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

Dursun Aras, MD a,1, Serkan Topaloglu, MD a,1, Serkan Cay, MD a,*, Ozcan Ozeke, MD a, Firat Ozcan, MD a, Goksel Cagirci, MD b

a Department of Cardiology, Division of Arrhythmia and Electrophysiology, Yuksek Ihtisas Heart-Education and Research Hospital, Ankara, Turkey
b Department of Cardiology, Division of Arrhythmia and Electrophysiology, Antalya Education and Research Hospital, Antalya, Turkey

ARTICLE INFO

Keywords:
Multi-electrode
Outcome
Point-by-point
Single-shot

ABSTRACT

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% Cl (−50.1 to −18.5)], p < 0.001 and mean difference = −7.1 min [95% Cl (−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% Cl (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.

Copyright © 2017, Indian Heart Rhythm Society. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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.
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.
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 PVC 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], 1–7-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 PVC® 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                | Study type      | AF type     | RF ablation strategy | Average follow-up duration, mean or median (days) | Reported end-point adverse events |
|----------------------|-----------------|-------------|----------------------|-----------------------------------------------|----------------------------------|
| Bulava et al. [16]   | 2010 Randomized | 100%        | Persistent AF         | 202                                          | Arrhythmia recurrence           |
| Bittner et al. [17]  | 2011 Randomized | 55%         | Multi-electrode      | 254                                          | Arrhythmia recurrence           |
| Choo et al. [13]     | 2011 Non-randomized | 67%       | Point-by-point        | 364                                          | Arrhythmia recurrence           |
| Beukema et al. [18]  | 2012 Non-randomized | 100%     | Persistent AF         | 204                                          | Tamponade, stroke               |
| Tivig et al. [12]    | 2012 Non-randomized | 71%       | Persistent AF         | 204                                          | Tamponade, TIA                  |
| Khaykin et al. [19]  | 2012 Non-randomized | 100%     | Persistent AF         | 576                                          | Tamponade, TIA                  |
| Looi et al. [20]     | 2013 Non-randomized | 100%     | Persistent AF         | 18 months (nMARQ®)                           | Arrhythmia recurrence           |
| McCready et al. [21] | 2014 Randomized | 100%        | 18.4 months (Point-by-point) | Arrhythmia recurrence           |
| De Greef et al. [14] | 2014 Non-randomized | 60%     | 18.4 months (Point-by-point) | Arrhythmia recurrence           |
| Gal et al. [22]      | 2014 Randomized | 81.5%       | 18.4 months (Point-by-point) | Arrhythmia recurrence           |
| Podd et al. [23]     | 2015 Randomized | 100%        | 18.4 months (Point-by-point) | Arrhythmia recurrence           |
| Wakili et al. [24]   | 2016 Non-randomized | 100%     | 18.4 months (Point-by-point) | Arrhythmia recurrence           |
| Rosso et al. [15]    | 2016 Non-randomized | 66%       | 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 [12,14,15,18,20,22]. 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 in 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 (I² = 95.5%, mean difference = –34.3 [95% CI (–50.1 to –18.5)], p < 0.001 and I² = 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 (I² = 95.9%, mean difference = –30.2 [95% CI (–50.1 to –10.3)], p < 0.01 and I² = 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 (I² = 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 Gender | Duration of AF or episode number | Baseline EF | LA diameter (mm) | ≥1 AAD use |
|----------------|-------------|-------------|----------------------------------|-------------|------------------|------------|
| Bulava et al. [16] | 57.6        | 64.7%       | 2.7a                             | 68.6%       | 40.3 (Point-by-point) | 97.1%      |
| Bittner et al. [17] | 58          | 63.8%       | 92 months                        | N/A         | 43 (PVAC)        | 100%       |
| Choo et al. [13] | 57.8        | 71.6%       | N/A                              | 57.1        | 41.6 (Point-by-point) | 100%       |
| Beukema et al. [18] | 55.9        | 76.8%       | N/A                              | 56%         | 40.6 (Point-by-point) | N/A        |
| Tivig et al. [12] | 61b         | 75.7%       | 4.9 years (PAF + PVAC)           | 62% (PAF + PVAC) | 40 (PAF + PVAC) | 93.3%      |
|                |             |             | 5.4 years (PAF + Point-by-point) | 61% (PAF + Point-by-point) | 40 (PAF + Point-by-point) |         |
|                |             |             | 3.0 years (Pers AF + PVAC)       | 53% (Pers AF + PVAC) | 46 (Pers AF + PVAC) |         |
|                |             |             | 4.0 years (Pers AF + Point-by-point) | 51% (Pers AF + Point-by-point) | 47 (Pers AF + Point-by-point) |         |
| Khaykin et al. [19] | 63 (PVAC)   | 58%         | 5 years (PVAC)                  | N/A         | 39 (PVAC)        |           |
| Looi et al. [20] | 57.7        | 77%         | 50.6 months (PVAC)              | N/A         | 43 (Point-by-point) |           |
| McCready et al. [21] | 62          | 61.7%       | 50.3 months (Point-by-point)     | N/A         | 48 (PVAC)        |           |
| De Greef et al. [14] | 60 (PVAC)   | 79.5%       | 48 months (PVAC)                | N/A         | 38 (PVAC)        |           |
| Gal et al. [22] | 56.3        | 75.4%       | 7.9 years (Point-by-point)       | N/A         | 41 (PVAC)        |           |
| Podd et al. [23] | 68.4 (PVAC) | 44%         | 89 months (PVAC)                | 60% (PVAC)  | 40.6 (Point-by-point) | 64%       |
| Wakili et al. [24] | 67.1 (nMARQ) | 66.5%       | 84 months (Point-by-point)       | 62% (Point-by-point) | 40 (Point-by-point) |       |
| Rosso et al. [15] | 58 (nMARQ)  | 64.3%       | 2.9 years (Point-by-point)       | 63.4% (Point-by-point) | 39.2 (Point-by-point) | 45%       |

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).
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 (I² = 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).
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 nMARS® 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 [4,5,29]. Similarly, with the nMARS® 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 Twieg 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 subgroups 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.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Acknowledgement

Study design: Cay, Cagirci.

Literature search and data collection: Cay, Ozcan, Ozkeze.

Statistical analyses and data interpretation: Cay, Cagirci, Aras.

Drafting: Cay, Cagirci, Ozkeze.

Revision: Cay, Topaloglu, Aras.

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.

References

[1] Jourda F, Providencia R, Marjion E, Bouzeman A, Hureche H, Khoueiry Z, et al. Contact-force guided radiofrequency vs. second-generation balloon cryotherapy for pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective evaluation. Eur Eur pacing, Arrhythm cardiac Electrophysiol J Work groups cardiac pacing, Arrhythm cardiac Cell Electrophysiol Eur Soc Cardiol 2013;17:225–31.
[2] Natale A, Reddy VY, Mourir C, Wilber DJ, Lindsay BD, McEllderry HT, et al. Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. J Am Coll Cardiol 2014;64:647–56.
[3] Kimura M, Sasaki S, Owada S, Horuchi D, Sasaki K, Itoh T, et al. Comparison of lesion formation between contact force-guided and non-guided circumferential pulmonary vein isolation: a prospective, randomized study. Heart rhythm official J Heart Rhythm Soc 2014;11:984–91.
[4] Beukema RP, Beukema WP, Smijt JJ, Bandaat Misier AR, Delnoij PP, Wellens H, et al. Efficacy of multi-electrode duty-cycled radiofrequency ablation for pulmonary vein disconnection in patients with paroxysmal and persistent atrial fibrillation. Eur Eur pacing, Arrhythm cardiac Electrophysiol J Work groups cardiac pacing, Arrhythm cardiac Cell Electrophysiol Eur Soc Cardiol 2010;12:502–7.
[5] Boersma LV, Wijffels MC, Oral H, Wefer EF, Morady F. Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter. Heart rhythm official J Heart Rhythm Soc 2008;5:1635–42.
[6] Piccone G, de Asmundis C, Sieira J, Conte G, Di Giovanni G, Mugnai G, et al. Single 3-minute freeze for second-generation cryoballoon ablation: one-year follow-up after pulmonary vein isolation. Heart Rhythm 2015;12:673–80.
[7] Scaglione M, Caponi D, Anselmino M, Di Clemente F, Blando A, Ferraris F, et al. Pulmonary vein isolation with a new multi-polar irrigated radiofrequency ablation catheter (nMARQ®): feasibility, acute and short-term efficacy, safety and impact on postablation silent cerebral ischemia. J Cardiovasc Electro-physiol 2014;25:1299–305.
[8] Sediva L, Petrui J, Skoda J, Janotka M, Chovanec M, Reddy V, et al. Visually guided laser ablation: a single-centre long-term experience. Eur Eur pacing, Arrhythm cardiac Electrophysiol J Work groups cardiac pacing, Arrhythm cardiac Cell Electrophysiol Eur Soc Cardiol 2014;16:1746–51.
[9] Garcia R, Sacher F, Oses P, Derval N, Barandon L, Denis A, et al. Electrophysiological study 6 months after Epicor high-intensity focused ultrasound atrial fibrillation ablation. J interventional cardiac Electrophysiol Int J Cardiol 2012;157:185–91.
[10] Zellerhoff S, Daly M, Lim HS, Denis A, Komatsuz Y, Jyel L, et al. Pulmonary vein isolation using a circular, open irrigated mapping and ablation catheter (nMARQ®): a report on feasibility and efficacy. Europace 2014;16:1296–303.
[11] Laish-Farkash A, Khamanevzer V, Fishman E, Cohen O, Yosef C, Cohen I, et al. Safety, efficacy, and clinical applicability of pulmonary vein isolation with circular multi-electrode ablation systems: PVAC®R vs. nMARQ® for atrial fibrillation ablation. Europace 2016;18:807–14.
[12] Tivig C, Dang L, Brunner-La Rocca HP, Ozcan S, Dufu F, Scharf C. Duty-cycled unipolar/bipolar versus conventional radiofrequency ablation in paroxysmal and persistent atrial fibrillation. Int J Cardiol 2013;157:815–20.
[13] Choo WK, Farwell D, Harris S. Experience of atrial fibrillation ablation in a new cardiac centre using three-dimensional mapping and multielectrode duty-cycled radiofrequency ablation. Archives Cardiovasc Dis 2011;104:396–402.
[14] De Greep Y, Buysschaert I, Schwagten B, Stockman D, Tavernier R, Duytschaever M. Duty-cycled multi-electrode radiofrequency vs. conventional irrigated point-by-point radiofrequency ablation for recurrent atrial fibrillation: comparative 3-year data. Eur Eur pacing, Arrhythm cardiac Electrophysiol J Work groups cardiac pacing, Arrhythm cardiac Cell Electrophysiol Eur Soc Cardiol 2014;16:820–5.
[15] Rosso R, Chorin E, Levi Y, Rogowski O, Viskin S. Radiofrequency ablation of atrial fibrillation: nonrandomized comparison of circular versus point-by-
point “smart” ablation for achieving circumferential pulmonary vein isolation and curing arrhythmic symptoms. J Cardiovasc Electrophysiol 2016 Jul 29. doi: http://dx.doi.org/10.1111/jce.13058. [Epub ahead of print].

[16] Belava A, Hanis J, Sitek D, Osmera O, Karpanus D, Smorek M, et al. Catheter ablation for paroxysmal atrial fibrillation: a randomized comparison between multielectrode catheter and point-by-point ablation. Pacing Clin Electrophysiol PACE 2010;33:1039–46.

[17] Bittner A, Monnig G, Zellerhoff S, Pott C, Kobe J, Decherding D, et al. Randomized study comparing duty-cycled bipolar and unipolar radiofrequency with point-by-point ablation in pulmonary vein isolation. Heart rhythm official J Heart Rhythm Soc 2011;8:1383–90.

[18] Beukema RJ, Elvan A, Smit JJ, Delnoy PP, Misier AR, Reddy V. Pulmonary vein isolation to treat paroxysmal atrial fibrillation: conventional versus multi-electrode radiofrequency ablation. J interventional cardiac Electrophysiol Int J Arhythm pacing 2012;34:143–52.

[19] Khaykin Y, Zaretsk I, Friedlander D, Wolffhurt ZA, Whaley B, Giewercer D, et al. Point-by-point pulmonary vein antrum isolation guided by intracardiac echocardiography and 3D mapping and duty-cycled multipolar AF ablation: effect of multipolar ablation on procedure duration and fluoroscopy time. J interventional cardiac Electrophysiol Int J Arhythm pacing 2012;34:303–10.

[20] Looi KL, Gajendragadkar P, Taha T, Elsik M, Scully E, Heck P, et al. Long-term clinical outcome after ablation with a novel multipolar irrigated ablation catheter in patients with paroxysmal atrial fibrillation. J interventional cardiac Electrophysiol Int J Arhythm pacing 2013;36:61–9. discussion 9.

[21] McCready J, Chow AW, Lowe MD, Segal OR, Ahsan S, de Bono J, et al. Safety and efficacy of multipolar pulmonary vein isolation catheter vs. irrigated radiofrequency ablation for paroxysmal atrial fibrillation: a randomized multicentre trial. Eur Eur pacing, Arrhythm cardiac Electrophysiol Eur Soc Cardiol 2014;16:1145–53.

[22] Gal P, Aarnitzen AE, Smit JJ, Adyayan A, Misier AR, Delnoy PP, et al. Conventional radiofrequency catheter ablation compared to multi-electrode ablation for atrial fibrillation. Int J Cardiol 2014;176:891–5.

[23] Dodd SJ, Sulke AN, Sugihara C, Furniss SS. Phased multipolar radiofrequency pulmonary vein isolation is as effective and safe as conventional irrigated point-to-point ablation. A prospective randomised 1-year implantable cardiac monitoring device follow-up trial. J interventional cardiac Electrophysiol Int J Arhythm pacing 2015;44:257–64.

[24] Waki R, Sieberhofer J, Fichtner S, Oesler M, Glocker E, Smorek M, et al. Catheter ablation for paroxysmal atrial fibrillation: a randomized comparison between multielectrode catheter and point-by-point ablation. Pacing Clin Electrophysiol PACE 2010;33:1383–90.

[25] Dello Russo A, Fassini F, Casella M, Di Monaco A, Riva S, Romano V, et al. Usefulness of intracardiac echocardiography during pulmonary vein isolation with the novel multipolar irrigated ablation catheter (nMARQ). J Interv Card Electrophysiol 2015;44:39–45.

[26] Shin DI, Kirmangolou K, Eckholt C, Schmidt J, Clasen L, Butzbach B, et al. Initial results of using a novel irrigated multielectrode mapping and ablation catheter for pulmonary vein isolation. Heart Rhythm 2014;11:375–83.

[27] Kuck KH, Hoffmanns BA, Ernst S, Wegscheider K, Tresel A, Metzner A, et al. Impact of complete versus incomplete circumferential lines around the pulmonary veins during catheter ablation of paroxysmal atrial fibrillation: results from the gap-atrial fibrillation-german atrial fibrillation competence network 1 trial. Circ Arhythm Electrophysiol 2016;9:e003317.

[28] Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, et al. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med 2015;372:1812–22.

[29] Vogler J, Willems S, Sultan A, Schreiber D, Luker J, Servatius H, et al. Pulmonary vein isolation versus defragmentation: the CHASE-AF clinical trial. J Am Coll Cardiol 2015;66:2743–52.

[30] Ruck KH, Brugada J, Furnkranz A, Metzner A, Ouyang F, Chun KR, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med 2016;374:2235–45.

[31] Cardoso R, Mendirizcaga R, Fernandes G, Healy C, Lambiase P, Viles-Gonzalez JF, et al. Cryoballoon versus radiofrequency catheter ablation in atrial fibrillation: a meta-analysis. J Cardiovasc Electrophysiol 2016 Oct;27(10):1151–9. doi: http://dx.doi.org/10.1111/jce.13047. Epub 2016 Aug 16.

[32] Provvidencia R, Defaye P, Lambiase PD, Pavin D, Debron JP, Halimi F, et al. Results from a multicentre comparison of cryoballoon vs. radiofrequency ablation for paroxysmal atrial fibrillation: is cryoablation more reproducible? Europace 2017 Jan;19(1):48–57. doi: http://dx.doi.org/10.1093/europace/eux080. Epub 2016 Jun 5.

[33] Bordignon S, Boehm MC, Klostermann A, Fuernkranz A, Perrotta L, Dugo D, et al. Visually guided pulmonary vein isolation in patients with persistent atrial fibrillation. Europace 2016;18:338–42.

[34] Dukkipati SR, Cuoco F, Kutinsky L, Aryana A, Bahnsen TD, Lakredddy D, et al. Pulmonary vein isolation using the visually guided laser balloon: a prospective, multicenter, and randomized comparison to standard radiofrequency ablation. J Am Coll Cardiol 2015;66:1350–60.

[35] Hocou M, Condic C, Stewart MT, Kirchhof N, Foell JD. Predictability of lesion durability for AF ablation using phased radiofrequency: power, temperature, and duration impact creation of transmural lesions. Heart Rhythm 2016;13:1521–6.

[36] Gal P, Buist TJ, Smit JJ, Adyayan A, Ramdat Misier AR, Delnoy PP, et al. Effective contact and outcome after pulmonary vein isolation in novel circular multi-electrode atrial fibrillation ablation. Neth Heart J 2017;25:16–23.

[37] Nagy-Balo E, Kiss A, Condie C, Stewart M, Edes I, Csandi Z. Predictors of cerebral microembolization during phased radiofrequency ablation of atrial fibrillation: analysis of biophysical parameters from the ablation generator. Heart rhythm official J Heart Rhythm Soc 2014;11:977–83.

[38] Herrera Siklody C, Deneka T, Hocou M, Lehrmann H, Shin DI, Miyazaki S, et al. Incidence of asymptomatic intracranial embolic events after pulmonary vein isolation: comparison of different atrial fibrillation ablation technologies in a multicenter study. J Am Coll Cardiol 2011;58:681–8.

[39] Deneka T, Muller P, Halkias P, Szollosi A, Roos M, Krug J, et al. Effect of different ablation settings on acute complications using the novel irrigated multipolar radiofrequency ablation catheter (nMARQ). J Cardiovasc Electrophysiol 2015;26:1063–8.

[40] Compier MG, Leong DP, Marsan NA, Delgado V, Zeppenfeld K, Schalij MJ, et al. Duty-cycled bipolar/unipolar radiofrequency ablation for symptomatic atrial fibrillation induces significant pulmonary vein narrowing at long-term follow-up. Eur Eur pacing, Arrhythm cardiac Electrophysiol J Work groups cardiac pacing, Arrhythm cardiac Cell Electrophysiol Eur Soc Cardiol 2013;15:190–6.