Predicting Likelihood for Coronary Artery Bypass Grafting After Non–ST-Elevation Myocardial Infarction: Finding the Best Prediction Model

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Background. **Up to half of patients with non–ST-elevation myocardial infarction (NSTEMI) do not receive dual antiplatelet therapy before angiography "pretreatment" because of the risk of increased bleeding if coronary artery bypass grafting (CABG) operation is needed. Several models have been published that predict the likelihood of CABG after NSTEMI, but they have not been independently validated. The purpose of this study was to validate these models and improve the best one.**

Methods. **We studied patients with NSTEMI who were enrolled in the 24-center Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) registry between 2005 and 2008. Previous CABG prediction models were assessed using c-statistics and calibration assessments to determine the best model. Variables from TRIUMPH likely to be associated with CABG were tested to see whether they could improve the best model's performance.**

Results. **Among 2,473 patients with NSTEMI, 11.8% underwent in-hospital CABG. C-statistics for the Modified Thrombolysis in Myocardial Infarction, Treat Angina With Aggrastat and Determine the Cost of Therapy With an Invasive or Conservative Strategy–Thrombolysis in Myocardial Infarction 18, Poppe, and Global Risk of Acute Coronary Events (GRACE) models were 0.54, 0.61, 0.61, and 0.62, respectively. The GRACE model showed the best discrimination and calibration. From the TRIUMPH registry, preselected variables were added to the GRACE model but did not significantly improve model discrimination. A GRACE model risk score of less than 9 had high sensitivity (96%), thus making it useful for predicting patients with NSTEMI who were at low risk for requiring CABG, which included approximately 21% of patients with NSTEMI.**

Conclusions. **This study could not improve on the GRACE model, which had the best predictive value for identifying a need for CABG after NSTEMI with a broader range of predicted risk levels and high sensitivity, especially in patients with scores lower than 9.**

(Ann Thorac Surg 2016;■:■–■)

The effectiveness of dual antiplatelet therapy (DAPT) before angiography "pretreatment" in patients with non–ST-elevation myocardial infarction (NSTEMI) remains controversial because of clinical challenges in managing patients found to have severe coronary artery disease requiring coronary artery bypass grafting (CABG) operations [1, 2]. The addition of a platelet adenosine diphosphate (ADP) receptor blocker to aspirin reduces adverse ischemic outcomes, but it increases the risk of bleeding [3–5], particularly in patients needing CABG [6, 7]. Data from real-world settings suggest that approximately half of patients with NSTEMI do not receive DAPT pretreatment, despite current guidelines to do so [8–10]. One reason for this discrepancy between guidelines and practice may relate to uncertainty about the need for subsequent CABG. A validated and reliable tool for identifying patients with NSTEMI who are at increased risk for requiring CABG could potentially reduce the variability in the use of DAPT before angiography. To address this clinical challenge, several studies

Dr Cohen discloses a financial relationship with Abbott Vascular, Medtronic, Merck, AstraZeneca, Biomet, Boston Scientific, Cardiovascular Systems, Daiichi-Sankyo, Edwards Lifesciences, and Eli Lilly; Dr Bach with Eli Lilly, Novo Nordisk, Relypsa, Wyeth/Pfizer, Bristol Myers Squibb, Eli Lilly, and Merck/Schering Plough Research Institute; Dr. Spertus with Healthcare, Genentech, Amgen, Janssen, Novartis, PCORI, ACCF, Gilead, Lilly, EvaHeart, Amorcyte, and Health Outcomes Sciences.

Accepted for publication March 22, 2016.

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Published by Elsevier

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.03.090

Abbreviations and Acronyms

ADP = adenosine diphosphate
CABG = coronary artery bypass grafting
DAPT = dual antiplatelet therapy
GRACE = Global Risk of Acute Coronary Events
MI = myocardial infarction
NSTEMI = non–ST-elevation myocardial infarction
PCI = percutaneous coronary intervention
TACTICS = Treat Angina With Aggrastat and Determine the Cost of Therapy With an Invasive or Conservative Strategy
TIMI = Thrombolysis in Myocardial Infarction
TRIUMPH = Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status

proposed models to predict the need for CABG, with the idea that delaying initiation of a platelet ADP receptor blocker until after angiography in patients likely to require CABG would be prudent.

Among four previously developed CABG prediction models [11–14], to our knowledge, none had been externally validated. Accordingly, we used a large multicenter registry of patients with acute myocardial infarction (MI) to validate these models and explore which one would be preferable for routine clinical use. We also sought to define additional variables that could further improve the performance of the best prediction model.

Patients and Methods

Data were obtained from the Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH) study. Details of the TRIUMPH methodology have been previously published [15]. In brief, this was a 24-center, prospective, observational registry of patients with acute MI who were 18 years old or older and were enrolled between April 2005 and December 2008. From the overall TRIUMPH cohort, patients with NSTEMI were identified and served as the final analytic cohort. The primary outcome for our study was the performance of CABG during the initial hospital stay after patients presented with an acute MI. This variable was collected by chart review from the procedures performed during the index hospital stay. Institutional research boards at each participating center approved the study, and each patient signed informed consent to participate.

Baseline differences between patients with NSTEMI who underwent CABG and those who did not undergo CABG were compared by the use of Student's t tests for continuous variables and χ^2 tests for categorical variables. From the TRIUMPH data we abstracted variables that constituted previous CABG prediction models including age, sex, history of angina, CABG, MI, percutaneous coronary intervention (PCI), stoke or transient ischemic attack, chronic kidney disease, congestive heart failure, peripheral vascular disease, hyperlipidemia, hypertension, and diabetes. Electrocardiographic findings of ST-segment depression, family history of coronary artery disease, and smoking status were also collected.

We then calculated four previously published prediction models: the Modified Thrombolysis in Myocardial Infarction (TIMI) model [11], the Treat Angina With Aggrastat and Determine the Cost of Therapy With an Invasive or Conservative Strategy (TACTICS)–TIMI 18 model [12], the prediction model proposed by Poppe and colleagues [13], and the Global Risk of Acute Coronary Events (GRACE) model [14] (Fig 1). To validate and compare these prediction models, we assessed their discrimination and calibration by using the data from our TRIUMPH registry. We used c-statistics to assess the models' discrimination, and for calibration we used the Hosmer-Lemeshow tests. We also plotted the observed versus predicted outcomes across deciles of predicted risk and determined whether the intercepts and slopes for the calibration plots were significantly different from 0 and 1, respectively, which would represent ideal performance of the models in the new data set. All these characteristics of the models were used to determine the one with the best predictive utility and clinical value.

The TRIUMPH registry collected many more details than were available in the data sets from which these original prediction models were built, so we explored whether the best CABG prediction model could be improved by adding additional variables that could be associated with the likelihood of undergoing CABG. The selection of these "potential predictor" variables was based on literature review and clinical criteria and included self-identified race, body mass index, marital status, education, work status, dialysis, history of lung disease, history of diabetes, history of cocaine use, use of warfarin on arrival, metabolic syndrome, left ventricular systolic function, initial hemoglobin, and platelet count. These variables were then added into a logistic regression model already containing the GRACE model's risk score. We calculated the Schwarz Bayesian information criterion and Akaike information criterion to assess the modified GRACE model's performance and used the likelihood ratio test to determine whether the extended model had a better fit than the model containing only the GRACE risk score. We also used the integrated discrimination improvement statistic to determine whether the modified GRACE model had improved discrimination. To avoid overestimation of the final models' discrimination, it was validated using 100 bootstrapped samples, and an optimism-corrected c-statistic was calculated. We further calculated the curves for sensitivities and specificities across different GRACE risk scores to identify important clinical thresholds that could best balance sensitivity and specificity for undergoing CABG.

In our study group, most patients (91%) were not missing covariate information; 99% of patients were