SYSTEMATIC REVIEW AND META-ANALYSIS

Is Atrial Fibrillation Noninducibility by Burst Pacing After Catheter Ablation Associated With Reduced Clinical Recurrence?

A Systematic Review and Meta-Analysis

Hualong Liu, MD*; Ping Yuan, MD*; Xin Zhu, MD*; Linghua Fu, MD; Kui Hong ២, MD, PhD; Jinzhu Hu, MD, PhD

BACKGROUND: To date, there is no cumulative evidence supporting the association of atrial fibrillation (AF) noninducibility after ablation and freedom from AF. We performed a systematic review and meta-analysis to determine whether AF noninducibility by burst pacing after catheter ablation is associated with reduced AF recurrence.

METHODS AND RESULTS: We searched PubMed, Embase, Web of Science, and Cochrane Library databases through July 2019 to identify studies that evaluated AF noninducibility versus inducibility by burst pacing after catheter ablation for freedom from AF. A fixed effects model was used to estimate relative risk (RR) with 95% Cls. Twelve prospective cohort studies with AF noninducibility (n=1612) and inducibility (n=1160) were included. Compared with AF inducibility, AF noninducibility by burst pacing after ablation was associated with a reduced risk of AF recurrence (RR, 0.68; 95% Cl, 0.60–0.77). Subgroup analysis showed that different AF types (paroxysmal AF and nonparoxysmal AF), different follow-up times (\leq 6, 6–12, and >12 months), and different degrees of burst pacing (mild, moderate, severe) had no significant impact on the RRs. However, different cut-off times for AF inducibility had a significant impact on the RR ($P_{interaction}=0.009$), and only the cut-off time of 1 minute showed a significant correlation (RR, 0.54; 95% Cl, 0.45–0.66).

CONCLUSIONS: AF noninducibility by burst pacing after catheter ablation is associated with reduced clinical recurrence of AF. Induction protocols with a different cut-off time for AF inducibility have a significant impact on the correlation, and the AF \geq 1 minute for AF inducibility is recommended.

Key Words: association a trial fibrillation induction protocol noninducibility recurrence

trial fibrillation (AF) is one of the most common arrhythmias and affects \approx 33.5 million people worldwide. Catheter ablation is an effective method for the treatment of symptomatic AF and an important alternative to pharmacological therapy, with the advantages of maintaining a longer duration of sinus rhythm, improving quality of life, and reducing hospitalizations.¹ Although the techniques of catheter

ablation of AF have been greatly developed, and its efficacy has been definitely established, the recurrence of AF after ablation remains a major concern.² Over the past decade, electrophysiologists have attempted to find better ablation strategies and prognostic factors to improve the success rate of AF ablation.

AF noninducibility by burst pacing is defined as the inability to induce AF with a prespecified

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Supplementary Materials for this article are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.015260

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For Sources of Funding and Disclosures, see page 11.

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CLINICAL PERSPECTIVE

What Is New?

- This systematic review and meta-analysis shows that atrial fibrillation (AF) noninducibility by burst pacing after ablation is significantly associated with freedom from AF, compared with AF inducibility.
- Different AF types (paroxysmal AF and nonparoxysmal AF), and different follow-up times (≤6, 6–12, and >12 months) have no significant impact on the relative risks, and all show a correlation.
- Induction protocols with different cut-off times (1, 2, and 5–10 minutes) for AF inducibility have a significant impact on the correlation, and AF ≥1 minute for AF inducibility is recommended.

What Are the Clinical Implications?

- AF noninducibility by burst pacing after ablation is a prognostic factor of freedom from AF, which can be employed as a main procedural end point in AF ablation.
- For the AF induction test, electrophysiologists should pay more attention to the cut-off time as AF inducible, rather than the degrees of burst pacing; "AF ≥1 minute (cut-off time) for AF inducibility" is recommended.
- In the AF ablation procedure, persistent AF inducibility suggests a higher risk of recurrence and thus a potential need for additional ablation to render AF noninducibility; patients with paroxysmal AF with AF noninducibility after pulmonary vein isolation may not require additional ablation, such as substrate or linear ablation, which is technically challenging for completely transmural injury and is potentially proarrhythmic.

Nonstandard Abbreviations and Acronyms

AF GRADE	atrial fibrillation grading of recommendations assessment, development and evaluation
MOOSE	Meta-analysis of Observational Studies in Epidemiology
NOS	Newcastle-Ottawa Scale
PAF	paroxysmal atrial fibrillation
PRISMA	preferred reporting items for systematic reviews and meta-analyses
RR	relative risk

electrophysiological induction protocol. AF noninducibility by burst pacing after ablation has been adopted as one of the common electrophysiological end points for guiding ablation strategies to improve clinical outcomes in both patients with paroxysmal AF (PAF)³⁻⁷ and those without PAF.^{3,8} More recently, studies targeting rotors or AF drivers responsible for AF maintenance have employed AF noninducibility as a main procedural end point.⁹ Is AF noninducibility after ablation really a prognostic factor of freedom from AF? The cumulative evidence supporting the AF noninducibility after catheter ablation as a prognostic factor is largely inconclusive.^{10–14}

Hence, the primary objective of this study was to compare the postoperative recurrence of AF between AF noninducibility and AF inducibility by burst pacing after catheter ablation in patients with symptomatic AF. The secondary objective is to determine which induction protocol is desirable for AF induction testing.

METHODS

All supporting data are available within the article and its online supplementary files.

This systematic review and meta-analysis was performed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines¹⁵ and MOOSE (Meta-analysis of Observational Studies in Epidemiology) for the reporting of our study.¹⁶ There was no registered protocol.

Search Strategy and Selection Criteria

We conducted a comprehensive systematic literature search of online databases including PubMed, Embase, Web of Science, and Cochrane Library from inception through July 2019. We conducted electronic searches using MeSH terms and corresponding key words (Data S1). The reference lists of all included studies and relevant review articles were further scrutinized to identify additional citations that may fit our inclusion criteria.

The inclusion criteria were as follows: *study pop-ulation*: patients with symptomatic AF underwent catheter ablation; *intervention*: noninducibility versus inducibility by burst pacing after catheter ablation; *study design*: prospective cohort studies (randomized controlled trial not available because of the peculiarity of the objective that patients with AF noninducibility and AF inducibility could not be randomly assigned); and *outcome measures:* recurrence of AF or freedom from AF.

Published studies meeting the following criteria were excluded: (1) AF inducibility using a pharmacological protocol, such as isoproterenol induction; (2) burst pacing not performed after catheter ablation; (3) without specific outcome or sufficient data for extraction; (4) fewer than 30 study patients; and (5) obvious bias in patient selection: only selected patients with repeat procedures of AF ablation or patients screened after the pharmacological protocol, which would affect the reliability and accuracy of the results.

Data Extraction and Quality Assessment

Three investigators (H.-L.L., P.Y., X.Z.) independently performed the initial search, screened the titles and abstracts for relevance, deleted duplicate records, and identified records as included, excluded, or uncertain. In case of uncertainty, the full-text article was acquired to determine eligibility. Any discrepancies were resolved through discussion with 2 additional investigators (J.-Z.H., K.H.). Collected data included the following: first author, year of publication, country, study type, number of patients in each group, number of events, clinical characteristics of patients, ablation lesions, induction protocols (degree of burst pacing and defined time as AF inducible), definition of recurrence, antiarrhythmics before and after ablation, and follow-up time.

The Newcastle-Ottawa Scale (NOS) was used for quality assessment of included cohort studies. A maximum of 9 stars was awarded to each study: selection (4 stars), comparability (2 stars), and outcome (3 stars). The scores of 0 to 3, 4 to 6, and 7 to 9 were assigned for low, moderate, and high quality of studies, respectively.

Statistical Analysis

The pooled relative risks (RRs) with 95% CIs were estimated for the dichotomous outcome of clinical recurrence of AF. Heterogeneity among studies was quantified using the Cochran chi-square test and l^2 , which described the percentage of total variation across studies that was attributable to heterogeneity rather than chance. A value of 0% indicated no observed heterogeneity, and larger values showed increasing heterogeneity. $l^2 >50\%$ indicated significant heterogeneity. We pooled outcome data using a fixed and random effects model. Publication bias was assessed using a visually inspected funnel plot and was also evaluated by Harbord test and Peter test. A 2-sided *P*<0.05 was considered as statistically significant.

The analyses were conducted using Review Manager (RevMan) version 5.3 (The Nordic Cochrane Center, http://ims.cochrane.org/revman) and STATA version 12.0 (StataCorp LLC). Quality of evidence was assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation) tools and manual guidelines, which are available online (https://gradepro.org/).

RESULTS

Study Selection

According to the search strategy, the processes of literature screening, study selection, and reasons for exclusion are shown on the PRISMA statement flowchart (Figure 1). Our initial search obtained 516 records. After removing duplicates and screening the titles and abstracts, 82 articles were assessed for eligibility. After reviewing the full texts, 12 prospective cohort studies were ultimately included. The following studies that Essebag 2005³ accord with exclusion criteria (1), Jaïs 2006¹⁷ accord with exclusion criteria (3), Katritsis 2007¹⁸ accord with exclusion criteria (4), Crawford 2010¹⁹ and Fiala 2015²⁰ accord with exclusion criteria (5), were not included.

Studies Characteristics and Quality Assessment

The main characteristics of the included studies are summarized in the Table. The studies were published between 2004 and 2019. Because of the peculiarity of the objective, a randomized controlled trial design was not available. All of the included studies were prospective cohort studies. Seven studies included only patients with PAF,^{4–7,13,14,21} 1 study included only patients without PAF,¹⁰ and 4 studies had a mix of patients with and those without PAF.^{8,11,12,22} Population sizes ranged from 60 to 1141, with a total of 2772 patients. The average age was older than 50 years, and the majority of patients were men (not available in 1 study: Skala et al¹³). The average left atrial diameter ranged from 37±4.8 to 46±8 mm. AF with structural heart disease accounted for 0% to 43% of cases (not available in 3 studies: Santangeli et al¹², Liu et al,⁷ and Oral et al⁴). Ablation lesions were different, depending on the type of AF and the operators. Pulmonary vein isolation was included in every study. The follow-up times ranged from 5 to 42.5±9.3 months. The definition of AF recurrence in most studies was the same (>30 seconds). Subgroup analysis was performed according to the AF type, follow-up time, and the induction protocol (degree of burst pacing and defined time for AF inducibility)

Details of the quality and risk of bias assessments of the included studies are outlined in Table S1. The average NOS score was 8.08, and the score for each study was \geq 7, indicating that all of the studies were of high quality.

AF Recurrence in Total Patients

Twelve studies with a total of 2772 patients provided data evaluating the effect of AF noninducibility versus inducibility by burst pacing after catheter ablation on



Figure 1. Flow diagram of the study selection process.

the recurrence of AF.^{4–8,10–14,21,22} Compared with AF inducibility, AF noninducibility by burst pacing after ablation was associated with a significantly reduced risk of AF recurrence (RR, 0.68; 95% CI, 0.60–0.77 [*P*<0.00001]) (Figure 2). No significant heterogeneity was revealed (*I*²=32%, *P*_{heterogeneity}=0.13), which indicated the consistency of results among these studies.

Subgroup Analysis AF Recurrence in Different AF Types

A subgroup analysis was performed by dividing patients with AF into PAF and non-PAF subgroups. Ten studies with a total of 2254 patients provided data on AF recurrence with PAF and 4 studies with a total of 374 patients provided data on AF recurrence with non-PAF.^{4–8,10,12–14,21,22} Different AF types (PAF and non-PAF) had no significant impact on the RR and showed a correlation ($P_{interaction}$ =0.28) (Figure 3A). For PAF, AF noninducibility by burst pacing after ablation showed a significantly reduced risk of AF recurrence compared with AF inducibility (RR, 0.64; 95% CI, 0.55–0.75 [*P*<0.00001]), with no significant heterogeneity (*I*²=11%, *P*_{heterogeneity}=0.34) (Figure 3A). For non-PAF, AF noninducibility was also associated with reduced AF recurrence (RR, 0.75; 95% CI, 0.59–0.96 [*P*=0.02]), with no heterogeneity (*I*²=0%, *P*_{heterogeneity}=0.91) (Figure 3A).

AF Recurrence in Different Follow-Up Time

Since the recurrence of AF was associated with follow-up time, we evaluated whether the correlation was affected by the follow-up time in a subgroup analysis by different follow-up times. Two studies with a total of 334 patients provided data with follow-up ≤ 6 months,^{4,22} 7 studies with a total of 1895 patients with 6< follow-up ≤ 12 months,^{5–7,10,11,13,22} and 4 studies with a total of 777 patients with follow-up

	Follow-Up, mo	<u>5</u>	12	42.5±9.3	19±7	с Ч	12.1 [6.5–20.3]*	42	16.1±8.2	12±6	Q	7±3	ω
	Antiarrhy thmics After Ablation (Using Time), mo	ΨZ	NA	1-2	AN	1.5–6 (partly continued)	AN	NA	-	NA	≥3	0	2-3
	Antiarrhythmics Before Ablation (Ceased Time)	2.1±2.5 d	≥3 d (Amiodarone >3 mo)	≥5 Half- lives (except amiodarone)	≥5 Half- lives (except amiodarone)	۲ ۷	Ceased (time NA)	ΨN	≥5 Half- lives (except amiodarone)	NA	Partly ceased (time NA)	≥5 Half- lives (except amiodarone)	≥5 Half- lives (except amiodarone)
	Defined Time as AF Recurrence	AF/AT >30 s	AF/AT/AFL >30 s	AF/AT >30 s	AF/AT >30 s	AF/AT/AFL >30 s	AF >30 s	AF/AT/AFL >30 s	AF/AT/AFL (time NA)	AF ≥60 s	AF (time NA)	AF/AFL (time NA)	AF/AFL (time NA)
	Defined Time as AF Inducible	AF/AT ≥5 min	AF ≥5 min	AF/AT ≥5 min	AF/AT ≥2 min	AF/AFL/AT ≥2 min	AF >1 min	AN	AF >10 min	AF/AFL >1 min	AF >1 min	AF ≥1 min	AF >1 min
	Burst Pacing	Decremental burst pacing to refractoriness or 187.5 ms (30 beats)	Decremental burst pacing to 200 ms (5 s)	Decremental burst pacing to 180 ms (5 s)	Decremental burst pacing to refractoriness or 180 ms (15 beats)	Decremental burst pacing to 2:1 atrial capture or 180 ms (15 beats)	Decremental burst pacing to refractoriness or 200 ms (5 s)	NA	Decremental burst pacing to refractoriness (10 s)	Decremental burst pacing to 150 ms (5–10 s)	Decremental burst pacing to refractoriness or 200 ms (5 s)	Decremental burst pacing to refractoriness (5 s)	Burst pacing at refractoriness (≥15 s)
	Ablation Lesions	PVI≞non-PV triggers	Z	PVI+CTI≞ CFAE±non-PV triggers	PVI≞non-PV triggers	PVI+non-PV triggers	PVI±CTI	M	Ā	PVI±LA lines (roofline or MI)	PVI±LA lines (roofline+MI) ±CTI	PVI+CTI±MI	PVI+LA lines (septum+roofline+ MI±anterior wall)
	Structural Heart Disease, No. (%)	11 (11.2)	(0) 0	17 (5.84)	AA	49 (34.1)	36 (30)	NA	9 (15)	34 (39)	52 (22.2)	30 (43)	AN
	LVEF	63.8±10.1	AN	64.6±7.9	59±8	57 [53, 62]*	54.2±2.9	62.2±6.9	NA	61±6	61.3±7.4	67±12	57±9
Š	LAD, mm	43.4±7.6	42.6±6.7	39.9±6.1	43±7	46±8	44.3±6.9	37±4.8	42.9±5.5	37±5	45±7	43±7	43±6
ed Studie	Men, No. (%)	77 (78.6)	ЧZ	249 (85.6)	242 (79)	114 (79.2)	76 (63)	730 (64.0)	45 (75)	61 (69.3)	168 (71.8)	52 (74.3)	80 (80)
f Include	Age, y	61±10	NA	59.8±10.7	55±11	60 [52-65]*	59.5±10.4	58.1±11.5	58.3±10.6	51±12	56.7±10.5	53±9	55±10
iphics o	Patients, No.	8	120	291	305	144	121	1141	60	88	234	02	100
emogra	AF Type	Non-PAF	PAF	PAF/ non-PAF	PAF/ non-PAF	PAF/ non-PAF	PAF	PAF	PAF	PAF	PAF/ non-PAF	PAF	PAF
stics and D	Study Type	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational	Prospective, observational
aracteri:	Country	Japan	Czech Republic	Japan	United States	United States	Austria	China	Germany	Taiwan	Austria	France	United States
Table. Ché	Study	Kawai, 2019 ¹⁰	Skala, 2019 ¹³	Otsuka, 2018 ⁸	Santangeli, 2018 ¹²	Leong-Sit, 2013 ¹¹	Adlbrecht, 2013 ²¹	Liu, 2012 ⁷	Satomi, 2008 ¹⁴	Chang, 2007 ⁵	Richter, 2006 ²²	Haïssaguerre, 2004 ⁶	Oral, 2004 ⁴

Characteristics and Demographics of Included Studies

	Noninduc	ibility	Inducib	oility		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Adlbrecht-2013	35	85	22	36	7.5%	0.67 [0.47-0.97]	
Chang-2007	14	77	6	11	2.5%	0.33 [0.16-0.68]	
Haïssaguerre-2004	6	46	9	24	2.9%	0.35 [0.14-0.86]	
Kawai-2019	12	48	15	50	3.6%	0.83 [0.44-1.59]	
Leong-Sit-2013	27	55	44	89	8.2%	0.99 [0.71-1.40]	+
Liu-2012	74	500	142	641	30.2%	0.67 [0.52-0.86]	-
Oral-2004	10	70	10	30	3.4%	0.43 [0.20-0.92]	
Otsuka-2018	71	236	25	55	9.8%	0.66 [0.47-0.94]	
Richter-2006	61	156	53	78	17.1%	0.58 [0.45-0.74]	-
Santangeli-2018	45	187	37	118	11.0%	0.77 [0.53-1.11]	
Satomi-2008	18	43	7	17	2.4%	1.02 [0.52-1.98]	
Skala-2019	27	109	3	11	1.3%	0.91 [0.33-2.52]	
Total (95% CI)		1612		1160	100.0%	0.68 [0.60, 0.77]	•
Total events	400		373				
Heterogeneity: chi ² =16.2	29, df=11 (F	P=0.13);	l ² =32%				
Test for overall effect: Z	=6.26 (P<0	.00001)					Favor Noninducibility Favor Inducibility

Figure 2. Atrial fibrillation (AF) noninducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in total patients.

>12 months.^{8,12,14,21} Our results showed that different follow-up times (≤6, 6–12, and >12 months) had no significant impact on the RR ($P_{\text{interaction}}$ =0.31) and showed a correlation (Figure 3B). Compared with AF inducibility, AF noninducibility by burst pacing after ablation significantly reduced the risk of AF recurrence in all 3 subgroups with ≤6 months (RR, 0.55; 95% CI, 0.41–0.74 [*P*<0.0001]), 6 to 12 months (RR, 0.67; 95% CI, 0.58–0.78 [*P*<0.00001]), and >12 months (RR, 0.73; 95% CI, 0.60–0.89 [*P*=0.002]), respectively. There was no significant heterogeneity in any of the 3 subgroups (l^2 =0%, $P_{\text{heterogeneity}}$ =0.46; l^2 =46%, $P_{\text{heterogeneity}}$ =0.07; and l^2 =0%, $P_{\text{heterogeneity}}$ =0.68, respectively) (Figure 3B).

AF Recurrence in Different Induction Protocols

Degrees of burst pacing

To determine which degree of burst pacing was desirable for the AF induction test, we classified it into 3 degrees of mild, moderate, and severe stimulation. The mild stimulation was defined as "burst pacing to refractoriness, 2:1 atrial capture, or 180 to 200 ms (maintaining ≤3 seconds per 15 beats)." Moderate stimulation was defined as "burst pacing to refractoriness, or 180 to 200 ms (maintaining 5 seconds per 30 beats)." Severe stimulation was defined as "burst pacing to refractoriness (maintaining ≥ 10 seconds), or 150 ms (maintaining 5–10 seconds)." Two studies with a total of 449 patients provided data with mild stimulation,^{11,12} 6 studies with a total of 934 patients with moderate stimulation, 6,8,10,13,21,22 and 3 studies with a total of 248 patients with severe stimulation^{4,5,14} (Figure 4B). The results showed that different degrees of burst pacing (mild, moderate, and severe stimulation) had

no significant impact on the RR ($P_{interaction}$ =0.09), which indicated that the degree of burst pacing was not decisive for the correlation. In the moderate and severe stimulation subgroups, AF noninducibility could significantly reduce the risk of AF recurrence (RR, 0.63; 95% CI, 0.53–0.74 [P<0.00001] and RR, 0.57; 95% CI, 0.38– 0.86 [P=0.007], respectively), with heterogeneity (l^2 =0% [$P_{heterogeneity}$ =0.61] and l^2 =64% [$P_{heterogeneity}$ =0.06]) (Figure 4B). While the mild stimulation subgroup showed the effect size was not statistically significant difference (RR, 0.86; 95% CI, 0.67–1.11 [P=0.31]), which could be explained by the small sample size (only 2 studies) resulting in a false-negative result (Figure 4B).

Defined cut-off time for AF inducibility

To determine which cut-off time for AF inducibility was desirable for the AF induction test, 3 subgroups with defined cut-off times of 1, 2, and 5 to 10 minutes were classified for analysis. Five studies with a total of 613 patients with a cut-off time of 1 minute, 4-6,21,22 2 studies with a total of 449 patients with a cut-off time of 2 minutes,^{11,12} and 4 studies with a total of 569 patients with a cut-off time of 5 to 10 minutes were evaluated^{8,10,13,14} (Figure 4A). The results showed that different cut-off times (1, 2, and 5-10 minutes) for AF inducibility had a significant impact on the RR (P_{interaction}=0.009). Only in the subgroup of cut-off time of 1 minute, AF noninducibility was associated with a significantly reduced risk of AF recurrence (RR, 0.54; 95% CI, 0.45-0.66 [P<0.00001]) (Figure 4A), with no significant heterogeneity (l²=13%, P_{heterogeneity}=0.33). In contrast, no statistical significance was revealed in the subgroups with cut-off times of 2 minutes (RR, 0.86; 95% Cl, 0.67-1.11 [P=0.26]) and 5 to 10 minutes (RR, 0.77; 95% CI, 0.58-1.01 [P=0.05])

Α	Noninduc	ibility	Inducib	oility		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
1.2.1 PAF							
Adlbrecht-2013	35	85	22	36	8.3%	0.67 [0.47, 0.97]	
Chang-2007	14	77	6	11	2.8%	0.33 [0.16, 0.68]	
Haïssaguerre-2004	6	46	9	24	3.2%	0.35 [0.14, 0.86]	
Liu-2012	74	500	142	641	33.4%	0.67 [0.52, 0.86]	-
Oral-2004	10	70	10	30	3.8%	0.43 [0.20, 0.92]	
Otsuka-2018	45	166	8	22	3.8%	0.75 [0.41, 1.37]	
Richter-2006	39	115	31	50	11.6%	0.55 [0.39, 0.76]	
Santangeli-2018	29	133	19	68	6.8%	0.78 [0.47, 1.29]	
Satomi-2008	18	43	7	17	2.7%	1.02 [0.52, 1.98]	
Skala-2019	27	109	3	11	1.5%	0.91 [0.33, 2.52]	
Subtotal (95% CI)		1344	•	910	77.8%	0.64 [0.55, 0.75]	•
Total events	297		257			• • •	
Heterogeneity: chi ² =10	16 df=9 (P=	=0 34)· 1 ²	=11%				
Test for overall effect: Z	=5.71 (P<0)	00001)	1170				
		00001)					
1.2.2 Non-PAF							
Kawai-2019	12	48	15	50	3.9%	0 83 [0 44 1 59]	
Otsuka-2018	26	70	17	33	6.2%	0 72 [0 46 1 13]	
Richter-2006	20	/1	22	28	7.0%	0.68 [0.48, 0.96]	
Septengeli 2019	16	54	10	20	F 0%	0.00 [0.40, 0.90]	
Subtotal (95% CI)	10	213	10	161	22 2%	0.75 [0.59 0.96]	•
Total events	76	210	70	101	44.4 /0	0.10 [0.00, 0.00]	•
Heteregeneity shi2=0 F	2 4(-2)(D-(0.01×1^2	.00/				
Test for events, cfir-0.5	3, UI=3 (P=0	J.91), 1 -	0%				
Test for overall effect: 2	.=2.32 (P=0.0	02)					
Total (95% CI)		1557		1071	100.0%	0 67 [0 50 0 76]	•
Total (95% CI)	070	1557	200	1071	100.076	0.07 [0.55, 0.70]	
l otal events	3/3	0.55	329				
Heterogeneity: cni*=11.	74, df=13 (F	/=0.55);	1=0%				0.02 0.1 1 10 50
Test for overall effect: Z	.=6.15 (P<0.	00001)		2	0.001		Favor Non-inducibility Favor Inducibility
Test for subgroup difference	ences: cni~=	1.15, df=	1 (P=0.28	3), 1-=12	2.8%		
В							
В	Noninduc	ibility	Inducib	oility		Risk Ratio	Risk Ratio
B Study or Subgroup	Noninduc Events	ibility Total	Inducib Events	ility Total	Weight	Risk Ratio M-H, Fixed, 95% C	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 mo	Noninduc Events onths	ibility Total	Inducib Events	ility Total	Weight	Risk Ratio M-H. Fixed. 95% C	Risk Ratio I M-H. Fixed, 95% Cl
B Study or Subgroup 1.3.1 Follow-up ≤6 mo Oral-2004	Noninduc Events onths 10	ibility Total 70	Inducib Events 10	ility Total 30	Weight 3.0%	Risk Ratio <u>M-H. Fixed. 95% Cl</u> 0.43 [0.20, 0.92]	Risk Ratio I M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 mo Oral-2004 Richter-2006	Noninduc Events onths 10 48	ibility Total 70 156	Inducib Events 10 41	illity <u>Total</u> 30 78	Weight 3.0% 11.7%	Risk Ratio <u>M-H. Fixed, 95% Cl</u> 0.43 [0.20, 0.92] 0.59 [0.43, 0.80]	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 me Oral-2004 Richter-2006 Subtotal (95% CI)	Noninduc Events onths 10 48	ibility Total 70 156 226	Inducib Events 10 41	ility <u>Total</u> 30 78 108	Weight 3.0% 11.7% 14.7%	Risk Ratio M-H. Fixed, 95% Cl 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74]	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 mc Oral-2004 Richter-2006 Subtotal (95% CI) Total events	Noninduc Events onths 10 48 58	ibility Total 70 156 226	Inducib Events 10 41 51	ility <u>Total</u> 30 78 108	Weight 3.0% 11.7% 14.7%	Risk Ratio M-H. Fixed, 95% C 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% Cl) Total events Heterogeneity: chi²=0.5:	Noninduc <u>Events</u> 10 48 58 5, df=1 (P=0	ibility Total 70 156 226 0.46); I ² =	Inducib Events 10 41 51 0%	illity Total 30 78 108	Weight 3.0% 11.7% 14.7%	Risk Ratio M-H. Fixed, 95% Cl 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74]	Risk Ratio I M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi²=0.5: Test for overall effect: Z	Noninduc Events onths 10 48 58 5, df=1 (P=0 (=3.96 (P<0.	ibility Total 70 156 226 0.46); I ² = .0001)	Inducits Events 10 41 51 0%	ility <u>Total</u> 30 78 108	Weight 3.0% 11.7% 14.7%	Risk Ratio M-H. Fixed, 95% Cl 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74]	Risk Ratio I M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.3.1 Follow-up ≤6 mc Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi²=0.5: Test for overall effect: Z	Noninduc Events onths 10 48 58 5, df=1 (P=0 =3.96 (P<0.	ibility Total 70 156 226 0.46); l ² = .0001)	Inducits Events 10 41 51 0%	ility <u>Total</u> 30 78 108	Weight 3.0% 11.7% 14.7%	Risk Ratio M-H. Fixed, 95% Cl 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74]	Risk Ratio M-H. Fixed, 95% Cl
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$\begin{array}{c} \textbf{B} \\ \hline \textbf{Study or Subgroup} \\ \hline \textbf{1.3.1 Follow-up} \leqslant 6 \mbox{ model} \\ \mbox{Oral-2004} \\ \mbox{Richter-2006} \\ \mbox{Subtotal (95\% Cl)} \\ \mbox{Total events} \\ \mbox{Heterogeneity: chi^2=0.5:} \\ \mbox{Test for overall effect: Z} \\ \hline \textbf{1.3.2 6 months $	Noninduc Events onths 10 48 58 5, df=1 (P=0 =3.96 (P<0. w-up≤12 m 14 6 12 27	ibility Total 70 156 226 0.46); l ² = 0.001) 1000ths 77 46 48 55	Inducit Events 10 41 51 0% 6 9 15 44	111 24 50 89	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2%	Risk Ratio <u>M-H. Fixed, 95% Cl</u> 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40]	Risk Ratio
$\begin{array}{c} \textbf{B} \\ \hline \textbf{Study or Subgroup} \\ \textbf{1.3.1 Follow-up} \leqslant 6 \mbox{ m} \\ Oral-2004 \\ Richter-2006 \\ \textbf{Subtotal (95% CI)} \\ Total events \\ Heterogeneity: chi2=0.5: \\ Test for overall effect: Z \\ \textbf{1.3.2 6 months $	Noninduc Events 10 48 5, df=1 (P=0 (=3.96 (P<0. w-up≪12 m 14 6 12 27 74	ibility Total 70 156 226 0.46); ² = 0001) ionths 77 46 48 55 500	Inducit Events 10 41 51 0% 6 9 15 44 44 142	ility Total 30 78 108 11 24 50 89 641	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7%	Risk Ratio M-H. Fixed, 95% Cl 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40] 0.67 [0.52, 0.86]	Risk Ratio
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B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi²=0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: chi²=12:</follow 	Noninduc Events 10 48 5, df=1 (P=0: (=3.96 (P<0. w-up≤12 m 14 6 12 27 74 61 27 74 61 27 221 97 df=6 (P:	ibility <u>Total</u> 70 156 226 0.46); l ² = 0.001) ionths 77 46 48 55 500 156 109 991	Induciti Events 10 41 51 0% 6 9 15 44 142 3 3 3 272 2=54%	ility Total 30 78 108 11 24 50 89 641 78 11 904	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7% 15.1% 1.2% 58.1%	Risk Ratio M-H. Fixed, 95% CI 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.67 [0.58, 0.78]	Risk Ratio
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B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi²=0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: chi²=12: Test for overall effect: Z</follow 	Noninducc Events 10 48 58 5, df=1 (P=0 =3.96 (P<0. w-up≤12 m 14 6 12 27 74 61 27 221 97, df=6 (P=0 (P<0. (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P<0.) (P	ibility Total 70 156 226 0.46); ² = 0001) ionths 77 46 48 55 500 156 109 991 =0.04); ²	Inducit Events 10 41 51 0% 6 9 15 44 142 53 3 272 2=54%	ility Total 30 78 108 111 24 50 89 641 78 11 78 1904	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7% 15.1% 1.2% 58.1%	Risk Ratio M-H, Fixed, 95% CJ 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.91 [0.33, 2.52] 0.67 [0.58, 0.78]	Risk Ratio
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B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% Cl) Total events Heterogeneity: chi²=0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% Cl) Total events Heterogeneity: chi²=12: Test for overall effect: Z 1.3.3 Follow-up > 12 m Adlbrecht-2013 Otsuka-2018 Satomi-2008 Subtotal (95% Cl) Total events Heterogeneity: chi²=1.5: Test for overall effect: Z Total (95% Cl)</follow 	Noninduc Events 10 48 58 5, df=1 (P=0 =3.96 (P<0. w-up≤12 m 14 6 12 27 241 97, df=6 (P= =5.13 (P<0 xonths 35 71 45 18 0, df=3 (P=(=3.05 (P=0) 412	ibility Total 70 156 226 0.46); ² = 0.001) ionths 77 46 48 55 500 156 109 991 =0.04); ² = 236 187 43 551 0.68); ² = 1768	Induciti Events 10 41 51 0% 6 9 15 44 142 53 3 3 272 25 37 7 91 :0%	ility Total 30 78 108 11 24 50 89 641 78 11 904 36 55 118 37 226 1238	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7% 15.1% 1.2% 58.1% 6.6% 8.7% 9.7% 21.2% 100.0%	Risk Ratio M-H. Fixed, 95% CI 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.35 [0.14, 0.86] 0.35 [0.14, 0.86] 0.39 [0.74, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.91 [0.33, 2.52] 0.67 [0.58, 0.78] 0.67 [0.47, 0.97] 0.66 [0.47, 0.94] 0.77 [0.53, 1.11] 1.02 [0.52, 1.33] 0.73 [0.60, 0.89] 0.67 [0.60, 0.75]	Risk Ratio
B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi ² =0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: chi²=12: Test for overall effect: Z 1.3.3 Follow-up > 12 m Adlbrecht-2013 Otsuka-2018 Santangeli-2018 Satomi-2008 Subtotal (95% CI) Total events Heterogeneity: chi²=1.5: Test for overall effect: Z Total (95% CI) Total events Heterogeneity: chi²=1.5: Test for overall effect: Z</follow 	Noninduc Events 10 48 58 5, df=1 (P=0 =3.96 (P<0.) w-up≤12 m 14 6 12 27 74 61 27 74 61 27 74 61 27 74 61 27 74 61 27 74 61 27 74 61 27 221 97, df=6 (P<0 w-up≤12 m 14 6 12 12 13 16 16 10 16 16 16 16 16 16 16 16 16 16	ibility <u>Total</u> 70 156 226 0.46); l ² = 0001) ionths 77 46 48 55 500 156 109 991 =0.04); l ² .00001) =0.04); l ² .00001) 85 236 187 43 551 0.68); l ² = 1768	Induciti Events 10 41 51 0% 6 9 15 44 15 44 15 33 272 53 3 272 25 37 7 91 10 414 10 10 41 10 41 10 10 41 10 10 10 10 10 10 10 10 10 1	ility Total 30 78 108 108 11 24 50 89 641 78 11 904 36 55 118 17 226	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7% 15.1% 1.2% 58.1% 6.6% 8.7% 9.7% 2.1% 27.2%	Risk Ratio M-H. Fixed, 95% CI 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.91 [0.53, 0.78] 0.67 [0.58, 0.78] 0.67 [0.53, 1.11] 1.02 [0.52, 1.98] 0.73 [0.60, 0.89] 0.67 [0.60, 0.75]	Risk Ratio
B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi ² =0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: chi²=12: Test for overall effect: Z 1.3.3 Follow-up > 12 m Adibrecht-2018 Satomi-2008 Subtotal (95% CI) Total events Heterogeneity: chi²=1.5: Test for overall effect: Z Total events Heterogeneity: chi²=1.5: Test for overall effect: Z Total (95% CI) Total events Heterogeneity: chi²=1.6: Total (95% CI)</follow 	Noninduc Events 000000000000000000000000000000000000	ibility Total 70 156 226 0.46); ² = 0001) ionths 77 46 48 55 500 156 109 991 =0.04); ² 156 236 157 43 551 0.68); ² = 0.002) 1768 2-022) 1768	Inducite Events 10 41 51 0% 6 9 15 44 142 53 3 272 2=54% 225 37 7 7 91 0% 91 414 1 ² =29%	111 111 24 50 89 641 78 11 904 366 55 118 17 226 1238	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 7.2% 26.7% 15.1% 1.2% 58.1% 6.6% 8.7% 9.7% 2.1% 27.2% 100.0%	Risk Ratio M-H, Fixed, 95% CJ 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.33 [0.16, 0.68] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.99 [0.71, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.91 [0.33, 2.52] 0.67 [0.58, 0.78] 0.66 [0.47, 0.94] 0.77 [0.53, 1.11] 1.02 [0.52, 1.98] 0.73 [0.60, 0.89] 0.67 [0.60, 0.75]	Risk Ratio M-H. Fixed. 95% Cl + + + + + + + + + + + + +
B Study or Subgroup 1.3.1 Follow-up ≤6 m Oral-2004 Richter-2006 Subtotal (95% CI) Total events Heterogeneity: chi ² =0.5: Test for overall effect: Z 1.3.2 6 months <follow Chang-2007 Haïssaguerre-2004 Kawai-2019 Leong-Sit-2013 Liu-2012 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: chi²=12. Test for overall effect: Z 1.3.3 Follow-up > 12 m Adlbrecht-2018 Santangeli-2018 Satumi-2008 Subtotal (95% CI) Total events Heterogeneity: chi²=1.5. Test for overall effect: Z Total (95% CI) Total events Heterogeneity: chi²=1.5. Test for overall effect: Z Total (95% CI) Total events Heterogeneity: chi²=16. Test for overall effect: Z</follow 	Noninduc Events 10 48 58 5, df=1 (P=0 =3.96 (P<0. w-up≤12 m 14 6 12 27 74 61 27 221 97, df=6 (P=0 x-up≤12 m 14 6 12 27 221 97, df=6 (P=0 x-up≤12 m 14 6 12 27 24 97, df=6 (P=0 x-up≤12 m 14 6 12 27 21 97, df=6 (P=0 x-up≤12 m 14 6 12 27 221 97, df=6 (P=0 x-up≤12 m 14 6 12 27 21 97, df=6 (P=0 x-up≤12 m 14 15 16 99, df=3 (P=0 448 99, df=12 (P=0 x-up≤12 m 16 97, df=6 (P=0 x-up≤12 m 18 18 18 18 19 99, df=12 (P=0 x-up≤12 m 18 18 18 18 19 18 18 18 18 18 18 18 18 18 18	ibility Total 70 156 226 0.46); ² = 0001) ionths 77 46 48 55 500 156 109 991 =0.04); ² =0.04); ² =0.001) 85 236 157 43 551 0.068); ² = 0.002) 1768 P=0.15); .00001) 0.068	Induciti Events 10 41 51 0% 6 9 15 44 142 53 3 272 25 37 7 91 :0% 414 1 ² =29% 0.4/2 - 14 1 ² =29%	111 24 50 89 641 78 11 24 50 89 641 78 11 904 366 55 118 17 226 1238	Weight 3.0% 11.7% 14.7% 2.2% 2.5% 3.1% 26.7% 15.1% 1.2% 58.1% 6.6% 8.7% 9.7% 2.1% 27.2% 100.0%	Risk Ratio M-H, Fixed, 95% CJ 0.43 [0.20, 0.92] 0.59 [0.43, 0.80] 0.55 [0.41, 0.74] 0.35 [0.41, 0.74] 0.35 [0.14, 0.86] 0.35 [0.14, 0.86] 0.39 [0.71, 1.40] 0.67 [0.52, 0.86] 0.58 [0.45, 0.74] 0.91 [0.33, 2.52] 0.67 [0.58, 0.78] 0.67 [0.47, 0.97] 0.66 [0.47, 0.94] 0.77 [0.53, 1.11] 1.02 [0.52, 1.98] 0.73 [0.60, 0.89]	Risk Ratio

Figure 3. Atrial fibrillation (AF) noninducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in different AF types (A) and different follow-up time (B). PAF indicates paroxysmal atrial fibrillation.

Δ	Noninduci	bility	Inducibi	lity		Risk Ratio	Risk Ratio
Study or subgroup	Evente	Total	Evente	Total	Weight	M-H Fixed 95% C	M-H Fixed 95% Cl
1.4.1 Cut off time 1 mit	Lventa	Total	LVCIILO	Total	Weight	M-11, 1 1Xeu, 3570 0	MI-11, 11XCC, 3578 OF
Address to 0040	05	05	00	20	40 70/	0 07 10 47 0 071	
Adibrecht-2013	35	85	22	36	10.7%	0.67 [0.47, 0.97]	
Chang-2007	14	77	6	11	3.7%	0.33 [0.16, 0.68]	
Haïssaguerre-2004	6	46	9	24	4.1%	0.35 [0.14, 0.86]	Concerne and Conce
Oral-2004	10	70	10	30	4.9%	0.43 [0.20, 0.92]	
Richter-2006	61	156	53	78	24.6%	0.58 [0.45, 0.74]	
Subtotal (95% CI)		434		179	47.9%	0.54 [0.45, 0.66]	•
Total events	126		100				
Heterogeneity: Chi ² = 4. Test for overall effect: Z	61, df = 4 (P = 6.30 (P <	e = 0.33) 0.00001	; I² = 13%)				
1.4.2 Cut-off time 2 min	n						
Leona-Sit-2013	27	55	44	89	11.7%	0.99 [0.71, 1.40]	-
Santangeli-2018	45	187	37	118	15.8%	0.77 [0.53, 1.11]	
Subtotal (95% CI)		242		207	27.5%	0.86 [0.67, 1.11]	◆
Total events	72		81				
Heterogeneity: $Chi^2 = 1$	04 df = 1/P	= 0.31	12 = 3%				
Test for overall effect: 7	- 1 14 (P -	0.26)	,1 = 070				
Test for overall effect. Z	– 1.14 (P –	0.26)					
1.4.3 Cut-off time 5-10	min						
Kawai-2019	12	48	15	50	5.1%	0.83 [0.44, 1.59]	
Otsuka-2018	71	236	25	55	14 1%	0.66 [0.47 0.94]	
Sotomi 2009	10	42	25	17	2 50/	1 02 [0.52 1 09]	
Satomi-2008	10	40	2	17	3.5%	1.02 [0.02, 1.90]	
Skala-2019	21	109	3	422	1.9%	0.91 [0.33, 2.52]	
Subtotal (95% CI)	100	430	= 0	133	24.0%	0.77 [0.58, 1.01]	•
l otal events	128		50				
Heterogeneity: Chi ² = 1. Test for overall effect: Z	54, df = 3 (P = 1.92 (P =	9 = 0.67) 0.05)	; l² = 0%				
Total (95% CI)		1112		519	100.0%	0.69 [0.60, 0.78]	•
Total events	326		231				
Heterogeneity: Chi ² = 16	30 df = 10	(P = 0.0)	19)· 12 = 39	%			
Tost for overall effect: 7	- 5 56 (P <	0.00001	\ \	/0			0.02 0.1 1 10 50
Test for subgroup differe	- 0.00 (1 <	0.00001	/ - 2 (D - 0	0000	2 - 70 00/		Favor Non-inducibility Favor Inducibility
rest for subgroup differe	inces. Chi -	9.41, ui	- 2 (F - U	.009),	- 70.070)	
-							
В							
В	Non-induci	bility	Inducibi	ility		Risk Ratio	Risk Ratio
B Study or Subgroup	Non-induci Events	bility Total	Inducibi Events	lity Total	Weight	Risk Ratio M-H. Fixed. 95% C	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation	Non-induci Events	bility Total	Inducibi Events	lity Total	Weight	Risk Ratio 	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013	Non-induci Events 27	bility Total 55	Inducibi Events 44	llity Total 89	<u>Weight</u> 11.7%	Risk Ratio <u>M-H. Fixed, 95% C</u> 0.99 [0.71, 1.40]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santanceli-2018	Non-induci Events 27 45	bility Total 55 187	Inducibi Events 44 37	lity Total 89 118	<u>Weight</u> 11.7% 15.8%	Risk Ratio <u>M-H. Fixed. 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53. 1.11]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI)	Non-induci Events 27 45	bility Total 55 187 242	Inducibi Events 44 37	lity Total 89 118 207	<u>Weight</u> 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events	Non-induci Events 27 45 72	bility Total 55 187 242	Inducibi Events 44 37 81	lity Total 89 118 207	Weight 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed. 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 11	Non-induci Events 27 45 72 04. df = 1 (P	bility Total 55 187 242	Inducibi Events 44 37 81 1 ² = 3%	lity <u>Total</u> 89 118 207	Weight 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed. 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect 7	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P =	bility <u>Total</u> 55 187 242 (= 0.31) 0.26)	Inducibi Events 44 37 81 ; I ² = 3%	lity <u>Total</u> 89 118 207	Weight 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed. 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P =	bility Total 55 187 242 = 0.31) 0.26)	Inducibi Events 44 37 81 ; I ² = 3%	lity <u>Total</u> 89 118 207	Weight 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H, Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion	bility <u>55</u> 187 242 () = 0.31) 0.26)	Inducibi Events 44 37 81 ; I ² = 3%	lity <u>Total</u> 89 118 207	Weight 11.7% 15.8% 27.5%	Risk Ratio <u>M-H. Fixed. 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11]	Risk Ratio M-H. Fixed, 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = 1.14 (P = 35	bility <u>55</u> 187 242 () = 0.31) () 0.26) 85	Inducibi Events 44 37 81 ; I ² = 3%	liity Total 89 118 207 36	Weight 11.7% 15.8% 27.5%	Risk Ratio M-H. Fixed. 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.67 [0.47, 0.97]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaquerre-2004	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = 1.14 (P = 35 6	bility Total 55 187 242 5 = 0.31) 0.26) 85 46	Inducibi Events 44 37 81 ; I ² = 3% 22 9	lity Total 89 118 207 36 24	Weight 11.7% 15.8% 27.5% 10.7% 4.1%	Risk Ratio M-H. Fixed. 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.67 [0.47, 0.97] 0.35 [0.14, 0.86]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019	Non-induci <u>Events</u> 27 45 72 04, df = 1 (P = 1.14 (P = 12 tion 35 6 12	bility <u>Total</u> 55 187 242 - = 0.31) 0.26) 85 46 48	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15	lity Total 89 118 207 36 24 50	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1%	Risk Ratio <u>M-H, Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.67 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1. Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = 12 12 71	bility <u>Total</u> 55 187 242 - = 0.31) 0.26) 85 46 48 236	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15 25	lity <u>89</u> 118 207 36 24 55	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1%	Risk Ratio M-H. Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.67 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Birbtore 2006	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 61	bility <u>Total</u> 55 187 242 • = 0.31) 0.26) 85 46 48 236 156	Inducibi Events 44 37 81 ; ² = 3% 22 9 15 25 53	llity Total 89 118 207 36 24 50 55 78	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6%	Risk Ratio M-H. Fixed. 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.67 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94]	Risk Ratio M-H. Fixed. 95% Cl
B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Richter-2006	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 61 27 45 8 8 8 9 10 10 10 10 10 10 10 10 10 10	bility Total 55 187 242 2 = 0.31) 0.26) 85 46 48 236 156 156	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15 25 53 25	lity <u>Total</u> 89 118 207 36 24 50 55 78 4	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6%	Risk Ratio <u>M-H, Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.65 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94] 0.68 [0.47, 0.94] 0.69 [0.47, 0.94]	Risk Ratio M-H. Fixed. 95% Cl
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B <u>Study or Subgroup</u> 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Richter-2006 Skala-2019 Subtotal (95% Cl) Total events	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = 1.14 (P = 10 35 6 12 71 71 61 27 212	bility <u>Total</u> 55 187 242 • = 0.31) 0.26) 85 46 48 236 156 109 680	Inducibi Events 44 37 81 ; ² = 3% 22 9 15 25 53 3 127	lity Total 89 118 207 366 24 50 558 11 254	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 1.9% 60.5%	Risk Ratio M-H, Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.65 [0.47, 0.97] 0.65 [0.47, 0.94] 0.68 [0.47, 0.94] 0.58 [0.45, 0.74] 0.91 [0.33, 2.52] 0.63 [0.53, 0.74]	Risk Ratio M-H. Fixed. 95% Cl
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B 	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = 12 71 6 12 71 6 12 71 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 5 6 12 71 15 5 6 12 71 15 5 16 12 71 15 5 16 12 71 16 12 71 12 71 12 71 12 71 21 27 212 5 5 (P = 5 (P = 5) 5 5 (P = 5) 5 (P = 5) 5 12 12 12 12 12 12 12 12 12 12	bility Total 55 187 242 = 0.31) 0.26) 85 46 48 236 6 109 680 = 0.61) 0.00001	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15 25 53 3 3 127 ; I ² = 0%)	lity Total 89 118 207 36 24 50 55 78 11 254	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 1.9% 60.5%	Risk Ratio M-H. Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.55 [0.14, 0.97] 0.55 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94] 0.58 [0.45, 0.74]	Risk Ratio M-H, Fixed, 95% Cl
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B .5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adibrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 3. Test for overall effect: Z 1.5.4 Severe stimulation Chang-2007	Non-induci 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 21 258, df = 5 (P = 5.40 (P < n 14	bility Total 55 187 242 = 0.31) 0.26) 85 46 48 236 156 109 680 = 0.61) 0.00001 77	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15 25 53 3 127 ; I ² = 0%)	liity Total 89 118 207 36 24 50 55 78 11 254	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 60.5% 3.7%	Risk Ratio M-H. Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.83 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94] 0.58 [0.45, 0.74] 0.53 [0.53, 0.74] 0.63 [0.53, 0.74]	Risk Ratio M-H, Fixed, 95% Cl
B 	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 61 27 212 58, df = 5 (P = 5.40 (P < yn 14 10	bility Total 55 187 242 = 0.31) 0.26) 85 46 48 236 156 109 680 = 0.61) 0.00001 77 70	Inducibi Events 44 37 81 ; ² = 3% 22 9 15 25 53 3 127 ; ² = 0%) 6 10	lity Total 89 118 207 36 24 50 55 78 11 254 11 30	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 1.9% 60.5% 3.7% 4.9%	Risk Ratio <u>M-H, Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.85 [0.47, 0.97] 0.65 [0.47, 0.94] 0.68 [0.47, 0.94] 0.68 [0.45, 0.74] 0.91 [0.33, 2.52] 0.63 [0.53, 0.74] 0.33 [0.16, 0.68] 0.43 [0.20, 0.92]	Risk Ratio M-H, Fixed. 95% Cl
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B 	Non-induci 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 212 58, df = 5 (P = 5.40 (P < n 14 10 18	bility Total 555 187 242 = 0.311) 0.26) 85 46 48 236 680 680 680 680 680 77 77 70 3 3190	Inducibi Events 44 37 81 ; I ² = 3% 22 9 15 25 53 3 127 ; I ² = 0%) 6 10 7	lity Total 89 118 207 366 24 555 78 11 254 11 300 17 58	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 1.9% 60.5% 3.7% 4.9% 3.5% 12.0%	Risk Ratio M-H. Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.83 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94] 0.58 [0.45, 0.74] 0.58 [0.45, 0.74] 0.63 [0.53, 0.74] 0.63 [0.53, 0.74] 0.33 [0.16, 0.68] 0.43 [0.20, 0.92] 1.02 [0.52, 1.98] 0.57 [0.38, 0.86]	Risk Ratio M-H, Fixed. 95% Cl
B Study or Subgroup 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneily: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimulat Adlbrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2019 Otsuka-2019 Otsuka-2019 Subtotal (95% CI) Total events Heterogeneily: Chi ² = 3. Test for overall effect: Z 1.5.4 Severe stimulation Chang-2007 Oral-2004 Satomi-2008 Subtotal (95% CI) Total events	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 61 27 212 58, df = 5 (P = 5.40 (P < yn 14 10 18 42	bility Total 55 187 242 = 0.31) 0.26) 85 46 156 109 680 = 0.61) 0.00001 77 70 43 190	Inducibi Events 44 37 81 ; ² = 3% 22 9 15 25 53 3 127 ; ² = 0%) 6 10 7 23	lity Total 89 118 207 36 24 50 55 78 11 254 11 30 17 58	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 24.6% 1.9% 60.5% 3.7% 4.9% 3.5% 12.0%	Risk Ratio <u>M-H, Fixed, 95% C</u> 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.65 [0.47, 0.97] 0.65 [0.47, 0.94] 0.68 [0.45, 0.74] 0.63 [0.53, 0.74] 0.33 [0.16, 0.68] 0.43 [0.20, 0.92] 1.02 [0.52, 1.98] 0.57 [0.38, 0.86]	Risk Ratio M-H. Fixed. 95% Cl
B Study or Subgroup 1.5.1 Mild stimulation Leong-Sit-2013 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimula Adibrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 3. Test for overall effect: Z 1.5.4 Severe stimulation Chang-2007 Oral-2004 Satomi-2008 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 5.	Non-induci Events 27 45 72 04, df = 1 (P = 1.14 (P = tion 35 6 12 71 61 27 212 58, df = 5 (P = 5.40 (P < m 14 10 18 42 56, df = 2 (P	bility Total 55 187 242 = 0.31() 0.26) 85 46 48 236 236 236 109 680 = 0.61() 0.00001 77 77 0 43 190 = 0.06()	Inducibi Events 44 37 81 $; ^2 = 3\%$ 22 9 15 55 53 3 127 $; ^2 = 0\%$) 6 10 7 23 $; ^2 = 64\%$	llity Total 89 118 207 36 24 50 55 78 11 254 11 300 17 58	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 24.6% 1.9% 60.5% 3.7% 4.9% 3.5% 12.0%	Risk Ratio M-H. Fixed. 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.58 [0.47, 0.97] 0.55 [0.14, 0.86] 0.63 [0.47, 0.94] 0.58 [0.45, 0.74] 0.53 [0.53, 0.74] 0.33 [0.16, 0.68] 0.43 [0.20, 0.92] 1.02 [0.52, 1.98] 0.57 [0.38, 0.86]	Risk Ratio M-H. Fixed. 95% Cl
B Study or Subgroup 1.5.1 Mild stimulation Leong-Sit-2013 Santangeli-2018 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1.1 Test for overall effect: Z 1.5.2 Moderate stimulat Adibrecht-2013 Haïssaguerre-2004 Kawai-2019 Otsuka-2018 Richter-2006 Skala-2019 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 3. Test for overall effect: Z 1.5.4 Severe stimulation Chang-2007 Oral-2004 Satomi-2008 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 5. Test for overall effect: Z	Non-induci Events 27 45 72 04, df = 1 (P = 1.14	bility Total 55 187 242 = 0.31) 0.26) 85 46 48 236 156 109 680 • • • • • • • • • • • • •	Inducibi Events 44 37 81 ; l ² = 3% 22 9 15 25 53 3 127 ; l ² = 0%) 6 10 7 7 23 ; l ² = 64%	llity Total 89 118 207 366 24 55 78 758 11 254 11 300 17 58	Weight 11.7% 15.8% 27.5% 10.7% 4.1% 5.1% 14.1% 5.1% 14.6% 1.9% 60.5% 3.7% 4.9% 3.5% 12.0%	Risk Ratio M-H. Fixed, 95% C 0.99 [0.71, 1.40] 0.77 [0.53, 1.11] 0.86 [0.67, 1.11] 0.86 [0.67, 1.11] 0.85 [0.47, 0.97] 0.35 [0.14, 0.86] 0.83 [0.44, 1.59] 0.66 [0.47, 0.94] 0.58 [0.45, 0.74] 0.51 [0.53, 0.74] 0.33 [0.16, 0.68] 0.43 [0.20, 0.92] 1.02 [0.52, 1.98] 0.57 [0.38, 0.86]	Risk Ratio M-H, Fixed. 95% Cl
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Figure 4. Atrial fibrillation (AF) noninducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in different induction protocols (cut-off time [A], degrees of burst pacing [B]).

Mild stimulation: burst pacing to refractoriness, 2:1 atrial capture, or 180 to 200 ms (maintaining \leq 3 seconds per 15 beats); Moderate stimulation: burst pacing to refractoriness, or 180 to 200 ms (maintaining 5 seconds per 30 beats); severe stimulation: burst pacing to refractoriness (maintaining \geq 10 seconds), or 150 ms (maintaining 5–10 seconds).



Figure 5. Funnel plot of all of the 12 included studies.

(Figure 4A). The results indicated that AF \geq 1 minute for AF inducibility is the recommended protocol for the AF induction test.

Publication Bias, Sensitivity Analysis, and Quality of Evidence

Inspection of the funnel plot indicated a symmetric distribution of the included 12 studies (Figure 5). Formal statistical tests (Harbord test, P=0.398; Peter test, P=0.702) demonstrated that there was no potential publication bias among studies. Sensitivity analyses have confirmed the robustness of the results (Figure S1). Meanwhile, the random effects model (Figures S2 through S4) was performed and showed almost the same results with the fixed effects model (Figures 2 through 4), which also indicated the robustness of the results. In addition, GRADE ratings of the quality of evidence in the 12 cohort studies are provided in Table S2. According to GRADE system categories, the quality of evidence for the main outcome (AF recurrence in total patients) was moderate.

DISCUSSION

Main Findings

Our study comprehensively and systematically reviewed the current available literature, including 12 publications with 2772 (1612 versus 1160) patients, and found that: (1) AF noninducibility by burst pacing after catheter ablation was significantly associated with reduced risk of AF recurrence; (2) different AF types (PAF and non-PAF) and different follow-up

times (≤6, 6–12, and >12 months) had no significant impact on the RRs, and all showed correlations; (3) induction protocols with different cut-off times (1, 2, and 5-10 minutes) for AF inducibility had a significant impact on the correlation, and the AF \geq 1 minute for AF inducibility is recommended; and (4) different degrees of burst pacing (mild, moderate, and severe stimulation) had no significant impact on the RR and seem not to be decisive for the correlation. To our knowledge, this study is the first systematic review and meta-analysis reflecting the cumulative evidence for evaluating the association of AF noninducibility by burst pacing after catheter ablation and postoperative AF recurrence. Although randomized controlled trials were not available because of the peculiarity of the objective, all of the included prospective cohort studies were of high quality according to the recommended quality evaluation of NOS. In addition, there was no significant heterogeneity among the main results of the included studies, and the sensitivity analysis also showed that the results were not affected by any individual study. All of these factors indicated the robustness of the results.

Possible Mechanisms for the Findings

The mechanism by which AF noninducibility by burst pacing after ablation is associated with reduced AF recurrence remains unclear. Chang et al⁵ found that patients with AF inducibility after ablation had lower left atrial and right atrial voltages compared with those with AF noninducibility, which indicated that the biatrial substrate of perpetuating activity may play a critical role in the outcome of AF induction testing. Patients with AF noninducibility after ablation have fewer substrates capable of maintaining AF, and therefore have a lower risk of AF recurrence. In contrast, patients with AF inducibility have more substrates capable of maintaining AF, and therefore have a higher risk of AF recurrence.

Different AF types (PAF and non-PAF) had no significant impact on the RRs, and all showed a correlation. However, the non-PAF shows the decreased tendency of RRs, which can be explained by the complicated multifactorial nature and the faster substrate deterioration of non-PAF, causing the relatively higher AF recurrence in the subgroup of AF noninducibility in non-PAF compared with PAF.

In addition, our results also show that different follow-up times (≤ 6 , 6–12, and >12 months) had no significant impact on the RRs, and all showed a correlation. It is interesting that the RR decreases gradually with the prolongation of follow-up time, despite the lack of a statistically significant difference and it cannot be distinguished from noise. However, this "tendency" is consistent with clinical practice and has strong external information to support such claims. This phenomenon can be well understood through the mechanism whereby as the time is prolonged, along with atrial remodeling, the substrates capable of maintaining AF progress and deteriorate, resulting in increases in AF recurrence in both groups (AF noninducibility and AF inducibility), which results in a disparity of AF recurrence between the 2 groups that was not as obvious as before, and therefore, the RR decreases.

It has been reported that 26% of patients without a history of AF had positive nonspecific AF inducibility using an aggressive electrophysiological induction protocol.23 The defined cut-off time of AF inducibility directly determines the assignment of patients to the noninducible and inducible groups. Obviously, different definitions of cut-off time produce different assignment of patients (noninducible and inducible). Thus, some patients in one study can be assigned to completely different groups as a result of changes in the induction protocol. Therefore, induction protocols have a potential impact on the RRs. It is particularly important for electrophysiologists to determine which induction protocol is desirable for AF induction testing. Our results show that different cut-off times for AF inducibility have a significant impact on the RR, and only the AF ≥1 minute for AF inducibility, which presents a significant correlation, is recommended. In contrast, the degrees of burst pacing have no significant impact on the RR and seem not to be decisive for the correlation. These results indicate that the cut-off time for AF inducibility is more important than the degrees of burst pacing in AF induction testing. Electrophysiologists should pay more attention to the cut-off time for AF inducibility rather than the degrees of burst pacing.

Implications for Clinical Practice

It is known that pulmonary vein isolation has been recognized as a basic strategy of AF ablation. However, other strategies applied to AF ablation to reduce recurrence of AF have not been well established and remain controversial.²⁴ Our study shows that AF noninducibility by burst pacing after ablation is significantly associated with freedom from AF, regardless of PAF or non-PAF, which can be employed as a main procedural end point in AF ablation. In the AF ablation procedure, persistent AF inducibility suggests a higher risk of recurrence and thus a potential need for additional ablation to render AF noninducibility. Attention should be paid to the balance of additional ablation rendering AF noninducibility to improve the outcome, the proarrhythmic potential, and other complications caused by excessive ablation. However, patients with PAF who have AF noninducibility by burst pacing after pulmonary vein isolation may not require additional ablation, such as substrate or linear ablation, which is technically challenging for complete transmural injury and potential proarrhythmia. For the AF induction test, electrophysiologists should pay more attention to the cut-off time for AF inducibility rather than the degrees of burst pacing. AF ≥1 minute for AF inducibility is the recommended protocol for AF induction after ablation.

Strengths and Limitations

Our study has several strengths. First, to our knowledge, this is the first systematic review and metaanalysis to investigate the association between AF noninducibility by burst pacing after ablation and postoperative clinical recurrence. Second, although this meta-analysis does not have a registered review protocol, we conducted this study in compliance with the PRISMA guidelines and MOOSE suggestions. Finally, there was no significant heterogeneity or potential publication bias among the results of the included studies, and the sensitivity analysis also indicated the robustness of the results. However, several limitations should be considered. First, a randomized controlled trial design is not available because of the peculiarity of the objective. Second, although all of the included studies were prospective and of high quality by NOS, the use of observational cohort studies and lack of adiusted models may increase the potential of confounding, which will affect our results.

CONCLUSIONS

AF noninducibility by burst pacing after catheter ablation is associated with a favorable clinical outcome of freedom from AF, regardless of a PAF or non-PAF condition and different follow-up times. In addition, we found that induction protocols with a different cut-off time for AF inducibility have a significant impact on the correlation, and the AF \geq 1 minute for AF inducibility is the recommended protocol. While the different degrees of burst pacing seem to not be decisive. Electrophysiologists should pay more attention to the cut-off time for AF inducibility rather than the degrees of burst pacing in the AF induction test.

ARTICLE INFORMATION

Received November 12, 2019; accepted April 30, 2020.

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Acknowledgments

Liu, Yuan, and Zhu contributed to the acquisition of data, analysis and interpretation of data, drafting of the article, and final approval of the version to be published. Fu contributed to acquisition of data and analysis and interpretation of data. Hong and Hu contributed to the conception and design of the study, analysis and interpretation of data, revision of the article, and final approval of the version to be published.

Sources of Funding

This work was supported in part by the National Natural Science Foundation of China (NSFC, 81860070 and 81400188), the Youth Science Foundation Project of Jiangxi Education Department (14189), and the Science and Technology Project of Jiangxi Public Health Department (20141084).

Disclosures

None.

Supplementary Materials Data S1 Tables S1–S2 Figures S1–S4

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Supplemental Material

Data S1.

Used search terms:

(Mesh exp "Atrial Fibrillation" and key words "atrial fibrillation", "atrial fibrillations", "paroxysmal atrial fibrillation", "paroxysmal atrial fibrillations", "persistent atrial fibrillation", "persistent atrial fibrillations" or "long-standing persistent atrial fibrillation"), (Mesh exp "Catheter Ablation", and key words "catheter ablation", "transvenous catheter ablation", "radiofrequency ablation", "radio-frequency ablation", "ablation", "circumferential pulmonary vein isolation", or "pulmonary vein isolation"), "(Mesh exp "Non-inducibility", "Inducibility" and key words "non-inducibility", "noninducibility", "non inducibility", "not inducible", "inducibility", "inducible", "induction", or "induce"), and (Mesh exp "Recurrence", "Prognosis" and key words "recurrence", "recurrences", "freedom from AF", "freedom from arrhythmia", "freedom from arrhythmias", "prognosis", "prognostic factor", "prognostic factors", "prognostic significance", "clinical value", "outcome", "outcomes", "clinical outcomes", "arrhythmias-free outcome" or "arrhythmia-free outcome").

Studies	Selection	Comparability	Outcome	Total score
Kawai-2019 ¹⁰	****	*	***	8
Skala-2019 ¹³	****	**	***	9
Otsuka-2018 ⁸	****	*	***	8
Santangeli-2018 ¹²	****	*	***	8
Leong-Sit-2013 ¹¹	****	*	***	8
Adlbrecht-2013 ²¹	****	*	***	8
Liu-2012 ⁷	****	*	***	8
Satomi-200814	****	*	***	8
Chang-2007 ⁵	****		***	7
Richter -2006 ²²	****	**	***	9
Haïssaguerre-2004 ⁶	****		***	7
Oral-2004 ⁴	****	**	***	9

 Table S1. Quality assessment according to the Newcastle-Ottawa scale for nonrandomized studies.

Average score: 8.08

Table S2. GRADE rating of the quality of evidence.

Author(s):

Question: AF non-inducibility compared to AF inducibility

Setting:

Bibliography:

	Certainty assessment							№ of patients				
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AF non-inducibility	AF inducibility	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance

AF recurrence rate (follow up: range 5 months to 42.5 months)

12	observational	not	not serious	not serious	not serious	strong	400/1612 (24.8%)	373/1160	RR 0.68	103 fewer	$\oplus \oplus \oplus$	
	studies	serious				association		(32.2%)	(0.60 to	per 1,000	\bigcirc	
									0.77)	(from 129	MODERATE	
										fewer to 74		
										fewer)		

PAF associated with AF recurrence rate (follow up: range 5 months to 42.5 months)

10	observational	not	not serious	not serious	not serious	strong	297/1344 (22.1%)	257/910	RR 0.64	102 fewer	$\oplus \oplus \oplus$	
	studies	serious				association		(28.2%)	(0.55 to	per 1,000	\bigcirc	
									0.75)	(from 127	MODERATE	
										fewer to 71		
										fewer)		

Non-AF associated with AF recurrence (follow up: range 5 months to 42.5 months)

4	observational	not	not serious	not serious	not serious	none	76/213 (35.7%)	72/161	RR 0.75	112 fewer	$\Theta \Theta \bigcirc$	
	studies	serious						(44.7%)	(0.59 to	per 1,000	\bigcirc	
									0.96)	(from 183	LOW	
										fewer to 18		
										fewer)		

Follow up less than 6 months associated with AF recurrence rate (follow up: mean 5 months)

2	observational	not	not serious	not serious	not serious	none	51/108 (47.2%)	58/226	RR 0.55	115 fewer	$\oplus \oplus \bigcirc$	
	studies	serious						(25.7%)	(0.41 to	per 1,000	\bigcirc	
									0.74)	(from 151	LOW	
										fewer to 67		
										fewer)		

Follow up between 6 months to 12 months associated with AF recurrence (follow up: range 6 months to 12 months)

8	observational	not	not serious	not serious	not serious	strong	296/956 (31.0%)	235/1041	RR 0.67	74 fewer	$\oplus \oplus \oplus$	
	studies	serious				association		(22.6%)	(0.58 to	per 1,000	\bigcirc	
									0.77)	(from 95	MODERATE	
										fewer to 52		
										fewer)		

Follow up longer than 12 months associated with AF recurrence rate (follow up: range 12 months to 42.5 months)

			Certainty as	sessment			Nº of pati	ients	Ef	fect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AF non-inducibility	AF inducibility	Relative (95% CI)	Absolute (95% Cl)	Certainty	Importance
4	observational studies	not serious	not serious	not serious	not serious	none	91/226 (40.3%)	169/551 (30.7%)	RR 0.73 (0.60 to 0.89)	83 fewer per 1,000 (from 123 fewer to 34 fewer)	⊕⊕⊖ ⊖ Low	

Cut-off time 1 minute associated with AF recurrence rate (follow up: range 6 months to 12 months)

5	observational	not	not serious	not serious	not serious	strong	100/179 (55.9%)	126/434	RR 0.54	134 fewer	$\oplus \oplus \oplus$	
	studies	serious				association		(29.0%)	(0.45 to	per 1,000	\bigcirc	
									0.66)	(from 160	MODERATE	
										fewer to 99		
										fewer)		

Cut-off time 2 minutes associated with AF recurrence rate (follow up: range 12 months to 19 months)

2	observational	not	not serious	not serious	not serious	none	81/207 (39.1%)	72/242	RR 0.86	42 fewer	⊕⊕⊖	
	studies	serious						(29.8%)	(0.67 to	per 1,000	\bigcirc	
									1.11)	(from 98	LOW	
										fewer to 33		
										more)		

Cut-off time 5-10 minutes associated with AF recurrence rate (follow up: range 12 months to 42.5 months)

4	observational	not	not serious	not serious	not serious	none	50/133 (37.6%)	128/436	RR 0.77	68 fewer	⊕⊕⊖	
	studies	serious						(29.4%)	(0.58 to	per 1,000	\bigcirc	
									1.01)	(from 123	LOW	
										fewer to 3		
l										more)		

Mild stimulation associated with AF recurrence rate (follow up: range 12 months to 19 months)

2	observational	not	not serious	not serious	not serious	none	81/207 (39.1%)	72/242	RR 0.86	42 fewer	⊕⊕⊖	
	studies	serious						(29.8%)	(0.67 to	per 1,000	\bigcirc	
									1.11)	(from 98	LOW	
										fewer to 33		
										more)		

Moderate stimulation associated with AF recurrence rate (follow up: range 12 months to 42.5 months)

6	observational	not	not serious	not serious	not serious	none	127/254 (50.0%)	212/680	RR 0.63	115 fewer	⊕⊕⊖	
	studies	serious						(31.2%)	(0.53 to	per 1,000	\bigcirc	
									0.74)	(from 147	LOW	
										fewer to 81		
										fewer)		

Severe stimulation associated with AF recurrence rate (follow up: range 6 months to 16 months)

			Certainty as	sessment			№ of pati	ents	Ef	fect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	AF non-inducibility	AF inducibility	Relative (95% Cl)	Absolute (95% Cl)	Certainty	Importance
3	observational	not	not serious	not serious	not serious	none	23/58 (39.7%)	42/190	RR 0.57	95 fewer	⊕⊕⊖	
	studies	serious						(22.1%)	(0.38 to	per 1,000	\bigcirc	
									0.86)	(from 137	LOW	
										fewer to 31		
										fewer)		

CI: Confidence interval; RR: Risk ratio



Figure S1. Sensitivity of the outcome (recurrence of AF).

Figure S2. (random effects models) AF non-inducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in total patients.

	Non-induc	ibility	Inducit	oility		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% Cl	M-H. Random, 95% CI
Adlbrecht-2013 21	35	85	22	36	11.1%	0.67 [0.47, 0.97]	-
Chang-2007 ⁵	14	77	6	11	4.0%	0.33 [0.16, 0.68]	
Haïssaguerre-20046	6	46	9	24	2.6%	0.35 [0.14, 0.86]	
Kawai-201910	12	48	15	50	4.8%	0.83 [0.44, 1.59]	
Leong-Sit-201311	27	55	44	89	12.0%	0.99 [0.71, 1.40]	+
Liu-20127	74	500	142	641	16.1%	0.67 [0.52, 0.86]	-
Oral-2004 ⁴	10	70	10	30	3.6%	0.43 [0.20, 0.92]	
Otsuka-2018 ⁸	71	236	25	55	11.7%	0.66 [0.47, 0.94]	
Richter-2006 ²²	61	156	53	78	16.5%	0.58 [0.45, 0.74]	-
Santangeli-2018 12	45	187	37	118	10.9%	0.77 [0.53, 1.11]	
Satomi-2008 14	18	43	7	17	4.5%	1.02 [0.52, 1.98]	
Skala-2019 ¹³	27	109	3	11	2.1%	0.91 [0.33, 2.52]	
Total (95% CI)		1612		1160	100.0%	0.68 [0.58, 0.79]	•
Total events	400		373				
Heterogeneity: Tau ² =	0.02; Chi ² =	16.29, df	= 11 (P =	0.13);	l ² = 32%		
Test for overall effect:	Z = 4.94 (P <	0.0000	1)				0.02 0.1 1 10 50 Favor Non-inducibility Favor Inducibility

Figure S3. (random effects models) AF non-inducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in different AF type and follow-up time.

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	Non-induc	ibility	Inducit	oility		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
1.2.1 PAF							
Adlbrecht-2013 ²¹	35	85	22	36	11.5%	0.67 [0.47, 0.97]	
Chang-2007 ⁵	14	77	6	11	3.0%	0.33 [0.16, 0.68]	
Haïssaguerre-2004 ⁶	6	46	9	24	1.9%	0.35 [0.14, 0.86]	
Liu-20127	74	500	142	641	23.3%	0.67 [0.52, 0.86]	
Oral-2004 ⁴	10	70	10	30	2.6%	0.43 [0.20, 0.92]	
Otsuka-2018 ⁸	45	166	8	22	4.1%	0.75 [0.41, 1.37]	
Richter-2006 ²²	39	115	31	50	13.6%	0.55 [0.39, 0.76]	
Santangeli-201812	29	133	19	68	6.1%	0.78 [0.47, 1.29]	
Satomi-200814	18	43	7	17	3.4%	1.02 [0.52, 1.98]	
Skala-2019 ¹³	27	109	3	11	1.5%	0.91 [0.33, 2.52]	
Subtotal (95% CI)		1344		910	71.0%	0.63 [0.54, 0.74]	◆
Total events	297		257				
Heterogeneity: Tau ² =	0.01; Chi ² = ⁻	10.16, df	= 9 (P =	0.34); l²	! = 11%		
Test for overall effect: 2	Z = 5.50 (P <	0.00001)				
1.2.2 Non-PAF							
Kawai-2019 ¹⁰	12	48	15	50	3.6%	0.83 [0.44, 1.59]	
Otsuka-2018 ⁸	26	70	17	33	7.5%	0.72 [0.46, 1.13]	
Richter-2006 ²²	22	41	22	28	12.9%	0.68 [0.48, 0.96]	
Santangeli-201812	16	54	18	50	5.0%	0.82 [0.47, 1.43]	
Subtotal (95% CI)		213		161	29.0%	0.73 [0.58, 0.92]	\bullet
Total events	76		72				
Heterogeneity: Tau ² =	0.00: Chi ² = 0	0.53. df =	= 3 (P = 0	.91): l² =	= 0%		
Test for overall effect: 2	Z = 2.65 (P =	0.008)		,.			
Total (95% CI)		1557		1071	100.0%	0 66 [0 58 0 75]	•
Total events	373	1001	320		100.070	0.00 [0.00, 0.10]	
Heterogeneity: Tau ² - 1	0.00. Chi² – ·	11 74 df	= 13 (P -	0.55)	$l^2 = 0\%$		· · · · · · · · · · · · · · · · · · ·
Test for overall effect:	7 = 657 (P < 100)	0.00001	- 13 (F =	- 0.55),	- 076		0.02 0.1 1 10 50
Test for subgroup diffe	= - 0.07 (P <	- 1 08 c	() f = 1 (D =	0.30)	12 - 7 7%		Favor Non-inducibility Favor Inducibility
rescior suburoub dille	ences. one	- 1.00.0		- 0.301.	- 1.170		

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	Non-induc	ibility	Inducik	oility		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% CI
1.3.1 Follow-up ≤6 r	nonths						
Oral-2004 ⁴	10	70	10	30	3.0%	0.43 [0.20, 0.92]	
Richter-2006 ²²	48	156	41	78	11.7%	0.59 [0.43, 0.80]	-
Subtotal (95% CI)		226		108	14.7%	0.56 [0.42, 0.75]	\bullet
Total events	58		51				
Heterogeneity: Tau ² =	0.00; Chi ² = ().55, df =	= 1 (P = 0	.46); I² :	= 0%		
Test for overall effect:	Z = 3.90 (P <	0.0001)					
1.3.2 6 months <foll< td=""><td>ow-up≪12 m</td><td>onths</td><td></td><td></td><td></td><td></td><td></td></foll<>	ow-up≪12 m	onths					
Chang-2007 ⁵	14	77	6	11	3.4%	0.33 [0.16, 0.68]	
Haïssaguerre-2004 ^e	6	46	9	24	2.2%	0.35 [0.14, 0.86]	
Kawai-2019 ¹⁰	12	48	15	50	4.0%	0.83 [0.44, 1.59]	
Leong-Sit-2013"	27	55	44	89	10.6%	0.99 [0.71, 1.40]	+
Liu-20127	74	500	142	641	14.7%	0.67 [0.52, 0.86]	
Richter-2006 ²²	61	156	53	78	15.1%	0.58 [0.45, 0.74]	-
Skala-2019 ¹³	27	109	3	11	1.8%	0.91 [0.33, 2.52]	
Subtotal (95% CI)		991		904	51.8%	0.65 [0.51, 0.84]	\bullet
Total events	221		272				
Heterogeneity: Tau ² =	0.05; Chi ² = '	12.97, df	= 6 (P =	0.04); l²	! = 54%		
Test for overall effect:	Z = 3.26 (P =	0.001)					
1.3.3 Follow-up > 12	months						
Adlbrecht-2013 ²¹	35	85	22	36	9.8%	0.67 [0.47, 0.97]	
Otsuka-2018 ⁸	71	236	25	55	10.3%	0.66 [0.47, 0.94]	
Santangeli-2018 ¹²	45	187	37	118	9.6%	0.77 [0.53, 1.11]	
Satomi-200814	18	43	7	17	3.8%	1.02 [0.52, 1.98]	
Subtotal (95% CI)		551		226	33.5%	0.72 [0.59, 0.88]	\bullet
Total events	169		91				
Heterogeneity: Tau ² =	0.00; Chi ² = '	1.50, df =	= 3 (P = 0	.68); l² :	= 0%		
Test for overall effect:	Z = 3.22 (P =	0.001)					
Total (95% CI)		1768		1238	100.0%	0.67 [0.58, 0.77]	♦
Total events	448		414				
Heterogeneity: Tau ² =	0.02; Chi ² = '	16.99, df	= 12 (P =	: 0.15);	l² = 29%		
Test for overall effect:	Z = 5.69 (P <	0.00001)				Eavor Non-inducibility Eavor Inducibility
Test for subaroup diffe	erences: Chi ²	= 2.01. c	if = 2 (P =	0.37).	l ² = 0.3%		ravor ron-inducionity ravor inducionity

PAF: paroxysmal AF; Non-PAF: non-paroxysmal AF.

Figure S4. (random effects models) AF non-inducibility vs AF inducibility by burst pacing after catheter ablation on the recurrence of AF in different induction protocols.

Α	Non-induc	ibility	Inducib	ility		Risk Ratio	Risk Ratio
Study or Subaroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H, Random, 95% Cl
1.4.1 Cut-off time 1 mi	in						
Adlbrecht-2013 ²¹	35	85	22	36	13.0%	0.67 [0.47, 0.97]	
Chang-2007 ⁵	14	77	6	11	5.3%	0.33 [0.16, 0.68]	
Haïssaguerre-20046	6	46	9	24	3.6%	0.35 [0.14, 0.86]	
Oral-2004 ⁴	10	70	10	30	4.8%	0.43 [0.20, 0.92]	
Richter-2006 ²²	61	156	53	78	17.9%	0.58 [0.45, 0.74]	-
Subtotal (95% CI)		434		179	44.6%	0.55 [0.44, 0.68]	◆
Total events	126		100				
Heterogeneity: Tau ² = 0).01; Chi ² = 4	l.61, df =	= 4 (P = 0.	33); l² =	= 13%		
Test for overall effect: 2	z = 5.42 (P <	0.00001)				
1.4.2 Cut-off time 2 mi	'n						
Leong-Sit-201311	27	55	44	89	13.9%	0.99 [0.71, 1.40]	+
Santangeli-201812	45	187	37	118	12.9%	0.77 [0.53, 1.11]	
Subtotal (95% CI)		242		207	26.8%	0.88 [0.68, 1.14]	•
Total events	72		81				
Heterogeneity: Tau ² = 0	0.00; Chi ² = 1	I.04, df =	= 1 (P = 0.	31); l² :	= 3%		
Test for overall effect: Z	2 = 0.97 (P =	0.33)					
1.4.3 Cut-off time 5-10	min						
Kawai-2019 ¹⁰	12	48	15	50	6.2%	0.83 [0.44, 1.59]	
Otsuka-2018 ⁸	71	236	25	55	13.6%	0.66 [0.47, 0.94]	
Satomi-2008 ¹⁴	18	43	7	17	5.9%	1.02 [0.52, 1.98]	_
Skala-2019 ¹³	27	109	3	11	2.9%	0.91 [0.33, 2.52]	
Subtotal (95% CI)		436	-	133	28.6%	0.75 [0.58, 0.99]	•
Total events	128		50				
Heterogeneity: Tau ² = 0	0.00; Chi ² = 1	l.54. df =	3 (P = 0	67); l ² :	= 0%		
Test for overall effect: 2	z = 2.05 (P =	0.04)		,,			
Total (95% CI)		1112		519	100.0%	0.68 [0.56, 0.81]	•
Total events	326		231	0.5		0.00 [0.00, 0.01]	
Heterogeneity: Tau ² = ($0.03 \cdot Chi^2 = 3$	6 30 df	= 10 (P =	0.09)	l ² = 39%		
Test for overall effect: 7	r = 4.16 (P < 100)	0.0001)	- 10 (1	0.00),	- 5570		0.02 0.1 1 10 50
Test for subgroup differ	ences: Chi ²	= 8.38 d	f = 2 (P =	0.02)	² = 76 1%		Favor Non-inducibility Favor Inducibility
reactor adduloub unler	choca. Off	0.50. 0		0.021.	- 70.176		

В Non-inducibility Inducibility **Risk Ratio Risk Ratio** M-H. Random, 95% CI Study or Subaroup Events Total Events Total Weight M-H. Random, 95% CI 1.5.1 Mild stimulation Leong-Sit-201311 89 13.9% 0.99 [0.71, 1.40] 27 55 44 Santangeli-201812 12.9% 26.8% 0.77 [0.53, 1.11] 0.88 [0.68, 1.14] 45 187 37 118 Subtotal (95% CI) 242 207 Total events 81 72 Heterogeneity: Tau² = 0.00; Chi² = 1.04, df = 1 (P = 0.31); I² = 3% Test for overall effect: Z = 0.97 (P = 0.33) 1.5.2 Moderate stimulation Adlbrecht-2013²¹ 35 85 22 36 13.0% 0.67 [0.47, 0.97] Haïssaguerre-2004 ⁶ Kawai-2019 ¹⁰ 6 46 9 24 3.6% 0.35 [0.14, 0.86] 12 48 15 50 6.2% 0.83 [0.44, 1.59] Otsuka-2018⁸ 71 236 25 55 13.6% 0.66 [0.47, 0.94] Richter-2006²² 61 156 53 78 17.9% 0.58 [0.45, 0.74] Skala-2019¹³ 27 109 3 2.9% 0.91 [0.33, 2.52] 11 Subtotal (95% CI) 680 254 57.3% 0.63 [0.53, 0.74] Total events 212 127 Heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 5 (P = 0.61); l² = 0% Test for overall effect: Z = 5.56 (P < 0.00001)1.5.4 Severe stimulation Chang-2007 5 77 5.3% 0.33 [0.16, 0.68] 14 6 11 Oral-2004⁴ 70 4.8% 0.43 [0.20, 0.92] 10 10 30 Satomi-200814 43 190 18 7 17 5.9% 1.02 [0.52, 1.98] Subtotal (95% CI) 58 16.0% 0.53 [0.27, 1.06] Total events 42 23 Heterogeneity: Tau² = 0.24; Chi² = 5.56, df = 2 (P = 0.06); l² = 64% Test for overall effect: Z = 1.79 (P = 0.07) Total (95% CI) 1112 519 100.0% 0.68 [0.56, 0.81] Total events 326 231 Heterogeneity: Tau² = 0.03; Chi² = 16.30, df = 10 (P = 0.09); l² = 39% 0.02 0.1 10 50 Test for overall effect: Z = 4.16 (P < 0.0001) Favor Non-inducibility Favor Inducibility Test for subaroup differences: Chi² = 5.42. df = 2 (P = 0.07). I^2 = 63.1%

Mild stimulation: burst pacing to refractoriness, 2:1 atrial captlure, or 180-200 ms (maintaining $\leq 3 \text{ sec/15 beats}$); Moderate stimulation: burst pacing to refractoriness, or 180-200 ms (maintaining 5 sec/30 beats); Severe stimulation: burst pacing to refractoriness (maintaining $\geq 10 \text{ sec}$), or 150 ms (maintaining 5-10 sec).