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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Assessment of the prognostic value of coronary angiography in patients with non-ST segment elevation myocardial infarction

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Abstract

Background: Management of patients with acute non-ST segment elevation myocardial infarction (NSTEMI) depends on risk evaluation. The recommended approach involves the use of risk stratification tools such as TIMI and GRACE risk scores. However, these clinical scores do not include variables derived from coronary angiography which is currently performed in most patients.

Aim: To evaluate the prognostic value of adding selected coronary angiographic parameters to the established TIMI and GRACE risk scores.

Methods: We studied consecutive patients with NSTEMI who underwent coronary angiography. We evaluated selected vascular variables (vessel score, lesion location, percent stenosis, presence of thrombus, lesion length, vessel size, TIMI flow, lesion type according to the ACA/AHA classification, and extent score) and estimated risk using the TIMI and GRACE scores. We assessed total mortality at 30 days, 180 days, and 3 years. To determine the prognostic value of vascular variables and risk scores, we used a logit model and the Hosmer-Lemeshow test. Diagnostic utility of the models was measured by the area under receiver operating characteristic (ROC) curves. To determine usefulness of selected vascular variables as outcome predictors in addition to the GRACE and TIMI scores, we used Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement (IDI) indices.

Results: The study included 237 patients (mean age 65.5 years, 62% men). The TIMI and GRACE risk scores were good predictors of mortality in the evaluated periods. Among vascular variables, independent prognostic factors included the extent score which predicted mortality at 30 days (odds ratio [OR] 12.7, 95% confidence interval [CI] 1.6–99, p = 0.016), 180 days (OR 8.8, 95% CI 2.3–33.7, p = 0.002), and 3 years (OR 3.5, 95% CI 1.6–8.0, p = 0.003), and distal lesion location which predicted mortality at 180 days (OR 3.1, 95% CI 1.0–9.4). Addition of the extent score to the TIMI risk score improved the prognostic value of the latter at all time points, as confirmed by NRI and IDI indices. The GRACE risk score itself had good prognostic value which was not significantly improved by any of the evaluated vascular variables.

Conclusions: The extent score added to the TIMI risk score improves the prognostic value of the latter in patients with NSTEMI. Angiographic variables should be more widely used in risk stratification models in patients with acute coronary syndromes.

Key words: non-ST segment elevation myocardial infarction (NSTEMI), coronary angiography, risk stratification

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INTRODUCTION

Risk evaluation in patients with non-ST segment elevation myocardial infarction (NSTEMI) is the approach recommended by the European Society of Cardiology (ESC) to choose the optimal management strategy [1, 2]. Among many risk scoring systems in patients with acute coronary syndromes (ACS), two classifications have gained most popularity in the recent years, the Thrombolysis in Myocardial Infarction (TIMI) risk score which was published in 2000, and the Global Registry of Acute Coronary Events (GRACE) risk score [3–5]. Indications for advanced drug therapy and early invasive strategy are based on these widely used risk classifications [1]. Early risk

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stratification allows selection of high risk patients who derive most clinical and pharmacoeconomic benefits from advanced strategies of pharmacological and invasive therapy. A routine approach in patients after an ACS includes performing a diagnostic coronary angiography followed by a decision whether to proceed with invasive (percutaneous coronary intervention or coronary artery bypass grafting or conservative therapy. In clinical practice, however, angiographic variables are not used for risk evaluation in this patient group.

Using data from the ACUITY study, Lansky et al. [6] evaluated the effect of clinical and angiographic variables on early and late complications in patients in NSTEMI treated invasively. These authors showed that vascular variables including vessel score, presence of calcifications, presence of stenoses, low ejection fraction as evaluated by ventriculography, excentric lesion, and the presence of a thrombus were more frequent in patients who reached the combined endpoint by 30 days and 1 year. Huang et al. [7] analysed coronary angiographic images in a group of patients with ACS. The authors used three complex systems to evaluate coronary stenoses: the Leaman score, the Gensini score and the ACC/AHA score [8–12]. All these scores were good predictors of coronary deaths at 6 months. An original aspect of the study by Huang et al. [7] was consideration of the prognostic role of atherosclerotic lesions in all coronary vessels and not only culprit lesions, and showing such a relationship in patients with ACS.

We believe that the use of an index describing the severity of atherosclerotic lesions in all coronary segments that takes into account not only the degree of the stenosis but also the degree of atherosclerotic process in general may have higher prognostic value in comparison to evaluation of the degree of coronary stenosis.

Sullivan et al. [13] suggested a new index of the severity of coronary atherosclerotic lesions, called the extent score. This score has been designed to reflect the proportion between "healthy" and diseased segments. The former are characterised by smooth coronary luminal surface, and the luminal surface of the latter indicates atherosclerotic lesions. In 2004, a Milan group of Bigi et al. [14] compared a traditional approach to evaluate coronary vessels by the vessel score and the use of the extent score to predict death and MI. It was shown that the extent score (χ^2 6.5, $p = 0.01$) and age (χ^2 11.4, $p = 0.001$) predicted occurrence of death or MI during 1-year follow-up of patients with stable coronary artery disease (CAD).

Many angiographic studies showed that atherosclerotic lesions are responsible for ACS, thus leading to premature mortality in some patients. These culprit lesions are initially haemodynamically non-significant or even develop in an apparently normal vessel segment. Lack of angiographically significant stenoses at the sites of atherosclerotic plaques may be explained by positive remodelling.

Available literature suggests that data are lacking on the comparison of established risk classifications with angiographic variables derived from cardiac catheterisation in patients with ACS. The aim of this study was to evaluate the prognostic value of coronary angiographic variables in predicting the 30-day, 6-month, and 3-year overall mortality in patients with NSTEMI, and to determine the value of adding selected vascular variables to non-invasive TIMI and GRACE risk scores with a view to improve prediction of early and late overall mortality in NSTEMI patients.

METHODS

This was a retrospective study that included consecutive patients with NSTEMI hospitalised in the Department of Cardiology of the Centre of Postgraduate Medical Education at the Grochowski Hospital, Warsaw, Poland, from Jan 01, 2004 to Jun 01, 2005 who underwent invasive coronary angiography during the index hospitalisation. On admission, GRACE and TIMI risk scores were calculated using a standard form of the hospital electronic medical record. We excluded patients with the diagnosis of ST-segment elevation myocardial infarction (STEMI) or chest pain due to causes other than MI, patient who were unable to provide reliable history, and patients participating in other clinical studies. During hospitalisation, conventional coronary angiography was performed via femoral artery access route. To image atherosclerotic lesions, at least 2 views were analysed for the right coronary artery and at least 5 views for the left coronary artery. Angiographic images were analysed by an invasive cardiologist using the Encompass system (Heartlab Cardiac Solutions). At the time of this analysis, the physician was not aware of the patient clinical data. We evaluated the following vascular variables:

Vessel score. Using the Cardiology Audit and Registration Data Standards (CARDS), 6 CAD categories were defined depending on the number of stenosed major coronary vessels and involvement of the left main coronary artery: 0-, 1-, 2- and 3-vessel disease, left main disease, and left main disease with right CAD [15].

Location of the culprit lesion. Infarct-related artery (IRA) was determined using the CARDS coronary artery segment classification [15]. For the purpose of this study, IRA location was categorised as proximal (segments 1, 2, 5, 6, 7, 11, and 13) or distal (segments 3, 4, 9, 12, 14, and 15).

Percent IRA stenosis. The degree of stenosis was defined as percentage lumen reduction compared to the reference segment. For the purpose of this study, coronary stenoses were categorised as $> 50\%$ and $\leq 50\%$.

Presence of a thrombus. We evaluated the presence of a thrombus within IRA, using the TIMI classification [16]. For the purpose of this study, patients were divided into groups without angiographic evidence of a thrombus (TIMI 1–0) and with indirect evidence of a thrombus (TIMI 1–4).

Length of the culprit lesion. In the study, we used the ACC/AHA criteria and divided IRAs into short culprit lesions (< 20 mm) and long culprit lesions (≥ 20 mm).

Vessel diameter. IRA diameter was measured within the reference segment for a given vessel. We categorised coronary vessels as narrow (< 3 mm) or wide (≥ 3 mm).

Extent score. We used the extent score which reflects the proportion between "healthy" and diseased coronary vessel segments [13]. Each vessel was weighted depending on its importance (left main coronary artery: 5; left anterior descending artery: 20, first diagonal branch: 10, left circumflex artery: 20, right coronary artery: 20, posterior descending artery: 10). Patients were divided depending on the median value for the overall study group.

Flow in the IRA. We used the TIMI classification [17]. Patients were categorised into the group with no or trace IRA flow (TIMI 0–1) and the group with preserved IRA flow (TIMI 2–3).

Culprit lesion type. We used the ACC/AHA working group classification that includes three lesion types: A, B1, B2, and C [18]. Simple lesions were defined as those fulfilling the criteria of the A type lesion, and complex lesions were defined as those fulfilling at least one criterion of the B or C type lesion.

The study endpoint was overall mortality. To determine mortality, we obtained survival data from the national PESEL database (National Electronic System of Population Records) referring to a 4-year follow-up period since the index coronary angiography.

Statistical analysis

Quantitative variables were described using mean values, standard deviations and medians. Categorical variables were described using frequency tables. We used a logit model to assess predictive value of the TIMI and GRACE risk scores for mortality. Relationship between selected vascular variables and mortality risk, taking into account the effect of the TIMI and GRACE risk scores, was tested using the likelihood ratio. We assessed the diagnostic utility of the models with or without a given vascular variable by comparing the areas under receiver operating characteristic (ROC) curves [19]. We also fitted multivariable logit models for the 30-day, 180-day, and 3-year mortality, including only vascular variables. Goodness of fit was tested using the Hosmer-Lemeshow test. To determine usefulness of selected vascular variables as outcome predictors in addition to the GRACE and TIMI scores, we used Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement (IDI) indices described by Pencina et al. [20].

RESULTS

We studied 237 consecutive patients hospitalised in the Department of Cardiology of the Centre of Postgraduate Medical Education with the initial diagnosis of an ACS, in whom the exclusion criteria were absent and who underwent coronary angiography during the index hospitalisation. Table 1 shows patient characteristics. During the follow-up, 13 (5%) patients died by 30 days, 21 (9%) patients died by 180 days, and 34 (14%) patients died by 3 years.

Table 1. Clinical characteristics of the study group — demographic and history data

Variable	Overall study group (n = 237)
Age (range) [years]	65.5 ± 11 (39–90)
Gender (male/female)	147/90 (62%/38%)
Diabetes	57 (24%)
Hypertension	167 (70%)
Hypercholesterolaemia	107 (45%)
Current smoking	88 (37%)
Resting chest pain before hospitalisation	136 (57%)
Renal failure	13 (5%)
Previous myocardial infarction	76 (32%)
Previous percutaneous coronary intervention	17 (7%)

Table 2. Prognostic value of vascular variables for predicting mortality at 30 days, 180 days, and 3 years

	Odds ratio	95% confidence interval	P
30-day mortality			
Extent score > median	12.7	1.6–99.0	0.02
180-day mortality			
Extent score > median	8.8	2.3–33.7	0.002
Distal culprit lesion	3.1	1.0–9.4	0.04
3-year mortality			
Extent score > median	3.5	1.6–8.0	0.003

In multivariate analysis of vascular variables, only the extent score was significantly associated with the 30-day, 180-day, and 3-year mortality. Distal IRA location was associated with the 180-day mortality (Table 2).

Our statistical analysis showed the predictive value of TIME and GRACE risk scores for short-, medium-, and long-term mortality in the studied population of NSTEMI patients (Table 3).

We evaluated the relationship between selected vascular variables and the 30-day, 180-day, and 3-year mortality, taking into account the effect of the TIMI and GRACE risk scores. We compared the prognostic value of models with or without a given vascular variable. Results are shown in Table 4. The extent score added to the TIMI risk score was shown to significantly improve the prognostic value of the latter at all analysed time points. The vessel score added to

Table 3. Prognostic value of the TIMI and GRACE risk scores

	Odds ratio	95% confidence interval	P	Hosmer-Lemeshow goodness of fit	Area under receiver operating characteristic curve
30-day mortality					
TIMI	1.93	1.3–2.9	0.001	0.61	0.77
GRACE	1.04	1.02–1.06	< 0.001	0.7	0.89
180-day mortality					
TIMI	1.56	1.2–2.1	0.003	0.23	0.68
GRACE	1.06	1.04–1.08	< 0.001	0.71	0.88
3-year mortality					
TIMI	1.93	1.03–1.6	0.027	0.76	0.61
GRACE	1.04	1.03–1.06	< 0.001	0.63	0.79

Table 4. Statistical significance (p) of comparisons of the TIMI or GRACE risk models vs. the TIMI or GRACE risk score + vascular variable

TIMI risk model + vascular variables												
	30 days				180 days				3 years			
	HL	ROC	NRI	IDI	HL	ROC	NRI	IDI	HL	ROC	NRI	IDI
Vessel score	O				**0.02**	**0.01**			NS			
Culprit lesion location	NS				NS				NS			
Percent stenosis	O				O				NS			
Thrombus by TIMI	O				NS				NS			
Lesion length	NS				NS				NS			
Vessel diameter	NS				NS				NS			
Extent score	**0.006**	**NS**	**NS**	**< 0.05**	**0.003**	**0.04**	**< 0.05**	**< 0.05**	**0.009**	**0.055**	**< 0.05**	**< 0.05**
TIMI flow	NS				NS				NS			
Lesion type	NS				NS				NS			
GRACE risk model + vascular variables												
	30 days				180 days				3 years			
	HL	ROC	NRI	IDI	HL	ROC	NRI	IDI	HL	ROC	NRI	IDI
Vessel score	O				NS				NS			
Culprit lesion location	NS				NS				NS			
Percent stenosis	O				O				NS			
Thrombus by TIMI	O				NS				NS			
Lesion length	NS				NS				NS			
Vessel diameter	NS				NS				NS			
Extent score	**0.06**	NS	NS	NS	**0.065**	NS	NS	NS	NS	NS	NS	NS
TIMI flow	NS				NS				NS			
Lesion type	NS				NS				NS			

Table shows p values for the Hosmer-Lemeshow test (HL), ROC curve, and NRI and IDI indices for the TIMI and GRACE risk models with added vascular variable. Statistically significant values are given in bold. NS indicates p > 0.05. O — statistical significance could not be calculated due to zero deaths in one of the groups.

the TIMI risk score significantly improved its prognostic value at 180 days. This positive effect of adding the extent score to the TIMI risk score was confirmed using the NRI and IDI indices. The GRACE risk score itself was a very good predictor of mortality. Only for the extent score added to the GRACE risk score at 30 and 180 days of follow-up, borderline values of the Hosmer-Lemeshow test indicated a small independent prognostic value of this variable. However, the p value for

the estimated effect of the extent score was not statistically significant (for 30 days: odds ratio [OR] 5.51, 95% confidence interval [CI] 0.66–46.36, p = 0.12; for 180 days: OR 3.23; 95% CI 0.84–12.42, p = 0.09). Based on the comparison of areas under ROC curves, adding the extent score to the GRACE risk score did not improve the prognostic value of the latter at 30 days, 180 days, and 3 years. The NRI and IDI indices also did not show the prognostic value of the GRACE risk score to be improved by adding any angiographic variables.

DISCUSSION

To evaluate the prognostic value of vascular variables, we created a multivariate model and identified those variables which were significant predictors of mortality at 30 days, 180 days, and 3 years. It was shown that only the extent score above the median was a significant predictor of the 30-day, 180-day, and 3-year mortality. The extent score is a parameter describing the severity of atherosclerotic lesions. Sullivan et al. [13] showed in a group of patients with stable CAD that the extent score correlated with patient age ($r = 0.30$, $p < 0.05$) and apolipoprotein B level ($r = 0.36$, $p < 0.05$) better than previously used vascular variables such as percent stenosis or the vessel score. Until now, this parameter has not been used to evaluate prognosis in ACS patients.

Our findings indicate a negative prognostic effect of distally located culprit lesions. In our study, such lesions were seen in 24% of patients. In a study by Kerensky et al. [21] in a group of NSTEMI patients included in the VANQWISH study, distal culprit lesions were found in 28% of patients. Such culprit lesions were more common in the left circumflex artery (46%) and the right coronary artery (21%) than in the left anterior descending artery (16%). Ischaemia resulting from a distal occlusion of the left circumflex artery or the right coronary artery is usually electrocardiographically silent and thus more difficult to be diagnosed early. This leads to treatment delays, including delayed invasive treatment, which might result in worse patient outcomes.

Our analysis confirmed good predictive value of the TIMI and GRACE risk scores for predicting short- and long-term mortality. These results are in agreement with previously published data [3, 4, 22, 23]. Yan et al. [22] compared clinical utility of three risk scores (TIMI, GRACE, and PURSUIT) and related their predictive value for in-hospital and 1-year mortality to clinical assessment undertaken by physicians who did not use either of these risk scores. The C-statistics for the risk of in-hospital mortality was highest for the GRACE risk score (OR 0.81, 95% CI 0.73–0.89, $p < 0.0001$) and differed significantly from the value calculated for the TIMI risk score (OR 0.68, 95% CI 0.59–0.77, $p < 0.001$). These authors showed that the use of established risk scores was superior to subjective physician clinical assessment.

We found that the extent score added to the TIMI risk score significantly improved its prognostic value at all analysed time points. The GRACE risk score itself was a very good predictor of mortality. Based on the comparison of areas under ROC curves, adding the extent score to the GRACE risk score did not improve the prognostic value of the latter at 30 days, 6 months, and 3 years.

In our study, we used novel NRI and IDI indices to evaluate the value of a adding a vascular variable to the established TIMI and GRACE risk scores. These methods, developed by Pencina et al. [20], allow evaluation of risk indicators supplemented with additional data using the C-statistics. Based on the NRI and IDI indices, we showed that adding the extent score to the TIMI risk score significantly improved the ability to categorise patient into various risk groups at 180-day and 3-year follow-up. At the same time, adding the extent score to the TIMI risk score improved its ability to predict mortality at all analysed time points. Use of the NRI and IDI indices for the GRACE risk model with added extent score confirmed no independent effect of the latter.

In the available literature, we identified two studies that added coronary angiographic data to clinical variables in a group of ACS patients to improve risk prediction. Authors of an ACUITY substudy showed that in moderate to high risk NSTEMI patients, angiographic variables such as myocardial contractility evaluated by ventriculography, severity of CAD, presence of vascular calcifications, and characteristics of the culprit lesion added to established clinical risk factors improved prediction of combined endpoint occurrence at 30 days and 1 year [6]. In the other study, Margonato et al. [24] used the Syntax score in a group of STEMI patients and showed its predictive value. High Syntax scores were associated with more frequent occurrence of a combined endpoint, and particularly of mortality at 18 months, and improved the predictive value of the TIMI risk score for the prediction of both combined endpoint (HR 1.63, CI 1.17–2.27, p = 0.04) and mortality (HR 1.52, CI 1.03–2.23, p = 0.04). In the available literature, we were unable to identify any studies that used the Syntax score in NSTEMI patients.

Showing improved risk stratification in NSTEMI patients by adding angiographic data reflected by the extent score to the TIMI risk score is important new clinical information. The C-statistics for that model was 0.83 for the 30-day follow-up, 0.76 for the 180-day follow-up, and 0.67 for the 3-year follow-up. The C-statistics for the GRACE risk score in the same follow-up periods was 0.89, 0.88, and 0.79, respectively, and thus its prognostic value was slightly superior to that of the TIMI risk score with addition of the extent score. Our findings indicate that coronary angiographic data should be included in the overall estimation of risk in NSTEMI patients.

Limitations of the study

This was a retrospective single-centre study. With a relatively low number of included patients, three vascular variables (vessel score, percent stenosis, and the presence of a thrombus)

could not be evaluated during the initial 30 days due to the fact that the number of observed events amounted to zero. In addition, we did not perform any external validation of the evaluated model. Other limitations include assessment of the angiographic data on atherosclerotic lesions by a single cardiologist, with no evaluation of intraobserver and interobserver variability. Finally, we evaluated overall mortality without specifying causes of death.

CONCLUSIONS

1. The extent score was the only evaluated vascular variable that showed a significant prognostic value for predicting short- and long-term mortality.
2. TIMI and GRACE risk scores predicted mortality in the study group at all analysed time points.
3. The extent score added to the TIMI risk score improved its prognostic value at all analysed time points. The GRACE risk score itself had good prognostic value which was not significantly improved by any of the evaluated vascular variables.

Conflict of interest: *none declared*

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Ocena wartości prognostycznej badania koronarograficznego u chorych z ostrym zespołem wieńcowym bez uniesienia odcinka ST

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Streszczenie

Wstęp: Postępowanie z pacjentami z ostrym zawałem serca bez uniesienia odcinka ST (NSTEMI) zależy od oceny ryzyka. Zalecanymi skalami oceny są TIMI i GRACE. Jednak skale te, oprócz zmiennych klinicznych, nie uwzględniają danych pochodzących z badania koronarograficznego, które obecnie jest wykonywane u większości chorych.

Cel: Celem badania była ocena wartości prognostycznej dodania wybranych zmiennych naczyniowych pochodzących z koronarografii do uznanych skal ryzyka TIMI i GRACE.

Metody: Do badania włączono kolejnych pacjentów z NSTEMI, u których wykonano koronarografię. Oceniono wybrane zmienne naczyniowe (*vessel score*, lokalizację zmiany, % zwężenia, obecność skrzepliny, długość zmiany, rozmiar naczynia, przepływ wg TIMI, typ zmiany wg ACC/AHA, *extent score* — ES) oraz oceniono ryzyko na podstawie skal TIMI i GRACE. Określono całkowitą śmiertelność chorych po 30 dniach, 180 dniach oraz po 3 latach. W celu oceny wartości prognostycznej zmiennych naczyniowych i skal ryzyka posłużono się modelem logitowym i testem Hosmer-Lemeshow. Wartość diagnostyczną modeli oceniono za pomocą wartości pola pod krzywą ROC. W celu zbadania przydatności wybranych wskaźników naczyniowych, jako dodatkowego czynnika prognostycznego, oprócz skal GRACE i TIMI, zastosowano miary *Net Reclassification Improvement* (NRI) i *Integrated Discrimination Improvement* (IDI).

Wyniki: Do badania włączono 237 pacjentów w średnim wieku 65,5 roku, w większości mężczyzn (62%). Skale TIMI i GRACE dobrze przewidywały wystąpienie zgonu w badanych okresach. Niezależnymi zmiennymi naczyniowymi okazały się ES, który przewidywał wystąpienie zgonu w ciągu 30 dni (OR 12,7; 95% CI 1,6–99; p = 0,016), 180 dni (OR 8,8; 95% CI 2,3–33,7; p = 0,002) i 3 lat (OR 3,5; 95% CI 1,6–8,0; p = 0,003) oraz dystalna lokalizacja zmian, która wykazała zdolność prognostyczną w okresie 180 dni (OR 3,1; 95% CI 1,0–9,4). Dodanie ES do skali TIMI poprawiało jej wartość rokowniczą we wszystkich badanych okresach, co potwierdziły testy NRI i IDI. Skala GRACE okazała się narzędziem o wysokiej wartości rokowniczej i dodanie zmiennych naczyniowych nie wpływało znacząco na jej zdolność rokowniczą.

Wnioski: ES dodany do skali TIMI podwyższa jej wartość rokowniczą w grupie pacjentów z NSTEMI. Dane angiograficzne powinny być powszechniej stosowane w modelach oceny ryzyka chorych z ostrym zespołem wieńcowym.

Słowa kluczowe: NSTEMI, koronarografia, stratyfikacja ryzyka

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