

## New-onset atrial fibrillation after percutaneous coronary intervention or coronary artery bypass grafting for left main disease

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### ABSTRACT

**Aim** To determine the prevalence of new-onset atrial fibrillation (NOAF) following percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for left main coronary artery disease (LMCAD) and its effect on 6-month cardiovascular outcomes.

**Methods** This prospective study included 40 patients diagnosed with LMCAD, in the period from 2017 to 2018. The patients with LMCAD and low or intermediate SYNTAX score were randomized to PCI with zotarolimus-eluting stents versus CABG. Outcomes were analyzed according to the development of NOAF during the initial hospitalization following revascularization.

**Results** Among 40 patients without atrial fibrillation on presentation, NOAF developed 3.1±1.3 days during hospitalization in three CABG treated patients, and one PCI treated patient. One patient that was CABG treated developed NOAF after two months. Patients with versus patients without NOAF had a significantly longer duration of hospitalization, probably because they were discharged on anticoagulant therapy. Myocardial infarction was presented in one CABG treated patient after 3 months, and also in one PCI treated patient after 4 months. One patient died 2 months after the operation, and one developed stroke 5 months after the CABG operation.

**Conclusion** The NOAF was common after CABG, but extremely rare after PCI, and it occurred almost exclusively following CABG. There was a clear statistical tendency for all-cause death, cardiovascular death and stroke at 6-month follow-up period.

**Key words:** atrial fibrillation, coronary artery disease, coronary bypass surgery, percutaneous coronary intervention, prognosis

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## INTRODUCTION

New-onset atrial fibrillation (NOAF) is a common post-operative complication of coronary artery bypass grafting (CABG), and in earlier studies (mostly in patients with multi-vessel disease), NOAF was associated with prolonged hospitalization, increased rates of adverse events, and greater health care costs (1,2). A recent analysis from the MAIN-COMPARE registry (Revascularization for Unprotected Left MAIN Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization From Multi-Center Registry) in Asia reported that preoperative atrial fibrillation (AF) was a predictor of a long-term morbidity and mortality after CABG in patients with left main coronary artery disease (LMCAD) (3); however, the incidence and prognostic impact of NOAF following contemporary percutaneous coronary intervention (PCI) and CABG in patients with LMCAD in sinus rhythm is still largely unknown. Recent randomized trials have suggested that PCI with contemporary drug-eluting stents is an acceptable alternative to CABG for selected patients with LMCAD (4,5). As such, identification of pre-procedural and post-procedural factors that affect outcomes after both revascularization modalities may affect the choice between PCI and CABG.

To our knowledge there were no published studies on this subject from Bosnia and Herzegovina (B&H), and assessing the NOAF and its burden as a frequent complication of CABG should add to the local and general pool of knowledge.

The aim of this study was to determine the prevalence, predictors, and outcomes of NOAF in patients with LMCAD who underwent percutaneous or surgical revascularization.

## PATIENTS AND METHODS

### Patients and study design

This prospective study included 40 patients diagnosed with LMCAD (20 treated with CABG and 20 treated with PCI), in the period from 2017 to 2018 at University Clinical Center Tuzla. The patients with LMCAD and low or intermediate SYNTAX score (depending of the vessel calcification and severity of the disease) (6) were randomized to PCI with zotarolimus-eluting stents versus CABG. Patients with left main stenosis

and left main equivalent - stenosis of the left descending artery (LAD) and circumflex artery (CX) ostium were included in the study. Outcomes were analyzed according to the development or no development of NOAF during the initial hospitalization following revascularization.

New onset atrial fibrillation was defined as the occurrence of any episode of atrial fibrillation (AF) or flutter following the index procedure through the time of discharge that lasted at least 30 s and was captured on a standard 12-lead electrocardiogram or cardiac telemetry, or that required medical treatment.

A follow-up was complete for all patients through 6 months. The median follow-up for clinical outcomes was 6 months.

The investigation was approved by the Institutional Review Board or Ethics Committee at University Clinical Center Tuzla, and all patients signed written informed consent forms.

### Methods

The goal of PCI was complete revascularization of all ischemic territories with the second generation drug eluting stent (DES) - zotarolimus eluting stents. Cardiac surgery was performed with or without cardiopulmonary bypass according to the discretion of the operator, with the goal of complete anatomic revascularization of all 1.5 mm wide coronary vessels and with >50% stenosis. Only antegrade cardioplegia was used. In patients undergoing on-pump CABG, the use of retrograde cardioplegia was a strong predictor of NOAF. All CABG-treated patients received beta-blockers post-procedure unless contraindicated.

### Statistical analysis

Assuming the prevalence of NOAF after PCI being roughly 0.1% and after CABG around 30%, a power of 80%, beta-error of 0.2 and alpha-error of 0.05, about 20 patients were needed in each study group. All numerical variables were first tested for normality using the Kolmogorov-Smirnov test. Numerical variables were then compared using the Student's t-test for normally distributed data and Mann-Whitney U-test for non-normally distributed data. Categorical variables were analyzed using  $\chi^2$  or Fisher exact test, as appropriate. For the purpose of this study, arrhythmic events during the hospitalization following the

index CABG or PCI procedure were analyzed. The results were expressed as mean ± standard deviation (SD) for numerical data and frequencies for categorical data.

**RESULTS**

The mean age of five patients in NOAF group was 66.5 years, while in the group of 35 patients without (No) NOAF it was 61.4 years (p=0.76). There was no gender difference (M:F) between NOAF (2:3) and No NOAF (7:28) group (p=0.32), although the dominance of females in both groups was obvious.

Among the NOAF patients, higher body mass index was noticed comparing to No NOAF group, 30.5 and 27.6, respectively (p=0.32). Also, there was higher Syntax score in the NOAF group comparing to No NOAF group, 32 and 31, respectively (Table 1).

**Table 1. Baseline characteristics according to the development of in-hospital new onset atrial fibrillation (NOAF)**

Variable	NOAF (n=5)	No NOAF (n=35)	P
Hyperlipidaemia (No)	2	12	0.80
Hypertension (No)	2	33	0.007
Prior stroke or TIA (No)	1	5	1.0
Diabetes mellitus (No)	1	5	1.0
Insulin treated diabetes mellitus (No)	2	6	0.26
COPD (No)	1	8	1.0
Prior myocardial infarction (No)	2	4	0.15
Recent myocardial infarction (within 7 days) (No)	1	1	0.24
STEMI (No)	1	1	0.24
NSTEMI (No)	0	2	1.0
SYNTAX Score (site reported) (No)	32	31	0.85
Low (0-22)	1	6	1.0
Intermediate (23-32)	0	5	1.0
High (≥33)	1	6	1.0
Left ventricular ejection fraction (%)	40 ±8.3	47±9.4	0.11
Body mass index	30.5	27.6	0.32

TIA, transitory ischemic attack; COPD, chronic obstructive pulmonary disease; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction;

Among 40 patients there were no patients with AF before hospitalization for procedure.

The NOAF developed 3.1±1.3 days during hospitalization in three patients in CABG treated patients, and one in PCI treated patient. One patient that was CABG treated developed NOAF after two months of discharge. However, although there were three times as many patients who developed in-hospital NOAF post-procedurally in the CABG group, a statistically significant difference between the groups was not found, three

(15%) patients in the CABG group and one (5%) patient in the PCI group (p=0.605) (Table 2).

**Table 2. Procedural characteristics according to the development of in-hospital new onset atrial fibrillation (NOAF)**

Patient's group	NOAF (n=4)	No NOAF (n=16)	P
<b>Coronary artery bypass grafted (CABG) patients</b>			
On pump CABG (3 patients as one was off-pump) (No)	3	16	1.0
Only antegrade cardioplegia (3 patients as one was off-pump) (No)	3	16	0.37
Other surgical procedures done	0	0	1.0
LIMA used (4 patients) (No)	4	16	1.0
Vessels bypassed per patient (%)	2.4	2.8	0.69
CPB duration (min)	84.5±39.2	80.9±41.3	0.43
Cross-clamp duration (min)	60.3±29.2	58.9±31.3	0.71
LAD grafted with LIMA (4 patients)	4	16	1.0
<b>PCI patients</b>			
<b>LM lesion</b>			
LM coronary segment (No) (1 patient)	1	17	1.0
LM equivalent disease (No)	0	2	1.0
Procedure duration (min)	32±5.2	21.6±4.2	0.14

CABG, coronary aortic bypass graft; LIMA, left internal mammary artery; CPB, cardiopulmonary bypass; LAD, left anterior descending artery; PCI, percutaneous coronary intervention; LM, left main coronary artery

Pre-procedural laboratory values and characteristic were similar in patients with NOAF and patients without NOAF. By the time of hospital discharge, NOAF had resolved in two of three CABG treated patients, and in one PCI treated patient. One CABG treated patient was discharged from hospital with NOAF and was treated with anticoagulant therapy. One patient had NOAF two months after discharge and was treated with amiodarone and anticoagulant therapy, and in 6-month follow up, he stayed in permanent AF. Aspirin was equally prescribed in both groups. The PCI and CABG had non-significantly different rates of the 6-month primary endpoint if NOAF did not occur.

Major complications in patients with NOAF after the 6-month follow up period was myocardial infarction which happened once, three months after CABG, and once after 4 months in PCI treated patient. One death happened 2 months and one stroke happened 5 months after CABG. All those patients were on anticoagulant therapy (with one anticoagulant drug).

One patient that had NOAF after PCI was the patient with high SYNTAX score and multiple comorbidities, in which the primary decision was to do CABG, respecting the current data and guidelines, but the patient declined. The PCI procedure had a longer duration, the patient had multiple risk factors, including type 2 diabetes and hypertension, and resulted with NOAF.

## DISCUSSION

In this study the patients with LMCAD and low or intermediate SYNTAX score, PCI with second generation DES were non-inferior to CABG with respect to primary composite end point of death, stroke, or myocardial infarction at 6-month follow up. The result of EXCEL trial suggests that PCI with the second generation DES is acceptable and alternative to CABG, which was confirmed in the new ESC/EACTS guidelines on myocardial revascularization, in which the recommendation is the same for CABG and PCI for low SYNTAX score, while intermediate and high SYNTAX score still prefer CABG (7). In our study, one patient with NOAF after PCI had high SYNTAX score, which declined CABG. The major findings from our study: although statistically not significant, NOAF was frequent after CABG but rare after PCI, NOAF was associated with prolonged hospitalization and there was a statistical tendency/signal for NOAF to predict 6-month rates of all-cause and cardiovascular death, myocardial infarction (MI), or stroke after CABG. Among patients with LMCAD and sinus rhythm, in-hospital NOAF was more frequent after CABG than after PCI. Although somewhat speculating, we believe that the reason lies in a relatively small sample size (20 patients per group). The 20% rate of NOAF after CABG for LMCAD in the present study is consistent with prior reports in which post-CABG AF developed in 11% to 40% of patients (8-11). Patients enrolled in our study were relatively stable and not high risk, with equipoise for revascularization by either PCI or surgery, except for the one patient which had high SYNTAX score and declined CABG. Nonetheless, in-hospital NOAF occurred in only 1 patient (5%) after PCI, markedly less than after CABG, although the statistical significance was not reached. The NOAF was a predictor of adverse outcomes during the 6-month follow-up after CABG, in particular stroke, myocardial infarction, cardiovascular death, and all-cause death. As shown in our study, PCI had superior 6-month event-free survival compared with CABG if NOAF after the surgery occurred. Consistent with previous reports (5,12,13), the strategy of surgical revas-

cularization (on-pump vs. off-pump) in our study was not a predictor of NOAF because we used only antegrade cardioplegia. However, total bypass duration and cross-clamp duration were not associated with an increased risk for AF. The higher per procedural rates of stroke with CABG compared with PCI that has been noted in most prior trials (14,15), in our study it might be in part explained by the greater rate of NOAF after surgical revascularization (16). Future studies are warranted to determine the extent to which recurrent AF during long-term follow-up contributed to the late stroke risk (17,18). In addition to affecting long-term prognosis, NOAF showed a tendency for being significant predictor in terms of 6-month rates of cardiovascular death, stroke and MI; however, due to a small sample size this was not proven as statistically significant in our case.

There are also important limitations of the study. Firstly, this is a rather small, single-center trial with only 40 enrolled patients. Secondly, the follow-up period for the primary outcome was only 6 months. Finally, the patients were monitored for paroxysms of atrial fibrillation only during their hospitalization; no data about possible paroxysms after the discharge are available.

In our study comparing PCI and CABG for the treatment of LMCAD in patients with low and intermediate SYNTAX scores, NOAF occurred almost exclusively following CABG and it was a statistical signal of all-cause death, cardiovascular death, stroke at 6-month follow up period.

Further studies are needed to identify patients at high risk for NOAF after CABG to guide prophylactic measures, to examine the potential role of implantable monitors to detect AF recurrence in patients with NOAF who convert to sinus rhythm before hospital discharge. They are also needed to determine whether the routine use of long-term oral anticoagulation in patients with in-hospital NOAF improves long-term prognosis after CABG for LMCAD.

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## TRANSPARENCY DECLARATION

Competing interests: None to declare.



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