

## Type of revascularization and outcome in patients with ischaemic cardiomyopathy and multivessel coronary disease

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### Abstract

**Background:** Several studies have compared outcome of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in the treatment of multivessel coronary disease, but a few were focused on patients with reduced left ventricular function. The aim of the study was to compare effectiveness of PCI and CABG in patients with ischaemic cardiomyopathy and multivessel coronary disease

**Methods:** This single-center study, included 178 patients, admitted because of symptomatic multivessel coronary disease, ejection fraction of left ventricle (EF)  $\leq 50\%$ , who underwent PCI or CABG, with two-years follow up of adverse cardiac and cerebrovascular events (MACCE), which included mortality, myocardial infarction (MI), target lesion/vessel revascularisation (TLR/TVR) and stroke.

**Results:** There was higher incidence of MACCE in PCI group (18.1% vs. 9.5%,  $p=0.145$ ). That was mainly because of higher incidence of MI (6% vs. 0%,  $p=0.021$ ) and TLR/TVR (6% vs. 0%,  $p=0.021$ ) in PCI group. There was no difference in mortality rate (9.6% in PCI group vs. 9.5% in CABG group,  $p>0.05$ ). Age, fibrinogen, C-reactive protein were predictors of stent thrombosis, while left ventricular dilatation, EuroSCORE and SYNTAXscore were predictors of mortality in our study.

**Conclusion:** There was no difference in mortality rate during 2-year follow-up after PCI and CABG in studied patients. Incidence of MI and TLR/TVR was higher after PCI comparing with CABG.

### Key words

Myocardial Ischemia; Angioplasty; Stents; Coronary Artery Bypass; Myocardial Revascularisation; Treatment Outcome.

## Introduction

Despite an enormous medical progress in the treatment of ischemic heart disease, the debate between cardiac surgeons and interventional cardiologists about which is the optimal method of myocardial revascularization is still present.<sup>1</sup>

Meta analysis of four studies: Arterial Revascularisation Therapies Study Part I (ARTS), Medicine, Angioplasty, or Surgery Study for Multivessel Coronary Artery Disease (MASS II), Argentine randomized Study of Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease (ERACI-II), Surgery or Stenting (SOS) compared the percutaneous coronary intervention (PCI) with bare-metal stents and coronary artery bypass grafting (CABG) in patients with multi-vessel coronary artery disease and showed similar survival, but a higher number of repeated revascularization in patients treated with

bare-metal stents<sup>2</sup>. SOS study highlighted the benefits of surgery in terms of long-term surviving especially in the subgroups of patients with diabetes, which was also highlighted in a Bypass Angioplasty Revascularisation Interventional trial (BARI).<sup>3,4</sup>

Results of randomized multicentre SYNTAX study (Synergy Between PCI with Taxus and Cardiac Surgery), which compared angioplasty with drug eluted stents and CABG for the treatment of patients with left main coronary disease or three-vessel disease, showed higher incidence of major adverse cardiac and cerebrovascular events in the PCI group during five years follow up period. The incidence of myocardial infarction (MI) and repeat revascularization were nearly twice as high in PCI group during five year follow up. There were higher incidence of stroke in CABG group, which mainly occurred at the time of bypass surgery. There was trend to better survival in CABG group but difference in mortality during follow up period was not statistically significant.<sup>5-7</sup>

**Table 1.** The basic clinical characteristics of patients according to the type of revascularization procedure

	PCI	CABG	p value
Men	60 (72.3%)	75 (78.9%)	0.360
Age (years)	63.9 ±9.7	61.94±7.92	0.126
Arterial hypertension, n (%)	69 (83.1%)	77 (81.1%)	0.869
Diabetes mellitus, n (%)	27 (32.5%)	31 (32.6%)	1.000
Hyperlipoproteinaemia, n (%)	60 (72.3%)	68 (71.6%)	1.000
Cigarette smoking, n (%)	40 (48.2%)	61 (64.2%)	<b>0.045</b>
Heredity, n (%)	41 (49.4%)	56 (58.9%)	0.260
CRP (mg/l)	7.6±12.7	12.09±22.70	0.184
Glucose (mmol/l)	6.9±3.4	6.83±2.63	0.753
Total cholesterol (mmol/l)	5.2±1.4	5.30±1.39	0.699
Triglycerides (mmol/l)	1.9±1.3	2.00±0.97	0.441
Uric acid (µmol/l)	338.3±102.1	299.88±86.21	<b>0.011</b>
BUN (mmol/l)	7.0±2.7	6.46±2.44	0.157
Creatinine (µmol/l)	97.9±23.9	91.27±19.24	0.051
Leukocyte count (×10 <sup>9</sup> /l)	7.9±2.3	7.81±1.99	0.681
Fibrinogen (g/l)	3.8±1.1	3.96±1.20	0.513
EF (%)	43.2±8.0	43.06±6.04	0.876
LVIDd (cm)	5.5±0.7	5.62±0.56	0.144
LVIDs (cm)	3.8±0.8	3.93±0.63	0.306
LA (cm)	3.9±0.4	3.98±0.42	0.163
IVSd (cm)	1.2±0.2	1.20±0.14	0.767
PLWd (cm)	1.2±0.2	1.18±0.15	0.736
RVSP (mmHg)	33.9±9.5	29.74±7.32	<b>0.011</b>
EuroSCORE	1.9±1.6	1.48±0.94	0.057
SYNTAXscore	14.4±6.1	24.32±8.08	<b>&lt;0.0005</b>
Previous myocardial infarction, n (%)	58 (69.9%)	78 (82.1%)	0.082
Previous cerebral infarction, n (%)	6 (7.2%)	6 (6.3%)	1.000
Peripheral arterial disease, n (%)	19 (22.9%)	21 (22.1%)	1.000
Chronic obstructive pulmonary disease, n (%)	4 (4.8%)	7 (7.4%)	0.547
Signs of congestion at the admission, n (%)	9 (10.8%)	3 (3.2%)	0.069
Unstable angina, n (%)	52 (62.7%)	39 (41.1%)	<b>0.006</b>
Ejection fraction below 30%, n (%)	10 (12.0%)	5 (5.3%)	0.175
Time to intervention (days)	2.6±2.9	4.4±5.9	<b>0.013</b>
Time to discharge (days)	3.1±2.4	9.8±6.7	<b>&lt;0.0005</b>

PCI-percutaneous coronary intervention, CABG-coronary artery bypass, CK-creatinine kinase, CKMB-creatinine kinase isoenzyme, CRP-C-reactive protein, BUN-blood urea nitrogen, EF-ejection fraction, LVIDd-the diameter of the left ventricle in diastole, LVIDs-the diameter of the left ventricle in systole, LA-left atrium, IVSd-interventricular septum

Above mentioned studies did not analyze outcome after PCI and CABG in subgroup of patients with reduced left ventricle function although it is well known that low ejection fraction (EF) is a strong predictor of mortality. Higher incidence of MI and repeat revascularization in PCI group may worsen prognosis during follow up period, especially in subgroup of patients with reduced left ventricle systolic function.<sup>8</sup> According to evidence, percutaneous and surgical revascularization are complementary approaches for effectively relieving symptoms of angina in heart failure with preserved ejection fraction – HFpEF, but whether these interventions improve outcomes is not entirely clear.<sup>9</sup> The same is and the recommendation from ESC guidelines on myocardial

revascularization, where CABG is more suitable for patients with significant left main stenosis and left main equivalent to improve prognosis.<sup>10</sup> What is the comprehensive influence of myocardial revascularisation procedure CABG or PCI in patients with heart failure with reduced ejection fraction - HFrEF is not clear as well. There is a need for more data to empower the knowledge because, there is a lack of studies including patients who have HFrEF.<sup>9</sup>

The aim of this study was to compare outcome and to determine predictors of outcome after PCI and CABG in patients with multivessel coronary disease and reduced left ventricular ejection fraction during two years follow up.

## Methods

This research is conducted as an observational, single center study, with two years follow up period. The study included patients hospitalized at the Institute of Cardiovascular Diseases of Vojvodina because of symptomatic coronary artery disease who had confirmed multi vessel coronary disease on coronarography and on echocardiography at admission verified EF≤50%. Patients were divided into two groups depending on the type of revascularization technique that was applied: PCI or CABG. Every patient has signed informed consent form.

Complete revascularization of significant coronary lesions was performed by PCI, if appropriate anatomical location and characteristics of the lesion, or by CABG, with consultative decision of cardiologist, interventional cardiologist and cardiac surgeon.

Exclusion criteria were: patients with less than 18 or more than 80 years of age, MI within 30 days, one vessel coronary disease, previous PCI or CABG, valvular heart disease that requires surgical correction, chronic renal failure with serum creatinine level >200 µmol/l.

Study end-point was incidence of Major Adverse Cardiac and Cerebrovascular Events (MACCE) during two years follow up. MACCE included mortality, MI, acute cerebrovascular infarction, target lesion/vessel revascularization (TLR/TVR) which included stent thrombosis (ST) and graft failure. ST was defined as early - within 30 days after PCI, late - within 30 days to 1 year after PCI and very late – more than 1 year after procedure. Early ST is further subdivided into acute (<24 hours) and subacute (1–30 days).<sup>11</sup> For each patient were collected data: gender, age, conventional risk factors for coronary disease, comorbidity, laboratory parameters (complete blood count, blood glucose level, C-reactive protein,

**Table 2.** Intervention characteristics

Intervention characteristics	Min.	Max.	Mean ± St. dev.
Total stents	2	6	2.7 ± 0.9
Total BMS	0	5	1.3 ± 1.3
Total DES	0	6	1.4 ± 1.4
Total stent length, (mm)	24	145	51.2 ± 20.7
Total BMS length, (mm)	0	97	22.5 ± 23.3
Total DES length, (mm)	0	145	28.7 ± 29.9
Total grafts	1	4	2.7 ± 0.9
Total saphenous venous grafts	0	3	1.9 ± 0.8

BMS-bare metal stent, DES-drug eluted stent

fibrinogen, blood urea nitrogen, serum creatinine level, cardiac enzymes, transaminases, serum cholesterol and triglycerides), clinical characteristics, KILLP class, echocardiography parameters, type and length of stents, type of grafts, length of hospital stay. SYNTAXscore and EUROscore were calculated for each patient using online calculators.<sup>12,13</sup>

Analysis of data was performed using the package SPSS for Windows 17.0 and Microsoft Excel. The statistical tests, used for data analysis were: T-test, X<sup>2</sup>, logistic regression.

## Results

The study included 178 patients of which 83 underwent PCI and in 95 CABG, p>0.05. Table 1 shows the basic clinical characteristics of the subjects.

There were no statistically significant difference in age and gender, presence of diabetes mellitus, arterial hypertension, dyslipidemia between groups, (p>0.05). Significantly higher number of past and current smokers

**Table 3.** Medical treatment in relation to the type of revascularization procedures

	PCI	CABG	p-value
	Number of patients, (%)	Number of patients, (%)	
Acetyl salicylic	81 (97.6 %)	91 (95.8 %)	0.687
Thienopyridine			
At discharge	81 (97.6 %)	2 (2.1 %)	<0.0005
1 month	68 (81.9 %)	0	<0.0005
6 months	58 (69.9 %)	0	<0.0005
12 months	38 (45.8 %)	0	<0.0005
24 months	1 (1.2 %)	0	0.466
Anticoagulants	2 (2.4 %)	9 (9.5 %)	0.064
Statins	78 (94.0 %)	91 (95.8 %)	0.735
Beta blockers	74 (89.2 %)	92 (96.8 %)	0.069
ACE inhibitors	62 (74.7 %)	87 (91.6 %)	0.005
Ca blockers	6 (7.2 %)	9 (9.5 %)	0.789
Angiotensin II receptor blockers	6 (7.2 %)	0	0.009
Antiarrhythmics	4 (4.8 %)	12 (12.6 %)	0.113
Digoxin	1 (1.2 %)	2 (2.1 %)	1.000
Diuretics	45 (54.2 %)	78 (82.1 %)	<0.0005
H2 blockers	32 (38.6 %)	10 (10.5 %)	<0.0005
PPIs	13 (15.7 %)	8 (8.4 %)	0.207

PCI-percutaneous coronary intervention, CABG-coronary artery bypass, ACE inhibitors-angiotensin-converting enzyme, AT blockers-angiotensin receptor blockers, H2-H2 receptor antagonists, PPIs-proton pump inhibitors

**Table 4.** Occurrence of adverse events in relation to the type of revascularization procedures

	<i>PCI</i>	<i>CABG</i>	
	Number of patients, (%)	Number of patients, (%)	P value
<b>Myocardial infarction</b>			
In-hospital	1 (1.2 %)	0	0.466
1 month	2 (2.4 %)	0	0.216
6 months	3 (3.6 %)	0	0.099
12 months	3 (3.6 %)	0	0.099
24 months	5 (6.0 %)	0	<b>0.021</b>
<b>TLR/TVR</b>			
In-hospital	2 (2.4 %)	0	0.216
1 month	3 (3.6 %)	0	0.099
6 months	3 (3.6 %)	0	0.099
12 months	5 (6.0 %)	0	<b>0.021</b>
24 months	5 (6.0 %)	0	<b>0.021</b>
<b>Cerebral infarction</b>			
24 months	0	1 (1.1 %)	1.000
<b>Mortality</b>			
In-hospital	2 (2.4 %)	2 (2.1 %)	1.000
1 month	3 (3.6 %)	3 (3.2 %)	1.000
6 months	3 (3.6 %)	3 (3.2 %)	1.000
12 months	5 (6.0 %)	4 (4.2 %)	0.735
24 months	8 (9.6 %)	9 (9.5 %)	1.000
<b>Total adverse events</b>			
In-hospital	4 (4.8 %)	2 (2.1 %)	0.419
1 month	5 (6.0 %)	3 (3.2 %)	0.476
6 months	6 (7.2 %)	3 (3.2 %)	0.307
12 months	10 (12.0 %)	4 (4.2 %)	0.091
24 months	15 (18.1 %)	9 (9.5 %)	0.145

PCI-percutaneous coronary intervention, CABG-coronary artery bypass, TLR/TVR-target lesion/vessel revascularization

was in surgically treated patients ( $p < 0.05$ ). Surgically treated patients more often had previous MI, but without statistical significance ( $p > 0.05$ ). Uric acid was higher in PCI group ( $p < 0.05$ ). Patients in PCI group had significantly higher right ventricular systolic pressure, signs of congestion at admission and were more likely to have symptoms of unstable coronary disease ( $p < 0.05$ ). The mean value of EuroSCORE was higher in the PCI group, but without statistic significance ( $p > 0.05$ ). While the mean value of the SYNTAX score was significantly higher in the CABG group ( $p < 0.01$ ), table 1.

Patients surgically treated spent a longer time in the hospital before and after the intervention ( $p < 0.05$ ), table 1.

Studied patients in PCI group had 2-6 implanted stents, of mean length 51.2mm, table 2. CABG group patient had 1-4 grafts, of which mean 1.9 saphenous venous grafts, table 2. Total 72 (76 %) patients had at least one arterial graft.

Medical treatment rendered after revascularization is presented in Table 3. Thienopyridines were not part of the standard treatment protocol after bypass surgery, and most are not applied, except in two patients. Patients in CABG group more frequently received anti-coagulant treatment with vitamin K antagonists, renin-angiotensin system blockers and diuretics. In PCI group

patients more frequently received gastroprotective drugs. Table 3.

MACCE were registered in 15 (18.1 %) patients PCI group and in 9 (9.5 %) patients in the CABG group during the 2-year follow-up ( $p = 0.145$ ), table 4. There was no significant difference in mortality rate during the 2-years follow-up (8 (9.6 %) patients in PCI group vs. 9 (9.5 %) patients in CABG group,  $p = 1.000$ ), table 4. MI was registered in 5 (6 %) patients in PCI group while there was no MI during follow up period in CABG group. Recoronarography was performed in 10 (12 %) patients in PCI group during 2-year follow up period while it was not performed in CABG group. In 5 (6 %) patients in PCI group recoronarography was performed due to acute MI, while in 5 (6 %) patients was because of symptoms and ECG signs of de novo myocardial ischemia, but on coronarography no significant coronary lesion was found. In 2 (2.4 %) patients MI was due to stent thrombosis (in 1 (1.2 %) patient acute in 1 (1.2 %) patient subacute). In 3 patients MI was due to de novo coronary lesion. TLR was registered in 5 (6 %) patients in PCI group: early ST in 3 (3.6 %) patients (in 2 (2.4 %) patients acute, 1 (1.2 %) patient subacute), and late ST in 2 (2.4 %) patients. There were no MI, symptomatic coronary disease and TVR registered in CABG group during 2-year follow up.

Cerebral infarction was detected in one patient in the CABG group, occurred at the time of bypass surgery, table 4.

Patients in PCI group with MACCE during 2-years follow up period had higher in-hospital fibrinogen level (4.7g/l vs. 3.6g/l,  $p=0.004$ ). Univariate predictor of MACCE in PCI group during 2-year follow up was also CRP (OR=1.065 (1.017-1.115),  $p=0.007$ ) and fibrinogen (OR=2.66 (1.239-5.471),  $p=0.008$ ). Patient with MACCE during 6-months period had higher BUN level (9.7 mmol/l vs. 6.9 mmol/l,  $p=0.037$ ) and greater left ventricle systolic diameter (4.5cm vs. 3.8cm,  $p=0.033$ ). Univariate 6-months predictor of MACCE was systolic diameter of left ventricle (OR=2.371 (1.010-5.567),  $p=0.047$ ), while univariate predictors of in-hospital MACCE were also diastolic diameter of left ventricle (6.2cm vs. 5.4cm,  $p=0.025$ ; OR=3.596 (1.047-12.348),  $p=0.042$ ), left ventricular ejection fraction (32 % vs. 44 %,  $p=0.004$ ; OR=0.082 (0.749-0.979),  $p=0.018$ ) and EF below 30 % (OR=8.875 (1.096-71.885),  $p=0.041$ ). Other examined patients characteristics were not predictors of MACCE in our study.

Univariate predictors of MI during follow up period in PCI group were higher blood level of fibrinogen (5g/l vs. 3.7g/l,  $p=0.40$ ; OR=2.589 (1.154-5.810),  $p=0.021$ ) and statin therapy which was associated with reduced risk (OR=0.053 (0.003-0.849),  $p=0.038$ ), while other examined patients characteristics were not predictors of MI occurrence in our study. Fibrinogen was independent predictor of MI, with cut off value  $\geq 3.85$  g/l (sensitivity 100 %, specificity 61.3 %). Univariate predictors of TLR (ST) during 2 years follow up period were: age (72.6 years vs. 63.4 years,  $p=0.039$ ; OR=1.302 (1.006-1.685),  $p=0.045$ ), CRP (21.2 mg/l vs. 6.5 mg/l,  $p=0.239$ ; OR=1.074 (1.018-1.134),  $p=0.010$ ), BUN (9.1mmol/l vs. 6.9mmol/l,  $p=0.078$ ; OR=1.471 (1.045-2.073),  $p=0.027$ ) and fibrinogen (5.8 g/l vs. 3.7 g/l,  $p=0.128$ ; OR=2.504 (1.132-5.541),  $p=0.023$ ). Age and fibrinogen level were independent predictors of ST (cut off values:  $\geq 68.5$  years of age (sensitivity 100 %, specificity 66.1%), fibrinogen level  $\geq 4.55$  g/l (sensitivity 75%, specificity 83.9%)). Acute ST occurred in patients with implanted only bare metal stents, and with greater total stent number (1.3 vs. 3,  $p<0.005$ ) and stent-length (21.5cm vs. 62.5cm,  $p=0.013$ ). Type and length of stents were predictors of acute ST. Length of bare metal stent (OR=1.070 (1.001-1.143),  $p=0.045$ ), CRP (50.6mg/l vs. 6.3mg/l,  $p=0.005$ ; OR=1.112 (1.020-1.221),  $p=0.015$ ) and fibrinogen (8.5 g/l vs. 3.7 g/l,  $p=0.005$ ; OR=3.422 (1.197-9.782),  $p=0.022$ ) were univariate predictors of early ST. CRP was independent predictor of early ST.

Patient in PCI group with lethal outcome during follow up period had enlarged left ventricle with thinner walls. Univariate predictors of one-year mortality in PCI group were higher systolic diameter of left ventricle (4.6 cm vs. 3.8 cm,  $p=0.027$ ; OR=2.579 (1.033-6.438),  $p=0.042$ ) and reduced interventricular septum and posterior wall thickness (1cm vs. 1.2cm,  $p=0.02$ ; OR=0.003 (0.000-0.955),  $p=0.049$ ), while other tested patients characteristics did not significantly influence 2-year mortality rate in our study.

In CABG group univariate predictors of mortality during 2-year follow up period were EuroSCORE and

SYNTAX score while other tested patients characteristics did not significantly influence 2-year mortality. EuroSCORE was the only two year mortality predictor (2.3 vs. 1.4,  $p=0.149$ ; OR=1.956 (1.120-3.417),  $p=0.018$ ). EuroSCORE was also predictor of in-hospital, 6-month, 1-year mortality, and was independent predictor of in-hospital mortality (cut off value  $\geq 3.39$  (sensitivity 100%, specificity 96.8%)). SYNTAX score was independent one year mortality predictor (37 vs. 23.7,  $p<0.0005$ ; OR=1.231 (1.050-1.443),  $p=0.010$ ), cut off value  $\geq 34.5$  (sensitivity 100%, specificity 91.7%), and also univariate 6-month mortality predictor.

## Discussion

In our study the overall incidence of MACCE during the two-year follow-up after PCI and CABG was similar, but the number of adverse events was higher in PCI group. There was no difference in mortality rate between PCI and CABG group, but patients in PCI group were more frequently undergone repeat revascularization.

With advances in technology, most coronary lesions can be solved by PCI, however, technical feasibility is only one element for the treatment decision. Contemporary medicine now faces the need to individualize treatment approach to each complex patient and another important criteria are: clinical presentation, severity of angina, extent of ischemia, co-morbidities, response to medical therapy and angiographic estimation of the coronary heart disease.<sup>1</sup>

According to results of meta analysis of earlier published studies (ARTS, MASS II, ERACI-II and AWESOME) that compare effectiveness of different types of myocardial revascularization and include only patients with bare metal stents, patients treated with PCI had higher incidence of repeat revascularization,<sup>2</sup> which is in accordance with our results. SOS and BARI studies showed benefit of surgery in patients with diabetes.<sup>3,4</sup> We did not registered differences in adverse events between diabetic and non diabetic patient, but we must emphasize that our study was conducted in era of DES, novel PCI technique, long time dual antiplatelet therapy and that these factors might be the reasons for better outcome of diabetic patients. We, also did not find statistically significant difference in MACCE rate in our study during follow up according to the type of implanted stents. Total length of BMS was predictor of acute ST, but the number of patients was too small and that should be confirmed in the larger studies.

Left ventricular ejection fraction is a predictor of mortality in patients with heart diseases.<sup>8,9</sup> Our study included only patients with reduced left ventricular ejection fraction and accordingly, mortality rate was highly associated with heart failure related factors. We also noticed significant influence of enlarged heart chambers on mortality in PCI group. Previous studies has also mention this significant finding, emphasizing that left ventricular diameter is a measure that can be easily obtained during echocardiography, with very little interobserver differences.<sup>14,15</sup> In the Studies of Left Ventricular Dysfunction (SOLVD), increased LV end systolic diameter was associated with cardiovascular death<sup>16</sup>.

Narayanan et al suggested that LV size may have additional value beyond left ventricular EF as a risk marker for sudden cardiac death in the community.<sup>15</sup>

In the SYNTAX study high SYNTAX score proved to be a good predictor of adverse events in the PCI group, which should be taken into account in the case of selection of the optimal treatment.<sup>5</sup> In our study patients in PCI group had lower mean SYNTAX score, without predictive significance for adverse events, but in the CABG group, which was consisted of patients with more severe coronary disease, it proved to be independent predictor of mortality. In CABG group mortality predictors were both EuroSCORE and SYNTAX score.

In the SYNTAX study, most cases of stent thrombosis occurred within 30 days after the intervention, and after 12 months, the incidence of ST was similar to the incidence of symptomatic graft occlusion in the CABG group.<sup>17,18</sup> In our study, the majority of ST occurred in the first 30 days (3.6 %), and late ST occurred in another 2.4 % of cases, with no difference depending on the type of stents, while we did not registered symptomatic graft occlusion during follow-up period in CABG group. This might be due to short follow up period.

Results of our study revealed that the predictors of early and late stent thrombosis were elevated inflammatory markers, while subacute and late thrombosis were affected also by the age of patients. It was found that acute thrombosis was influenced by the length of BMS. The largest published observational study that aimed to compare revascularization strategy - ASCERT study, which included 103549 patients from PCI and CABG register, concluded that in a population of patients older than 65 years with multiple coronary disease coronary bypass provides better long term survival than PCI.<sup>19</sup> Similarly, subgroup analysis of BARI and SoS study showed that among patients younger than 55 years outcome is better if they were treated by percutaneous angioplasty, and at the age of 55 and more CABG provides better surviving.<sup>20</sup>

A number of inflammatory biomarkers were investigated in order to determine their predictive power for MACCE after BMS implantation. Recent meta-analysis demonstrated that basal CRP value is significant predictor of angiographic restenosis.<sup>21</sup> Hoshida et al. found that basal CRP is significant risk factor for in-stent restenosis among patients who had not received statins.<sup>22</sup> Fibrinogen and plasminogen activator inhibitor (PAI)-1 are associated with in-stent restenosis after BMS implantation, but this correlation is less strong compared with CRP. It is due to their short half-life, which affects the variability of the measurements.<sup>23,24</sup> In accordance with these studies, our results showed that baseline values of CRP and fibrinogen were predictors of early and late stent thrombosis.

Measurement of inflammatory markers before stent implantation may be useful in order to determine the non-specific inflammatory hyperreactivity, which can lead to increased incidence of stent thrombosis. Niccoli et al. found that biomarkers of hypersensitivity, such as eosinophilic cationic protein were useful in identifying patients at increased risk of developing an allergic reaction to the stent polymer and late stent thrombosis.<sup>25</sup> Other biomarkers (IL-5, leukotrienes, etc.) or diagnostic tests for allergy

(intradermal or patch tests) might be examined. Interestingly, patients with allergic patch test reactions to nickel or molybdenum have a higher incidence of in-stent restenosis after implantation BMS.<sup>26</sup> Allergy and inflammation may be therapeutic targets in patients with an implanted stent. Use of statins proved effective in reducing the risk of MACE after BMS implantation.<sup>27</sup>

Potential limitations of our study were: small number of patients who were included, study was not randomized, follow up period was only two years. Because of that, our results had to be confirmed in further larger, randomized studies with longer follow up period.

## Conclusion

In our survey there was no statistically significant difference in the overall incidence of adverse cardiovascular and cerebrovascular events during the two-year follow-up of patients with multi-vessel coronary disease and reduced ejection fraction treated with PCI and CABG, although the number of adverse events was higher in PCI group. There was no difference in mortality rate between PCI and CABG group, but patients in PCI group were more frequently undergone repeat revascularization. Inflammatory biomarkers CRP and fibrinogen were predictors of early and late in-stent restenosis, while incidence of late stent restenosis increases with the age of patients. Enlarged heart chambers and reduced wall thickness were leading predictors of mortality in PCI group. In CABG group mortality predictors were EuroSCORE and SYNTAX score.

This study is part of PhD thesis of dr Tanja Popov.

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## Sažetak

### ***Način revaskularizacije miokarda i ishod kod pacijenata sa ishemijskom kardiomiopatijom i višesudovnom koronarnom bolešću***

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**Uvod:** Poređenje hirurške revaskularizacije miokarda (CABG) i perkutane koronarne intervencije (PCI) u lečenju višesudovne koronarne bolesti tema je nekoliko velikih studija, međutim nijedno istraživanje nije fokusirano isključivo na bolesnike sa smanjenom ejectionom frakcijom leve komore (EF). Cilj rada je bilo poređenje ishoda lečenja nakon primenjene neke od revaskularizacionih tehnika CABG ili PCI kod bolesnika sa ishemijskom kardiomiopatijom i višesudovnom koronarnom bolešću.

**Metodi:** Istraživanje je obuhvatilo 178 pacijenata, hospitalizovanih zbog simptomatske višesudovne koronarne bolesti, sa sniženom ejectionom frakcijom leve komore (EF) ≤50%, kod kojih je učinjena neka od revaskularizacionih tehnika CABG ili PCI. Pacijenti su praćeni tokom dve godine nakon otpusta i u tom periodu su prikupljeni podaci o pojavi neželjenih kardiovaskularnih i cerebrovaskularnih događaja (MACCE), koji su podrazumevali smrtni ishod, infarkt miokarda (MI), ponovnu revaskularizaciju ranije tretirane lezije i moždani infarkt.

**Rezultati:** Uočena je veća incidenca MACCE u PCI grupi (18,1% vs. 9,5%,  $p=0,145$ ). To je pretežno zbog veće učestalosti MI (6% vs. 0%,  $p=0,021$ ) i ponovne revaskularizacije (6% vs. 0%,  $p=0,021$ ). Ne postoji razlika u mortalitetu tokom dvogodišnjeg praćenja (9,6% u PCI grupi, a 9,5% u CABG grupi,  $p>0,05$ ). Životna dob, fibrinogen, C-reaktivni protein su prediktori tromboze stenta, a dilatacija leve komore, EURO skor i SYNTAX skor su prediktori mortaliteta.

**Zaključak:** Ne postoji razlika u stopi mortaliteta tokom dvogodišnjeg praćenja nakon učinjene revaskularizacije miokarda putem CABG i PCI kod pacijenata sa sniženom EF. Incidenca infarkta miokarda i ponovne revaskularizacije je veća nakon učinjene PCI.

**Gljučne reči:** Ishemija miokarda; Angioplastika; Stentovi; Koronarno arterijsko premošćavanje; Miokardna revaskularizacija; Ishod lečenja