Original article

Renal dysfunction at hospital admission, high complexity of coronary artery disease and short term prognosis in acute ST-segment elevation myocardial infarction

Disfuncția renală la internare, complexitatea crescută a bolii coronariene şi prognosticul pe termen scurt în infarctul miocardic acut cu supradenivelare de segment ST

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Abstract

Introduction: Renal dysfunction predicts worse outcomes after ST elevation myocardial infarction (STEMI), even if interventional reperfusion therapy is available. The SYNTAX score is an angiographic tool for assessing the complexity of coronary artery disease. Higher values correspond to a more affected vasculature and are associated with increased complication and mortality rates after primary percutaneous coronary intervention (pPCI). Kidney dysfunction is more prevalent in patients with stable coronary artery disease and high SYNTAX score values. However, this association was not prospectively studied in STEMI patients undergoing pPCI. Material and methods: All STEMI patients admitted between 2011.01.01-2011.12.31 were included in a prospective clinical study. The SYNTAX score was calculated on the basis of emergency coronary angiograms; glomerular filtration rate (GFR) was determined according to the Cockroft-Gault equation, using the serum creatinine levels measured at admission. If GFR was <60 ml/min, renal dysfunction was considered. Three different SYNTAX score tertiles were defined, with low (<11), medium (11-19.5) and high (≥20) values. Results: GFR and SYNTAX score were calculated in 135 of the 137 patients included in the study. Impaired GFR (<60ml/min) was found in 36 cases (26.6%). A negative correlation was observed between the GFR and SYNTAX score values (r=-0.2191, p=0.0107). The GFR was significantly lower in the high SYNTAX score tertile (p=0.029). In-hospital mortality was significantly increased in the high SYNTAX score group (p=0.0397), and also if renal dysfunction was present (p=0.0008). Conclusion: renal dysfunction at hospital admission for STEMI is associated with more complex coronary artery disease. Both conditions increase in-hospital mortality after pPCI.

Keywords: SYNTAX score, acute myocardial infarction, glomerular filtration rate

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Rezumat

Introducere: disfuncţia renală prezice rezultate clinice nefavorabile după un infarct miocardic acut cu supradenivelare de segment ST (STEMI). Scorul SYNTAX este un instrument angiografic pentru gradarea complexităţii bolii coronariene. Valorile mari corespund unui pat arterial mai afectat şi se asociază cu creşterea complicaţiilor şi a mortalităţii după intervenţia coronariană percutană primară (pPCI). Disfuncţia renală este mai prevalentă la pacienţii cu boală coronariană stabilă şi valori crescute ale scorului SYNTAX. Această asociere nu s-a studiat însă în mod prospectiv la pacienţii cu STEMI trataţi cu pPCI. Materiale şi metode: toţi pacienţii internaţi cu STEMI în perioada 01.01.-31.12.2011 s-au inclus într-un studiu clinic prospectiv. Scorul SYNTAX s-a calculat pe baza coronarografiei de urgenţă, iar rata filtrării glomerulare (GFR) conform ecuaţiei Cockroft-Gault, din valoarea creatininei serice, măsurată la internare. Disfuncţia renală a fost definită printr-o valoare a GFR de <60ml/min. Pacienţii s-au împărţit în trei loturi în funcţie de valoarile mici (<11), medii (11-19.5) şi crescute (≥20) ale scorului SYNTAX. Rezultate: GFR şi scorul SYNTAX s-a calculat la 135 din cei 137 de pacienţi incluşi. Disfuncţia renală s-a observat în 36 cazuri (26.6%). Am găsit o corelaţie negativă între GFR şi scorul SYNTAX (r=-0.2191, p=0.0107); GFR a fost semnificativ redusă în lotul cu scor SYNTAX crescut (p=0.0294). Mortalitatea intraspitalicească a fost semnificativ mai mare în grupul pacienţilor cu scor SYNTAX crescut (p=0.0397) şi în cazul disfuncţiei renale (p=0.0008). Concluzii: prezenţa disfuncţiei renale în momentul internării pentru STEMI se asociază cu boală coronariană mult mai complexă. Ambele condiţii cresc mortalitatea intraspitalicească după pPCI.

Cuvinte cheie: *scor SYNTAX, infarct mocardic acut, rata filtrării glomerulare*

Introduction

The negative impact of impaired kidney function on clinical outcomes after acute coronary syndromes is well documented (1-9). Even mild to moderate impairment of the glomerular filtration rate predicts a higher risk of complications, including major bleeding and a three to five-fold increase in long-term mortality (2, 8). The association was described before the era of primary percutaneous coronary intervention (pPCI) (7), and after emergency interventional revascularization became a common practice (2-6, 8, 9). However, pPCI is capable to improve prognosis even in patients on renal replacement therapy (4) .

When pPCI is performed, a precise description of the coronary vasculature is obtained. The SYNTAX score is a unique tool which is used for assessing the complexity of coronary artery disease (11). High values of the SYNTAX score describe a more affected coronary circulation, and are associated with higher complication- and mortality rates after pPCI (12). Mul-tivessel coronary artery disease (13), as well as kidney dysfunction (3) were found to be linked with impaired myocardial reperfusion after pPCI, a possible explanation of the above observations. Although impaired renal function can predict higher SYNTAX score values in patients with stable coronary artery disease (15, 16), this association was not studied in a prospective fashion in STEMI patients undergoing pPCI, in which the process of successful myocardial reperfusion is a primary goal.

Material and methods

Patients

As a part of a prospective clinical study, we analyzed the clinical, laboratory and angiographic data of all patients admitted with STEMI in the Center of Cardiovascular Diseases, Tîrgu Mureş between 2011 January 01 and 2011 December 31. The baseline characteristics are illustrated in *Table 1*. The patients who met the following inclusion criteria were eligible: acute ischemic chest pain lasting ≥30

Table 1. Baseline characteristics of the enrolled patients

Age (years±SD)	61.4±11.4
Male	88 (65.1)
History of hypertension	91 (67.9)
History of diabetes mellitus	29 (21.8)
History of dyslipidemia	67 (52.7)
Current smoking	63 (47.3)
BMI (kg/m^2)	27.7±4.4
Killip class >1	25 (18.5)
Anterior STEMI	55 (40.7)
LVEF (%, median)	40
Ischemic time (hours, median)	5

Values are N (%), unless otherwise stated. BMI=body mass index; SD=standard deviation; STEMI=ST segment elevation myocardial infarction.

minutes, associated with ≥1 mm ST segment elevation in ≥2 contiguous electrocardiographic leads, pPCI as reperfusion therapy performed in the first 24 hours after symptom onset.

Kidney dysfunction

Renal function was assessed by estimating the glomerular filtration rate from the serum creatinine values determined at hospital admission. The Cockroft-Gault equation was preferred for calculating the GFR (17) as it has been previously shown to have a higher predictive value when compared to other formulae (9). Kidney dysfunction was considered in patients with an estimated GFR <60ml/min.

Coronary artery disease

The SYNTAX score was calculated for each patient on the basis of the emergency coronary angiography, (i.e. before performing the angioplasty) using the Version 2.11 of the SYNTAX Score calculator (available online at www.syntaxscore.com). All coronary lesions with a diameter stenosis of ≥50% in any artery with a diameter of minimum 1.5mm received a separate score. A multiplication factor of 2 was applied in case of stenoses 50-99% and 5 for total occlusions. Other adverse lesion characteristics (localization within the coronary artery tree, bi- or trifurcation disease, vessel angulation,

aorto-ostial localization, severe tortuosity, long/calcified/thrombotic lesions and "diffuse" disease) had an additive value (12, 19, 18).

Outcomes

In-hospital mortality was registered and analyzed according to SYNTAX score tertiles and in both patients with and without impaired renal function.

Statistical analysis

After data collection, statistical analysis was performed using the Version 6.01 of the GraphPad Prism software. All variables were stratified according to SYNTAX SCORE tertiles. Discrete data were summarized as frequencies (%), parametric continuous data were expressed as mean ± standard deviation, whereas nonparametric continuous data were expressed as median. Gaussian distribution was evaluated with the Kolmogorov-Smirnov test. The Chi-square test (categorical variables), ordinary analysis of variance (ANOVA, for parametric, continuous variables), and the Kruskal-Wallis test with the Dunn's multiple comparisons post-test (nonparametric, continuous variables) were used to analyze the differences between the 3 study groups. The relation between the SYNTAX score and GFR was also tested using Spearman correlation analysis. In-hospital mortality was analyzed with the help of the

Table 2. Characteristics of the three different patient groups

SYNTAX score tertiles (values)	Low (<11)	Medium (11-19.5)	High (≥20)	p (test)
Age (years±SD)	58.4±13.2	61.8±10.7	64.0±9.7	0.0676 (ANOVA)
Male	29 (64.4)	31 (70.4)	28 (60.8)	0.6292 (Chi-square)
Hypertension	26 (57.7)	29 (65.9)	36 (80.0)	0.0736 (Chi-square)
Diabetes mellitus	9 (20)	9 (20.4)	11 (25)	0.8202 (Chi-square)
Dyslipidemia	18 (42.8)	26 (60.4)	23 (56)	0.2400 (Chi-square)
BMI, kg/m^2 (mean±SD)	27.28±4.9	27.30±3.5	28.54±4.6	0.2991 (ANOVA)
Current smoking	28 (63.6)	20 (45.4)	15 (33.3)	0.0158[1] (Chi-square)
Killip class >1	4 (8.8)	5 (11.3)	16 (34.7)	0.0021[2] (Chi-square)
Anterior location of STEMI	7 (15.5)	23 (52.2)	25 (54.3)	0.0001[3] (Chi-square)
LVEF at admission (%, median)	45	41	36	0.0001[2] (Kruskal-Wallis)
Ischemic time (hours, median)	5.5	4.75	5.5	0.5752 (Kruskal-Wallis)

Significant differences are present as follows: [1]between low and high; [2]between low vs. high and medium vs. high. [3]between low vs. medium and low vs. high SYNTAX score tertiles. Values are N (%), unless otherwise stated. ANOVA=analysis of variance; BMI=body mass index; LVEF=left ventricular ejection fraction; SD=standard deviation; STEMI=ST segment elevation myocardial infarction.

chi-square test. A probability value of <0.05 was considered significant; all tests were two-tailed.

Results

One hundred and thirty-seven patients fulfilled the inclusion criteria during the enrolling period; 135 of them were included in the present substudy (missing data in two cases).

Calculated SYNTAX scores ranged between 3 and 42 with a non-Gaussian distribution (median=16). The three patient groups defined according to complexity of the coronary morphology were homogenous with regard to age, sex, duration of the ischemic time, history of hypertension, dia-

betes mellitus and dyslipidemia. However, in the case of higher SYNTAX score values patients tend to be older (p=0.0676) and to have high blood pressure in clinical history (p=0.0736). We found significant difference between the SYNTAX score tertiles regarding the smoking status (more frequent at lower scores), clinical signs of heart failure at admission (Killip class >1), anterior location of the infarction and impaired left ventricular ejection fraction – the three last conditions being more frequent in patients with higher SYNTAX scores. Characteristics of the three patient groups are summarized in *Table 2*.

The estimated GFR values ranged between 9 and 214.5ml/min, with nonparamet-
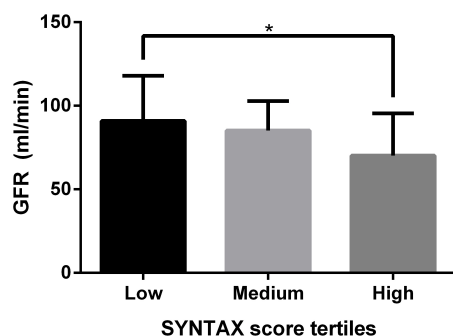
Figure 1. Glomerular filtration rates (GFRs) in different SYNTAX score groups. A significant difference is noted between the median GFRs calculated in low vs. high SYNTAX score tertiles (*p=0.0294, Kruskal-Wallis test with Dunn's multiple comparisons). The plotted values are medians+interquartile range.

ric distribution and a median value of 82.6. Kidney dysfunction (GFR <60ml/min) at hospital admission was present in 36 (26.6% of) the patients. The GFR values were significantly increased in the low SYNTAX score tertile (median GFR in case of low vs. medium vs. high complexity of coronary artery disease: 90.9ml/min vs. 85.2ml/min vs. 70.1ml/min, p=0.0294, *Figure 1*), and Spearman correlation analysis showed an inverse relationship between the absolute values of GFR and SYNTAX score (r=-0.2191, p=0.0107).

In-hospital mortality was significantly increased in case of high SYNTAX score values (mortality in low vs. medium vs. high SYNTAX score groups: 6.66% vs. 4.54% vs. 19.5%, p=0.0397, *Figure 2*) and also in the presence of renal dysfunction (mortality in subjects with GFR <60ml/min vs. ≥60ml/min: 25.0% vs. 5.0% p=0.0008, *Figure 3*).

Discussion

Renal dysfunction is an important issue of pPCI, not only due to the possible negative effects of the contrast media administered during the procedure itself, but also because an-

giographic and clinical outcomes after STEMI are worse in the presence of this condition, with and without reperfusion therapy (1-9). The post-procedural myocardial perfusion was found to be impaired in the case of elevated serum creatinine levels on admission (3), partially explaining the observed higher mortality. On the other hand, there is a known association between multivessel coronary artery disease and poor myocardial reperfusion after pPCI (13). Whereas the term "multivessel" describes only the simple fact that more than one coronary artery is significantly affected by atherosclerosis, the SYNTAX score provides a more complete definition of the coronary artery disease (11). Originally developed to assess the lesions of stable patients, the score was recently evaluated in non-STEMI and STEMI cases, and a significant impact on short- and long term clinical outcomes (death, reinfarction and target vessel revascularization) was described (12, 19), as confirmed by the higher in-hospital mortality rates observed in our population. The same works evidenced a negative relationship between the left ventricular ejection fraction and the SYNTAX score values. This explains the higher incidence of anterior-wall infarction and congestive heart failure in these subsets. Kidney dysfunction is a predictor of higher SYNTAX score values in stable coronary artery disease (15, 16). However, this association probably occurs due to other reasons than the atherosclerotic burden "per se": a meta-analysis of coronary intravascular ultrasound studies found no association between impaired GFR and progression rates of total atheroma volume and percent atheroma volume (20). In the case of acute infarction, the patient's prognosis is highly dependent on successful reperfusion too. The exact pathophysiological mechanism responsible for impaired reperfusion in the presence of renal insufficiency is unknown. However, this last condition at admission can reflect mechanisms like low cardiac output and subsequently impaired myocardial and renal blood flow (3). Processes like endothelial dysfunction, oxidative stress,
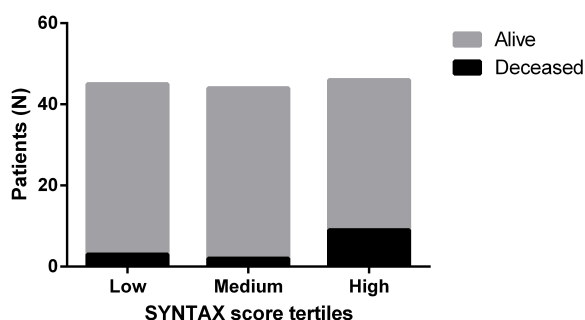
Figure 2. In-hospital mortality according to the SYNTAX score tertiles. Although there was no difference between mortality rates in the low and medium SYNTAX score groups, the number of deaths was significantly more elevated in the high SYNTAX score tertile (p=0.0397, Chi-square test).
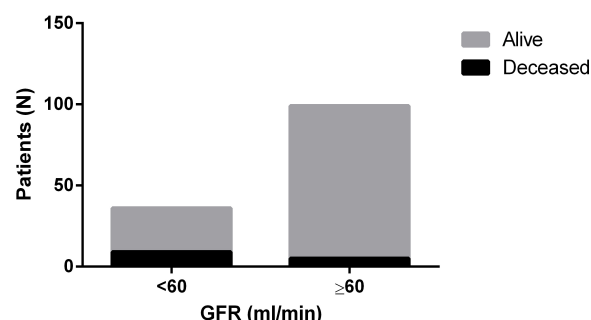

Figure 3. In-hospital mortality in acute myocardial infarction patients with and without impaired glomerular filtration rates (GFR). Significantly more subjects died if renal dysfunction was present (p=0.0008, Chi-square test).

pro-inflammatory and pro-coagulation conditions may have an additional role, as they were found to be associated with high serum creatinine concentration (1, 21-23).

Our findings confirm that there is a gradual, negative correlation between the complexity of the coronary artery disease and the estimated GFR. This probably contributes to the increased mortality rates observed in patients with acute STEMI and renal dysfunction.

Study limitations: The study was elaborated analyzing prospectively an "all-comers" (e.g. real-world) population. However, the research was conducted in a single centre which could only provide a relatively small number of patients. Renal function was only assessed once at hospital admission in the majority of the subjects. Consequently, additional information on further (nephrologic/urologic) investigations leading to a specific ethiological diagnosis was not available.

Conclusion

Renal dysfunction at hospital admission for STEMI is associated with more complex coronary artery disease. Both conditions increase in-hospital mortality after pPCI.

Acknowledgement

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