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The use of minimal fluoroscopy for cardiac electrophysiology procedures: A meta-analysis and review of the literature

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Abstract

Background: Conventional catheter ablation involves prolonged exposure to ionizing radiation, potentially leading to detrimental health effects. Minimal fluoroscopy (MF) represents a safer alternative, which should be explored. Data on the safety and efficacy of this technique are limited.

Hypothesis: Our hypothesis is that MF is of equal efficacy and safety to conventional catheter ablation with the use of fluoroscopy by performing a meta-analysis of both randomized controlled trials (RCTs) and real-world registry studies.

Methods: Pubmed and Embase were searched from their inception to July 2020 for RCTs, cohort and observational studies that assessed the outcomes of catheter ablation using a MF technique versus the conventional approach.

Lorraine Lok Wing Chiang and Christien Li share first authorship.

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Results: Fifteen studies involving 3795 patients were included in this meta-analysis. There was a significant reduction in fluoroscopy and procedural time with no difference in acute success (odds ratio [OR]:0.74, 95% CI: 0.50–1.10, p = .14), long-term success (OR:0.92, 95% CI: 0.65–1.31, p = .38), arrhythmia recurrence (OR:1.24, 95% CI: 0.75–2.06, p = .97) or rate of complications. (OR:0.83, 95% CI: 0.46–1.48, p = .65). Additionally sub-group analysis for those undergoing catheter ablation for atrial fibrillation (AF) did not demonstrate a difference in success or complication rates (OR:0.86, 95% CI: 0.30–2.42, p = .77). Multivariate meta-regression did not identify the presence of moderator variables.

Conclusion: This updated meta-analysis demonstrated an overall reduction in procedural and fluoroscopy time for those undergoing a minimal fluoroscopic approach. There was no significant difference in either acute or chronic success rates or complications between a MF approach and conventional approach for the management of all arrhythmias including those undergoing catheter ablation for AF.

KEYWORDS

catheter ablation, fluoroscopy, radiation, X-ray

1 | INTRODUCTION

Conventionally, the anatomical localization of catheters has relied on fluoroscopic imaging during catheter ablation for cardiac arrhythmias. It is well known that ionizing radiation is a proven (Class 1) carcinogen, therefore conventional fluoroscopy-based techniques carry potential risks to both the operator and the patient. Prolonged radiation exposure has been shown to be associated with an increased prevalence of certain malignancies, genetic defects, cataracts, and dermatitis, especially for high-risk populations such as children, pregnant women, and people who are immunocompromised.¹⁻³ The current standard practice is to use as low as reasonably achievable (ALARA) levels of radiation as well as lead protection where possible.⁴⁻⁶ Although electroanatomic mapping has been used in conjunction with fluoroscopic imaging there has been an increasing interest in the use of minimal fluoroscopy (MF). This has been helped with advancements in intracardiac echocardiography (ICE), 3-D mapping technology and contact force-sensing catheters.

Given the significant increase in the clinical volume of EP procedures there have been multiple studies about MF published since the last meta-analysis in 2016 on this topic.⁷ We conducted an updated meta-analysis to compare the efficacy and safety parameters of MF with conventional fluoroscopically guided procedures for ablation of cardiac arrhythmias. The main outcomes analyzed include fluoroscopy time, radiation dose, ablation time, procedural duration, acute success, long-term success, complication rates, and recurrence rates. We also performed a meta-analysis on MF and conventional fluoroscopy in the catheter ablation of atrial fibrillation (AF), including its acute success, long-term success, complications rates, and recurrence rates. Finally, we review the current state of adoption of MF technology and areas of future work.

2 | METHODS

2.1 | Search strategy, inclusion, and exclusion criteria

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISM) statement.⁸ Ethics was obtained from University of Hong Kong, PubMed and Embase were searched for studies which compared low or zero fluoroscopy to conventional fluoroscopy in the ablation of cardiac arrhythmia. The following search terms were used for both databases: (radiation or X-ray or fluoroscopy or fluoroscopic or fluoroscopically) and (catheter ablation). The search period was from January 1974 through to July 2020 without language restrictions. Only fully published studies were used. The following inclusion criteria were used: (i) Studies involving patients with cardiac arrhythmia requiring catheter ablation, (ii) difference in outcome between the two procedures, conventional ablation and zero or nonzero fluoroscopy, were compared. These outcomes included fluoroscopic time, radiation dose, ablation time, procedure duration, acute success, long-term success, complications, or arrhythmia recurrence.

The Newcastle–Ottawa Quality Assessment Scale (NOS) was used for quality assessment of the included studies.⁹ The NOS system evaluated the categories of study participant selection, results comparability, and quality of the outcomes. Specifically, the following characteristics were assessed: (a) Representativeness of the exposed cohort; (b) selection of the nonexposed cohort; (c) ascertainment of exposure; (d) demonstration that outcome of interest was not present at the start of study; (e) comparability of cohorts based on study design or analysis; (f) assessment of outcomes; (g) follow-up periods that were sufficiently long for outcomes to occur; and (h) adequacy of 816 WILEY CLINICAL

follow-up of cohorts. This scale varied from 0 to 9 stars, which indicated that studies were graded as poor quality if the score was <5, fair if the score was 5 to 7, and good if the score was >8. Studies with a score equal to or higher than six were included. The details of the NOS quality assessment are shown in Supplementary Tables 1.

2.2 Data extraction and statistical analysis

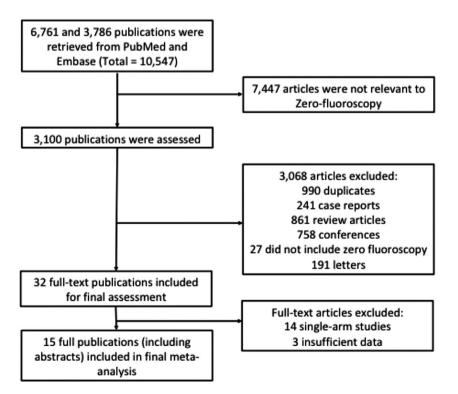
Data from different studies were entered in pre-specified spreadsheets in Microsoft Excel. All potentially relevant studies were retrieved as complete manuscripts, which were assessed fully to determine their compliance with the inclusion criteria. The following data were extracted from the included studies: (i) Publication details: last name of first author, publication year, and locations; (ii) study design; (iii) outcomes(s); and (vi) characteristics of the population including sample size, gender, age, and number of subjects. Two reviewers (L. C. and C. L.) reviewed each included study independently. Disagreements were resolved by adjudication with input from a third reviewer (G. T.). Heterogeneity across studies was determined using Cochran's Q-value and the l^2 statistic from the standard chisquare test. Cochran's Q-value is the weighted sum of squared differences between individual study effects and the pooled effect across studies. The l^2 statistic from the standard chi-square test describes the percentage of variability in the effect estimates resulting from heterogeneity. l^2 >50% was considered to reflect significant statistical heterogeneity. The random-effects model using the inverse variance heterogeneity method was used with l^2 >50%. To locate the origin of the heterogeneity, sensitivity analysis excluding one study at a time was also performed. Funnel plots showing standard errors or precision

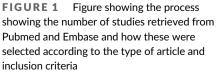
against the logarithms of the odds ratio were constructed. The Begg and Mazumdar rank correlation test and Egger's test were used to assess for potential publication bias (Figure 3). Associations between population co-variables and study outcomes were explored using multivariate meta-regression. To account for missing data, we used mean imputation (<10% missing) or random imputation (>10% missing). All statistical analysis was conducted using the Review Manager 5.3 for MacOS and Comprehensive Meta-Analysis (CMA) version 3.0 (Biostat, Inc, Englewood, NJ, USA). Statistical significance was set as p-value of less than .05.

RESULTS 3

A total of 15 studies involving 3795 patients met our inclusion criteria and were included in this meta-analysis. The PRISMA flow chart diagram (Figure 1) shows the study selection process. Of the 15 included publications. 5 were randomized trials while the remaining 10 were non-randomized studies. All studies included patients with attempted MF ablation. Baseline characteristics of the included studies are summarized in Supplementary Table 2. Overall, this shows that catheter ablations were performed for AVRT, AVNRT, atrial flutter, AF, and VT. The mean follow up ranged from 42 to 389 ± -217 days.

The results of our meta-analysis on fluoroscopic time (available in 11 out of 15 studies), radiation dose (available in 4 out of 25 studies), ablation time (available in 7 out of 25 studies) and procedure duration (available in 9 out of 15 studies) are shown in Figure 2(A)-(D). In these figures, the term 'total' refers to the number of cases recorded Significant reductions in fluoroscopic time, radiation dose and ablation time were observed in the MF group, vielding a standardized mean





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difference (SMD) of -2.21 (95% confidence interval [CI]: -2.89 to -1.54, p < .001), -1.62 (95% CI: -2.22 to -1.02, p < .001) and -0.25 (95% CI: -0.39 to -0.11, p = .0006), respectively, (Figure 2 (A)-(C)). By contrast, mean procedural times were not significantly different between MF and conventional ablation (SMD: -0.11, 95% CI: -0.27 to 0.04, p = .15) (Figure 2(D)). Subgroup analyses revealed that fluoroscopic time and radiation dose were significantly reduced for both randomized and non-randomized studies (Figure 2(A), (B)). However, ablation time and procedural duration were only shorter in non-randomized studies but not in randomized studies. No significant changes in pooled effects estimates were observed after the trimand-fill adjustment and Egger's tests showed no evidence of publication bias (Egger's regression test p-values >.05; Figure 3(A)-(C)).

Forest plots for all other clinical outcomes including acute success, long-term success, complication rate and recurrence rate are shown in Figure 4(A)-(D). The acute success, long-term success, complication rate, and recurrence rate were recorded in 14, 4, 10, and

5 studies for each outcome, respectively. With the addition of new articles into the meta-analysis since 2016, there were no significant differences between the MF and conventional groups in terms of acute success (OR: 0.74, 95% Cl: 0.50–1.10, p = .14), long-term success (OR: 0.92, 95% Cl: 0.65–1.31, p = .38), complication rates (OR: 0.83, 95% Cl: 0.46–1.48, p = .65) or recurrence rates (OR: 1.24, 95% Cl: 0.75–2.06, p = .97) (Figure 4(A)–(D)).

Of the publications included in this review, two randomized studies exclusively examined AF procedures. A meta-analysis of these two studies included 416 patients with AF treated either with MF or conventional fluoroscopic techniques. Both studies showed that MF and conventional techniques achieved 100% acute success. Long-term success rates were only reported and therefore only estimable in Zhang et al. (OR: 0.83, 95% CI: 0.52–1.32, p = .42), which showed no significant difference between the two groups after 1 year. Furthermore, no significant increase in complication rates was observed in the MF experimental group compared to conventional

(A)

h)		luorosc	••		entiona			Std. Mean Difference	Std. Mean Difference
tudy or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1 Randomised									
ulava 2015	0.2	1	40	180	84	40	9.1%	-3.00 [-3.64, -2.35]	
un 2011	28.4	43.1	23	339.3	162.6	23	8.7%	-2.57 [-3.37, -1.77]	
2hang 2017 Subtotal (95% CI)	168	24	170 233	600	60.7	166 229		-9.38 [-10.12, -8.64] -4.98 [-9.23, -0.73]	
leterogeneity: Tau ² :	= 13.98;	$Chi^2 = 2$	205.01,	df = 2 (P	< 0.000	001); I ²	= 99%		
est for overall effect	t: Z = 2.3	0 (P = 0)	0.02)						
.1.2 Non-randomis	sed								
Alvarez 2009	282	222	50	324	306	50	9.5%	-0.16 [-0.55, 0.24]	+
Deutsch 2017	16.5	89.5	219	533.5	422.2	241	9.7%	-1.66 [-1.87, -1.44]	
Giaccardi 2016	14	6	145	1,159	833	297	9.7%	-1.67 [-1.90, -1.45]	
eizer 2016	0	0	91	798	732	93	9.6%	-1.53 [-1.86, -1.20]	
mith 2007	63	178	30	1,282.2	11	30	6.1%	-9.54 [-11.38, -7.71] +	
Stec 2014	12	54	188	486	444	714	9.7%	-1.20 [-1.37, -1.03]	•
Vang 2017	0	0	163	450	570	326	9.7%	-0.96 [-1.16, -0.77]	+
Vannagat 2018 Subtotal (95% CI)	117.9	226.8	57 943	604.3	410.8	100 1851	9.5% 73.3%	-1.36 [-1.72, -1.00] -1.57 [-2.01, -1.13]	→
leterogeneity: Tau ²	= 0.35; C				0.0000	01); I ² =	95%		
Test for overall effect	t: Z = 6.9	6 (P < 0	0.00001	.)					
	t: Z = 6.9	6 (P < 0	0.00001 1176	.)		2080	100.0%	-2.73 [-3.47, -1.99]	•
lest for overall effect			1176		< 0.000				
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Test for overall effect Total (95% CI) Teterogeneity: Tau ² Test for overall effect Test for subgroup diffect	= 1.46; C t: Z = 7.2 fferences	hi ² = 62 4 (P < 0	1176 20.71, c 0.00001 2.45, c	if = 10 (P .) if = 1 (P =		001); I ² I ² = 59.	= 98%		
est for overall effect otal (95% CI) leterogeneity: Tau ² est for overall effect est for subgroup dif B) tudy or Subgroup	= 1.46; C t: Z = 7.2 fferences	hi ² = 62 4 (P < 0 : Chi ² = uorosco	1176 20.71, c 0.00001 2.45, c	if = 10 (P .) if = 1 (P =	0.12), vention	001); I ² I ² = 59. al	= 98% 1%		Favours [Zero fluoroscopy] Favours [Conventional] Std. Mean Difference
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rest for overall effect Fotal (95% CI) Heterogeneity: Tau ² + Fost for subgroup dif B) Study or Subgroup Lal Randomised Julava 2015 Subtotal (95% CI) Heterogeneity: Not ap Test for overall effect 2.2 Non-randomised Jaccardi 2016 eizer 2016 Vannagat 2018 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect	= 1.46; C t: Z = 7.2 fferences Zero Fl Mean 0.6 oplicable : Z = 8.62 ed 283.4 0 62.3 = 0.22; Ct : Z = 4.65	$hi^{2} = 62$ $4 (P < 0)$ $Chi^{2} =$ $4 (P < 0)$ 3.3 $3 (P < 0.0)$ 56.8 0 116.1 $hi^{2} = 21.$ $5 (P < 0.0)$	1176 20.71, 6 0.00001 2.45, c ppy Total 40 40 00001) 297 91 57 445 77, df 00001) 485	if = 10 (P) if = 1 (P = <u>Con</u> <u>Mean</u> 306.2 10,963.3 500 850 = 2 (P < 0	vention. 158 10,472 758 .0001);	$\begin{array}{c} \text{(0)} \text{(1)}; \text{(1)}; \text{(2)} \\ \text{(2)} \text{(2)}; \text{(2)}$	= 98% 1% al Weigl 0 21.6 0 21.6 15 26.8 13 26.1 10 25.4 18 78.4 6 18 100.0	Std. Mean Difference IV, Random, 95% CI % -2.70 [-3.31, -2.09] % -2.70 [-3.31, -2.09] % -1.78 [-2.01, -1.55] % -0.89 [-1.19, -0.58] % -1.29 [-1.64, -0.93] % -1.32 [-1.88, -0.77]	Favours [Zero fluoroscopy] Favours [Conventional]

FIGURE 2 (A) Forest plots demonstrating the changes in fluoroscopic time (s) between zero or near-zero fluoroscopy with conventional approach. (B) Forest plots demonstrating the changes in radiation dose (cGy/cm²) between zero or near-zero fluoroscopy with conventional approach. (C) Forest plots demonstrating the changes in ablation time (s) between zero or near-zero fluoroscopy with conventional approach. (D) Forest plots demonstrating the changes in procedural duration (min) between zero or near-zero fluoroscopy with conventional approach.

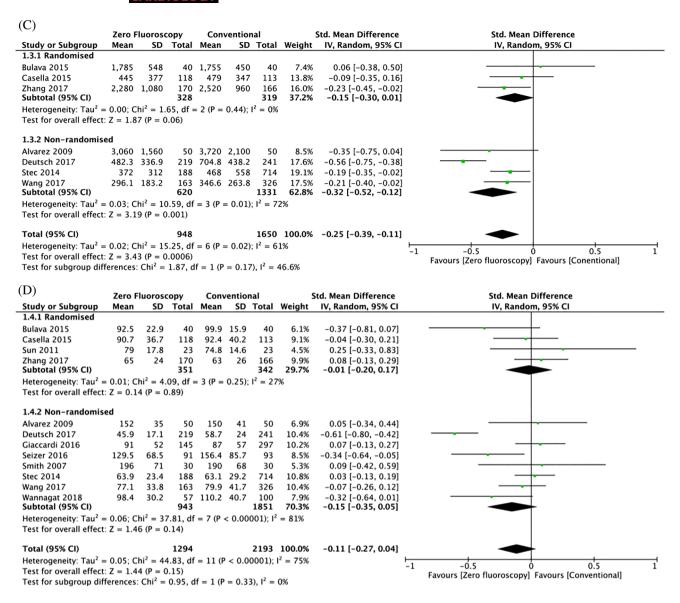


FIGURE 2 (Continued)

fluoroscopic techniques (OR: 0.86, 95% CI: 0.30–2.42, p = .77) (Figure 5(A)–(D)).

3.1 | Multivariate regression analysis for outcomes

We conducted a multivariate meta-regression, using all covariates that were common across any of the 15 studies that included the three outcomes: acute success, complication rates, and recurrence rates. Long-term success as an outcome was omitted from the multivariate regression due to lack of reporting from the included articles. Covariates used were mean population age, male gender, fluoroscopy time, ablation time, and procedure time. Both acute success and complication outcomes utilized all covariates while the recurrence rate outcome included only two covariates (fluoroscopy time and ablation time) for multivariate analysis (Supplementary Table 3). None of the covariates tested significantly moderated the acute success, complication rate and recurrence rate outcomes. Beta-coefficients for each covariate did not differ significantly from zero other than male gender (p > .05).

4 | DISCUSSION

There has been an increased interest in performing MF techniques particularly since the last meta-analysis was published on this topic.⁷ This study provides an update to a previously published meta-analysis by including five additional studies (one randomized and four non-randomized studies).¹⁰⁻¹⁴ In total, we included 15 clinical studies involving 3795 patients who underwent catheter ablation with MF or conventional fluoroscopy for cardiac arrhythmias. Our results demonstrate a significant reduction in fluoroscopic time, radiation dose and

ablation time in the MF group with no difference in total procedural time, short-term success, long-term success, complication rates, and recurrence rates. This is a very important finding as the use of MF is not associated with an increase in the duration of the procedure, success rates and most important rate of complications. This should be encouraging for operators who are looking at adopting this approach.

Furthermore, Zhang et al. and Bulava et al. were meta-analyzed to compare the two techniques specifically for AF (AF) procedures.^{12,15} The two outcomes analyzed–acute success and complication rates, did not differ significantly between the two approaches.

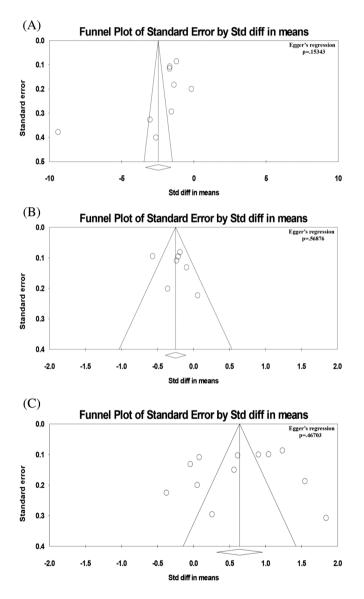


FIGURE 3 (A) Funnel plot with Egger's regression test in changes in fluoroscopic time (s) between zero or near-zero fluoroscopy with conventional approach. (B) Funnel plot with Egger's regression test in changes in ablation time (s) between zero or near-zero fluoroscopy with conventional approach. (C) Funnel plot with Egger's regression test in changes in procedural duration (min) between zero or near-zero fluoroscopy with conventional approach approach

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Subsequently, multivariate meta-regression was conducted on common covariates, including mean age, male gender, fluoroscopy time, ablation time, and procedural time for all outcomes except for long-term success. This analysis showed that these variables had no impact on acute success, complication and recurrence outcomes.

4.1 | Cancer risk associated with fluoroscopy and operator preference

There is sparse evidence regarding the long-term radiation effects in interventional-cardiac electrophysiology, thus emphasizing the need for additional studies in this area.^{16,17} In a study by Casella et al., they estimated that a switch from a fluoroscopic to MF approach would result in a 96% reduction in the estimated risks of cancer incidence, mortality, estimated years of life lost and years of life affected.¹⁸

The use of MF approaches becomes especially important in children, pregnant women and women of childbearing potential.^{19,20} In a survey published in 2017 by the European Society of Cardiology, the percentage of female trainees in electrophysiology is only 11%, with female cardiologists making more changes in their training and careers to reduce or avoid radiation exposure because of concerns related to risk to a developing fetus.²¹

Furthermore, it also appears that there is a higher incidence of sperm DNA fragmentation and hyper-methylated spermatozoa, suggesting that occupational exposure has substantial detrimental effects on sperm function, genetic and epigenetic integrity in healthcare workers.²² Unsurprisingly, surveys have shown that healthcare professionals favored the zero fluoroscopy approach over the conventional approach.^{10,23} Even though the use of lead aprons is useful in reducing radiation exposure, it has been shown to only effectively reduce one-third of the scattered radiation²⁷ Wang et al. also observed lower mean fatigue score with the zero fluoroscopy approach as compared to the conventional group (2.1 \pm 0.7 vs. 3.9 \pm 1.6, p < .05),¹⁰ which may partially be due to the use of lead aprons. This data underscores the importance of both development and adoption of MF technology for the field of electrophysiology in terms of reducing occupational health burdens on healthcare workers.

4.2 | Zero fluoroscopy in specific arrhythmias

Finally, it is worth noting that 13 out of 15 studies included in this meta-analysis included a broad range of arrhythmias ranging from atrial flutter to idiopathic ventricular arrhythmias, as illustrated in Supplementary Table 2. Considering two studies with similar patient populations,^{24,25} Alvarez et al. only used AVNRT patients while Razminia et al. utilized a population with a wide arrhythmic background. This resulted in a significantly different odds ratio in acute success favoring different ablation approaches. Furthermore,

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Walsh et al. reported significantly less ablation time was required to achieve cavo-tricuspid isthmus block in typical atrial flutter using MF. This may reflect the fact that three dimensional electroanatomical mapping may increase the accuracy of the ablation lesions compared with fluoroscopy making it more straightforward for the operator to ascertain any potential conduction gaps. Minimizing ablation time and instances might have the potential to reduce ablation-related complications.¹⁴ As such, the utility of MF over conventional ablation cannot be confirmed in arrhythmia-specific instances.

4.3 | Current barriers to adoption-cost and training

Currently available data suggest that the use of MF technique for individual patients is predicted by the type of arrhythmia, operator experience and patient's age.²⁶ Another common concern is the difficulty of learning to use a different modality. However, studies have shown that the MF learning curve is not unreasonably steep with the learning burden occurring over the first 20, 15, and 40 cases for SVT, PVC, and PVI ablation, respectively.²⁷

	Zero Fluoro		Convent			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.1.1 Randomised							
Bulava 2015	40	40	40	40		Not estimable	
Casella 2015	112	113	117	118	2.0%		
Earley 2006	44	45	51	51	1.5%		
Sun 2011	23	23	23	23		Not estimable	
Thang 2017 Subtotal (95% CI)	170	170 39 1	166	166 398	3.5%	Not estimable 0.57 [0.07, 4.72]	
Fotal events Heterogeneity: Tau² = Fest for overall effect:			397 f = 1 (P =	0.58); l ³	² = 0%		
2.1.2 Non-randomise	ed						
Alvarez 2009	50	50	48	50	1.7%	5.21 [0.24, 111.24]	
Deutsch 2017	217	219	239	241	4.0%	0.91 [0.13, 6.50]	
Giaccardi 2016	285	297	140	145	13.9%	0.85 [0.29, 2.45]	
Razminia 2012	59	60	60	60	1.5%		
Smith 2007	30	30	29	30	1.5%	3.10 [0.12, 79.23]	
Stec 2014	185	188	701	714	9.8%	1.14 [0.32, 4.06]	
Valsh 2018	50	50	42	42	5.0/0	Not estimable	
Vang 2017	130	163	281	326	64.0%		_
Vannagat 2018	57	57	100	100	01.0/0	Not estimable	
ubtotal (95% CI)	57	1114	100	1708	96.5%		•
otal events	1063		1640				
leterogeneity: Tau ² = Test for overall effect:			f = 6 (P =	0.74); l ⁱ	² = 0%		
Fotal (95% CI)		1505		2106	100.0%	0.74 [0.50, 1.10]	•
otal events	1452		2037				
1-1				a a m 13	2 00/		
Heterogeneity: Tau ² =	= 0.00; Chi* =	3.89, df	F = 8 (P =	0.87); I	·= 076		
Fest for overall effect:			f = 8 (P =	0.87); I	- = 076		
	Z = 1.49 (P =	= 0.14)					0.01 0.1 1 10 1 Favours [Zero fluoroscopy] Favours [Conventional]
Test for overall effect: Test for subgroup diff	Z = 1.49 (P = ferences: Chl ²	= 0.14) = 0.06,	df = 1 (P	= 0.81)			Favours [Zero fluoroscopy] Favours [Conventional]
Test for overall effect: Test for subgroup diff (B)	Z = 1.49 (P = ferences: Chl ² Zero Fluoro	= 0.14) = 0.06, scopy	df = 1 (P Convent	= 0.81) ional	, ² = 0%	Odds Ratio	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect: Test for subgroup diff (B) Study or Subgroup	Z = 1.49 (P = ferences: Chl ²	= 0.14) = 0.06, scopy	df = 1 (P	= 0.81) ional	, ² = 0%	Odds Ratio M-H, Random, 95% Cl	Favours [Zero fluoroscopy] Favours [Conventional]
Test for overall effect: Test for subgroup diff (B) Study or Subgroup 2.2.1 Randomised	Z = 1.49 (P = ferences: Chl ² Zero Fluoro Events	= 0.14) = 0.06, scopy Total	df = 1 (P Convent Events	= 0.81) ional Total	, ² = 0% Welght	M-H, Random, 95% Cl	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect: Test for subgroup diff B) Study or Subgroup 2.2.1 Randomised Casella 2015	Z = 1.49 (P = ferences: Chl ² Zero Fluoro Events 110	= 0.14) = 0.06, scopy Total 113	df = 1 (P Convent Events 111	= 0.81) ional Total 118	, ² = 0% <u>Welght</u> 6.6%	M-H, Random, 95% Cl 2.31 [0.58, 9.17]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) Study or Subgroup 2.2.1 Randomised Casella 2015 Zhang 2017	Z = 1.49 (P = ferences: Chl ² Zero Fluoro Events	= 0.14) = 0.06, scopy Total	df = 1 (P Convent Events 111 119	= 0.81) ional Total	, ² = 0% Welght	M-H, Random, 95% Cl	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
rest for overall effect: rest for subgroup diff B) 2.2.1 Randomised Casella 2015 Zhang 2017 Subtotal (95% CI) Fotal events	: Z = 1.49 (P = ferences: Chl ² Zero Fluoro <u>Events</u> 110 115 225	= 0.14) = 0.06, scopy Total 113 170 283	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230	= 0.81) ional Total 118 166 284	, ² = 0% Welght 6.6% 55.2% 61.8%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect: Test for subgroup diff (average) (average	Z = 1.49 (P = ferences: Chl ² Zero Fluoro Events 110 115 225 • 0.26; Chl ² =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230	= 0.81) ional Total 118 166 284	, ² = 0% Welght 6.6% 55.2% 61.8%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) (B) (Caselia 2015 Chang 2017 Subtotal (95% Cl) Fotal events Heterogeneity: Tau ² = Fest for overall effect:	zero Fluoro Events 110 115 225 0.26; Chi ² = z = 0.24 (P =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230	= 0.81) ional Total 118 166 284	, ² = 0% Welght 6.6% 55.2% 61.8%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
rest for overall effect: rest for subgroup diff B) 2.2.1 Randomised Casella 2015 chang 2017 Subtotal (95% Cl) rotal events leterogeneity: Tau ² = rest for overall effect: 2.2.2 Non-randomise	zero Fluoro Events 110 115 225 0.26; Chi ² = z = 0.24 (P =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230	= 0.81) ional Total 118 166 284	, ² = 0% Welght 6.6% 55.2% 61.8%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect: Test for subgroup diff B) C.2.1 Randomised C.2.1 Randomised C.2.1 Randomised C.2.1 Randomised C.2.1 Randomised C.2.1 Randomised C.2.1 Randomised C.2.2 Non-randomised tec 2014 Vannagat 2018	z z = 1.49 (P = ferences: Chl ² Zero Fluoro Events 110 115 225 0.26; Chl ² = z = 0.24 (P =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P =	= 0.81) ional <u>Total</u> 118 166 284 0.17); I ² 714 100	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect: Test for subgroup diff B) 2.2.1 Randomised Casella 2015 Chang 2017 Subtotal (95% Cl) Total events Test for overall effect: 2.2.2 Non-randomise tice 2014 Vannagat 2018 Subtotal (95% Cl)	Zero Fluoro Events 110 115 225 0.26; Chi ² = Z = 0.24 (P = ed 174 54	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91	= 0.81) ional <u>Total</u> 118 166 284 0.17); I ² 714	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) (B) (Casella 2015 Chang 2017 Subtotal (95% Cl) Fotal events Heterogeneity: Tau ² = Fest for overall effect: 2.2.2 Non-randomise Site 2014 Wannagat 2018 Subtotal (95% Cl) Fotal events	z z = 1.49 (P = ferences: Chl ² Zero Fluoro <u>Events</u> 110 115 225 0.26; Chl ² = z = 0.24 (P = ed 174 54 228	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762	= 0.81) ional <u>Total</u> 118 166 284 0.17); l ² 714 100 814	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Test for overall effect:	Zero Fluoro Events 110 115 225 0.26; Chi ² = Z = 0.24 (P = ed 174 54 228 0.04; Chi ² =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245 1.13, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762	= 0.81) ional <u>Total</u> 118 166 284 0.17); l ² 714 100 814	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) (B) (Caselia 2015 Chang 2017 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: 2.2.2 Non-randomise Sitec 2014 Wannagat 2018 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² =	Zero Fluoro Events 110 115 225 0.26; Chi ² = Z = 0.24 (P = ed 174 54 228 0.04; Chi ² =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245 1.13, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762	= 0.81) ional Total 118 166 284 0.17); l ² 714 100 814 0.29); l ²	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) Study or Subgroup diff (Casella 2015 Casella 2017 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: 2.2.2 Non-randomise Site 2014 Wannagat 2018 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% CI)	z = 1.49 (P = ferences: Chl2 $zero Fluoro: Events$ 110 115 225 0.26; Chl ² = Z = 0.24 (P = ference) ed 174 54 228 0.04; Chl ² = Z = 0.17 (P = ference)	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245 1.13, df = 0.87)	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762	= 0.81) ional Total 118 166 284 0.17); l ² 714 100 814 0.29); l ²	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2% = 11%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86] 0.95 [0.49, 1.81]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
Fest for overall effect: Fest for subgroup diff (B) (B) (Casella 2015 Chang 2017 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: 2.2.2 Non-randomise Stec 2014 Wannagat 2018 Subtotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect: Total events Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% CI) Fotal events	Zero Fluoro Events 110 115 225 0.26; Chi ² = Z = 0.24 (P = ed 174 54 228 0.04; Chi ² = Z = 0.17 (P = 453	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245 1.13, df = 0.87) 528	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762 = 1 (P = 992	= 0.81) ional Total 118 166 284 0.17); l ² 714 100 814 0.29); l ² 1098	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2% = 11% 100.0%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86] 0.95 [0.49, 1.81]	Favours [Zero fluoroscopy] Favours [Conventional]
Test for overall effect: Test for subgroup diff B) 2.2.1 Randomised Casella 2015 Chang 2017 Subtotal (95% Cl) Total events Heterogeneity: Tau ² = Test for overall effect: 2.2.2 Non-randomise Stoc 2014 Vannagat 2018 Subtotal (95% Cl) Total events Heterogeneity: Tau ² = Test for overall effect: Total (95% Cl)	Zero Fluoro Events 110 115 225 0.26; Chi ² = Z = 0.24 (P = 24 228 0.04; Chi ² = Z = 0.17 (P = 453 0.00; Chi ² =	= 0.14) = 0.06, scopy Total 113 170 283 1.93, df = 0.81) 188 57 245 1.13, df = 0.87) 528 3.05, df	df = 1 (P <u>Convent</u> <u>Events</u> 111 119 230 = 1 (P = 671 91 762 = 1 (P = 992	= 0.81) ional Total 118 166 284 0.17); l ² 714 100 814 0.29); l ² 1098	, ² = 0% Welght 6.6% 55.2% 61.8% = 48% 31.3% 6.9% 38.2% = 11% 100.0%	M-H, Random, 95% Cl 2.31 [0.58, 9.17] 0.83 [0.52, 1.32] 1.12 [0.45, 2.80] 0.80 [0.43, 1.49] 1.78 [0.46, 6.86] 0.95 [0.49, 1.81]	Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio

FIGURE 4 (A) Forest plots comparing the number of acute success between zero or near-zero fluoroscopy with conventional approach. (B) Forest plots comparing the number of long-term success between zero or near-zero fluoroscopy with conventional approach. (C) Forest plots comparing the number of complications between zero or near-zero fluoroscopy with conventional approach. (D) Forest plots comparing the number of recurrence between zero or near-zero fluoroscopy with conventional approach.

	Zero Fluoro		Convent			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Welght	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.3.1 Randomised							
Bulava 2015	3	40	3	40	12.3%	1.00 [0.19, 5.28]	
Casella 2015	1	113	2	118	5.9%	0.52 [0.05, 5.79]	
arley 2006	1	45	0	50	3.3%	3.40 [0.14, 85.71]	
Zhang 2017 Subtotal (95% CI)	4	170 368	5	166 374	19.2% 40.7%	0.78 [0.20, 2.94] 0.89 [0.36, 2.23]	
Total events	9		10				
eterogeneity: Tau ² =		= 0 92 df		0 82)- 1	² = 0%		
est for overall effect				0.02/, 1	- 0/0		
.3.2 Non-randomis	ed						
lvarez 2009	1	50	4	50	6.9%	0.23 [0.03, 2.18]	
Giaccardi 2016	13	297	3	145	21.1%	2.17 [0.61, 7.73]	
lazminia 2012	1	60	2	60	5.8%	0.49 [0.04, 5.57]	
tec 2014	2	188	10	714	14.7%	0.76 [0.16, 3.48]	
Vang 2017	1	163	3	326	6.6%	0.66 [0.07, 6.44]	
Vannagat 2018	ō	57	8	100	4.1%	0.09 [0.01, 1.67]	←
ubtotal (95% CI)	Ŭ	815	Ũ	1395	59.3%	0.72 [0.31, 1.69]	
otal events	18		30				
eterogeneity: Tau ² =		= 5.93. df		0.31): 1	² = 16%		
est for overall effect			5 (.		20/0		
cation overall effect	•						
	•• ••••	1183		1769	100.0%	0.83 [0.46, 1.48]	
Fotal (95% CI)	27	1183	40	1769	100.0%	0.83 [0.46, 1.48]	-
Fotal (95% CI) Fotal events	27 = 0.00: Chi ² =		40 F = 9 (P =			0.83 [0.46, 1.48]	
F otal (95% CI) Fotal events Heterogeneity: Tau ² =	= 0.00; Chi ² =	= 6.87, di				0.83 [0.46, 1.48]	0.02 0.1 1 10
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect Fest for subgroup diff	= 0.00; Chi ² = :: Z = 0.64 (P	= 6.87, di = 0.52)	F = 9 (P =	0.65); l ⁱ	² = 0%	0.83 [0.46, 1.48]	
Fotal (95% CI) Fotal events Heterogeneity: Tau ² = Fest for overall effect Fest for subgroup dif	= 0.00; Chi ² = :: Z = 0.64 (P	= 6.87, di = 0.52)	F = 9 (P =	0.65); l ⁱ	² = 0%	0.83 [0.46, 1.48]	0.02 0.1 1 10
Total (95% CI) Total events leterogeneity: Tau ² = Test for overall effect Test for subgroup diff	= 0.00; Chi ² = :: Z = 0.64 (P	= 6.87, di = 0.52) ² = 0.11,	F = 9 (P =	0.65); l ² ? = 0.74)	² = 0%	0.83 [0.46, 1.48] Odds Ratio	0.02 0.1 1 10
iotal (95% CI) iotal events leterogeneity: Tau ² = est for overall effect est for subgroup dif	= 0.00; Chi ² = :: Z = 0.64 (P ferences: Chi	= 6.87, di = 0.52) ² = 0.11, oscopy	f = 9 (P = df = 1 (P	0.65); i ² ? = 0.74) tional	² = 0% , ² = 0%		0.02 0.1 i 10 Favours [Zero fluoroscopy] Favours [Conventional]
iotal (95% CI) otal events leterogeneity: Tau ² = est for overall effect est for subgroup dif)) tudy or Subgroup	= 0.00; Chi ² = : Z = 0.64 (P ferences: Chi Zero Fluoro Events	= 6.87, di = 0.52) ² = 0.11, oscopy	f = 9 (P = df = 1 (P Convent	0.65); i ² ? = 0.74) tional	² = 0% , ² = 0%	Odds Ratio	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio
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iotal (95% CI) iotal events leterogeneity: Tau ² = est for overall effect est for subgroup dif)) tudy or Subgroup .4.1 Non-randomis lvarez 2009	= 0.00; Chi ² = :: Z = 0.64 (P ferences: Chi Zero Fluoro <u>Events</u> ed	= 6.87, df = 0.52) ² = 0.11, oscopy Total	f = 9 (P = df = 1 (P Convent Events	0.65); ² ? = 0.74) tional Total	² = 0% , ² = 0% <u>Weight</u>	Odds Ratio M-H, Random, 95% CI	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio M-H, Random, 95% Cl
Total (95% CI) Total events leterogeneity: Tau ² = est for overall effect test for subgroup diff tudy or Subgroup (4.1 Non-randomis livarez 2009 mith 2007	= 0.00; Chi ² = :: Z = 0.64 (P ferences: Chi Zero Fluoro Events red 3	= 6.87, df = 0.52) ² = 0.11, oscopy <u>Total</u> 50	f = 9 (P = df = 1 (P Convent Events 2	0.65); l ² ? = 0.74) tional <u>Total</u> 50	² = 0% , ² = 0% <u>Weight</u> 7.7%	Odds Ratio M-H, Random, 95% CI 1.53 [0.24, 9.59]	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio M-H, Random, 95% Cl
Total (95% CI) Total events leterogeneity: Tau ² = est for overall effect test for subgroup diff tudy or Subgroup t.4.1 Non-randomis lvarez 2009 mith 2007 tec 2014	= 0.00; Chi ² = :: Z = 0.64 (P ferences: Chi Zero Fluore Events ed 3 4	= 6.87, df = 0.52) ² = 0.11, oscopy <u>Total</u> 50 30	F = 9 (P = df = 1 (P <u>Convent</u> <u>Events</u> 2 3	0.65); i ² 2 = 0.74) tional Total 50 29	² = 0% , ² = 0% <u>Weight</u> 7.7% 10.2%	Odds Ratio M-H, Random, 95% CI 1.53 [0.24, 9.59] 1.33 [0.27, 6.56]	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio M-H, Random, 95% Cl
Total (95% CI) iotal events leterogeneity: Tau ² = est for overall effect est for subgroup diff)) tudy or Subgroup :.4.1 Non-randomis .lvarez 2009 mith 2007 tec 2014 Valsh 2018	= 0.00; Chi ² = : Z = 0.64 (P ferences: Chi Zero Fluoro <u>Events</u> ed 3 4 14	= 6.87, df = 0.52) ² = 0.11, oscopy Total 50 30 188	F = 9 (P = df = 1 (P <u>Convent</u> <u>Events</u> 2 3 43	0.65); i ² = 0.74) tional <u>Total</u> 50 29 714	² = 0% , ² = 0% <u>Weight</u> 7.7% 10.2% 65.9%	Odds Ratio M-H, Random, 95% CI 1.53 [0.24, 9.59] 1.33 [0.27, 6.56] 1.26 [0.67, 2.35]	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional] Odds Ratio M-H, Random, 95% Cl
iotal (95% CI) iotal events leterogeneity: Tau ² = est for overall effect est for subgroup diff 	= 0.00; Chi ² = : Z = 0.64 (P ferences: Chi Zero Fluoro <u>Events</u> ed 3 4 14 14	= 6.87, di = 0.52) ² = 0.11, oscopy Total 50 30 188 50	F = 9 (P = df = 1 (P <u>Events</u> 2 3 43 0	0.65); i ² = 0.74) tional Total 50 29 714 42 326	² = 0% , ² = 0% <u>Weight</u> 7.7% 10.2% 65.9% 2.5%	Odds Ratio M-H, Random, 95% CI 1.53 [0.24, 9.59] 1.33 [0.27, 6.56] 1.26 [0.67, 2.35] 2.58 [0.10, 64.90]	0.02 0.1 1 10 Favours [Zero fluoroscopy] Favours [Conventional]
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FIGURE 4 (Continued)

Furthermore, in a study by Gist et al. they found that procedure time significantly shortens as a function of experience, reaching acceptable time frames in comparison to current fluoroscopic approaches after 12 months of use.²⁸ Despite such benefits, higher cost incurred with zero fluoroscopy has been previously reported.²⁹ This issue was elegantly addressed by Casella et al., whose analysis found that the additional cost of MF technology is approximately equal to the extra costs associated with increased cancer treatment and reduction in quality of life associated with traditional fluoroscopic techniques.¹⁸

4.4 | Current and future directions

Currently, through this meta-analysis, we found no significant difference in outcome measures between conventional and MF techniques. This is a reassuring finding, confirming a previous important study.⁷ It would be beneficial for future studies to compare the two approaches in specific arrhythmia types. Moving forward, subgroup analysis of the effectiveness of MF approaches to different procedures, which vary widely in their baseline radiation exposure and technical difficulty, would be useful to inform practitioners that specialize in specific procedures. Long-term follow-up studies should focus on long-term patient outcomes and healthcare use experiences to better elucidate how to implement MF technology into established practices.

5 | LIMITATIONS

Several limitations of this study should be noted. First, a high degree of heterogeneity is still observed (>50%) between the different study populations. This was addressed by conducting a sensitivity analysis excluding one study at a time along with Egger's test, which overall showed a nonsignificant publication bias. A multivariate meta-regression analysis also confirmed that patient characteristics and procedural

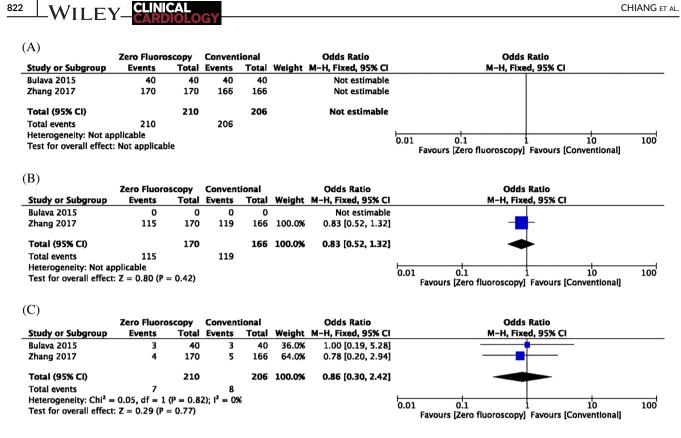


FIGURE 5 (A) Forest plots comparing the number of acute success between zero or near-zero fluoroscopy with conventional approach in atrial fibrillation patients. (B) Forest plots comparing the number of long-term success between zero or near-zero fluoroscopy with conventional approach in atrial fibrillation patients. (C) Forest plots comparing the number of complications between zero or near-zero fluoroscopy with conventional approach in atrial fibrillation patients.

parameters have no impact on outcome measures. Second, abstracts presented at scientific meetings and non-English studies were excluded from this meta-analysis, which may result in a small degree of selection bias. Finally, all studies listed the arrhythmia subtypes that were included in the comparison (Supplementary Table 2) but only two authors (Earley, et al. and Smith, et al.) went on to briefly specify the complications with each subtype. As such, a sub-analysis of each arrhythmia subtype was not possible.

6 | CONCLUSIONS

This systematic review and meta-analysis confirmed that the use of MF does not result in an increase in procedural time, success rates or complication rates when compared with conventional techniques. These parameters were also not significantly different for patients undergoing catheter ablation for AF. This is highly encouraging data for those who are seeking to adopt this technique for the management of cardiac arrhythmias.

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None.

CONFLICT OF INTEREST

Authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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

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