Epicardial thoracoscopic ablation versus endocardial catheter ablation for management of atrial fibrillation: a systematic review and meta-analysis

Hyun Jung Kim, Jin Suk Kim and Tae Sik Kim

Abstract

OBJECTIVES: In the treatment of patients with atrial fibrillation (AF), the efficacy and safety of epicardial thoracoscopic ablation (TA) versus endocardial catheter ablation (CA) using radiofrequency energy remains unclear. This meta-analysis was performed to assess the efficacy and safety of each ablation technique using a pooled comparative analysis.

METHODS: Studies comparing the efficacy and safety of TA and CA were identified by searching electronic databases. Those that reported patients’ freedom from atrial arrhythmia and significant side effects were included.

RESULTS: Three randomized controlled trials (RCTs) and two retrospective cohort studies with a total of 587 patients were included in the meta-analysis (273 patients underwent TA and 314 patients underwent CA). The proportion of patients who were free of atrial arrhythmia without antiarrhythmic drugs during 12 months of follow-up was significantly higher after TA than after CA in the RCTs (\( P < 0.001; \) relative risk (RR), 1.77; 95% confidence interval (CI), 1.34–2.32) and in the retrospective cohort studies (\( P = 0.010; \) RR, 1.68; 95% CI, 1.12–2.51). The incidence of significant side effects during the post-procedural period was significantly higher in the TA group than in the CA group in both the RCT (\( P = 0.007; \) RR, 7.23; 95% CI, 1.71–30.49) and the retrospective cohort studies (\( P = 0.020; \) RR, 4.39; 95% CI, 1.33–14.46).

CONCLUSIONS: Based on the available data, TA was found to be more effective than CA in achieving freedom from atrial arrhythmia; however, TA had a higher rate of immediate post-procedural complications than CA.

Keywords: Atrial fibrillation • Thoracoscopy • Catheter ablation • Meta-analysis

INTRODUCTION

Endocardial catheter ablation (CA) using radiofrequency energy for the treatment of atrial fibrillation (AF) has varying success rates [1, 2]. This procedure basically involves pulmonary vein isolation (PVI), with or without ablations of other sites, using endocardial catheter-based techniques via a transvenous approach. Epicardial surgical ablation using radiofrequency energy under video-assisted thoracoscopy mimics the PVI lesion sets used in CA. This surgical technique on the beating heart can be extended to a left atrial lesion, and resection of the left atrial appendage [3–5]. Epicardial thoracoscopic ablation (TA), as a single procedure, has had promising outcomes, with success rates ranging from 65 to 96% [4, 6–11]. However, since these reports were single-centre experiences, rather than comparative studies or randomized trials, the effectiveness of TA has not yet been demonstrated.

Previous systematic reviews and meta-analyses of surgical ablation included various types of surgical techniques: classic Cox–maze procedure, under mini-thoracotomy, using cardiopulmonary bypass, on the beating heart or video-assisted thoracoscopy [12–15]. However, there has been no systematic review and meta-analysis focusing on the clinical outcomes of the TA technique. In this systematic review and meta-analysis, we aimed to review all studies that compared the clinical outcomes of TA and CA in order to assess the efficacy and safety of TA compared with CA for the management of AF.

MATERIALS AND METHODS

We used multiple comprehensive databases to find publications comparing TA and CA for the treatment of AF. This study was based on the Cochrane Review Methods and reported according to an earlier proposal [16].
Literature source

We searched MEDLINE (1 January 2005 to 12 February 2015), EMBASE (1 January 2005 to 12 February 2015) and Cochrane Central Register of Controlled Trials (CENTRAL) (1 January 1987 to 12 February 2015). We placed no restrictions on language in our search. A search for important keywords and MeSH was carried out through Medline; E-Method includes the comprehensive list. Search strategies were adapted for other databases based on the MEDLINE strategy. After the initial electronic search, we hand-searched further relevant articles and the bibliographies from identified studies. Articles identified were assessed individually for inclusion.

Study selection

The decision whether to include each study was made independently by two investigators (Tae Sik Kim and Jin Suk Kim), based on the selection criteria. Study selection involved two levels of screening: at the first level, we screened titles and abstracts of identified studies; at the second level, we screened the full text. Studies were included in our meta-analysis if they: (i) concerned patients with AF; (ii) included clinical results of TA and (iii) included clinical results of CA.

Data extraction

Two investigators (Tae Sik Kim and Jin Suk Kim) independently extracted data from each study using a predefined data extraction form. We considered patients who underwent TA as the intervention group, and patients who underwent CA as the control group. Any disagreement unresolved by discussion was reviewed by a third author (Hyun Jung Kim).

The following variables were extracted from each included study for both the TA (intervention) and CA (control) groups: (i) demographic characteristics; (ii) number of patients who were free of atrial arrhythmia without antiarrhythmic drugs (AAD), number free of atrial arrhythmia with AAD and incidence of significant adverse events (SAEs); (iii) treatment protocol; (iv) method of assessment and (v) inclusion and exclusion criteria. If the above variables were not mentioned in the studies, we requested the data via e-mail.

Assessment of methodological quality

Two investigators (Tae Sik Kim and Jin Suk Kim) independently assessed the methodological quality of each study, using the Cochrane Collaboration’s tool (see Supplementary Table 1) for assessing the risk of bias for randomized controlled studies (RCTs) and the Newcastle–Ottawa Scale (see Supplementary Table 2) for retrospective cohort studies. Any unresolved disagreements between the two investigators (Tae Sik Kim and Jin Suk Kim) were resolved through discussion after review by a third author (Hyun Jung Kim).

Statistical analysis

Freedom from atrial arrhythmia without AAD over a follow-up of 12 months’ duration was the primary outcome measure of interest. Secondary measures included freedom from atrial arrhythmia with AAD at 12 months of follow-up, and SAEs during the post-procedural period and 12 months of follow-up, such as death, stroke, transient
<table>
<thead>
<tr>
<th>Author, publication year</th>
<th>Study design</th>
<th>TA:CA (n)</th>
<th>TA technique</th>
<th>CA technique</th>
<th>Efficacy (E), Safety (S) outcomes</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Rhythm measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boersma, 2012 [17]</td>
<td>RCT</td>
<td>61:63</td>
<td>VATS, PVI, ganglionic plexi ablation, LAA excision</td>
<td>Wide antral PVI, mitral isthmus</td>
<td>E: freedom from any LA arrhythmia without AAD, freedom from LA arrhythmia with AAD&lt;br&gt;S: rate of significant adverse events&lt;br&gt;a</td>
<td>PAF or PersAF for at least 12 months refractory to or intolerant of at least 1 AAD, age between 30 and 70 years</td>
<td>Longstanding AF &gt;1 year, cardiac CA or a surgical cardiac procedure in the last 3 months, previous stroke, LA thrombus, LA size &gt;65 mm, LV EF &lt;45%, MR or AR &gt;grade 2, moderate to severe MS or AS, active infection or sepsis, pregnancy, UAP, MI ≤3 months, AF secondary to electrolyte imbalance, thyroid disease, other reversible or non-cardiovascular causes for AF, history of blood-clotting abnormalities, known sensitivity to heparin or warfarin, life expectancy of &lt;12 months, pleural adhesions, prior thoracotomy, prior cardiac surgery, elevated hemidiaphragm&lt;br&gt;CHF, LA thrombus, LV EF &lt;35%, LA &gt;65 mm, prior thoracotomy, prior cardiac surgery, elevated hemidiaphragm</td>
<td>12-lead ECG, 7-day Holter at 6, 12 months</td>
</tr>
<tr>
<td>Pokushalov, 2013 [18]</td>
<td>RCT</td>
<td>32:32</td>
<td>VATS, PVI, ganglionic plexi ablation, LAA excision</td>
<td>PVI, roof, mitral isthmus</td>
<td>E: recurrence of atrial tachyarrhythmia without any cardioversion&lt;br&gt;S: rate of significant adverse events&lt;br&gt;a</td>
<td>PAF or PersAF after a previous failed first radiofrequency CA</td>
<td></td>
<td>Implantable loop recorder at 12 months</td>
</tr>
<tr>
<td>Wang, 2014 [19]</td>
<td>CT</td>
<td>66:72</td>
<td>VATS, PVI, ganglionic plexi ablation, resection of ligament of Marshall, LAA excision</td>
<td>PVI</td>
<td>E: sinus rhythm rate&lt;br&gt;S: major adverse events&lt;br&gt;b</td>
<td>PAF</td>
<td>UAP, shock, cardiac failure, indication for additional surgical procedures, hyperthyroidism</td>
<td>ECG, Holter at 1, 3, 6, 12 months</td>
</tr>
<tr>
<td>Wang, 2011 [20]</td>
<td>Retrospective cohort</td>
<td>83:83</td>
<td>VATS, PVI, ganglionic plexi ablation, resection of ligament of Marshall, LAA excision</td>
<td>PVI, roof, mitral isthmus</td>
<td>E: Maintenance of sinus rhythm without AAD, maintenance of sinus rhythm with AAD&lt;br&gt;S: clinical events&lt;br&gt;c</td>
<td>Longstanding PersAF ≥1 year resistant to electrical or pharmacological cardioversion</td>
<td>For TA: LV EF &lt;30%, sick sinus syndrome, severe pleural adhesions as well as prior attempts with CA&lt;br&gt;For CA: LV EF &lt;30%, LA thrombus, prior attempts with CA or surgical ablation</td>
<td>12-lead ECG, 24- or 48-h Holter at visit [mean duration: 2.2 years (range, 1.0–3.6 years)]</td>
</tr>
</tbody>
</table>

Continued
### Table 1: (Continued)

<table>
<thead>
<tr>
<th>Author, publication year</th>
<th>Study design</th>
<th>TA:CA (n)</th>
<th>CA technique</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.J. Kim [21]</td>
<td>Retrospective cohort</td>
<td>33:66 VATS, PVI, 12 months</td>
<td>VA &gt;55 mm, prior CA, prior heart or lung surgery, significant coronary artery disease or pulmonary disease, CHF, MR, AR, MS, AS, UAP, MI, LVH &gt;12 mm, previous hospitalization for HF, high comorbidity, or patient refusal</td>
<td>For TA: PAF or PersAF, freedom from atrial arrhythmia with AAD, quality of life, at least one episode of atrial fibrillation, total atrial volume and covariates, age, sex, and duration of AF in the same calendar period</td>
<td></td>
</tr>
</tbody>
</table>

####RESULTS

**Identification of studies**

The search of the databases yielded 6220 articles. Of these, 6213 publications were excluded as it was clear from the title and abstract that they did not fulfill the selection criteria. For the remaining seven articles, we obtained full manuscripts, and following scrutiny of these, we identified five potentially relevant studies [17–21]. Two publications were excluded due to different criteria of populations, and nearly the same population with other studies of the same authors. Thus, the total number of studies included in this review was five (Fig. 1).

**Study characteristics**

We identified five studies (three RCTs and two retrospective cohort studies) that enrolled a total of 587 patients: 273 patients underwent TA and 314 patients underwent CA (Table 1) [17–21]. For the TA technique, all studies involved endoscopically performed bipolar radiofrequency ablation on the beating heart, including epicardial bilateral PVI, ablation of ganglionic plexi and left atrial appendage excision. Two studies (one RCT, one cohort study) added resection of the ligament of Marshall [19, 20]. Different methods were used for PVI, namely circumferential [17, 21] and segmental ostial [18–20] ablation. Ablation of additional lines (roof or mitral isthmus) was performed in three studies at the clinician’s discretion [17, 18, 20]. The inclusion and exclusion criteria of each group, and the assessment tools and follow-up durations used in the included studies are also described in Table 1.

**Patients’ characteristics**

Patients had either paroxysmal or permanent AF. One study only enrolled patients with paroxysmal AF [19], and one only those with persistent AF [20], whereas the remaining studies included patients with both paroxysmal and persistent AF [17, 18, 21]. Most of the patients included in the studies were relatively young (age <60 years), had few comorbidities, normal ejection fraction...
 (>55%) and a left atrial dimension less than 50 mm (Table 2). None of the patients enrolled in the two retrospective cohort studies had a history of previous CA [20, 21]. The trials of Pokushalov et al. [18] covered only patients with previous failed CA.

Quality of the included studies

We assessed the quality of the included studies using the Cochrane Collaboration’s tool for assessing risk of bias for the three RCTs and the Newcastle–Ottawa Scale for the two retrospective cohort studies. Blinding of participants and personnel was not feasible and blinding of outcome assessment was not reported in the three RCTs (see Supplementary Table 3). However, the trials of Boersma et al. [17] and Pokushalov et al. [18] were finally considered to have a low risk of bias, because their outcome assessment was an objective measurement and the allocation was adequately concealed. The trial of Wang et al. [19] was considered to have a high risk of bias due to domains of unclear risk (random sequence generation, allocation concealment, incomplete outcome data, selective outcome reporting). The two retrospective cohort studies were evenly awarded a star in the domain of Selection, Comparability and Outcome (see Supplementary Table 4). Overall, the quality of the included studies was generally good, with only one exception.

Table 2: Baseline characteristics of the patients in the included studies

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Male (%)</th>
<th>PAF: PersAF (n)</th>
<th>HTN (n)</th>
<th>DM (n)</th>
<th>Stroke (n)</th>
<th>CHADS2 score</th>
<th>AF duration (months)</th>
<th>Prior AAD (n)</th>
<th>Prior CA (n)</th>
<th>EF (%)</th>
<th>LAD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boersma 2012</td>
<td>TA (61)</td>
<td>56 ± 8</td>
<td>73.8</td>
<td>45:16</td>
<td>-</td>
<td>-</td>
<td>≤1 (86.6%)</td>
<td>-</td>
<td>61</td>
<td>45</td>
<td>57.7 ± 8</td>
<td>42.5 ± 6.5</td>
</tr>
<tr>
<td></td>
<td>CA (63)</td>
<td>56.0 ± 7.2</td>
<td>87.3</td>
<td>37:26</td>
<td>-</td>
<td>-</td>
<td>≤1 (91.6%)</td>
<td>-</td>
<td>63</td>
<td>38</td>
<td>55.5 ± 8</td>
<td>43.2 ± 4.8</td>
</tr>
<tr>
<td>Pokushalov 2013</td>
<td>TA (32)</td>
<td>56 ± 7</td>
<td>71.9</td>
<td>20:12</td>
<td>13</td>
<td>3</td>
<td>3</td>
<td>0.6 ± 0.8</td>
<td>62.4</td>
<td>32</td>
<td>55 ± 5</td>
<td>46 ± 5</td>
</tr>
<tr>
<td></td>
<td>CA (32)</td>
<td>57 ± 7</td>
<td>78.1</td>
<td>18:14</td>
<td>11</td>
<td>4</td>
<td>2</td>
<td>0.6 ± 0.9</td>
<td>58.8</td>
<td>32</td>
<td>57 ± 6</td>
<td>45 ± 7</td>
</tr>
<tr>
<td>Wang 2014</td>
<td>TA (66)</td>
<td>52 ± 10</td>
<td>57.6</td>
<td>66:0</td>
<td>26</td>
<td>9</td>
<td>7</td>
<td>-</td>
<td>71 ± 52</td>
<td>56</td>
<td>-</td>
<td>64 ± 6</td>
</tr>
<tr>
<td></td>
<td>CA (72)</td>
<td>51 ± 10</td>
<td>63.9</td>
<td>72:0</td>
<td>27</td>
<td>11</td>
<td>5</td>
<td>-</td>
<td>76 ± 74</td>
<td>62</td>
<td>-</td>
<td>65 ± 5</td>
</tr>
<tr>
<td>Wang 2011</td>
<td>TA (83)</td>
<td>57 ± 11</td>
<td>69.9</td>
<td>0.83</td>
<td>37</td>
<td>10</td>
<td>13</td>
<td>-</td>
<td>71 ± 65</td>
<td>80</td>
<td>0</td>
<td>62 ± 9</td>
</tr>
<tr>
<td></td>
<td>CA (83)</td>
<td>55 ± 12</td>
<td>62.7</td>
<td>0.83</td>
<td>40</td>
<td>11</td>
<td>7</td>
<td>-</td>
<td>70 ± 74</td>
<td>74</td>
<td>0</td>
<td>61 ± 7</td>
</tr>
<tr>
<td>De Maat 2014</td>
<td>TA (33)</td>
<td>51 ± 10</td>
<td>82 ± 10</td>
<td>28:5</td>
<td>10</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>41</td>
<td>27</td>
<td>0</td>
<td>41.7 ± 5.4</td>
</tr>
<tr>
<td></td>
<td>CA (66)</td>
<td>53 ± 9</td>
<td>82 ± 48:18</td>
<td>28</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>58</td>
<td>50</td>
<td>0</td>
<td>40.8 ± 5.4</td>
</tr>
</tbody>
</table>

PAF: paroxysmal atrial fibrillation; PersAF: persistent atrial fibrillation; EF: ejection fraction; LAD: left atrial diameter; TA: thoracoscopic ablation; CA: catheter ablation; –: not reported; AAD: antiarrhythmic drugs; HTN: hypertension; DM: diabetes mellitus.

Figure 2: Freedom from atrial fibrillation without antiarrhythmic drugs in the randomized controlled studies (A) at 6 and 12 months of follow-up and retrospective cohort studies (B) after 12 months of follow-up, comparing TA with CA. TA: thoracoscopic ablation; CA: catheter ablation; CI: confidence interval; M-H: Mantel–Haenszel estimation method; random: random-effects model.
Efficacy: freedom from atrial arrhythmia

Our analysis showed that TA was associated with a significantly higher rate of freedom from AF without AAD at 12 months of follow-up in the RCTs (P < 0.001, RR 1.77, 95% CI 1.34–2.32, I² = 0%) (Fig. 2A) and after 12 months of follow-up in the retrospective cohort studies (P = 0.010, RR 1.68, 95% CI 1.12–2.51, I² = 71%) (Fig. 2B). The success rates and risk differences between both procedures of freedom from AF without AAD are described in Table 3.

In the RCTs, a trend towards a higher rate of freedom from atrial arrhythmia with AAD in the TA group was detected at 12 months of follow-up, but did not reach statistical significance (P = 0.12, RR 1.45, 95% CI 0.91–2.32, I² = 86%) (Fig. 3A). TA was associated with a significantly higher rate of freedom from AF with AAD after 12 months of follow-up in the retrospective cohort studies (P < 0.001, RR 1.35, 95% CI 1.16–1.58, I² = 0%) (Fig. 3B). The success rates and risk differences between both procedures of freedom from AF with AAD are described in Table 3.

Table 3: Success rates and risk differences between TA and CA

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TA</th>
<th>CA</th>
<th>Risk difference [95% CI]</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Success rate</td>
<td>Events</td>
</tr>
<tr>
<td>Freedom from AF without AAD RCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Boersma, 2012</td>
<td>41</td>
<td>61</td>
<td>0.67</td>
</tr>
<tr>
<td>12 months</td>
<td>Boersma, 2012</td>
<td>40</td>
<td>61</td>
<td>0.66</td>
</tr>
<tr>
<td>Pokushalov, 2013</td>
<td>26</td>
<td>32</td>
<td>0.81</td>
<td>15</td>
</tr>
<tr>
<td>RetrspCohrt</td>
<td>De Maat, 2014</td>
<td>27</td>
<td>31</td>
<td>0.87</td>
</tr>
<tr>
<td>6 months</td>
<td>Wang, 2011</td>
<td>51</td>
<td>83</td>
<td>0.61</td>
</tr>
<tr>
<td>Freedom from AF with AAD RCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Wang, 2014</td>
<td>60</td>
<td>66</td>
<td>0.91</td>
</tr>
<tr>
<td>12 months</td>
<td>Boersma, 2012</td>
<td>48</td>
<td>61</td>
<td>0.79</td>
</tr>
<tr>
<td>Wang, 2014</td>
<td>59</td>
<td>66</td>
<td>0.89</td>
<td>54</td>
</tr>
<tr>
<td>RetrspCohrt</td>
<td>De Maat, 2014</td>
<td>28</td>
<td>31</td>
<td>0.90</td>
</tr>
<tr>
<td>Wang, 2011</td>
<td>62</td>
<td>83</td>
<td>0.75</td>
<td>49</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; AAD: antiarrhythmic drug; TA: thoracoscopic ablation; CA: catheter ablation; CI: confidence interval; RCT: randomized controlled studies; RetrspCohrt: retrospective cohort studies; NA: not available.

Figure 3: Freedom from atrial fibrillation with antiarrhythmic drugs in the randomized controlled studies (A) at 6 and 12 months of follow-up and retrospective cohort studies (B) after 12 months of follow-up, comparing TA with CA. TA: thoracoscopic ablation; CA: catheter ablation; CI: confidence interval; M-H: Mantel-Haenszel estimation method; random: random-effects model.
Safety: significant adverse events

During the periprocedural period, SAEs were significantly more frequent in the TA group than in the CA group in both the RCT ($P = 0.007$, RR 7.23, 95% CI 1.71–30.49) and the retrospective cohort studies ($P = 0.020$, RR 4.39, 95% CI 1.33–14.46, $I^2 = 0\%$) (Fig. 4A).

During the follow-up period of over 12 months, SAEs showed no significant differences between groups either in the RCTs ($P = 0.78$, RR 1.10, 95% CI 0.56–2.15, $I^2 = 0\%$) or the retrospective cohort studies ($P = 0.70$, RR 0.75, 95% CI 0.17–3.25) (Fig. 4B).

DISCUSSION

A major finding of this meta-analysis was that epicardial surgical ablation under thoracoscopy using radiofrequency energy was more effective than endocardial radiofrequency CA in achieving freedom from atrial arrhythmia during 12 months of follow-up. However, the CA technique was safer than the TA technique, with fewer periprocedural complications.

Epicardial surgical ablation using a radiofrequency energy source under video-assisted thoracoscopy is a relatively new technique for the control of AF [3–5, 22, 23]. Previous studies of TA or CA have reported a wide range of success rates, due to the diverse characteristics of AF, various follow-up durations, different procedural methods, more or less experienced operators, etc. Taking these aspects into consideration, a comparison of the merits of the two strategies for the treatment of AF requires close attention. Furthermore, RCTs for the assessment of clinical outcomes of surgical or percutaneous intervention seem to have several limitations and inevitable bias. Therefore, very few well-designed, statistically powerful, comparative studies of TA and CA using radiofrequency energy have been published. We reviewed and analysed the efficacy and safety of these newly developed techniques using a limited number of publications—cohort studies as well as RCTs—aimed at a proper assessment of the clinical results [24].
Heterogeneity could be investigated by means of metaregression analysis; however, this was not performed in our meta-analysis owing to the small number of studies included. Moreover, the investigation of heterogeneity would be mainly associated with the magnitude of the pooled estimate rather than its direction of favour (efficacy or safety) [25]. Instead of metaregression, we conducted subgroup analyses, based on factors such as study design or follow-up duration, to determine clinical heterogeneity. Using the $I^2$ statistic, the heterogeneity of retrospective cohort studies with regard to the freedom from arrhythmia without AAD was considered as high ($I^2 = 71\%$) (Fig. 2B).

We believe that this was attributable to the difference in follow-up duration between studies; De Maat et al. measured outcomes after 12 months of follow-up, whereas the mean follow-up duration in the study by Wang et al. was 2.2 years (range, 1.0–3.6 years).

In the random-effects model, the difference between groups in the rate of freedom from arrhythmia with AAD had no statistical significance, with only a trend to favour TA (the rate of freedom from arrhythmia with AAD had no statistical significance with only a trend to favour TA; $P = 0.12$, RR $1.45$, 95% CI $0.91–2.32$, $I^2 = 86\%$) (Fig. 3A). In the fixed-effects model, however, a higher rate of freedom from arrhythmia with AAD was demonstrated in the TA group ($P < 0.001$, RR $1.41$, 95% CI $1.21–1.65$, $I^2 = 86\%$) (see Supplementary Fig. 2). This finding could be interpreted as reflecting the high risk of bias in the trial of Wang et al. (see Supplementary Table 1). In other words, the poor quality of the trial by Wang et al. caused a high heterogeneity of analysis, and consequently expanded the CI of RR.

The medical history of prior CA in the studies we analysed was not uniform. In two of the three RCTs, all or the majority of patients had undergone previous failed CA, whereas the other study did not mention previous ablation history. It was important that the patients in the CA arm of the three RCTs underwent the same endocardial ablation technique in each trial, regardless of the history of prior CA, because the clinical outcomes, i.e. efficacy or safety, were the final result of the intervention in each study, not of the ablation history. On the other hand, the two retrospective cohort studies excluded patients with prior CA. However, this might not affect any bias of the pooled estimate because the subgroup analysis was performed separately according to the study design.

Wang et al. did not mention significant adverse clinical events. Therefore, we assessed the safety of the ablation procedures in four studies: two RCTs and two retrospective cohort studies.

Publication bias was not assessable in these studies. Tests for funnel plot asymmetry are generally only performed when at least 10 studies are included in the meta-analysis. As our analysis included only five studies, tests for asymmetry would be ineffective as they would be unable to differentiate asymmetry from chance.

**Limitations**

Many different factors in the included studies might have led to the heterogeneity of our meta-analysis: the detailed technique used for radiofrequency ablation, rhythm measurement tools, type of AF, prior use of AAD, etc. Because the patient characteristics, such as relatively young age, fewer comorbidities, preserved ejection fraction and a non-enlarged left atrium, were not similar to those of the general population with AF, no definite conclusion favouring one treatment modality over the other can be drawn at present.

**CONCLUSIONS**

Epicardial TA was more effective than endocardial CA in achieving freedom from atrial arrhythmia over 12 months of follow-up; however, TA had a higher rate of immediate post-procedural complications than did CA. More definitive evidence regarding the long-term outcomes needs to be provided by systematic reviews and meta-analyses based on more RCTs.

**SUPPLEMENTARY MATERIAL**

Supplementary material is available at ICVTS online.

**Conflict of interest:** none declared.

**REFERENCES**


I have read with great attention the article by Kim et al [1]. In the setting of the Cox-maze III “cut-and-sew”, it is clear that we need to evolve from complex original surgical techniques to easier and more feasible techniques to treat atrial fibrillation (AF). These techniques often use alternative energy sources (radiofrequency, cycloisoles, microwaves, high-intensity focused ultrasound). Two examples of this are epicardial thoracoscopic ablation (TA) and endocardial catheter ablation (CA) with radiofrequency energy, both described in this meta-analysis [1]. The great concern is that both techniques here use unipolar radiofrequency (RF) ablation. It is well known that unipolar RF ablation is able to assure neither transmurality nor uniformity of the burn in the atrial tissue [2,3]. Unexpectedly, the TE was better than the CA, despite the well-known fact that the bloodstream in normothermia could cool the heat wave of RF applied from the outside. However, the lower effectiveness of CA can be explained by the difficulty in creating precise lesions within the heart without a direct view of the anatomic structures. In particular, during the course of a Cox-maze III “cut-and-sew” procedure in patients previously treated with CA, I found large areas of scarred tissue instead of a precise burn line.

The techniques studied in this review [1] represent a great effort in order to reach Dr. Cox’s ideal regarding to surgery for AF. According to Cox, surgery for AF should meet the following conditions: 1) the procedure should be preferably epicardial by nature; 2) the energy source should be capable of penetrating epicardial fat and ablating all types of AF; 3) cardiopulmonary bypass must be avoided; 4) the procedure should be amenable to endoscopic or minimally invasive techniques; 5) it should be performed in less than 1 hour; 6) hospital discharge should be possible on the first postoperative day [4]. Finally, standard Cox-maze III “cut-and-sew” remains the gold standard to surgically treat AF, regardless its type [5].

Conflict of interest: None declared.

References