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Persistent atrial fibrillation: A systematic review and meta-analysis of invasive strategies

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ABSTRACT

Background: Persistent atrial fibrillation (AF) is associated with higher stroke and mortality risk than paroxysmal AF (pAF). Outcomes of catheter or surgical ablation are worse in patients with persistent AF than in pAF, and the optimal invasive rhythm control strategy has not been established.
Purpose: We provide a contemporary systematic overview on efficacy and safety of catheter and minimally-invasive surgical ablation for persistent AF.
Methods: We systematically searched EMBASE, MEDLINE and CENTRAL from inception to July 2018 for randomized trials on surgical and catheter ablation, and included all study arms on persistent AF. Outcome was AF freedom after ≥12 months follow-up without AAD use. Random effects models were used to calculate proportions with 95%-confidence intervals. Safety consisted of adverse events during treatment and follow-up.
Results: We included 6 studies on minimally-invasive surgical ablation and 56 on catheter ablation, involving 7624 patients with persistent AF. AF Freedom at 12 months was 69% (95%CI 64–74%) after surgical and 51% (95%CI 46–56%) after catheter ablation. More severe procedural adverse events occurred with surgery than with catheter ablation.
Conclusions: In persistent AF patients, minimally-invasive surgical ablation is associated with more procedural complications, but higher AF freedom. As adverse events after surgical ablation appear more severe than in catheter ablation, a patient-tailored therapy choice is warranted.

1. Introduction

Persistent Atrial Fibrillation (PeAF) is associated with higher AF burden and higher stroke and mortality risk compared to paroxysmal AF (pAF) [1]. Approximately 50% of AF patients have peAF [2]. However, despite the considerable prevalence and higher stroke risk of this particular AF group, there is no consensus on the optimal invasive strategy for PeAF, contrary to paroxysmal atrial fibrillation (pAF). The aggregate evidence for the efficacy of catheter ablation for peAF is weaker than for pAF [3,4].

The total number of patients with AF is increasing and estimated at >8 million in the USA by 2050 and 14 to 17 million in Europe by 2030 [2,5]. Furthermore, AF is associated with decreased quality of life, a five-fold increased risk of stroke, increased risk of heart failure and dementia and mortality [6] [7]. Annual AF costs are estimated between $6 to $26 billion dollars in the USA and €6.2 billion in five European countries [8,9]. Hence, AF imposes a large and increasing burden on health and on healthcare systems [10], largely caused by treatment.

When restoration of sinus rhythm is required in patients with paroxysmal AF, refractory for anti-arrhythmic drugs (AAD), pulmonary vein isolation (PVI) through catheter ablation is indicated, and a large body of evidence supports this therapy. Some studies advocate catheter ablation as first line treatment in pAF, without prior use of AAD [11–14]. However, evidence is limited, and essentially insufficient to proof that catheter ablation is the optimal invasive strategy for maintaining sinus rhythm in PeAF patients. Moreover, the frequent need for multiple catheter ablations in PeAF patients may have impact on the cumulative risk and burden of procedural complications. Minimally-invasive surgical techniques are therefore increasingly being employed in peAF patients [15].

The current literature on catheter ablation for the treatment of PeAF has recently been reviewed [16]. Whether sinus rhythm is restored most effectively with catheter ablation or minimally-invasive surgical ablation in peAF is uncertain. Limited randomized comparisons exist on these treatment strategies. Similarly, how complication rates of

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both strategies compare is unknown. However, as the population of patients with PeAF is large and growing, and despite the scarce data, the need for a systematic overview of the available evidence is evident. We therefore provide a contemporary overview, and conducted two meta-analyses on rhythm control interventions for peAF. We describe efficacy and safety using all randomized study arms on minimally-invasive surgical and catheter ablation.

2. Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines [17]. The protocol was registered in the International Prospective Register of Systematic Reviews, registration number: CRD42015026621.

2.1. Search strategy

A medical information specialist (J.L.) performed a comprehensive search in OVID MEDLINE, OVID EMBASE and CENTRAL (the Cochrane Central Register of Controlled Trials from inception to July 5th 2018. Supplementary Table S1 displays the complete MEDLINE search strategy.

The search strategy consisted of controlled terms and text words for the concepts of AF persistence and the two interventions (catheter and minimally-invasive surgical ablation). A broad search filter was applied to identify all randomized controlled trials (RCTs). We cross-checked reference lists and citing articles of identified relevant papers and adapted the search in case of additional relevant studies. The bibliographic records retrieved were imported and de-duplicated in ENDNOTE X7©.

2.2. Study selection and critical appraisal

Two investigators (W.R.B and E.R.M.) independently screened studies for eligibility using Covidence©, 2015. Inclusion criteria were: PeAF or longstanding peAF (LPeAF). Studies on patients with paroxysmal or permanent AF exclusively were excluded, as were studies not written in English. Studies comprising patients with both paroxysmal and PeAF were included when peAF or LPeAF data was extractable for efficacy, defined as freedom of AF or any atrial tachycardia. We included different catheter ablation strategies including: radiofrequency, cryoballoon, or any other type of AF ablation. Minimally-invasive surgical ablation studies that used both mini-thoracotomy and (hybrid) thoracoscopy were allowed, however, concomitant AF ablation during open-chest cardiac surgery was excluded. Supplementary Table S2 details in- and exclusion criteria. When studies reported serial data on the same cohort, the study with the largest number of patients was included. Abstract, case reports, reviews were excluded. The Cochrane Collaboration Tool for assessing risk of bias [18] was applied for all RCTs.

2.3. Data collection and analysis

Baseline and procedure characteristics, follow-up design and duration, and data on efficacy and safety were independently extracted by two investigators (W.R.B. and E.R.M.). Disagreements were resolved by consensus or by consultation of a third reviewer (J.R.d.G.). Efficacy rates at 12 months were extracted. All AF freedom definitions reported by the original articles were accepted, provided that at least one electrocardiographic recording was performed during ≤12 months follow-up.

We extracted the following pre-specified adverse events: death, procedure-related death, thrombo-embolism, bleeding, hemothorax, cardiac tamponade, sternotomy, pacemaker implantation, phrenic nerve paralysis, atriaoesophageal fistula, pulmonary vein stenosis, pneumothorax, pericarditis, (non-embolic) neurologic event, ventricular arrhythmia, bradycardia, atrioventricular block, thyroid dysfunction, infection, gastrointestinal- and hepatic complications.

2.4. Sensitivity analyses

In the catheter ablation group, we performed a sensitivity analysis for PVI ablation alone, and PVI + additional lesions. Furthermore, we performed sensitivity analyses comparing (i) studies reporting AF freedom at 12 months vs. at >12 months, (ii) those reporting AF freedom in PeAF vs. LPeAF patients, (iii) those reporting AF freedom following the HRS/EHRA/ECAS expert consensus statement vs. those using alternative outcome [19], (iv) those published before 2010 vs. between 2010 and 2015 vs 2016–2018, (v) those reporting on studies with <100 vs. >100 patients, (vi) those reporting on studies with mean study population age < 60 vs. >60 years, (vii) those reporting on studies where mean left atrial diameter < 47 mm vs. >47 mm or where left atrial volumes index was <38 mL/m^2 vs. >38 mL/m^2.

2.5. Statistical analysis

We used 'meta' package in R for Windows version 3.2.4 and SPSS for Windows (IBM) version 23. Meta-analyses were performed to calculate proportions (rates) with corresponding 95%-confidence intervals (CI). Random-effects modelling was used, taking into account the heterogeneity of effects estimates across the studies. Heterogeneity was assessed by Q-statistics and I^2. A p-value < 0.05 for the Q-statistic defined statistical significance. An I^2 > 40% indicated substantial heterogeneity. Meta-regression analyses were conducted testing the relation between publication year and efficacy outcomes. For continuous data, sample size-weighted means and standard deviations of sample means were calculated. Categorical data were described in percentages. Funnel plots were used to assess publication bias.

3. Results

3.1. Search results and risk of bias

Supplementary Fig. S3 shows the flowchart of included studies. We identified 1016 unique publications. After exclusion based on title and abstract, 158 articles were retrieved for full-text analysis. The study arms on patients with PeAF were extracted from 60 articles that met our inclusion criteria, of which 2 articles provided study arms for both catheter and minimally-invasive surgical ablation, comprising 56

Table 1
Characteristics of patients with AF undergoing catheter ablation or minimally-invasive surgical ablation.

	Catheter ablation			Surgical ablation		
Baseline characteristics	t	n	Mean (range)	t	N	Mean (range)
Total patients						
Mean age, y	110	9710	59.0 (50–69)	8	557	59.8 (56–67)
Mean duration of AF since diagnosis, m	95	8691	46.3 (9–96)	7	545	58.0 (48–89)
Mean LA size, mm	87	7721	45.0 (39–51)	7	545	44.8 (42–47)
Mean LV ejection fraction, %	85	7980	56.6 (22–65)	7	545	54.3 (48–58)
Mean BMI	48	5218	27.6 (23–34)	7	545	27.9 (27–30)

	Catheter ablation			Surgical ablation		
Baseline characteristics	t	n/N	%	t	n/N	%
Sex						
Male	107	7181/9480	76	7	400/557	72
Female	107	2299/9480	24	7	157/557	28
AF type						
Persistent	110	4501/9710	46	7	366/557	66
Persistent/longstanding	110	398/9710	0.04	7	7/557	1
Longstanding	110	2337/9710	24	7	15/557	3
Comorbid conditions						
History of PVI	18	80/1305	6	3	59/161	37
Structural heart disease	43	756/5933	13	6	29/464	6
Valvular heart disease	29	236/3664	6	1	1/36	3
Hypertension	86	4203/8027	52	7	222/496	45
Diabetes mellitus	76	820/6415	13	6	39/460	8
Coronary artery disease	57	393/3633	12	4	35/416	8
History of MI	6	51/2313	2	3	13/276	5
Stroke/TIA	41	444/5286	8	7	49/496	10
COPD	5	18/275	7	1	2/36	6
CHA_2DS_2-VASc -score						
CHA_2DS_2-VASc = 0	14	531/1352	39	4	177/389	46
CHA_2DS_2-VASc = 1	12	504/1234	41	3	93/301	31
CHA_2DS_2-VASc ≥ 2	13	1293/3179	41	6	148/513	29
NYHA-Class						
NYHA I	5	359/444	81	–	–	–
NYHA II	6	83/470	18	–	–	–
NYHA III	3	16/470	3	–	–	–
NYHA IV	3	1/444	0	–	–	–
Anti-arrhythmic drugs						
Class IA	5	67/410	16	2	6/240	3
Class IC	12	243/1148	21	2	81/240	34
Class III	35	1030/2502	41	3	122/301	41
Beta-blockers	16	850/1387	61	2	122/240	51
Digoxin	10	163/1030	16	2	30/240	13
Anticoagulants						
Anti-platelets	9	331/2992	11	2	15/240	6
OAC	9	2702/2992	90	2	240/240	100

t indicates No. of treatment groups reporting characteristics, n; No. of patients with this characteristic, LA; left atrium, LV; left ventricle, BMI; body mass index, AF; atrial fibrillation, PVI; pulmonary vein isolation, MI; myocardial infarction, TIA; transient ischemic attack, COPD; chronic obstructive pulmonary disease, NYHA: New York Heart Association, OAC; oral anticoagulants.

catheter and 6 minimally-invasive surgical ablation RCTs. Supplementary Fig. S4 shows the risk-of-bias scores. Only two studies had all quality criteria, the remainder had >1 criterion for bias. Supplementary Table S5 shows reference lists of the included studies.

3.2. Patient characteristics

Table 1 displays the patient characteristics of the catheter ablation- and minimally-invasive surgical ablation-studies. The studies overall described 9710 patients, of whom 7624 with PeAF or LPeAF. Numerically, the majority of patients were male, had enlarged atria and had an AF duration >12 months. The comorbidities of the study subjects were not consistently reported among the study arms, hence caution should be taken comparing comorbidities from Table 1.

3.3. Treatment characteristics

Pulmonary veins were isolated in all 56 catheter ablation-studies. In 97% of the treatment arms, radiofrequency energy was used. The following additional lesions in 94 treatment arms were described: none (n = 16), ganglion plexus ablation (n = 3), complex fractionated atrial electrogram (CFAE) ablation (n = 36), cavotricuspid ablation (n = 32), mitral isthmus ablation (n = 44), additional left atrial roof line (n = 43), left posterior wall ablation (n = 1) or right atrial ablation (n = 7).

PVI was performed in all 8 treatment arms of minimally-invasive surgical ablation studies. Additional lesions were the following: ganglion plexus ablation (n = 3), additional left atrial lines (roof line n = 4, inferior line n = 2, mitral isthmus line n = 1, trigone line n = 3 respectively) or other additional ablations. Two studies described a hybrid approach, where electrophysiologists collaborate with the surgeon for mapping and ablation. Supplementary Tables S6 and S7 summarize study and treatment characteristics respectively.

3.4. AF monitoring during follow-up

Post-procedural rhythm monitoring varied strongly between studies. All studies used Holter monitoring, a combination of Holter and ECG or continuous rhythm monitoring during follow-up, except for one catheter ablation study that used only ECGs. Fig. 1 summarizes AF absence rates for the different meta-analyses, using the endpoint definition and monitoring strategy of the original studies.

3.5. Randomized trials directly comparing treatment strategies

Two RCTs were performed on minimally-invasive surgical versus catheter ablation in 67 patients with persistent AF [20,21]. These studies showed a numerically, but not statistically higher AF freedom after surgical ablation compared to catheter ablation (OR 2.58, 95%CI 0.83–8.03).

3.6. AF freedom after 12 months; catheter ablation

Forty-one studies with 7502 PeAF or LPeAF patients, reported outcome after catheter ablation without AAD after 12 months. AF freedom was 51% (95%CI 46–56%) (Fig. 2A). With AAD use allowed, AF freedom increased to 58% (95%CI 54–63%) in 29 studies (3133 patients). In patients with peAF, AF freedom after PVIalone was 53% (95%CI 42–62%) without AAD and 57% (95%CI 46–67%) with AAD. AF freedom after PVI + additional lesions was 49% (95%CI 42–55%) without and 55% (95%CI 50–60%) with AAD. The blanking period, during which arrhythmia episodes are considered no recurrence, ranged from 0 to 3 months.

3.7. AF freedom after 12 months; minimally-invasive surgical ablation

In 5 randomized trials on minimally-invasive surgical ablation (339 patients), AF freedom was 69% (95%CI 64–74%), after 12 months, without AAD (Fig. 2B). Three studies (196 patients) reported outcome with and without AAD, AF freedom increased to 71% with AAD. The blanking period ranged from 0 to 3 months.

3.8. Heterogeneity and sensitivity analyses

All meta-analyses demonstrated heterogeneity ($I^2 > 40\%$). Despite, sensitivity analysis demonstrated similar outcomes in peAF patients (50%, (95%CI 42–58)) vs. LPeAF (51% (95%CI 44–58%)) after catheter ablation. Only one minimally-invasive surgical ablation reported outcome in LPeAF patients. No difference in AF freedom was found between studies that reported according to the HRS/EHRA/ECAS consensus statement (i.e. serial Holter monitoring and reporting every recurrence of atrial tachyarrhythmia lasting >30 s as a recurrence), versus those that did not.

No difference was found between studies that reported on patients ≥60 years compared to study patients<60 years (Supplementary Fig. S8). Furthermore, there was no difference when studies were divided according to study population size or left atrial dimensions.

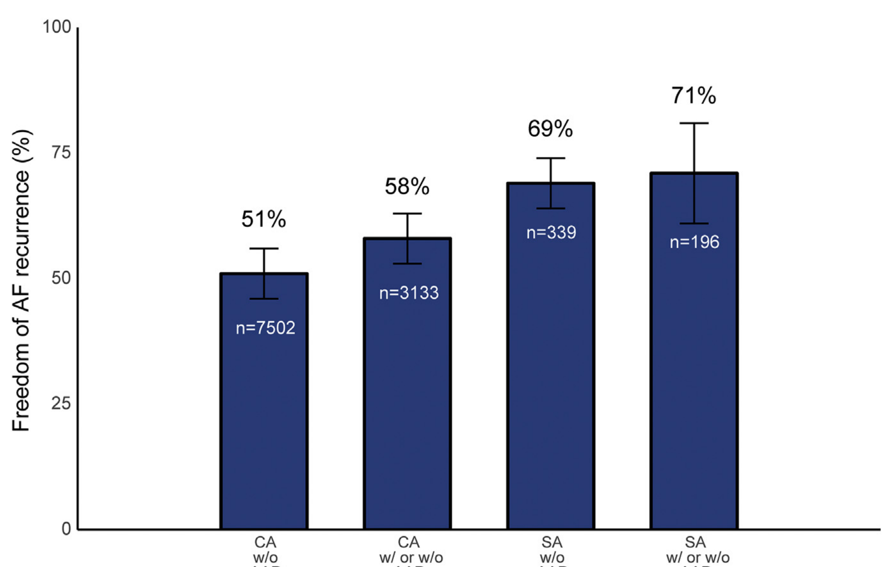

Fig. 1. Freedom of AF after both treatment strategies for persistent atrial fibrillation. AF, atrial fibrillation; w/o, without; w/,with; AAD; antiarrhythmic drugs, *; significant difference, ns; non-significant difference.

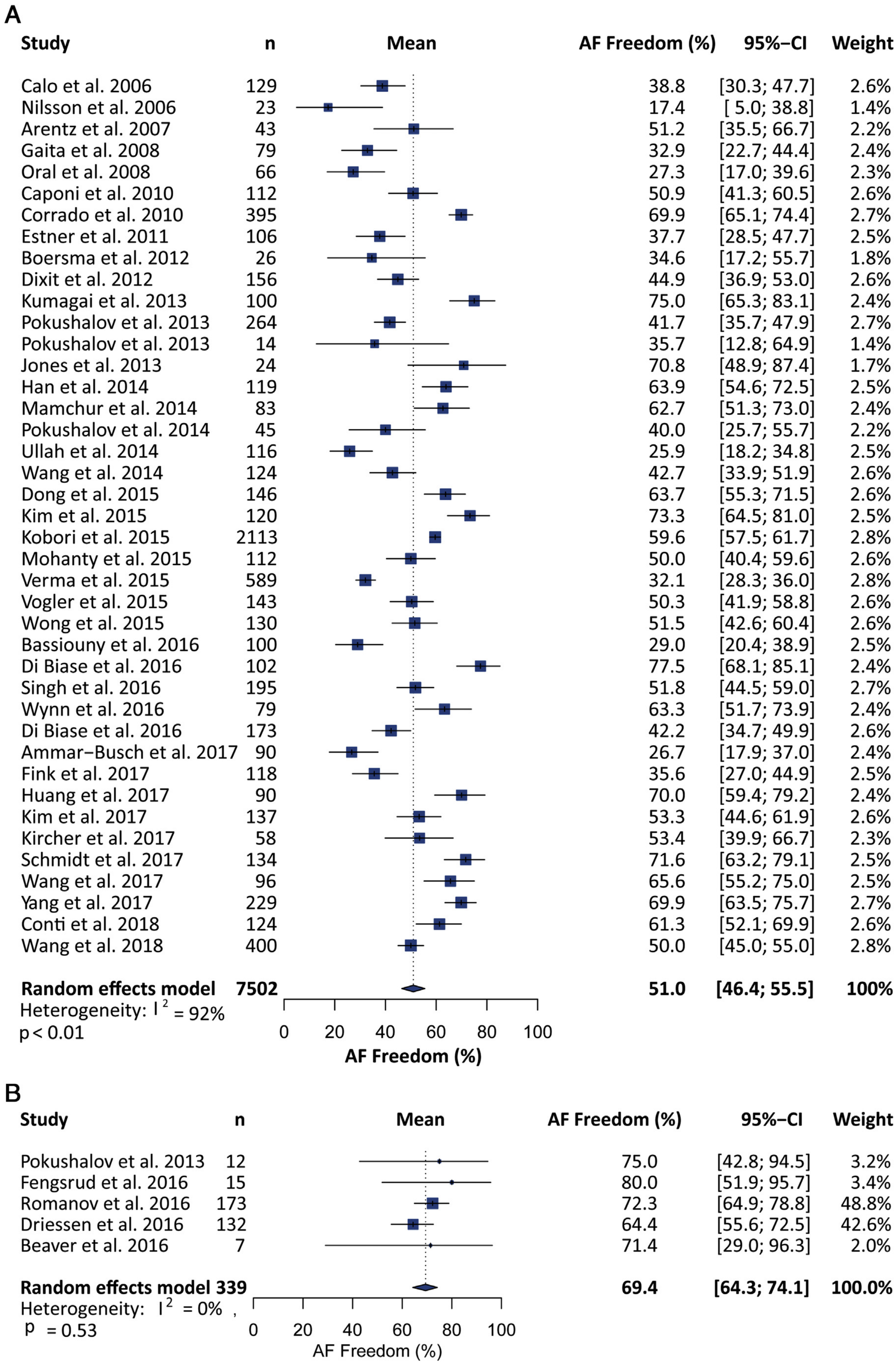

Fig. 2. Forest plots showing rates of AF freedom of persistent AF patients 12 months after (A) catheter ablation or (B) minimally-invasive surgical ablation.

Meta-regression testing for the relation between publication year and outcome showed higher efficacy rates in more recent catheter ablation-studies ($p = 0.03$), but not minimally-invasive surgical ablation-studies. Funnel plots showed publication bias in catheter ablation-studies, but not in minimally-invasive surgical ablation-studies (Supplementary Table S9).

3.9. Safety outcomes

Table 2 displays adverse events and complications following catheter and minimally-invasive surgical ablation.

Adverse events after catheter ablation were infrequent. Mortality during the study course was 1.1%, procedure-related death 0.1%. The commonest complications were pacemaker implantations (0.9%), any bleeding (1.7%) and pericarditis (1.4%). Thrombo-embolic events occurred in 0.7% of patients.

Mortality was 1.1%; procedure-related death 0% after minimally-invasive surgical ablation. Pulmonary vein stenoses were not reported. Combined major and minor bleeding rate was 7.7% and 8 patients (1.6%) were converted to sternotomy. Pneumothorax occurred in 6.1% of patients and 2.7% required pacemaker implantation. Thrombo-embolic events occurred in 1.4%. Taken together, particularly irreversible adverse events occurred more frequently after minimally-invasive surgery than after catheter ablation.

4. Discussion

We performed a comprehensive systematic review, using all treatment arms of randomized controlled trails available to date. We included both catheter ablation- and minimally-invasive surgical ablation-studies and show that in patients with peAF: 1) Minimally-invasive surgery is associated with numerically more irreversible adverse events than catheter ablation 2) AF freedom after 12 months is 69% in randomized studies on minimally-invasive surgical ablation compared to 51% in catheter ablation studies. In patients with or without AAD, AF freedom was 58% in catheter ablation studies, and 71% in minimally-invasive surgical ablation studies. These numbers do not reflect direct treatment comparisons, but the confidence intervals did not overlap. Procedural complications are reported inconsistently and cannot be compared directly between both invasive strategies. The higher procedural complications rate reported in minimally-invasive surgical ablation seems to accompany higher efficacy rates.

Table 2
Safety outcomes for patients with AF after catheter ablation or minimally-invasive surgical ablation.

	Catheter ablation			Surgical ablation		
Safety outcomes	Studies	n/N	%	Studies	n/N	%
Mortality						
Overall death	17	38/3264	1.1	4	5/464	1.1
Prodecure-related death	15	3/3052	0.1	4	0/464	0
Thrombo-embolic event	29	53/7169	0.7	6	8/557	1.4
Bleeding						
Small bleeding	34	124/7515	1.7	2	21/272	7.7
Hemathorax	1	1/80	1.3	3	6/448	1.3
Cardiac tamponade	36	81/8090	1.0	2	2/301	0.6
Sternotomy	–	–		4	8/489	1.6
Phrenic nerve paralysis	5	9/2934	0.3	1	2/240	0.8
LA-esophageal fistula	9	7/3937	0.2	–	–	–
Pulmonary vein stenosis	11	14/1690	0.8	–	–	–
Pneumothorax	–	–		4	31/509	6.1
Pericarditis	10	54/3981	1.4	–	–	–
Atrioventricular block	1	1/230	0.4	–	–	–
QT-prolongation	–	–		–	–	–
Pacemaker implantation	2	3/345	0.9	2	8/301	2.7
Thyroid dysfunction	1	1/230	0.4	–	–	
Gastro-intestinal complications	2	7/2286	0.3	–	–	–
Infection (pneumonia, urinary tract infection etc.)	3	21/2754	0.7	2	3/301	1.0

n; No. of patients with adverse events, N; No. of patients evaluated in studies reporting this adverse event, %; percent of patients with adverse event of interest.

4.1. Treatment strategies

Inherent to our aim to include all available data, patient characteristics, endpoint reporting and follow-up strategy varied among the included publications.

Our aim was to numerically estimate efficacy and safety of different treatment modalities. However, as studies generally did not compare different strategies directly, care must be taken in comparing absolute numbers.

While PVI remains the cornerstone of invasive AF treatment. However, different combinations of additional lesion sets and energy sources were applied, resulting in considerable variation among studies. The dogma that PVI alone is insufficient for PeAF was challenged in the STAR-AF-2 trial, randomizing PeAF patients to PVI alone, PVI + linear ablation or PVI + CFAE ablation [3]. No difference in efficacy was found in that study. In our meta-analysis on catheter ablation studies, sensitivity analysis showed no difference in AF freedom after PVI alone compared to PVI + additional lesions, with AF freedom after PVI alone being slightly higher than PVI + additional lesions (53% vs 49% respectively). A recent meta-analysis reported even higher success rates (67%) after a single PVI procedure, but this study also included cohort studies and allowed for AAD use [22]. Contrarily, another meta-analysis supported combining PVI with additional ablations in PeAF [23].

Minimally-invasive surgical ablation was developed to combine the success rates of the (open heart surgery) Cox-Maze procedure with a less invasive intervention. Epicardial PVI is usually performed with RF energy through clamps around the PVs.

Furthermore, additional left, and right, atrial ablation lines can be created with linear devices and the left atrial appendage can be removed, possibly reducing stroke risk [15].

New approaches need to be evaluated in clinical trials and treatment of concomitant diseases is important adjunct to ablation strategies [24].

4.2. Clinical implications

Guidelines designate class IA indications for AAD class I and III and for catheter ablation in patients with symptomatic (paroxysmal) AF, reflecting the current (randomized) literature [4,19,25]. RCTs in PeAF patients showed higher AF freedom with catheter ablation compared to AAD [26,27]. In general the ESC and the HRS/EHRA/ECAS consensus document are more conservative on the indication for stand-alone minimally-invasive surgery to treat AF, potentially because of the higher complication rate.

The variation among the studies was large, and insufficient direct comparison between invasive treatment strategies for peAF is available. AF freedom was higher in the minimally-invasive surgical ablation-group than in the catheter ablation-group. This effect was further enhanced when AAD use was permitted during follow-up. The majority of the 5 RCTs with 7 treatment arms on minimally-invasive surgical ablation studies were small and/or single-center studies, whereas larger, more frequently multi-center RCTs were available on catheter ablation. Potentially, the minimally-invasive surgery studies reflect dedicated programs in specialized centers.

Two RCTs directly compared minimally-invasive surgical ablation to catheter ablation in patients with paroxysmal or PeAF, with a prior failed catheter ablation or hypertension and enlarged left atria (potentially representing a more advanced patient group), and showed higher AF freedom in minimally-invasive surgical ablation, at the cost of more procedural complications [20,21]. The number of peAF patients in these studies was low, but the results of both studies were consistent with the data in this review.

We describe efficacy rates after the index procedure, notwithstanding that patients may have had previous ablations. A single catheter ablation procedure may often not be sufficient, and multiple procedures combined with AAD can increase success to 69% [16]; numerically comparable with the success rates of minimally-invasive surgical ablation. Furthermore, the increasing safety of catheter ablation over time, makes a multiple procedure approach feasible [19]. However, adverse events rates for minimally-invasive surgical ablation are similarly improving.

The characteristics and timing of adverse events vary between the included studies. Procedure related death was similarly infrequent in both strategies. However, irreversible complications, such as sternotomy, pacemaker implantation, phrenic nerve paralysis and thrombo-embolic events appeared more frequent in minimally-invasive surgical ablation. However, these patients more often had high CHA_2DS_2-VASc -scores. In general, the extent of reporting of adverse events in all studies included in our meta-analyses was limited in both treatment strategies, and most studies did not meet the criteria of complete reporting of complications resulting in permanent injury, death, requiring interventions or hospitalization [19]. However, these are the published data available on peAF.

4.3. Generalizability and limitations

A limitation of our analysis is the heterogeneity between the different studies and treatment strategies. Different catheter ablation strategies were studied, while the minimally-invasive surgical ablation strategies are relatively uniform. Also, there are only two prospective, randomized studies comparing both treatment strategies. Furthermore, only studies on catheter ablation with >40 patients were included in this analysis, since a plethora of randomized studies was available in this treatment arm, while studies on minimally-invasive surgical ablation are small, with only two studies with >40 patients with PeAF. However, omitting minimally-invasive studies with <40 patients did not change our conclusions on procedural efficacy. Despite the high and growing prevalence of PeAF, the data reported here are the only aggregate data available for clinical decision making. Using detailed inclusion criteria, and including all available evidence, we attempted to select equivalent studies reporting outcome after PeAF treatment.

We performed extensive sensitivity analysis to detect concomitant conditions driving the results reported, and found no differences among subgroups that alter our main conclusions. However, more recent catheter ablation studies seemed more efficacious. Consistent reporting procedural outcome and complications, such as advocated by the HRS/EHRA/ECAS consensus statement remains of utmost importance [19]. The definitions of peAF and LPAF evolved over time, and have not been used similarly strictly across studies. Furthermore, we appreciate that peAF is a clinical classification that poorly reflects AF temporal persistence [28].

AF freedom is defined as absence of any atrial arrhythmia (AF, atrial flutter and atrial tachycardia) lasting >30 s, without AAD use [19]. The majority of studies included in our meta-analyses employed this endpoint. Studies included in our meta-analyses used different monitoring protocols, varying between continuous monitoring to only one ECG at 12 months follow-up. This may limit direct comparison and emphasizes the necessity for consistency in monitoring and outcome reporting. Evidently, contemporary rhythm follow-up is more extensive than before, and more often includes long term rhythm monitoring. For the particular case of peAF, continuous monitoring may be less relevant than for pAF.

Therefore, and despite the limitations listed here, this systematic review comprising >7500 patients with peAF, provides the most comprehensive available evidence on the invasive treatment to date.

5. Conclusions

Minimally-invasive surgery for peAF is associated with more severe complications than catheter ablation, although underreporting of adverse events appeared present in all included studies. Minimally-invasive surgical ablation appears more efficacious in restoring sinus rhythm than catheter ablation, however the number of randomized studies directly comparing both treatment strategies is limited and cohorts are small.

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Disclosures and potential conflict of interest

Dr. de Groot and Dr. Driessen are consultants for Atricure; Dr. de Groot is consultant for Daiichi Sankyo and received research funding from St Jude Medical. All other authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.11.127.

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