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Comparison of phase mapping and electrogram-based driver mapping for catheter ablation in atrial fibrillation

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Abstract

Introduction: Adjunctive driver-guided ablation in addition to pulmonary vein isolation has been proposed as a strategy to improve procedural success and outcomes for various populations with atrial fibrillation (AF). First, this study aimed to evaluate the different mapping techniques for driver/rotor identification and second to evaluate the benefits of driver/rotor-guided ablation in patients with paroxysmal and persistent AF (PerAF).

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AUTHOR CONTRIBUTIONS

Chin-Yu Lin, Yun-Yu Chen, and Yenn-Jiang Lin generated the research topic, did the literature search, and prepared the first manuscript. Yun-Yu Chen ran the statistical tests. Sanjiv M. Narayan, Tina Baykaner, Men-Tzung Lo, Fa-Po Chung, Shih-Lin Chang, Li-Wei Lo, Yu-Feng Hu, Jo-Nan Liao, Ta-Chuan Tuan, and Tze-Fan Chao conceived the study concept and contributed important parts in data interpretation. Chin-Yu Lin, Yenn-Jiang Lin, and Shih-Ann Chen analyzed and interpreted the data. Tina Baykaner, Abigail Louise D. Te, Ling Kuo, Jennifer Jeanne B. Vicera, Ting-Yung Chang, and Simon Salim collected the data. Yenn-Jiang Lin, Sanjiv M. Narayan, Kuo-Liong Chien, and Shih-Ann Chen critically read the manuscript and made vital suggestions in revision. All authors reviewed and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Methods: We searched the electronic database in PubMed using the keywords “atrial fibrillation,” “rotor,” “rotational driver,” “atrial fibrillation source,” and “drivers” for both randomized controlled trials and observational controlled trials. Clinical studies reporting efficacy or safety outcomes of driver-guided ablation for paroxysmal AF or (PerAF) were identified. We performed subgroup analyses comparing different driver mapping methods in patients with PerAF. The odds ratios (ORs) with random effects were analyzed.

Results: Out of 175 published articles, seven met the inclusion criteria, of which two were randomized controlled trials, one was quasiexperimental study, and four observational studies (three case-controlled studies and one cross-sectional study). Overall, adjunctive driver-guided ablation was associated with higher rates of acute AF termination (OR: 4.62, 95% confidence interval [CI]: 2.12–10.08; $P < 0.001$), lower recurrence of any atrial arrhythmia (OR: 0.44, 95% CI: 0.30–0.065; $P < 0.001$), and comparable complication incidence.

Conclusions: Adjunctive driver-guided catheter ablation suggested an increased freedom from AF/AT relative to conventional strategies, irrespective of the mapping techniques. Furthermore, phase mapping appears to be superior to electrogram-based driver mapping in PerAF ablation.

Keywords

atrial fibrillation; catheter ablation; driver; meta-analysis; phase-mapping

1 | INTRODUCTION

Atrial fibrillation (AF) is the most frequently occurring sustained arrhythmia, which causes significant morbidity and mortality.[1] Has-saïguerre et al[2] and Chen et al[3] first reported the dominant and pathologic role of pulmonary vein (PV) triggers in the arrhythmogenesis of AF. Owing to the advancement of mapping techniques and broader knowledge on pathogenesis, catheter ablation has been considered as an effective and alternative treatment option for AF patients. Electrical isolation of PV has become the cornerstone for catheter ablation in AF with achievement of rhythm control in approximately 70%−75% cases of paroxysmal AF (PAF).[4] However, it is less effective in patients with persistent AF (PerAF), and repeat procedures are often required.[5] Additional targeting of signals with high frequencies for catheter ablation during AF has been previously proposed as a treatment strategy.[6–10] However, randomized controlled trials (RCTs) did not show any benefit of performing additional linear ablation or of complex fractionated atrial electrograms ablation in addition to PV isolation (PVI) in patients with PerAF.[11]

Because of the advancement of signal processing systems, mapping systems, and mapping catheters, several recent studies have demonstrated successful driver identification during AF ablation. Lin et al, Haïssaguerre et al, and Narayan et al used phase-mapping-based strategy to identify drivers during procedure,[9,12,13] whereas Atienza et al, Jadidi et al, and Seitz et al used electrogram-based driver mapping strategy to identify small radius reentry responsible for the maintenance of AF.[14–16] Owing to the advances in mapping techniques and understanding of the pathogenesis, driver-guided ablation has emerged as a potential therapeutic target for PerAF ablation.

Several meta-analyses have been conducted by different groups to evaluate the benefit of driver-guided ablation in addition to the standard approach, and the results are controversial. These meta-analyses did not focus on PerAF ablation only but also included PAF and PerAF patients. Additionally, the driver mapping methodology (phase mapping or electrogram-based mapping) was not investigated. We, therefore, systematically reviewed the published literature to compare the reported efficacy and safety of phase mapping and electrogram-based driver mapping for AF and PerAF patients.

2 | MATERIALS AND METHODS

2.1 | Search strategy and study eligibility

We searched the electronic database in PubMed for both experimental and observational studies published before 1 September 2017. The search strategy included “atrial fibrillation,” “rotor,” “rotational driver,” “atrial fibrillation source,” and “drivers” as the medical subject headings and text keywords. We aimed to systematically review the literature for evidence of clinical effectiveness of driver/rotor ablation of AF in RCT, quasiexperimental studies, and observational studies with a comparison group following the recommendations for the reporting of meta-analysis of observational studies.[17] For the subgroup analyses in subjects with persistent AF, we conducted an individual patient meta-analysis, which focused on patients with PerAF. The trials investigating only patients with PAF were excluded from the subgroup analysis. There is currently no consensus or guidelines for driver/rotor identification, and thus, we classified mapping strategy for drivers during AF using the two predominant methods as[1] phase-mapping and[2] electrogram-based driver mapping strategies. Four studies used phase-mapping-based driver identification, and three studies used electrogram-based driver identification strategy. These studies were included in the pooled analyses along with a discussion about any impact they may have had on the results.

2.2 | Definitions of driver mapping

The studies were classified into phase mapping and electrogram-based driver mapping based on the methodology used in each study. Several studies demonstrated successful driver identification by phase mapping of simultaneous recordings using a basket catheter,[13] noninvasive array of body surface electrodes,[12] or nonlinear processing technique to identify the morphological repetitiveness of waveform patterns by using double spiral catheters.[9] Some studies also revealed the successful driver identification by recognizing the localized high-frequency source,[14] electrogram dispersion during AF,[16] and local rotational activity[15] by using the electrogram-based driver mapping strategy.

2.3 | Study end points

We grouped studies according to the following analysis areas for patients with AF who underwent driver-guided ablation:

Analysis 1: Efficacy (AF termination and 1-year freedom from AF/atrial tachycardia [AT] recurrence) of driver-guided ablation compared to conventional ablation therapy.

Analysis 2: Subgroup analysis of efficacy (1-year freedom from AF/AT recurrence) of phase mapping and electrogram-based driver mapping strategy.

Analysis 3: Complications in driver mapping strategy compared to those in conventional ablation therapy.

2.4 | Assessment of study quality

Comparison of interventions usually does not allow a blinded study design; hence, we did not assess for blinded studies. Two independent cardiac electrophysiologists screened the eligible abstracts and full texts of all controlled trials, with disagreements solved by the opinions of a third cardiac electrophysiologist. The methodological quality of the studies was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines,[18,19] Newcastle-Ottawa Scale,[20] and Cochrane Collaboration's tool.[9]

2.5 | Statistical analyses

Data were pooled by the use of the Cochran-Mantel-Haenszel method, and the outcomes were compared with the results obtained from a random-effects model, which considered the heterogeneity among the trials. To avoid unnecessary heterogeneity, we formed a homogeneous group of studies according to the adjustment status of the estimated risk. The Cochran Q and I^2 statistic were applied for the estimation of heterogeneity, and the funnel plots with Egger's test for small-study effects were applied to evaluate the risks of bias. The pooled odds ratios (ORs) and the 95% confidence intervals (CIs) were determined for the outcomes. P value of <0.05 was considered statistically significant. The analyses were performed using the software RevMan 5.3 (Cochrane, London, UK) and Stata 11.0 (StataCorp LLC, College Station, TX, USA).

3 | RESULTS

3.1 | Study selection and characteristics

Of the 175 relevant full-text articles/clinical trials identified from database search or manual search, seven full manuscripts met the inclusion criteria for this present study (Figure 1). Two full RCTs,[9,14] one quasiexperimental study,[13] and four observational studies (three case-controlled studies[12,15,16] and one cross-sectional study[21]) were found. The remaining reports were observational studies, predominantly descriptive studies, or small case series. Study characteristics and quality are summarized in Table 1 and in Supporting Information Tables S1–S3. Funnel plot with Egger's test on the small-study effects of 1-year freedom from AF/AT recurrence with driver-guided versus conventional ablation for PAF plus PerAF patients revealed that there was no bias of heterogeneity in this study (Supporting Information Figure S1). Metaregression with the adjustment with heterogeneity of AF duration in the selected studies demonstrates no significant impact on the outcomes (adjusted $R^2 = -82.7\%$, $P = 0.67$, Supporting Information Figure S2).

3.2 | Analysis 1: Efficacy (AF termination and 1-year freedom of AF/AT recurrence) of driver-guided ablation compared to conventional ablation therapy

Six studies with control groups reported relevant efficacy outcomes for both treatment and control groups in PAF and PerAF (Table 1). One study was excluded from this analysis because there was no control group.[21] Five studies were extracted for evaluation of the driverguided ablation efficacy on PerAF.[9,12–15] Overall, driver-guided ablation was associated with significantly improved 1-year freedom (OR: 0.44, 95% CI: 0.30–0.65, $P < 0.001$) from recurrent AF/AT and higher AF termination rate (OR: 4.62, 95% CI: 2.12–10.08, $P < 0.001$) than conventional AF ablation strategies (Figures 2A and 3A). In the subgroup analysis for PerAF, driver-guided ablation was associated with higher 1-year freedom from recurrent AF/AT (OR: 0.36, 95% CI: 0.22–0.60, $P < 0.001$) and higher AF termination rate (OR: 7.12, 95% CI: 1.24–41.04, $P = 0.03$) than conventional AF ablation strategies.

3.3 | Analysis 2: Subgroup analysis of efficacy (1-year freedom of AF/AT recurrence) by phase mapping and electrogram-based driver mapping strategy

Three studies used phase-mapping-based strategy[9,12,13] and three used the electrogram-based driver mapping strategy to identify the drivers.[14–16] One study that used phase mapping was excluded from this analysis because there was no control group.[21] Five studies were extracted for evaluation of the driver-guided ablation efficacy on PerAF.[9,12–15] In the pooled database, both phase mapping and electrogram-based driver mapping significantly improved the 1-year freedom from recurrent AF/AT (OR: 0.35, 95% CI: 0.21–0.59, $P < 0.001$ and OR: 0.51, 95% CI: 0.28–0.94, $P < 0.001$, respectively, Figures 2B and 2C). In the subgroup analysis of PerAF, phase mapping (OR: 0.33, 95% CI: 0.19–0.56, $P < 0.001$) significantly improved the 1-year freedom of recurrent AF/AT compared to electrogram-based driver mapping (OR: 0.41, 95% CI: 0.12–1.37, $P = 0.15$).

3.4 | Analysis 3: Complications in driver mapping strategy compared to those in conventional ablation therapy

Seven studies with control groups reported relevant complications for both treatment and control groups in PAF or PerAF. One study was excluded from this analysis because there was no report regarding complications.[12] Four studies were extracted for evaluation of the efficacy of driver-guided ablation on PerAF.[9,13–15] Overall, driver-guided ablation-related complications did not differ from that in the control group in overall AF procedure and PerAF procedure (OR: 0.96, 95% CI: 0.55–1.65, $P = 0.87$ and OR: 1.33, 95% CI: 0.44–3.99, $P = 0.62$, respectively, Figure 3B).

4 | DISCUSSION

4.1 | Main findings

The current meta-analysis demonstrated that adjunctive driver-guided ablation in addition to conventional ablation could improve 1-year AF/AT freedom and increase AF termination rate during the procedure without risking additional potential complication. In patients with

PerAF, phase mapping may be beneficial compared to electrogram-based driver mapping in the 1-year AF/AT freedom after ablation.

4.2 | AF driver mapping technologies

A driver of a spiral wave is a rotation center with excitation rotating outward. Phase mapping has been the standard method to identify drivers in animal models of fibrillation.[22] On the phase maps, a driver is defined as a phase singularity point around which the phase transitions through a complete cycle from $-\pi$ to $+\pi$.[23,24] There are mainly three phase mapping-guided settings used for driver detection: invasive focal impulse and driver modulation (Abbott, Abbott Park, IL, USA),[13] noninvasive electrocardiographic imaging (ECGI),12 and electrogram similarity/phase mapping combined techniques.[9] Several electrogram-based driver mapping techniques have also been used to demonstrate successful driver identification and ablation.

The heterogeneity of methodology used for AF driver mapping in published studies is a major limitation of the current data. Moreover, the available mapping systems capable of detecting AF drivers have major differences related to signal acquisition and processing.[1] Focal Impulse and Rotor Mapping (FIRM) mapping[13] used basket contact mapping and electrogram-based driver mapping technique,[2] Haïssaguerre et al[12] reported using noninvasive ECGI mapping technique with an array of body surface electrodes and phase-mapping-based technique,[3] Lin et al[9] reported using 20-poles double spiral catheter (1-mm electrodes with 4-mm spacing, St. Jude Medical, St. Paul, MN, USA) and nonlinear processing technique in signal processing with phase-mapping-based technique in high similarity index areas,[4] Jadidi et al[15] used doubleloop 20-pole catheter AFocus II HD (1-mm electrodes with 4-mm spacing, St. Jude Medical) or a 20-pole variable Lasso-Nav catheter (1 mm electrodes with 2–5-2 mm spacing, Biosense Webster, Diamond Bar, CA, USA) to identify repetitive rotational activity >70% of AF cycle length with electrogram-based driver mapping technique,[5] Radiofrequency Ablation of Drivers of AF (RADAR-AF)[14] used ablation catheter or circular mapping catheter with a dominant frequency/electrogram-based driver mapping technique, and[6] Seitz et al[16] used the 20-pole PentaRay catheter to identify the local regions displaying electrogram dispersion during AF. Because of the nonuniformed mapping technique and mapping materials, it is unknown if these mapping tools would detect the same drivers. The pooled efficacy effect estimates provided in this meta-analysis are based on the premise that these mapping tools are adequate for detecting AF drivers.

4.3 | Comparison with previous meta-analyses

Previous meta-analyses of trials comparing additional driver-guided ablation with the traditional approach have supported the possible benefit of a combined approach of driver-guided ablation, which includes the phase mapping and electrogram-based technique, and PVI in improving single-procedure freedom from all arrhythmias in the population with mixed AF type.[25,26] Another meta-analysis focused on studies using FIRM mapping (phase mapping based, RhythmView, Abbott Medical) to identify rotors in the mixed AF type.[27] Although the pooled dataset favor the rotor ablation by using FIRM mapping, there was a marked heterogeneity between studies and wide variability in success rates between different centers performing rotor ablations.[27] Mohanty et al[28] conducted another meta-analysis

comparing the PVI alone and PVI plus FIRM ablation. Unlike the previous meta-analysis, the PVI only group was extracted from other randomized trials, which were not related to FIRM ablation studies. Although the study design is debatable by comparing different strategies from different studies, the overall pooled estimate did not show any therapeutic benefit of PVI plus FIRM approach over PVI alone.[28]

These above-mentioned meta-analyses did not focus on ablation in PerAF patients alone, but on both PAF and PerAF patients. Additionally, the different driver mapping methodologies (phase mapping or electrogram-based mapping) have not been investigated. To the best of our knowledge, this is the first systematic review and meta-analysis reporting the comparison of the efficacy and safety of phase mapping and electrogram-based driver mapping for AF and PerAF patients. Our systematic review suggests that phase mapping may be superior to electrogram-based driver mapping technique for catheter ablation in PerAF patients.

4.4 | Consideration of PerAF ablation

The optimal ablation strategy for persistent AF remains undetermined and an alternative approach must be explored. The results of the substrate and trigger ablation for reduction of AF—part II (STAR-AF II) trial have cast doubts on the efficacy of widely adopted strategies to modify the atrial substrate and have underscored an urgent need to identify the optimal ablation strategy for PerAF. Adjuvant ablation of the ganglion plexus failed to achieve significant improvement in PerAF ablation.[29] Adjuvant elimination of drivers and non-PV triggers have been proposed as a potential strategy in PerAF patients.[30]

RADAR-AF and the study by Lin et al are the only full RCTs that test targeting the presumed AF drivers (defined as high-frequency sources using dominant frequency mapping in the former and as sites with high similarity indices using nonlinear phase-mapping in areas exhibiting complex fractionated atrial electrograms in the latter).[9,14] The studies by Haïssaguerre et al, Narayan et al, and Jadidi et al were prospective studies with matched control patients to test the efficacy of driver elimination (defined as focal or reentrant activity by phase mapping using commercially available ECGI in the first study [against historical controls] and rotational activity with multiple electrodes in the latter two).[12,15] The pooled data on the efficacy of PerAF driver-guided catheter ablation showed increased freedom from AF/AT relative to conventional strategies.

Additionally, phase mapping rather than electrogram-based driver mapping seemed to provide better freedom from AF/AT relative to conventional strategies. Although the data are promising, and the results favored phase-mapping driver identification, our meta-analysis included primarily nonrandomized studies. Overall, the evidence for the efficacy of AF driver ablation remains inconclusive. Further prospective randomized study with standardized driver identification and validation are warranted.

4.5 | Limitations

Although the results are promising, existing studies are limited owing to the lack of consistent mapping tools. Therefore, the evidence to support ablative strategies targeting AF drivers remains inconclusive. Further, randomized and clinical trials with standardized

mapping materials are needed. This study also included differences in clinical management between centers, reflecting differences in anticoagulation protocols, transseptal technique, and PVI ablation strategy between individual operators. Furthermore, the number of published RCT trials on driver-guided ablation is limited.

5 | CONCLUSIONS

Pooled data on the efficacy of AF driver-guided catheter ablation suggested increased freedom from AF/AT relative to conventional strategies. Phase mapping appears to be superior to electrogram-based driver mapping technique to achieve better ablation outcomes in PerAF patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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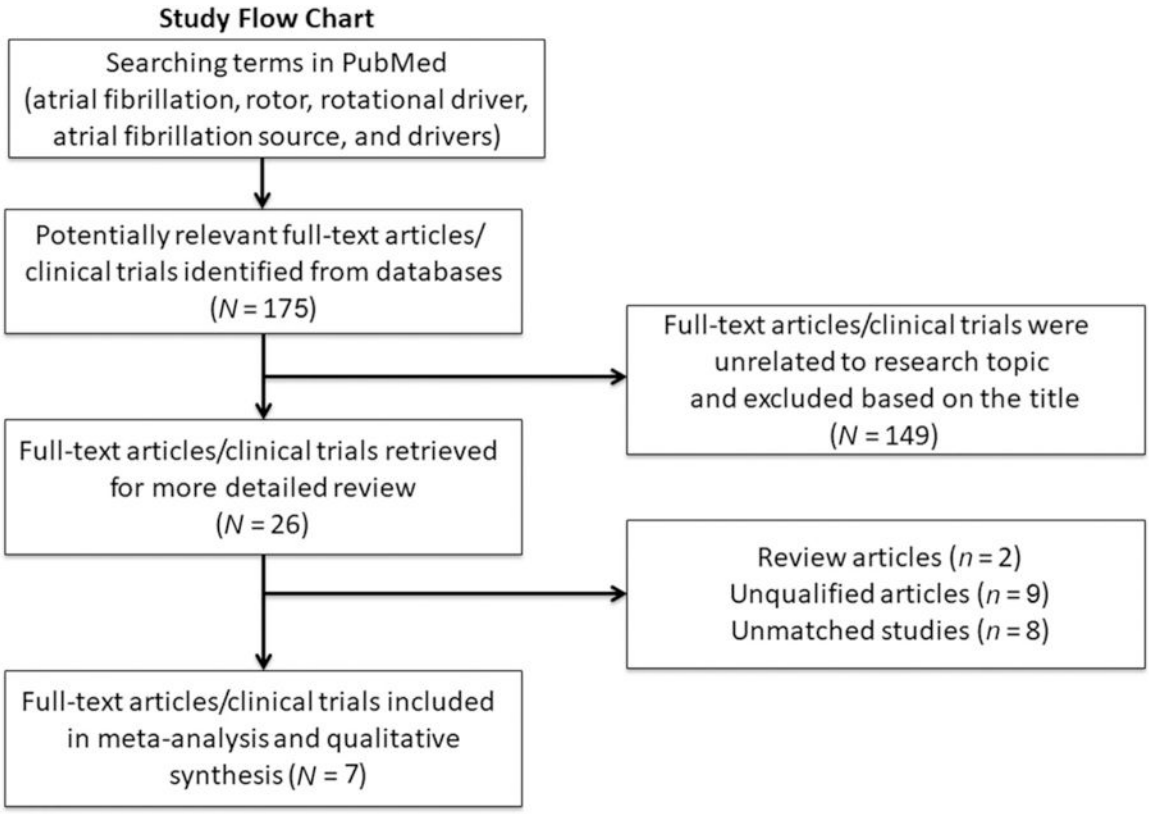

FIGURE 1.
Flow diagram of literature search

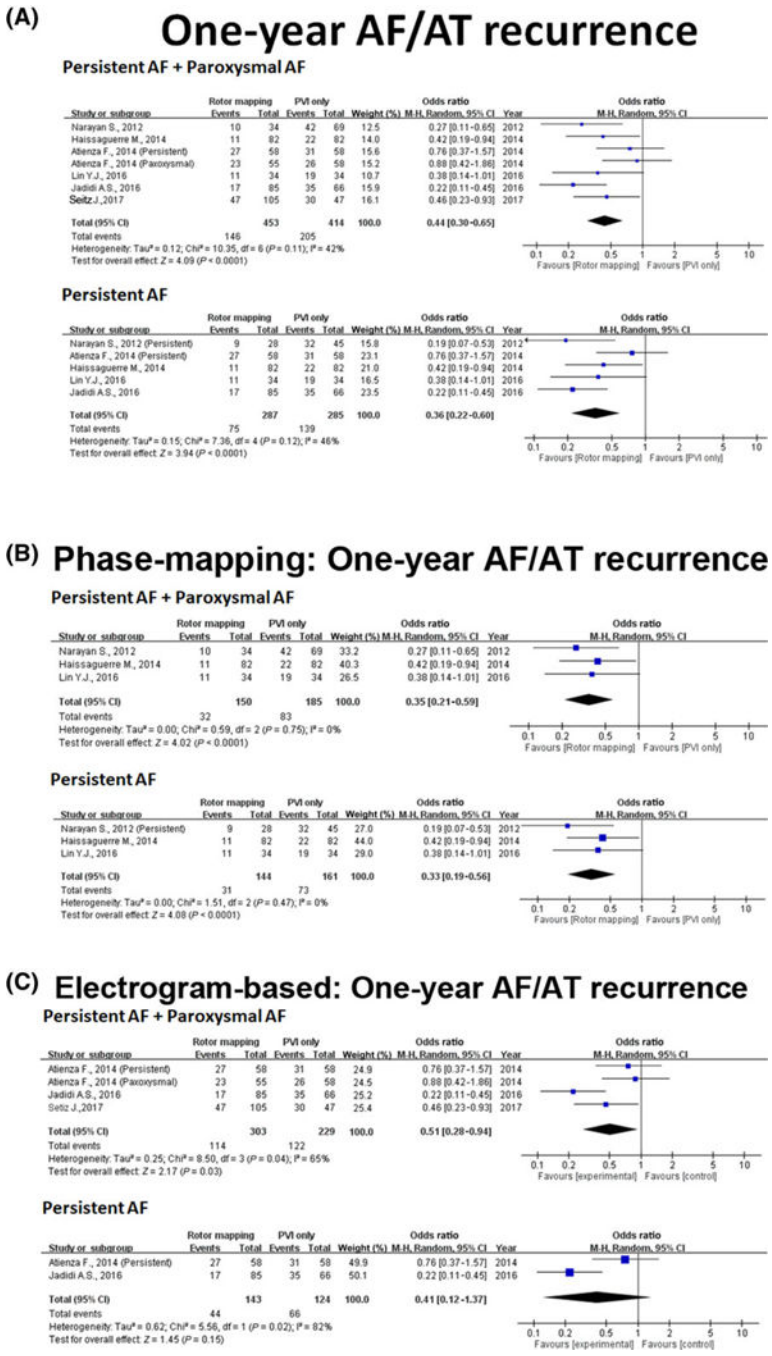

FIGURE 2.

One-year freedom from AF/AT recurrence at 1 year. (A) Forest plot of 1-year freedom from AF/AT recurrence at 1 year with driver-guided versus conventional ablation. (B) Forest plot of 1-year freedom from AF/AT recurrence at 1 year with phase-mapping-based driver-guided versus conventional ablation. (C) Forest plot of 1-year freedom from AF/AT recurrence at 1 year with electrogram-based driver mapping versus conventional ablation. AF = atrial fibrillation; AT = atrial tachycardia [Color figure can be viewed at wileyonlinelibrary.com]

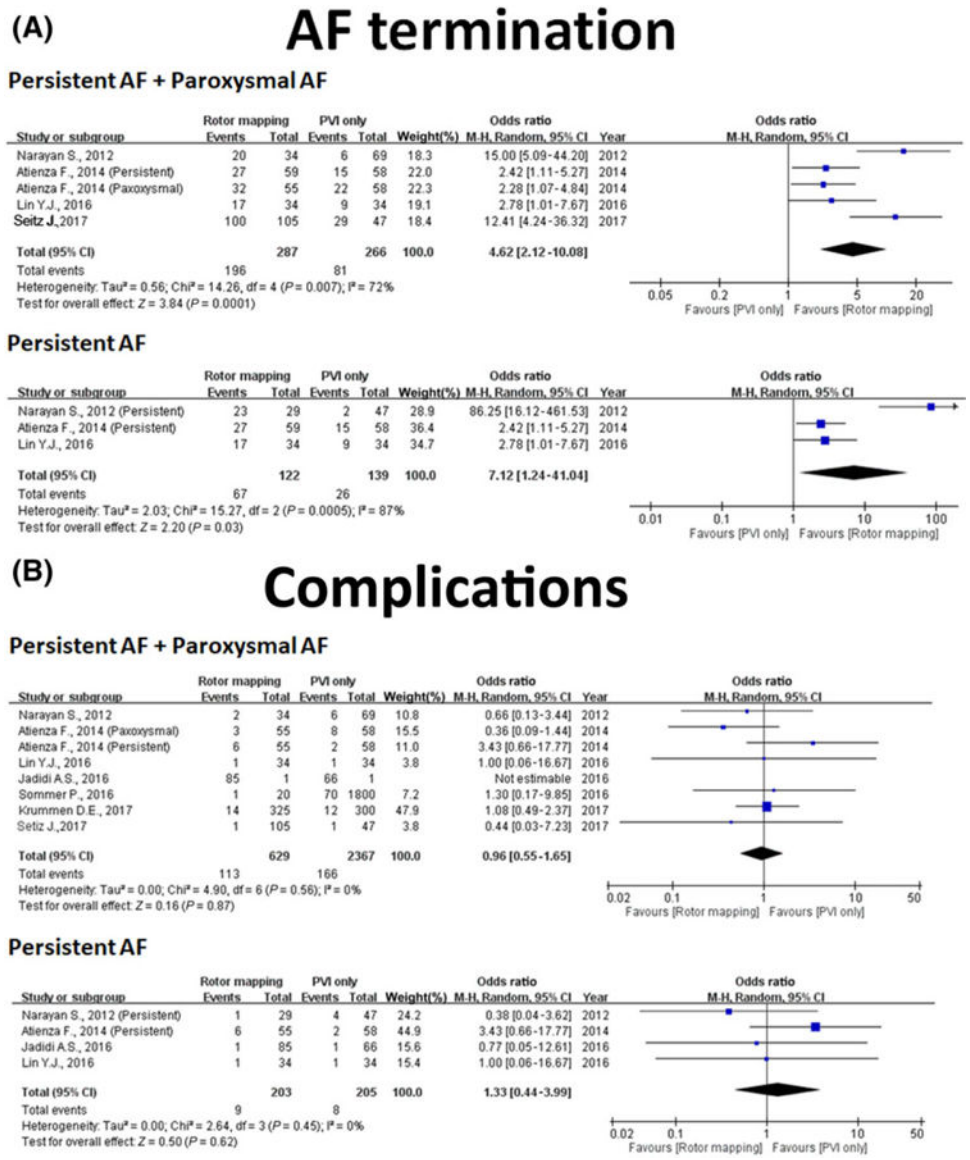

FIGURE 3.

Analysis of AF termination and complication. (A) Forest plot of acute AF termination with driver-guided versus conventional ablation. (B) Forest plot of complication with driver-guided versus conventional ablation. AF = atrial fibrillation [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1

Details of selected studies

First author	Study type	Total number	PerAF	Control group	Treatment group	Risk of bias	Quality of methodology[b]
Atienza[14]	RCT	232	117	PVI	Driver (PAF) ± PVI (PerAF)	No serious limitation	High
Lin[9]	RCT	68	68	PVI + CFAE	PVI then rotor ablation within CFAE regions	No serious limitation	High
Narayan[13]	Quasiexperimental study	107[a]	76	PVI ± LA roof line, AT/AFL ablation (PerAF)	Driver then PVI (PAF) ± LA roof line, AT/AFL ablation (PerAF)	Serious	Moderate
Haïssaguerre[12]	Case-controlled study	103	103	PVI	Driver then LA roof + mitral isthmus line if AF persisted then PVI	Serious	Moderate
Jadidi[15]	Case-controlled study	85	85	PVI	PVI then rotor in low-voltage areas (<0.5 mV)	Serious	Low
Seitz[16]	Case-controlled study	105	81	PVI	Driver	Serious	Moderate
Sommer[21]	Cross-sectional study	20	20	N/A	Driver then PVI (PAF) ± LA roof line, AT/AFL ablation (PerAF)	Serious	Low

AF = atrial fibrillation; AT/AFL = atrial tachycardia/atrial flutter; CFAE = complex fractionated atrial electrogram; LA = left atrium; PAF = paroxysmal atrial fibrillation; PerAF = persistent atrial fibrillation; PVI = pulmonary vein isolation; RCT = randomized controlled trial.

[a] Procedure numbers.

[b] Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidelines.

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