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Immediate clinical and angiographic outcomes after delayed percutaneous coronary interventions in patients with acute coronary syndrome

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Abstract

Objective: Coronary artery disease (CAD) remains the leading cause of premature death. Clinical management of patients with such disorders as acute coronary syndrome (ACS) is still one of the most important and debated issues in modern medicine. Some patients fail to come in the most relevant and recommended time for percutaneous coronary interventions (PCI) to receive an effective treatment. This study analyzed the results of the practical approach to the "compelled" delayed percutaneous coronary interventions (DPCI) in patients with acute coronary syndrome.

Methods: The study was performed retrospectively. From 2013 to 2016, there were 141 patients with CAD. The DPCI group with an average admission time when symptoms onset counts 89.4 (17.5) hours was compared with the groups with medical therapy only (MT) and PCI after stabilization (PPCI).

Results: The revascularization Index in DPCI was 0.90 (0.18) and in PPCI made 0.89 (0.2) ($p>0.05$). The percentage of ST segment recovery in the DPCI was 72.8% in patients with elevation, and 87% with ST segment depression. At the same time in comparison with the medical therapy group, a significant difference was found according to this criterion (45.2% and 67.2%, respectively) ($p<0.05$). There were marked changes in DPCI in the data of the echocardiogram due to the reduction in the size of the left ventricle after delayed PCI. The main role in increasing the ejection fraction in DPCI group was the contraction of the left ventricle cavity during the end of systolic phase. In DPCI, group 39 convalescents (92.9%) reached condition stabilization. All-cause mortality during hospitalization in the DPCI was noted for 3 patients (7.1%) and 9 patients (18%) in the MT ($p<0.05$). The PPCI group had no lethal cases.

Conclusion: Delayed PCI in patients with ACS is safe and effective procedure. The use of delayed PCI in combination with optimal drug therapy is the most appropriate non-surgical method of myocardial revascularization in the studied cohort of patients. Delayed PCI results showed greater efficacy in the dynamics of the clinical and functional patient's status compared to PCI performed after ACS stabilization.

Key words: delayed percutaneous coronary interventions, acute coronary syndrome, coronary artery disease

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Abbreviations

ACS-Acute coronary syndrome, CAD-Coronary artery disease, CCS-Canadian Cardiovascular Society, EDD-end-diastolic dimension, EF-Ejection fraction, ESD-end-systolic dimension, LV-Left ventricle, NYHA- New York Heart Association, OMT-Optimal medical therapy, PCI-Percutaneous coronary intervention, RI-Revascularization index, TLT-Thrombolytic therapy

Introduction

Cardiovascular diseases caused by the progression of the atherosclerotic process such as coronary artery disease (CAD) remain the leading cause of premature death. Clinical

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management of patients with such disorders as acute coronary syndrome (ACS) is still one of the most important and debated issues in modern medicine. There are several approaches in the treatment of patients with ACS such as optimal medical therapy (OMT), percutaneous coronary intervention (PCI), coronary artery bypass grafting. Each of these areas can be used to eliminate the root cause of an acute condition. Myocardial reperfusion attempts should be timely and optimal in terms of the volume. This study analyzed the results of the practical approach to the tactics of "compelled" delayed percutaneous coronary interventions (DPCI) in patients with ACS.

Methods

The study was performed retrospectively. It included 141 patients with ACS who were divided into three groups. The first group included 42 patients who, from 2013 to 2016, were exposed to DPCI. The second group (MT) consisted of 50 patients admitted urgently with ACS to the intensive care department in the clinic without the possibility of angiography and received optimal medical therapy. In 40% (20 patients) of cases thrombolytic therapy (TLT) was used in MT group. The third group consisted of 49 patients who underwent planned PCI at various periods after their stabilization (PPCI). The results obtained in the PPCI group were compared to determine the necessity of delayed PCI. Exclusion criteria were myocardial infarction (MI) with right ventricle involvement, patients with congenital heart disease, organic valvular lesions, severe concomitant diseases in the terminal stage (chronic kidney disease, and those of oncological nature).

Cases of achieving condition stabilization, dynamics of the heart failure class, all - cause mortality, dynamics of ST segment deviation on the ECG, recovery of left ventricular function according to echocardiography at the end of hospitalization were recorded and analyzed.

Patients of DPCI and PPCI groups had "Ad-hoc" PCI. PCI was performed after the consent was obtained. All patients received a loading dose of acetylsalicylic acid - 500 mg, clopidogrel - 600 mg and 5000 IU of heparin. The number of stents in stable patients depended on the affected arteries with hemodynamically significant stenosis / occlusion and the patient's physical condition. In patients with ACS, mainly stented artery was infarct-related artery (IRA). Whenever possible on part of the patient the stenting of the remaining hemodynamically significant stenosis of various localizations to increase the completeness of myocardial revascularization was carried out after stents implantation into IRA. Stenting of the arteries not connected with the infarction / ischemia zone was performed only with an adequate clinical picture available. The revascularization index (RI) was calculated.

Statistical analysis: The obtained data was processed on a computer using the statistical program SPSS statistics version 17. Comparison of mean findings was made using standard methods of variation statistics of a medical-biological profile. The distribution of variables was checked using the Kolmogorov-Smirnov test. In the case of a normal distribution of variables, Student's t-test and ANOVA tests were applied. For an out-of-standard distribution of variables, the U-criterion of Mann-Whitney, the criterion of the Wilcoxon signs and the criteria of Kruskal-Wallis, Friedman were calculated. Nominal variables were compared using criterion Chi-square.

Results

The majority of DPCI and MT groups' patients were in the II and III functional classes according to the Killip classification (92.7% and 78%, respectively). The groups differed significantly only in the number of IV class patients. All patients of the PPCI group were in II and III angina pectoris classes according to the Canadian Cardiovascular Society (CCS) classification and only one patient (2%) had New York Heart Association (NYHA) class IV heart failure. Patients were distributed depending on the diagnosis upon admission in the acute period (disease exacerbation), which is presented in Table 1.

In all three groups, the number of men was significantly higher ($p<0.05$). There were no significant differences in the three groups according to the age ($p>0.05$). In patients with ACS, the time from the symptoms onset to the types of treatment (MT and PCI) ranged from an hour to several days. The median time for DPCI patients was 89.4(17.5) hours. Patients admitted before 12 hours threshold prevailed in the MT group 35 (70%) ($p<0.05$). Most of PPCI patients 33 (67.3%) underwent PCI a month after medical treatment stabilization.

The basic characteristics are shown in Table 2.

Table 1. The distribution of patients depending on the diagnosis upon admission in the acute period

Diagnosis at admission	DPCI (N=42)	MT (N=50)	PPCI (N=49)
Refractory unstable angina, n(%)	10(23.8)	13(26)	27(55.1)*
Non Q-wave MI, n(%)	14(33.3)*	7(14)	8(16.3)
Q-wave MI, n(%)	18(42.9)	30(60)*	14(28.6)
*- $p<0.05$, Data are presented as n(%), DPCI- delayed percutaneous coronary intervention, MI –myocardial infraction, MT – medical treatment, PPCI- primary percutaneous coronary intervention			

Table 2. Baseline characteristics

Variables	DPCI (N= 42)	MT (N= 50)	PPCI (N= 49)
Age, years	55.6 (9.6)	61.5 (13.4)	56.3 (8.4)
Male sex, %	76.2	62.0	81.6
Mean delay time/ h/days	89.4 (17.5) *	5.3 (4.1)	>30 days
Killip class > 2, %	30.9	44.0	-
NYHA > 2/ CCS > 2, %	-	-	46.9 / 57.1
Anterior infarct/ischemia localization %	85.7	70.0	73.4
STEMI, %	61.9	68.0	44.9*
Affected arteries number (angiographically) > 1,%	59.5	-	49.0
GRACE score > 140, %	60.0	78.0	-
Euroscore II, %	7.8 (5.1)	9.0 (6.2)*	1.4 (0.8)
SYNTAX score (in points)	13.9 (6.0)	-	12.5 (7.6)
Cholesterol, mmol / l	5.2 (1.4)	5.0 (1.1)	5.2 (1.1)
GFR (MDRD) ml / min / 1.73 m^2	73.3 (16.7)	70.4 (33.2)	74.1 (19.3)
Creatinine, µmol / l	96.8 (21.6)	110.7 (48.1)	96.6 (20.9)
GFR (MDRD) < 70 ml / min / 1.73 m^2	33.3	56	42.8
EF < 50%,%	45.2	52.0	20.4*
Smoking, n(%)	15 (35.7)	20 (40)	11 (22.4)*
Diabetes mellitus, n(%)	14 (33.3)	18 (36)	16 (32.7)
Hypertension, n(%)	27 (64.3)	29 (58)	35 (71.4)
Lung disorders, n(%)	12 (28.6)	25 (50)*	2 (4.1)
Peripheral artery disease, n(%)	4 (9.5)*	14 (28)	14 (28.5)
Cardiogenic shock, n(%)	9 (21.4)	9 (18)	0
LV aneurysm, n(%)	11 (26.2)	14 (28)	7 (14.3)
AV blockade or BBB/atrial fibrillation , n(%)	9 (21.4) / 0	9 (18) / 4 (8)	2 (4.1) / 4 (8.2)
Previous MI, n(%)	11 (26.2)	6 (12)	22 (44.9)*
Previous GABG, n(%)	1 (2.4)	0	0
Previous PCI, n(%)	1 (2.4)	0	0

*- p<0.05, Continuous data are presented as Mean(SD), categorical variables as n(%)
AV-atrioventricular, BBB- bundle branch block, CABG-coronary bypass surgery, DPCI- delayed PCI, EF – ejection fraction, GFR-glomerular filtration rate, LV – left ventricle, MI –myocardial infraction, MT – medical treatment, PCI – percutaneous coronary intervention, PPCI- primary PCI, STEMI – ST-elevation myocardial infarction

It is worth noting that the number of patients with ST segment elevation in all groups was significantly higher compared with other forms of ACS. In the DPCI group, 34 (80.9%) patients had ST segment elevation and only 8 patients (19%) had depression. Among patients with ST-segment elevation, 24 (70.5%) patients had ischemia in the LV anteroseptal area, which was significantly higher than in other groups of patients (p<0.05), in 6 patients (17.6%) that was in the inferior wall of the LV, in three patients (9%) anterolateral LV area was ischemic. LVEF in patients of DPCI and MT groups did not statistically differ when admitted to hospital (49.3 (12.7) and 47.7 (13.1)mm, respectively) as well as the LV end-systolic dimension (ESD) (40.45(7.9) and 41.0(9.4) mm, respectively). The initial LVEF in the DPCI was significantly less than in PPCI (57.3 (9.8)) whereas the LVESD was significantly higher (p<0.05). LVESD in the PPCI group was 36.5 (6.1) mm. The mean values of the LV end-diastolic size (EDD) did not differ among the groups (55.1(5.6); 56 (6.7) and 53.3 (5.5) mm, respectively). Patient characteristics by the various risk assessment scales are presented in Table 3.

Table 3. Patient characteristics by risk stratification systems

	DPCI (N=42)	MT (N=50)	PPCI (N=49)
Euroscore в%	7.8 (5.1)	9.0 (6.2)*	1.4 (0.8)
GRACE в %	6.2 (3.2)	11.9 (5.6)*	-
SYNTAX score	13.9 (6.0)	-	12.5 (7.6)
BCIS-J Score before PCI	5.7 (2.7)	-	5.8 (2.2)
*- p<0.05, Data are presented as Mean (SD) DPCI- delayed percutaneous coronary intervention, MT – medical treatment, PPCI- primary percutaneous coronary intervention			

In accordance with the basic angiographic characteristics (Table 4) of the infarct / symptom-related artery (IRA) the left anterior descending artery (LAD) was affected in 71.4% of cases, in 8 patients (19%) it was the right coronary artery (RCA), and in 4 patients (9.5%) the circumflex artery (Cx) in DPCI group (p<0.05). The blood flow in IRA in most cases (54.8%) was at the TIMI 2 level (p<0.05). Blind occlusion was recorded in 10 (23.8%) patients, occlusion with recanalization elements in 7 (16.7%) patients. Blood flow TIMI 3 was observed in only 2 patients. The presence of collaterals to IRA, which were found in 12 (28.6%) patients, was also important. According to the American Heart Association classification, the type C of stenosis prevailed in both groups in the IRA (p<0.05).

In the PPCI group LAD was the most common lesion among 34 symptom-related cases (69.4%). The incidence rate of symptoms due to Cx in this group was 7 (14.3%) patients and 8 RCA (16.3%) patients. The most frequent was TIMI 2 blood flow through IRA during the period of stabilization in the PPCI group overall in 27 (55.1%) patients. Along with this, the number of blind occlusions with the TIMI 0 bloodstream was only 3 (6.1%), which proves the effectiveness of the optimal MT performed in these patients. The presence of collaterals to the IRA channel was detected in 13 (26.5%) patients.

After admission to the hospital, patients began to receive medical treatment for ACS and stable form of CAD. Almost all patients received antiplatelet and anticoagulant therapy, and according to these criteria, the groups were equal (p>0.05). There was also no difference in the percentage ratio in beta-blockers, nitrates, statins, angiotensin converting enzyme inhibitors / angiotensin receptor blockers (p>0.05). It is also important that inotropic drugs were used more often in the MT group (38.2%), which points to more unstable hemodynamic parameters (p<0.05). The use of Ca++ channel blockers and glycoprotein 2b / 3a inhibitor was also more frequent (p<0.05) in DPCI. It should be noted that the number of patients receiving TLT in the DPCI group was significantly less than in the MT group (4.8% and 40%, respectively) (p<0.05).

Table 4. Angiographic characteristics of IRA

IRA	DPCI	PPCI
	(N=42)	(N=49)
LAD, n(%)	30 (71.4)	34 (69.4)
Cx, n(%)	4 (9.5)	7 (14.3)
RCA, n(%)	8 (19)	8(16.3)
Blood flow by TIMI in IRA, n(%)		
0	10 (23.8)*	3 (6.1)
1	7 (16.7)	7 (14.3)
2	23 (54.8)	27 (55.1)
3	2 (4.8)	12 (24.5)
The presence of collaterals to the IRA, n(%)	12 (28.6)	13 (26.5)
Type of Stenosis in IRA by AHA, n(%)		
A	8 (19)	8 (16.3)
B	9 (21.4)	19 (38.8)
C	25 (59.5)	22 (44.9)
*- p<0.05, Data are presented as n(%) Cx- left circumflex artery, DPCI- delayed percutaneous coronary intervention, IRA – infract-related artery, PPCI- primary percutaneous coronary intervention, RCA – right coronary artery		

Characteristics of revascularization

One-vessel disease patients prevailed in the PPCI group (51%), while the number of patients with a two-vessel disease prevailed in the DPCI (52.4%). The BCIS-JS indicator can also specify the completeness of revascularization after PCI, which was 0.77 (1.4) in the DPCI group and 0.69 (0.3) in the PPCI group ($p>0.05$). RI in DPCI was 0.90 (0.18) and 0.89 (0.2) in PPCI ($p>0.05$).

Characteristics of ECG changes

The percentage of ST segment recovery in the DPCI was 72.8% in patients with elevation, and 87% with ST segment depression. At the same time in comparison with the MT group, a significant difference was found according to this criterion (45.2% and 67.2%, respectively) ($p<0.05$). PPCI group patients at the time of hospitalization and PCI were in stable condition and did not have a tendency to obvious ST segment deviation. As exceptions there were patients with LV aneurysms (7 patients) and rhythm disorders (blockade of the His bundle branch). However, there were no significant differences in ST deviation in this group ($p>0.05$). In the TLT subgroup (MT group), the percentage of ST segment recovery to baseline was 50%, which was also significantly different from the DPCI patients ($p<0.05$).

Characteristic of echocardiography data

After the treatment (3-5 days), DPCI LV EF was 54.4 (11.6)%, which was significantly different from the MT group 51.18 (10.2)% ($p<0.05$). There was also a significant difference before and after procedures in the DPCI group (49.3 (12.7) vs. 54.4 (11.6)%, respectively) ($p<0.05$). Despite the fact that the mean value of LVEF after stenting was the highest in the PPCI group (57.2 (8.9)%); there were no significant changes in intragroup comparison ($p>0.05$). There was also no difference in dynamics of EDD (53.88 (4.6) and 53.0 (5.5) mm, respectively) and ESD (37.75 (6.0) and 37.08 (5.5) mm, respectively) in the MT and PPCI groups after the treatment. On the contrary, in DPCI group a pronounced dynamics was observed in decreasing ventricular cavity size after delayed PCI (EDD- 53.55 (6.7) mm, ESD - 37.93 (7.2) mm). The main role in increasing the ejection fraction (EF) in DPCI group was about the contraction of the left ventricle (LV) cavity during the end systolic phase.

Hospitalization outcomes characteristics

In DPCI group, 39 convalescents (92.9%) reached condition stabilization. They moved from acute heart failure class by Killip to CCS I-II class and NYHA I-II. In the MT group, 41 (82%) patients gained the same results ($p>0.05$). In the PPCI group all stented patients move to CCS I class. In contrast, no reliable dynamics was found as far as NYHA heart failure after the procedure in PPCI group 21 (42.8%), which was combined with the lack of LV EF dynamics. All-cause mortality rate during hospitalization in the DPCI was 3 patients (7.1%) and 9 patients (18%) in the MT ($p<0.05$). In the PPCI group, there were no lethal cases.

Discussion

A very important factor in the effectiveness of revascularization in ACS is its timeliness. Numerous controlled studies showed the relationship of the total ischemia time, i.e. between the symptoms onset and reperfusion (thrombolysis, mechanical reperfusion or PCI) with a prediction of the revascularization success (1, 2). Reperfusion by primary PCI is to be administered to all patients with symptomatic duration <12 hours and persistent ST elevation or complete left bundle branch block (3-5). According to many authors, reperfusion by the method of primary PCI should be considered for patients and after 12-48 hours from the symptoms onset (6 -9).

In ACS without ST elevation, the time of angiography and revascularization is ambiguous. The choice of management is based on the patient risk profile. Very high-risk patients should undergo immediate angiography (within 2 hours). High-risk patients with at least one primary criterion (a regular increase or decrease in troponin, dynamic changes in ST and T, GRACE>140) should receive invasive care within 24 hours, which looks like an adequate time interval (10).

Obviously, in patients with ACS the timeliness of interventions has great importance. However, it is not always possible to meet the deadlines in accordance with the established international criteria and standards due the socio-economic and logistical difficulties.

The main result of this study is that PCI provides the best immediate results, even if they are performed late after the ACS symptoms onset. Primary PCI despite the delaying procedure proved to be most effective in restoring LV function, even compared with patients who received early thrombolytic therapy. Moreover, hospital mortality was significantly lower in the DPCI group, compared with the MT group.

Conclusion

Delayed PCI in patients with ACS are safe and effective procedures. The use of delayed PCI in combination with optimal drug therapy is the most appropriate non-surgical method of myocardial revascularization in the studied cohort of patients. Delayed PCI results showed greater efficacy in the dynamics of the clinical and functional patient's status compared to PCI performed after ACS stabilization.

Conflict of interest: None to declare

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