction and revascularization were determined from the electronic medical records using standard definitions. However, the definition of reinfarction could suffer from some misclassification bias due to the sole reliance on troponin T to define recurrence, without the inclusion of electrocardiographic changes. Re-infarction and revascularization procedures occurring outside our institution were not captured in the current analysis. However, the event rates noted in our study are comparable to those reported by other investigators [33]. Finally, we are unable to directly compare our results with the GRACE score due to non-capture of EKG variables. Validation of the currently identified predictors in other ACS registries is necessary to determine the generalizability of our findings.

Conclusions

In our analysis of a contemporary cohort of patients presenting with ACS, we identified a number of demographic, past medical history, laboratory, pharmacological and angiographic parameters that are associated with adverse ischemic outcomes at 30 days and 1 year in patients discharged alive from the hospital. These models have comparative or superior discriminatory power as currently available models. Our easy-to-use online nomogram allows for accurate risk characterization of these patients at discharge. Future studies are necessary to validate our findings in other ACS registries.

Disclosures

D.J. Kumbhani: Honoraria: American College of Cardiology, SomahLutions. B.J. Wells: None.

Address correspondence to: Dr. Michael W Kattan, Department of Quantitative Health Sciences, Cleveland Clinic, 9500 Euclid / JJN3-01,Cleveland, OH 44195, USA. Phone: 216-539-4731; Fax: 216-445-2781; E-mail: kattanm@ccf.org

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Supplemental material

Instructions to read the paper-based nomogram

The nomogram provides a visual way to express relationships between the predictor variables and the outcome. Moving to the right along any axis indicates greater risk. Variables with greater impact have longer axes. Continuous variables may have a U-shaped relationship reflected by numbers on the bottom and top of the axis. Use the following steps to calculate a patient's risk. Locate the patient's age and draw a line straight up. Where this line crosses the "points" axis reflects the number of points contributed by age. Repeat this process for each of the variables. Sum the points and locate this value on the total points axis. Draw a line straight down to identify the predicted risk.