Editorial

Value of community-derived risk models for stratifying patients with non-ST elevation acute coronary syndromes

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This editorial refers to ‘TIMI, PURSUIT, and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS’† by P. de Araújo Gonçalves et al., on page 865

In their paper, de Araújo Gonçalves et al.1 from Portugal compared three risk-stratification algorithms—the Thrombolysis in Myocardial Infarction (TIMI) score,2 the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) score,3 and the Global Registry of Acute Coronary Events (GRACE) score4 in predicting 1-year outcome in 460 consecutive patients aged $63.4 \pm 10.8$ presenting with non-ST elevation acute coronary syndromes (NSTE-ACS). Predictive accuracy of each risk score was fair to good for death or myocardial infarction (MI) at 1-year, which occurred in 15.4% of patients (including 32 deaths and 49 MIs) with the C index ranging from 0.585 [95% confidence interval (CI) 0.539–0.631] with the TIMI score, to 0.630 (95% CI 0.584–0.674) with the PURSUIT score, and 0.715 (95% CI 0.672–0.756) with the GRACE score.

Of interest in this paper is the fact that the GRACE risk score algorithm (a score based on a community registry) performed better than the score algorithms derived for 30-day outcomes from trials (the TIMI and PURSUIT scores). Predictive accuracy of each risk score was fair to good for death or myocardial infarction (MI) at 1-year, which occurred in 15.4% of patients (including 32 deaths and 49 MIs) with the C index ranging from 0.585 [95% confidence interval (CI) 0.539–0.631] with the TIMI score, to 0.630 (95% CI 0.584–0.674) with the PURSUIT score, and 0.715 (95% CI 0.672–0.756) with the GRACE score.

Of interest in this paper is the fact that the GRACE score algorithm (a score based on a community registry) performed better than the score algorithms derived for 30-day outcomes from trials (the TIMI and PURSUIT scores). Table 1 of their paper summarizes the algorithms for the calculation of these three scores. The fact that the investigators used a computer programme available from the GRACE project website to calculate the GRACE score is worthy of note.

Why should the GRACE risk score perform slightly better than the TIMI and PURSUIT risk scores? One explanation is that the clinical trial populations from TIMI and PURSUIT were selected on the basis of restricted entry criteria, whereas the registry data from GRACE are much more likely to reflect real-life practice.4,5 In the TIMI trial, exclusions included planned revascularization within 24 h. It is likely that unstable patients and patients with heart failure were not recruited into TIMI-11 because of their possible need for early intervention. Also, the trial excluded patients who were thought to have a high bleeding risk from enoxaparin treatment, and this would include the many patients who had significant renal dysfunction. In the PURSUIT trial, exclusions included renal failure.

The GRACE registry is based on 94 hospitals of different sizes and with a wide range of interventional and non-interventional centres from 14 countries in Europe, North America, South America, Australia, and New Zealand. Only the GRACE score algorithm gives any weighting to renal function. Impaired renal function is commonly seen in daily practice with most patients $\geq 75$ years having some renal impairment, and patients with renal impairment have high event rates. In the de Araújo Gonçalves et al.1 study, those who suffered death and MI had higher creatinine levels than those who did not ($2.8 \pm 1.9$ vs. $1.2 \pm 0.5$ mg/dL for 30-day events, $P < 0.001$ and $2.2 \pm 1.7$ vs. $1.2 \pm 0.5$ mg/dL for 1-year events, $P < 0.005$).

There are other major differences between the three score algorithms. The notable absence of a heart failure variable in the TIMI score is a likely consequence of the lower number of patients with heart failure in the TIMI-11 trial,6 and the dichotomous age cut-off may at least partly explain the slightly lower performance of the TIMI score for prognostication. Although risk prediction from the TIMI risk score could be improved by adding more factors, this would be at the expense of simplicity.

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The inherent difference in case collection between registries and trials deserves further attention. In the GRACE registry, two methods were used to identify patients—the so-called warm pursuit and cold pursuit. With the latter approach, cases were identified retrospectively after discharge or death of patients on the basis of the International Classification of Disease codes and, even with the warm pursuit, the patients may be identified some time after presentation. Thus, there may be some missing data fields when compared with prospective data collection in clinical trials, and differences in the collection of data may explain why different parameters are retained in the different algorithms. The TIMI risk score includes coronary risk factors, documented CAD, and the use of aspirin, which are not in the PURSUIT or GRACE scores.

Risk scores are clearly important for informing the patient and family about prognosis and may also be useful to target therapies. de Araújo Gonçalves et al. found that higher risk patients as defined by the PURSUIT and GRACE scores benefited more from revascularization. This observational finding is very interesting as revascularization is often performed in low-risk patients and not in high-risk patients, who are more likely to benefit. For example, in the recent CRUSADE registry from the United States, lower risk patients (such as younger patients and those without heart failure) were more likely to undergo early revascularization. In this registry, 44.8% of patients underwent cardiac catheterization within 48 h of presentation with NSTE-ACS. Predictors of ‘early invasive management’ included cardioselective care, young age, lack of prior or current heart failure, lack of renal insufficiency, no ischaemic ECG changes, no positive cardiac markers, white race, and male gender. In addition, patients treated with the invasive strategy were also more likely to receive other therapies recommended by ACC/AHA guidelines, and they had a lower risk of in-hospital mortality after adjusting for other risk factors (2.5 vs. 3.7%; P < 0.001).

In the TACTICS TIMI-22 trial where revascularization was randomized, revascularizations decreased the composite of death MI, and this benefit was seen only in patients with a TIMI risk score > 3. The TIMI risk score has also been found to stratify those who may benefit more from glycoprotein IIb/IIIa inhibition with tirofiban in the PRISM-PLUS study and from enoxaparin in the TIMI IIb and ESSENCE trials. It is, however, important to recognize that these risk scores are relevant to predict prognosis when the patients receive the standard of care provided by the participating centres and/or specified by the trials.

Dynamic risk assessment with serial assessments can identify changing risk in patients with NSTE-ACS who may need more intensive therapies. For example, serial N-terminal pro-BNP levels over the first 48–72 h have recently been found to help stratify patients. Those with a rapidly falling BNP levels within 48–72 h after medical therapy had improved outcome, and the reverse was seen in those with rising BNP levels.

There is not much information available as to how often risk assessment is actually performed in daily clinical practice. The TIMI risk tool is the commonest used risk assessment tool. It is widely available on a palm pilot and has high user friendliness, with seven easily obtained clinical variables. Clearly, risk models will need to be defined further, perhaps with a multibiomarker approach and the addition of novel markers such as myeloperoxidase and monocyte chemotactic protein-1. Dynamic risk assessment will also be important, but as in other areas of medicine, the major challenge is for clinicians to use the tools currently available.

References