INTRODUCTION

As a global epidemic, atrial fibrillation (AF) is the commonest form of arrhythmia and a well-established risk factor of mortality and morbidities such as stroke and heart failure.1,2 The four facets for AF management include lifestyle modification, anticoagulation, rate, and rhythm control.3,4 Antiarrhythmics and ablation procedures are strategies for rhythm control, and recent trials have shown potential benefits of catheter ablation to reducing cardiovascular events and death in AF patients especially with heart failure.5,6 Catheter (CA) and thoracoscopic (TA) ablation are the two approaches for AF ablation, however, the optimal approach remains controversial because of the paucity of randomized trials. This meta-analysis aimed to compare the efficacy and safety outcomes for CA vs TA at treating AF across randomized trials.

METHODS

We searched Pubmed, Embase, and Cochrane databases from 1 January 1980 to 31 December 2019 using search terms "atrial fibrillation," "ablation" or "pulmonary vein isolation," "catheter or percutaneous," and "minimally invasive or thoracoscopy." Eligible studies must be original randomized trials reporting both CA and TA outcomes. Two authors screened studies for inclusion, and data pertaining to study design, characteristics, efficacy, and adverse events were recorded. Reviewer Manager (Version 5.3.5, The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) program was used for meta-analyses using random effects models. Pooled odds ratios (OR) with 95% confidence intervals (95% CI) were calculated and Forrest Plots constructed. The primary efficacy endpoint was AF recurrence at 1-year, and primary safety endpoint was total adverse events. Cochrane Q and I² statistic were used to assess studies’ heterogeneity.
heterogeneity, and Funnel plots for publication bias. The PRISMA guidelines were followed during the conduct of this meta-analysis.

3 | RESULTS

There were 652 articles generated from the search, and the abstract screening excluded 122 duplicate studies, 193 unrelated studies, 162 reviews, 148 single arm studies, and eight nonrandomized studies. Amongst 19 full-text articles reviewed, five reviews, five nonrandomized studies and three incomplete randomized trials were excluded, leaving six randomized trials totaling 465 patients (254 CA and 211 TA) eligible.\(^7,12\) The study design and clinical characteristics for included studies are listed in Tables 1 and 2.

Results of the meta-analysis are shown in Table 3, and Forrest plots for the main efficacy and safety outcomes illustrated in Figure 1. Pooled rates of AF recurrences at 6 months were CA 38% vs TA 19%, OR 2.91, 95% CI 1.64-5.16 in three studies; AF recurrences at 1-year

### Table 1

| Author          | Year | Country                  | Center | Date              | N (CA/TA) | Follow-up (mo) | AF recurrence detection |
|-----------------|------|--------------------------|--------|-------------------|-----------|----------------|------------------------|
| Boersma\(^7\)   | 2012 | Spain, Netherlands       | 2      | 2007/7-2010/6     | 63/61     | 12             | 7-day Holter at 12 mo  |
| Pokushalov\(^8\) | 2013 | Russia                   | 1      | 2011/1-2011/11    | 32/32     | 12             | Loop recorder 0-12 mo |
| Wang\(^9\)      | 2014 | China                    | 1      | 2008/3-2012/3     | 72/66     | 12             | 24-hour Holter at 1, 3, 6, and 12 mo |
| Adiyaman\(^10\) | 2018 | Netherlands              | 1      | 2007/11-2015/2    | 27/23     | 24             | 7-day Holter at 12 and 24 mo |
| Sindby\(^11\)   | 2018 | Denmark                  | 1      | 2011/4-2014/1     | 11/10     | 12             | 7-day Holter at 6 and 12 mo |
| Sugihara\(^12\) | 2018 | United Kingdom           | 1      | 2012/4-2015/8     | 49/19     | 12             | Loop recorder/ pacemaker 0-12 mo |

### Table 2

|                          | Number of studies | CA (y)   | TA (y)   
|--------------------------|-------------------|----------|----------|
| N                        | 6                 | 254      | 211      |
| Demographics             |                   |          |          |
| Age (y)                  | 6                 | 57 ± 9   | 55 ± 8   |
| Male                     | 6                 | 173/254 (68%) | 145/211 (69%) |
| Body mass index (kg/m²)  | 3                 | 28 ± 4   | 28 ± 5   |
| Past history             |                   |          |          |
| Hypertension             | 5                 | 80/191 (42%) | 60/150 (40%) |
| Diabetes                 | 5                 | 25/191 (13%) | 14/150 (9%)  |
| Stroke                   | 3                 | 7/153 (5%)   | 10/117 (9%) |
| Ischemic heart disease   | 2                 | 10/112 (9%)  | 2/80 (3%)  |
| Atrial fibrillation      |                   |          |          |
| Paroxysmal               | 6                 | 214/254 (84%) | 183/211 (87%) |
| Duration (years)         | 4                 | 5.9 ± 5.2 | 5.9 ± 5.2 |
| Antiarrhythmic use       | 5                 | 195/205 (95%) | 181/192 (94%) |
| Prior failed catheter ablation | 5         | 78/182 (43%) | 81/145 (56%) |
| Echocardiography         |                   |          |          |
| Left ventricular ejection fraction (%) | 5   | 60 ± 7 | 59 ± 6 |
| Left atrial diameter (mm) | 5                | 44 ± 8   | 44 ± 8   |
| Procedure                |                   |          |          |
| Procedure time (min)     | 6                 | 144 ± 39 | 213 ± 68 |
| Fluoroscopy time (min)   | 4                 | 16 ± 9   | 0 ± 0    |
| Left atrial appendage ligation | 5        | 0/182 (0%)  | 144/145 (99%) |
TABLE 3 Summary of meta-analysis findings of catheter (CA) vs thoracoscopic (TA) ablation for atrial fibrillation (AF)

| Outcome                  | Number of studies | CA (%) | TA (%) | Odds ratio | 95% confidence interval | P value |
|--------------------------|-------------------|--------|--------|------------|-------------------------|---------|
| **Efficacy**             |                   |        |        |            |                        |         |
| AF recurrence at 6 mo    | 3                 | 38     | 19     | 2.91       | 1.64-5.16               | <.001   |
| AF recurrence at 12 mo   | 6                 | 46     | 26     | 2.90       | 1.32-6.38               | .008    |
| Repeat ablation          | 2                 | 25     | 2.0    | 10.4       | 1.85-59.7               | .008    |
| **Safety**               |                   |        |        |            |                        |         |
| Total adverse events     | 5                 | 10     | 25     | 0.35       | 0.14-0.86               | .02     |
| Death                    | 5                 | 0.0    | 0.7    | 0.12       | 0.00-3.20               | .21     |
| Stroke                   | 4                 | 1.5    | 0.8    | 1.59       | 0.19-13.2               | .67     |
| Pacemaker implantation   | 2                 | 0.0    | 1.7    | 0.19       | 0.01-3.98               | .28     |
| Pneumothorax             | 3                 | 0.0    | 7.8    | 0.09       | 0.01-0.74               | .03     |
| Hemothorax and hydrothorax | 5             | 0.0    | 5.5    | 0.15       | 0.03-0.69               | .02     |
| Pericardial effusion     | 3                 | 0.8    | 2.6    | 0.48       | 0.08-2.81               | .41     |

were 46% vs 26%, OR 2.90, 95% CI 1.32-6.38 in six studies; and total adverse events CA 10% vs TA 25%, OR 0.35, 95% CI 0.14-0.86. CA also had higher pooled rates of repeat ablation during follow-up, but lower rates of pneumothorax, hemothorax, or hydrothorax complications (all P < .05). There was no significant heterogeneity observed for all outcomes except AF recurrences at 1-year, and no significant publication bias found (Funnel plots not shown).

4 DISCUSSION

This meta-analysis has some key findings. First, TA had higher efficacy shown by lower rates AF recurrence and repeat ablation than CA. Second, TA also had higher rates of adverse events particularly thoracic complications. The key clinical characteristics of eligible randomized trials include middle-aged patients with a high prevalence of paroxysmal AF in 85%, AF duration of 5.9 years, high antiarrhythmic use in 95%, prior failed CA in approximately half, and normal mean left ventricular ejection fraction, but mildly dilated left atrial dimensions on echocardiography.7–12 Therefore, patients with paroxysmal AF refractory to antiarrhythmic drugs and previous failed CA, but with preserved left ventricular function, are those that our findings best apply to.

The greater efficacy seen in five of six trials for TA7–9,11,12 may be explained by TA being more extensive with additional left atrial lines, targeting of epicardial ganglionic plexi and left atrial appendage ligation.3 Only one study showed no difference in efficacy, in patients without previous CA,10 suggesting TA should probably not be attempted as a first-line therapy before CA. Furthermore, the lower rate of repeat ablation during follow-up (25% vs 2%) is another distinct advantage of TA. However, the high adverse event rates in up to 25% of TA even in randomized trials is important, observed across four of five studies reporting this.7,8,10,11 In particularly, thoracic complications much higher in TA are detrimental because of their frequent need of invasive procedures, prolonging of intensive care and/or hospital stay, and potential for long-term sequelae. Two previous meta-analyses reported similar findings for CA compared to TA, however, both of these included observational studies subjective to confounding bias, and being earlier did not contain the three recent important randomized trials since 2018, so our findings are the most contemporary and least biased.13,14

Therefore, although TA has higher efficacy, its adverse event rates strongly cautions and diminishes its role in AF management. The Heart Rhythm Society consensus statement for AF ablation in 2017 and the European Society of Cardiology guidelines 2016 both suggest isolated TA can be performed in paroxysmal or persistent AF patients who failed both antiarrhythmic drugs and one or more CA, with a review of relative efficacy and safety compared to CA and consideration of patient choice by a multidisciplinary AF Heart Team.3 Local expertise of CA and especially TA with sufficient experience and volume are also important for referral.3,4 Our results incorporating more recent trials consolidate the evidence that support these statements. In the setting of concomitant cardiothoracic surgery, however, TA can be performed at a lower threshold in appropriate AF candidates.3

This meta-analysis has some limitations. Several clinically relevant endpoints were not reported including AF burden, symptoms, heart failure, and cost-effectiveness. The total sample size was moderate at best, restricting the power to identify significant differences in outcomes especially for rare events. Patient-level
data were not available for in-depth analysis and identification of predictors of efficacy and safety endpoints. There were some heterogeneity in study design, patient characteristics, procedures, medical therapy, and outcome definitions, and studies remain susceptible to publication bias. Our findings also may not necessarily apply to AF patients with very different characteristics to the studies we included. Follow-up duration of studies was restricted at 12-24 months.

In conclusion, TA not only had greater efficacy but also higher adverse event rates than CA, particularly thoracic complications. The safety data provide a compelling case for CA to remain the AF ablation strategy of choice. TA should be reserved only for selected patients with AF refractory to antiarrhythmic medications and multiple failed CA, but with ongoing symptoms requiring rhythm control, and our findings support contemporary AF guidelines in terms of the roles of CA and TA.

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CONFLICT OF INTEREST
Authors declare no conflict of interests for this article.

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