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Predicting Post-operative Atrial Fibrillation in Cardiac Surgery – The Added Value of Echocardiography

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Abstract

INTRODUCTION: Post-operative atrial fibrillation (POAF) is a frequent rhythmic complication in cardiac surgery with the potential to cause sudden hemodynamic instability and catastrophic thromboembolic complications. Despite vast scientific research, it is still hard to predict and prevents its occurrence.

AIM: The aim of this study was to determine whether selected pre-operative and intraoperative echocardiographic variables would be of added value in POAF prediction.

MATERIAL AND METHODS: This prospective observational follow-up study included 178 cardiac surgery patients undergoing coronary artery bypass graft intervention. Demographic as well as echocardiographic variables of interest were examined to detect significant independent predictors for POAF.

RESULTS: POAF was detected in 90 (50.56%) patients versus 88 (49.44%) patients without POAF. Patients who developed POAF were significantly older and burdened with multiple comorbidities. In multiple regression analysis pre-operative echocardiographic variables-diastolic dysfunctions, enlarged left atrial (LA) volume indexed for body surface area, mitral annular calcification, and secondary mitral regurgitation were predictive of POAF. LA appendage flow velocity obtained by intraoperative transesophageal echocardiography was also a significant intraoperative predictor for POAF.

CONCLUSION: The results of this study confirmed that two-dimensional echocardiography is a valuable diagnostic and prognostic tool in relation to POAF. The addition of the aforementioned echocardiographic independent predictors to traditional demographic variables could be a solid foundation of a new predictive model for POAF.

Introduction

Due to its frequency and clinical importance, post-operative atrial fibrillation (POAF) has been a subject of numerous scientific studies and investigations. Several perioperative risk factors have been associated with POAF; however, its etiology remains unclarified. POAF contributes to a prolonged ICU and hospital stay in general and it significantly increases the costs of medical treatment. Moreover, it multiplies the risk of thromboembolic complications and increases the post-operative morbidity and mortality of cardiac surgery patients. Hence, the need to predicts and prevents its occurrence.

Having in mind the multifactorial nature of POAF, it would be reasonable to assume that any model aiming to achieve high specificity and sensitivity would have to take into account not only preoperative but also intraoperative variables that play a significant role in its manifestation.

Although several markers have been proposed, the last decade of research in this field has not come up with one that is highly specific and sensitive for POAF prediction. Moreover, search of the published literature offers somewhat conflicting data. Therefore, further attempts to determine the significance of several perioperative risk factors are needed.

Materials and Methods

This was a prospective monocenteric observational clinical study performed at the University Clinic for State Cardiac Surgery in Skopje, Republic of North Macedonia. A total of 178 adult patients of both genders undergoing a cardiac surgical intervention were enrolled in the study after obtaining their written informed consent. Ineligibility criteria were preexisting atrial fibrillation as well as contraindication to open heart surgery. All eligible patients were divided into two groups based on the occurrence or absence of POAF.

Demographic data from the medical chart of each patient were taken which included: Gender, age, BMI, BSA, smoking history, and comorbidities: DM

Type 2, CMP, HF, TIA/CVA, PAD, CKD, and COPD. Pharmacological anamnesis for each patient was screened for the use of calcium channel blockers, beta blockers, angiotensin converting enzyme inhibitors (ACE inhibitors)/angiotensin receptor antagonists, statins, aspirin, and diuretics. Standard 12-lead ECG recording was done with the use of Philips Page Writer TC30 (Philips-USA) standard paper speed 25 mm/s and amplification of 10 mm/mv.

Two-dimensional pre- and post-operative transthoracic echocardiography was done using GE's VIVID 7 machine with cardiac probe M5Sc-D and according to the recommendations from the European Association for Cardiovascular Imaging (EACVI). Ejection fraction was calculated according to Simpsons formula. Left and right ventricular dimensions and volumes were reported. More than mild valve pathologies were reported and quantified with the use of pulsed and continuous as well as color Doppler mode according to EACVI recommendation. Simpson's biplane method was used for left atrial (LA) volume calculation and indexed for BSA. Apical 4-chamber view was used for E and A wave and deceleration time (DT) for diastolic function assessment. Tissue Doppler obtained –s`TDI was analyzed as a mean value from lateral and medial mitral annulus, as well as e` wave to calculate E/e` ratio.

Tricuspid annular plane systolic excursion as a measure of right ventricular longitudinal systolic function was obtained as well as fractional area change of the RV. We also reported the presence of mitral and aortic valve annular calcification.

Intraoperative transesophageal echocardiography (TEE) (as a standard perioperative procedure done in each patient) using GE's VIVID 7 machine with 6VT-D probe was used to obtain LA appendage flow velocity (LAA vel) with pulsed wave Doppler from standard TEE midesophageal short axis view at the level of aortic valve 30–60 omniplane angle and 2-chamber midesophageal view 80–100 omniplane angle.

Data collected were entered in a separate worksheet for each patient and kept confidential. The study was conducted in accordance with the ethical principles of the current Declaration of Helsinki and was approved by the Ethical Committee of the Faculty of Medicine in Skopje, North Macedonia.

Statistical analysis

Statistical analysis was performed with the use of SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA). Analysis of attributive (qualitative) series was done by determining the coefficient of relations, proportions and rates. Numerical series were analyzed using central tendency and dispersion measures. Pearson Chi-square test, Yates corrected, Fischer exact test, and Fisher Feeman Halton exact test were used to determine the association between certain attributable dichotomous features. Spearman rank correlation coefficient was used to determine the relationship between numerical variables with incorrect frequency distribution. The analysis of the dependent samples was done with McNemar Chi-square.

Risk factors were quantified through the use of odd ratio (OR) and confidence intervals (CI). Univariate and multiple logistic regression analysis was used to determine and quantify the independent significant predictors of POAF (+) status. $p < 0.05$ was considered statistically significant.

Results

The incidence of POAF in our study was 50.56%. Demographic data of the patients are given in Table 1.

Table 1: Baseline characteristics

	POAF (+) N=90	POAF (-) N=88	p-value
Age (years)	67.21 ± 8.41	60.62 ± 9.40	0.003
Sex (ref. female)	33.3%	34.09%	0.914
BSA (m^2)	1.87 ± 0.19	1.87 ± 0.20	0.996
BMI (kg/m^2)	28.22 ± 4.57	27.95 ± 4.38	0.337
Smokers	45.56%	45.45%	0.989
Comorbidities			
HTA	10/9 (11.11%)	19/88 (21.59%)	0.058
HF	22/90 (24.44%)	15/88 (17.05%)	0.223
CMP	21/90 (23.33%)	16/88 (18.18%)	0.397
DM2	31/90 (34.44%)	36/88 (40.91%)	0.373
TIA/CVA	12/90 (13.33%)	7/88 (7.95%)	0.245
PAD	19/90 (21.11%)	15/88 (17.05%)	0.490
CKD	50/90 (55.56%)	24/88 (27.27%)	0.0001*
COPD	55/90 (66.11%)	25/88 (28.41%)	0.00001*

Results are shown as mean ± SD. BSA: Body surface area, BMI: Body mass index, HTA: Hypertension, HF: Heart failure, CMP: Cardiomyopathy, DM2: Diabetes mellitus type 2, TIA/CVA: Transitory ischemic attack/stroke, PAD: Peripheral artery disease, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease.

No gender difference was noted between the two groups ($p = 0.914$). Patients developing POAF were significantly older and burdened with multiple comorbidities. Univariate logistic regression analysis of predictive role of selected variables regarding POAF s is given in Figure 1.

Age was significantly positively associated with POAF, with each year of age increasing POAF probability by 1091 times.

Univariate logistic regression analysis of predictive role of selected comorbidities regarding POAF is given in Figure 2.

In our study, patients with CKD were 3.33 times more likely to develop POAF compared to those without CKD. COPD patients in our study had 396 times higher likelihood of POAF.

Data regarding pharmacological anamnesis is given in Figure 3.

We found significant association between regular preoperative use of loop diuretics and POAF. No other class of drug in our study was found to be significantly related to a POAF episode.

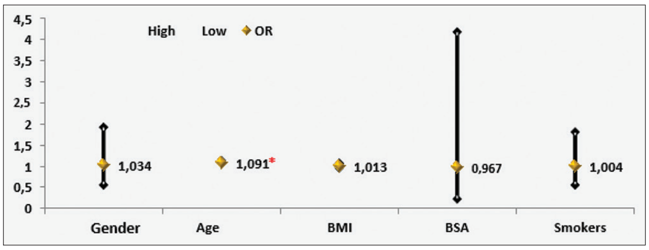

Figure 1: Univariate logistic regression analysis of predictive role of selected variables regarding post-operative atrial fibrillation

We analyzed a total of 23 echocardiographic variables from pre-operative two-dimensional transthoracic echocardiography exam (Table 2).

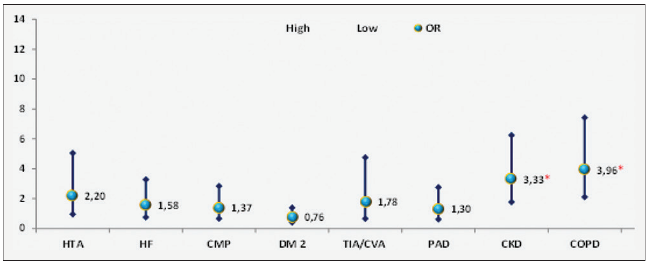

Figure 2: Univariate logistic regression analysis of predictive role of selected comorbidities regarding post-operative atrial fibrillation. HTA: Arterial hypertension, HF: Heart failure, CMP: Cardiomyopathy; DM2: Diabetes mellitus type 2, TIA/CVA: Transitory ischemic attack/ stroke, PAD: Peripheral artery disease, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease.

Multiple logistic regression analysis distinguished 4 of them as significant independent POAF predictors. Specifically, those were:

1. LAVi (ml/m^2) – indexed volume of left atrium – each unit of increased volume significantly increases the risk for POAF by 1450 times (OR = 1450 [1313–1188] 95% CI; p = 0.0001)
2. Calcified mitral annulus – significantly increases the risk for POAF by 5423 times (OR = 5423 [1639–17,949] 95% CI; p = 0.006)
3. Secondary mitral regurgitation –significantly increases POAF risk by 5912 times (OR = 5912 [1107–31,571] 95% CI; p = 0.038)
4. DD – diastolic dysfunction – significantly increases POAF risk by 5968 times (OR = 5968 [1030–34,577] 95% CI; p = 0.046).

Mean LAA flow velocity of blood was significantly higher in the group that developed POAF and it was confirmed as independent significant POAF predictor in a model of multiple logistic regression analysis. Each unit of increasing LAA flow velocity lowers the patient's likelihood of developing POAF by 13% (OR = 0.875 [0.839–0.913] 95% CI; p = 0.0001) (Table 2).

Discussion

Recent studies report an incidence of 25–40% after CABG and up to 62% after combined cardiac surgery intervention [1-7]. The incidence of POAF that was observed in our study is in accordance with previously published literature.

Some studies report higher incidence of POAF in male patients. Our study, however, as well as several others did not find significant association between male gender and POAF [8,9].

The incidence of POAF increases with age, and older age has been the only consistent risk factor for POAF in all studies published so far. It could be attributed to a growing number of comorbidities.[10] However, it is considered more a direct consequence of aging (structural changes of the atria, fibrosis, muscle atrophy, and dilation) rather than prolonged hospital stay and other age-related complications.

Data from previously published studies are conflicting regarding significance of several comorbidities. The significant association between COPD and CKD with POAF found in our study is in concordance with the results of several published studies [11-16].

The strong association between regular use of loop diuretics and subsequent POAF in our study could be explained by the fact that those patients with volume overload, more frequent episodes of subclinical and manifest decompensations, have more often and more advanced stage of diastolic dysfunction and greater stretch and remodeling of the atria. On the other hand, loop diuretics cause *per se* electrolyte disbalance – a known arrhythmia trigger.

Review studies suggest that LA dysfunction is at least partially responsible for POAF development. Hence, the idea that LA appendage function as assessed by TEE could be predictive for POAF [17-19]. Yet, studies report conflicting results. Monocenteric retrospective study of Ngai *et al*. concluded that the risk of POAF rises as LAA flow velocity decreases [19]. On the other hand, Sarin *et al*. did not find a significant difference in LAA flow velocity between groups with and without POAF [20]. Analyzing LAA in our study, we came to conclusion that the average LAA flow velocity in patients developing POAF was significantly lower compared to those without POAF and it appeared as significant independent POAF predictor in multiple logistic regression analysis of five intraoperative parameters. LAA flow velocity as a potential risk factor for POAF remains to be determined by further studies.

In this study, we sought to determine the potential predictive value of 23 echocardiographic parameters obtained from standard pre-operative two-dimensional echocardiography in regard to POAF.

Despite greater left ventricular dimensions and lower EF in the POAF group, our study did not find significant association between these parameters and POAF.

LA dilation has already been confirmed as significant risk factor for POAF in a multitude of published

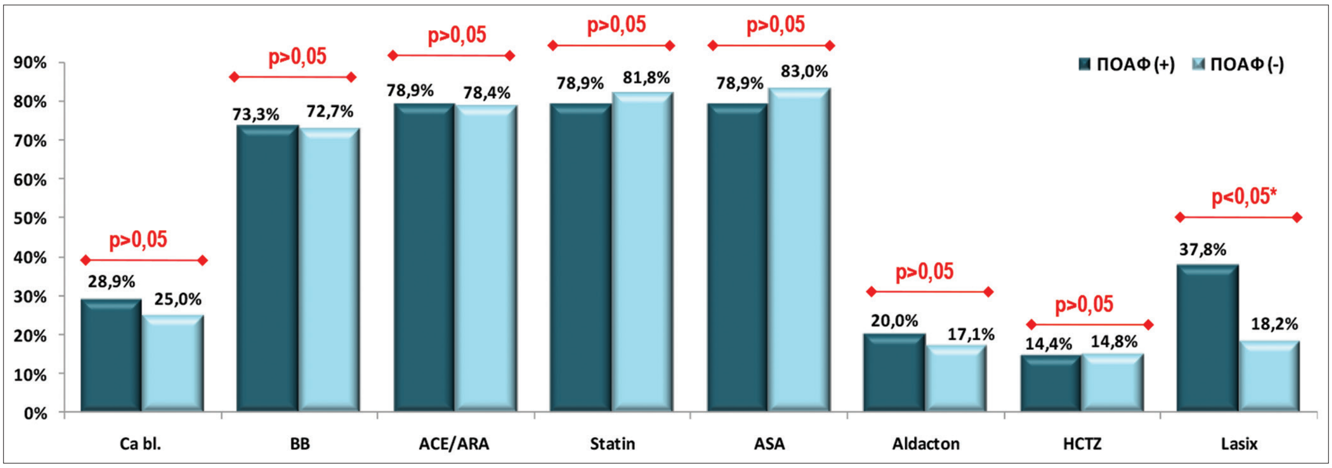

Figure 3: Analysis of POAF status in regards to pre-operative therapy. Ca bl.: Calcium channel blockers, BB: Beta blockers, ACE/ARA: Angiotensin converting enzyme/angiotensin receptor blocker, ASA: Acetyl salicylic acid, HCTZ: Hydrochlorothiazide.

Table 2: Multivariate logistic regression analysis of predictive role of selected echocardiographic variables for POAF

Echocardiographic variables	B	S.E.	Wald	Df	Sig.	Exp (B)	95% C.I. for EXP (B)	
							Lower	Upper
LVEDD	0.060	0.068	0.778	1	0.378	10.062	0.929	1.214
LVESD	– 0.014	0.062	0.049	1	0.825	0.987	0.874	1.113
LVEDV	– 0.010	0.019	0.314	1	0.575	0.990	0.954	1.027
LVESV	0.000	0.028	0.000	1	0.993	1.000	0.946	1.056
EF	0.048	0.040	1.452	1	0.228	1.049	0.970	1.135
LA	– 0.161	0.066	5.998	1	0.150	0.851	0.986	1.968
LAVi	0.272	0.051	28.648	1	0.000*	1.313	1.188	1.450
IVS	0.027	0.091	0.090	1	0.764	1.028	0.859	1.230
PW	– 0.122	0.170	0.515	1	0.473	0.885	0.634	1.235
RV	– 0.061	0.065	0.896	1	0.344	0.941	0.829	1.068
TAPSE	– 0.032	0.070	0.205	1	0.651	0.969	0.845	1.111
FAC	– 0.006	0.033	0.028	1	0.866	0.994	0.933	1.060
sTDI	0.229	0.147	2.436	1	0.119	1.258	0.943	1.677
E/é	0.037	0.084	0.191	1	0.662	1.038	0.879	1.224
AS – yes/no	– 0.350	0.783	0.200	1	0.654	0.704	0.152	3.266
AR – yes/no	0.423	1.025	0.170	1	0.680	1.526	0.205	11.375
MS – yes/no	– 0.185	3.694	0.003	1	0.960	0.831	0.001	1158.900
Ca mitral annulus – yes/no	1.691	0.611	7.665	1	0.006*	5.423	1.639	17.949
Ca aortic annulus – yes/no	0.708	0.742	0.910	1	0.340	2.030	0.474	8.690
Functional TR – yes/no	– 0.466	0.676	0.475	1	0.491	0.628	0.167	2.362
MR – secondary/none	1.777	0.855	4.322	1	0.038*	5.912	1.107	31.571
DD -yes/normal	1.786	0.896	3.972	1	0.046*	5.968	1.030	34.577

Dependent variable – POAF Independent variables – Echocardiographic variables *Significant for P < 0.05

studies [21]. LA volume, as more precise parameter for its actual size can easily be measured preoperatively. It is a significant independent predictor for AF in the general population [22]; however, its role in POAF prediction is still not well established. Increased LAVi hemodynamically coincides with chronically increased LV filling pressure and with diastolic dysfunction [22,23]. A more important finding in our study was the predictive role of LAVi for POAF. Our results are in concordance with those of Osranek *et al*. They considered it a surrogate for chronically increased LV filling pressure and found it to be a significant independent predictor for POAF and a useful tool for risk stratification [21]. It is interesting to note that we did not find a significant difference in LA diameter obtained by parasternal long axis view. We suppose that it is the result of the insufficiency of linear measurements to precisely quantify geometrically irregular structure such as the LA. Moreover, when LA dilates, it additionally changes its morphology and it's challenging to measure its true size from two-dimensional axis.

We noted that patients who did not develop POAF had more often normal diastolic function. Our study found DD to be a significant predictor of POAF in multiple regression analysis. The study of Melduni *et al*. was the first to show that DD is a POAF predictor [24]. Yet, there are scientific papers in which no significant association was found between DD and POAF. Such is the study of Barbara *et al*. who found that LAVi is a significant multivariant POAF predictor, but this was not true for DD as well [25]. Cameron *et al*. found only weak correlation and limited power for pre-operative identification of patients with high risk of developing POAF [26]. Our study, however, contributes to the growing amount of evidence that DD is a significant POAF predictor after cardiac surgical interventions.

Multivariant regression analysis in our study distinguished secondary MR as independent POAF predictor. Our findings are supportive of previously published literature. Kievisas *et al*. also found significant association between left heart valve pathology [27]. In their study, pre-operative MR and AR independently increased risk for POAF by 7.5 and 1.9 times accordingly. The influence of valve pathology in relation to POAF has not been extensively studied. The influence of MR on POAF occurrence has been studied in the study of Osranek *et al*. and they found significant association only in univariate regression analysis. Multivariate regression, however, confirmed only age and LAVi as independent POAF predictors [21]. MR significantly increases LA pressure and contributes to atrial dilation, electrophysiological remodeling, fibrosis, and arrhythmia. The influence of AR has not been thoroughly studied. However, one possible explanation derives from the observation that this valve pathology results in compensatory LV hypertrophy, and as disease progresses, potentially triggers similar pathophysiological mechanisms as seen in MR.

In November 2019, results from a systematic review and meta-analysis of 16 studies were published, which included 23.958 patients. It demonstrated significant association between mitral annular calcification and AF [28]. Mitral annular calcification is a frequent echocardiography finding seen in about 9% of female and 3% of male population older than 60 years [29]. It has been independently correlated with significant structural heart abnormalities. To the best of our knowledge, our study is one of the very first to observe significant correlation with POAF.

Recent advancement and expanding use of 3D echo techniques confirmed its superiority over traditional 2D techniques for volume and function analysis. It provides more accurate quantification of volumes and ejection fraction of ventricles, as well as shape, size, and volume of atria. Although we recognize the advantages of this technique, it is still far from routine practice worldwide. Many of us practicing echocardiography in cardiac surgery ICU will continue to rely and make the most of “the good, old 2D echo”. Indeed, once again this study confirmed it to be invaluable clinical tool, offering several potential POAF predictors. We believe that they should be integrated with traditional risk factors for POAF into new scoring systems, whose testing and validation would be the subject of future prospective studies.

Conclusion

Traditional two-dimensional echocardiography is a powerful and widely available diagnostic tool which offers several potential independent predictors for POAF. LAVi, diastolic dysfunction, secondary MR, calcified mitral annulus, and LAA flow velocity in combination with traditional risk factors for POAF would be a solid basis for constructing an algorithm for POAF prediction. Further larger scale randomized studies are needed to confirm these observations.

Limitations of the study

Our study included 178 patients, which is relatively small number considering the pathology studied. However, it is fair statistical sample given its almost equal the total number of cardiac surgeries at our institution annually. We did not analyze data from 3D echocardiography. It is still not widely available in routine practice, so we continue to rely on 2D echocardiography modes for such measurements and assessment.

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