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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Predictors of post-operative atrial fibrillation in patients undergoing isolated coronary artery bypass grafting

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Abstract

Background: Post-operative atrial fibrillation (POAF) is the most common cardiac arrhythmia occurring after coronary artery bypass grafting (CABG). Arrhythmia leads to prolonged hospitalisation and may have an impact on both short-term and long-term prognoses.

Aim: The aim of this paper was to evaluate the incidence of POAF in patients after CABG as well as to identify its predictors.

Methods: The study was performed on 791 patients (selected from a group of 1031 patients who underwent CABG in the Clinical Department of Cardiology in the years 2009–2011) who did not suffer from atrial fibrillation (AF) prior to isolated CABG. Data on co-existing diseases, as well as data collected at the time of surgery and in the post-operative period, were evaluated.

Results: The average age of patients in the examined group was 64.6 ± 9.1 years. Emergency CABG was performed on 38% of patients, whereas 75.1% of patients underwent CABG with the use of extracorporeal circulation. Based on the incidence of POAF, the post-CABG patients were classified into a POAF(+) group that comprised 166 (21%) patients, and a POAF(–) group involving 625 (79%) patients. The first occurrence of arrhythmia during the first three days after surgery was observed in 76.5% of patients. The average age of POAF(+) and POAF(–) patients was 68.7 ± 8.8 years and 63.5 ± 8.9 years, respectively ($p < 0.0001$). The respective incidence rates of co-existing diseases in patients with POAF and those without POAF were as follows: arterial hypertension, 80.1% vs. 75.8% ($p = 0.29$); heart failure, 18.7% vs. 21.1% ($p = 0.56$); type 2 diabetes, 24.1% vs. 26.2% ($p = 0.64$). Stable angina pectoris was diagnosed in 22.3% of patients with POAF and 15% of patients without POAF ($p = 0.034$). The following conditions were more frequently observed in patients with POAF compared with those without POAF: low cardiac output syndrome, 28.9% vs. 14.2% ($p < 0.0001$) and cardiac tamponade, 9% vs. 4.6% ($p = 0.044$), respectively. Red blood cell transfusions were performed more often in patients with POAF compared to those without POAF (70.5% vs. 55.7%, respectively, $p = 0.0008$). Multivariate analysis revealed the following potential predictors of POAF: age ≥ 70 years (HR 2.3), preoperative stable angina pectoris (HR 1.7), and post-CABG low cardiac output syndrome (HR 1.8).

Conclusions: POAF was diagnosed in 21% of post-CABG patients, and the major predictors were: age ≥ 70 years, preoperative stable angina, as well as low cardiac output syndrome following CABG.

Key words: atrial fibrillation, coronary artery bypass grafting, risk factors

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INTRODUCTION

Coronary artery bypass grafting (CABG) is an effective method of coronary revascularisation, which is used more and more commonly in the treatment of coronary artery disease, also in elderly patients who are significantly more exposed to arrhythmias than younger people. The retrospective study by Mahoney et al. [1] performed in 10,550 patients demonstrated that post-operative atrial fibrillation (POAF) occurred in 33.8% of patients after CABG and cardiac valve surgery. Another retrospective study revealed that POAF was observed

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in 44% of patients who underwent CABG and aortic-valve replacement [2]. Shen et al. [3] indicated a higher percentage of patients (44%) who suffered from POAF after CABG combined with valve surgery. The pathogenesis of POAF is multi-factorial and not fully elucidated. Numerous proarrhythmic factors have been found during the perioperative period. Disorders of the interatrial impulse conduction resulting from hypertension-induced atrial remodelling, ischaemic heart disease, or valvular heart diseases are of significant importance [4]. Additionally, the role of degenerative disorders that occur with age in the cardiac conduction system and myocardium is also underlined by experts.

The aim of this paper was to evaluate the POAF incidence in post-CABG patients and to identify its predictors.

METHODS

The study was conducted on 791 patients selected from a group of 1031 patients undergoing CABG in the Clinical Department of Cardiac Surgery in the years 2009–2011. The inclusion criteria were isolated CABG and no atrial fibrillation (AF) in medical history, whereas the exclusion criteria included CABG combined with the following conditions: valve surgery, cervical carotid angioplasty, angioplasty of post-infarction ventricular septal defect (VSD), angioplasty of ventricular aneurysm, and AF prior to CABG.

According to the 2010 guidelines of the European Society of Cardiology, AF was diagnosed on the basis of abnormalities on electrocardiogram (ECG), which lasted for at least 30 s and was characterised by sustained arrhythmia, irregular RR intervals, absent P waves, and different intervals between atrial contractions (cycle < 200 ms). All patients were monitored using 72-h telemetry throughout the post-operative period.

Arterial hypertension was defined as a systolic or a diastolic blood pressure measurement consistently higher than 139 mm Hg and/or 89 mm Hg, respectively, in two measurements or chronic antihypertensive treatment.

Diabetes was diagnosed in the presence of any one of the following: fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL), plasma glucose ≥ 11.1 mmol/L (200 mg/dL) 2 h after a 75 g oral glucose load as in a glucose tolerance test, symptoms of high glycemia and casual plasma glucose ≥ 11.1 mmol/L (200 mg/dL), or chronic antidiabetic treatment.

Acute coronary syndrome (ACS) was diagnosed as ST segment elevation myocardial infarction, non-ST elevation myocardial infarction, or unstable angina.

The local Bioethics Committee (No. 20/2013) approved the study.

Statistical analysis

The following models of statistical analysis were used in the present study: χ^2 test for the evaluation of statistically significant differences in single classifications as well as the evaluation of the correlation between pairs of characteristics in double classifications; t-student test used for variables with Gaussian distribution; and Mann-Whitney U test for variables with non-normal statistical distribution. The evaluation of differences was designated with a p value whereby $p < 0.05$ indicates a statistically significant difference. Single-factor and multi-factor logistic regression analyses were applied to determine prognostic value of specific variables.

RESULTS

The average age of the 791 patients from the examined group (males, 74.3%) was 64.6 ± 9.1 years. Hypertension, which was diagnosed in 607 (76.7%) patients, co-existed most frequently with coronary artery disease (Table 1). ACS resulted in coronary angiography in 660 (83.4%) subjects. Unstable angina was the most common condition leading to coronary angiography (258 patients, i.e. 39% of patients with ACS), which was performed due to stable angina in only 131 (16.6%) patients. 297 (37.5%) patients from the examined group underwent emergency CABG. In patients who underwent emergency surgery, critical stenosis of the left main coronary artery was demonstrated in 99 subjects (33% of those operated on emergency), while haemodynamic instability was observed in 172 (57.9%) patients. In addition, stenosis of the left main coronary artery co-existed with haemodynamic instability in 26 (8.8%) patients. The average number of implanted grafts in the present group amounted to 2.7 ± 0.5. Arterial grafts were implanted in 43 (5.4%) patients and venous grafts in 40 (5.1%) patients, while both arterial and venous grafts were implanted in 173 (21.9%) patients. In the examined group, grafts were most frequently implanted in the left anterior descending artery (LAD) (787 patients, 99.5%). CABG duration was 206.2 ± 53.6 min on average, while in 594 (75.1%) patients CABG was performed in combination with extracorporeal circulation (ECC). Complications in the post-operative period occurred in 339 (42.9%) post-CABG patients. The most common complication in that period was low cardiac output syndrome, which was observed in 166 (21%) patients. Intra-aortic balloon pump (IABP) was performed in 29 (3.7%) patients. Local complications were demonstrated in 68 (8.6%) operated patients. In the examined group, 69 (8.7%) patients underwent rethoracotomy, while 465 (58.8%) patients were subject to red blood cell transfusions in the post-operative period.

Post-operative AF was diagnosed in 166 (21%) patients undergoing isolated CABG during hospitalisation after surgery. In the group of 166 patients with POAF, only one arrhythmic event occurred in 54 (32.5%) patients and 62 of (37.4%) patients suffered from at least four POAF events (Fig. 1). The first POAF event occurred in 127 (76.5%) patients during the first three days after surgery. In 29 (23.5%) patients, the first arrhythmic event occurred after three days following CABG. In 11 (6.6%) subjects, the first POAF event was to be observed on the seventh day of hospitalisation or on the following day (Fig. 2).

Table 1. Co-existing diseases in POAF(+) and POAF(–) groups

Co-existing diseases	Total		POAF(+)		POAF(–)		p
	n = 701	% patients	n = 166	% patients	n = 625	% patients	
Arterial hypertension	607	76.7	133	80.1	474	75.8	0.2905
Dyslipidaemia	421	53.2*	93	56*	328	52.5*	0.4679
Hypercholesterolaemia	336	42.5	76	45.8	260	41.6	0.3784
Hypertriglyceridaemia	9	1.1	3	1.8	5	0.8	0.4737
Combined dyslipidaemia	76	9.6	14	8.4	62	9.9	0.6676
Type 2 diabetes mellitus	204	25.8	40	24.1	164	26.2	0.6445
Chronic kidney disease (GFR < 60 mL/min)	193	24.4	50	30.1	143	22.9	0.0691
Heart failure	163	20.6	31	18.7	132	21.1	0.5589
Thyroid diseases	62	7.8	9	5.4	53	8.5	0.2540
Hyperthyroidism	32	4	4	2.4	28	4.5	0.3185
Hypothyroidism	24	3	4	2.4	20	3.2	0.7797
Nodular goitre of the thyroid	6	0.8	1	0.6	5	0.8	0.8109
Chronic obstructive pulmonary disease	42	5.3	13	7.8	29	4.6	0.1512
Lower-extremity AAD	41	5.2	10	6	31	5	0.7276
Transient ischaemic attack	38	4.8	8	4.8	30	4.8	0.8463

*Due to hypolipaemic treatment prior to the surgery, the percentage of patients with dyslipidaemia is underestimated; AAD — atherosclerotic arterial disease; GFR — glomerular filtration rate; POAF — post-operative atrial fibrillation

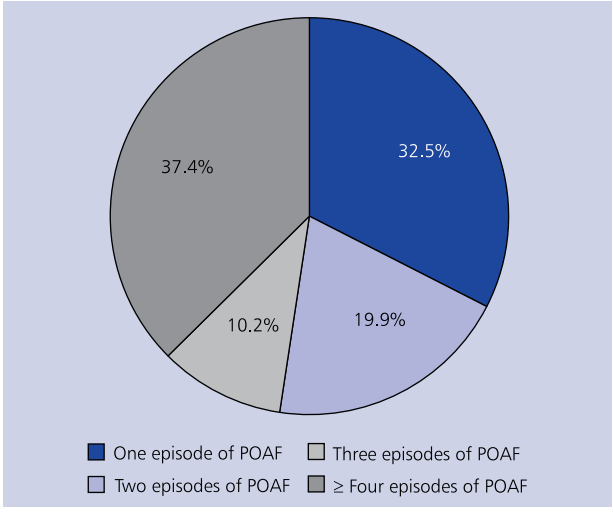

Figure 1. The number of atrial fibrillation events in patients after coronary artery bypass grafting; POAF — post-operative atrial fibrillation

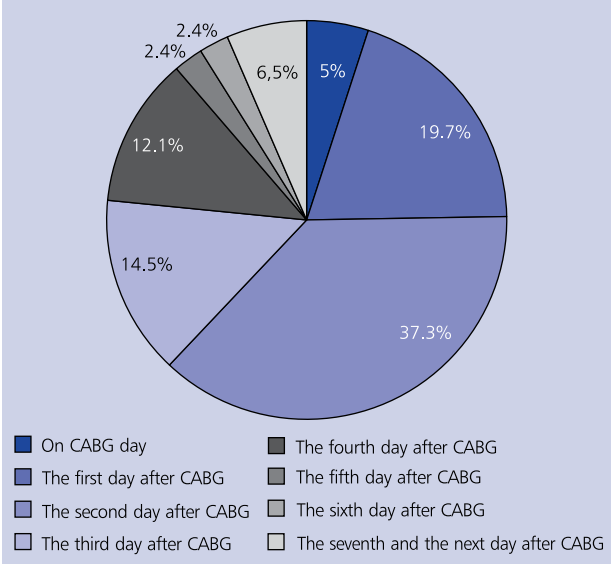

Figure 2. The timepoint the occurrence of the first atrial fibrillation event in the examined group; CABG — coronary artery bypass grafting

The examined group of 791 post-CABG patients was classified into two groups, based on the incidence of POAF during hospitalisation after surgery:

— POAF(+) group comprising 166 (21%) patients who suffered from POAF;
— POAF(–) group comprising 625 (79%) patients who did not suffer from POAF.

The mean age of patients in the POAF(+) group was 68.7 ± 8.8 years and in the POAF(–) group 63.5 ± 8.9 years ($p < 0.0001$). In both groups, no statistically significant differences in the incidence of cardiovascular risk factors were observed (Table 1). Stable angina led to coronary an-

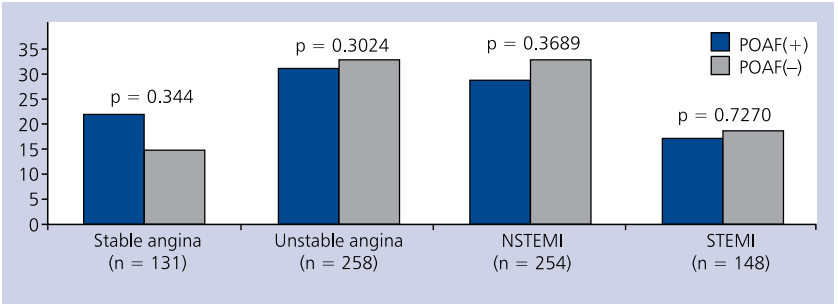

Figure 3. Diagnosis of coronary heart disease in POAF(+) and POAF(–) patients; POAF — post-operative atrial fibrillation; NSTEMI — non-ST-segment elevation myocardial infarction; STEMI — ST-segment elevation myocardial infarction

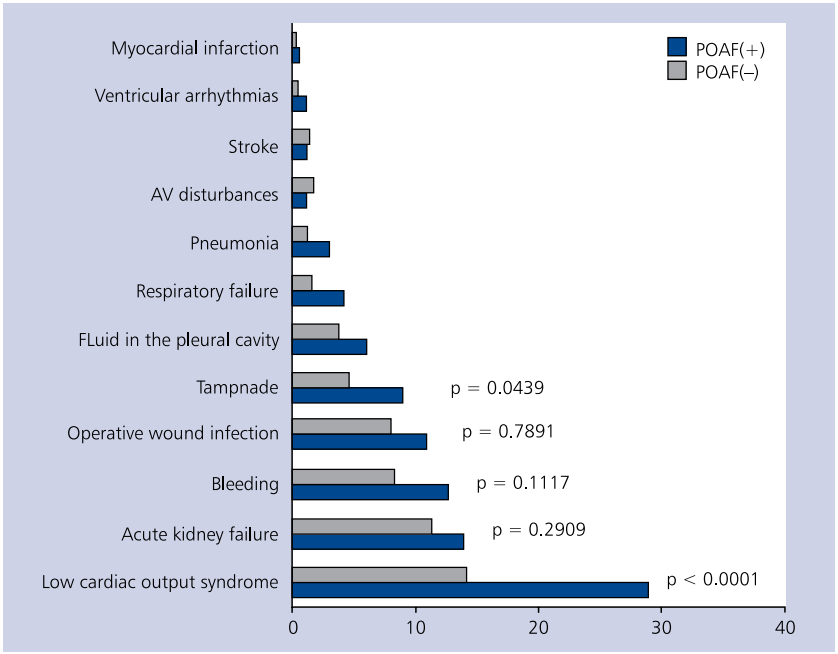

Figure 4. Post-operative complications in POAF(+) and POAF(–) groups; POAF — post-operative atrial fibrillation

giography in 37 (22.3%) patients in the POAF(+) group and 94 (15%) patients in the POAF(–) group (p = 0.034) (Fig. 3). 153 (92.2%) POAF(+) patients and 570 (91.2%) POAF(–) patients scored ≥ 2 $CHADS_2$ points (p = 0.0442). In both groups, no statistically significant differences in the incidence of left ventricular ejection fraction < 35% were observed (POAF(+) 18 (10.8%) vs. POAF(–): 65 (10.4%); p = 0.95). No differences in left atrium dimension were observed in patients with POAF compared to those without POAF (39.9 vs. 39.6 mm, p = 0.58).

Critical stenosis of the left main coronary artery was observed in 37 (22.3%) patients with POAF and 136 (21.8%) without arrhythmia (p = 0.97). Right coronary artery was revascularised in 31.3% of patients with POAF and in 30.6% of patients without POAF (p = 0.93). Arterial grafts were implanted in 10 (6%) POAF(+) patients and 33 (5.3%) POAF(–) patients (p = 0.86). Venous grafts were implanted in a similar number of patients compared to those with arterial grafts, i.e. 13 (7.8%) POAF(+) patients and 27 (4.3%) POAF(–) patients (p = 0.10). The POAF(+) and POAF(–) groups did not differ in terms of the incidence of venous and arterial grafting: 86.1% and 90.4%, respectively (p = 0.15). The average surgery duration was 203.4 ± 47.4 min in POAF(+) patients and 207 ± 55.2 min in POAF(–) patients, p = 0.4231. CABG in combination with ECC was performed in 127 (76.5%) patients with POAF and 467 (74.4%) without arrhythmia (p = 0.71). Ventilation after surgery lasting over 6 h was demonstrated in 80 (48.2%) POAF(+) patients and 281 (45%) POAF(–) patients. The difference was not statistically significant. Complications in the postoperative period occurred in 86 (51.8%)

Table 2. Multivariate logistic regression analysis of predictors of atrial fibrillation after CABG

Predictor	HR	95% CI for HR	p
Age ≥ 70 years	2.3	1.6136–3.3316	< 0.0001
Post-CABG low cardiac output syndrome	1.8	1.0935–3.1117	0.0217
Stable angina	1.7	1.1185–2.7312	0.0142
Tamponade after CABG	1.4	0.7179–2.9062	0.3026
Red blood cell transfusion after CABG	1.4	0.9392–2.1251	0.0971
$CHADS_2 \geq 2$ score	1.1	0.7387–1.5572	0.7128
Post-operative complications	0.9	0.5766–1.5009	0.7671

CABG — coronary artery bypass grafting; CI — confidence interval; HR — hazard ratio

patients from the POAF(+) group and in 253 (40.5%) patients from the POAF(–) group (p = 0.011). Figure 4 shows the incidence of postoperative complications in both POAF(+) and POAF(–) groups.

The univariate analysis revealed the following predictors of POAF: age over 69 years (hazard ratio [HR] 2.6), stable angina (HR 1.62), and low cardiac output syndrome after CABG (HR 2.12). The multi-factor analysis also indicated that these factors significantly increased the risk of POAF. In the univariate analysis, POAF risk was also increased by the following factors: $CHADS_2$ score ≥ 2 (HR 1.44) prior to surgery, post-operative complications (HR 1.58), cardiac tamponade (HR 2.04), and red blood cell transfusions after CABG (HR 1.9). However, this was not confirmed by the multivariate analysis. The multivariate logistic regression analysis identified factors related to the POAF incidence after CABG (Table 2). Age over 70 years as well as low cardiac output syndrome and stable ischaemic heart disease significantly increased the risk of POAF.

DISCUSSION

Despite the enhancement of surgery techniques and increasing quality of post-operative care, the incidence of POAF has not decreased in recent years. More and more often, elderly patients with increased arrhythmia risk, suffering from numerous co-existing conditions, undergo myocardial revascularisation. In the present paper, POAF occurred in 21% of operated patients during hospitalisation. The percentage of POAF patients varies in clinical trials, which results from different incidence of POAF predictors, but it is also related to a type of cardiac surgery and applied criteria of diagnosing arrhythmia. In the meta-analysis of 24 randomised clinical trials, Andrews et al. [5] revealed that the incidence of POAF amounts to 26%. The POAF incidence rate in the present study is similar to the incidence of arrhythmia in the study performed by Banach et al. [6] (23%). In comparison to Banach's study, the patients in the present study were older (average age 65 years vs. 61 years), and most frequently suffered from co-existing diseases such as arterial hypertension (77% vs. 68%) andr heart failure (21% vs. 4.3%). On the other hand, Sobczyk et al. [7] showed a lower percentage of POAF patients (12%) compared to the present study.

It was revealed that changes occurring with age in the cardiac conduction system contribute significantly to arrhythmia in post-CABG patients. In the present study, POAF patients were older than those without arrhythmia (average age 69 vs. 64 years, p < 0.0001), which is in line with the findings of the Polish authors. Banach et al. [6] showed that the mean age in patients with POAF was 66 years, and in those without POAF the average age was 60 years (p < 0.01). Similar results were achieved in the study conducted on patients operated at the Collegium Medicum Department of Cardiovascular Surgery and Transplantology of Jagiellonian University in Krakow. Patients with POAF were older than those without post-operational arrhythmia (mean age 69 vs. 64 years, p < 0.0001) [7]. Dąbrowski et al. [8] also revealed that the average age of POAF patients was higher than that of patients without POAF (65 vs. 61 years, p = 0.0033). In the present study, age was the most significant factor increasing the risk of POAF. It was shown that age over 70 years increased the risk of arrhythmia by more than 100% in univariate and multivariate analyses. Banach et al. [6] demonstrated that age over 70 years is an independent factor increasing the risk of POAF (odds ratio [OR] 2.6, 95% confidence interval [CI] 1.7–4.3). According to Dąbrowski et al. [8], age over 60 years increased the risk of post-CABG arrhythmia over eight-fold (OR 8.54, 95% CI 2.19–57.54). The study performed in a group of patients undergoing CABG and/or valve surgery indicated that with every past decade, the risk of POAF has increased by 74% [9]. Taking into account the fact that age is the most significant factor increasing the POAF risk, as well as the fact that the number of operated patients among older people is constantly increasing, a higher incidence of POAF is expected to be seen.

The role of conditions that co-exist with coronary artery disease in the pathogenesis of POAF is widely disputed. The present study did not reveal that patients with POAF and those without POAF differ in terms of the incidence of arterial

hypertension, heart failure, dyslipidaemia, renal failure, or lower-extremity peripheral a arterial disease. Also, the study by Filardo et al. [10] conducted on 6899 patients without AF history, who underwent isolated CABG, did not demonstrate that the incidence rates of arterial hypertension, diabetes, and renal failure differ between patients with POAF and those without POAF. Although $CHADS_2$ and CHA_2DS_2VASc scores are used to evaluate the risk of cardiovascular complications in patients with AF, the results can sometimes be useful while evaluating the risk of AF. This results from the fact that factors that are relevant for $CHADS_2$ and CHA_2DS_2VASc also increase the risk of AF. In the present study, the patients with POAF achieved a higher average $CHADS_2$ score than those without POAF (1.6 vs. 1.5 patients, $p = 0.0476$). Moreover, a greater number of POAF patients compared to that of non-POAF patients scored at least 2 points in the $CHADS_2$ scale. The single-factor analysis revealed that a $CHADS_2$ score ≥ 2 points increases the risk of POAF by 44%. The study conducted by Piccini et al. [9] on 2177 operated patients demonstrated that $CHADS_2$ score of ≥ 2 points was achieved by 81% of POAF patients and 74% of non-POAF patients ($p = 0.0002$). Chua et al. [11] showed that both $CHADS_2$ and CHA_2DS_2VASc score of at least 2 points were predictors of POAF. Therefore, $CHADS_2$ and CHA_2DS_2VASc scores can be used as simple tools for the evaluation of the risk of post-CABG arrhythmia. Interestingly, the present study did not reveal that factors which are relevant for these scales, i.e. hypertension, heart failure, and diabetes, increase the risk of POAF while being analysed separately. On the other hand, their presence in the scoring system was significant for the incidence of POAF. Possibly, this is related with the fact that age, which can be linked to the increased POAF risk, was one of the $CHADS_2$- and CHA_2DS_2VASc-factors.

In the present study, 25% of patients underwent off-pump coronary artery bypass grafting (OPCABG). It is claimed that ECC-induced inflammatory response increases the POAF risk. In the present study, OPCABG was not related to the incidence of POAF. Filardo et al. [10], similarly to the results of the present study, did not demonstrate differences in the number of OPCABG in patients with POAF and those without POAF (14% vs. 11%, $p = 0.207$). The results of numerous studies confirm the hypothesis of inflammatory response during ECC and arrhythmia trigger mechanisms. The meta-analysis of Wijeysundera et al. [12], which included 290,000 patients, revealed that OPCABG decreases POAF risk (OR 0.59, 95% CI 0.46–0.72).

The present study did not provide evidence that POAF occurrence is related with the following intra-operative parameters: surgery duration, ECC duration, or the clamping of the aorta. The results of experimental and clinical studies on the possible impact of these parameters on the occurrence of arrhythmia are disputable. Several studies revealed that prolonged ECC duration and the clamping of the aorta can be related to ECC occurrences. Creswell et al. [13] showed that prolonging the duration of the aorta by 1 h led to the increase of POAF occurrences by 2.7%. Zaman et al. [14] demonstrated that the average ECC duration in a group of POAF patients was statistically longer than in a group of non-POAF patients. However, the duration of the clamping of the aorta was equal in both groups. Numerous studies did not confirm that there is any relation between the number of POAF occurrences and prolonged ECC duration or the clamping of the aorta [7, 15, 16]. In the present study, for all patients who were operated using ECC, blood cardioplegia was applied. It is claimed that crystalloid cardioplegia can have an impact on the incidence of POAF, which occurs as a consequence of atrial ischaemia due to the lack of complete systolic dysfunction [7]. The fact that blood cardioplegia was applied in all patients operated with the use of ECC might result in a relatively low percentage of patients with POAF in the present study.

In the examined group, no difference in the duration of artificial ventilation after surgery was shown among patients with POAF and those without arrhythmia. The majority of patients were subject to artificial ventilation for no longer than six hours after surgery. The authors from the Collegium Medicum Department of Cardiovascular Surgery and Transplantology of Jagiellonian University in Krakow presented different findings on the potential relation between the duration of artificial ventilation and POAF occurrence [7]. Prolonged artificial ventilation, defined as ventilation time of over 24 h, was applied in 17% of patients with POAF and 9% of operated patients without POAF. On the other hand, Erdil et al. [16] claimed that prolonged ventilation (of over 6 h) was the most significant factor having an impact on the incidence of POAF.

In the examined group, complications in the post-operative period occurred in 52% of POAF patients and 41% of non-POAF patients. The most common complication in both groups was low cardiac output syndrome, which occurred in 29% of POAF patients and 14% of patients without arrhythmia. The present study demonstrated that low cardiac output syndrome after CABG increased POAF risk by 80%. Interestingly enough, IABP was applied significantly more often in patients without POAF than in those with POAF. The percentage of patients with low cardiac output syndrome in the present study is higher than that indicated in the studies of other authors. Pastuszek et al. [17] showed that low cardiac output syndrome occurred in 10% of POAF patients and 3% of patients without arrhythmia, whereas in the study of Banach et al. [6], low cardiac output syndrome was observed in 14% of patients with POAF and 10% of patients without POAF. The differences in the number of occurrences of low cardiac output syndrome might result from the fact that patents in the present study were older than the operated patients in the previously mentioned studies. In the present study, preoperative heart failure occurred more often than in the studies published by other authors, which could have an impact on

diagnosing low cardiac output syndrome after surgery. That difference could also result from different diagnostic criteria.

In the present study, red blood cell transfusion during surgery and in the post-operative period was conducted statistically more often in POAF patients than in those without arrhythmia. In univariate analysis, red blood cell transfusion increased POAF risk by 90%. It is claimed that the triggering of inflammatory processes as well as the volume overload of atria during transfusion are responsible for the proarrhythmic effect of red blood cell transfusion.

Limitations of the study

In addition to the usual limitations of a retrospective study, there are several other shortcomings to these results. The database did not include information about medical treatment before CABG, including beta-blockers, statins, or angiotensin converting enzyme inhibitors/angiotensin receptor blockers. In the present study, continuous-ECG recordings were only performed for 72 h after surgery. A prolonged registration could have resulted in an increased number of patients with POAF.

CONCLUSIONS

The incidence of AF increases significantly with age in both the overall population and in post-CABG patients. POAF occurred in 21% of patients undergoing CABG. In addition to age, the major predictors of POAF after CABG were stable coronary disease prior to surgery and low cardiac output syndrome following CABG. It was not revealed that predictors of arrhythmia in the overall population, such as hypertension or heart failure, could potentially lead to POAF. This counts as indirect evidence of a different pathomechanism of arrhythmia compared to that which is observed in the overall population. This implies different methods of treatment as well as different prognosis in patients with POAF than in those with arrhythmia in the overall population.

Conflict of interest: *none declared*

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