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Review

Remote magnetic navigation versus manual control navigation for atrial fibrillation ablation: A systematic review and meta-analysis

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ABSTRACT

Background: The aim of this review was to evaluate the efficacy and safety between remote magnetic navigation (RMN) and manual control navigation (MCN) for atrial fibrillation (AF) ablation.
Methods: We searched the PubMed, EMBASE and Cochrane library databases using the key words AF, ablation and magnetic navigation.
Results: Eighteen studies were identified in this analysis including 4046 patients comparing RMN and MCN in AF ablation, which were all non-randomized controlled studies. No significant difference of AF recurrence rate (40% vs. 38%, OR 1.00, 95% CI 0.82–1.22, $p = 0.97$) and acute success rate in achieving pulmonary vein isolation (91% vs. 93%, OR 0.44, 95% CI 0.16–1.17, $p = 0.10$) was found between RMN and MCN. However, compared with MCN, RMN was associated with significantly lower complication rate (2% vs. 5%, OR 0.44, 95% CI 0.28–0.69, $p = 0.0003$) and shorter fluoroscopy time (MD −9.71 min, 95% CI -15.80 to −3.63, $p = 0.002$). Procedure time (MD 47.05 min, 95% CI 27.5–66.58, $p < 0.00001$) and ablation time (MD 15.90 min, 95% CI 9.62–22.18, p < 0.00001) of RMN guided AF ablation were significantly longer than those of MCN.
Conclusion: The results of this study suggest that RMN is as effective as MCN in achieving pulmonary vein isolation and freedom from AF recurrence, and has superior safety with less complications and shorter fluoroscopy time.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice, which is also one of the major causes of stroke, heart failure, sudden death and cardiovascular morbidity in the whole world [1]. Catheter ablation of AF has evolved to an effective treatment option for AF patients during the past three decades and is recommended for patients with AF refractory to one or more antiarrhythmic drugs (AADs) in the latest international guidelines [2]. However, manual control navigation (MCN) ablation of AF is still a challenging procedure especially when there are complicated clinical or anatomical situations. Conventional approach also requires electrophysiologists to be more experienced and is associated with more radiation exposure [3]. Remote magnetic navigation (RMN) is a technique that uses magnetic field to control the mapping and ablation catheter inside the heart [4]. This technique has many advantages including increased precision, stability and decreased fluoroscopy exposure for both patients and physicians [5]. RMN catheter ablation has been used in human since 2003 [6] and numerous studies have assessed the efficacy and safety of this system by comparing RMN with MCN [7–16], but the results regarding the efficacy and safety of RMN are inconsistent. Although two meta-analysis were published in 2013 [17,18], more recent studies comparing RMN and MCN have now been published and provide more evidence about this issue. Therefore, we conducted a systematic review and meta-analysis using the most recent data to assess the efficacy and safety between RMN and the conventional approach.

Methods

We performed this meta-analysis according to the Cochrane Handbook for Systematic Reviews of Interventions [19] and reported it based on PRISMA checklist 2009 [20]. The protocol of our meta-analysis is available in PROSPERO(CRD42018093310).

Search strategy

We searched the PubMed, Cochrane library, and EMBASE databases from the inception dates to 5 March 2018, using the key words: 'atrial fibrillation', 'ablation' and 'magnetic navigation'. There were no language restrictions. The literature was searched by one researcher.

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Eligibility criteria

Studies were included based on the following criteria. Inclusion criteria:1) studies enrolling AF patients older than 18 years; 2) studies comparing RMN group with MCN group; 3) studies providing at least one relevant outcome; 4) randomized controlled trials, non-randomized controlled studies. Exclusion criteria: case reports, case series, editorials, literature review, conference abstract.

Studies selection

The studies were selected by two researchers independently according to the eligibility criteria. Disagreements were resolved by consensus. If there was no agreement, a third researcher was introduced and made the decision.

Data extraction

Two researchers extracted the data independently from each study: 1) first author; publication year; participant characteristics (mean age, sex and type of AF—paroxysmal, persistent or permanent), follow up time and ablation characteristics (remote magnetic navigation system, ablation catheter, mapping catheter, ablation lesion design, ablation setting and intracardiac echocardiography usage); 2) primary outcomes: AF recurrence rate and complication rate. Complications included two types: a) major complications consisted of acute myocardial infarction, stroke, major bleeding, cardiac tamponade, atrial-esophageal fistulae, severe pulmonary vein stenosis and procedure-related death; b) minor complications included pericarditis and inguinal hematoma [21]; 3) secondary outcomes: acute success rate, procedure time, fluoroscopy time and ablation time.

AF recurrence was defined as AF recurrence based on symptom and/or electrocardiographic documentation at the end of the follow-up independently from the length and intensity of the follow-up in each study. Acute success was defined as complete electrical pulmonary vein isolation (PVI). Procedure time was skin-to-skin time which is time of the whole procedure from the first venous puncture to the sheath withdrawal. Fluoroscopy time was defined as the duration of fluoroscopy during the procedure. Ablation time was defined as the duration of radiofrequency (RF) ablation during the procedure [18].

Disagreements were resolved by consensus. If there is no agreement, a third researcher was introduced and made the decision.

Risk of bias assessments

For non-randomized studies (NRS) the quality of the studies was independently evaluated by two authors using the Newcastle–Ottawa Scale (NOS) [22]. The NOS scale consists of eight items classified under three groups: selection of the study group, comparability and ascertainment of the exposure (case control studies) or outcome (cohort studies). Each item was graded with a maximum score of 1, except for those related to comparability whose maximum score was 2. The score ranged from 0 (lowest) to 9 (highest). Studies that scored a score ≥ 6 were considered high quality, whereas those with scores <6 were considered low quality.

We also used the GRADE (Grading of Recommendations Assessment, Development, Evaluation) approach to rate the quality of the evidence. In this approach, 5 factors including risk of bias, imprecision, indirectness, inconsistency and publication bias can result in rating down the quality of evidence for specific outcomes and, thereby, reduce confidence in the estimate of the effect. Large magnitude of an effect, dose-response gradient and effect of plausible residual confounding are 3 factors that can increase the confidence in the estimate of effect. The quality of the evidence is categorized into four levels, ranging from very low to high [23].

Statistical analysis

We followed the recommendations of chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions [19]. Continuous outcomes were reported as a mean difference (MD) with 95% confidence intervals (CIs). Dichotomous outcomes were reported as odds ratios (OR) with 95%CI. We used the random effects model of Der Simonian and Laird to combine results from the included individual studies. Publication bias was assessed by examining funnel plots only when there are at least 10 studies included in the meta-analysis. Sensitivity analysis was performed to ensure that conclusions of the meta-analysis was not affected by different decisions such as the choice of the effect measures and the effect models. All tests were 2-tailed and statistical significance was set as a $p < 0.05$. All statistical calculations were performed with the use of Revman version 5.3 (downloaded from the Cochrane Community).

Results

Search results

There were 321 published studies identified by our search. After duplicates were removed, there remained 198 references. Then, 138 articles were excluded after reviewing the titles and abstracts for clearly irrelevant or not meeting the eligibility criteria. The full texts of the remaining 60 citations were examined in detail and 42 studies did not meet the inclusion criteria. Eventually 18 studies were included in our analysis. The detailed process of study selection is shown in Fig. 1.

Study characteristics

We included 18 non-randomized controlled studies. Table 1 shows the baseline characteristics of included studies. To sum up, 4046

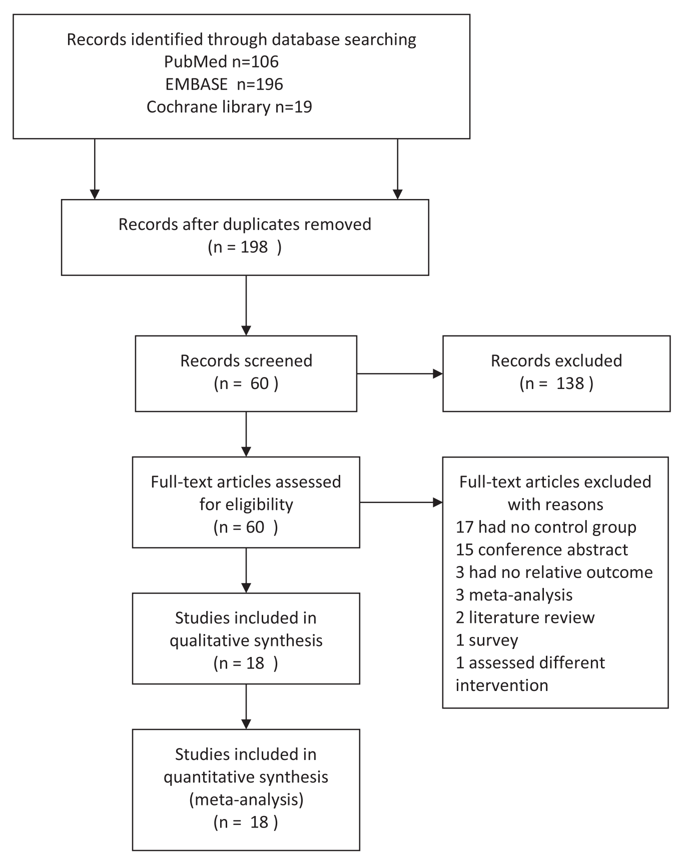

Fig. 1. Flow diagram of study selection.

Table 1
Characteristics of included studies.

Studies	Year	Sample size	Mean age (years)	Male (%)	Paroxysmal AF (%)	Persistent or permanent AF (%)	Left atrial diameter (mm) or left atrial size (ml)	Mean follow up time (months)
Yuan, s et al. [28]	2017	112:102	60.7 ± 10.8:60.1 ± 10.2	68%:71%	69.6%:70.6%	30.4%:29.4%	76.4 ± 17.9: 76.9 ± 20.4 ml	39 ± 9:44 ± 10
Lim, P et al. [29]	2017	214:229	54.9 ± 10.4:54.0 ± 9.3	74.6%:77.1%	75.2%:67.2%	24.8%:32.8%	–	–
Kataria et al. [26]	2017	114:222	61.3 ± 9.6:59.8 ± 16.2	65.7%:61.2%	100%:100%	–	40.7 ± 4.7:39.6 ± 5.3 mm	27.2 ± 8.8: 27.2 ± 8.8
Adragão, P et al. [30]	2016	287:287	58.3 ± 10.7:57.9 ± 11.2	70.0%:67.6%	74.2%:72.1%	25.8%:27.9%	–	31.2 ± 18: 31.2 ± 18
Weiss et al. [31]	2016	315:312	66.1 ± 10.1:64.1 ± 11.1	64.4%:63.8%	42.2%:46.5%	27.8%:53.5%	–	36:36
Akca, F et al. [32]	2015	108:306	48.4 ± 18.3:51.7 ± 16.6	60.7%:62.5%	–	–	–	–
Koutalas, E et al. [33]	2015	70:70	59.50 + 9.12:56.89 + 15	65.7%:71.4%	50%:50%	50%:50%	41.28 + 4.92:45.64 + 6.28 mm	30.34 ± 18.60:27.32 ± 19.23
Akca, F et al. [34]	2013	33:34	49.6 ± 18.2:52.8 ± 15.2	64.3%:64.6%	75.8%:67.6%	24.2%:32.2%	43.1 ± 6.4:44.9 ± 6.4 mm	19 ± 11: 19 ± 11
Bauernfeind et al. [13]	2011	56:76	48 ± 19:52 ± 16	57%:62%	0:78.9%	100%:21.1%	–	15 ± 9.5:14 ± 9.5
Choi et al. [14]	2011	41:70	57 ± 11:55 ± 11	77%:75%	58.5%:61.4%	41.5%:38.6%	43.7 ± 6.3:41.2 ± 6.3 mm	3:3
Lüthje et al. [15]	2011	107:54	62 ± 10:61 ± 10	62%:63%	31.8%:33.3%	68.2%:66.7%	47 ± 6:45 ± 7 mm	12: 12
Arya, A et al. [12]	2011	70:286	58.3 + 13.9:57.9 + 10.1	65.7%:66.1%	50%:75.5%	50%:24.5%	40.5 ± 2.9:42.8 ± 6.6 mm	6:6
Solheim, E et al. [16]	2011	23:65(irrigated catheter)	59 ± 7:57 ± 9	96%:79%	65%:61%	35%:39%	–	12.2 ± 5.4: 12.2 ± 5.4
		26:65(non-irrigated catheter)	55 ± 8:57 ± 9	77%:79%	54%:61%	46%:39%	–	12.2 ± 5.4: 12.2 ± 5.4
Sorgente et al. [11]	2010	35:29	55.7 ± 10.0:56.1 ± 7.2	83.3%:89.7%	80%:69%	20%:31%	41.1 ± 5.0:42.4 ± 4.2 mm	11.8 ± 5.1:10.9 ± 8.2
Miyazaki et al. [10]	2010	30:44	60.2 ± 9.4: 57.6 ± 11.3	76.7%:84.1	100%:100%	–	42.0 ± 6.3:40.7 ± 6.0 mm	14 ± 5:15 ± 5
Katsiyiannis, W.T et al. [9]	2008	20:20	–	–	65%:70%	35%:30%	46.1: 45.3 mm	12: 12
Kim et al. [8]	2008	91:75	–	–	–	–	–	–
Pappone et al. [7]	2006	40:28	57(28–75):57(31–75)	60%:57.1%	62.5%:57.1%	37.5%:42.9%	42.5(30–52):41.5(30–52) mm	–

patients were analyzed in our review. Sample size varied from 40 to 627 patients. The differences of weighted mean age, weighted percentage of male patients and left atrial diameter or size between two groups were not significant. There was no statistical difference in the percentage of paroxysmal AF and persistent or permanent AF between RMN and MCN group as well. We also summarized the follow-up of included studies. After the blanking period of 3 months, follow-up including clinical interview, physical examination, ECG or 1–7 days' Holter recording was done at different length, frequency and intervals. Although follow-up time ranged from 3 to 43 months and the frequency and intervals of follow-up were different among these studies, within each study the same criteria were applied equally to these two groups, which thereby would not affect the results of our analysis. Table 2 illustrates the ablation characteristics of included studies which are clinically relevant. We summarized the usage of remote magnetic navigation system, ablation catheter, circular mapping catheter and intracardiac echocardiography. We also summarized the ablation lesion design, specifically for persistent cases, and ablation settings including ablation temperature, power and flow rate.

AF recurrence rate

The data on AF recurrence rate was recorded in 13 studies that included 2881 patients. The difference between RMN and MCN was not statistically significant. (40% vs. 38%, OR 1.00, 95% CI 0.82–1.22, $p = 0.97$ (Fig. 2a).

Complication rate

Complication rate was evaluated in 12 studies that included 3327 patients. The difference between the two groups favored RMN and was statistically significant (2% vs. 5%, OR 0.44, 95% CI 0.28–0.69, $p = 0.0003$) (Fig. 2b). The use of RMN reduced the risk of complications by 56% when compared with MCN during the AF ablation procedure and in follow-up.

Acute success rate

Nine studies that included 1570 patients, assessed the acute success rate were included in this meta-analysis. Although 5 other studies also assessed the acute success rate at the end of the procedure, both groups in these studies all achieved pulmonary vein isolation, which means two groups had the same acute success rate. Therefore, these 5 studies would not have an influence on the results in acute success rate. The difference of acute success rate between RMN and MCN was not statistically significant. (91% vs. 93%, OR 0.44, 95% CI 0.16–1.17, $p = 0.10$) (Fig. 3a).

Procedure time

Sixteen studies that included 3365 patients, assessed the procedure time. Compared with MCN group, the procedure time of RMN group was significantly longer. The use of RMN increased procedure time by a mean duration of 47.05 min. (MD 47.05 min, 95% CI 27.51–66.58, $p < 0.00001$) (Fig. 3b).

Fluoroscopy time

Sixteen studies included 3831 patients assessed the fluoroscopy time at the end of the procedure. Compared with MCN group, the fluoroscopy time of RMN group was significantly shorter. The use of RMN reduced fluoroscopy time by a mean duration of 9.71 min. (MD −9.71 min, 95% CI -15.80 to −3.63, $p = 0.002$) (Fig. 3c).

Table 2
Summary of ablation characteristics.

Studies	Year	System	Ablation catheter		Circular mapping catheter	ICE usage
			RMN	MCN		
Yuan, s et al. [17]	2017	Niobe ES/Epoch	3.5-mm irrigated-tip Thermocool/C3/RMT	3.5-mm irrigated-tip Navistar Thermocool or contact force catheter SmartTouch	Yes (Lasso)	Not mentioned
Lim, P et al. [18]	2017	NIOBE II	3.5-mm irrigated Navistar RMT Thermocool	3.5 mm Navistar thermocool or Flexibility or Tacticath	Yes (Lasso)	Yes
Kataria et al. [15]	2017	the NIOBE/EPOCH	3.5 mm irrigated tip Navistar RMT Thermocool,	3.5 mm open-irrigated tip Navistar Thermocool or Navistar Thermocool Smart-touch	Yes (Lasso)	Not mentioned
Adragão, P et al. [19]	2016	NIOBE II	irrigated catheter (without details)		Yes (without details)	Not mentioned
Weiss et al. [20]	2016	the Niobe II and EPOCH	3.5-mm open-irrigated Navistar Thermocool RMT	3.5-mm open- irrigated Navistar Thermocool or 3.5-mm open-force-sensing irrigated Thermocool Smarttouch	Yes (Lasso)	Yes
Akca , F et al. [21]	2015	NIOBE II	not mentioned		Not mentioned	Yes
Koutalas, E et al. [22]	2015	the Niobe Stereotaxis MNS	3.5-mm irrigated tip Navistar-RMT Thermocool	3.5-mm irrigated-tip CoolPath or Navistar Thermocool	Yes (Inquiry Optima)	Not mentioned
Akca, F et al. [23]	2013	NIOBE II	NaviStar RMT ThermoCool	Navistar ThermoCool	Not mentioned	Yes
Bauernfeind et al. [24]	2011	NIOBE II	NaviStar RMT ThermoCool	Navistar ThermoCool	Yes (Lasso)	Yes
Choi et al. [25]	2011	the Niobe Stereotaxis MNS	3.5 mm irrigated Navistar thermocool RMT	3.5 mm Navistar thermocool	Yes (Lasso)	Not mentioned
Lüthje et al. [26]	2011	NIOBE II	3.5 mm open-irrigated Navistar Thermocool RMT	3.5 mm open-irrigated Navistar Thermocool	Not mentioned	Not mentioned
Arya, A et al. [27]	2011	the Niobe Stereotaxis MNS	8-mm Navistar-RMT or 3.5-mm irrigated tip Navistar-RMT Thermocool	irrigated tip CoolPath	Yes (Inquiry Optima)	Not mentioned
Solheim, E et al. [28]	2011	NIOBE II	Navistar® RMT ThermoCool or Navistar Celsius RMT	irrigated RFA ThermoCool or Navistar ThermoCool	Yes (Lasso or Optima)	Not mentioned
Sorgente et al. [29]	2010	NIOBE II	3.5 mm irrigated Thermocool RMT NaviStar	3.5 mm irrigated tip Navistar Thermocool	Yes (Lasso)	Not mentioned
Miyazaki et al. [16]	2010	the Niobe Stereotaxis MNS	3.5-mm tip externally irrigated magnetic tip ThermoCool RMT	3.5-mm externally irrigated tip	Yes (Lasso)	Not mentioned
Katsiyiannis, W.T et al. [30]	2008	NIOBE II	4-mm tip magnetic Celsius	an 8-mm-tip Blazer	Yes (Lasso)	Not mentioned
Kim et al. [31]	2008	NIOBE II	CARTO:4-mm or 8-mm tipped Navistar RMT; ESI/NavX or No mapping: 4-mm tipped Celsius	4-mm or 8-mm tip EPT	Not mentioned	Not mentioned
Pappone et al. [32]	2006	NIOBE II	4-mm tip Navistar RMT	not mentioned	Not mentioned	Not mentioned

Studies	Year	Ablation lesion design	Temperature (°C)		Power (W)		Flow rate (ml/min)	
			RMN	MCN	RMN	MCN	RMN	MCN
Yuan, s et al. [17]	2017	PVI+ linear lesions	48		30–35 for the posterior wall,35–40 for other areas		–	–
Lim, P et al. [18]	2017	PVI+ superior vena cava+ CTI+ CFAE	40		40		–	–
Kataria et al. [15]	2017	PVI	48		20–35		20 cc/min	
Adragão, P et al. [19]	2016	PVI + CTI	–	–	–	–	–	–
Weiss et al. [20]	2016	PVI	–	–	40-50 W (25-35 W for posterior wall)	30-40 W (20-30 W for posterior wall)	–	–
Akca, F et al. [21]	2015	Not mentioned	–	–	–	–	–	–
Koutalas, E et al. [22]	2015	PVI+ linear ablations between the left and right PVs (box lesion) at the posterior wall +between the inferior borders of the left inferior PV to the lateral mitral annulus	48		35		30	
Akca, F et al. [23]	2013	PVI+ linear ablations in the first roof line and mitral line+ postero-inferior line + ablation in the LA and coronary sinus	–	–	–	–	–	–
Bauernfeind et al. [24]	2011	PVI+ linear ablation in the left and/or right atrium	–	–	–	–	–	–
Choi et al. [25]	2011	PVI, antral ablation with carina, roof and posterior lines+ anterior ablation line connected roof line and anterior mitral annulus through the medial side of the left atrial appendage	39		40	35	–	–
Lüthje et al. [26]	2011	PVI	45		40(30 for posterior wall)		30(17 for posterior wall)	

(continued on next page)

Table 2 (*continued*)

Studies	Year	Ablation lesion design	Temperature (°C)		Power (W)		Flow rate (ml/min)	
			RMN	MCN	RMN	MCN	RMN	MCN
Arya, A et al. [27]	2011	PVI+ linear ablations between the circular lesions along the roof and posterior wall of the left atrium (box lesion) + between the circular lesion and the mitral annulus	48		35		30	
Solheim, E et al. [28]	2011	PVI + CTI+ additional ablation between the two PVs if needed + two lines connecting the two contra-lateral superior and inferior veins + CAFE + combinations	55	50	40	30–35	20	15–20
Sorgente et al. [29]	2010	PVI	48		35		–	–
Miyazaki et al. [16]	2010	PVI + CTI	45		35		30	
Katsiyiannis, W. T et al. [30]	2008	PVI, WACA+ linear lesions from the left inferior pulmonary vein to the mitral valve + across the anterior left atrial roof	50	55	30	45	–	–
Kim et al. [31]	2008	PVI	–	–	–	–	–	–
Pappone et al. [32]	2006	PVI + mitral isthmus ablation line	65	–	50	–	–	–

ICE = intracardiac echocardiography; WACA = Wide area circumferential ablation; CTI = Cavotricuspid isthmus; CAFÉ = complex atrial fractionated electrograms; PVI = pulmonary vein isolation; RMT = Remote Magnetic Technology.

Ablation time

Eight studies that included 1762 patients, assessed the ablation time at the end of the procedure. Compared with MCN group, the ablation time of RMN group was significantly longer. The use of RMN increased ablation time by a mean duration of 15.90 min (MD 15.90 min, 95% CI 9.62–22.18, $p < 0.00001$) (Fig. 3d).

Test of heterogeneity

The tests of heterogeneity for AF recurrence rate ($p = 0.23$, $I^2 = 21\%$) and complication rate ($p = 0.84$, $I^2 = 0\%$) were not significant. However, the tests of heterogeneity for acute rate success ($p = 0.008$, $I^2 = 70\%$), procedural time ($p < 0.00001$, $I^2 = 95\%$), fluoroscopy time ($p < 0.00001$, $I^2 = 99\%$), and ablation time ($p < 0.00001$, $I^2 = 91\%$) were significant. In order to find the source of heterogeneity, meta-regression analysis was performed using publish year and sample size, but it turned out these two factors are not the reasons which caused high heterogeneity.

Publication bias

A Funnel plot was performed to evaluate the publication bias when there were at least 10 studies. Four funnel plots were produced, and they were all obvious asymmetry. It suggests that there may be publication bias in our analysis.

Sensitivity analysis

Sensitivity analysis was performed by changing the effect measures and effect models. For instance, we replaced OR with RR and used SMD instead of MD and changed random effect model to fixed effect model, the conclusions of our meta-analysis remained the same. That means results of the meta-analysis were not affected by different decisions such as the choices of effect measures and the effect models.

Risk of bias

We evaluated the quality of our included studies using the Newcastle–Ottawa Scale. According to the criterion, these observation studies were all scored ≥6, thereby high quality NRSs. (Table 3).

We made the GRADE summary of finding table to summarize the findings of included outcomes and evaluate the quality of the evidence. It turned out only certainty of the evidence of complication rate was low, while other outcomes were very low. (Table 4).

Discussion

Efficacy of RMN

In our meta-analysis, efficacy outcomes such as AF recurrence rate and acute success rate between the two groups were similar. This study demonstrates that RMN is at least as effective as manual navigation ablation. However, it is important to mention that some studies have a small sample size and might be unable to detect the differences due to low statistical power. That is why large randomized controlled studies are needed to confirm our conclusions.

RMN is associated with longer procedure time and ablation time compared with MCN. Several reasons could be used to explain this observation. First, the flaccid nature of the RMN catheter determines its lower contact force during ablation, resulting in the need for longer ablation time to create similar lesions as conventional manual approach [24]. Second, the navigation speed of RMN in the earlier version is slower than MCN. And there is a short delay in the catheter movement when changing the magnetic vector, and subsequently this may increase the time spent on navigating the catheter and therefor increase the procedure and ablation time [3]. In some cases, the learning curve of this new technology may play a role as well. Moreover, when using the circular mapping catheter, electrophysiologists may need to move between the control room and operating room to manually manipulate the Lasso catheter when using RMN, therefore increasing procedure time. Use of the Stereotaxis Vdrive® System would allow remote movements of the Lasso catheter thus eliminating this step [25].

Safety of RMN

Our meta-analysis indicates that the complication rate of RMN group is statistically lower than MCN. This result is also consistent with the former two meta-analysis published in 2013 and confirms that RMN has an improved safety profile [17,18]. The possible reasons are as follows. As it is known, the catheter of manual navigation is stiff. When moving this kind of catheter, high contact force is often applied and can increase the risk of perforating the atrial wall. However, the catheter of RMN is flaccid, leading to potential advantages like increased precision with catheter movement and control, improved catheter stability with constant tissue contact. In addition, remote magnetic navigation with 3D reconstruction based on CT scan before the ablation procedure can be beneficial to some challenging anatomical variations. All these

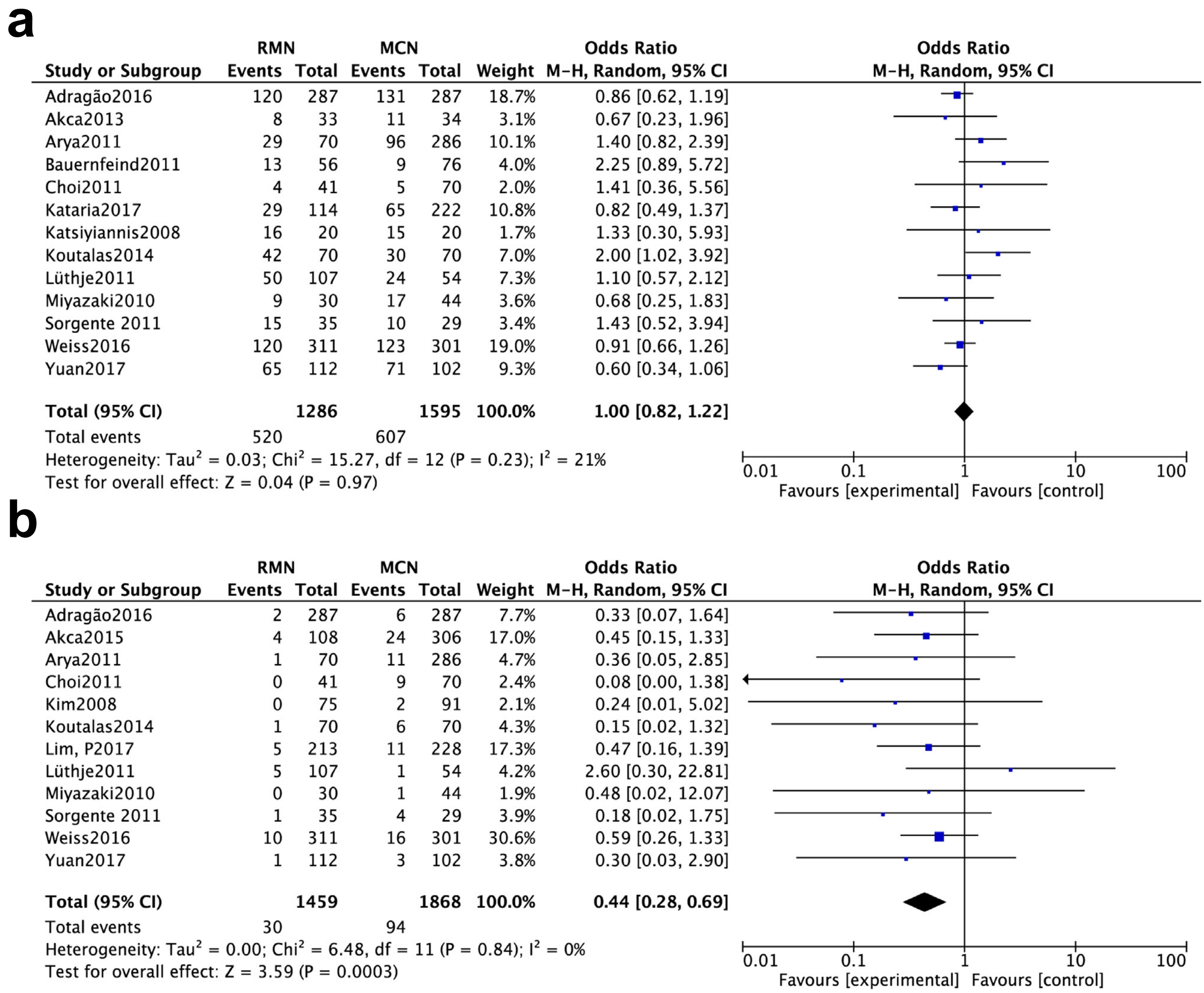

Fig. 2. Forest plot of the primary outcomes. Panel a shows the forest plot of the AF recurrence rate. In panel b, we show the forest plot of complication rate.

characteristics of the RMN catheter can contribute to decreased risk of pericardial effusion and tamponade [5].

In addition, the most important advantage of RMN is reduced fluoroscopy time, which still remains a major component contributing to the total radiation dose to the physician and operator. The use of RMN allows the catheters to be maneuvered remotely from the control room. Which means decreased reliance on continuous fluoroscopy for intracardiac navigation therefore less radiation exposure [4]. This is especially true for young patients and electrophysiologists, who keep receiving the highest radiation exposure as part of occupational hazard. In the long run, the benefits are obvious.

Limitations

The first limitation in our review is that the tests for heterogeneity for acute success rate, procedure, fluoroscopy and ablation time were significant. We performed a meta-regression analysis using publish year and participate numbers but failed to find the source of heterogeneity. The original data of included studies was not available, we cannot further evaluate the source of heterogeneity. We can assume that there may be the confounding factors like different level of experience among operators, type of AF, even different ablation technique and strategy including the number of trans-septal punctures [18]. All these differences between studies may introduce a bias to our analysis. Additionally, we cannot perform the subgroup analysis because the population of our included studies was almost mixed by paroxysmal, persistent and permanent AF patients, and only two studies ([10,26]) enrolled all paroxysmal AF patients. Another limitation is that the studies included are all non-randomized controlled studies (NRSs). Remote magnetic navigation is a developing technology and systematic reviews of the this technology, particularly when focused on devices rather than a medical therapy, face a number of challenges when the numbers of RCTs is limited [27]. Although studies included are high quality observational studies, NRSs is susceptible to bias inherently. Therefore, studies included in our meta-analysis are still at high risk of bias. Along with publication bias, these limitations mentioned above makes the evidence of our meta-analysis uncertain. Since the baseline data of some included studies is incomplete, especially data of some critical factors affecting outcomes such as left atrial diameter, it may add to potential bias to our analysis. According to the summary of findings, only the quality of evidence of complication rate is low, and the quality of evidence of the rest of the

Fig. 3. Forest plot of the secondary outcomes. Panel a shows the forest plot of the acute success rate. Panel b, c and d shows the forest plot of procedure time, fluoroscopy time and ablation time respectively.

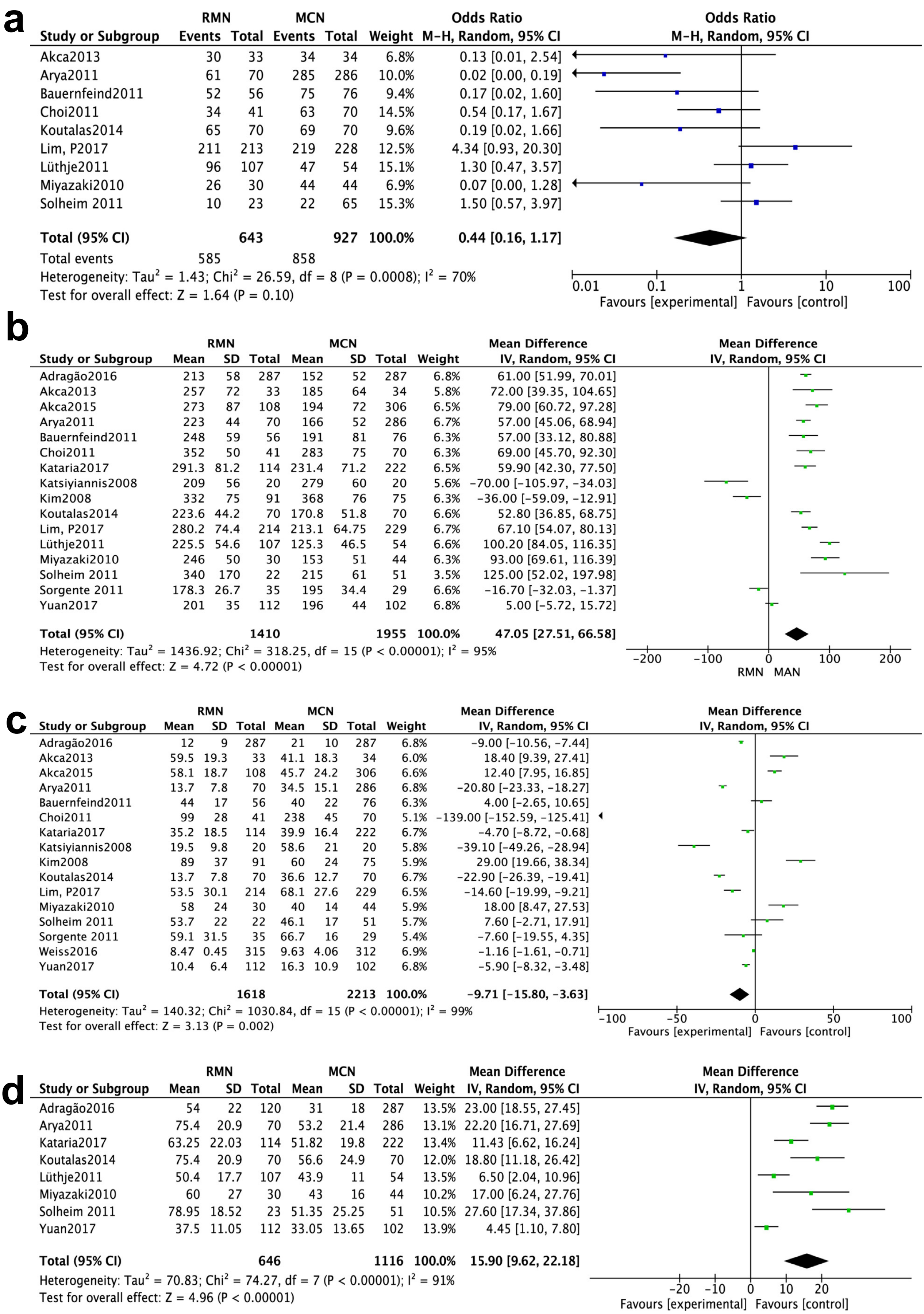
a
Study or Subgroup | RMN Events | Total | MCN Events | Total | Weight | Odds Ratio M-H, Random, 95% CI
Akca2013 30 33 34 34 6.8% 0.13 [0.01, 2.54]
Arya2011 61 70 285 286 10.0% 0.02 [0.00, 0.19]
Bauernfeind2011 52 56 75 76 9.4% 0.17 [0.02, 1.60]
Choi2011 34 41 63 70 14.5% 0.54 [0.17, 1.67]
Koutalas2014 65 70 69 70 9.6% 0.19 [0.02, 1.66]
Lim, P2017 211 213 219 228 12.5% 4.34 [0.93, 20.30]
Lüthje2011 96 107 47 54 15.1% 1.30 [0.47, 3.57]
Miyazaki2010 26 30 44 44 6.9% 0.07 [0.00, 1.28]
Solheim 2011 10 23 22 65 15.3% 1.50 [0.57, 3.97]
Total (95% CI) 643 927 100.0% 0.44 [0.16, 1.17]
Total events 585 858
Heterogeneity: Tau² = 1.43; Chi² = 26.59, df = 8 (P = 0.0008); I² = 70%
Test for overall effect: Z = 1.64 (P = 0.10)
Odds Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours [experimental] Favours [control]
b
Study or Subgroup | RMN Mean | SD | Total | MCN Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI
Adragão2016 213 58 287 152 52 287 6.8% 61.00 [51.99, 70.01]
Akca2013 257 72 33 185 64 34 5.8% 72.00 [39.35, 104.65]
Akca2015 273 87 108 194 72 306 6.5% 79.00 [60.72, 97.28]
Arya2011 223 44 70 166 52 286 6.7% 57.00 [45.06, 68.94]
Bauernfeind2011 248 59 56 191 81 76 6.3% 57.00 [33.12, 80.88]
Choi2011 352 50 41 283 75 70 6.3% 69.00 [45.70, 92.30]
Kataria2017 291.3 81.2 114 231.4 71.2 222 6.5% 59.90 [42.30, 77.50]
Katsiyiannis2008 209 56 20 279 60 20 5.6% −70.00 [−105.97, −34.03]
Kim2008 332 75 91 368 76 75 6.3% −36.00 [−59.09, −12.91]
Koutalas2014 223.6 44.2 70 170.8 51.8 70 6.6% 52.80 [36.85, 68.75]
Lim, P2017 280.2 74.4 214 213.1 64.75 229 6.7% 67.10 [54.07, 80.13]
Lüthje2011 225.5 54.6 107 125.3 46.5 54 6.6% 100.20 [84.05, 116.35]
Miyazaki2010 246 50 30 153 51 44 6.3% 93.00 [69.61, 116.39]
Solheim 2011 340 170 22 215 61 51 3.5% 125.00 [52.02, 197.98]
Sorgente 2011 178.3 26.7 35 195 34.4 29 6.6% −16.70 [−32.03, −1.37]
Yuan2017 201 35 112 196 44 102 6.8% 5.00 [−5.72, 15.72]
Total (95% CI) 1410 1955 100.0% 47.05 [27.51, 66.58]
Heterogeneity: Tau² = 1436.92; Chi² = 318.25, df = 15 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.72 (P < 0.00001)
Mean Difference IV, Random, 95% CI
−200 −100 0 100 200
RMN MAN
c
Study or Subgroup | RMN Mean | SD | Total | MCN Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI
Adragão2016 12 9 287 21 10 287 6.8% −9.00 [−10.56, −7.44]
Akca2013 59.5 19.3 33 41.1 18.3 34 6.0% 18.40 [9.39, 27.41]
Akca2015 58.1 18.7 108 45.7 24.2 306 6.6% 12.40 [7.95, 16.85]
Arya2011 13.7 7.8 70 34.5 15.1 286 6.8% −20.80 [−23.33, −18.27]
Bauernfeind2011 44 17 56 40 22 76 6.3% 4.00 [−2.65, 10.65]
Choi2011 99 28 41 238 45 70 5.1% −139.00 [−152.59, −125.41]
Kataria2017 35.2 18.5 114 39.9 16.4 222 6.7% −4.70 [−8.72, −0.68]
Katsiyiannis2008 19.5 9.8 20 58.6 21 20 5.8% −39.10 [−49.26, −28.94]
Kim2008 89 37 91 60 24 75 5.9% 29.00 [19.66, 38.34]
Koutalas2014 13.7 7.8 70 36.6 12.7 70 6.7% −22.90 [−26.39, −19.41]
Lim, P2017 53.5 30.1 214 68.1 27.6 229 6.5% −14.60 [−19.99, −9.21]
Miyazaki2010 58 24 30 40 14 44 5.9% 18.00 [8.47, 27.53]
Solheim 2011 53.7 22 22 46.1 17 51 5.7% 7.60 [−2.71, 17.91]
Sorgente 2011 59.1 31.5 35 66.7 16 29 5.4% −7.60 [−19.55, 4.35]
Weiss2016 8.47 0.45 315 9.63 4.06 312 6.9% −1.16 [−1.61, −0.71]
Yuan2017 10.4 6.4 112 16.3 10.9 102 6.8% −5.90 [−8.32, −3.48]
Total (95% CI) 1618 2213 100.0% −9.71 [−15.80, −3.63]
Heterogeneity: Tau² = 140.32; Chi² = 1030.84, df = 15 (P < 0.00001); I² = 99%
Test for overall effect: Z = 3.13 (P = 0.002)
Mean Difference IV, Random, 95% CI
−100 −50 0 50 100
Favours [experimental] Favours [control]
d
Study or Subgroup | RMN Mean | SD | Total | MCN Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI
Adragão2016 54 22 120 31 18 287 13.5% 23.00 [18.55, 27.45]
Arya2011 75.4 20.9 70 53.2 21.4 286 13.1% 22.20 [16.71, 27.69]
Kataria2017 63.25 22.03 114 51.82 19.8 222 13.4% 11.43 [6.62, 16.24]
Koutalas2014 75.4 20.9 70 56.6 24.9 70 12.0% 18.80 [11.18, 26.42]
Lüthje2011 50.4 17.7 107 43.9 11 54 13.5% 6.50 [2.04, 10.96]
Miyazaki2010 60 27 30 43 16 44 10.2% 17.00 [6.24, 27.76]
Solheim 2011 78.95 18.52 23 51.35 25.25 51 10.5% 27.60 [17.34, 37.86]
Yuan2017 37.5 11.05 112 33.05 13.65 102 13.9% 4.45 [1.10, 7.80]
Total (95% CI) 646 1116 100.0% 15.90 [9.62, 22.18]
Heterogeneity: Tau² = 70.83; Chi² = 74.27, df = 7 (P < 0.00001); I² = 91%
Test for overall effect: Z = 4.96 (P < 0.00001)
Mean Difference IV, Random, 95% CI
−20 −10 0 10 20
Favours [experimental] Favours [control]

Table 3
NOS scale for case control study and cohort study.

Case control study

Studies	Selection				Comparability	Exposure			Score
	Adequate definition of cases	Representativeness of the cases	Selection of controls	Definition of controls		Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-Response rate	
Lim, P et al	★	★	☆	★	★☆	★	★	★	7
Koutalas, E et al 2015	★	★	☆	★	★★	★	★	★	8
Arya, A et al 2011	★	★	☆	★	★☆	★	★	★	7
Pappone et al. 2006	★	★	☆	★	★☆	★	★	★	7
Kim et al. 2008	★	★	☆	★	★☆	★	★	★	7

Cohort study

Studies	Selection				Comparability of cohorts	Outcomes			Score
	Representativeness of cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome lacking at the beginning		Outcome assessment	Sufficient follow-up time	Follow up adequacy	
Yuan, s et al. 2017	★	★	★	☆	★☆	★	★	★	7
Kataria et al. 2017	★	★	★	☆	★☆	★	★	☆	6
Adragão, P et al. 2016	★	★	★	★	★☆	★	★	☆	7
Weiss et al. 2016	★	★	★	☆	★☆	★	★	★	7
Akca, F et al. 2015	★	★	★	★	★☆	★	★	★	8
Akca, F et al. 2013	★	★	★	★	★★	★	★	★	9
Bauernfeind et al. 2011	★	★	★	★	★☆	★	★	★	8
Choi et al. 2011	★	★	★	★	★☆	★	☆	★	7
Lüthje et al. 2011	★	★	★	★	★★	★	★	★	9
Solheim, E et al. 2011	★	★	★	★	★☆	★	★	★	8
Sorgente 2011	★	★	★	☆	★☆	★	★	★	7
Miyazaki 2010	★	★	★	★	★☆	★	★	★	8
Katsiyiannis, W.T et al 2008	★	☆	★	★	☆☆	★	★	★	6

Table 4
Summary of findings table.

RMN compared to MCN in AF ablation					
Bibliography					
Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with MCN	Risk difference with RMN
AF recurrence rate	2881 (13 observational studies)	⊕◯◯◯ VERY LOW[a]	OR 1.00 (0.82 to 1.22)	381 per 1000	0 fewer per 1000 (46 fewer to 48 more)
Complication rate	3327 (12 observational studies)	⊕⊕◯◯ LOW [b]	OR 0.44 (0.28 to 0.69)	50 per 1000	28 fewer per 1000 (36 fewer to 15 fewer)
Acute success rate	1570 (9 observational studies)	⊕◯◯◯ VERY LOW [c]	OR 0.44 (0.16 to 1.17)	926 per 1000	80 fewer per 1000 (260 fewer to 10 more)
Procedure time	3365 (16 observational studies)	⊕◯◯◯ VERY LOW [d, e]	–	The mean procedure time was 0	MD 47.05 higher (27.51 higher to 66.58 higher)
Fluoroscopy time	3831 (16 observational studies)	⊕◯◯◯ VERY LOW [f, g]	–	The mean fluoroscopy time was 0	MD 9.71 lower (15.8 lower to 3.63 lower)
Ablation time	1762 (8 observational studies)	⊕◯◯◯ VERY LOW [h]	–	The mean ablation time was 0	MD 15.9 higher (9.62 higher to 22.18 higher)

CI: Confidence interval; OR: Odds ratio; MD: Mean difference.
GRADE Working Group grades of evidence.
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.
*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

five outcomes is very low. These limitations should not impact our conclusions.

Our study summarizes the state of the art of RMN technology through large populations up to 4046 patients and provides valuable information about the efficacy and safety between remote magnetic navigation and manual navigation for AF ablation.

Conclusion

Our results suggest that the RMN is as effective as MCN in achieving PVI and freedom form AF recurrence, and has superior safety with less complication and shorter fluoroscopy time, but longer procedure and ablation time. Since included studies were all non-randomized studies, which is inherit to bias, randomized studies need to be performed to better test this hypothesis with stronger evidence.

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