ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

Can we improve the accuracy of risk assessment in patients with non ST-segment elevation acute coronary syndromes?

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Abstract

Background: In patients with non-ST segment elevation acute coronary syndromes (NSTE-ACS), the long-term risk of death and myocardial infarction (MI) is estimated by scores based on noninvasively derived variables. Much less is known about the relation between the degree of atherosclerotic burden in the coronary tree and the long-term risk of patients with NSTE-ACS.

Aim: To evaluate the accuracy of a wide spectrum of coronary angiographic and clinical data in predicting outcomes in a long-term follow-up of patients successfully treated invasively for NSTE-ACS.

Methods: The study group consisted of 112 consecutive patients (age 62 ± 10 years; 76 men) treated invasively for NSTE-ACS. 27 (24%) patients had a history of diabetes mellitus (DM) and 37 (33%) patients a history of MI. The coronary angiograms prior to intervention were evaluated blindly for the four angiographic scores: (1) Stenosis score derived from the assessment of the degree of stenosis in 15 segments of the coronary tree; (2) Vessel score showing the number of main vessels stenosed > 70%; (3) Extensity score assessing the proportion of lumen length irregularity in 15 segments; and (4) Complexity score describing the number of complex plaques. The angiographic analysis also focused on the flow, presence of thrombus and collateral supply prior to intervention (according to TIMI) and the size of the culprit lesion vessel. The intervention was successful in 95% of cases. All patients were followed-up for 6–24 months for the occurrence of death or MI.

Results: In the follow-up period, the composite end point of death or MI occurred in 20 (17%) patients. In order to indicate the risk predictors from the group of clinical and angiographic variables (age, sex, history of DM, history of MI, four angiographic scores and culprit lesion vessel characterisation), logistic regression analysis was performed. The independent angiographic predictors of composite end point (selected by forward conditional selection) were stenosis score (OR 1.13; 95% CI 1.05–1.2; p < 0.001) and size of the vessel (OR 0.08; 95% CI 0.01–0.6; p = 0.02)

Conclusions: Our preliminary data shows that attempting to add angiographic variables into the risk assessment scoring systems in order to strengthen their predictive accuracy is justified.

Key words: coronary angiography, NSTE-ACS, risk assessment

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INTRODUCTION

The relation between the angiography and prognosis of the short and long-term risks of patients with non-ST segment

elevation acute coronary syndromes (NSTE-ACS) has been widely studied [1–8]. The results of these studies strengthen the conviction that the complexity of the culprit lesion de-

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termines the short-term clinical outcome, and the extent of atherosclerotic plaques in main branches influences the long-term risk [7–9].

When comparing the angiographic findings in patients with chronic stable angina to those having unstable angina, the latter exhibited a higher frequency of complex lesions and thrombus presence [10–12]. Elevated troponin levels in NSTE-ACS are confirmed to be strongly associated with the presence of coronary thrombus [13, 14]. Furthermore, it has been proved that the angiographic appearance of the culprit lesion with increased complexity carries a high risk of complication in the event of angioplasty, and worsens short-term outcome (early hazard and late gain) [15, 16].

However, the availability of comprehensive antiplatelet pharmacotherapy, suction devices and a new generation of stents lowers the risk of failed angioplasty in this subset of patients to below 5% [17]. There is only limited data available in the literature showing a direct relation between the complexity of the culprit lesion and the occurrence of major cardiac events in cases of successful invasive treatment [16–19]. The European Society of Cardiology (ESC) recommends a combined approach (i.e. non-invasive variables and angiographic data) for a reliable assessment of short-term risk in everyday practice [13]. However, the contemporary scores for the short-term risk stratification of patients with NSTE-ACS (TIMI, GRACE) are based on non-invasive variables, even when an invasive strategy is implemented [20, 21].

This raises the question as to whether the prognostic value of the angiographic data in this subset of patients is undisputed or requires re-evaluation.

Our current knowledge about the relation between the degree of atherosclerotic burden in the coronary tree and the long-term risk is mainly based on the results of studies performed in the 1970s and early 1980s, which showed morbidity and mortality were related to the number of major epicardial arteries with significant diameter reduction [1–4]. These studies, however, have considerable limitations. The study populations were not treated invasively and medical therapy has improved greatly since that time. It remains unclear whether the modern cardiovascular treatment combining current pharmacotherapy and intervention may change the role of traditional angiographical assessment based on evaluation of the lumen narrowing in the main branches in the prediction of long-term risk. This assumption is strengthened by two recently published trials [6, 7].

The purpose of this study was to evaluate the accuracy of a wide spectrum of coronary angiographic and clinical data in the prediction of outcomes in long-term follow-ups of patients successfully treated invasively for NSTE-ACS. We focused particularly on the impact of culprit lesion assessment and evaluation of the severity of the atherosclerotic burden in the coronary tree, as well as on the impact of successful or failed intervention.

Table 1. Study group characteristics (n = 112)

Clinical	
Age [years]	62 ± 10
Men	76 (67%)
History of MI	37 (33%)
History of CHF	14 (13%)
Diabetes mellitus	27 (24%)
Troponin (+)	68 (67%)
Invasive treatment	
PCI	106 (95%)
Stents	63 (59%)
GP IIb/IIIa	51 (48%)
CABG	6 (5%)
Discharged home on	
Aspirin	105 (93%)
Beta-receptor antagonists	103 (91%)
Statins	100 (89%)
ACE inhibitors	98 (87%)
Clopidogrel	60 (53%)

ACE — angiotensin-converting enzyme; CABG — coronary artery bypass graft; GP — glycoprotein; CHF — congestive heart failure; MI — myocardial infarction; PCI — percutaneous coronary intervention

METHODS The study population

The study group consisted of 112 consecutive high risk NSTE-ACS patients hospitalised in the Cardiology Department of the Postgraduate Medical School. High risk was defined as the presence of resting angina lasting for at least 30 min, troponin rise (> 0.5 mg/mL) and/or ST segment depression (> 0.5 mm in at least two contiguous leads) on ECG. All patients were diagnosed and treated invasively. Culprit lesion was clearly depicted in the majority of patients (n = 106, 95%) and treated by percutaneous coronary intervention (PCI). Six (5%) patients were treated surgically. Among those who had PCI performed, TIMI 3 flow was achieved in 86 (81%) patients. The characteristics of the study population are presented in Table 1.

Angiographic assessment

Two independent observers, blinded to the follow-up results, reassessed the angiograms performed prior to the intervention. Each angiogram was reassessed according to the culprit lesion characteristics and severity of the atherosclerotic burden in the entire coronary tree. As in everyday clinical practice, the interpretation of the angiographic picture was based on visual estimation. Lumen vessel narrowing equal to or greater than 70% was interpreted as haemodynamically essential. The coronary vessels were binary divided into two groups: small (equal to or smaller than 2.5 mm) and others. The lesion most

likely to be the angina producing one was identified using the method of Ambrose et al. [10, 11]. The culprit lesion characteristics prior to intervention were described by flow, collateral supply, thrombus presence (graded by TIMI scales) and size of the vessel.

Four different scores were used to measure the severity of the atherosclerotic involvement:

- The traditional vessel score presenting the number of main vessels with a greater than 70% reduction of lumen diameter.
- The complexity score showing the number of plaques with irregular morphology, scalloped borders and overhanging or abrupt borders perpendicular to the vessel wall, ulcerations and/or filling defects according to the method described by Kaski et al. [12].
- 3. The stenosis score describing the most severe stenosis within each segment of the coronary tree. This score, first implemented by Gensini [22], can measure the stenosis in each of eight proximal segments. In our study, this score was further modified to a 15-segment model covering the entire coronary tree. Each segment was graded according to the severity: Grade 0 for less than 10% reduction in lumen diameter, Grade 1 for 11% to 50%, Grade 2 for 51% to 75%, Grade 3 for 76% to 99%, and Grade 4 for total occlusion. The scores in each of the 15 segments were added together to give a total score.
- 4. The extensity score, first developed by Sullivan et al. [23], was used to indicate the proportion of the coronary arterial tree involved by angiographically detectable atheroma. In our study we implemented a further modification of this score by Bogaty et al. [24]. This score was also based on a 15-segment model of the coronary tree. Briefly, the segment was given a score of 0 if it appeared angiographically normal; 1 if less than 10% of its length appeared narrowed or irregular; 2 if > 10% up to 50% of its length was abnormal, and 3 if more than 50% of segment length was occupied. The extent score was the total score of 15 segments of coronary tree.

In a subgroup of patients treated by PCI, flow following the procedure was also assessed, according to the TIMI classification.

Examples of stenosis and extensity scores measurements are presented in Figure 1.

Clinical outcome

The patients were followed-up for 6–24 months. The occurrence of death or myocardial infarction (MI) was recorded as the study end point. The follow-up data was collected prospectively through direct contact with the patients.

Statistical analysis

Statistical analysis was performed using the SPSS 11.0 statistical package. Descriptive statistics for categorical variables

Stenosis score	Extensity score
0 — < 10% stenosis	0 — no irregularities
1 — < 50% stenosis	1 - < 10% of length irregular
2 — < 75% stenosis	2 - < 50% of length irregular
3 — < 99% stenosis	3 - > 50% of length irregular
4 — occlusion	
Example 1	Example 2
Stenosis score — 3	Stenosis score — 1
Extensity score — 2	Extensity score — 3

Figure 1. Angiographic assessment of the severity of atherosclerotic burden in a 15-segment model

were calculated as group percentages and for continuous as mean \pm SD. The presence of relationship between treatment outcomes and predictor variables was tested using the χ^2 test or Fisher exact test for categorical variables and ANOVA for continuous variables. A probability value < 0.05 was considered statistically significant.

A binary logistic regression analysis was performed to identify independent predictors of treatment outcomes. The forward conditional variable selection method with entry p-value of 0.05 was used. Parameter significance in the final model was tested using Wald statistic.

RESULTS Clinical outcome

During the follow-up period, 20 (17%) of the study population died or had MI (15 MIs and five deaths as first event).

Clinical assessment

Among the variables describing clinical status, only a history of previous MI and a history of congestive heart failure (CHF) were related to death or MI during follow-up. Univariate analyses of the treatment modalities showed that patients who were less likely to receive therapy with beta-blockers, statins and clopidogrel had a worse outcome. Surprisingly, stent and glycoprotein IIb/IIIa antagonist use were not related to the occurrence of death or MI in the follow-up period. The univariate analyses of clinical data are presented in Table 2.

Angiographic assessment

Culprit lesion characteristics. Among the four variables describing culprit lesion characteristics, only the vessel size was related to the occurrence of the study end point. Unfavourable outcome occurred more frequently in patients in whom PCI of small vessels was performed. Neither the frequency of severely impaired flow prior to the intervention (TIMI 0 or 1),

Table 2. Univariate analyses of clinical and treatment data

	Death or MI		P <
	YES	NO	
	(n = 20)	(n = 92)	
Clinical assessment			
Age [years]	66 ± 11	62 ± 10	NS
Women	7 (35%)	29 (31%)	NS
History of MI	12 (60%)	25 (27%)	0.01
History of CHF	8 (40%)	6 (6%)	0.001
Diabetes mellitus	5 (25%)	22 (23%)	NS
Treatment			
Stents	9 (53%)	54 (61%)	NS
GP IIb/IIIa	10 (59%)	41 (46%)	NS
Aspirin	18 (90%)	87 (94%)	NS
Beta-receptor antagonists	14 (70%)	89 (96%)	0.01
Statins	13 (65%)	87 (94%)	0.01
ACE inhibitors	15 (75%)	83 (90%)	NS
Clopidogrel	7 (35%)	53 (57%)	0.05

Abbreviations as in Table 1

frequency of weak collateral supply (TIMI grade 0 or 1) nor angiographic evidence of thrombus presence (grade higher than 1 by TIMI) showed any relation with the death or MI during follow-up.

The severity of atherosclerotic burden. The results of univariate analyses of four scores describing the severity of atherosclerotic involvement in coronary arteries were consistent. However, only the traditional vessel score showed a trend toward worse outcome in patients with multivessel disease. The three other scores showed a strong relation between the level of atherosclerotic burden and the occurrence of study end point. In a subgroup of patients treated by PCI, impaired flow post PCI was strongly related to an adverse outcome. The univariate analyses of angiographical data are presented in Table 3.

Multivariate analysis

In binary logistic regression analysis of clinical data and angiographic variables (prior to intervention), three independent predictors of study end point were found. Previous history of CHF and stenosis score indicated increased probability of death or MI (OR 5.3; 95% CI 1.1–25, p < 0.04 and OR 1.1; 95% CI 1.05–1.2, p < 0.001, respectively) and medical therapy with beta-blockers indicated a protective effect (OR 0.07; 95% CI 0.007–0.8, p < 0.04). In a subgroup of patients treated by PCI, the regression analysis was performed with adjustment for the impact of successful intervention, defined as TIMI flow grade 3 after PCI. The stenosis score was the only independent predictor of adverse outcome. The PCI

Table 3. Univariate analyses of angiographical data

	Death or MI		P <		
	YES	NO			
	(n = 20)	(n = 92)			
Severity of atherosclerotic burden					
Vessel score: > 2	16 (80%)	55 (60%)	NS		
Complexity score: 3 or more	13 (65%)	22 (24%)	0.001		
Stenosis score	30 ± 11	17 ± 9	0.001		
Extensity score	31 ± 9	20 ± 10	0.001		
Culprit lesion characteristics					
Flow by TIMI (0 and 1 pre PCI)	11 (55%)	44 (40%)	NS		
Collateral supply by TIMI	16 (80)	79 (86)	NS		
(0 and 1)					
Thrombus presence by TIMI (> 1)	8 (40%)	44 (47%)	NS		
Vessel size (≤ 2.5 mm)	4 (20%)	3 (3%)	0.02		
Effectiveness of angioplasty					
Flow post PCI by TIMI (< 3)	10 (50%)	10 (11%)	0.001		

Abbreviations as in Table 1

of large vessels and medical therapy with beta-blockers were found to be independent factors lowering the risk of death or MI during follow-up (results shown in Fig. 2).

DISCUSSION Long-term risk assessment

The ESC recommendations for long-term risk stratification are based on evaluation of clinical, biological and angiographical markers of the underlying disease [9]. However, the current everyday approach to long-term risk stratification of patients with NSTE-ACS is based mainly on noninvasive variables. Analysis of the structure of commonly used risk scores reveals the marginal role of angiographic data in the process of risk calculation [20, 21]. This tendency aligns with the modern concept of atherothrombosis involving the entire circulation, as a major factor limiting life expectancy.

The results of our study show that the value of the coronary angiographic data should not be forgotten for this purpose, and they strengthen the importance of measuring the extent of coronary disease. Our results agree with the recently published data by Huang et al. [7] and Song et al. [8], focusing on the importance of complex angiogram analysis, despite culprit lesion treatment, for long-term risk assessment.

Stenosis score

The traditional assessment of the extent of coronary artery disease (CAD) limited to the evaluation of major epicardial arteries with significant diameter reduction seems not to be sensitive enough for accurate risk prediction.

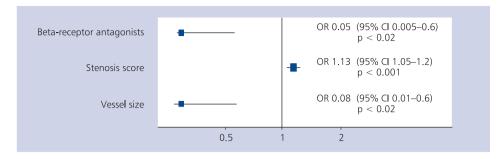


Figure 2. Independent predictors of study end point; OR — odds ratio; CI — confidence interval

The modern invasive approach to the treatment of a high-risk subset of patients with NSTE-ACS ends up with the mechanical stabilisation of plaques narrowing significantly main and possibly secondary branches. However, a large proportion of the coronary tree still remains inaccessible for stents. Rupture of the plaque in smaller branches may also have a deleterious effect.

The concept of measuring the extent of CAD more precisely than by the vessel score was first proposed by Gensini [22]. The Gensini Stenosis Score was based on the analysis of lumen narrowing in eight proximal segments of coronary circulation only. This score was subsequently replaced by the Extent Score (Sullivan group), which was proved to correlate better with the CAD risk factors [23]. The advantage of this score over traditional vessel score in predicting death and MI was further positively evaluated by Bigi et al. [25] in a population of patients with stable angina, and its predictive accuracy has also been recently shown by Arroyo-Espligueroa et al. [26], if angiographic data was combined with C-reactive protein level. The SYNTAX angiographic score is most widely implemented for the proper selection of patients who may benefit from surgical or percutaneous revascularisation. It has recently also been positively evaluated in the context of calculating risk in a population of STEMI patients [27]. The importance of analysing coronary angiograms profoundly in NSTE-ACS patients in terms of risk prediction has been strengthened by the findings of the ACUITY angiographic substudy, which focused once again on the value of jeopardy score as well as the presence of calcifications. However, no attempt has been made so far to adopt any of those angiographic scores for routine risk stratification.

In our study, we aimed to find the most reliable prognostic angiographic score related to hard end points (death or MI) in a long term follow-up period. The stenosis score based on a 15-segment model of the coronary tree has the potential to predict adverse outcome in a high-risk subset of patients treated invasively for NSTE-ACS, independently of other clinical and angiographical markers. It allows simultaneously the measurement of the severity of stenosis and the extent of atherosclerotic involvement.

We believe that the advantage of the stenosis score proposed by our group is mainly due to its proven prognostic

power and simplicity of scoring, which could lead to implementation in everyday practice.

Limitations of the study

Angioplasty of small vessels. Traditional interpretation of the relation between culprit lesion localisation and prognosis assumes that the proximal plaques localised in bigger vessels jeopardise a larger part of the myocardium and may lead to a worse outcome. On the contrary, in our study the angioplasty of small vessels resulted in a worse outcome. The question of why PCI of small vessels worsens the prognosis cannot be easily answered. The concept of the presence of few culprit lesions within small branches or the failure to choose the right vessel for PCI might explain it. The number of PCIs performed in the angiographic territory of small vessels also influences the stenting practice. The low percentage of stent use (compared to contemporary practice) was probably also due to the thrombus presence despite thrombectomy use and the accessory risk of distal embolisation. Nevertheless, we cannot draw a definite conclusion because the number of observations was small.

The culprit artery occlusion. The same limitation has to be kept in mind when interpreting our initial observation showing comparable outcomes in patients with severely impaired or diminished flow in the culprit artery and in patients with a good flow prior to PCI. This result might suggest that the occlusion of the culprit artery surprisingly does not influence the prognosis. This concept needs further evaluation although pathological studies in the literature support this observation. Blumgart et al. [28] described in his pioneering work coronary occlusions in the absence of necrosis and fibrosis in the myocardium, when collateral circulation was well developed. Rissanen [29] found coronary occlusions in 12% of a control group without any myocardial signs of necrosis. Hangartner et al. [30] described recanalised coronary arteries in ten of 16 patients with stable angina in the absence of any signs of infarction.

Diabetes mellitus. Surprisingly our observation found that diabetes mellitus did not influence the prognosis. This subgroup included a large proportion of patients with prediabetic states and also patients with newly diagnosed diabetes. Therefore a longer follow-up period is probably needed.

Patients treated surgically. The results of this registry also include follow-up data of surgically treated patients. We must admit the lack of study group uniformity to be a limitation of the study. However, the idea behind this was to illustrate the true picture of an everyday practice with the need to avoid preselection bias.

CONCLUSIONS

Our intention was to focus on the clinical necessity of searching for an angiographic scale which might have an independent value in long-term risk stratification. Our preliminary data shows that in a high-risk population of patients with NSTE-ACS, treated invasively, the long-term risk is influenced by the atherosclerotic burden of the entire coronary tree, which can easily by measured by the stenosis score.

The value of this score is independent of successful intervention and of culprit lesion characteristics. The question as to whether this parameter could be added to currently used noninvasive risk scores requires further evaluation.

Conflict of interest: none declared

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Czy można poprawić dokładność oceny ryzyka u chorych z ostrymi zespołami wieńcowymi bez uniesienia odcinka ST?

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Streszczenie

Wstęp: Odległe rokowanie chorych z ostrymi zespołami wieńcowymi bez uniesienia odcinka ST (NSTE-ACS) w zakresie ryzyka wystąpienia zgonu lub zawału serca (MI) opiera się na skalach ryzyka zbudowanych na podstawie zmiennych nieinwazyjnych. Relacje między obrazem koronarograficznym i odległym klinicznym ryzykiem są znacznie mniej poznane, podczas gdy u podłoża choroby leży zmienione chorobowo łożysko naczyniowe.

Cel: Celem pracy była ocena, czy rozszerzenie aktualnie stosowanych skal określających ryzyko chorych na podstawie zmiennych wynikających z obrazu angiograficznego może wpłynąć na ich wartość predykcyjną.

Metody: Grupę badaną stanowiło 112 kolejnych chorych (w wieku 62 ± 10 lat, 76 mężczyzn) leczonych inwazyjnie z powodu rozpoznanego NSTE-ACS. Chorzy na cukrzycę (DM) stanowili grupę 27 (24%) chorych; 37 (33%) osób przebyło w przeszłości MI. Badania koronarograficzne wykonane przed interwencją były analizowane pod kątem 4 skal angiograficznych: 1. "Skala zwężeń" uzyskana po ocenie stopnia zwężenia naczyń wieńcowych w modelu 15-segmentowym; 2. "Skala naczyniowa" określająca liczbę głównych naczyń wieńcowych zwężonych > 70%; 3. "Skala rozległości zmian" określająca proporcję zmian miażdżycowych zajmujących każdy z 15 segmentów naczyń wieńcowych, niezależnie od stopnia zawężania; 4. "Skala złożoności zmian" opisująca liczbę złożonych zmian miażdżycowych, których morfologia sugeruje niestabilność. Analiza angiograficzna obejmowała ponadto przepływ w naczyniu odpowiedzialnym za niedokrwienie, obecność skrzepliny, stopień rozwinięcia krążenia obocznego (wg TIMI) i wielkość naczynia w miejscu obecności blaszki miażdżycowej odpowiadającej za niedokrwienie. Angioplastyka była skuteczna w 95% przypadków. Chorych objęto obserwacją dotyczącą zgonu i MI przez okres 6–24 miesięcy.

Wyniki: Złożony punkt końcowy wystąpił u 20 (17%) chorych. Spośród analizowanych zmiennych klinicznych i angiograficznych (analiza regresji) niezależnymi czynnikami ryzyka wystąpienia złożonego punktu końcowego były: skala zwężeń (OR 1,13; 95% CI 1,05–1.2; p < 0,001) i wielkość naczynia (OR 0,08; 95% CI 0,01–0,6; p = 0,02).

Wnioski: Wstępne wyniki badania sugerują, że próby rozszerzenia aktualnie obowiązujących skal oceniających ryzyko długoterminowe chorych z NSTE-ACS o zmienne angiograficzne są uzasadnione i mogą się przyczynić do poprawy ich wartości predykcyjnej.

Słowa kluczowe: koronarografia, NSTE-ACS, ocena ryzyka

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