

EVOLUTION OF PATIENTS WITH MYOCARDIAL INFARCTION WITHOUT ST-SEGMENT ELEVATION DEPENDING ON THE TIME OF CORONAROGRAPHY

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Rezumat

Introducere. *Tratamentul de elecție al infarctului miocardic constă în revascularizare miocardică prin intervenție coronariană percutană. La pacienții cu STEMI este recomandată o abordare cât mai precoce, fiind stabilit un interval sub 2 h de la momentul diagnosticului. Lucrurile nu sunt la fel de clare în ceea ce privește infarctul miocardic fără supradenivelare de segment ST. Recomandările actuale propun împărțirea pacienților cu NSTEMI în 4 grupe de risc și efectuarea coronarografiei într-un interval de sub 2 h până la peste 72 de h în funcție de grupa de risc în care este încadrat pacientul. Au fost efectuate mai multe studii, cu scopul de a determina beneficiul unei abordări invazive în detrimentul recomandărilor actuale, dar nu s-a ajuns la un consens până în acest moment.*

Obiectiv. *Studiul de față și-a propus să analizeze evoluția pe termen scurt și mediu a unui grup de 125 de pacienți cu infarct miocardic fără supradenivelare de segment ST, în funcție de momentul efectuării coronarografiei.*

Material și metodă. *Au fost analizate toate cazurile de NSTEMI internate în spitalul nostru în perioada 1.01.2017-31.12 2017. Pentru fiecare pacient au fost notate :vârsta, sexul, prezența factorilor de risc cardiovascular, antecedentele personale patologice, tratamentul anterior, clasa Killip, scorul GRACE, fracția de ejeție a ventriculului stâng la internare, grupa de risc în care a fost încadrat, momentul efectuării coronarografiei. S-au urmărit: complicațiile apărute, numărul de zile de spitalizare, mortalitatea intraspitalicească și la externare pe o durată de un an de zile.*

Rezultate. *Dintre cei 125 de pacienți cu NSTEMI, 86 (68,8%) au fost bărbați. Pacienții au fost împărțiți în 4 grupe de risc, după cum urmează : risc foarte înalt (n =31; 16,8%), risc înalt (n =80; 43,5%), mediu (n =58; 31,5%) și scăzut (n =15; 8,2%). Coronarografia a fost efectuată în primele 2 ore de la prezentare în 13 cazuri (10,40%), în 24 de ore pentru 48 de cazuri (38,40%), între 24-72 ore la 26 de bolnavi (20,80%) și tardiv, după 72 ore la 38 de bolnavi (30,40%). Cel mai frecvent, coronarografia a fost efectuată în primele 24 de ore la bolnavii aflați în clasele Killip I și II. În funcție de grupa de risc, 11 dintre cei 15 bolnavi (73,34%) cu risc foarte înalt au beneficiat de angiografie de urgență (în primele 24 de ore). În schimb, bolnavii cu risc înalt au efectuat procedura după 24*



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de ore. Pe durata spitalizării, un număr de 19 bolnavi (15,20%) au prezentat complicații. Analiza multivariată arată că predictorii cei mai puternici pentru apariția complicațiilor au fost vârsta ($p = 0,02$), scorul Grace ($p = 0,004$) și grupa de risc în care este încadrat pacientul. Momentul efectuării PCI nu a influențat apariția complicațiilor. Numărul zilelor de spitalizare a fost de $5,92 \pm 3,56$ zile la pacienții care au efectuat PCI sub 2 ore, $7,47 \pm 5,41$ zile pentru cei care beneficiază de procedura în 24 ore, $7,80 \pm 3,67$ zile între 24-72 ore, $10,28 \pm 3,79$ pentru cei care au efectuat procedura tardiv. Aplicând regresia multiplă, cei mai puternici predictorii pentru numărul zilelor de spitalizare au fost vârsta, momentul efectuării PCI și scorul GRACE. Mortalitatea intraspitalicească a fost de 1,6 %, iar la un an de 11,20%. Regresia multiplă a arătat că dintre variabilele studiate, predictorii pentru decesul la un an au fost complicațiile survenite și clasa de risc a bolnavilor.

Concluzie. Efectuarea coronarografiei precoce la pacienții cu NSTEMI poate reprezenta o strategie cost eficientă, prin reducerea numărului de zile de spitalizare, dar nu influențează rata de apariție a complicațiilor, nici mortalitatea pe termen scurt și mediu. În schimb vârsta și scorul GRACE la internare reprezintă predictorii ai complicațiilor intraspitalicești. Mortalitatea pe termen scurt și mediu este corelată cu grupa de risc din care face parte bolnavul și complicațiile apărute pe durata spitalizării.

Cuvinte cheie: grupe de risc, complicații cardiovasculare, mortalitate pe termen scurt și mediu, coronarografie

Abstract

Introduction. The standard treatment for myocardial infarction is percutaneous revascularization. In patients with STEMI, is recommended an approach as early as possible, being established a period of less than 2 hours from the moment of diagnosis. Things are not as clear regarding myocardial infarction without ST segment elevation. The current guideline proposes to divide the patients with NSTEMI into 4 risk groups, and to perform coronarography in a range of less than 2 hours up to over 72 hours, depending on the risk group of which the patient is part. Several studies have been conducted to determine the benefit of an invasive approach to the detriment of current recommendations, but no consensus has been reached so far.

Objective. The present study aims to analyze the short and medium term evolution, of a group of 125 patients, with NSTEMI, depending on the time of coronarography.

Material and methods. We have analyzed all cases of NSTEMI, admitted in our hospital, between 1.01.2017-31.12 2017. The following parameters were noted: age, sex, presence of

cardiovascular risk factors; personal pathological history, previous treatment, Killip class, GRACE score, left ventricular ejection fraction at admission, risk group, the moment of the coronarography. We have followed: complications, number of days of hospitalization, in-hospital and one year mortality.

Results. Of the 125 patients with NSTEMI, 86 (68.8%) were men. They were divided into 4 risk groups as follows: very high risk ($n=31$; 16.8%), high risk ($n=80$; 43.5%), medium ($n=58$; 31.5%) and low risk ($n=15$; 8.2%). Coronarography was performed in the first 2 hours after presentation in 13 cases (10.40%), in 24 hours for 48 cases (38.40%), between 24-72 hours in 26 patients (20.80%) and late, after 72 hours in 38 patients (30.40%). Most commonly, coronarography was performed in the first 24 hours in patients in Killip I and II classes. Depending on the risk group, 11 of the 15 patients (73.34%) with very high risk received emergency angiography (within the first 24 hours). In contrast, high risk patients performed the procedure after 24 hours. During the hospitalization, 19 patients (15.20%) had complications. The multivariate analysis shows that the most powerful predictors for the onset of complications were age ($p=0.02$), Grace score ($p=0.004$) and the risk group in which the patient is classified. The timing of PCI did not influence the appearance of complications. The number of hospitalization days was 5.92 ± 3.56 days in patients who had PCI under 2 hours, 7.47 ± 5.41 days for those who received the procedure in 24 hours, 7.80 ± 3.67 days between 24-72 hours, 10.28 ± 3.79 for those who performed the procedure late. Applying multiple regression, the most powerful predictors for the number of hospitalization days were age, time of PCI and GRACE score. Intra-hospital mortality was 1.6%, and 11.20% at 1 year. Multiple regression showed that among the variables studied, the predictors for death at 1 year were the complications that occurred and the risk class of the patients.

Conclusion. Performing early coronarography in patients with NSTEMI may represent a cost-effective strategy, by reducing the number of days of hospitalization, but it does not influence the rate of complications, nor the short and medium term mortality. In contrast, the age and the GRACE score are predictors of the cardio-vascular complications. Short- and medium-term mortality is correlated with the risk group and with the complications that occurred during the hospitalization.

Keywords: risk groups, cardiovascular complications, short and medium term mortality, coronarography.

Introduction

The most common cause of morbidity and mortality worldwide are cardio-vascular disease. Of these, myocardial infarction is responsible for 15% of deaths annually, with a predominance of myocardial infarction without ST segment elevation (NSTEMI), compared to myocardial infarction with ST segment elevation (STEMI). Prevention,

diagnosis and treatment of this entity representing a current problem of the health system⁽¹⁾. In 90% of cases, the etiology of both types of infarction is given by atherosclerosis. Erosion and rupture of the atheroma plate leads to the formation of occlusive or non-occlusive thrombus in the coronary arteries, with impaired blood flow, ischemia and necrosis, myocardial reperfusion through percutaneous coronary intervention being



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the treatment of choice. The timing of the procedure depends on the type of infarction⁽²⁾. In patients with STEMI, is recommended an approach as early as possible, being established a period of less than 2 hours from the moment of diagnosis, with a decrease in mortality among these patients⁽³⁾. Things are not as clear regarding myocardial infarction without ST segment elevation. The guide of the European Society of Cardiology from 2015 proposes to divide the patients with NSTEMI into 4 risk groups, and to perform coronarography in a range of less than 2 hours up to over 72 hours, depending on the risk group of which the patient is part, as it follows:

1. Very high risk (PCI below 2 h): patients with cardiogenic shock or haemodynamic instability, with acute heart failure, with cardiac arrest or malignant arrhythmias, with recurrent angina or refractory angina at treatment, with recurrent ST-T changes or transient ST segment elevation
2. High risk (PCI in 24 h): suggestive enzymatic dynamics for a heart attack, GRACE score over 140, dynamics ECG changes (ST-T)
3. Medium risk (PCI in 72 h): GRACE score between 109 and 140, patients with early post-infarction angina, diabetes, chronic kidney disease, history of aorto-coronary bypass or angioplasty, FEVS below 40% or heart insufficiency

4. Low risk (conservative treatment, elective PCI): without the criteria mentioned above⁽⁴⁾

However, the wide variety of presentation of this type of infarction and the number of comorbidities that these patients associate, make it difficult to choose an opportune moment for performing coronarography⁽²⁾. Several studies have been conducted to determine the benefit of an invasive approach to the detriment of current recommendations, but no consensus has been reached so far.

Objective

The present study aims to analyze the short and medium term evolution of a group of 125 patients with myocardial infarction without ST segment elevation admitted in our hospital, depending on the time of coronarography.

Material and methods

We have analyzed all cases of myocardial infarction, hospitalized in Emergency County Clinical Hospital of Oradea, between 1.01.2017-31.12 2017. The diagnosis of myocardial infarction was established according to the latest ESC guideline (increase and / or decrease of cardiac

Parameter	Interventional treatment
Age	63,65±11,54
Sex (m)	86 (68,8%)
Diabetis	41 (32,8%)
History of MI	12 (9,60%)
History of CAGB	1 (0,8%)
Hystory of angioplasty	11(8,8%)
Hypertension	79 (63,20%)
Dyslipidemia	43 (34,40%)
Chronic kidney disease	19 (15,20%)
Smoking	38 (30,40%)
Previous treatment	71 (56,80%)
GRACE score	118,80±26,97
Killip class	
I N=120 (65,2%)	100 (83,33%)
II N=45 (24,5%)	22 (48,89%)
III N=6 (3,3%)	1 (16,66%)
IV n=13 (7,1%)	2 (15,38%)
Risk groups	
Very high risk n= 31 (16,8%)	15 (48,38%)
High risk n=80 (43,5%)	46 (57,5%)
Medium risk n=58 (31,5%)	50 (86,2%)
Low risk n=15 (8,2%)	14 (93,33%)
ECG changes N=125	100 (65,36%)
Left ventricular ejection fraction at admission(%)	46,37%±7,39%

Table 1. Characteristics of the patients included in the study



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troponin, preferably high sensitive, with at least one value above the 99th percentile of the upper reference limit, accompanied by at least one of the following: ischemia symptoms, new or presumed new ST-T changes on ECG or major left bundle branch block (LBBB), development of pathological Q waves on ECG, imaging evidence of viable myocardial loss, or changes in parietal kinetics, intracoronary thrombus detected at angiography or autopsy). We selected patients with myocardial infarction without ST segment elevation (based on the ECG aspect) who performed coronarography. Patients with major LBBB or persistent ST segment elevation and those with NSTEMI who did not benefit from the interventional procedure were excluded from the study. At the beginning of the study, each patient signed the informed consent that allowed us to use personal data. For each patient the following parameters were noted: age, sex, presence of cardiovascular risk factors such as smoking, dyslipidemia, high blood pressure; personal pathological history, especially the presence or absence of diabetes, chronic kidney disease, old myocardial infarction, history of angioplasty or coronary aortic bypass, previous drug treatment, Killip class, GRACE score, ECG changes, left ventricular ejection fraction at admission. Depending on the characteristics mentioned above, we divided the patients

into the four risk groups. It was followed the moment of the coronarography, the complications that occurred, the number of days of hospitalization, the in-hospital mortality and at discharge for a period of one year.

Results

The study included 125 patients with NSTEMI, who performed coronarography. The patients were divided into 4 groups, according to the time of the procedure. The characteristics of the patients included are shown in table 1.

Coronarography was performed in the first 2 hours after presentation in 13 cases (10.40%), in the first 24 hours in 48 cases (38.40%), between 24-72 hours in 26 patients (20, 80%) and late, after 72 hours in 38 patients (30.40%)($p = 0.0001$) (Figure 1). Depending on the time of the PCI, it was observed that the younger patients benefited from the procedure within the first 24 hours, compared to the older patients to whom the procedure was performed later. Instead, it was not noted a significant differences of the GRACE score or of the ejection fraction at the hospitalization between the 4 groups of patients (Table nr. 2).

Most commonly, coronarography was performed in the first 24 hours in patients in

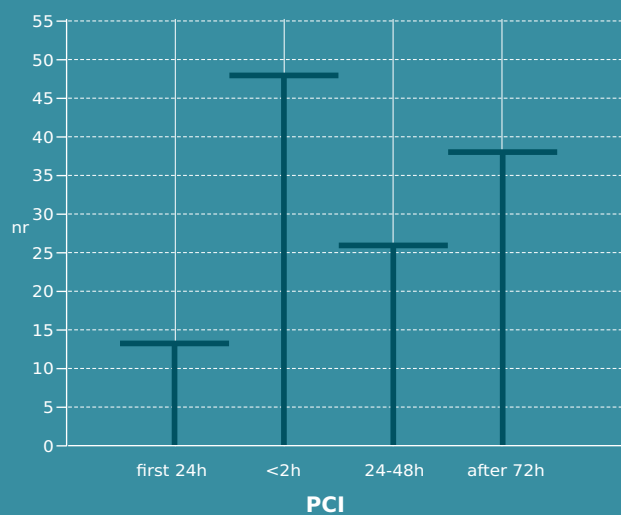


Figure 1. Distribution of patients according to the time of coronary artery intervention

	PCI				P
	< 2 h	First 24 h	24-72 h	After 72 h	
Age	60,12 ±12,47	60,41 ±12,04	67,69± 9,37	66,10 ±10,84	0,0100
GRACE score	116,53± 66,21	112,66 29,59	121,80 17,89	125,26 26,97	0,1660
FEVS	48,84± 6,76	47,02 ± 6,71	46,57± 7,48	46,37 ±7,39	0,609

Table 2. Distribution of patients according to, age, Grace score, FEVS and time of PCI



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Killip I and II classes. The main factors incriminated in the delay of the procedure were the critical condition of the patients on admission (hemo-dynamic instability) and associated comorbidities. Distribution of patients according to Killip class and time of PCI is presented in Table 3.

Depending on the risk group, 11 of the 15 patients (73.34%) with very high risk received emergency interventional treatment (within the first 24 hours). In contrast, high risk patients performed the procedure after 24 hours. Distribution of patients according to risk group and time of PCI is presentet in Table 4.

The number of intraprocedural complications was small ($n = 3$; 2.4%). One of them appeared during the procedure performed in the first 24 hours, and two of them appeared during the procedures performed after 72 hours (third -degree atrioventricular block, ventricular tachycardia). There were no intraprocedural deaths.

During the hospitalization, 19 patients (15.20%) had complications: acute pulmonary edema, arrhythmias, cardiogenic shock or refractory angina. The multivariate analysis shows that the most powerful predictors for the onset of complications were age ($p = 0.02$), Grace score ($p = 0.004$) and the risk group in which the patient was enrolled. The timing of PCI did not influence

the appearance of complications in the patients followed.

The number of days of hospitalization was 5.92 ± 3.56 days in patients who had PCI under 24 hours, 7.47 ± 5.41 days for those who received the procedure in 24 hours, 7.80 ± 3.67 days. between 24-72 hours, 10.28 ± 3.79 for those who performed the late procedure. Applying multiple regression, the strongest predictors for the number of hospitalization days were age, time of PCI and GRACE score at admission.

Intra-hospital mortality was 1.6%. During the hospitalization there were two deaths, in patients who had PCI during the first 24 hours after hospitalization and between 24-72 hours. These occurred in patients with ejection fraction <30 , with trivascular coronary disease, in whom no stenting was performed, the indication being by aorto-coronary bypass. At 1 year there were 14 deaths (11.20%). Multiple regression showed that among the variables studied, the predictors for death at 1 year were the complications that occurred and the risk group of the patients (Table 5).

Discussions

The timing of the coronarography in the group studied by us did not influence the development of complications such as acute pulmonary edema, arrhythmias, cardiogenic

	PCI	KILLIP class - 1	KILLIP class - 2	KILLIP class - 3	KILLIP class - 4	Row - Totals
Count	< 2 h	13	0	0	0	13
Column Percent		13,00%	0,00%	0,00%	0,00%	
Row Percent		100,00%	0,00%	0,00%	0,00%	
Total Percent		10,40%	0,00%	0,00%	0,00%	10,40%
Count	First 24 h	38	8	0	2	48
Column Percent		38,00%	36,36%	0,00%	100,00%	
Row Percent		79,17%	16,67%	0,00%	4,17%	
Total Percent		30,40%	6,40%	0,00%	1,60%	38,40%
Count	Between 24-72 h	22	4	0	0	26
Column Percent		22,00%	18,18%	0,00%	0,00%	
Row Percent		84,62%	15,38%	0,00%	0,00%	
Total Percent		17,60%	3,20%	0,00%	0,00%	20,80%
Count	After 72 h	27	10	1	0	38
Column Percent		27,00%	45,45%	100,00%	0,00%	
Row Percent		71,05%	26,32%	2,63%	0,00%	
Total Percent		21,60%	8,00%	0,80%	0,00%	30,40%

Table 3. Distribution of patients according to Killip class and time of PCI



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shock or refractory angina. It also did not influence the intra-hospital mortality and 1 year mortality, but shows that an earlier approach leads to a decrease in the number of days of hospitalization.

Our data were similar to those in the LIPSIA-NSTEMI trial (Leipzig Immediate vs. early and late Percutaneous Coronary Intervention in NSTEMI), which included 602 patients; they performed coronarography randomly, either immediately (<2 h), early (10 -48 h) or selectively.

There were no significant differences between the 3 groups in terms of death, the rate of occurrence of new myocardial infarction and recurrent ischemia during hospitalization and at 6 months. Complications such as arrhythmias, cardiogenic shock and acute pulmonary edema have not been studied.

The number of days of hospitalization was lower for patients who performed the procedure immediately or early, 4 days compared to 5 days for patients who performed it selectively⁽⁵⁾. The RIDDLE NSTEMI trial, which enrolled 323 patients who randomly performed the procedure immediately below 2h (mean 1.4 h) or delayed before 2 and 72 h (mean 61 h), demonstrated a decrease of myocardial infarction and death at 30 days (12.3% vs 22.5%, hazard ratio 0.50, 95% confidence interval 0.29 to 0.87, $p = 0.014$) and one

year. GRACE score was associated with a significant increase in mortality regardless of when coronarography was performed, while in our group it did not have a statistical significance. The one year mortality was correlated in our study with the risk group and the complications experienced, variables that were not part of the RIDDLE NSTEMI trial analysis^(5,6,7).

Limitations of the study

Coronarography was not always performed according to the risk group in which the patient was enrolled, we have observed a tendency to urgent procedure in younger patients, instead a late approach is preferred in the case of older patients, hemo-dynamic unstable and with many comorbidities; the times for performing the procedures were not entirely identical to those recommended by ESC guideline, most probably due to the poorer access to the catheterization room, in favor of STEMI cases.

Conclusion

Early coronarography in patients with myocardial infarction without ST-segment elevation may be a cost-effective strategy by reducing the number of days of hospitalization. However it does not influence the rate of complications during

	PCI	High risk	Medium risk	Very high risk	Low risk	Total
Number of patients	<2 h	1	6	4	2	13
% of the total number of patients in the risk class		2,17%	12,00%	26,67%	14,29%	
% of the total number of patients who underwent PCI <2 hours		7,69%	46,15%	30,77%	15,38%	
% of the total number of patients		0,80%	4,80%	3,20%	1,60%	10,40%
Number of patients	first 24 h	14	20	7	7	48
% of the total number of patients in the risk class		30,43%	40,00%	46,67%	50,00%	
% of the total number of patients who underwent PCI in 24 h		29,17%	41,67%	14,58%	14,58%	
% of the total number of patients		11,20%	16,00%	5,60%	5,60%	38,40%
Number of patients	24-72 h	16	9	0	1	26
% of the total number of patients in the risk class		34,78%	18,00%	0,00%	7,14%	
% of the total number of patients who underwent PCI in 24 -72h		61,54%	34,62%	0,00%	3,85%	
% of the total number of patients		12,80%	7,20%	0,00%	0,80%	20,80%
Number of patients	> 72 h	15	15	4	4	38
% of the total number of patients in the risk class		32,61%	30,00%	26,67%	28,57%	
% of the total number of patients who underwent PCI >72h		39,47%	39,47%	10,53%	10,53%	
% of the total number of patients		12,00%	12,00%	3,20%	3,20%	30,40%

Table 4. Distribution of patients according to risk class and time of PCI



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	Beta	Std.Err. - of Beta	Beta	Std.Err. - of Beta	t(110)	p-level
Age	0,258386	0,195157	0,006908	0,005218	1,32399	0,188251
KILLIP class	0,183152	0,109076	0,103178	0,061448	1,67912	0,095966
Scor Grace	-0,325370	0,226392	-0,003715	0,002585	-1,43719	0,153501
Group Risk	0,193327	0,096040	0,070122	0,034835	2,01298	0,046559
Time of PCI	-0,001858	0,088609	-0,000570	0,027184	-0,02097	0,983306
Ejection fraction at admission	-0,017930	0,087538	-0,000771	0,003766	-0,20483	0,838084
Complication	0,235092	0,090651	0,204582	0,078887	2,59337	0,010797

Table 5. Predictors for 1 year death (mutiple regression)

*Correlation is significant at the 0.05 level

hospitalization nor the short- and medium-term mortality. On the other hand, the age and the GRACE score at admission represent predictors for the intra-hospital, cardiovascular complications. Mortality in the short and medium term is correlated with the risk group and with the complications that occurred during the hospitalization.

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