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Additional Statistical Methods, Califf et al. "Prediction of 1-year Survival After Thrombolysis for Acute Myocardial Infarction in the GUSTO-I Trial"

Four sets of characteristics were evaluated statistically. These included all significant variables from the 30-day model,1 and those available that were considered potential prognostic factors by the authors: 1) baseline clinical characteristics (age, race, height, weight, enrollment in the U.S. versus elsewhere, diabetes, hypertension, prior cerebrovascular disease, prior bypass surgery, previous MI, previous angina, smoking status, sex, systolic and diastolic pressures, pulse, Killip class, MI location, and thrombolytic assignment); 2) baseline ECG characteristics (atrioventricular block, MI location, left posterior hemiblock, right bundle branch block, supraventricular tachycardia, junctional rhythm, previous MI, heart block, ST-segment depression, ST-segment elevation, number of leads with ST-segment elevation, absolute ST-segment deviation, QRS duration, and heart rate);
3) in-hospital factors (congestive heart failure or pulmonary edema, arrhythmias, stroke, bypass surgery, angiography, moderate or severe bleeding, angioplasty, intra-aortic balloon pump, ventilator, cardioversion, shock, Swan-Ganz catheter, pacemaker, nonarrhythmic complications, reinfarction, and ischemia); and 4) angiographic factors (number of diseased vessels, Thrombolysis In Myocardial Infarction [TIMI] flow grade, left ventricular ejection fraction, and percent stenosis of the infarct artery, the left main, the left anterior descending coronary artery, the left circumflex artery, and the right coronary artery). For each set of factors, we followed the process below, using Cox proportional-hazards modeling techniques.

The assumption of proportional hazards was tested for each potential factor using the method based on weighted residuals.[2] The tests for most factors resulted in a P value >0.05 for violating proportional hazards. In the stepwise-regression process, all factors were incorporated assuming proportional hazards. Any factor remaining in the model after this process that did not meet this assumption was included as a stratification factor. All factors retained in the final model met the proportional-hazards assumption.

First, we determined the univariable relation of each factor with 1-year survival. If the factor was nondiscrete, then we evaluated its linearity with respect to the hazard ratio. For continuous factors, spline transformations were used.[3] Formal comparisons of a model assuming linearity versus models allowing very flexible relations (through the use of splines) showed how much the relation deviated from linear. A plot of the hazard ratio versus the characteristic of interest from the spline-transformed model allowed us to better understand the true relation and to determine appropriate transformations of the factor to test.

References:
1. Lee KL, Woodlief LH, Topol EJ, Weaver WD, Betriu A, Col J, Simoons M, Aylward P, Van de Werf F, Califf RM, for the GUSTO-I Investigators. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. Circulation. 1995;91:1659-1668.

2. Grambsch P, Therneau T. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika. 1994;81:515-526.

3. Devlin TF, Weeks BJ. Spline functions for logistic regression modeling. Proceedings of the 11th Annual SAS Users Group International Conference. Cary, NC: SAS Institute; 1986:646-651.

Appendix: Risk Models for 1-year Mortality in 30-day Survivors of Acute Myocardial Infarction

Baseline clinical and ECG factors and in-hospital factors:

Survival at 1 year = $0.985066^{\exp(\text{Hazard})}$, where Hazard = –1.5853023 + 0.01638428 age + 0.044018939 age' + 0.75244916 [Black race] – 0.015000536 weight + 0.025582448 weight' – 0.015682044 pulse + 0.023901944 pulse' – 0.024982014 [past smoking] – 0.2496803 [never smoked] + 0.46009279 [prior CVD] + 0.56956146 [prior bypass surgery] + 0.59984122 [prior MI, patient history] + 0.011979328 QRS duration – 0.01597942 QRS duration' + 0.20225188 [prior MI, ECG] + 0.26170738 [anterior MI, ECG] + 0.012247884 ECG heart rate – 0.01787625 ECG heart rate' + 0.62321612 [CHF or pulmonary edema] + 0.84275344 [stroke] + 0.40951015 [shock] + 0.47282049 [arrhythmic complication] – 0.28964427 [angioplasty] – 0.34479417 [angiography] + 0.59822106 [intra-aortic balloon pump] – 0.98537247 [bypass surgery] + 0.69659347 [ventilator]

Baseline clinical and ECG factors, in-hospital factors, and angiographic factors:

Survival at 1 year = $0.983692^{\exp(\text{Hazard})}$, where Hazard = 26.940418 + 0.016277666 age + 0.042333059 age' + 0.76459178 [Black race] – 0.016833525 weight + 0.024611701 weight' – 0.00060159774 [past smoking] – 0.27376711 [current smoking] + 0.49513479 [prior CVD] + 0.74383678 [prior bypass surgery] + 0.52745145 [prior MI, history] + 0.012148437 QRS duration – 0.016054066 QRS duration' + 0.2377906 [anterior MI, ECG] + 0.016381804 ECG heart rate – 0.015930691 ECG heart rate' + 0.60133561 [CHF or pulmonary edema] + 0.80042621 [stroke] + 0.45409322 [shock] + 0.46239202 [arrhythmic complication] – 28.532817 [angiography] – 0.88673642 [bypass surgery] + 0.72785356 [ventilator] – 0.029539989 ejection fraction.

Notes:

1. Brackets are interpreted as [c] = 1 if the patient falls into the category, [c] = 0 otherwise.
2. Age' = 0 if age ≤52 or (age - 52) if age >52 years.
3. Weight' = 0 if weight ≤80 or (weight - 80) if weight >80 kg.
4. Pulse' = 0 if pulse ≤62 or (pulse - 62) if pulse >62 beats per minute.
5. QRS Duration' = 0 if duration ≤125 or (duration - 125) if duration >125 ms.
6. ECG heart rate' = 0 if rate ≤115 or (rate - 115) if rate >115 per minute.

Age is measured in years, weight in kg, pulse and ECG heart rate in beats per minute, QRS duration in ms, and ejection fraction as %.