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Pulmonary vein isolation using multi-electrode radiofrequency vs conventional point-by-point radiofrequency ablation: A meta-analysis of randomized and non-randomized studies

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Aims: Pulmonary vein isolation is effective in reducing atrial fibrillation (AF) episodes. Previous studies suggest single-shot techniques are effective and safe for this purpose. Procedural and clinical outcomes were compared between multi-electrode and point-by-point radiofrequency ablations by performing a meta-analysis of all randomized and non-randomized studies.
Methods and results: Systematic reviews of MEDLINE and Cochrane Library databases were performed. Studies comparing procedural (procedure and fluoroscopy times) and clinical (AF recurrence) outcomes were included in the meta-analysis. A total of 13 clinical studies (5 randomized and 8 non-randomized) including 2152 patients met the inclusion criteria. In patients underwent multi-electrode ablation, there were significant reductions in both total procedure and fluoroscopy times, compared with point-by-point ablation (mean difference = −34.3 min [95% CI (−50.1 to −18.5)], $p < 0.001$ and mean difference = −7.1 min [95% CI (−12.0 to −2.2)], $p < 0.01$, respectively). These significances also continued in patients with paroxysmal AF. No such difference was observed in regard to AF recurrence between the 2 ablation strategies (RR = 0.90 [95% CI (0.80−1.01)], $p = 0.066$). This insignificance was also observed in patients with paroxysmal AF.
Conclusions: In a heterogeneous AF population, multi-electrode ablation is as effective as point-by-point ablation, with better procedural and fluoroscopy durations.

1. Introduction

Pulmonary vein isolation (PVI) is the cornerstone of atrial fibrillation (AF) management, especially in patients with paroxysmal AF. Various energy sources and specially designed catheters have been introduced for catheter ablation of AF [1]. Conventional point-by-point radiofrequency ablation using thermocouple catheters whether irrigated tip or not have been widely used for circumferential isolation of pulmonary veins [2,3]. However, this technique requires a long-lasting learning-curve and needs substantial time to achieve complete isolation of all pulmonary veins. To overcome these disadvantages single-shot catheters using multiple energy sources such as radiofrequency, cryo-energy, laser, and ultrasound have been developed [4–9]. Performing PVI using multi-electrode radiofrequency ablation is one of the above-mentioned single-shot techniques. Specially designed circumferential multi-electrode catheters giving radiofrequency energy (PVAC®, Medtronic, Minneapolis, MN, USA) (nMARQ®, Biosense Webster, Irwindale, CA, USA) have been proposed to fast circumferential ablation of pulmonary veins over the past few years [4,5,7,10,11]. The effect of this novel treatment modality on procedural and clinical outcomes in patients with AF has not been systematically examined across the studies, either randomized or non-randomized. Therefore, our aim was to evaluate the effect of multi-electrode radiofrequency ablation, in comparison with conventional point-by-point radiofrequency ablation on procedural and clinical outcomes using data from randomized and non-randomized studies.

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2. Methods

2.1. Literature search

A systematic search of MEDLINE and Cochrane Library Databases from inception to August 2016 was performed to determine all published randomized and non-randomized trials of multi-electrode radiofrequency vs. conventional point-by-point radiofrequency ablation that reported procedural characteristics (including procedure and fluoroscopy times) and clinical outcomes (including AF recurrences and adverse events). Database search terms of duty-cycled radiofrequency ablation, phased radiofrequency ablation, Pulmonary Vein Ablation Catheter (PVAC®), multi-electrode ablation, nMARQ®, and atrial fibrillation returned 129 published articles. Additional search of the ClinicalTrials.gov website returned 3 trials of PVAC® vs. conventional radiofrequency ablation; one study is currently recruiting participants, the second study has been terminated and the third one is ongoing, but not recruiting participants. An additional trial comparing nMARQ® and conventional ablation is also ongoing, but not recruiting participants. None of the trials has posted the study results. The complete results of the literature search were shown in Fig. 1.

2.2. Study selection

Trials which reported procedural outcomes (i.e. procedure and fluoroscopy times) and clinical outcomes (i.e. AF recurrences and procedure-related adverse events) of groups or subgroups with either radiofrequency ablation method were included in the meta-analysis. All of the 129 articles identified from the literature search were reviewed for such information. Trials were excluded from the analysis if they did not have a comparative control group with conventional radiofrequency ablation, had a control group with other ablation energy sources such as cryo-ablation, did not report procedural and clinical outcomes of interest, or reported outcomes <6 months.

2.3. Data extraction

Information on the inclusion criteria, study intervention and control, type of AF, follow-up duration, definitions of procedural and clinical outcomes, drop-out and cross-over rates, and baseline patient characteristics were extracted from each trial independently by 2 of the investigators. Subsequently, data on the mean ± SD and event numbers or rates, whichever is available, for the study groups according to ablation method were extracted. Data of the last follow-up were extracted from the main text, tables or survival curves, whichever is available, if trials had follow-up duration >6 months.

2.4. Statistical analysis

Data was analyzed using Comprehensive Meta-Analysis software (Biostat Inc. Englewood, NJ). The differences in the meta-analytic mean value and risk ratio in AF patients according to radiofrequency ablation strategy were assessed with heterogeneity analysis. Statistical heterogeneity was tested by Cochran's Q statistic and reported as I^2. Random effects model was used when there was an evidence of heterogeneity ($I^2 > 40\%$) and *vice versa*. Sensitivity analyses were performed using the one-study out method to evaluate whether any single study was primarily responsible for the main findings. Additional sensitivity analyses were performed for trials reported patients with paroxysmal AF in both treatment arms. Funnel plot was created according to ablation strategy to assess the possibility of publication bias. The Egger's regression test was also used for this purpose. Separate groups of paroxysmal and persistent AF for total procedural and fluoroscopy times were used for analyses due to separate reported data in the study of Tivig [12]. In subgroup analyses of paroxysmal AF for arrhythmia recurrence, data extracted from studies by Choo, De Greef and Rosso were also used [13–15]. In addition, in subgroup analyses of paroxysmal AF for total procedural and fluoroscopy times, data extracted from the study by Rosso were used [15].

The authors of the current meta-analysis are solely responsible from the design, literature search and data collection, analyses, and editing of the paper.

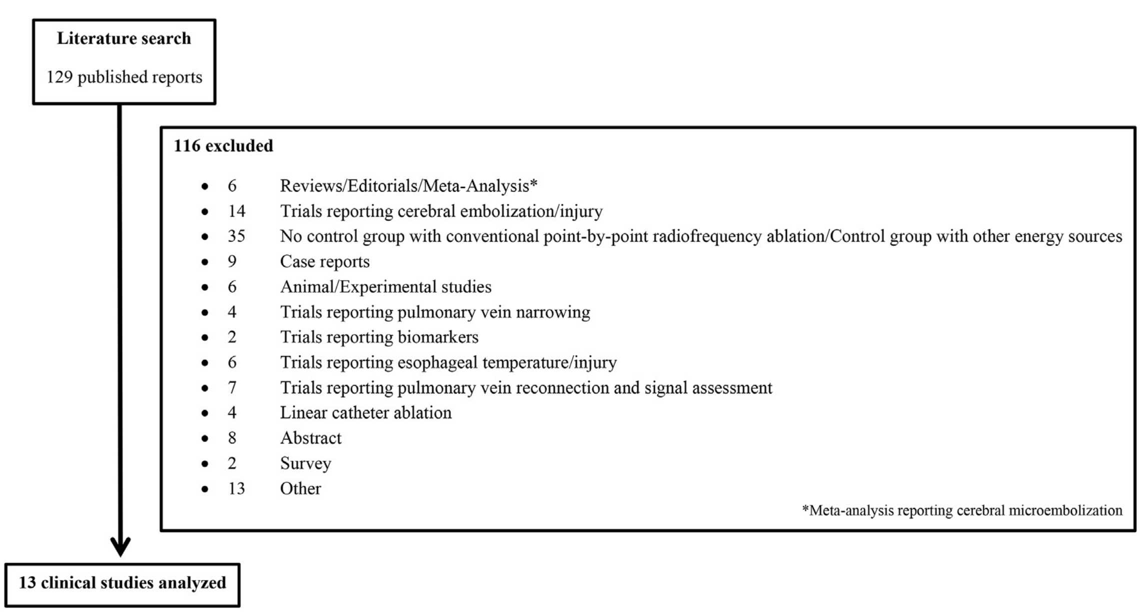

Fig. 1. Flowchart of multi-electrode radiofrequency ablation of AF studies.

3. Results

3.1. Search results

The literature search results were presented in Fig. 1. A total of 5 randomized and 8 non-randomized trials enrolling 2152 AF patients (1026 multi-electrode radiofrequency ablation and 1126 conventional radiofrequency ablation) were included in this meta-analysis [12–24]. The numbers of excluded articles and the brief reasons for exclusion were included in Fig. 1.

3.2. Trial characteristics

All study characteristics were presented in Table 1. In studies by Bulava, Beukema, Khaykin, Looi, McCready, Podd, and Wakili [16,18–21,23,24] only patients with paroxysmal AF were included although both paroxysmal AF and persistent AF were inclusion criteria in studies by Bittner, Choo, Tivig, De Greef, Gal, and Rosso [12–15,17,22]. Five studies had randomization with a 1:1 fashion according to radiofrequency ablation strategy. According to the study arm of point-by-point ablation, performed 2 different electro-anatomic mapping and ablation technologies were CARTO in studies by Bulava, Choo, Beukema, Tivig, Khaykin, Looi, McCready, De Greef, Gal, Podd, Wakili, and Rosso [12–16,18–24] and Ensite NavX in trials by Bittner, Choo, Tivig, Looi, and McCready [12,13,17,19,21]. The PVAC® catheter applying duty-cycled bipolar/unipolar radiofrequency energy was used as an active comparator in 11 studies whereas the nMARQ® catheter was studied in studies by Wakili and Rosso [15,24]. Blanking period was 1 month in studies by Bulava and Bittner [16,17], 3 months in remaining studies [13–15,18–24]. Arrhythmia recurrence was investigated using 12-lead electrocardiogram in the study by Looi [20], 24-h Holter recording in the studies of Gal and Rosso [15,22], 7-day Holter recording in the studies by Bulava and Wakili [16,24], 24- to 96-h Holter recording in the study by Bittner [17], 24–48-h Holter monitoring in the studies by Choo and Khaykin [13,19], 24- to 168-h Holter monitoring and 1 week AF alarm monitoring in the study of Beukema [18], 7-day ECG external loop recorder in the study by Tivig [12], 72-h Holter recording in the study of McCready [21], 1- to 7-day Holter recording or event recording in the study by De Greef [14], and implantable cardiac monitor and dual chamber pacemaker in the study by Podd [23]. Additional linear ablations were performed in patients with persistent AF in the study performed by Choo [13] and in both patients with paroxysmal and persistent AF in the study of Tivig [12]. In the study of Tivig et al. Multi-Array catheters and conventional irrigated-tip catheters were used to ablate complex fractionated electrograms in patients with persistent AF in the PVAC® and conventional groups respectively [12]. Rosso et al. performed complex fractionated atrial electrograms and additional linear ablations in patients with persistent AF who were in AF at the time of the procedure [15].

Redo procedures were applied with the same ablation strategy as in the index procedure in the study by Tivig et al. [12], with the conventional PVI in the studies of Beukema, and De Greef [14,18]. No redo ablation was performed in the study by Podd [23]. No clear data was present in the other studies.

All trials were analyzed using the intention to treat principle except for the study of McCready [21] that study outcomes were presented as on treatment analysis because 5 patients who were lost to follow-up and failed to achieve the ablation strategy were excluded from the analysis.

The baseline characteristics of patients enrolled in the studies

Table 1
Characteristics of the studies included in the meta-analysis.

Study	Year	Study type	AF type		RF ablation strategy		Average follow-up duration, mean or median (days)[a]	Reported end-point	Reported major adverse events
			Paroxysmal AF	Persistent AF	Multi-electrode	Point-by-point			
Bulava et al. [16]	2010	Randomized	100%	–	n = 51	n = 51	202	Arrhythmia recurrence	–
Bittner et al. [17]	2011	Randomized	55%	45%	n = 40	n = 40	254	Arrhythmia recurrence	–
Choo et al. [13]	2011	Non-randomized	67%	33%	n = 38	n = 71		Arrhythmia recurrence	Tamponade, stroke
Beukema et al. [18]	2012	Non-randomized	100%	–	n = 89	n = 96	364	Arrhythmia recurrence	–
Tivig et al. [12]	2012	Non-randomized	71%	29%	n = 209	n = 211	204[b]	Arrhythmia recurrence	Tamponade, TIA
Khaykin et al. [19]	2012	Non-randomized	100%	–	n = 31	n = 19	[a]	Arrhythmia recurrence	–
Looi et al. [20]	2013	Non-randomized	100%	–	n = 75	n = 128	576	Arrhythmia recurrence	Tamponade, TIA
McCready et al. [21]	2014	Randomized	100%	–	n = 94	n = 94	[c]	Arrhythmia recurrence	PV stenosis, tamponade, stroke
De Greef et al. [14]	2014	Non-randomized	60%	40%	n = 79	n = 82	[d]	Arrhythmia recurrence	PV stenosis, tamponade
Gal et al. [22]	2014	Randomized	81.5%	18.5%	n = 230	n = 230	1315[e]	Arrhythmia recurrence	Infarction, perforation
Podd et al. [23]	2015	Randomized	100%	–	n = 25	n = 25	[c]	Arrhythmia recurrence	Tamponade
Wakili et al. [24]	2016	Non-randomized	100%	–	n = 29	n = 29	373	Arrhythmia recurrence	Phrenic nerve palsy
Rosso et al. [15]	2016	Non-randomized	66%	34%	n = 36	n = 50	19 months (nMARQ®) 18.4 months (Point-by-point)	Arrhythmia recurrence	–

AF, atrial fibrillation; PV, pulmonary vein; RF, radiofrequency; TIA, transient ischemic attack.
[a] Only 6-month results were reported.
[b] Converted from month (6.7 months).
[c] Only 12-month results were reported.
[d] 3-year results were reported.
[e] Converted from month (43.2 months).

were presented in Table 2. Within each arm of the included studies, there were no statistically significant differences concerning age (except for the studies by Looi et al. [20] 60 years for the PVAC® group and 56 years for the conventional group, and by McCready et al. [21] 58 years for the PVAC® group and 62 years for the conventional group, all $p < 0.05$), gender (except for the study by Looi et al. [20] 55% male for the PVAC® group and 74% male for the conventional group, $p < 0.05$), duration of AF or episode numbers, baseline ejection fraction, or left atrial diameter (except for the study by Khaykin et al. [19] $p = 0.03$, see Table 2), where available.

3.3. Quantitative data and sensitivity analyses

The impact of ablation strategy on total procedure time and fluoroscopy time in patients with AF regardless of AF type was shown in Figs. 2 and 3. There was a statistically significant reduction in total procedure time in most of the studies except for the studies by Tivig, Khaykin and Rosso that no significant difference on total procedure times was observed between the 2 ablation strategies [12,15,19]. On the other hand, nMARQ® significantly increased the procedure time in the study of Wakili [24]. There was also a statistically significant reduction in total fluoroscopy time in most of the studies except for the studies by Beukema, Tivig (persistent AF subgroup), Looi, De Greef, Gal, and Rosso that no significant difference on total fluoroscopy times was observed between the 2 ablation strategies [12,14,15,18,20,22]. Similar to procedure time, nMARQ® significantly increased the fluoroscopy time in the study of Wakili [24]. On meta-analysis, patients assigned to multi-electrode radiofrequency ablation had a statistically significant 34 min reduction in total procedure time and 7 min reduction in fluoroscopy time compared to point-by-point radiofrequency ablation ($I^2 = 95.5\%$, mean difference = −34.3 [95% CI (−50.1 to −18.5)], $p < 0.001$ and $I^2 = 94.9\%$, mean difference = −7.1 [95% CI (−12.0 to −2.2)], $p < 0.01$, respectively).

Subgroup analysis of patients with paroxysmal AF, including studies by Bulava, Beukema, Tivig, Khaykin, Looi, McCready, Podd, Wakili, and Rosso [12,15,16,18–21,23,24] showed that there was also a statistically significant reduction in total procedure and fluoroscopy times in the majority of the studies except for the studies by Tivig, Khaykin (for total procedure time), Beukema, Looi and Rosso (for total fluoroscopy time) that no significant difference on total times was observed between the multi-electrode radiofrequency ablation and conventional point-by-point radiofrequency ablation [12,15,18–20]. In the study of Wakili, both total procedure and fluoroscopy times were higher with nMARQ® [24]. On meta-analysis, patients assigned to multi-electrode radiofrequency ablation had a statistically significant 30 min reduction in total procedure time and nearly 8 min reduction in fluoroscopy time compared to point-by-point radiofrequency ablation ($I^2 = 95.9\%$, mean difference = −30.2 [95% CI (−50.1 to −10.3)], $p < 0.01$ and $I^2 = 93.6\%$, mean difference = −7.6 [95% CI (−13.4 to −1.7)], $p = 0.01$, respectively) (Online supplementary material 1).

In sensitivity analyses both in total AF population and in patients with paroxysmal AF using the one study out method, there remained a statistically significant difference in the impact of multi-electrode radiofrequency ablation on total procedure and fluoroscopy times, demonstrating that the observed differences were not predominated by one single study (Online supplementary material 2).

Fig. 4 demonstrated that in AF patients regardless of arrhythmia type meta-analysis showed a statistically insignificant 10% reduction in the risk for arrhythmia recurrence by multi-electrode radiofrequency ablation ($I^2 = 0\%$, RR = 0.90 [95% CI (0.80–1.01)], $p = 0.066$). When examined separately, sensitivity analyses were performed by sequentially excluding each single study. In each sensitivity analysis carried out using the one study out method,

Table 2
Characteristics of patients included in the meta-analysis.

Study	Age (years)	Male	Duration of AF or episode numbers	Baseline EF	LA diameter (mm)	≥1 AAD use
Bulava et al. [16]	57.6	64.7%	2.7[a]	68.6%	40.3	97.1%
Bittner et al. [17]	58	63.8%	92 months	N/A	43 (PVAC®) 42 (Point-by-point)	100%
Choo et al. [13]	57.8	71.6%	N/A	57.1	41.6	100%
Beukema et al. [18]	55.9	76.8%	N/A	56%	40.6	N/A
Tivig et al. [12]	61[b]	75.7%	4.9 years (PAF + PVAC®) 5.4 years (PAF + Point-by-point) 3.0 years (Pers AF + PVAC®) 4.0 years (Pers AF + Point-by-point)	62% (PAF + PVAC®) 61% (PAF + Point-by-point) 53% (Pers AF + PVAC®) 51% (Pers AF + Point-by-point)	40 (PAF + PVAC®) 40 (PAF + Point-by-point) 46 (Pers AF + PVAC®) 47 (Pers AF + Point-by-point)	93.3%
Khaykin et al. [19]	63 (PVAC®) 57 (Point-by-point)	58%	5 years (PVAC®) 7 years (Point-by-point)	N/A	39 (PVAC®) 43 (Point-by-point)	[c]
Looi et al. [20]	57.7	77%	50.6 months (PVAC®) 50.3 months (Point-by-point)	N/A	48 (PVAC®) 44 (Point-by-point)	N/A
McCready et al. [21]	62	61.7%	[d]	64% (PVAC®) 62% (Point-by-point)	38 (PVAC®) 39 (Point-by-point)	100%
De Greef et al. [14]	60 (PVAC®) 58 (Point-by-point)	79.5%	48 months (PVAC®) 45 months (Point-by-point)	N/A	41 (PVAC®) 42 (Point-by-point)	100%
Gal et al. [22]	56.3	75.4%	7.9 years (PVAC®) 8.6 years (Point-by-point)	N/A	41.7 (PVAC®) 40.6 (Point-by-point)	100%
Podd et al. [23]	68.4 (PVAC®) 66.5 (Point-by-point)	44%	89 months (PVAC®) 84 months (Point-by-point)	60% (PVAC®) 62% (Point-by-point)	37 (PVAC®) 40 (Point-by-point)	64%
Wakili et al. [24]	67.1 (nMARQ®) 64.3 (Point-by-point)	55.2%	3.2 years (nMARQ®) 2.9 years (Point-by-point)	61.5% (nMARQ®) 63.4% (Point-by-point)	40.5 (nMARQ®) 39.2 (Point-by-point)	45%
Rosso et al. [15]	58 (nMARQ®) 62 (Point-by-point)	68.6%	N/A	N/A	43.4 (nMARQ®) 44.4 (Point-by-point)	100%

AAD, anti-arrhythmic drug; AF, atrial fibrillation; EF, ejection fraction; LA, left atrium; N/A, not available; PAF, paroxysmal atrial fibrillation; Pers AF, persistent atrial fibrillation; PVAC, pulmonary vein ablation catheter.

[a] Number of AF episodes during last month.

[b] The mean age was 59 years in the group with PAF and point-by-point ablation.

[c] Numbers of failed AAD were reported.

[d] Described as AF frequency (daily, weekly, and monthly).

Study name	Statistics for each study						
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Bulava et al.	-101,0	7,8	60,3	-116,2	-85,8	-13,0	0,000
Bittner et al.	-53,0	7,6	58,2	-68,0	-38,0	-6,9	0,000
Choo et al.	-84,0	10,9	118,6	-105,3	-62,7	-7,7	0,000
Beukema et al.	-37,0	6,9	48,0	-50,6	-23,4	-5,3	0,000
Tivig et al. PAF	-6,0	4,7	22,2	-15,2	3,2	-1,3	0,203
Tivig et al. PeAF	10,0	7,5	56,5	-4,7	24,7	1,3	0,183
Khaykin et al.	-10,0	7,4	54,7	-24,5	4,5	-1,4	0,176
Looi et al.	-43,0	6,9	47,4	-56,5	-29,5	-6,2	0,000
McCready et al.	-27,0	6,2	38,9	-39,2	-14,8	-4,3	0,000
De Greef et al.	-48,0	6,6	43,9	-61,0	-35,0	-7,2	0,000
Gal et al.	-43,8	4,1	16,9	-51,8	-35,8	-10,7	0,000
Podd et al.	-60,0	6,8	45,8	-73,3	-46,7	-8,9	0,000
Wakili et al.	23,0	8,8	78,2	5,7	40,3	2,6	0,009
Rosso et al.	-4,0	4,6	21,6	-13,1	5,1	-0,9	0,389
	-34,3	8,1	65,0	-50,1	-18,5	-4,3	0,000

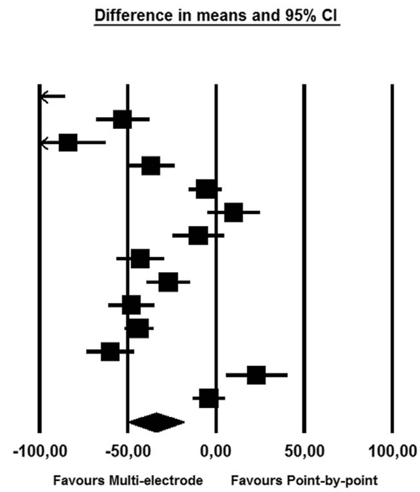

Fig. 2. Effect of multi-electrode radiofrequency ablation on total procedure time (Random effects model).
PAF, paroxysmal AF; PeAF, persistent AF.

Study name	Statistics for each study						
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Bulava et al.	-12,0	1,3	1,7	-14,6	-9,4	-9,1	0,000
Bittner et al.	-9,0	1,9	3,6	-12,7	-5,3	-4,7	0,000
Choo et al.	-36,0	4,5	20,6	-44,9	-27,1	-7,9	0,000
Beukema et al.	-1,0	1,8	3,1	-4,5	2,5	-0,6	0,571
Tivig et al. PAF	-10,0	2,0	3,9	-13,9	-6,1	-5,1	0,000
Tivig et al. PeAF	2,0	2,9	8,4	-3,7	7,7	0,7	0,490
Khaykin et al.	-14,0	4,3	18,5	-22,4	-5,6	-3,3	0,001
Looi et al.	-2,0	3,7	13,6	-9,2	5,2	-0,5	0,588
McCready et al.	-7,0	2,7	7,0	-12,2	-1,8	-2,6	0,008
De Greef et al.	1,0	2,1	4,3	-3,1	5,1	0,5	0,631
Gal et al.	2,2	1,1	1,3	-0,0	4,4	1,9	0,055
Podd et al.	-29,0	2,9	8,3	-34,7	-23,3	-10,1	0,000
Wakili et al.	8,0	2,9	8,4	2,3	13,7	2,8	0,006
Rosso et al.	1,9	1,7	2,8	-1,4	5,2	1,1	0,256
	-7,1	2,5	6,2	-12,0	-2,2	-2,9	0,004

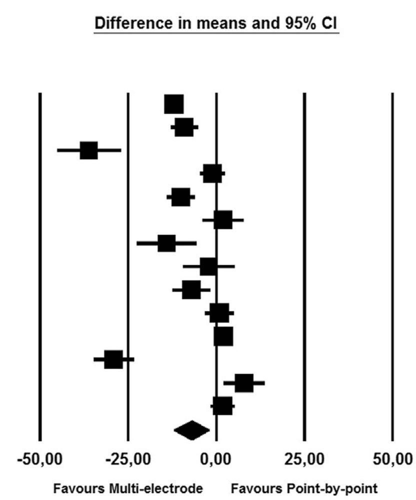

Fig. 3. Effect of multi-electrode radiofrequency ablation on total fluoroscopy time (Random effects model).
PAF, paroxysmal AF; PeAF, persistent AF.

statistical significance in the impact of multi-electrode radiofrequency ablation on arrhythmia recurrence was found when the study by Gal (p = 0.042) were removed [12,22] and statistical insignificance was continued when the remaining studies were removed from the analysis (Online supplementary material 2).

Subgroup analysis of patients with paroxysmal AF, including studies by Bulava, Choo, Beukema, Tivig, Khaykin, Looi, McCready, De Greef, Podd, Wakili, and Rosso showed that there was a statistically insignificant 14% risk reduction in arrhythmia recurrence by multi-electrode radiofrequency ablation ($I^2 = 0\%$, RR = 0.86 [95% CI (0.72–1.02)], p = 0.078) compared to point-by-point radiofrequency ablation [12–16,18–21,23,24]. In each sensitivity analysis carried out using the one study out method, there remained no statistically significant difference in the impact of multi-electrode radiofrequency ablation on arrhythmia recurrence, except for the study of Looi et al. [20] (p = 0.048) (Online supplementary material 1 and 2).

In the current meta-analysis, no evidence of publication bias was detected with the Egger's regression method for all analyses including procedure time, fluoroscopy time and arrhythmia recurrence (all $P > 0.1$). Funnel plots examining publication bias according to total procedure time, total fluoroscopy time and arrhythmia recurrence were presented in online supplementary material 3.

Lastly, no change in the results including procedure time, fluoroscopy time and arrhythmia recurrence was seen when the studies using nMARQ catheter were excluded from the analyses (Online supplementary material 4).

3.4. Complication rate

Complication rates including cerebrovascular accidents and tamponade were low and not significantly different between the 2 ablation strategies (Table 3).

Study name	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value
Bulava et al.	0,80	0,42	1,54	-0,67	0,503
Bittner et al.	0,85	0,43	1,66	-0,49	0,626
Choo et al.	0,52	0,31	0,86	-2,53	0,011
Beukema et al.	0,90	0,48	1,67	-0,34	0,737
Tivig et al.	0,97	0,62	1,53	-0,13	0,893
Khaykin et al.	0,41	0,13	1,26	-1,55	0,120
Looi et al.	1,01	0,68	1,49	0,04	0,966
McCready et al.	0,91	0,65	1,29	-0,51	0,609
De Greef et al.	0,79	0,54	1,15	-1,24	0,215
Gal et al.	0,96	0,81	1,14	-0,47	0,640
Podd et al.	0,92	0,50	1,67	-0,28	0,777
Wakili et al.	1,00	0,43	2,30	0,00	1,000
Rosso et al.	1,23	0,53	2,89	0,49	0,627
	0,90	0,80	1,01	-1,84	0,066

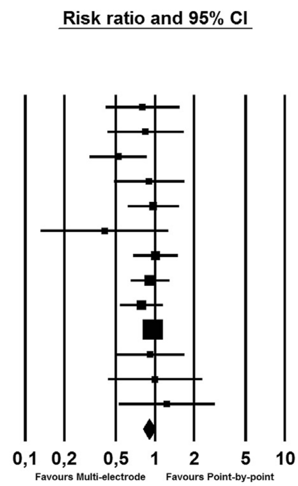

Fig. 4. Effect of multi-electrode radiofrequency ablation on AF recurrence (Fixed effects model).

4. Discussion

4.1. Main findings

The current meta-analysis showed that in patients with AF, the procedural outcomes which include procedural and fluoroscopy times improved with multi-electrode radiofrequency ablation in comparison with conventional point-by-point radiofrequency ablation with a mean reduction of 34 min and 7 min respectively. In addition, there was a trend for lower arrhythmia recurrence by a non-significant 10% relative risk reduction with multi-electrode radiofrequency ablation.

4.2. Need for single-shot technology

Fast technologic advancement has been occurred in arrhythmia and electrophysiology sections, especially in AF mechanism and ablation, as in all fields of life. From simple catheters giving radiofrequency energy to complex catheters with multiple processors measuring applied forces and giving various energy sources such as cryo-energy, laser and ultrasound [1–9]. Faster mapping and easier application of energy have been the focus of aim in AF ablation as well as minimum harm related to the procedure itself and radiation, to both the operator and the patient. For these purposes single-shot catheters have been developed to shorten the procedure and fluoroscopy times and to accelerate the learning curve without sacrificing success [4–7]. The PVAC® and nMARQ® seem as having these characteristics according to the current meta-analysis. Initial experiences with the PVAC® ablation have demonstrated that the mean procedural time ranged between 84 min and 176 min, the mean fluoroscopy time ranged between 18 min and 32 min [4,5,25]. In these studies freedom from AF rate has been reported between 61% and 83% without procedure-related complications [4,5,25]. Similarly, with the nMARQ® ablation the reported ranges for the mean procedural and fluoroscopy times were 69–160 min and 2–31 min, respectively [7,24,26,27]. With a single procedure, freedom from arrhythmia recurrence has been reported between 65% and 81% [11,28,29].

4.3. PVI with novel catheters

The most important issue to prevent AF recurrence is complete and durable PVI after catheter ablation [30]. Therefore, circumferential ablation for complete electrical isolation of pulmonary veins is the cornerstone and, PVI only seems enough if persistent AF is present [31,32]. It has been shown that PVI using cryoballoon is effective as point-by-point radiofrequency ablation with better procedural time and less operator dependence [33–35]. Encouraging novel balloon application using laser energy had also comparable outcome of freedom from arrhythmia recurrence [36,37]. Circumferential ablation using circumferential multi-electrode catheters can create contiguous, transmural lesions to achieve complete and durable PVI, which can result in less occurrence of arrhythmia recurrence [38]. Achieving durable PVI with any technology is strongly related to arrhythmia free survival. Durable PVI can be obtained by performing lesion transmurality using multi-electrode catheters. It has been shown that an ablation strategy with a temperature >50 °C and radiofrequency power >3 W for >30 s using PVAC Gold™ was associated with effective lesion creation, as a surrogate marker for lesion transmurality, resulted in less arrhythmia recurrence [39].

Table 3
Complications related to 2 ablation strategies.

Complication, n (%)	RF ablation strategy		P value
	Multi-electrode (n = 1026)	Point-by-point (n = 1126)	
CVA	6 (0.6)	2 (0.2)	0.121
Tamponade	2 (0.2)	5 (0.4)	0.311
Total	8 (0.8)	7 (0.6)	0.660

Note that procedure related complications were not reported in some studies.
Three tamponade cases were reported in all study population in the study by Tivig et al. [12].
CVA, cerebrovascular accident.

4.4. Controversies related to PVAC® and nMARQ®

The most important drawback related to this technology is micro-embolization whether asymptomatic or not. This adverse effect has been found to be higher compared with conventional ablation although some manipulations regarding energy giving (software) and catheter design such as removal of the most distal and proximal pairs (hardware) have been introduced to minimize the formation of micro-bubbles/thermal coagulum and so micro-embolization [40,41]. Silent cranial embolism reported with the nMARQ® ablation can be reduced with lower energy settings [42]. A potentially lethal complication, atrio-oesophageal fistula can develop with the nMARQ® catheter [26,28]. In addition, the scientific evidence for pulmonary vein narrowing related with the PVAC® ablation is controversial although it has been found to be higher with the PVAC® ablation [43]. In the current meta-analysis, there was no significant difference between the multi-electrode and conventional ablation groups in regard to major procedure-related complications including cerebrovascular events although no data for asymptomatic cerebral micro-embolization were presented.

In addition, all techniques have a learning curve, and almost always multi-electrode procedures are being performed by cardiac electrophysiologists with experience in point by point RF ablation.

4.5. Limitations

Our meta-analysis has certain limitations. Although a comprehensive literature search was performed some eligible studies not indexed in the databases used in the meta-analysis could be missed. Both randomized and non-randomized studies were included due to relatively small sample sizes of the randomized studies. The outcome data varied slightly amongst the included studies, but always included AF recurrence. The study patients included in this meta-analysis were heterogeneous in AF type. Half of the studies included patients with persistent AF whereas subgroup analyses for paroxysmal AF were performed. In some studies additional ablation attempts such as linear lines and complex fractionated electrograms were performed. After removal of studies including additional ablations from the meta-analysis [12,13], significant reductions in both procedural and fluoroscopy times and non-significance regarding AF recurrence were continued to be present in both total and paroxysmal AF patients (data not presented). Also, some inherent differences regarding catheter technology are present between the PVAC® and nMARQ® although both apply multi-electrode ablation. Therefore, given the above-mentioned limitations, the results of the meta-analysis should be interpreted with caution.

5. Conclusion

The PVI with a multi-electrode catheter ablation reduces both procedural and fluoroscopy times while maintaining similar clinical outcome for freedom from AF. These findings have important clinical implications for ablation of AF patients with this single-shot ablation technique.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ipej.2017.02.004.

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