Prospective Comparison of the 5 Most Popular Risk Scores in Clinical Use for Unselected Patients With Acute Coronary Syndrome
– Basis for Design of the Banach Score –

Krzysztof J. Filipiak, MD, PhD; Łukasz Koltowski, MD; Marcin Grabowski, MD, PhD; Grzegorz Karpinski, MD; Renata Glowczynska, MD, PhD; Zenon Huczek, MD, PhD; Janusz Kochman, MD, PhD; Franciszek Majstrak, MD, PhD; Grzegorz Opolski, MD, PhD

**Background:** A limited number of studies comparing the main risk scores (RS) for acute coronary syndromes (ACS) have been conducted and there is a limited number of long-term observations of unselected patient cohorts evaluated with the various RS. The aim of this study was to validate 5 RS (TIMI STEMI RS, TIMI NSTEMI/UA RS, GRACE RS, SIMPLE RS and ZWOLLE RS) in a Polish population and to develop a new RS that would specifically predict 1-year mortality in the unselected ACS patient cohort.

**Methods and Results:** Single-center ACS registry analysis with 1-year follow-up of 931 patients and prospective comparison of 5 RS was conducted. Creation of an RS was attempted. Risk factors were evaluated in a multivariate logistic regression model. The predictive value of the model was assessed with evaluation of the area under curve (AUC) in receiver-operating characteristic analysis. Twelve independent factors influencing 1-year mortality were identified and of them, clerking, physical findings on admission, first ECG and myocardial necrosis markers demonstrated sufficiently high predictive value. All 5 RS were successfully validated in the target registry and although they all displayed high predictive value, the TIMI RS STEMI (AUC=0.84) and GRACE RS (AUC=0.84) proved superior.

**Conclusions:** The developed Banach score offers both high goodness-of-fit and predictive value and may be used irrespective of ACS type. (Circ J 2011; 75: 167–173)

**Key Words:** Acute coronary syndrome; Risk score; Risk stratification

The key aspect of successful management of patients with acute coronary syndrome (ACS) is acting quickly. A quick and accurate decision may prevent life-threatening delays that occur when additional logistic arrangements are required, such as transfer to an invasive cardiology suite. To facilitate the clinical decision process in a prompt, precise and cost-saving manner a number of risk scores (RS) have been developed and locally validated.\(^1\)\(^2\) Comparative validation of different RS has been rarely reported in either retrospective\(^3\) or prospective\(^4\) studies, and to date there is no prospective study that compares different RS in terms of their long-term prognostic accuracy for unselected group of patients with ACS in the Polish setting.

The aim of our study was to evaluate prospectively the 5 most popular RS (ie, the Antman scale (TIMI RS NSTEMI), Morrow-Antman scale (TIMI STEMI RS), SIMPLE RS, ZWOLLE RS and Global Registry of Acute Coronary Events scale (GRACE RS)) in a large Polish cohort of ACS cases. Secondly, we aimed to identify the clinical features and independent prognostic factors that influenced 1-year total mortality in this population. Consequently, we aimed to design a RS that would specifically address characteristics of Polish ACS patients.

**Methods**
A group of 931 unselected, consecutive patients with ACS admitted from January 2002 till June 2003 to the 1st Chair and Department of Cardiology, Medical University of Warsaw were included in the study. As per hospital protocol, all patients were stratified using the TIMI STEMI RS and TIMI NSTEMI RS. Additionally, for the sake of the study, 3 more
RS were calculated: the GRACE RS, SIMPLE RS and ZWOLLE RS.

The inclusion criteria consisted of ACS on admission and age >18 years old. The patients were excluded from the study if they did not meet the inclusion criteria, did not sign the consent form or because the history of presenting complains was missing or coming from an unreliable source (ie, confused patient). Less than 0.5% of cases were excluded from the study among all the patients referred to the center.

The data for calculating the RS were collected directly from the patient at the bedside by the clerking physician and extracted from the medical records and the study forms that were completed together with the clinical care. A long-term follow-up form was completed at the 30-day, 6-month and 1-year outpatient clinic follow-up visits, or by telephone, mail or incidentally at home visit. No one was lost to follow-up. All data were entered into an electronic database and here we present the 1-year follow-up data.

The in-hospital data included: prehospital drug history, admission ECG reports, blood results, in-hospital diagnostic tests and medical events, medical interventions and discharge summary. The long-term follow-up data contained: total mortality, cardiac mortality, non-cardiac mortality, confirmed myocardial infarction (MI), interventional cardiology treatment (>30 days after discharge), cardiothoracic surgery treatment (>30 days after discharge), incidence of stroke and cardiac/non-cardiac hospitalization. The total mortality, an objective measure widely used in major clinical trials, was used as the main endpoint for our study and was adopted by the authors of the other commonly used RS. We have no knowledge of the causes of death.

All patients with ACS were treated according to the current hospital management algorithm for chest pain, based on the ACS European Society of Cardiology (ESC) guidelines from year 2002 and which included the interventional pathway for acute ST-elevation MI (STEMI) patients as a default treatment. However in 45 cases this therapeutic option was missed or coming from an unreliable source (ie, confused patient). We have no knowledge of the causes of death.

All patients with ACS were treated according to the current hospital management algorithm for chest pain, based on the ACS European Society of Cardiology (ESC) guidelines from year 2002 and which included the interventional pathway for acute ST-elevation MI (STEMI) patients as a default treatment. However in 45 cases this therapeutic option was missed or coming from an unreliable source (ie, confused patient). We have no knowledge of the causes of death.

Coronary angiography was performed in 795 (85.4%) cases (87.7% of STEMI and 81.2% of non-STEMI). Of the entire group, 610 patients (65.5%) underwent primary percutaneous coronary intervention (PCI: angioplasty), significantly more in the STEMI group (453; 75.4%) vs. the NSTEMI group (157; 47.6%). Coronary artery bypass grafting (CABG) was used mainly in the NSTEMI patients (40; 12.1%) compared with STEMI patients (29; 4.8%).

The initial risk stratification was performed according to existing hospital practice, which is the Antman scale for patients with NSTEMI or unstable angina (UA) and the Marrow-Antman scale for STEMI patients. Both scales, often referred to as the TIMI RS, are derived from 2 large fibrinolytic therapy studies and include electrocardiographic and clinical features. They became quite popular in day-to-day practice because of their easy to remember structure (7-point and 14-point, respectively) and straightforward mode of application.

The 3 additional RS (SIMPLE, ZWOLLE, GRACE) were calculated prospectively in the course of the clinical progression. The SIMPLE scale is a simplified model that also originates from the registry of the fibrinolytic InTime II study. It is extremely easy to use, as it has 3 parameters only, but at the same time is characterized by low prognostic value, especially in patients with bradycardia (<50 beats/min) or tachycardia (>150 beats/min).

The ZWOLLE scale is a 16-point scale and one of the few that incorporates the coronary flow measure expressed as the post reperfusion TIMI Grade Flow. It is characterized by a relatively high predictive value of c-statistics up to 0.91 and assesses the feasibility of early discharge in low-risk patients.

Finally, the GRACE RS score is based on a wide spectrum of ACS patients from a prospective, multicenter, global registry and it takes into consideration more additional risk factors, such as sudden cardiac arrest. Although it was designed to predict in-hospital mortality or the 6-month outcome, there is increasing evidence for its usefulness in predicting the long-term outcome, so we used it in this study.

The TIMI RS were calculated prospectively accordingly for STEMI and NSTEMI/UA patients. Consequently the GRACE and SIMPLE scores were calculated for all cases, were as the Antman scale (TIMI RS NSTEMI/UA) and Morrow-Antman scale (TIMI RS STEMI) were applied for NSTEMI/UA or STEMI patients, respectively. The ZWOLLE scale was applied only for patients with a known coronary blood flow (TIMI Grade Flow).

Statistical Analysis
The comparative analysis of features within the STEMI vs. the NSTEMI group was performed using Student’s t-test, the Kruskal-Wallis test, chi-square test and Fisher’s exact probability test as required.

The adequacy of the analyzed RS for our data was assessed by fitting corresponding models and investigating the area under curve (AUC) in the receiver-operating characteristic (ROC) analysis. Each model’s goodness-of-fit was checked by the Pearson or Hosmer-Lemeshow test and their predictive values were investigated by the ROC method. All tests were 2-sided and the level of significance was chosen to be 0.05.

A multivariate logistic regression model was used to investigate the relationship between 1-year mortality and important clinical factors. A backward selection procedure, with 0.1 level for staying in the model, was used to select important predictors at the 0.05 level of significance.

All categorical variables with more than 2 categories were replaced with the appropriate number of binary indicators. Subgroups with a small number of observations were combined. All continuous variables were replaced with binary indicators choosing the median as a cut-point, except for age, which was dichotomized at the level of 65 years.

Development of the New RS
All collected data were arranged into 6 homogeneous subgroups: past medical history, clinical examination, echocardiography, laboratory results, interventional procedures and preadmission pharmacotherapy. A multifactor analysis was performed to identify the independent predictors of the endpoint, namely the total 1-year mortality, among all recorded variables and within the subgroups. Using logistic regression analysis we determined the variables that had a significant influence on the main endpoint in the entire study group. The multifactor analysis of the logit model enabled us to assess the predictive variables in an unselected ACS population and to develop a primary model of a new RS that included 12 risk factors and 2 preventive factors. After the famous Polish mathematician the new RS was called the Banach score.

The usage of intraaortic balloon pumping (IABP) depends
The prognostic indexes in the final simplified model oscillate between 0.51 and 1.22 for the predictor variables. Eventually, the model consisted of 10 risk factors. In the Banach Scale, the risk score for 1-Year Mortality in ACS Patients is calculated as follows:

1. Aborted sudden cardiac death before or on admission (1 point)
2. Pulmonary edema before or on admission (1 point)
3. Age >65 years (1 point)
4. His bundle block on first ECG on admission (1 point)
5. Heart failure (NYHA III/IV) in patient’s history (1 point)
6. ST-depression on first ECG on admission (1 point)
7. Heart rate >78 beats/min in admission findings (1 point)
8. ST elevation (anterolateral) on first ECG on admission (1 point)
9. Elevated cardiac markers on admission (1 point)
10. Q wave in any lead on first ECG on admission (1 point)
11. Angina de novo <2 weeks in patient’s history as presenting complaint (−1 point)
12. SBP >130 mmHg on admission (−1 point)

ACS, acute coronary syndrome. Other abbreviations see in Table 1.

Table 2. Banach Scale: Risk Score for 1-Year Mortality in ACS Patients

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aborted sudden cardiac death</td>
<td>1 point</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>1 point</td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td>1 point</td>
</tr>
<tr>
<td>His bundle block on first ECG</td>
<td>1 point</td>
</tr>
<tr>
<td>Heart failure (NYHA III/IV)</td>
<td>1 point</td>
</tr>
<tr>
<td>ST-depression on first ECG</td>
<td>1 point</td>
</tr>
<tr>
<td>Heart rate &gt;78 beats/min</td>
<td>1 point</td>
</tr>
<tr>
<td>ST elevation (anterolateral)</td>
<td>1 point</td>
</tr>
<tr>
<td>Elevated cardiac markers</td>
<td>1 point</td>
</tr>
<tr>
<td>Q wave in any lead on first ECG</td>
<td>1 point</td>
</tr>
<tr>
<td>Angina de novo &lt;2 weeks in history</td>
<td>−1 point</td>
</tr>
<tr>
<td>SBP &gt;130 mmHg on admission</td>
<td>−1 point</td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome. Other abbreviations see in Table 1.

on the therapeutic decision taken by the physician, therefore it could not be treated as a sovereign predisposing feature. Additionally, the usage of IABP is an indirect manifestation of cardiogenic shock, which is already included in the assessment of pulmonary oedema covered by the Killip classification. The IABP was used solely in patients with cardiogenic shock, a group that had a rather severe prognosis. Unfortunately, we do not have the data on coexistent post-procedural slow-flow in this group, which would allow us to perform the analysis. All cases of post-procedural no-reflow were successfully treated with a pharmacological approach, mainly abciximab administration. There were, however only a few of such cases.

Consequently, we decided to remove the IABP factor from the primary RS model. We also combined the variables “elevated troponin (0.5 ng/ml)” and “elevated CK-MB on admission” as 1 predictor termed “elevated myocardial necrosis markers” and eventually built the modified model.

We collected the data for the Killip classification separately for each class (I, II, III, IV) and looked at their predictive value. There was no significant difference, in terms of the endpoint prediction, between classes II and III. There were only 14 patients in Killip class IV, which made it impossible for further statistical analysis. Therefore we decided to combine them into 1 group, which helped us to simplify the RS for the end user. However, we fully agree that from the clinical point of view such a simplification should not be used outside of the model and purposes of calculating the RS. There was a significant difference between Killip classes I and IV as far as prognosis was concerned.

The last step in the process of developing the Banach Scale was to simplify the modified RS model, to increase its usability and to propose a final prognostic model that was more user friendly. We reduced the number of variables by merging some of them into broader categories: left or right bundle branch blocks (LBBB and RBBB) into “bundle branch block (BBB)”, ST-depression in leads V1–V5, II, III and aVF into “ST depression on admission ECG”, ST-elevation in leads V1–V4 or V5,6 into “anterior wall ST elevation on admission ECG”, Q wave in leads V1–V4, V5,6, II, III and aVF into “pathologic Q wave on admission ECG”. The new set of independent predictive variables was analyzed in the repeated logit model and implemented in the final simplified model. The prognostic indexes of the predictive factors are presented in Table 1. Eventually, the model consisted of 10 risk factors and 2 preventive factors that decrease the 1-year mortality risk.

The prognostic indexes in the final simplified model oscill-
lated around 1, ranging from 0.5 for “pathologic Q wave” to 1.27 for “sudden cardiac arrest”. Consequently, we assumed that each negative factor increases the score by +1 and each positive factor decreases the score by −1, making the scale range from −2 to +10. The final version of the Banach Scale is shown in Table 2.

Results

In 601 cases the ACS was eventually identified as STEMI, 298 as NSTEMI and in 32 as UA. The latter 2 groups were combined and analyzed together as NSTEMI/UA (330 patients). There were 322 (35.7%) women in the study group.
194 (32.3%) in the STEMI group and 138 (41.9%) in NSTEMI/UA. The average age was 63 years and was significantly higher in the NSTEMI/UA group (65.5 vs. 62). In the STEMI group there were significantly more smokers (42.6% vs. 25.2%), less hypertension (51.6% vs. 69.7%), less diabetes (14.5% vs. 19.7%), less dyslipidemia (26.8% vs. 45.8%) and less history of previous MI (20.3% vs. 37.6%). The complete characteristics are presented in Table 3.

The overall 1-year mortality in the present study group was 13.5%, higher in the STEMI patients (14.9%) than in the NSTEMI group (11%). The 12 independent factors influencing 1-year mortality that we identified are presented in Table 2. For all 5 scales, we determined the relationship between the score and 1-year mortality. Ultimately a validation the 5 RS within the study group was achieved and all 5 scales accurately predicted the long-term outcome in the setting of a Polish population.

As mentioned in the Methods, we excluded the usage of IABP from the model on clinical bases, but it is worth pointing out that it appeared to be the strongest predicting factor determining the increased 1-year mortality risk (odds ratio = 6.27, 95% confidence interval 2.36–16.64).

Additionally, we tested the invented Banach RS and established the relationship between this scale and the 1-year total mortality (Figure 2). Because in the study group there were 194 (32.3%) in the STEMI group and 138 (41.9%) in NSTEMI/UA. The average age was 63 years and was significantly higher in the NSTEMI/UA group (65.5 vs. 62). In the STEMI group there were significantly more smokers (42.6% vs. 25.2%), less hypertension (51.6% vs. 69.7%), less diabetes (14.5% vs. 19.7%), less dyslipidemia (26.8% vs. 45.8%) and less history of previous MI (20.3% vs. 37.6%). The complete characteristics are presented in Table 3.
no patients with a Banach score >8, the 1-year mortality is not presented for these scores. The risk groups were defined as low (≤2 to +1 point), average (+2 to 3 points) and high (≥4 points). The 1-year mortality in the high-risk group was equal to 42%, which is comparable with the other scales. The average and low-risk groups had 1-year mortality of 10.8% and 2.5%, respectively. Medical data collected on admission enabled us to develop a new and more accurate RS for this population, the Banach RS (AUC=0.84).

**Discussion**

**Main Findings**

The predictive values of the SIMPLE, ZWOLLE, GRACE, TIMI STEMI RS and TIMI NSTEMI/UA RS were successfully validated for a Polish population of unsedated ACS patients. The Banach RS has been developed based on the collected data.

**Comparison With Other Scores**

The 5 analyzed RS showed moderate and high predictive value of 1-year mortality in the study cohort (AUC=0.63–0.84), the Banach score was also high.

The superior predictive accuracy of the TIMI and GRACE scales of long-term outcome has been previously recognized. To some extent the scales are based on similar predicting factors; for example, “older age”, defined as >65 or >75 years old, appears in all scales. Four of them (Banach score, Morrow-Antman, SIMPLE, GRACE) also included tachycardia and low blood pressure. All but 1 (SIMPLE) recognize changes in the ST segment as a potential risk predictor. The Banach score, however, included novel predictors not found in the other RS: “sudden cardiac arrest” (also in GRACE RS) and “pathologic Q wave on admission ECG”. Although the present study included unsedated group of ACS patients presenting to hospital, only the GRACE scale and Banach score are dedicated to be using commonly in both STEMI and NSTEMI/UA groups of patients. The other scores are used only in predefined groups, either STEMI or NSTEMI/UA. This prerequisite makes them harder to use in day-to-day clinical practice compared with the universal Banach and GRACE scales. In contrast to the GRACE scale, the Banach score is much easier to use. In the present study 2 protective factors were identified and included in the Banach score: systolic blood pressure ≥130mmHg on admission and angina de novo defined as the first episode of chest pain in the 2 weeks before admission with no other coronary history. In our view, an extremely important value of this study is its local character. The majority of the RS and guidelines used in Polish healthcare are directly adopted from international sources and guidelines. The Banach score is the first comprehensive model explicitly addressing local needs. The similarities of health profiles in countries in our region suggest that the model could be also applicable in the other hospitals of Central and Eastern Europe.

**Risk Scores in the Era of PCI**

The rapid progress and development that takes place in cardiology result in constant change in clinical practice and multiple updates of the guidelines. The past decade brought a major shift in the management of ACS from pharmacological methods, mainly thrombolysis, to interventional methods, such as PCI. The RS that are commonly used in current practice have been created from data from the thrombolysis era; for instance, the TIMI RS NSTEMI/UA is predominantly based on TIMI 11B (Thrombolysis In Myocardial Infarction 11B) and ESSENCE (Efficacy and Safety of Subcutaneous Enoxaparin in unstable angina non-Q-wave MI). The data that served the GRACE RS development include patients already treated with PCI; however, as those authors conclude, there was an increase in the use of PCI with a corresponding decrease in the frequency of fibrinolysis in ST-segment elevation MI. As the treatment strategies for and the views on the underlying causes of ischemic heart disease change, it seems reasonable to ask if the RS developed in the past will still efficiently serve the current population of cardiac patients. The long-term outcome of ACS does depend on the therapeutic strategy undertaken, so we would assume that the predictive value of the RS could be improved by adjusting it for the type of treatment used (PCI or fibrinolysis). This, however, implies the need for separate RSs that would be used according to the particular circumstances. Is this the right direction? In our view such a strategy seems to be less feasible, mainly for 2 reasons. Firstly the clerking physician would have to anticipate what type of treatment will eventually be used—very difficult in the early stages of the admission. Secondly, it would increase the complexity associated with risk stratification and potentially lead to lower compliance in terms of proper risk stratification. The Banach RS has been developed from real and unsedated data. The treatment strategies applied in the cohort were consistent with ESC guidelines; the majority of patients (93%) underwent PCI. The Banach RS is therefore designed with a primary focus on invasive treatment of ACS and should be applied in centers that possess the necessary capacity to fulfill patient management according to current cardiology guidelines. We would suggest therefore that the Banach RS is an optimal prognostic tool in the primary PCI era. In our view this feature is its main advantage over other common RS. The Banach RS was developed in Poland, a country with 1 of the highest rates of PCI performed in ACS patients in Europe. These rates are also improving in other countries in Europe, putting more pressure on physicians to use RS that are suitable in the PCI era.

**Study Limitations**

A common limitation of any single center study is the restricted size of the cohort. Most studies that developed RS are based on large observations of thousands of patients. However, they are usually not primarily designed with the purpose of RS development. This process is usually performed secondary to the primary analysis and the data is analysed retrospectively as a subanalysis of such study. In our case, the study was predominantly commenced with an objective to deliver relevant data for developing the Banach score. Any new RS should be tested in an internal and external validation process. Up until now the proposed Banach score has been examined only in the study group (internal validation) and would benefit from an external validation in a separate population, before wider usage is recommended. As observed in other studies this process requires a much smaller group of patients than in the original study; in the case of the Banach score we would estimate that a group 250 cases would be sufficient to prove the model.

We are aware that our research is based on a relatively small population size, especially when compared with the other studies that served for creation of the main RS used in cardiology. Furthermore, we have performed it as a single center study. For these reasons, before the Banach RS becomes wide-spread and applied in everyday clinical practice, further research in a larger population and preferably in other


