

# Hybrid ablation versus transcatheter ablation for atrial fibrillation

## A meta-analysis

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### Abstract

**Background:** Despite the successful creation of complex lesion sets during hybrid ablation (HA), reoccurrence of atrial fibrillation (AF), and/or atrial arrhythmia and procedural complications still occur. The main objective of this study was to compare the efficacy and safety between HA and transcatheter ablation (TA).

**Methods:** We searched Pubmed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) database up to October 2017. Studies that satisfied our predefined inclusion criteria were included. Of the 894 records, 4 studies encompassing 331 patients were included in our study. We assessed pooled data using random-effect or fixed-effect model. The main endpoint was freedom of atrial arrhythmia after follow-up duration, secondary results were procedure time and intraoperative and postoperative adverse events. Similarly, tertiary outcomes were endocardial time, fluoroscopy time, and postoperative hospitalization.

**Results:** Compared with TA, HA treatment through mini-thoracotomy access improved superiority in freedom of atrial arrhythmia after follow-up duration (odds ratio [OR]=6.67, 95% confidence interval [CI]: 2.63–16.90), but HA increased the incidence of intraoperative and postoperative adverse events for AF patients (OR=2.98, 95% CI: 1.30–6.83). HA through either mini-thoracotomy or transdiaphragmatic/subxiphoid access had longer procedure time and postoperative hospitalization than TA. However, endocardial time was shorter than TA.

**Conclusions:** For AF patients, HA possessed of an overall superior outcome using mini-thoracotomy way to TA. Although HA had longer procedure time, it yielded a reduction in endocardial time. Meanwhile, we should pay attention to the significantly high risk of intraoperative and postoperative adverse events that the HA generated.

**Abbreviations:** AADs = antiarrhythmic drugs, AF = atrial fibrillation, CI = confidence interval, HA = hybrid ablation, MD = mean difference, OR = odds ratio, Per or LSPer AF = persistent or long-standing persistent atrial fibrillation, PRISMA = the Preferred Reporting Items for Systematic Reviews and Meta-analysis, SA = surgical ablation, SD = standard deviation, TA = transcatheter ablation.

**Keywords:** atrial fibrillation, hybrid ablation, surgical ablation, transcatheter ablation

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## 1. Introduction

Atrial fibrillation (AF) is the most common sustained supraventricular arrhythmia, with the summary annual incidence of 5.38 per 1000 population in Asian countries.<sup>[1]</sup> It is associated with mortality and detrimental events including palpitations and cardiac hemodynamic disorders which increase the risk of thromboembolism and stroke.<sup>[1]</sup> The application of antiarrhythmic drugs (AADs) has encountered challenges due to their limited efficacy and safety. Transcatheter ablation (TA) which regards pulmonary veins isolation as a cornerstone is well established for the satisfactory effectiveness in termination of paroxysmal AF. As such, choosing TA as the first-line treatment of paroxysmal AF has reached an agreement among cardiologists.<sup>[2]</sup> Although promising, it is suboptimal, particularly in persistent or long-standing persistent AF (Per or LSPer AF) which is partly due to the absence of gaps in ablation as well as unavailable of other arrhythmogenic atrium substrates. To our knowledge, over the last decades, with the stand-alone surgical treatment of AF advances toward minimally invasive and off-pump procedures, Cox-maze III has been rendered obsolete for its complexity and high complication rates.<sup>[3]</sup> In addition, minimally invasive surgical ablation (SA) is gradually completing more complex procedures in order to be as similar as Cox-maze III/IV lesion sets.

Whereas, neither TA nor minimally invasive SA could accomplish the complete ablation lesion for stand-alone AF.

AF is regarded to be a progressive arrhythmia. For Per or LSPer AF, which is often transitioned from paroxysmal AF, a few clinical factors have been associated with the progression of the disease and continued efforts are underway to identify additive strategies to improve outcome.<sup>[4]</sup> In order to achieve this demanding requirement of cure rate, cardiovascular surgeons collaborated with electrophysiologists to proceed the minimally invasive SA followed by TA which are 2 complementary but totally different approaches. First characterized by Pak et al, this integrated method is also known as “hybrid” ablation and seems to be a very attractive treatment option for nonparoxysmal AF patients.<sup>[5]</sup> This approach produces perfect transmural lesions from the epicardial side, while allowing endocardial confirmation of ablation targets to customize lesion sets and endocardial touch-up to close conduction gaps. Since then, a few heart centers around the world have initiated to apply hybrid ablation (HA) treatment for AF patients who have failed one or more previous ablation and with evidence of enlarged left atrium. A meta-analysis demonstrated that minimally invasive SA may achieve superior success rates to TA in the short term, although the complications may be higher than TA.<sup>[6]</sup> Unfortunately, we are still unclear whether the relatively complex HA is superior to TA. Therefore, it is necessary for us to conduct this meta-analysis which aims to search for relevant literature and find solutions.

## 2. Methods

### 2.1. Search strategy

This study was prepared in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.<sup>[7]</sup> The review protocol has been registered in PROSPERO (CRD42017081847). All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

We retrieved Pubmed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) up to October 2017. No language restriction was applied. We used the following terms: ((atrial fibrillation [MeSH term] OR atrial fibrillation [Text Word]) AND (hybrid [Text Word] OR epicardial-endocardial [Text Word] OR surgical-transcatheter [Text Word] OR thoracoscopic-transcatheter [Text Word])). We searched all potentially eligible studies for review, such as conference literature. Reference lists of included studies were also reviewed for identification of further relevant studies.

### 2.2. Study selection

Included studies must accord with the following inclusion criteria: study involved comparison of HA with TA for AF; availability of data on patients' baseline characteristics, intra-operative and postoperative outcomes; and the follow-up duration should exceed 6 months after ablation.

The main exclusion criteria are as follows: “hybrid” treatment was not represented to minimally invasive SA and TA; no comparison between HA and TA; ablation procedure was concomitant with other cardiac surgery or on-pump surgery; and case report, review article, and duplicate data. We also acquired some conference abstracts and emailed to authors for more information. Two reviewers independently reviewed the searched literature and evaluated them according to the criteria. A third

reviewer resolved the discrepancies and checked the whole meta-analysis procedure again.

### 2.3. Data extraction

Data were extracted according to the criteria above. We recorded data including age (mean [standard deviation (SD)]), number of males, body mass index (mean [SD]), number of hypertension and diabetes, CHADS2 score (mean [SD]), and left atrial diameter (mean [SD]), which are associated with the occurrence and prognosis of AF. Other data including number of previous treatment, the percentage of Per or LSPer AF patients, ejection fraction (mean [SD]), postoperative hospitalization (mean [SD]), number of freedom from arrhythmia with or without AADs and procedure-related adverse events were also recorded. Mean [SD] format data of postoperative hospitalization and procedure time were utilized in data combining. In 2 studies, we transformed median values to mean values and interquartile range to SD according to the Cochrane Handbook of Systematic Review.<sup>[8]</sup> Two independent reviewers assessed the risk of bias according to the PRISMA recommendations.

### 2.4. Statistical analysis

The primary outcome was freedom of atrial arrhythmia after follow-up duration. Secondary outcomes were the procedure time, intraoperative and postoperative adverse events which contained cardiac tamponade, phrenic nerve paralysis, cerebrovascular accident, and so on. In addition, tertiary results were endocardial time, fluoroscopy time during ablation procedures, and postoperative hospitalization.

We analyzed freedom of atrial arrhythmia after follow-up duration, intraoperative and postoperative adverse events as dichotomous variables. For analysis of the proportion of patients who achieve sinus rhythm after the operation and those who have any adverse episodes related to the procedure, we calculated pooled estimates of odds ratio (OR). For continuous variables such as procedure time, we calculated pooled estimates of the mean difference (MD).

We used the Cochrane  $Q$  test to assess heterogeneity between studies. We also used  $I^2$  test to assess the magnitude of the heterogeneity. When  $P$  value for heterogeneity was  $>.10$  and  $I^2 < 50\%$ , indicating minor heterogeneity between studies, and the fixed-effect model was used to calculate the pooled OR and MD.<sup>[9]</sup> If the  $P$  value for heterogeneity was  $\leq .10$  or  $I^2 \geq 50\%$ , indicating moderate to higher heterogeneity between studies, and the random-effect model was used to calculate the pooled OR and MD.<sup>[10]</sup> We analyzed data with the Review Manager Version 5.3 software package (Revman, The Cochrane Collaboration). To investigate possible sources of heterogeneity, we performed subgroup analysis.

## 3. Results

### 3.1. Basic characteristics of AF patients with HA and TA

Our study searched 894 articles for selection. According to the inclusion criteria, we finally sorted out 4 articles encompassing 331 patients for further study. The selection protocol is summarized in Fig. 1. The 4 studies were all cohort studies published between 2011 and 2017 (Table 1).

All studies considered the definition of AF recurrence as any atrial arrhythmia lasting more than 30 seconds after the several months blanking period. Follow-up duration ranged from 6 to 27

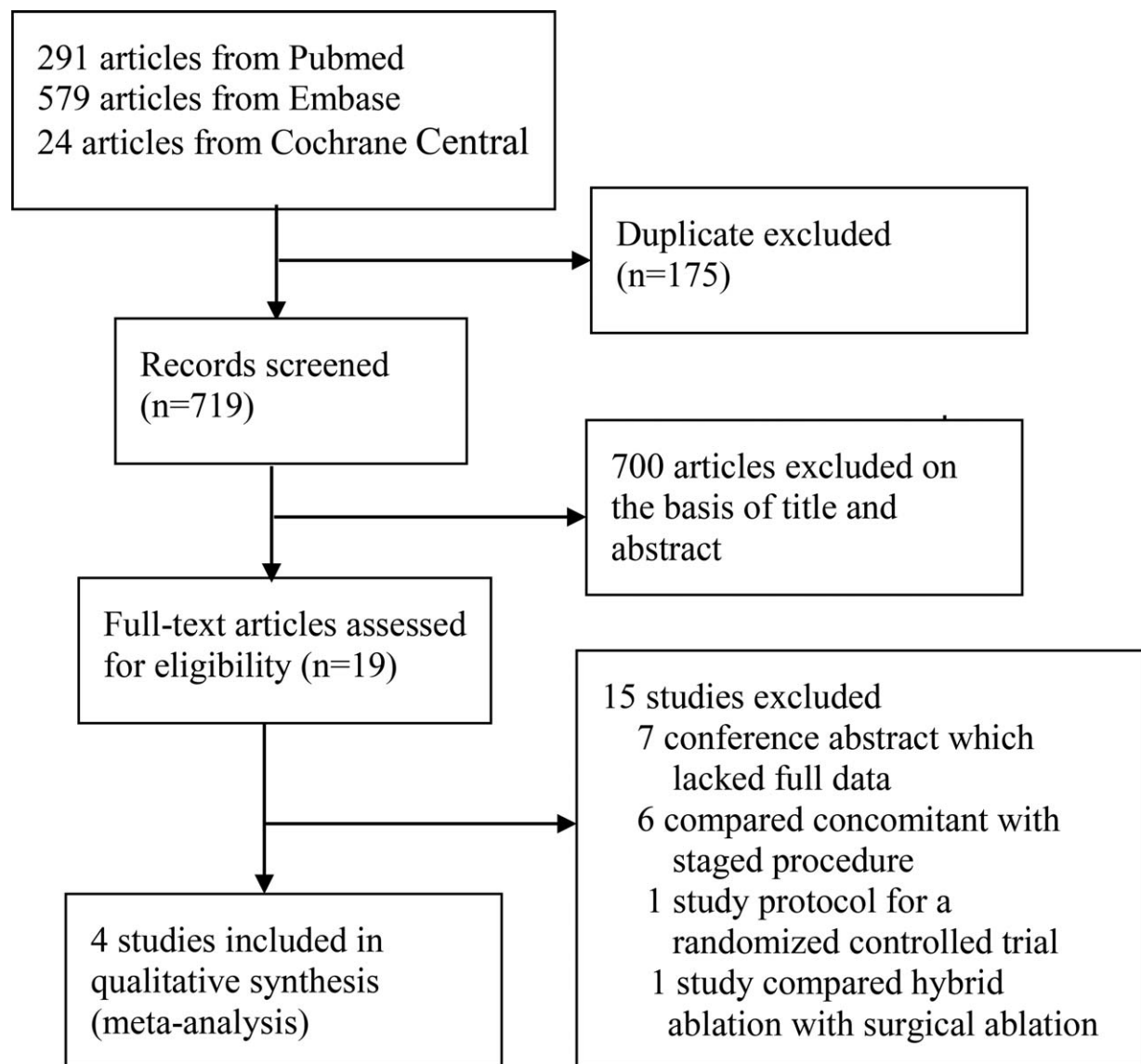


Figure 1. Flowchart of literature selection.

months. One study compared long-term efficacy and complication rates of HA to other more commonly utilized invasive procedures—TA and the complete Cox-maze, while the rest of studies compared with TA. All studies compared the success rate of sinus rhythm with or without AADs and adverse events between HA and TA. Three studies compared HA with TA on procedure time, postoperative hospitalization, fluoroscopy time, and endocardial time. Two studies performed HA via transthoracic approach, one via transdiaphragmatic access and another one via subxiphoid incision.

The concrete ablation lesion sets, ablation device, ablation energy, and ablation sequence of each study were summarized in Table 2. Mahapatra et al<sup>[11]</sup> permitted AADs and warfarin usage for at least 3 months and warfarin (goal INR 2–3) was continued indefinitely for CHADS2 score  $\geq 2$ . One patient in the TA group had cardiac tamponade requiring pericardiocentesis. Kress et al reported that in HA group, 1 death caused by a gastrointestinal bleed occurred approximately 2 weeks after the procedure, 1 presented with an acute right posterior cerebral

artery stroke on day 2 after the procedure, 1 of pericardial effusion, and 2 with groin complication that required surgical intervention. Meanwhile, cardiac tamponade occurred in 2 TA patients.<sup>[12]</sup> Edgerton et al showed 1 patient in HA group and 1 patient in TA group developed cardiac tamponade, 1 patient in HA group had transient phrenic nerve paralysis, which completely resolved at the 6-month follow-up. Three patients in HA group died within the blanking period of 3 months (1 died of esophageal fistula, 1 died of large thromboembolic stroke, 1 died suddenly at home) and they were not included in the recurrence of atrial arrhythmia analysis.<sup>[13]</sup> The study of Genev et al indicated that 4 patients underwent cardiac tamponade and another 4 patients presented complications at the catheter insertion site of groin in TA group. Besides, 1 suffered procedure-related death, 2 experienced Dressler syndrome and pneumonia, respectively, and 2 had pleural effusion in HA group. However, they did not introduce the method of procedure and all patients were prescribed postoperative AADs and anticoagulation treatment.<sup>[14]</sup>

**Table 1****Baseline characteristics of included studies.**

Characteristics	Kress <sup>[12]</sup>		Edgerton <sup>[13]</sup>		Genev <sup>[14]</sup>		Mahapatra <sup>[11]</sup>	
	HA (n=64)	TA (n=69)	HA (n=24)	TA (n=35)	HA (n=22)	TA (n=72)	HA (n=15)	TA (n=30)
Age, y	60.7±10.2	62.3±8.0	63.8±8.9	63.0±10.4	68.1±10.9	61.4±8.5	59.5±2.4	59.2±1.5
Male	59	51	22	29	16	49	8	19
BMI	35±6.2	34.6±7.5	30.8±5.0	29.2±4.0	NA	NA	NA	NA
Hypertension	38	53	15	22	19	57	7	20
Diabetes	9	13	1	4	4	25	3	4
CHADS2 score	1.8±1.2	2.1±1.4	1.13±0.95	1.11±0.99	3.5±2.5	3.5±3.5	NA	NA
LA diameter, cm	4.8±0.6	4.7±1.2	5.15±0.28	5.24±0.47	NA	NA	52.3±10.3	45.3±5.3
EF, %	53.6±11.4	53.4±7.5	52.6±8.6	49.2±9.3	NA	NA	47.0±3.0	54.7±2.1
Per-LSPer AF, %	100	100	100	100	NA	NA	100	100
Previous amiodarone	NA	NA	2	2	NA	NA	9	18
Previous ablation	37	17	NA	NA	0	0	15	30
Follow-up duration, mo	13 (12–23)	23 (12–27)	24	24	≥12	NA	450±20	302.0±65.0
Procedure time, min	313.7±60.8	233.1±53.1	276.9±63.5	203.1±67.3	NA	NA	450±20	302.0±65.0
Endocardial time, min	NA	233.1±53.1	101.3±23.2	203.1±67.3	NA	NA	172.0±45.0	302.0±65.0
Fluoroscopy time, min	58.3±20.3	66.8±23.5	36.2±15	40.3±11.6	NA	NA	17.6±1.3	42.3±2.1
Days of hospitalization	3.1±1.9	1.9±1.1	5 (3.25–8)	1 (1–3)	NA	NA	5.3±0.1	1.13±0.1
Procedural complication	5 (1 death)	2	5 (3 death)	1	5 (1 death)	8	0	1
Free of arrhythmia after follow-up	41	29	4	19	13	14	14	17

BMI = body mass index, EF = ejection fraction, HA = hybrid ablation, LA = left atrium, NA = not available, Per-LSPer AF = persistent and long-standing persistent atrial fibrillation, TA = transcatheter ablation.

The assessment of the risk of bias in included studies is available as an appendix (see Figure, Supplemental Content, which illustrates the risk of bias in each study, <http://links.lww.com/MD/C748>).

### 3.2. Primary outcome

Pooled results (Fig. 2) showed no statistical difference in freedom of atrial arrhythmia after follow-up duration for HA compared with TA (OR=2.10, 95% confidence interval [CI]: 0.45–9.88). However, significant heterogeneity was also revealed ( $P < .0001$  for heterogeneity,  $I^2 = 86\%$ ).

To reduce heterogeneity, we conducted a subgroup analysis. We divided the studies into transthoracic group and transdiaphragmatic/subxiphoid group and re-assessed the outcomes of freedom from atrial arrhythmia after follow-up duration.

Pooling the data of transthoracic group of HA showed better outcome of freedom from atrial arrhythmia after follow-up duration with or without AADs (OR=6.67, 95% CI: 2.63–16.90;  $P = .62$ ,  $I^2 = 0$ , Fig. 2.1.1), compared with TA. In transdiaphragmatic/subxiphoid group, no statistical difference was observed in the OR, whereas, significant heterogeneity still appeared in the pooled data of freedom from atrial arrhythmia after follow-up duration (Fig. 2.1.2).

### 3.3. Secondary outcomes

In a pooled analysis of 3 studies, we found that the procedure time of HA is longer than TA (MD=101.16, 95% CI: 54.48–147.84;  $P < .0001$  for heterogeneity,  $I^2 = 90\%$ , Fig. 3). Pooling the data of 4 studies, HA was associated with relatively higher risk of intraoperative and postoperative adverse events which

**Table 2****Ablation lesion set, ablation timing, ablation access, and part of follow-up information of included studies.**

Studies	Timing	Hybrid procedure (Minimally invasive SA)	Hybrid procedure (TA)	Transcatheter procedure	Follow-up
Mahapatra <sup>[11]</sup>	Staged, TA performed 3–5 d after minimally invasive SA	RFA, bilateral thorascopic PVs were ablated and tested for evidence of entrance/exit block. Isolation of SVC, placement of roof line, mitral line, elimination of ganglia response, LOM ablation, and LAA exclusion	RFA. If atrial flutter was induced, it was mapped and ablated. If AF was induced, checking PVs isolation, roof line, then mitral isthmus line and CFAEs were performed	RFA. Antral ablation, roof line, and CTI line. Mitral line was made in 17 cases, CS ablation performed in 9 cases, SVC isolated in 11 cases, and CFAEs performed in 12 cases	EKG, 7-d Holter, 24-h Holter, telephone
Edgerton <sup>[13]</sup>	Concomitant	RFA, subxiphoid. Using irrigated unipolar RF ablator to perform PVs, posterior wall, LOM (without dissection) and the lateral right atrium isolation. Assessing PVs entrance and exit block	RFA. Verification of the surgical lesions Further ablation: CS and LAA. If CFAEs were detected in the LA, they were ablated	RFA. Isolation of PVs, posterior wall, LOM, CS, LAA, and right atrium	EKG, 7-d Holter, AADs was continued after 3 mo
Kress <sup>[12]</sup>	Concomitant	Cryo or RFA, transdiaphragmatic. Isolation of PVs, posterior LA wall with a 3-cm Numeris probe which was saline-irrigated and vacuum attached, at 30W for 90s	Isolation of PVs with catheter ablation or the cryoballoon, CFAEs and linear lesions with RFA	Isolation of PVs with RFA or cryoballoon, CFAEs and linear lesions with RFA	EKG, loop recorder, Holter, AADs was permitted
Genev <sup>[14]</sup>	NA	Mini thoracotomy	NA	NA	NA

AADs = antiarrhythmic drugs, CFAEs = complex fractionated atrial electrograms, Cryo = cryoablation, CS = coronary sinus, CTI = cavotricuspid isthmus, EKG = Electrocardiogram, LA = left atrium, LAA = left atrial appendage, LOM = ligament of Marshall, NA = not available, PVs = pulmonary veins, RFA = radiofrequency ablation, SA = surgical ablation, SVC = superior vena cava, TA = transcatheter ablation.

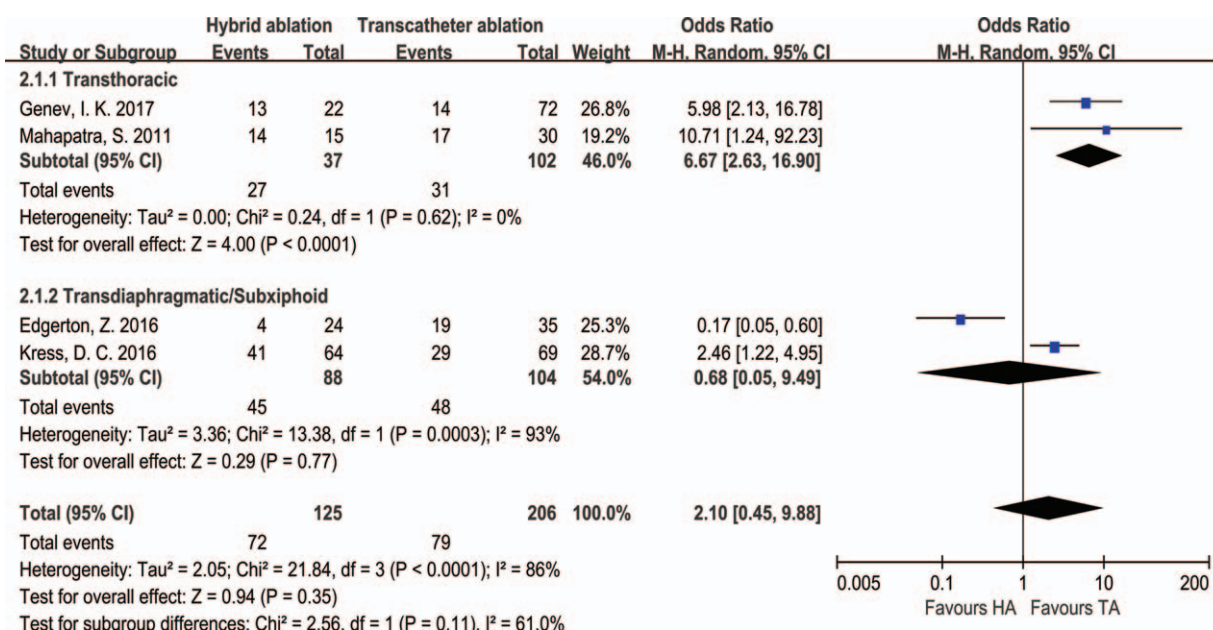


Figure 2. Freedom of atrial arrhythmia after follow-up duration; 2.1.1, freedom of atrial arrhythmia through mini-thoracotomy access after follow-up duration; 2.1.2, freedom of atrial arrhythmia through transdiaphragmatic/subxiphoid access after follow-up duration.

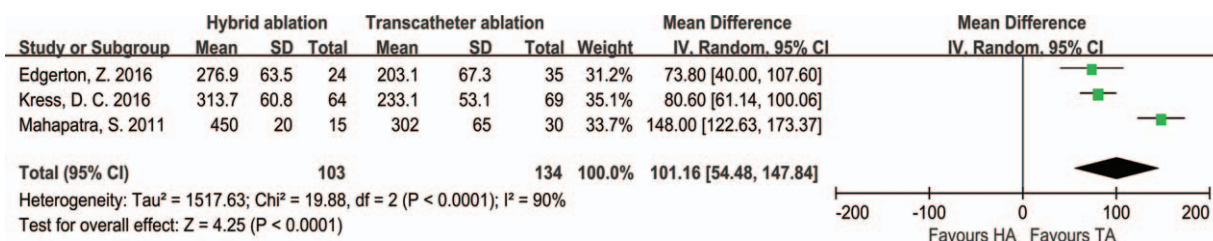


Figure 3. Procedure time in the included studies.

contained cardiac tamponade, phrenic nerve paralysis, cerebrovascular accident, and so on with no heterogeneity for risk estimate in comparison to TA (OR=2.98, 95% CI: 1.30–6.83, P = .52, I<sup>2</sup>=0, Fig. 4).

3.4. Tertiary outcomes

Another pooled analysis indicated the endocardial time of HA is shorter than TA (MD = -138.08, 95% CI: -191.47 to -84.69; P < .0001 for heterogeneity, I<sup>2</sup>=94%, Fig. 5A). On the contrary, no statistical significance was found in the fluoroscopy time compared among HA and TA (Fig. 5B). Anyway, there was high

heterogeneity for the risk estimate in endocardial time and fluoroscopy time.

Furthermore, pooled analysis of 3 studies showed statistical significance in postoperative hospitalization between HA and TA (Fig. 6). The problem of high heterogeneity for risk estimate existed yet.

4. Discussion

Our meta-analysis compared effectiveness and safety of HA procedure with TA procedure for AF patients and got the following findings: HA was associated with a longer procedure

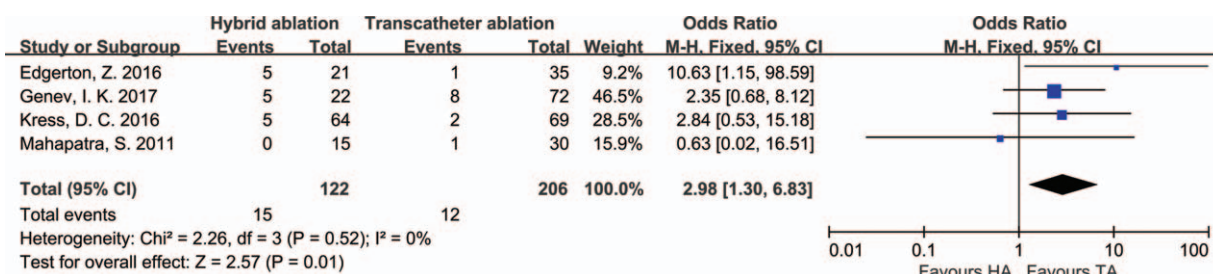


Figure 4. Intraoperative and postoperative adverse events in the included studies.

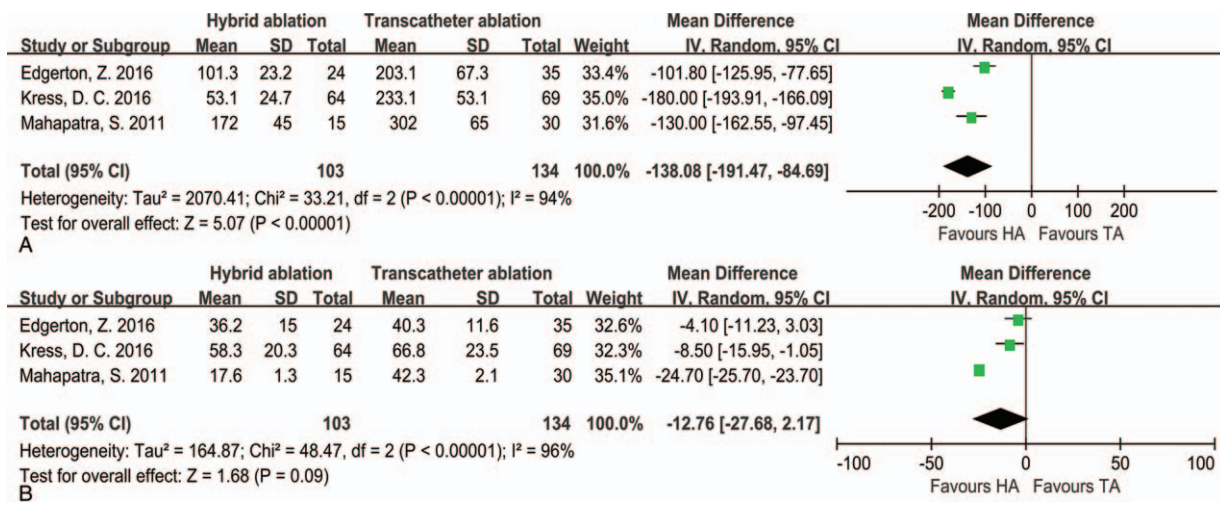


Figure 5. (A) Endocardial time in the included studies. (B) Fluoroscopy time in the included studies.

time and postoperative hospitalization than TA while a shorter endocardial time than TA; HA through mini-thoracotomy led to a better outcome in freedom of atrial arrhythmia with or without AADs compared with TA after follow-up duration; HA had a higher risk of intraoperative and postoperative adverse episodes than TA. In general, our finding data supported the efficacy of HA by means of mini-thoracotomy for AF patients. On the other hand, we could never neglect the side effects the procedure resulted in.

With electrophysiologists' in-depth study on the mechanism of AF, 3 concepts competed to explain the initiation, perpetuation, and progression of AF: multiple reentrant wavelets, rapidly discharging automatic foci and a single reentrant circuit with fibrillatory conduction.<sup>[15]</sup> Finally, structural remodeling and electrical remodeling of atrium induced by AF further transformed AF from paroxysmal to persistent and long-standing persistent status, and this is also the result of multiple factors.<sup>[4]</sup> For instance, inflammation and myocardial oxidative stress are acknowledged to play a pivotal role in the development and perpetuation of AF, which are also associated with AF recurrence post-TA.<sup>[16,17]</sup> Complicated pathophysiological mechanisms make the treatment of AF no longer restricted to AADs. The ablative procedure is therefore aimed to either eliminate the trigger sites initiating AF or modify the arrhythmogenic substrate. Cardiologists believe that circumferential pulmonary veins isolation is the cornerstone of AF ablation procedures and they use radiofrequency energy or cryotherapy to interrupt the abnormal conduction pathway.<sup>[18]</sup> Electrophysiologists avoid the effect of general anesthesia and single lung ventilation to complete lesion sets. They can ablate cavotricuspid isthmus,

mitral isthmus and identify any epicardial ablation lines gaps to decrease the occurrence of atrial flutter and atrial tachycardia after the operation. But the point-to-point lesions hardly achieve a transmural lesion, and it is impossible to resect the left atrial appendage and cut the ligament of Marshall otherwise surgeons are accessible from the epicardial side. In 2005, Dr Wolf first completed lesion sets similar to Cox-maze IV through thoracoscopic approach without on-pump.<sup>[19]</sup> Surgeons have access to ablate more ganglionic plexuses which can also be attained from endocardial side, dividing the ligament of Marshall and resecting the left atrial appendage for reducing stroke risk which is the most common place to form thrombosis and the trigger site of AF.<sup>[20]</sup> At the same time, the phrenic nerve and esophagus injury caused by catheter ablation can be avoided due to a clearer vision. Nevertheless, some inaccessible sites could not ablate by surgeons from the epicardial side and they lack mapping systems designed for epicardial use.

In fact, the ideal ablation strategy for Per or LSPer AF remains uncertain at the present. Some electrophysiologists put forward that combined cryoballoon and radiofrequency ablation may improve the AF termination rates and long-term arrhythmia-free survival in Per or LSPer AF patients. In their opinion, the cryoballoon catheter may cause wider antral circumferential ablation and achieve additional substrate modification due to the physical contact with remote atrial tissue away from the pulmonary vein orifice.<sup>[21]</sup> However, present studies failed to demonstrate whether this combined approach improve the rate of event-free survival by ablation compared with totally radiofrequency ablation.<sup>[22]</sup> In the regard, the addition of percutaneous endocardial catheter ablation and thoracoscopic epicardial

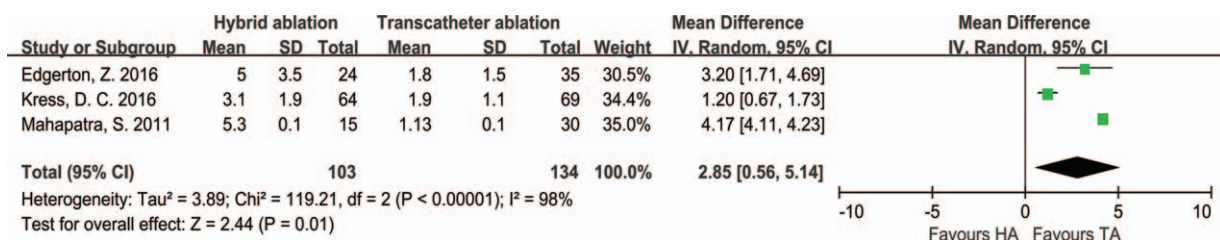


Figure 6. Postoperative hospitalization in the included studies.

ablation may increase the success rate by combining some of the potential advantages of the separate procedures theoretically. However, several patients suffer from Per or LSPer AF are often accompanied by enlargement of left atrium, history of previous ablation, and other related risks which facilitate AF occurrence. We found that 2 of 4 included studies selected patients with refractory AF for clinical studies. And all the researchers selected a proportion of patients with basic diseases, such as hypertension and diabetes, which were associated with the occurrence of AF and promoted the maintenance of AF.<sup>[23]</sup> For this reason, the treatment is difficult to achieve optimistic and satisfactory results and may require repeated ablation to improve the cure rate of AF. As an emerging treatment for AF, HA is still in the fledgling period and only a small fraction of clinical centers are available to perform HA independently because the cost of building a hybrid operating room is a formidable obstacle. Khoynzhad et al summarized outcomes of 15 HA studies from 2011 and pointed out that different ablation methods yielded various outcomes of HA including the overall AF cure rate ranged from 19% to 94% and the incidence of complications ranged from 0% to 24%.<sup>[24]</sup> The results of different clinical centers vary widely. The application of unipolar radiofrequency devices and immaturity of the ablation procedure may lead to the low success rate which reported by Gehi.<sup>[25]</sup> In our study, 2 researchers used transdiaphragmatic/subxiphoid approach to complete ablation procedure in which unipolar ablation device was applied and the lesion sets were incomplete. Currently, there are 2 multicenter clinical prospective trials comparing HA with TA for Per or LSPer AF including CONVERGE and DEEP studies which unified HA strategy, ablation lesions, and follow-up method and promoted reliability for future study.

Findings from our meta-analysis show a beneficial effect on freedom from atrial arrhythmia of HA through mini-thoracotomy access versus TA. In another word, HA was progressive in AF treatment in some sense. However, a recent study by Edgerton et al deserves mention on account of their lower efficacy of hybrid approach in patients with large atrium and Per or LSPer AF, possibly tempering our viewpoint.<sup>[13]</sup> They used a unipolar radiofrequency device through subxiphoid way to perform trigger site ablation and substrate modification and reported the success rate of sinus rhythm was only 19%. The result undoubtedly confirms the existing concerns about the ability of monopolar devices to create transmural lesions with a bidirectional conduction block on the beating heart. While mini-thoracotomy allows for circular electrical isolation of pulmonary veins, left atrial appendage closure, and ligament of Marshall, it requires chest incisions and sequential lung deflation. This can be difficult to achieve in patients suffering from chronic pulmonary disease or after pulmonary surgery. Transdiaphragmatic/Subxiphoid access used in the HA is independent of lung function and anatomy, allowing for extensive ablation in the posterior wall of left atrium. Additionally, the left atrial appendage exclusion represents an advantage of the thoroscopic approach, but it can also be combined safely with transdiaphragmatic/subxiphoid access in a selected population.<sup>[26]</sup> So, transdiaphragmatic/subxiphoid way in HA procedure should continue to be explored and improved no matter there is no statistical significance of the included 2 studies compared with TA.

Our study indicated the more frequent incidence of procedural complications and longer procedure time in HA group. Actually, we note that 5 patients died after operation especially after transdiaphragmatic/subxiphoid access. As far as we know, there has been an elevated adverse event rate through the convergent

transdiaphragmatic way in most published series, mostly related to atrial-esophageal fistula and sudden death.<sup>[25]</sup> But then again, any attempt tackling such a challenge is going to be tough. The combined expertise of electrophysiological and surgical specialists working together as a heart team improves the likelihood that any difficulty or complication can be quickly recognized and addressed and a reasonable ablation strategy can be worked out and improves the durability and satisfaction of HA for AF patients. To date, different heart centers have used the rather variable surgical-transcatheter procedure. Experience and proficiency in HA procedure between heart centers are also not the same. So, achieving obvious therapeutic efficacy and safety in a short period of time is difficult.

The limitations of the article: Our review was based on data from mostly observational studies. No researchers have conducted randomized controlled trials that inclusion of them would allow a more robust comparison; the including studies and research data are less, the findings require further validation of robust data from larger, longer studies in the future. And more high level of evidence need to be included in the meta-analysis in the future; the timing of the different stages of HA is still a matter of debate, prolonged procedural time of combined approach might be deleterious in some patients. We need to compare staged procedure with TA in the future; and data of procedure time and postoperative hospitalization were not all recorded as mean (SD). One study was excluded when comparing the procedure time, postoperative hospitalization, endocardial time, and fluoroscopy time.

## 5. Conclusions

This meta-analysis preliminarily demonstrated that HA by means of mini-thoracotomy was more efficacious than TA after follow-up duration with or without AADs. However, this procedure has still a considerable occurrence rate of intraoperative and postoperative adverse events even in experienced centers and longer procedure time despite the endocardial time was shorter than TA.

## Author contributions

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**Funding acquisition:** Yongfeng Shao.

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