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ORIGINAL ARTICLE



Prediction of postoperative atrial fibrillation with postoperative epicardial electrograms

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ABSTRACT

Objectives. New-onset postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. The arrhythmia often entails a longer hospital stay, greater risk of other complications, and higher mortality both short- and long-term. An investigation of the use of early atrial electrograms in predicting POAF in cardiac surgery was performed. **Design.** In this prospective observational study, a total of 99 consecutive adult patients undergoing coronary artery bypass grafting, valve surgery or both were included. On the first postoperative morning, standard 12-lead electrograms (ECG), unipolar atrial electrograms (aEG), and vital values were recorded. The outcome was new-onset POAF within one month postoperatively. **Results.** Three multivariable prediction models for POAF were formed using measurements derived from the ECG, aEG, and patient characteristics. Age, body mass index, and two unipolar electrogram measurements quantifying local activation time and fractionation were strongly associated with the outcome POAF. The performance of the POAF prediction models was assessed through receiver operating curve characteristics with cross-validation, and discrimination using the leave-one-out-method to internally validate the models. The cross-validated area under the receiver operating characteristic curve (AUC) was improved in a prediction model using atrial-derived electrogram variables (AUC 0.796, 95% CI 0.698–0.894), compared with previous ECG and clinical models (AUC 0.716, 95% CI 0.606–0.826 and AUC 0.718, 95% CI 0.613–0.822, respectively). **Conclusions.** This study found that easily obtainable measurements from atrial electrograms may be helpful in identifying patients at risk of POAF in cardiac surgery.

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Cardiac surgery; new-onset postoperative atrial fibrillation; atrial electrocardiogram; ECG; prediction model



Introduction


Approximately one-fourth to one-third of all patients undergoing cardiac surgery develops new-onset postoperative atrial fibrillation (POAF). These patients have a higher morbidity and mortality than patients who do not suffer from this postoperative arrhythmia [1,2]. Efforts to predict and reduce the incidence of POAF may improve patient outcomes and reduce hospitalization costs. Furthermore, the introduction of a routine risk score before the event would lead to a targeted strategy to prevent this complication. Because of the potential significant side effects of antiarrhythmic drugs, it is desirable to establish which patients are at high and low risk of POAF.

Several studies have shown an association between pathophysiological changes in the atria and the development of POAF [3,4]. Well-known risk factors for POAF are atrial enlargement and interstitial fibrosis, which may result in delayed or slowed conduction or perhaps the blockage of

electric impulses [5]. One of the methods used to quantify these properties of the atria, which is prone to POAF, is electrocardiographic measurements. Both preoperative and early postoperative measurements have been used for the development of a predictive tool for POAF [6,7]. In particular, the variables derived from atrial functioning, e.g. P-wave duration and left atrial enlargement (LAE), have been shown to be potential predictors of POAF.

In an earlier study from our research group [7], we showed that routine preoperative ECG variables (LAE, QRS duration, and PR interval) together with age could be used to identify patients at high risk of POAF. We aimed to improve this model by adding variables derived from atrial functioning as the variables associated with atrial enlargement served as the strongest predictors in the earlier study. ECG measurements from temporarily placed epicardial pacing wires can be used for the diagnosis of possible cardiac arrhythmias [8]. It allows for the possibility of recording

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atrial electrograms (aEGs) from epicardial pacing wires to aid in the differentiation between ventricular and supraventricular arrhythmias in early postoperative care.

The present study aimed to investigate whether it is possible to predict early POAF after cardiac surgery from a combination of patient characteristics and early postoperative electrocardiograms derived from right atrial epicardial pace wires. We hypothesized that specific atrial electrocardiogram measurements in combination with patient characteristics are associated with an increased risk of developing POAF after cardiac surgery and can therefore be used to identify patients at high risk of developing POAF. A decisive risk score for early prediction of POAF will allow clinicians to make informed decisions on whether to initiate prophylactic antiarrhythmic interventions.

Methods

Study design

The present study was conducted as a single-center prospective, observational study and was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. All measurements and recordings were collected in the Department of Cardiothoracic Surgery and the Cardiothoracic Intensive Care Unit at Aalborg University Hospital, Denmark, which performs approximately 400 open heart surgeries a year. This study was approved by the Institutional Review Board at Aalborg University Hospital (ID No. 2019–92). Ethical approval for this study was waived by The North Denmark Region Committee on Health Research Ethics because of the observational nature of the study, where only routine measurements were used.

Study data were collected and managed using the REDCap (Research Electronic Data Capture) database hosted at Region Nordjylland [9]. To reduce errors, double entry of all of the data were performed.

Subjects

All adult patients undergoing cardiac surgery at our hospital were screened from June 2019 to March 2020. The surgical procedures were either coronary artery bypass grafting (CABG), valve surgery, combined procedures as well as closures of atrial or ventricular septal defects. Patients were excluded if they had preoperative atrial fibrillation (AF) at the time of surgery, at the time of ECG recording, or had a history of AF, a pacemaker or total dependence on external pacing postoperatively, or the patient was placed in an ICU bed without the required software installed in monitors. Only the initial aEG and ECG recordings were used if patients underwent reoperation due to bleeding or ischemia during the same admission.

Most patients were discharged within six to seven days postoperatively and were then booked for an outpatient visit, including a 12-lead ECG, one month later.

All patients were on continuous telemonitoring three days postoperatively and for longer if the patient presented with arrhythmic episodes. POAF was documented by AF on the ECG. AF was defined as the absence of a P-wave and an irregular rhythm on a 12-lead ECG regardless of the duration and whether the patient received treatment for POAF.

Clinical variables

Baseline characteristics and information regarding the surgical procedure, as well as possible events of POAF up to 30 days postoperatively, were retrieved from the patient records. Details on the surgical procedure and postoperative events incl. POAF were registered by the surgeon responsible for the treatment of the patient. The pre- and postoperative variables sex, age, hypertension (requiring medical treatment), chronic pulmonary obstructive disease (defined as the need for long-term use of bronchodilators and/or steroids for lung disease), diabetes mellitus, dialysis, peripheral vascular disease (either carotid occlusion > 50%, claudication, or amputation due to arterial disease), ejection fraction, preoperative medication, body mass index (BMI), alcohol and smoking habits, euroSCORE II [10], type of surgery, use of cardiopulmonary bypass, and aortic cross-clamp were collected because each has been described as a predictor of POAF in previous studies [11–14]. Routine quality data checks for incorrect entries and missing values were made.

Electrograms, ECG, and hemodynamic recordings

Four temporary epicardial pacemaker wires (TME T quadripolar, Osypka TME, Dr. Osypka GmbH, Rheinfelden, Germany) are routinely sutured to the heart at the end of all cardiac procedures in Aalborg University Hospital. Two wires are placed on the right atrium, and two wires are placed on the right ventricle or one on the right ventricle and one on the left ventricle, depending on the surgeon's preferences. The percutaneous pace wires can be connected to a temporary external pacemaker if the patient's hemodynamic condition requires pacing assistance. Furthermore, atrial wires can be used to record an aEG with augmented P-waves when they are not used for pacing.

ECG recordings from these pace wires can be performed by connecting two precordial leads (e.g. V1 and V2) to the atrial wires or by adding two separate unipolar atrial wires to the conventional 12-lead ECG. The latter method was used in the present study. A 12-lead standard ECG and the two atrial unipolar electrograms were recorded for least one minute, and the most noise-free 10-s segment was selected for analysis. All ECG recordings were performed using Cardiosoft version 6.73 (GE Health care, Milwaukee, USA) on the first postoperative morning (time of ECG recording, $t=0$), while the patients were in the intensive care unit (ICU). If the patient had an external pacemaker connected, then it was paused during the recording. Simultaneously, the hemodynamic parameters detected by the right heart catheter (Swan-Ganz catheter; CCombo catheter, Edwards

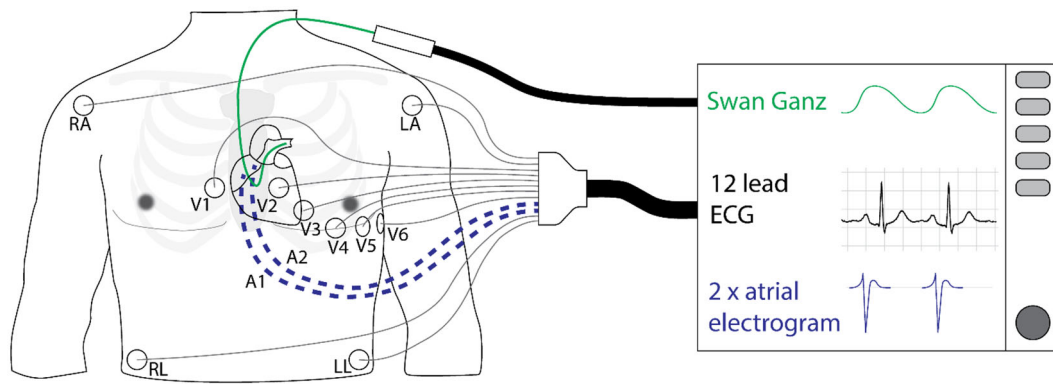


Figure 1. Experimental setup. Simultaneous recordings of hemodynamics, 12-lead ECG, and unipolar electrograms. Unipolar electrograms were recorded from temporary pacing wires placed on the right atrium.

Lifesciences, Irvine, CA, USA) were recorded, when possible, with Vital Recorder [15]. Some intensive care beds did not have this option; therefore, vital parameters were recorded from the patient records.

The experimental setup is shown in Figure 1.

ECG parameters

Clinically obtained sinus rhythm ECGs were imported to the GE MUSE Cardiology Information System (version 9.0) and reanalyzed with 12SL analysis software (version 243; GE Healthcare, Wauwatosa, WI, USA). The 12SL algorithm uses all 12 leads to construct a median beat in each lead from nonectopic P-QRS-T complexes and measures global intervals from the earliest onset in any lead to the latest offset in any lead as well as the lead specific intervals and amplitudes in all 12 leads. A single investigator blinded to the outcome (CG) manually overrode the fiducial points and corrected it if necessary. The following ECG measurements were derived from the 12SL algorithm and used in the present study: PR interval, P-wave duration (Pdur), QRS duration, and left atrial enlargement (LAE), which was defined as a P-wave duration in lead II greater than 120 milliseconds (ms) or a P-terminal force in V1 exceeding 40 mm × ms (Figure 2).

Electrogram parameters

Two unipolar electrograms recorded from the right atrium were used to measure the two variables: local atrial activation time (uLAT) and the degree of fractionation (uFRAC) of the electrograms (Figure 3). The stability over time of the electrograms allowed for median electrograms to be obtained and used for subsequent analyses. This is advantageous because it eliminates small negative deflections caused by noise while retaining the true deflections caused by physiological properties. The local activation time was manually measured in each unipolar lead as the duration from P-wave onset to the steepest negative slope of the electrogram that fell within the P-wave duration. The latest of the two activation times was used to define uLAT.

Upon visual inspection, the degree of electrogram fractionation was quantified by counting the number of negative slopes, regardless of the magnitude, within the P-wave

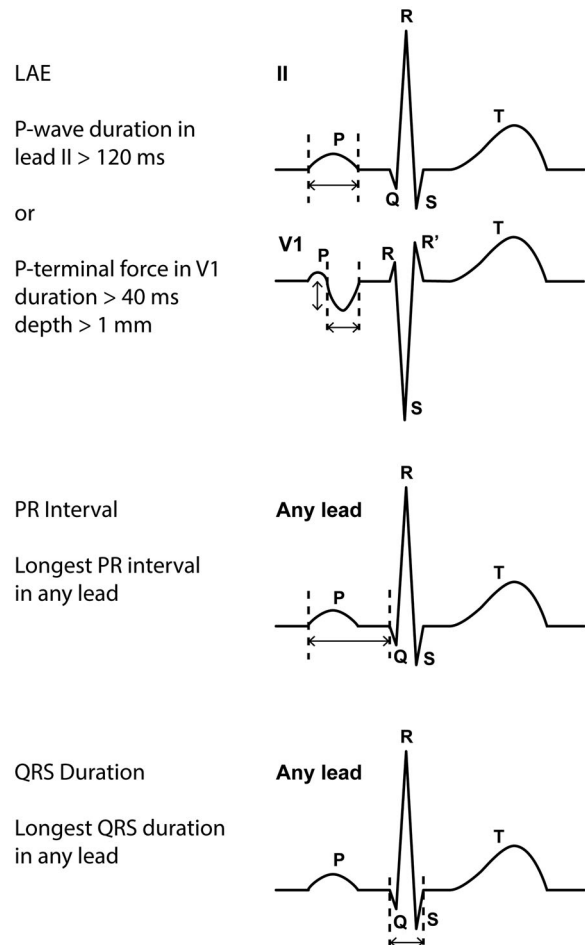


Figure 2. 12-lead ECG measurements. Measurement of the PR interval, QRS duration, and left atrial enlargement (LAE) from the 12-lead ECG. LAE was defined as a P-wave duration in lead II > 120 ms or a P-terminal force V1 greater than 40 mm × ms.

boundaries. An electrogram with a single negative slope was categorized as a single nonfractionated electrogram, whereas electrograms with more than one negative slope were categorized as fractionated (two negative slopes) or complex fractionated (more than two negative slopes). The degree of fractionation was assessed in both electrograms, and uFRAC was defined as a dichotomous parameter that quantifies the presence (more than one negative slope in either electrode) or absence (a single negative slope in both electrodes) of fractionation.

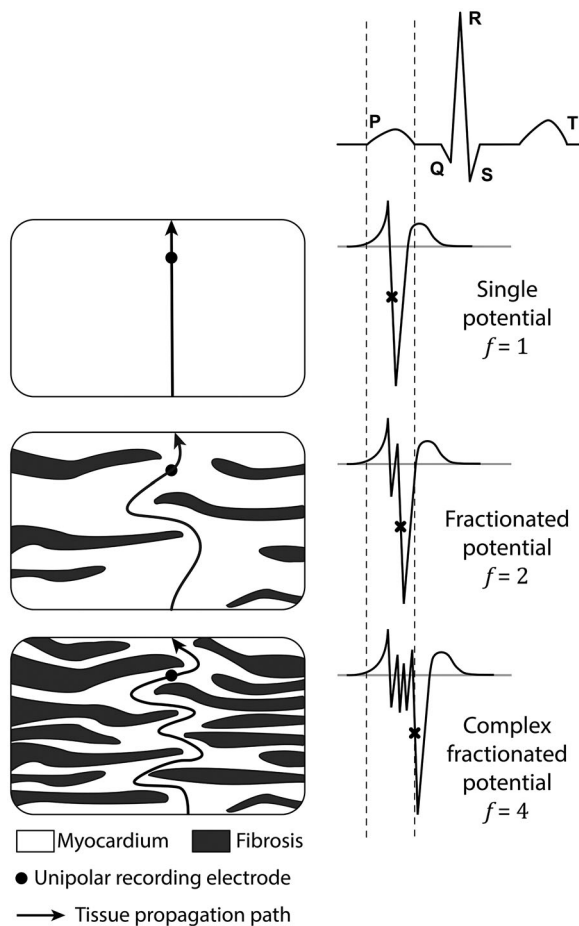


Figure 3. Measurement of unipolar electrogram parameters from temporary atrial pacing wires. In a healthy myocardium with little or no atrial structural changes and wavefront barriers (i.e. fibrosis or scarring), unipolar electrograms recorded from atrial pacing wires will have a single negative deflection without fractionation. With more advanced atrial structural changes, the electrogram will become fractionated, and the activation time indicated on the steepest negative slope of the electrogram will occur later. Structural changes in the atrium may therefore be reflected in the later atrial activation time on the electrogram (uLAT) and likely on more fractionated electrograms (uFRAC).

Statistical analysis and prediction models for POAF

Continuous data are summarized as the mean values with standard deviations. Categorical data are reported as counts and percentages. Differences between groups were tested using two sample t-tests and Fisher's exact tests. Because we were unsuccessful in identifying other studies using atrial ECG data for predicting POAF, no formal sample size calculation was performed.

All prediction models were univariable or multivariable logistic regression models with POAF as the outcome. All predictors were screened for linear or nonlinear associations using fractional polynomials [16] and they were included in the multivariate analysis when a p value $< .2$ was observed in the univariate analysis. We sought an easy clinically obtainable and reliable prediction model and used the common rule, which requires at least 10 events per variable, thus restricting models to four variables at the most.

The following three multivariable models for the prediction of POAF were produced: (1) a clinical model using only clinical predictors of POAF, including age, sex, and BMI (M1: clinical); (2) a combined ECG and clinical model

using the PR interval, QRS duration, LAE, and age (M2: ECG-clinical), as previously described by our group [7]; and (3) a combined electrogram and clinical model using the unipolar electrogram parameters uLAT and uFRAC, together with age and BMI (M3: atrial-clinical). The three models' scores were calculated from a linear combination of the three or four variables with no specific cutoff level for the individual components of the model. Thus, the chosen prediction models were an internal validation of two existing prediction models and a validation of a new potentially improved model.

Assessment of the prediction model performance

Multivariable prediction models were evaluated using the area under the receiver operating characteristic curve (AUC) and cross-validated using the leave-one-out method. The standard errors for the AUC were calculated with bootstrapping with 5000 replications. The optimal threshold value (cutoff point) for the best model was identified using the Youden index [17], and the sensitivity, specificity, and predictive ability of the model were calculated. Analyses were conducted using Stata/MP (version 16; StataCorp LP, College Station, Texas).

Results

A total of 260 patients were screened, and among these, 161 were excluded from the study (43 had AF at admission, 53 were unstable/dependent on pacemakers, and 65 had logistic obstacles). Among the 99 patients analyzed, 37 developed postoperative AF (37.4%).

Patient characteristics and information about the surgical procedures are shown in Table 1. The patients with POAF were older and had a higher body mass index than those without POAF. Although not all patients had a right heart catheter at the time of the ECG recording, the available results showed that only mixed venous oxygen saturation (SvO₂) reached significance and it was significantly lower in the POAF group. The majority of patients who developed POAF did so within three days of surgery (30 out of 37, 81%), and 89% of the patients who developed POAF were identified within five days of the surgery. Patients who developed POAF were treated according to surgeons' decision. If POAF persisted after 48 h OAC were initiated until successful Direct Current-conversion.

Compared with those who did not develop POAF, patients with POAF had, on average, a longer duration of the P-wave and signs of left atrial enlargement (LAE) but not a significantly longer QRS duration (Table 2). The atrial electrogram parameters uLAT and uFRAC showed that the patients who developed POAF had later atrial activation times and were more likely to have fractionated electrograms (Figure 4).

In univariate regression analyses, age (OR: 1.08 (95%CI: 1.03–1.13), BMI (OR: 1.10 (95%CI: 1.01–1.21), P-wave duration (OR: 1.04 (95% CI: 1.01–1.07), LAE (OR: 2.57 (95%CI: 1.05–6.30), uLAT (OR: 1.04 (95%CI: 1.01–1.07),

Table 1. Descriptive characteristics of the patients.

	No POAF n = 62	POAF n = 37	p Value
Male, n (%)	42 (67.74)	31 (83.78)	.100
Female, n (%)	20 (32.26)	6 (16.22)	
Age, mean, year (SD)	60.8 (13.2)	70.3 (9.3)	<.001
Comorbidities, n (%)			
Hypertension	37 (59.68)	24 (64.86)	.673
COPD	8 (12.90)	5 (13.51)	1
Diabetes (NIDDM)	5 (8.06)	3 (8.11)	1
Diabetes (IDDM)	10 (16.13)	2 (5.41)	.201
Dialysis	2 (3.23)	0	.527
Peripheral vascular disease	6 (9.68)	2 (5.41)	.706
LVEF, mean (SD)	52.94 (1.27)	54.19 (1.71)	.5524
Medication, n (%)			
Beta blocker	22 (35.48)	12 (32.43)	.829
Thrombocyte inhibitor	31 (50)	22 (59.46)	.409
ACE inhibitor	16 (25.81)	11 (29.73)	.816
Calcium antagonist	17 (27.42)	10 (27.03)	1
Oral anticoagulation	1 (1.61)	1 (2.70)	1
Steroid	2 (3.23)	2 (5.41)	.628
Statin	37 (59.68)	24 (64.86)	.673
BMI (kg/m ²), mean (SD)	26.24 (4.21)	28 (4.77)	.0344
Alcohol consumption			.180
0 units/week	4 (6.45)	0	
<7/14 units/week for women/men	52 (83.87)	34 (91.89)	
>7/14 units/week for women/men	6 (9.68)	2 (5.41)	
Not given	0	1 (2.7)	
Smoking			.897
No	25 (40.32)	17 (45.95)	
Former ^a	20 (32.26)	11 (29.73)	
Active	17 (27.42)	9 (24.32)	
EuroSCORE II, mean (SD)	1.92 (2.54)	2.15 (1.92)	.6377
Type of operation			.231
CABG	30 (48.39)	14 (37.84)	
Valve	23 (37.10)	12 (32.43)	
CABG + valve	3 (4.84)	6 (16.22)	
Other	6 (9.68)	5 (13.51)	
CPB(On-pump)	52 (83.87)	35 (94.59)	.201
Aortic cross-clamp time (minutes), mean	63.61 (31.10)	75.06 (30.85)	.0897
Postoperative ICU data, mean			
SvO ₂ (%)	68.63 (7.67)	65.49 (6.64)	.0437
CO (L/min)	5.59 (1.63)	5.50 (1.14)	.8211
CI (L/min/m ²)	3.23 (0.93)	2.81 (0.69)	.0223
MAP (mmHg)	77.21 (11.22)	73.86 (9.93)	.1377
SBP (mmHg)	119.13 (16.35)	119.57 (18.71)	.9029
DBP (mmHg)	55.94 (10.72)	55.46 (8.60)	.0971
MPAP (mmHg)	21.58 (7.16)	20.17 (5.24)	.3104
PASP (mmHg)	27.47 (5.87)	27.93 (6.34)	.7703
PADP (mmHg)	15.39 (5.10)	15.33 (5.25)	.9664
CVP (mmHg)	11.95 (8.03)	10.53 (5.45)	.3550

Notes: Continuous data are presented as the mean \pm standard deviation, and categorical data are presented as numbers (percentages). COPD: chronic obstructive pulmonary disease; NIDDM: noninsulin-dependent diabetes mellitus; IDDM: insulin-dependent diabetes mellitus; LVEF: left ventricular ejection fraction; ACE: angiotensin-converting enzyme; BMI: body mass index; ^aFormer smoker; stopped >1 month prior to the day of operation; EuroSCORE: European System for Cardiac Operative Risk Evaluation; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; SvO₂: mixed venous oxygen saturation; CO: cardiac output; CI: cardiac index; SBP: systolic arterial blood pressure; DBP: diastolic arterial blood pressure; MPAP: mean pulmonary artery pressure; PASP: systolic pulmonary artery pressure; PADP: diastolic pulmonary artery pressure; CVP: central venous pressure.

and uFRAC (OR: 2.68 (1.12–6.39) were found to be independent predictors of POAF (Table 3). As can be seen from Table 3, multivariate analyses for the three prediction models showed that age, sex, LAE, uLAT, and uFRAC were independent predictors of POAF.

Prediction models

The apparent best model for the prediction of POAF was M3 using the atrial-derived electrogram parameters uLAT

and uFRAC, together with age and BMI (Figure 5 and Supplementary Figure 1). This model had the highest ROC area both with and without cross-validation as follows: AUC 0.796 (95% CI 0.698–0.894) and AUC 0.837 (95% CI 0.750–0.923), respectively (Table 4). Furthermore, calibration plots revealed a reasonable risk assessment of the M3 model (Supplementary Figure 1). Table 5 shows the ability of the M3 model to predict the outcome POAF when calculated from the optimal cutoff point of the model (cutpoint = −0.13585592). The M3 model had a sensitivity

of 73% with a cutpoint determined by maximizing the Youden index. As shown in Figure 5, the sensitivity of 73% would correspond to a specificity of approx. 60–65% for M2, whereas we have calculated a specificity of 80.6% for M3. Although the M3 model seemingly had a higher AUC score, it performed in a statistically similar matter to that of the ECG-clinical model combining the PR interval, QRS duration, LAE and patient age and the model using only the clinical measurements of age, sex, and BMI.

Discussion

The present study found that variables derived from atrial electrograms together with age and BMI in a prediction model increased its ability to predict POAF. The two predictors, uLAT and uFRAC, were both strongly associated with the development of POAF, and they may therefore act as

indicators of the underlying structural atrial changes, potentially related to increased fibrotic myocardial tissue in the atria. A strong relationship between atrial remodeling due

Table 3. Univariable and multivariable regression analyses for odds of postoperative atrial fibrillation using the variables in the M1, M2, and M3 models.

Variable	Univariable OR (95% CI)	p Value
Clinical		
Age	1.08 (1.03–1.13)	.001
Sex	2.46 (0.88–6.85)	.085
BMI	1.10 (1.01–1.21)	.038
ECG		
PR, ms	1.01 (0.99–1.02)	.419
Pdur, ms	1.04 (1.01–1.07)	.009
LAE, %	2.57 (1.05–6.30)	.039
QRS, ms	1.01 (0.99–1.03)	.167
Atrial electrogram		
uLAT	1.04 (1.01–1.07)	.006
uFRAC, %	2.68 (1.12–6.39)	.026
Variable	Multivariable OR (95% CI)	p Value
M1: age, sex, BMI		
Age	1.09 (1.04–1.15)	.001
Sex	3.71 (1.16–11.82)	.026
BMI	1.09 (0.98–1.21)	.111
M2: age, PR, QRS, LAE		
Age	1.09 (1.04–1.16)	<.001
PR	0.98 (0.97–1.00)	.136
QRS	1.02 (0.99–1.04)	.144
LAE	4.06 (1.27–12.97)	.018
M3: age, BMI, uLAT, uFRAC		
Age	1.10 (1.04–1.16)	.001
BMI	1.10 (0.97–1.24)	.123
uLAT	1.05 (1.02–1.09)	.003
uFRAC	4.39 (1.50–12.81)	.007

Table 2. Electrocardiogram and atrial electrogram parameters.

	No POAF (n = 62)	POAF (n = 37)	p Value
ECG			
PR, ms (SD)	168.5 (27.2)	173.4 (32.1)	.4231
Pdur, ms (SD)	108.8 (13.6)	117 (14.3)	.0061
LAE, %	13 (21)	15 (41)	.042
QRS, ms (SD)	97.7 (22.4)	103.9 (19.8)	.1636
aEG			
uLAT (SD)	38.2 (14.3)	47.8 (16)	.0029
uFRAC, %	28 (45)	25 (68)	.049

Notes: Data are presented as the mean ± standard deviation (SD) or as a count and percentage. Pdur: P-wave duration; LAE: left atrial enlargement (see Figure 2 for the ECG parameter definition); uLAT: unipolar local activation time; uFRAC: unipolar fractionation (see Figure 4 for the electrogram parameter definitions).

Abbreviations: BMI: body mass index; Pdur: P-wave duration; LAE: left atrial enlargement (see Figure 2 for ECG parameter definition); uLAT: unipolar local activation time; uFRAC: unipolar fractionation (see Figure 4 for electrogram parameter definitions).

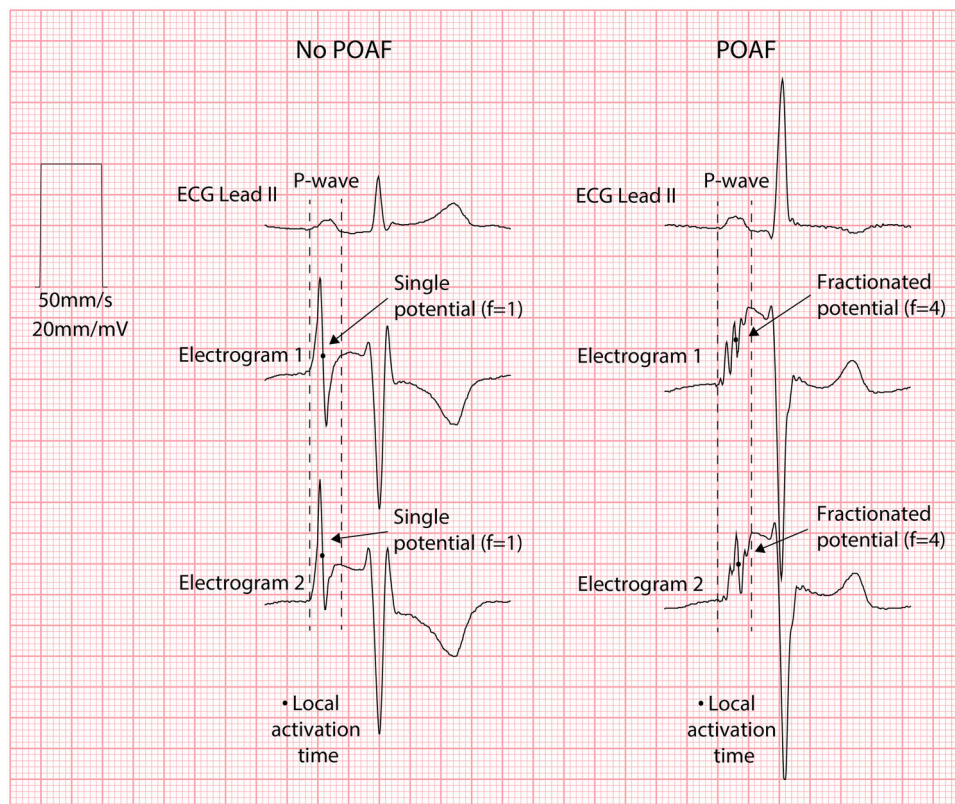


Figure 4. Examples of the configuration of the electrograms depending on the outcome POAF. The figure shows how the variables local activation time (uLAT) and fractionation (uFRAC) were calculated.

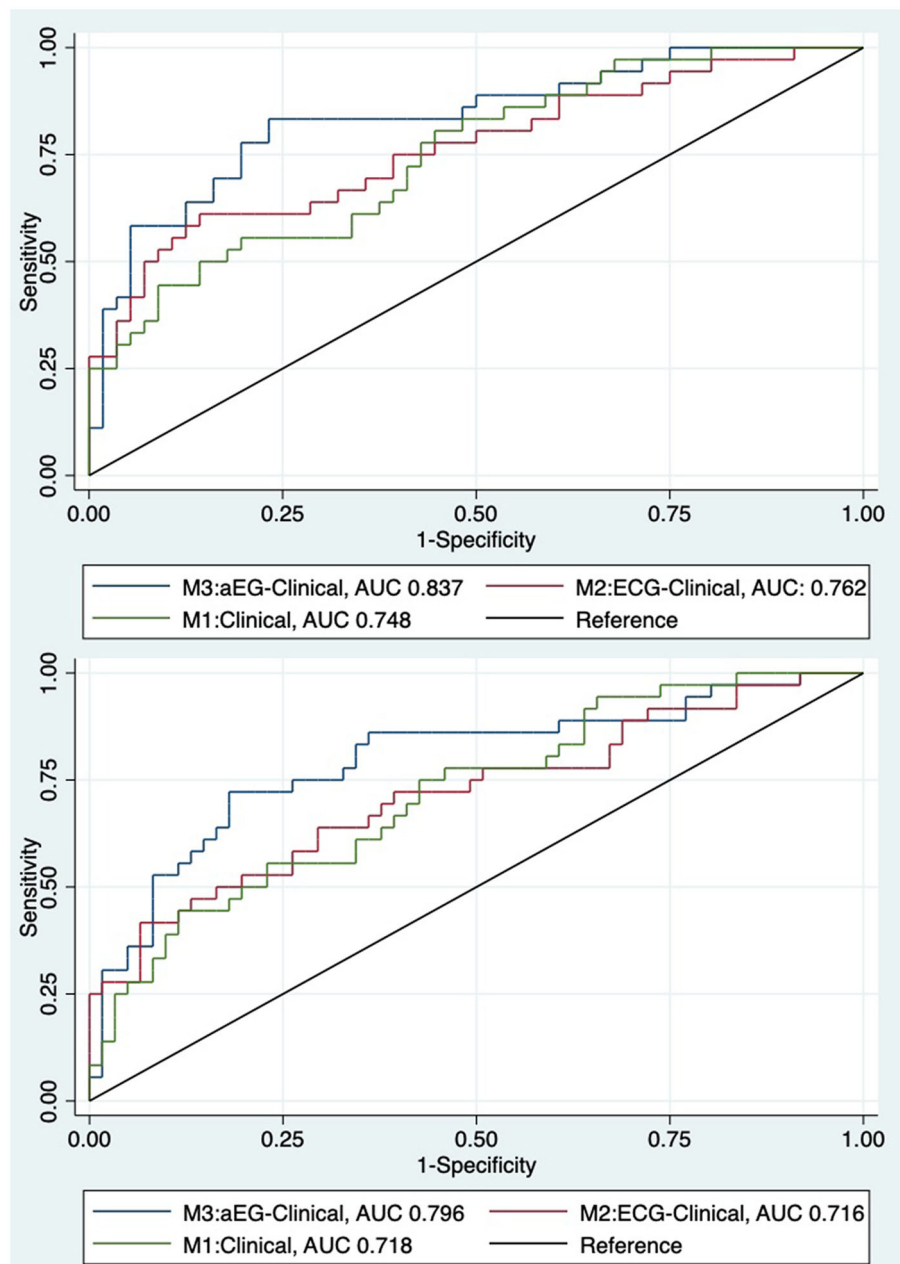


Figure 5. Receiver operating characteristic curves for multivariable POAF prediction models. The best prediction model for POAF was the atrial-clinical model using the atrial electrogram parameters uLAT and uFRAC, together with age and BMI. (A) Model without cross-validation. (B) Model with 10-fold cross-validation.

Table 4. Area under the curve for the prediction models.

	AUC	[95% CI]
Clinical model:		
Model 1: age, sex, BMI	0.748	0.646 0.849
With cross-validation	0.723	0.623 0.823
ECG-clinical model:		
Model 2: PR interval, QRS-dur, LAE, age	0.762	0.658 0.866
With cross-validation	0.716	0.607 0.825
Atrial ECG-clinical:		
Model 3: age, BMI, uLAT, uFRAC	0.837	0.750 0.923
With cross-validation	0.796	0.698 0.894

Abbreviations: AUC: area under the curve; BMI: body mass index; CI: confidence interval; ECG: electrocardiogram; QRS-dur: QRS duration; LAE: left atrial enlargement; uLAT: local activation time; uFRAC: presence of fractionation of the electrograms.

to aging (used here as a measure of the left atrial size) and POAF has been reported in the literature [5,18]. Comparisons of the present findings with those of other

studies confirmed that advanced age and BMI are independent predictors of POAF.

POAF is the most common complication after cardiac surgery, and it is most likely related to a combination of predisposing factors as well as reactions to the surgical procedure. The pathophysiology behind the development of POAF has not been fully established, but an increasing number of studies have confirmed that structural and electrical changes can be detected in patients prone to POAF [19–22].

The variables used in the prediction model developed in the present study are easy to collect in daily routines involved in patient care. The atrial-derived measurements used in the prediction model are applicable even when the temporary electrodes are not placed in the exact same place on the heart. This is because obstructive barriers to

Table 5. Sensitivity, specificity, and other characteristics of the M3 atrial-clinical model with an estimated optimal cut-off point.

Outcome of M3: atrial-clinical	True incidence of POAF		Row total
	Positive	Negative	
Positive	27 (TP)	12 (FP)	39 (TP + FP)
Negative	10 (FN)	50 (TN)	60 (FN + TN)
Column total	37 (TP + FN)	62 (FP + TN)	N = 99 (TP + TN + FP + FN)
Accuracy: $(TP + TN)/(TP + TN + FP + FN) = 78\%$			
Sensitivity: $TP/(TP + FN) = 73\%$			
Specificity: $TN/(TN + FP) = 80.6\%$			
Positive predictive value: $TP/(TP + FP) = 69.2\%$			
Negative predictive value: $TN/(TN + FN) = 83.3\%$			

TP: true positive; FP: false positive; TN: true negative; FN: false negative.

wavefront propagation, such as fibrosis in the atria, most often are not localized to a single focal point but instead are more diffuse and thus cover the entire epicardial surface. It is also unlikely that fractionation was caused by wavefront collision or irregular re-entries in the atria because the morphology of the P-waves indicates a regular sinus rhythm.

This study supports evidence from previous observations of electrocardiographic measures for the prediction of POAF. Chandy et al. [23] found an association with increased P-wave dispersion and POAF. Gu et al. [7] showed a good predictive value of different ECG parameters in combination with the clinical characteristics of patients for predicting POAF with an AUC of 0.780 (0.696; 0.865). We observed a similar AUC in our population (AUC 0.716 (0.606;0.826) with the same model, but a larger AUC (0.837) was obtained for the model including atrial electrograms. Thus, compared to earlier prediction models of ECG parameters, the measured AUC for the model with atrial-derived variables in this study was significantly higher [22,24,25], and thus it appears that the use of electrograms adds value to POAF prediction. Of note, we did not find a significant difference for the type of surgery or the duration of the QRS interval, which contradicted previous studies [7,26].

Hemodynamic parameters (particularly pulmonary capillary wedge pressure and pulmonary artery systolic pressure) have been previously reported to be useful for the prediction of POAF [27]. We included variables from the Swan-Ganz catheter in the preliminary screening but could not confirm the earlier reported association.

Prediction of POAF with ECG and electrogram measurements might help identify the proportion of patients at high risk of POAF, who then can be targeted with prophylactic measures. A recent systematic review found that the use of beta blockers, sotalol, amiodarone, and atrial pacing reduces the rate of POAF after cardiac surgery [28]. Due to the potential side effects of these medications, which include hypotension, prolongation of the QT interval, and bradycardia, a more targeted strategy is necessary to avoid their application to patients not at risk. The calculated Youden index offers the best possible sensitivity and specificity in this specific model. In a clinical setting, however, the model should be adjusted to achieve a higher positive predictive value to offer patients over a certain threshold prophylactic medication early on.

Limitations

There were several limitations to this study. Due to the small sample size, the following results may have occurred: (1) overfitting of the model, which was not captured in the cross-validation; (2) selection bias, in which the most comorbid/complicated procedures/patients were excluded from evaluation and furthermore, that only two ICU beds had the software installed in the monitors enabling the recording of data; and (3) distortion of the data due to different procedures in both elective and acute patients. Most likely, the ECG and electrogram characteristics in patients with chronic valvular lesions will differ from those in patients with coronary artery disease with regard to atrial remodeling and ventricular dysfunction and it may be advantageous to study the prediction model in patients undergoing the same type of surgery. Furthermore, there may be patients with incidents of POAF not captured *via* early postoperative telemetry or after discharge, which could underestimate the incidence rate of POAF. However, the composition and incidence of POAF are probably applicable to most cardiac surgery centers and we have no reason to believe that the patients were systematically excluded because of the availability of the software in the monitors, and hence skew the applicability of the risk score.

Although the present study must be viewed as a hypothesis-generating study that requires further validation studies, these results suggested that atrial-derived electrogram recordings may be of assistance in predicting POAF. Additional studies with larger study populations are necessary to test and externally validate the model.

Conclusion

We demonstrated that measurements from atrial electrograms may be helpful in identifying patients at risk of POAF in cardiac surgery. Further studies are needed to validate the use of the prediction model before implementation in a clinical setting.

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Data availability statement

The data underlying this article cannot be shared publicly due to patient privacy. The data will be shared on reasonable request to the corresponding author.

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