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# Transseptal or retrograde approach for transcatheter ablation of left sided accessory pathways: a systematic review and meta-analysis

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**Key words:** Accessory pathway, Wolff-Parkinson-White, transcatheter ablation, transseptal access, transaortic access

**Abstract**

**Background.** Transcatheter ablation is the most effective treatment for patients with symptomatic or high-risk accessory pathways (AP). At present, no clear recommendations have been issued on the optimal approach for left sided AP ablation. We performed this meta-analysis to compare the safety and efficacy of transaortic retrograde versus transseptal approach for left sided AP ablation.

**Methods and Results.** MEDLINE/PubMed and Cochrane database were searched for pertinent articles from 1990 until 2016. Following inclusion/exclusion criteria application, 29 studies were selected including 2030 patients (1013 retrograde, 1017 transseptal) from 28 observational single Centre studies and one randomized trial. Patients approached by transseptal puncture presented a significantly higher acute success (98% vs. 94%, p=0.040). The incidence of late recurrences (p=0.381) and complications (p=0.301) did not differ among the two groups, but the pattern of complications differed: vascular complications were more frequent with transaortic retrograde approach, while cardiac tamponade was the main transseptal complication. No difference was noted in terms of procedural duration and fluoroscopy time (p=0.230 and p=0.980, respectively). Meta-regression analysis showed no relation between year of publication and acute success (p=0.325) or incidence of complications (p=0.795); additionally, no direct relation was found between age and acute success (p=0.256) or complications (p=0.863).

**Conclusions.** Left sided AP transcatheter ablation is effective in around 95% of the cases, with a very limited incidence of complications. Transseptal access provides higher acute success in achieving AP ablation; late recurrences are rare but observed similarly following both approaches. Retrograde approach is affected by a relatively high incidence of vascular complications.

Abstract word count: 250

## Introduction

Wolff-Parkinson-White syndrome is characterized by the concomitant presence of cardiac pre-excitation and arrhythmias as atrio-ventricular re-entrant tachycardia or atrial fibrillation (AF). Less than 1% of patients with cardiac pre-excitation may present a significant risk of sudden cardiac death, due to very high conduction properties of the atrioventricular accessory pathway (AP) [1]. Treatment is warranted to prevent this risk of sudden death in high-risk asymptomatic patients, or to prevent re-entrant tachycardias in symptomatic patients [2,3].

The APs can be situated everywhere in the tricuspid or mitral annuli, with the exception of the mitral-aortic continuity. Transcatheter ablation of the AP is the most effective treatment for patients affected by Wolff-Parkinson-White syndrome and for high-risk asymptomatic pre-excitation. The most recent guidelines recommend transcatheter ablation as first-line treatment for these patients [2], due to its high efficacy and safety in experienced Centres.

Bearing in mind the different possible localizations, right APs can be approached for ablation from the femoral or subclavian veins, while left sided APs can be approached by transaortic retrograde pathway or transseptal puncture. These two approaches differ in terms of technique, materials, potential complications and easy access to the AP, and are usually chosen alternatively according to the operators' comfort level and preference. However, no clear recommendation has been proposed on the ideal approach for transcatheter ablation of left sided APs. In particular, common practice is mainly based on single-Centre, observational studies, and no large randomized trials or registries have been published.

We therefore performed this systematic review and meta-analysis including randomized and observational studies comparing the outcome of transaortic retrograde versus transseptal approach, aiming to assess the optimal approach for left sided AP transcatheter ablation, in terms of both safety and efficacy.

## Materials and Methods

### *Search strategy and studies selection*

The present study was conducted in accordance with current guidelines, including the recent Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [4] amendment to the Quality of Reporting of Meta-analyses (QUOROM) statement, as well as recommendations from The Cochrane Collaboration and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) [5]. All subjects included in the studies gave informed consent.

MEDLINE/PubMed and Cochrane database were searched for pertinent articles published in English from 1990 until December 2016. The following terms: ("Left accessory pathway" OR "left Wolff Parkinson White") AND "catheter ablation" AND "radiofrequency" were used. Retrieved citations were screened through abstract reading independently by two reviewers (M.M. and A.S.), and divergences resolved after consensus. If the citations were deemed potentially pertinent, they were then appraised as complete full-text reports according to the following explicit selection criteria: (i) human observational or randomized studies, (ii) published in English between 1990 and 2016, (iii) investigating patients with left accessory pathways, (iv) including any duration of follow-up. Exclusion criteria were (one enough for exclusion): (i) non-human setting, (ii) duplicate reporting (in which case the manuscript reporting the largest sample of patients was selected), (iii) case reports or papers including less than 10 patients; (iv) surgical AP ablation. Data concerning study design and year of publication, population characteristics, intervention, complications, acute and mid- or long-term outcome were extracted by two Authors and reviewed independently by a third one (M.A.), being inserted in a single study database.

### *Statistical analysis*

Since most of the included studies had an observational design, meta-analysis and meta-regressions were performed using random effect models. Primary outcomes of this systematic review were: proportions of initial success (calculated as the ratio between successful procedures and number of patients or as the ratio between successfully ablated pathways and the total number of treated pathways), proportion of recurrences after a mid-term follow-up and proportion of complications. Secondary outcomes were: total procedural time, fluoroscopy time (excluding those studies characterized by a "zero-fluoroscopy" approach) and number of energy applications per procedure. Meta-analysis of proportions was performed using STATA command "metaprop" [6], while meta-analysis of continuous variables was performed using STATA command "metan" [7]. Aiming to assess the impact of the type of procedural access (retrograde aortic vs transseptal), subgroup meta-analysis was performed for both primary and secondary outcomes and a Q test for heterogeneity between subgroups was computed. In addition, aiming to reduce the impact of potential biases derived from patients' characteristics or year of publication, using the primary outcomes as dependent variables, pre-specified meta-regression analysis was performed through STATA command "metareg" [8] to test whether interactions with (i) year when the study was published and (ii) mean age of study participants were present.

Continuous variables were reported as mean (standard deviation) and categorical variables as counts (percentage). Statistical analysis was performed using STATA version 12.0 (StataCorp, College Station, TX, USA), considering p values $< 0.05$ statistically significant.

## Results

### *Search Results*

The search identified 269 abstracts referring to transcatheter ablation of left sided APs; among this group, 233 were excluded following application of the inclusion and exclusion criteria; 36 of them were selected and full text was read by two Authors; 7 were excluded because reporting repeated data. Twenty-nine studies were finally included meeting all the pre-specified inclusion criteria. All included articles were single-Centre studies; overall 28 observational studies and one randomized trial were included. Complete details of the study flow-chart are described in in the Supplementary Material, Supplementary Figure 1.

First Author, study design, publication date and complete main characteristics of each included study are reported in the Supplementary Material, Supplementary Table 1 [9-37].

Overall, 2030 patients have been included in the analysis, 1013 approached by retrograde transaortic access and 1017 by transseptal puncture. Baseline characteristics of the included population in both groups are described in Table 1. Briefly, population included mainly young adults, two thirds of whom were males. The most common location for left sided AP was left lateral, followed by left posterior.

### *Efficacy and safety endpoints*

As shown in Figure 1, patients approached by transseptal puncture presented a significantly higher acute success of the ablation (98% vs. 94%, p=0.040) compared to transaortic retrograde approach. Conversely, the incidence of late recurrences of cardiac pre-excitation did not differ significantly among the two groups (3% vs. 2%, p=0.381; Figure 2). Concerning safety, the incidence of overall complications was equally low in both groups (0.4% vs. 1.2%, p=0.301; Figure 2). Of note, complications pattern was different: vascular complications (hematoma, pseudoaneurysm, aortic regurgitation and coronary damage) were more frequent with transaortic retrograde approach, while cardiac tamponade was the main complication of transseptal approach. Detailed complications are reported in the Table 2.

Additionally, procedural duration and fluoroscopy time were investigated, and no difference was noted between the two groups (p=0.230 and p=0.980, respectively; Figure 2).

Aiming to assess the impact of the currently available knowledge and technologies employed for transcatheter ablation on the outcome and complications of the procedure, a meta-regression analysis was performed to assess the impact of year of publication, showing no relation between year of publication and acute success (p=0.325) or incidence of complications (p=0.795). Additionally, due to the wide age range of the included patients, varying from children to middle age, a meta-regression analysis was performed to assess the impact of age (Supplementary Figure 2), showing no direct relation with acute success (p=0.256) or complications (p=0.863).

## Discussion

The present meta-analysis, although mainly based on single high-volume Centres, observational studies, includes the largest series of patients comparing the outcome of left sided AP transcatheter ablation approaching alternatively by transseptal or retrograde transaortic access. This series emerges due to the absence of large randomized trials or prospective registries assessing the comparison between the two approaches for left sided AP ablation, resulting a potentially useful tool to help Electrophysiologists in planning the access for left sided APs catheter ablation procedures.

Overall, transseptal approach reported a higher acute success compared to transaortic retrograde approach. In fact, in experienced Centres transseptal approach may lead to easier manoeuvrability of the ablation catheters in the left atrium, compared to the more challenging manipulation approaching from the left ventricle across the aortic arch. Additionally, a more direct approach, as conferred by transseptal access through the catheter “entrapment” within the interatrial septum, may result in improved catheter stability and optimal contact on the mitral annulus, leading to a more effective radiofrequency delivery towards the left sided AP. Failure of an ablation attempt is in fact usually related to a suboptimal catheter stability and catheter-tissue contact during ablation. Of note, the only randomized trial included in the analysis, limited by the very small case sample (only 22 patients), did not find any difference between the two approaches [32].

Concerning recurrence of conduction over the AP, the incidence was limited between both groups, without significant difference. In fact, the mechanism leading to recurrence is related to a transient effect provided by suboptimal site of ablation, along with the oedema generated by the energy delivery [38]. The majority of difficulties for obtaining good stability through the transaortic approach seem therefore to impair acute efficacy, while the incidence of recurrences, although rare, occurs similarly with both approaches.

The overall incidence of complications did not differ between the two groups. It should be noted that pattern of complication is different, as transaortic approach was affected by a significantly higher incidence of vascular complications, while pericardial effusion was the most common complication following transseptal approach (although not reaching statistical significance, see Suppl Table 2). However, transseptal puncture needs specific training, and some Electrophysiology labs are not trained for this approach and therefore mandatorily manage left sided AP by transaortic approach. Of note, the number of transseptal access publications increased during recent years: this trend probably relates to the spread of left atrial ablation for atrial fibrillation, which increasingly favours the comfort level for transseptal puncture. However, in the absence of specific training, transseptal access may provide additional risk; therefore, the results of this analysis should not be generalized to all Electrophysiology Centres.

Of note, the overall incidence of complications did not differ compared to the incidence reported for other left-sided arrhythmias ablation approached by transseptal access [39]. Additionally, also vascular complications were comparable to those reported by other electrophysiological procedures [39], although higher than those reported by coronary artery interventional procedures, probably related to the need of anticoagulation during the procedure. Conversely, thromboembolic events did not differ between the two approaches, highlighting that this is not an access-related complication.

The meta-regression analysis, performed to assess the impact of the available knowledge and technologies on the outcome of accessory pathway ablation, showed no significant relation between acute efficacy or complications and year of publication. This finding suggests that left sided AP ablation can be safely and effectively performed even using conventional diagnostic and ablation catheters. In fact, although being related to reduction of radiological exposure for patients and physicians (40), the impact on the outcome of AP ablation seems not to be relevant, as previously reported concerning atrial fibrillation ablation. Of note, the overall procedural duration and the fluoroscopy time did not differ between the two approaches. Due to the different tools and technologies, both approaches reported a wide range of both procedural duration and radiological exposure, which appear shorter in the most recent publications. However, decreasing procedural and fluoroscopy durations were parallel between the two approaches, demonstrating that both access types benefit from technological improvements in terms of global simplification and shortening of the procedure, but not in terms of safety or efficacy.

Finally, age was not related to different outcome, in terms of both safety and efficacy. This finding emphasizes that left sided AP ablation can be safely performed even in children, in case of clear indication to perform catheter ablation, such as in case of symptomatic, high anterograde conduction APs.

**Limitations**

The present analysis includes a large and heterogeneous group of single Centre, observational studies: although heterogeneity was appraised by random effect, the inclusion of non-randomized, retrospective studies may limit the reproducibility of the results. Although excluding case samples and very small series, the experience of each single Centre in performing transcatheter ablation procedures or even left chambers access, including individual operators' comfort level with both the approaches, may have affected the access choice and the outcome of each single study results. Additionally, publication bias cannot be excluded, as a more favourable outcome would have driven the potential interest for publication of these series, compared to other single-Centres series that did never reach publication. However, it should be noted that parameters as year of publication, or age of the included patients, did not affect safety or efficacy of the ablation procedure. Finally, meta-regression analysis does not allow clinicians to drive causative inferences, but only speculative.

## Conclusion

Left sided AP transcatheter ablation is effective in around 95% of the patients in trained operators hands, and can be performed with a very limited incidence of complications even in younger patients, when indicated. Transseptal access provides a higher acute success in achieving left sided AP ablation, while late recurrences are limited, but occur similarly following both approaches. While procedural duration and fluoroscopy use are similar, retrograde approach is affected by a relatively higher incidence of vascular complications.


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## Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

## Figure legends

**Figure 1.** Acute success (A; 2030 patients from 29 studies) and incidence of recurrences (B; 1338 patients from 23 studies) following left-sided accessory pathways ablation.

**Figure 2.** Complications of left-sided accessory pathways ablation (1750 patients from 23 studies), procedural duration (1238 patients from 22 studies) and fluoroscopy times (1108 patients from 18 studies) of left-sided accessory pathways transcatheter ablation procedures.

**Table 1.** Pooled clinical features of included studies (2030 patients, 29 studies).

| | Transseptal approach (1017 patients) | Transaortic approach (1013 patients) | p-value |
|---|---|---|---|
| Age, years (IQR) | 27.8 (17.9-37.6) | 34.5 (30.1-39.0) | 0.10 |
| Males, % (IQR) | 67 (62-72) | 67 (59-65) | 0.90 |
| Concealed accessory pathways, % (IQR) | 34 (20-48) | 31 (8-59) | 0.76 |
| Site of accessory pathway, % (IQR): | | | |
| - Left anterolateral (%) | 7 (0.0-15) | 7 (2-11) | 0.68 |
| - Left lateral (%) | 54 (36-70) | 67 (57-76) | 0.08 |
| - Left posterior (%) | 32 (20-44) | 12 (4-21) | 0.02 |
| - Left posteroseptal (%) | 7 (3-12) | 14 (7-21) | 0.60 |
| Symptoms, % (IQR): | | | |
| - AVRT (%) | 82 (38-100) | 86 (76-95) | 0.81 |
| - AF (%) | 13 (8-20) | 31 (15-51) | 0.05 |
| Acute success, % (IQR) | 98 (96-100) | 94 (90-97) | 0.02 |
| Number of RF/Cryo applications, n (IQR) | 6.7 (4.6-8.6) | 6.1 (4.2-8.0) | 0.63 |
| Procedural duration, min (IQR) | 179.0 (139.7-218.3) | 145.5 (109.2-181.8) | 0.23 |
| Fluoroscopy time, min (IQR) | 32.2 (19.0-45.3) | 32.9 (22.7-43.1) | 0.98 |
| Complications, % (IQR) | 0.4 (0.0-1.2) | 1.2 (0.3-2.6) | 0.30 |
| Follow-up duration, months (IQR) | 14.5 (10.8-18.1) | 12.75 (9.4-16.1) | 0.62 |
| Recurrences, % (IQR) | 3.2 (1.6-6.1) | 2.3 (0.5-4.6) | 0.31 |

AVRT: atrioventricular re-entrant tachycardia; AF: atrial fibrillation; RF: radiofrequency; Cryo: cryoablation; IQR: interquartile range.

**Table 2.** Complication pattern reported by transseptal and retrograde transaortic approach

| | Transseptal approach (1017 patients) | Transaortic approach (1013 patients) | p-value |
|---|---|---|---|
| Vascular complications (hematoma, pseudoaneurysm) | 0 | 8 | 0.03 |
| Cardiac tamponade | 6 | 3 | 0.51 |
| Stroke/TIA | 2 | 1 | 1.00 |
| Death | 0 | 0 | 1.00 |
| Peripheral embolism | 0 | 3 | 0.12 |
| Coronary artery dissection/infarction | 1 | 3 | 0.37 |
| Mitral regurgitation | 1 | 2 | 0.62 |
| Aortic regurgitation | 0 | 4 | 0.06 |
| Aortic dissection | 0 | 1 | 1.00 |

TIA: transient ischemic attack.

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**Figure 1.**

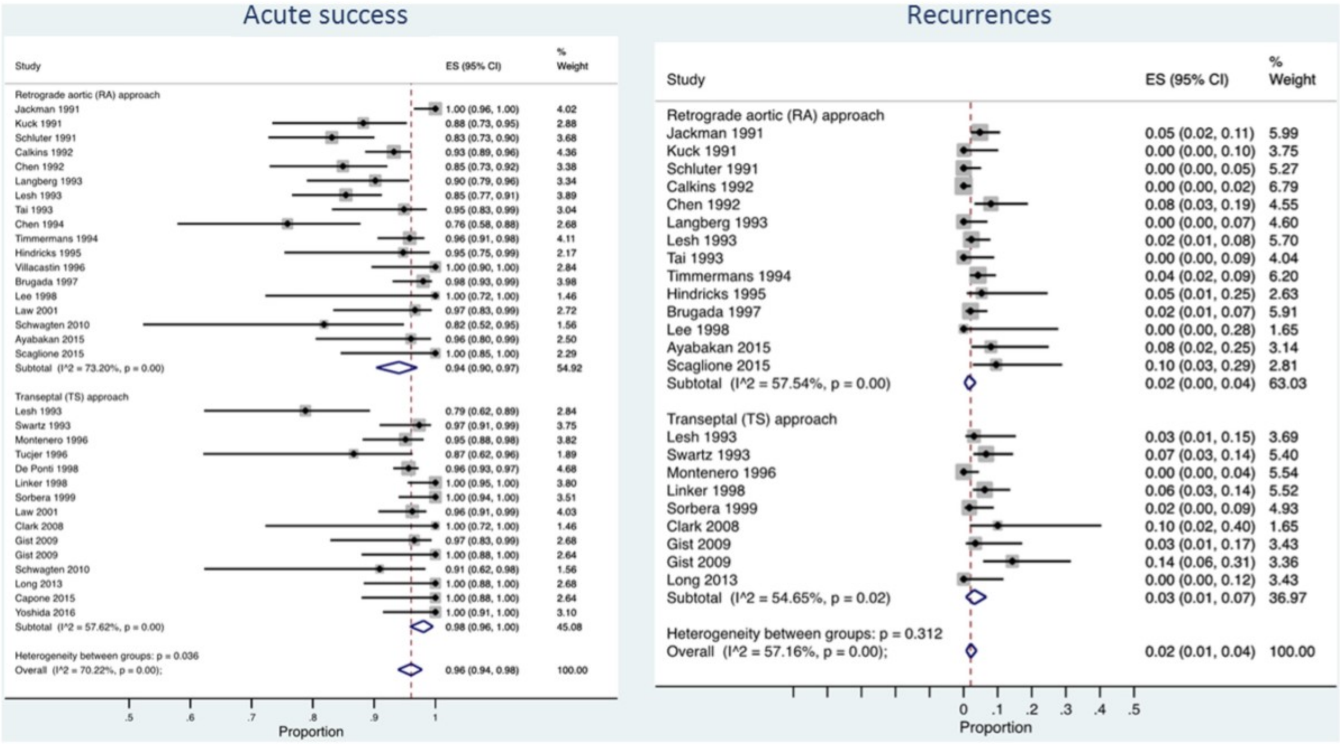


**Figure 2.**