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META-ANALYSIS

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Preoperative P-wave parameters and risk of atrial fibrillation after cardiac surgery: a meta-analysis of 20 201 patients

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Key question

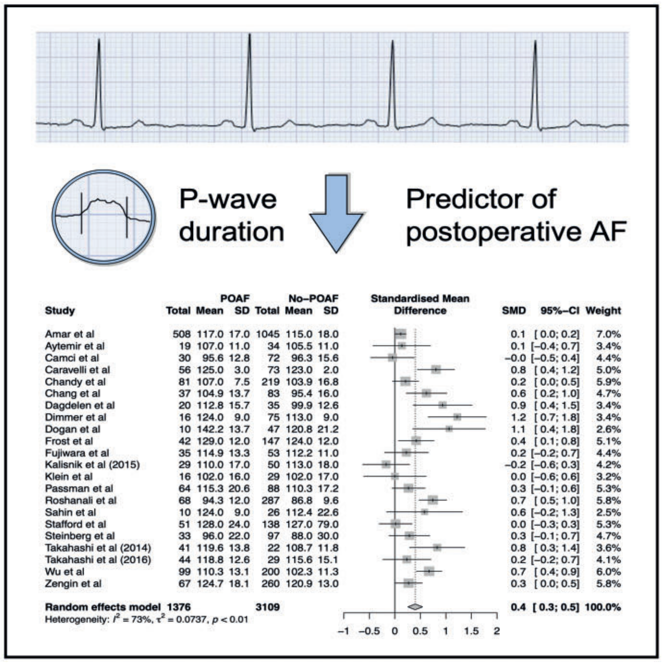
To evaluate P-wave parameters, defined on electrocardiography, in predicting atrial fibrillation after cardiac surgery.

Key finding(s)

Increased P-wave duration was associated with increased POAF occurrence independently from left atrial size.

Take-home message

Increased P-wave duration is a valuable parameter for predicting POAF in patients undergoing cardiac surgery.



Abstract

OBJECTIVES: To evaluate the role of P-wave parameters, as defined on preprocedural electrocardiography (ECG), in predicting atrial fibrillation after cardiac surgery [postoperative atrial fibrillation (POAF)].

METHODS: PubMed, Cochrane library and Embase were searched for studies reporting on P-wave parameters and risk of POAF. Meta-analysis of P-wave parameters reported by at least 5 different publications was performed. In case of receiver operator characteristics (ROC-curve) analysis in the original publications, an ROC meta-analysis was performed to summarize the sensitivity and specificity.

[†]These authors contributed equally to this work.

RESULTS: Thirty-two publications, with a total of 20 201 patients, contributed to the meta-analysis. Increased P-wave duration, measured on conventional 12-lead ECG (22 studies, Cohen's $d = 0.4$, 95% confidence interval: 0.3–0.5, $P < 0.0001$) and signal-averaged ECG (12 studies, Cohen's $d = 0.8$, 95% confidence interval: 0.5–1.2, $P < 0.0001$), was a predictor of POAF independently from left atrial size. ROC meta-analysis for signal-averaged ECG P-wave duration showed an overall sensitivity of 72% (95% confidence interval: 65–78%) and specificity of 68% (95% confidence interval: 58–77%). Summary ROC curve had a moderate discriminative power with an area under the curve of 0.76. There was substantial heterogeneity in the meta-analyses for P-wave dispersion and PR-interval.

CONCLUSIONS: This meta-analysis shows that increased P-wave duration, measured on conventional 12-lead ECG and signal-averaged ECG, predicted POAF in patients undergoing cardiac surgery.

Keywords: Postoperative atrial fibrillation • Electrocardiography • Cardiac surgery • Receiver operating curve meta-analysis

INTRODUCTION

Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery and it has been associated with the incidence of early and late postoperative stroke, mortality and prolonged hospitalization [1]. POAF is thought to be an expression of a pre-existing substrate resulting from cardiovascular comorbidities which also predict POAF recurrences after discharge from hospital [1, 2]. P-wave parameters, measured on conventional electrocardiography (ECG), have previously been used to determine the underlying substrate for atrial fibrillation (AF) in the general population and to predict AF in non-surgical patients [3, 4]. However, the clear diagnostic value and the usefulness of these P-wave parameters in POAF prediction are debated. The purpose of this systematic review and meta-analysis is to evaluate the value of preoperative P-wave parameters in predicting POAF.

METHODS

Protocol registration and literature search

The study protocol was registered in PROSPERO international prospective register of systematic reviews (CRD42021261119). For this systematic review, the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed [5]. In June 2022, a systematic literature search was conducted, after consultation of a trained medical librarian, in PubMed, Cochrane database and Embase (Supplementary Material, Tables S1–S3). Citation tracking was performed to identify additional publications.

Study selection and data extraction

After removal of duplicates, all identified studies were screened on titles and abstracts by 2 (M.J.K. and S.V.D.W.) researchers. Studies in patients not undergoing cardiac surgery, studies not published in English or without description of preoperative ECG-workup and postoperative monitoring for POAF were excluded after screening the titles and abstracts. Full texts of the remaining articles were screened. The inclusion criteria for the systematic review were a preoperative P-wave assessment, cardiac surgery and postoperative monitoring for POAF.

Two authors independently extracted the data (M.J.K. and S.V.D.W.). Data on the following variables were extracted: age, sex, diabetes mellitus, hypertension, left ventricular ejection fraction, chronic obstructive pulmonary disease, right coronary artery occlusion, body mass index, left atrial diameter, definition of POAF and history of AF. Also, the following study characteristics were analysed: study size, type of study (prospective or retrospective) and type of surgery performed. In case of disagreements during the study selection and data extraction process, a third independent author was consulted (E.B.).

Quality assessment

The Downs and Black tool for quality assessment in cohort studies was used to determine the quality of the studies included in the meta-analyses [6]. In addition, the description of the ECG protocol and monitoring for POAF were added to the quality assessment.

Study outcomes

The primary outcome of this study was occurrence of POAF in the early postoperative period after cardiac surgery. POAF had to be registered either by a 12-lead ECG or by telemetric monitoring. No distinction was made between the different definitions of POAF, such as episode duration and monitoring duration. Ultimately, this was corrected for in various subgroup analyses.

The exposure parameters of interest were all P-wave parameters, as determined by ECG, associated with the occurrence of POAF in patients undergoing cardiac surgery.

Statistical analysis

For parameters identified by a minimum of 5 publications, a continuous variables meta-analysis using inverse variance method was performed to assess the overall Cohen's d, which is a measure of effect size (ES). A minimum of 5 publications was set to obtain the robustness of the models. The following cut-offs for the interpretation of Cohen's d were selected: $0 <$ Cohen's $d < 0.2$ = no effect, $0.2 \leq$ Cohen's $d < 0.5$ = small effect, $0.5 \leq$ Cohen's $d < 0.8$ = intermediate effect, Cohen's $d \geq 0.8$ = large effect. Cochran's Q-test and I^2 statistics were used to assess heterogeneity of the models with a significant cut-off value of $P < 0.10$ and $I^2 > 50\%$, respectively. To explore the patterns of heterogeneity, a leave-one-out analysis or a graphic display of heterogeneity plot was performed [7]. Subgroup analyses and meta-regression were performed to examine the between-study differences and different patterns of ES distribution. The subgroups were predefined based on the suspected contributors to between-study differences (patient characteristics, outcome measures and definitions, or interventions).

To determine pooled diagnostic accuracy of receiver operator characteristics curves (ROC curves) in the original publications, an ROC meta-analysis was performed using a bivariate approach in a linear mixed model [8]. Based on given pairs of sensitivity and specificity for a certain cut-off value, true positives, true negatives, false positives and false negatives were back-calculated and fitted in the ROC meta-analysis. The results were presented in a summary receiver operating curve (SROC) with a range of sensitivity and specificity based on a range of cut-off values. The discriminative power of the model was assessed based on the area under the curve (AUC) with the following cut-off values: AUC < 0.75 = low accuracy, 0.75 ≤ AUC < 0.85 = moderate accuracy, AUC ≥ 0.85 = high accuracy. To assess study differences and their influence on SROC, a meta-regression was performed [8].

The presence of potential publication bias was visually assessed in a funnel plot and by performing the Egger's test with a *P*-value <0.05 regarded as statistically significant [9]. In addition, between-study heterogeneity and outliers were considered as potential causes of funnel plot asymmetry. Significant publication bias was explored using a Duval & Tweedie's trim-and-fill procedure to estimate the actual ES [10]. Trim-and-fill analysis was performed with 3 different estimators (L_0, R_0 and Q_0) to provide more insight into patterns of publication bias [11].

All statistical values were computed with a 95% confidence interval in random-effects models. The 2-tailed *P*-value cut-off for statistical significance was set at $P < 0.05$. All statistical models were created in 'Rstudio Version 1.2.1335' by using the 'meta' (version 4.18–1), 'metafor' (version 3.0–2), 'mada' (version 0.5.10) and 'dmetar' (version 0.0.9000) packages available for performing meta-analyses [12, 13].

RESULTS

Study selection

The search generated 2627 results. Additional 6 records were identified by scanning the studies included in a previous meta-analysis [14]. After exclusion of duplicates, 2633 studies were screened on title and abstracts and 65 publications were deemed suitable for full-text evaluation. Eventually, 33 records were excluded with reasons (Supplementary Material, Table S4) and 32 studies were included in the quantitative analysis. An overview of the study selection process is presented in Fig. 1.

Quality of studies

The overall quality of the studies included in the meta-analyses was high (Supplementary Material, Figs S1 and S2). All studies clearly described the objectives, study outcomes, interventions and their main findings. Also, majority of the studies provided extensive descriptions of ECG protocols, monitoring for POAF and statistical methodology.

Study outcomes

Thirty-two studies (20 201 patients) were included in the current meta-analysis (Table 1). Study subjects were predominantly males (71.2%). The average incidence of POAF was 33.7%. Patients with POAF were significantly older compared to patients without POAF (67.3 vs 61.7 years, $P < 0.001$, respectively). The studies were conducted between 1993 and 2020 [15–46].

P-wave dispersion. Eight studies were included in a meta-analysis of P-wave dispersion [ES = 0.7, 95% confidence interval (CI): 0.2–1.3; I^2 = 92%, $P < 0.01$; Fig. 2A]. Heterogeneity analysis showed that omitting the study by Achmad *et al.* reduced overall heterogeneity (I^2 = 87%) and ES (ES = 0.1, 95% CI: -0.1 to 0.3) (Supplementary Material, Fig. S3).

PR-interval. Eleven studies were included in a meta-analysis of PR-interval (ES = 0.1, 95% CI: 0.03–0.3) (Fig. 2B). Differences in PR interval are shown in Fig. 3A. Subgroup analysis showed that larger cohort size was associated with a greater ES (ES = 0.2, 95% CI: 0.1–0.3, $P = 0.03$) (Table 2). There was no significant difference for ES in the subgroup analysis for PR-interval based on rhythm history, however, there was a greater ES for patients with history of AF (ES = 0.2, 95% CI: 0.1–0.3) (Table 2). Also, higher prevalence of hypertension was associated with a lower ES (Beta = -0.04, $P < 0.01$), whereas increased average body mass index and increased percentage of patients with diabetes mellitus were associated with increased ES (Beta = 0.82, $P = 0.02$, and Beta = 0.03, $P = 0.01$, respectively) (Table 2). Heterogeneity analysis determined study by Kališnik *et al.* (2019) as the main source of heterogeneity (Supplementary Material, Fig. S4). Sensitivity analysis after omitting this study showed a small ES of 0.2 (95% CI: 0.2–0.3), with still substantial model heterogeneity (I^2=63%, Cochran's Q: $p < 0.01$) (Supplementary Material, Fig. 4).

P-wave duration (12-leads electrocardiography). Twenty-two studies were included in a meta-analysis of P-wave duration measured on 12-lead ECG (ES = 0.4, 95% CI: 0.3–0.5) (Fig. 4). Patients with history of AF had a greater P-wave duration as compared to patients without history of AF (115.2 ms; 95% CI: 112.3–118.2 ms, vs 109.8 ms; 95% CI: 104.5–114.9 ms, $p = 0.04$, respectively). Also, there was a gradual increase in P-wave duration between no-POAF patients without history of AF, and POAF-patient with history of AF (105.7 ms; 95% CI: 97.9–115.5 ms, vs 118.2 ms; 95% CI: 112.9–123.4 ms, $p = 0.03$, respectively) (Fig. 3B). Subgroup analysis and meta-regression showed no statistically significant results (Table 2). Heterogeneity analysis revealed studies by Kališnik *et al.* (2015), Dimmer *et al.* and Roshanali *et al.* as main sources of heterogeneity (Supplementary Material, Fig. S5–S7). Sensitivity analysis after omitting these studies showed a small ES (ES = 0.4 95% CI: 0.2–0.5), with still substantial model heterogeneity (I^2 = 67%, Cochran's Q: $P < 0.01$) (Supplementary Material, Fig. S8).

P-wave duration (signal-averaged electrocardiography). Twelve studies were included in a meta-analysis of signal-averaged ECG (SAECG) P-wave duration (ES = 0.8, 95% CI: 0.5–1.2) (Fig. 4). Patients with history of AF had a slightly greater P-wave duration as compared to patients without history of AF (140.7 ms; 95% CI: 133.6–147.8 ms, vs 138.8 ms; 95% CI: 133.1–144.6 ms, $P = 0.69$, respectively) (Fig. 3C). Also, there was a gradual increase in P-wave duration from no-POAF patients without history of AF, to POAF-patient with history of AF (133.0 ms; 95% CI: 124.7–141.3 ms, vs 144.9 ms; 95% CI: 138.1–151.7 ms, $P = 0.03$, respectively) (Fig. 3C). Meta-regression showed that higher

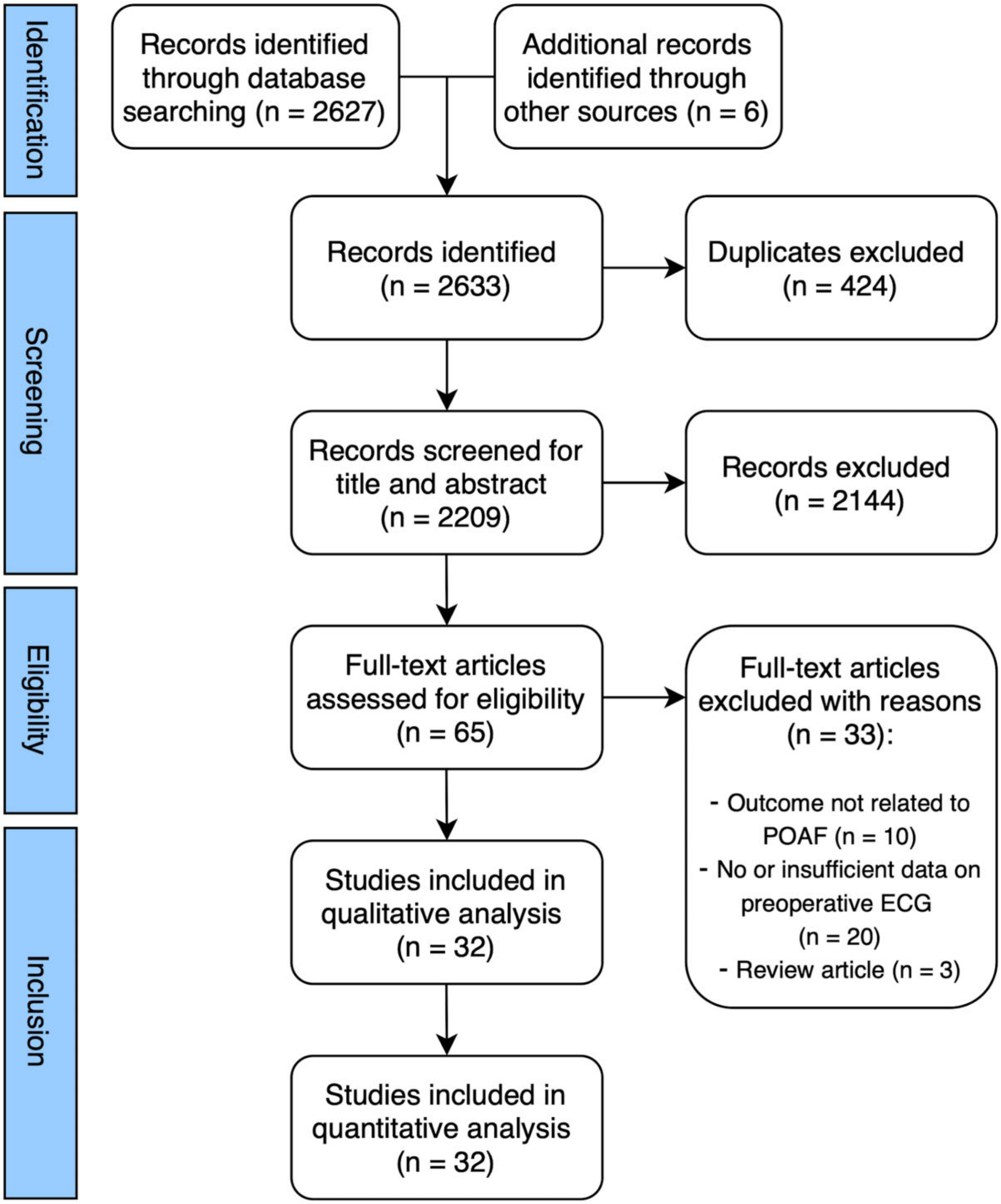


Figure 1: Study selection diagram.

percentage of male subjects was associated with a lower ES (Beta = -0.06, $P < 0.01$), whereas increased prevalence of chronic obstructive pulmonary disease was associated with increased ES (Beta = 0.07, $P = 0.01$) (Table 2). Heterogeneity analysis identified study by Caravelli *et al.* as the main source of heterogeneity (Supplementary Material, Fig. S9). Sensitivity analysis after omitting this publication showed a moderate ES of 0.6 (95% CI: 0.4–0.8), with still moderate model heterogeneity (I^2 = 56%, Cochran's Q: $P = 0.01$) (Supplementary Material, Fig. S10).

Ten studies were included in an ROC meta-analysis (Table 3). Pooled results of the SROC are presented in Fig. 5. Overall sensitivity was 72% (95% CI: 65–78) and specificity was 68% (95% CI: 58–77) for a range of cut-off values (122.3–155 ms). AUC (0.76) revealed a good discriminative power for the SROC. Meta-regression showed that studies published before year 2000 had lower specificity (Beta = -0.76, $P = 0.03$) (Table 3).

Publication bias

Meta-analyses for P-wave dispersion and P-wave duration (12-lead ECG) showed significant publication bias (Egger's test:

Table 1: Summary of studies included in the meta-analyses

Study	Number of participants	Timing of preoperative ECG	Type of ECG	Type of surgery	POAF %	Definition of POAF	Reported parameters
Prospective studies							
Amar *et al.*	1851	NA	12-lead	CABG	33	>5 min	P-wave duration PR-interval
Aytemir *et al.*	59	1 day prior	12-lead/SAECG	CABG	35.8	>30 min	P-wave duration
Budeus *et al.*	101	Day of surgery	SAECG	CABG	37	>10 min	P-wave duration
Camci *et al.*	102	1 day prior	12-lead	CABG	29.4	Any episode.	P-wave duration P-wave dispersion
Caravelli *et al.*	129	1 day prior	12-lead/SAECG	CABG	43	>30 s	P-wave duration
Dagdelen *et al.*	148	1 day prior	12-lead	CABG	38	Any episode.	P-wave duration P-wave dispersion PR-interval
Dimmer *et al.*	91	NA	12-lead/SAECG	CABG	17.5	Any episode.	P-wave duration
Dogan *et al.*	57	NA	-12-lead	CABG	17	Any episode.	P-wave duration P-wave dispersion
Frost *et al.*	189	NA	12-lead/SAECG	CABG	22	Any episode.	P-wave duration
Fujiwara *et al.*	88	NA	12-lead	OPCAB	39.8	Any episode.	P-wave duration
Gang *et al.*	205	1 day prior	12-lead/SAECG	CABG	26	>10 min	P-wave duration P-wave dispersion PR-interval
Hayashida *et al.*	95	1-3 days prior	SAECG	CABG/AVR	29	>1 h	P-wave duration
Kališnik *et al.* (2019)	150	1 day prior	12-lead	CABG/AVR	21	Any episode.	PR-interval
Kališnik *et al.* (2015)	79	1 day prior	12-lead	CABG/AVR	36.7	>1 min	P-wave duration PR-interval
Klein *et al.*	45	1 week prior	12-lead/SAECG	CABG	35.6	>1 h	P-wave duration
Magne *et al.*	169	1 day prior	12-lead	CABG	38	>10 min	PR-interval
Rader *et al.*	13356	NA	12-lead	CABG/AVR/MV surgery	35	Any episode.	PR interval
Roshanali *et al.*	355	NA	12-lead	CABG	19.2	>5 min	P-wave duration
Sigurdsson *et al.*	1227	30 days prior	12-lead	CABG/valve surgery	31	Any episode leading to change in treatment.	PR-interval
Stafford *et al.*	189	1 day prior	12-lead/SAECG	CABG	27	>1 h	P-wave duration
Steinberg *et al.*	130	1 day prior	12-lead/SAECG	CABG/valve surgery	25	>30 min	P-wave duration
Wu *et al.*	299	2 days prior	12-lead	CABG	33.1	>5 min	P-wave duration
Zaman *et al.* (1997)	102	NA	SAECG	CABG	26.5	Any episode.	P-wave duration
Zaman *et al.* (2000)	326	NA	SAECG	CABG	28	Any episode.	P-wave duration
Retrospective studies							
Achmad *et al.*	42	NA	12-lead	CABG	29	Any episode identified by ECG	P-wave dispersion
Chandy *et al.*	300	1 week prior	12-lead	CABG	27	>30 min	P-wave duration P-wave dispersion PR-interval
Chang *et al.*	120	NA	12-lead	CABG	31	>30 min	P-wave duration P-wave dispersion
Passman *et al.*	152	NA	12-lead	CABG	42.1	Any episode.	P-wave duration PR-interval
Sahin *et al.*	36	1 day prior	12-lead	LA myxoma exclusion	27.8	Any episode.	P-wave duration P-wave dispersion
Takahashi *et al.* (2014)	63	NA	12-lead	AVR	65	>5 min	P-wave duration
Takahashi *et al.* (2016)	73	NA	12-lead	MV surgery	60	>5 min	P-wave duration
Zengin *et al.*	327	Within 30 days prior	12-lead	CABG	20	Any episode.	P-wave duration P-wave dispersion PR-interval

AF: atrial fibrillation; AVR: aortic valve replacement; CABG: coronary artery bypass grafting; ECG: electrocardiography; LA: left atrium; MV: mitral valve; NA: not available; OPCAB: off-pump coronary artery bypass grafting; POAF: postoperative atrial fibrillation; SAECG: signal-averaged electrocardiography.

$P = 0.01$ and $P = 0.04$, respectively) (Supplementary Material, Figs S11–S14). Trim-and-fill analysis was performed for P-wave duration using 3 different model estimators (L_0, R_0 and Q_0) to correct for the presence of publication bias and it showed potentially 2 studies missing on the left side of the funnel plot (Supplementary Material, Fig. S15). Adjustment for these studies showed a lower ES of 0.3 (95% CI: 0.2–0.5) for P-wave duration (12-lead ECG). Trim-and-fill analysis for P-wave dispersion could not be performed due to significant outliers leading to funnel plot asymmetry.

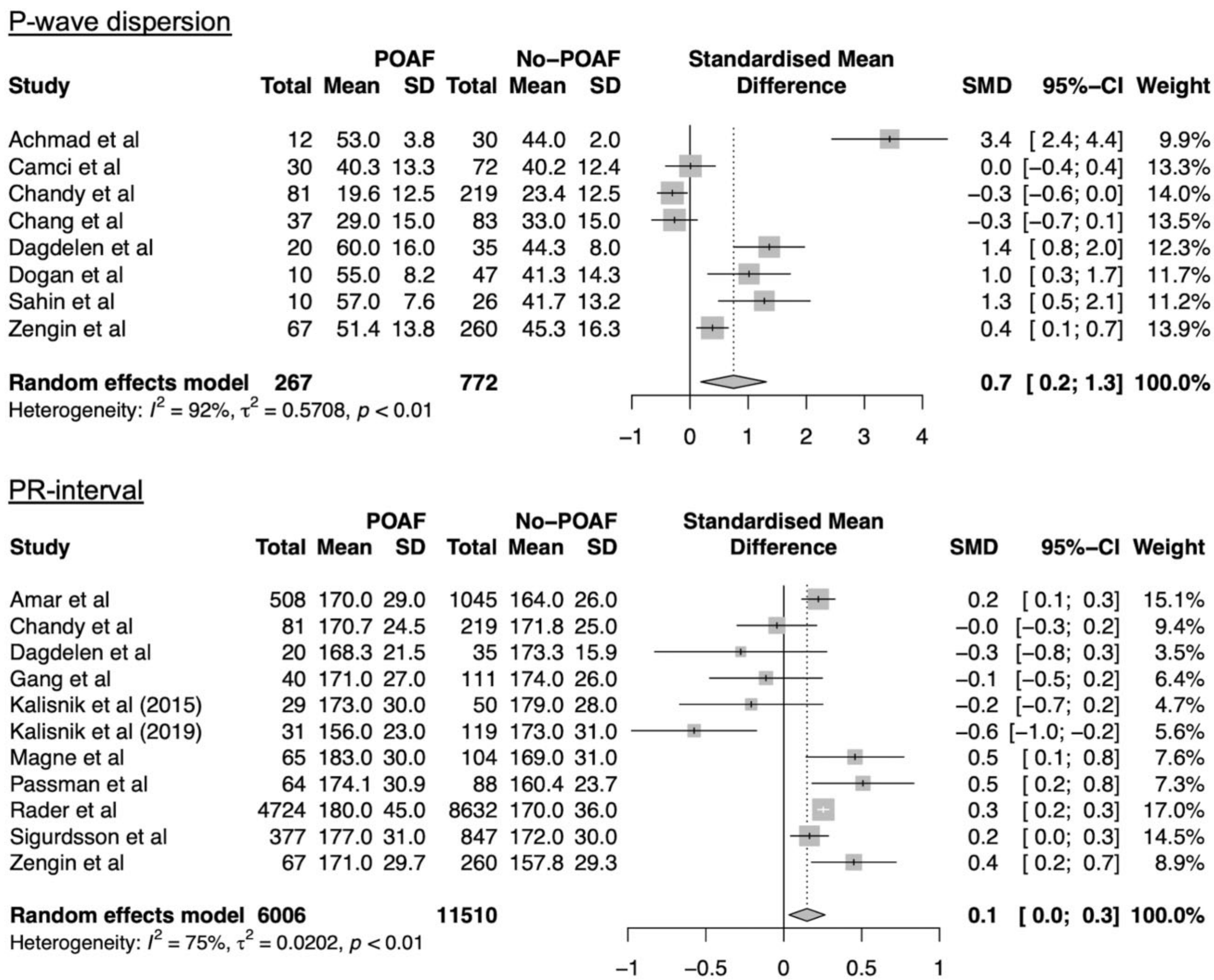


Figure 2: Forest plots for meta-analyses for P-wave dispersion and PR-interval. Studies included in meta-analysis, mean preoperative values for patients with and without POAF, corresponding standard deviations, numbers of subjects, standardized mean differences (SMD), corresponding standard deviations and the weight of the studies are presented. Overall effect size is presented in a diamond shape. CI: confidence interval; POAF: postoperative atrial fibrillation; SD: standard deviation.

DISCUSSION

In this meta-analysis, we analysed the predictive value of preoperative P-wave parameters for POAF prediction in patients undergoing cardiac surgery. We found that prolonged preoperative P-wave duration, as defined on conventional 12-lead ECG or SAECG, is an important predictor of POAF in the inherently heterogeneous population undergoing cardiac surgery. ROC meta-analysis was only performed for SAECG P-wave duration since other studies did not provide sufficient data for this analysis. This analysis showed that SAECG P-wave duration has an adequate predictive value for POAF (AUC = 0.76), although with a variety of cut-off values across studies (122.3 ms to 155 ms). Differences in cut-off values were mainly caused by different P-wave filtering techniques and distinct study populations, which impeded the selection of a single cut-off value. Nevertheless, our findings are in line with several studies which identified increased P-wave duration as a predictor of AF in the general population further emphasizing its importance as an indicator of AF substrate [3, 4].

In this meta-analysis, we found a significant relationship between preoperative P-wave dispersion and incidence of POAF. However, there was substantial heterogeneity in the model resulting from contradicting evidence in the original articles. Previous studies suggested that P-wave dispersion might be a useful predictor of paroxysmal AF and AF recurrence after catheter ablations, however, its role in predicting POAF is still questionable [47]. Notably, Chandy *et al.* [20] found a greater increase in postoperative P-wave dispersion in POAF patients as compared to patients without POAF suggesting that intra- and interatrial conduction delays and inhomogeneous wave propagation may intensify due to surgery itself, possibly as a result of atrial ischaemia.

The relationship between atrioventricular conduction, defined as PR-interval, and risk of POAF is still not fully understood, and our meta-analysis showed contradicting results with substantial model heterogeneity even after sensitivity analyses. Since PR-interval is a combination of atrial conduction time and atrioventricular-conduction time, it is influenced by multiple factors which are not directly associated with AF, such as atrioventricular-node dysfunction. Interestingly, subgroup analysis and meta-regression revealed that hypertension was associated with a lower ES of PR-interval, while PR-interval was

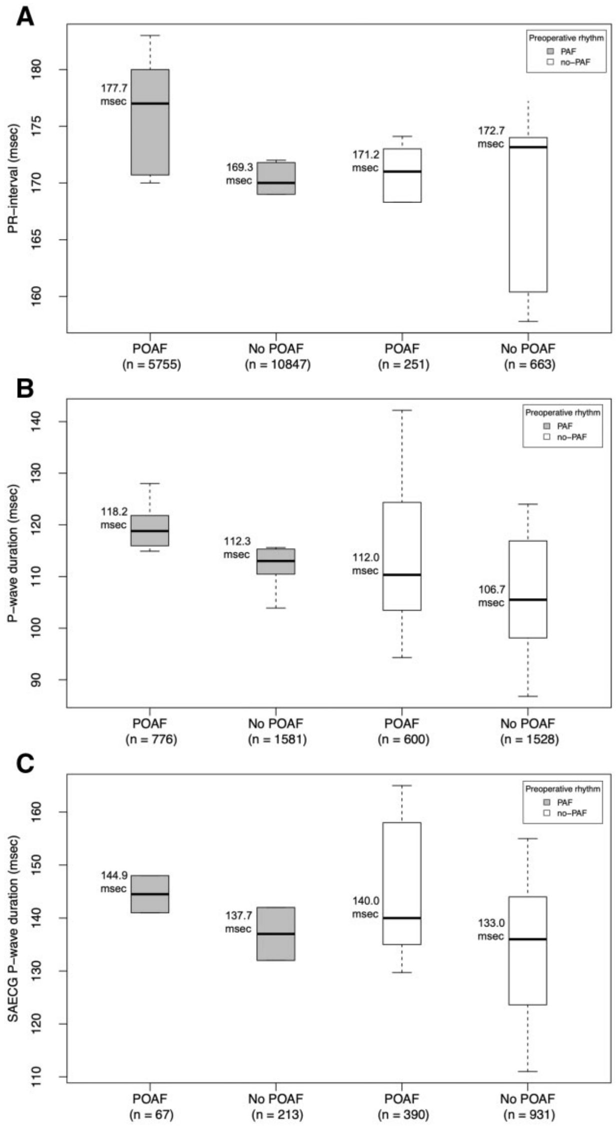


Figure 3: Box plots showing the differences between patients with and without POAF for PR-interval (**A**), P-wave duration (**B**), and signal-averaged electrocardiography P-wave duration (**C**). Patients with history of paroxysmal atrial fibrillation were separated from patients without history of paroxysmal atrial fibrillation. The exact values are provided in milliseconds (msec). POAF: postoperative atrial fibrillation.

significantly longer in patients with pre-existing AF developing POAF compared to no-AF patients without POAF. This suggests that PR-interval reflects the underlying substrate for AF development.

On the other hand, P-wave duration was a strong predictor of POAF, independently from the left atrial diameter (Table 2). In fact, P-wave duration seems to provide information on the different phases of electrical remodelling increasing from lowest duration of 106.7 ms in patients without a history of AF and no-POAF to highest duration up to 118.2 ms in patients with a history of AF and POAF development (Fig. 4B and C). From the electrophysiological point of view, prolonged P-wave duration is most likely caused by disturbances in atrial electrical conduction and in lesser degree by atrial dilatation [48]. Previous post-mortem studies have reported that fatty infiltration and fibrosis in major atrial conduction routes, such as Bachmann's bundle and the crista terminalis, are associated with prolonged P-wave duration [49]. These processes might lead to local areas with conduction blocks which are able to facilitate re-entry wavelets and eventually induction of AF [20]. Accordingly, previous electroanatomical mapping studies reported the relationship between lower atrial conduction velocities, especially in the Bachmann's bundle, and AF incidence [50]. Furthermore, epicardial mapping of patients without a history of AF undergoing cardiac surgery showed more complex propagation patterns in patients developing POAF as compared to patients without POAF [2]. Also, previous studies have demonstrated the predictive value of total atrial activation time, which is a parameter quantifying intra- and interatrial conduction disturbances, in predicting POAF in a variety of cardiac surgical patients [14].

Clinical implications

Currently, there is accumulating evidence suggesting that POAF is not only limited to the early postoperative phase but that it is associated with long-term AF recurrences [2]. Also, POAF is associated with the incidence of early- and late postoperative stroke, long-term mortality and prolonged hospitalization [51]. Therefore, preoperative prediction of new-onset POAF after cardiac surgery might be of tremendous interest to prevent these complications. Moreover, considering POAF as a surrogate marker for an AF substrate, the identification of patients at risk for POAF during the hospitalization period might provide indications for long-term rhythm follow-up in this select group of patients. This approach might help to identify patients which show progression of the arrhythmia and therefore potentially facilitate timely therapeutic interventions to prevent further progression to sustained AF. Whereas current prediction scores for POAF mostly focus on clinical parameters, we believe that additional parameters, which focus on quantification of an AF-substrate, might contribute to POAF prediction. This meta-analysis shows that P-wave duration, measured on standard 12-lead ECG and SAECG, might be a helpful tool to identify patients at risk for POAF. Additionally, previous studies described the potential of clinical parameters and preoperative transthoracic echocardiography in predicting POAF [1, 14]. However, even though these non-invasive diagnostic modalities are standard of care in the preoperative setting, they are yet to be implemented as a standardized predictive tool for POAF. Future studies should be performed to develop POAF prediction tools consisting of a combination of clinical, echocardiographic and electrocardiographic parameters to improve POAF prediction accuracy.

Limitations

The quality of studies included in a meta-analysis is always a limiting factor for the overall results. As the quality of the studies included in our meta-analyses was high, we believe our results are robust. The first limitation of our study was the substantial heterogeneity of the meta-analyses even after extensive sensitivity analysis and several subgroup analyses. The second limitation was significant publication bias in the meta-analyses for P-wave dispersion and P-wave duration. Trim-and-fill analysis suggested that the results for P-wave duration might be slightly overestimated. The third limitation was the variation in cut-off values of the studies included in the ROC meta-analysis for SAECG P-wave

Table 2: Subgroup analysis and meta-regression

		PR-interval			P-wave duration			SAECG P-wave duration		
Subgroups		Number of studies	SMD 95% CI	*P*-value	Number of studies	SMD 95% CI	*P*-value	Number of studies	SMD 95% CI	*P*-value
Study size (*n*)	<100	2	-0.24 (-0.59 to 0.12)	**0.03**	10	0.48 (0.18 to 0.78)	0.50	4	0.98 (0.64 to 1.31)	0.47
	>100	9	0.19 (0.07 to 0.30)		12	0.36 (0.20 to 0.53)		8	0.76 (0.29 to 1.23)	
Type of study	Prospective	8	0.11 (-0.02 to 0.24)	0.33	15	0.41 (0.21 to 0.61)	0.65	12	NA	NA
	Retrospective	3	0.30 (-0.06 to 0.65)		7	0.35 (0.20 to 0.50)		0	NA	
Type of surgery	CABG	7	0.21 (0.03 to 0.39)	0.20	17	0.42 (0.26 to 0.58)	0.24	10	0.86 (0.43 to 1.29)	0.69
	AVR	0	NA		1	0.23 (-0.24 to 0.71)		0	NA	
	Diverse[a]	4	0.02 (-0.19 to 0.24)		3	0.18 (-0.22 to 0.57)		2	0.75 (0.45 to 1.05)	
	Mitral Valve	0	NA		1	0.24 (-0.24 to 0.71)		0	NA	
Definition of POAF[b]	Any	6	0.17 (-0.01 to 0.34)	0.40	9	0.47 (0.23 to 0.71)	0.14	4	0.44 (0.27 to 0.61)	0.07
	Short episode	1	-0.04 (- 0.30 to 0.21)		7	0.46 (0.16 to 0.76)		3	1.25 (-0.24 to 2.75)	
	Long episode	4	0.14 (-0.11 to 0.38)		6	0.22 (0.05 to 0.40)		5	0.84 (0.51 to 1.16)	
History of AF	No	6	-0.01 (-0.38 to 0.35)	0.24	15	0.43 (0.27 to 0.60)	0.44	10	0.89 (0.46 to 1.33)	0.16
	Yes	5	0.21 (0.13 to 0.30)		7	0.32 (0.09 to 0.55)		2	0.53 (0.24 to 0.80)	

Meta-regression	Number of studies	Beta 95% CI	*P*-value	Number of studies	Beta 95% CI	*P*-value	Number of studies	Beta 95% CI	*P*-value
Age, per 1 year	10	-0.05 (-0.11 to 0.001)	0.05	22	-0.003 (-0.04 to 0.03)	0.85	12	0.04 (-0.06 to 0.15)	0.44
DM2, per 1%	8	0.03 (0.006 to 0.05)	**0.01**	15	-0.004 (-0.02 to 0.008)	0.49	5	0.005 (-0.04 to 0.04)	0.82
%Male, per 1%	10	0.005 (-0.01 to 0.02)	0.57	20	-0.007 (-0.02 to 0.009)	0.41	12	-0.06 (-0.09 to 0.03)	**<0.01**
Hypertension, per 1%	8	-0.04 (-0.06 to 0.01)	**<0.01**	17	-0.003 (-0.01 to 0.006)	0.54	6	0.002 (-0.02 to 0.02)	0.84
LVEF, per 1%	4	-0.009 (-0.07 to 0.05)	0.77	17	0.01 (-0.02 to 0.04)	0.44	10	-0.03 (-0.09 to 0.03)	0.37
COPD, per 1%	5	-0.01 (-0.21 to 0.19)	0.94	10	0.01 (-0.01 to 0.02)	0.23	4	0.07 (0.01 to 0.13)	**0.01**
RCA occlusion, per 1%	0	NA	NA	6	0.01 (-0.005 to 0.02)	0.20	7	-0.01 (-0.02 to 0.01)	0.22
BMI, per 1 kg/m^2	3	0.82 (0.16 to 1.48)	**0.02**	10	-0.03 (-0.13 to 0.08)	0.62	0	NA	NA
LAD, per 1 mm	0	NA	NA	12	-0.08 (-0.89 to 1.05)	0.88	6	-0.68 (-4.37 to 3.01)	0.72

AF: atrial fibrillation; AVR: aortic valve replacement; BMI: body mass index; CABG: coronary artery bypass grafting; CI: confidence interval; COPD: chronic obstructive pulmonary disease; DM2 : diabetes mellitus type 2; LAD: left atrial diameter; LVEF: left ventricle ejection fraction; POAF: postoperative atrial fibrillation; RCA: right coronary artery; SAECG: signal-averaged electrocardiography; SMD: standardized mean difference. Bold values are marked as statistically significant with a P-value threshold of 0.05.

[a]Coronary artery bypass grafting, valvular surgery, combined surgery.

[b]Short episodes are defined as POAF duration less than 30 min, whereas long episodes only included POAF duration over 30 min.

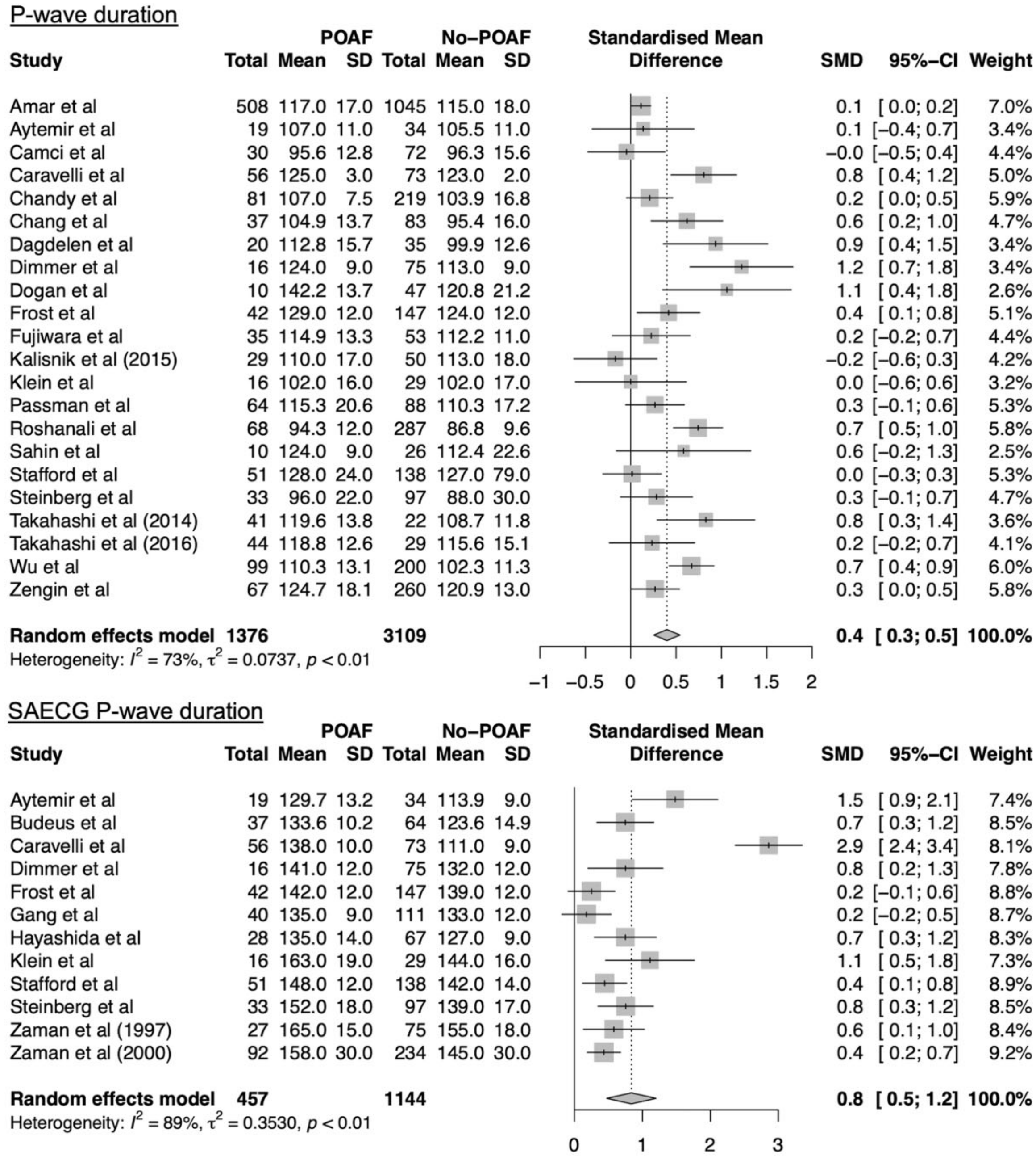


Figure 4: Forest plots for meta-analyses for P-wave duration (12 leads and signal-averaged electrocardiography). Studies included in meta-analysis, mean preoperative values for patients with and without POAF, corresponding standard deviations, numbers of subjects, standardized mean differences, corresponding standard deviations and the weight of the studies are presented. Overall effect size is presented in a diamond shape. CI: confidence interval; POAF: postoperative atrial fibrillation; SD: standard deviation.

duration what impeded the selection of a single optimal cut-off value. However, we could establish the study-differences that attributed to variance in diagnostic accuracy by performing a meta-regression. The fourth limitation was the broad range of publication dates of the articles included (1993–2020). Nevertheless, we believe that P-wave analysis has remained consistent over the years despite changes in risk factor modifications, clinical practice, surgical techniques and perioperative managements. The fifth and last limitation was the lack of consistency in POAF definition among studies included in the meta-analyses. To explore this bias, we have performed a subgroup-analysis which showed no significant differences for the different definitions of POAF. Despite all these limitations, our results provide a thorough insight into the ECG parameters associated with a higher risk of POAF.

CONCLUSION

In this meta-analysis including 20 201 patients, we found that increased preoperative P-wave duration, measured on conventional 12-lead ECG or SAECG, is a useful tool for POAF prediction

Table 3: SAECG P-wave duration diagnostic test accuracy meta-analysis and meta-regression

Overview of diagnostic accuracy data

Study	Cut-off value (ms)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Aytemir *et al.*	122.3	68	88	76	83	79.6
Budeus *et al.*	124	75	78	64	86	77.2
Caravelli *et al.*	135	84	73	70	85	77.0
Dimmer *et al.*	134	75	57	28	91	60.4
Hayashida *et al.*	135	50	81	52	79	71.9
Klein *et al.*	155	69	79	65	82	75.6
Stafford *et al.*	141	73	48	34	83	54.5
Steinberg *et al.*	140	77	55	37	87	60.9
Zaman *et al.* (1997)	155	86	45	37	89	55.9
Zaman *et al.* (2000)	155	63	74	49	84	70.9

ROC meta-analysis (Reitsma model)

	Cut-off value (ms)	Sensitivity (%)	95% CI	Specificity (%)	95% CI	AUC
Summary results	122.3–155	72	65–78	68	58–77	0.756

Subgroup analysis and meta-regression

Variable		Number of studies	Sensitivity			Specificity		
			Beta	95% CI	P-value	Beta	95% CI	*P*-value
Study size	>100[a]	6	0.55	-0.14 to 1.25	0.12	0.65	0.20 to 1.50	0.14
	<100	4						
History of AF	Yes[a]	2	0.02	-0.95 to 0.99	0.97	0.83	-0.10 to 1.75	0.08
	No	8						
Publication year	<2000[a]	6	-0.27	-0.99 to 0.46	0.47	-0.76	-1.44 to 0.07	**0.03**
	≥2000	4						
Age, per 1 year		10	-0.03	-0.15 to 0.08	0.60	-0.07	-0.20 to 0.07	0.32
%Male, per 1%		10	0.01	-0.04 to 0.05	0.80	0.05	-0.003 to 0.10	0.06
LVEF, per 1%		9	-0.02	-0.08 to 0.04	0.46	0.03	-0.03 to 0.09	0.17
RCA occlusion, per 1%		6	0.01	-0.02 to 0.04	0.41	0.01	-0.03 to 0.04	0.64
LAD, per 1 mm		6	1.31	-1.15 to 3.77	0.30	1.56	-0.45 to 3.57	0.13
Hypertension, per 1%		4	0.01	-0.03 to 0.05	0.67	-0.01	-0.07 to 0.07	0.99

AF: atrial fibrillation; AUC: area under the curve; CI: confidence interval; LAD: left atrial diameter; LVEF: left ventricle ejection fraction; ms: milliseconds; NPV: negative predictive value; POAF: postoperative atrial fibrillation; PPV: positive predictive value; RCA: right coronary artery. Bold values are marked as statistically significant with a P-value threshold of 0.05.

[a]Reference category.

after cardiac surgery. Implementation of P-wave duration in substrate-based risk scores for POAF will provide valuable information on the presence and severity of intra- and interatrial conduction disturbances, independently from left atrium size. Future studies should combine these easily accessible and standardized risk prediction models to identify patients at risk of developing POAF and find potential associations with long-term outcomes such as late POAF and stroke.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

Conflict of interest: none declared.

Data availability

Data are available upon reasonable request.

Author contributions

Michal J. Kawczynski: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Software; Validation; Visualization; Writing—original draft; Writing—review & editing. **Sophie Van De Walle:** Conceptualization; Data curation; Methodology. **Bart Maesen:** Data curation; Methodology; Supervision; Writing—review & editing. **Aaron Isaacs:** Conceptualization; Methodology; Writing—review & editing. **Stef Zeemering:** Conceptualization; Writing—review & editing. **Ben Hermans:** Conceptualization; Methodology; Writing—original draft; Writing—review & editing. **Kevin Vernooy:** Conceptualization; Supervision; Validation; Writing—review & editing. **Jos Maessen:** Conceptualization; Methodology; Validation; Writing—review & editing. **Ulrich Schotten:** Conceptualization; Methodology; Supervision; Writing—review & editing. **Elham Bidar:** Conceptualization; Data curation; Investigation; Methodology; Supervision; Validation; Writing—original draft; Writing—review & editing.

Reviewer information

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ADULT CARDIAC

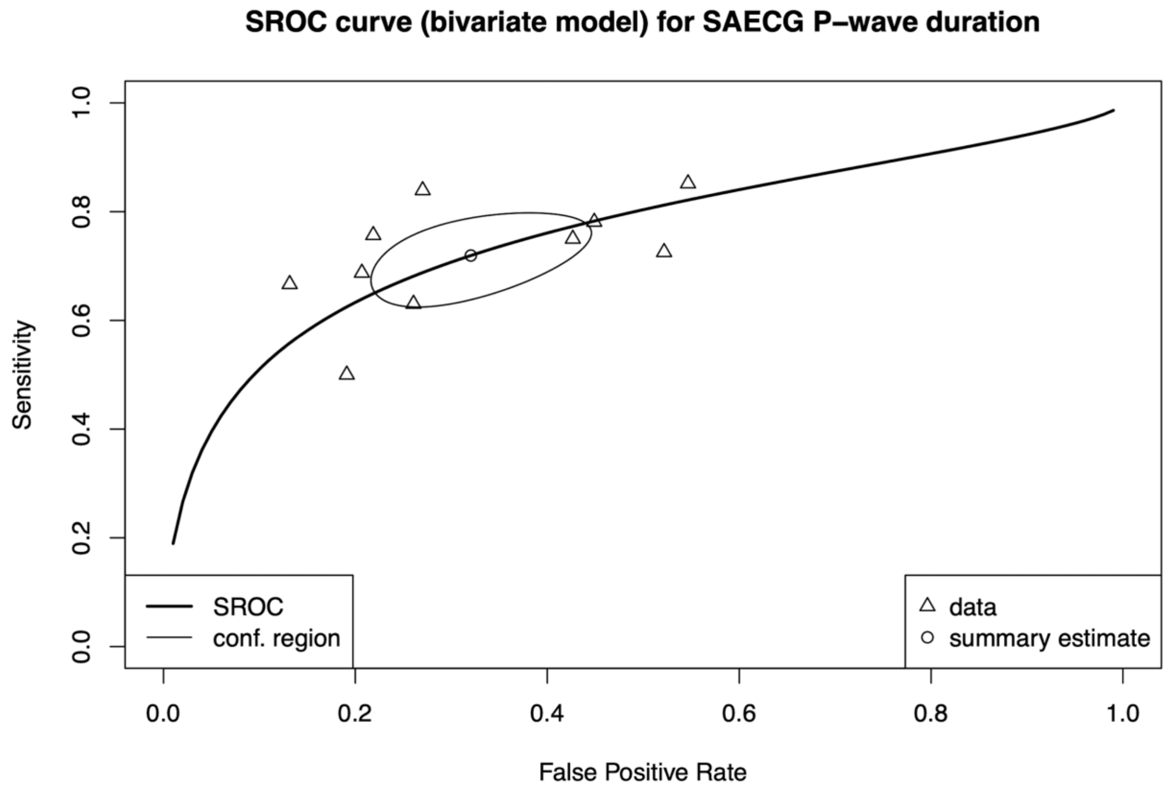

Figure 5: Summary receiver operator curve (SROC) for ROC meta-analysis of SAECG P-wave duration. Triangles represent the individual studies, whereas the round shape shows the summary estimate. Ellipse surrounding the summary estimate depicts the confidence region of the summary estimate. SAECG: signal-averaged electrocardiography; SROC: summary receiver operator curve.

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