

Systematic Review

A Meta-Analysis Comparing General Anesthesia, Deep Sedation, and Conscious Sedation for Catheter Ablation of Atrial Fibrillation

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Abstract

Background: The optimal anesthesia strategy during catheter ablation of atrial fibrillation (AF) remains controversial. This meta-analysis compared general anesthesia, deep sedation, and conscious sedation in terms of procedural time and complications. **Methods:** Literature searches were conducted in PubMed, EMBASE, and Web of Science databases. Mean differences (MDs) and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using fixed- and random-effect models on the basis of the heterogeneity among studies, as assessed by I^2 statistics. The random-effect model was used when the heterogeneity was high ($I^2 > 50\%$). Publication bias was evaluated through funnel plots and Egger's tests. **Results:** Sixteen studies were included in this study. No significant difference was observed in procedural time between the general anesthesia and conscious sedation groups (MD: -8.1479 minutes, 95% CI: from -27.6836 to 11.3878 , seven studies). Deep sedation was associated with procedural time (MD: 131.8436 minutes, 95% CI: 99.6540 – 164.0332 , eight studies). The rate of serious intraprocedural complications was 1.5% (95% CI: 1.2%–1.9%) with deep sedation (seven studies). Conscious/analog sedation had 26%–29% higher odds of perioperative complications than general anesthesia (OR: 1.2622, 95% CI: 1.0273–1.5507, nine studies). Significant heterogeneity was present across studies. **Conclusions:** This meta-analysis found no significant difference in procedural time between general anesthesia and conscious sedation for AF ablation. Deep sedation was associated with longer procedural time. Conscious sedation appeared to have a higher risk of perioperative complications than general anesthesia. Further randomized trials are warranted to determine the optimal anesthesia strategy.

Keywords

meta-analysis; general anesthesia; deep sedation; conscious sedation; catheter ablation; atrial fibrillation; procedural time; complications; perioperative complications

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting over 30 million individuals worldwide. Catheter ablation has emerged as an effective treatment strategy to electrically isolate the pulmonary veins, which are the predominant triggers of AF. The primary catheter ablation procedures employed are radiofrequency ablation and cryoablation techniques [1,2]. Radiofrequency ablation utilizes a catheter delivering high-frequency electrical energy for localized thermal tissue destruction, whereas cryoablation involves a catheter delivering freezing temperatures to induce tissue necrosis [3,4]. Specifically, a 4 mm-tip catheter is used for radiofrequency ablation under fluoroscopic guidance, with energy delivery adjusted on the basis of impedance and temperature monitoring for optimal lesion formation [5]. Cryoablation utilizes a 6 mm-tip cryoablation catheter guided to the target site to achieve controlled tissue freezing [3]. While the surgical procedure is crucial, the choice of anesthesia administered during the operation can remarkably influence a patient's recovery process [6].

The optimal anesthesia strategy during AF ablation remains controversial. Recent studies have compared general anesthesia, deep sedation, and conscious sedation in terms of efficacy and safety outcomes [7]. They are different levels of anesthesia that affect the patient's consciousness, pain perception, and respiratory function. General anesthesia is the most profound level of anesthesia, in which the patient is completely unconscious, does not feel any pain, and requires mechanical ventilation [8]. Deep sedation is a level of anesthesia in which the patient is nearly unconscious, has a reduced response to painful stimuli, and may need assistance with breathing [9]. Conscious sedation is a level of anesthesia in which patients are awake but relaxed, can respond to verbal commands, and can breathe on their own [10]. The choice of anesthesia for AF ablation depends on various factors, such as the patient's preference, medical condition, procedural complexity, and the operator's experience [11]. Each level of anesthesia has its advantages and disadvantages and may affect the procedural time and complications of AF ablation differently. Therefore, comparing

the outcomes of different anesthesia strategies for AF ablation is important.

Grimaldi *et al.* [12], 2022 reported no difference in fluoroscopy time, radiofrequency time, or long-term success between deep sedation and general anesthesia. Wutzler *et al.* [13], 2013 found similar complication rates between deep sedation and general anesthesia groups. However, results have been conflicting. Some studies reported shorter procedure time with general anesthesia than with conscious sedation, whereas others found no difference.

Given the inconsistent results, a systematic review and meta-analysis was performed to compare general anesthesia, deep sedation, and conscious sedation for catheter ablation of AF in terms of procedural time and complications to provide evidence on the optimal anesthesia strategy during AF ablation.

Methods

Search Strategy and Study Selection

A systematic literature search was conducted in PubMed, EMBASE, and Web of Science databases to identify relevant studies comparing different sedation methods for catheter ablation of AF. The search terms included various combinations of keywords such as “atrial fibrillation”, “catheter ablation”, “anesthesia”, and “sedation”. No limits were applied to publication date nor language. The study selection process is outlined in a PRISMA flow diagram.

Inclusion and Exclusion Criteria

In this systematic review and meta-analysis of studies investigating the effect of different methods of sedation or anesthesia on the outcomes of catheter ablation of AF, the following inclusion and exclusion criteria were applied to select relevant studies for analysis.

Inclusion Criteria

- (1) Studies published in peer-reviewed journals.
- (2) Studies that focused on catheter ablation procedures for symptomatic AF.
- (3) Studies that reported data on the sedation or anesthesia strategy used during catheter ablation (e.g., general anesthesia, conscious sedation, and deep sedation).
- (4) Studies with a sample size of at least 10 patients.
- (5) Studies that provided sufficient data for analysis.
- (6) Studies conducted on human subjects.

Exclusion Criteria

- (1) Reviews, meta-analyses, conference abstracts, or case reports.
- (2) Studies with a sample size of less than 10 patients.

(3) Studies lacking information on the sedation or anesthesia strategy.

(4) Studies with insufficient data for analysis.

(5) Studies conducted on animal subjects.

(6) Non-English language studies, if translation resources were not available.

(7) Duplicate publications from the same study.

(8) Studies with incomplete or inadequately reported outcomes.

(9) Studies that were not randomized controlled trials (RCTs) or retrospective/prospective studies because these were the least common study types among the eligible studies.

Statistical Methods

(1) Effect sizes (e.g., risk ratio and standardized mean difference) were computed for each study.

(2) A meta-analysis was conducted by amalgamating the effect sizes from the studies to derive the pooled effect size and confidence intervals (CIs).

(3) Inter-study heterogeneity was evaluated. For instance, heterogeneity was detected using methods like Q-test or I^2 statistic.

(4) Subgroup or sensitivity analyses were conducted to investigate the resilience and coherence of the study findings.

Data Extraction and Quality Assessment

Data extraction and quality assessment were conducted systematically and rigorously to ensure the validity and reliability of the meta-analysis. This section outlines the process of data extraction and quality evaluation for the 16 selected studies, and any additional sources of potential bias specific to each study.

Quality assessment aimed to determine the overall risk of bias for each study, and it was carried out independently by two assessors. Discrepancies were resolved through discussion, and a third assessor was consulted when consensus could not be reached. The results of the quality assessment were taken into consideration when interpreting the findings of the meta-analysis and assessing the overall strength of the evidence. This systematic approach to data extraction and quality assessment ensures the reliability and credibility of the meta-analysis results.

Group Assignment and Comparison

The studies included in this meta-analysis assigned the patients to different groups on the basis of sedation or anesthesia strategy used during catheter ablation of AF. The control group received general anesthesia, which is the most profound level of anesthesia, in which the patient is completely unconscious, does not feel any pain, and requires mechanical ventilation. The test group received ei-

ther conscious sedation, analgosedation, or local anesthesia, which are different levels of sedation that affect the patient's consciousness, pain perception, and respiratory function to varying degrees.

Statistical Analysis

This study is based solely on the PRISMA (Supplementary Materials) guidelines. We analyzed all data using R software 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). The meta-analysis was performed using R packages meta, dmetar, and metaphor [14]. Mean differences (MD) and odds ratios (OR) with 95% CIs were calculated for continuous and dichotomous outcomes, respectively. Heterogeneity was assessed using I^2 statistic. Publication bias was evaluated through funnel plots, Begg's test, and Egger's test. Influence analysis was conducted to determine the effect of excluding individual studies. Leave-one-out analysis assessed the effect on the pooled effect size. Baujat and Galbraith plots were used to visually examine heterogeneity. P -curve analysis was conducted to evaluate the evidential value and statistical power. GOSH diagnostics was applied to identify potential outlier studies.

Results

Search Results and Study Characteristics

The results of the systematic literature search and meta-analysis of the effect of different methods of sedation or anesthesia on the outcomes of catheter ablation of AF are presented. The literature search was conducted in three databases: PubMed, EMBASE, and Web of Science. A total of 667 records were identified through the database search. After 513 duplicates were removed, 154 records were screened by title and abstract. Among them, 78 records were excluded for not meeting the inclusion criteria. The remaining 76 records were assessed for eligibility by full-text articles. Among them, 60 records were excluded for various reasons such as being reviews or meta-analyses, having a sample size of less than 10, or having insufficient data. Finally, 16 studies were included in the meta-analysis (Fig. 1). The characteristics of the 16 studies are summarized in Table 1 (Ref. [12,13,15–27]).

Procedural Time of Deep Sedation for Catheter Ablation of AF

This meta-analysis of eight studies compared the procedural time of deep sedation for catheter ablation of AF, as shown in Fig. 2A. The total number of patients in the deep sedation group was 4474. The results showed that the pooled MD = 131.8436 minutes, the 95% CI = 99.6540–164.0332, $z = 8.0277$, the p value < 0.0001. The hetero-

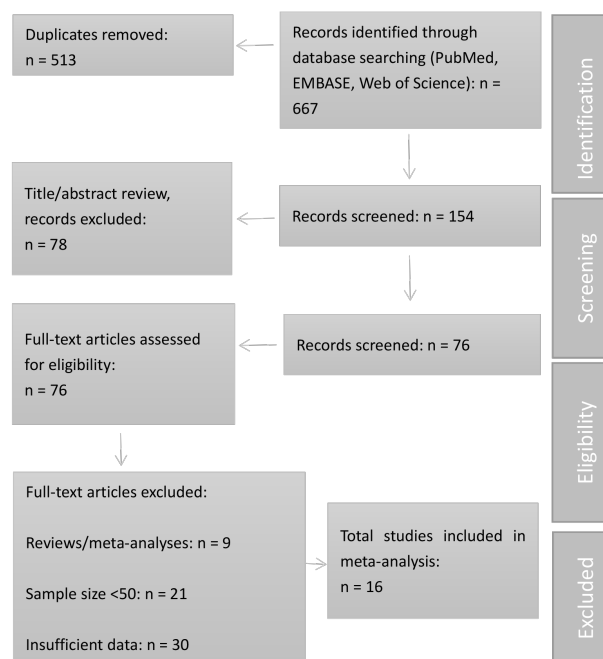


Fig. 1. Flow diagram for study identification and inclusion.

geneity was moderate, $\tau^2 = 841.4662$, $\tau = 29.0080$, $I^2 = 42.63\%$, $H^2 = 1.74$, $Q = 11.1638$, $df = 7$, and $p = 0.1316$. This finding indicated some variation between the studies but not sufficient to reject the null hypothesis of homogeneity ($p > 0.05$). The funnel plot showed a roughly inverted funnel shape, with a symmetrical distribution of studies on both sides (Fig. 2B).

Meta-Analysis of Procedural Time for General Anesthesia and Conscious/Analgosedation Groups

A meta-analysis of seven studies was conducted to compare the procedural time of catheter ablation of AF between the general anesthesia (control) group and the conscious sedation/analgosedation/local anesthesia (test) groups. The total numbers of patients in the control and test groups were 730 and 752, respectively. The mean and standard deviation of the procedural time for each study and each group were entered as input data. The results showed that the pooled MD = -8.1479 minutes, the 95% CI $[-27.6836; -11.3878]$, $z = -0.82$, and $p = 0.41$ under the random-effect model. This finding indicated no significant difference between the control and test groups in procedural time across all studies ($p > 0.05$).

The heterogeneity was high, $\tau^2 = 636.565$, $\tau = 25.2302$, $I^2 = 94\%$, $H^2 = 1.74$, $Q = 105.80$, the degree of freedom was 6, indicating considerably variation in procedural time between the studies (shown in Fig. 3A).

The meta-analysis used three graphical and statistical tools to assess the presence of publication bias or other sources of heterogeneity among the studies: funnel plot, Begg's rank correlation test, and Egger's linear regression

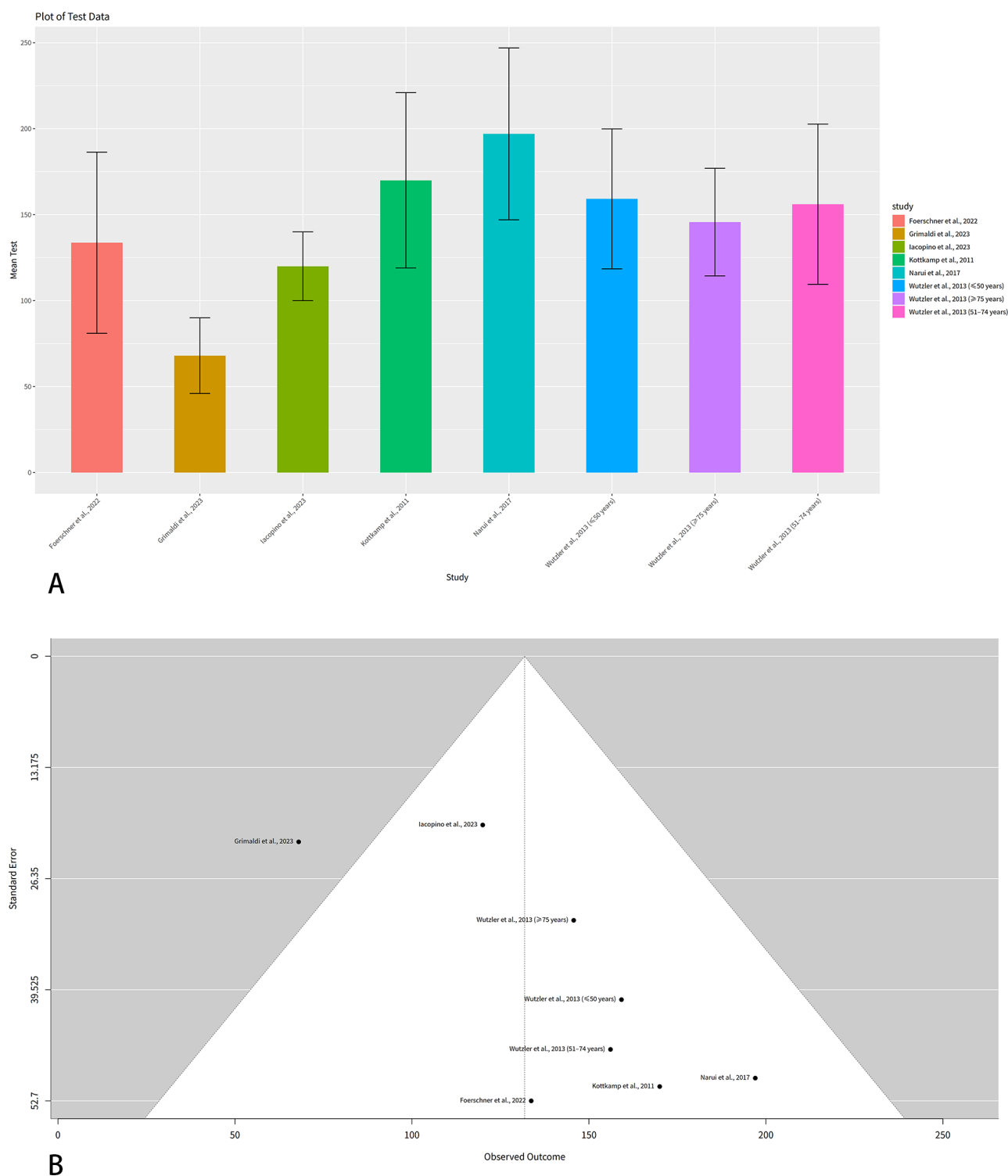


Fig. 2. Illustrations of procedural time plot and funnel plot. (A) Plot of procedural time (in minutes). (B) Funnel plot of procedural time (in minutes).

test. The funnel plot in Fig. 3B shows that the studies are roughly distributed in an inverted funnel shape, with a symmetrical pattern on both sides. This finding suggested no significant publication bias nor heterogeneity among the

studies. The Begg's rank correlation test in Fig. 3C shows that $z = -0.75$ and $p = 0.45$, indicating no significant correlation between the effect size and its variance rank, hence no publication bias nor heterogeneity. The Egger's linear

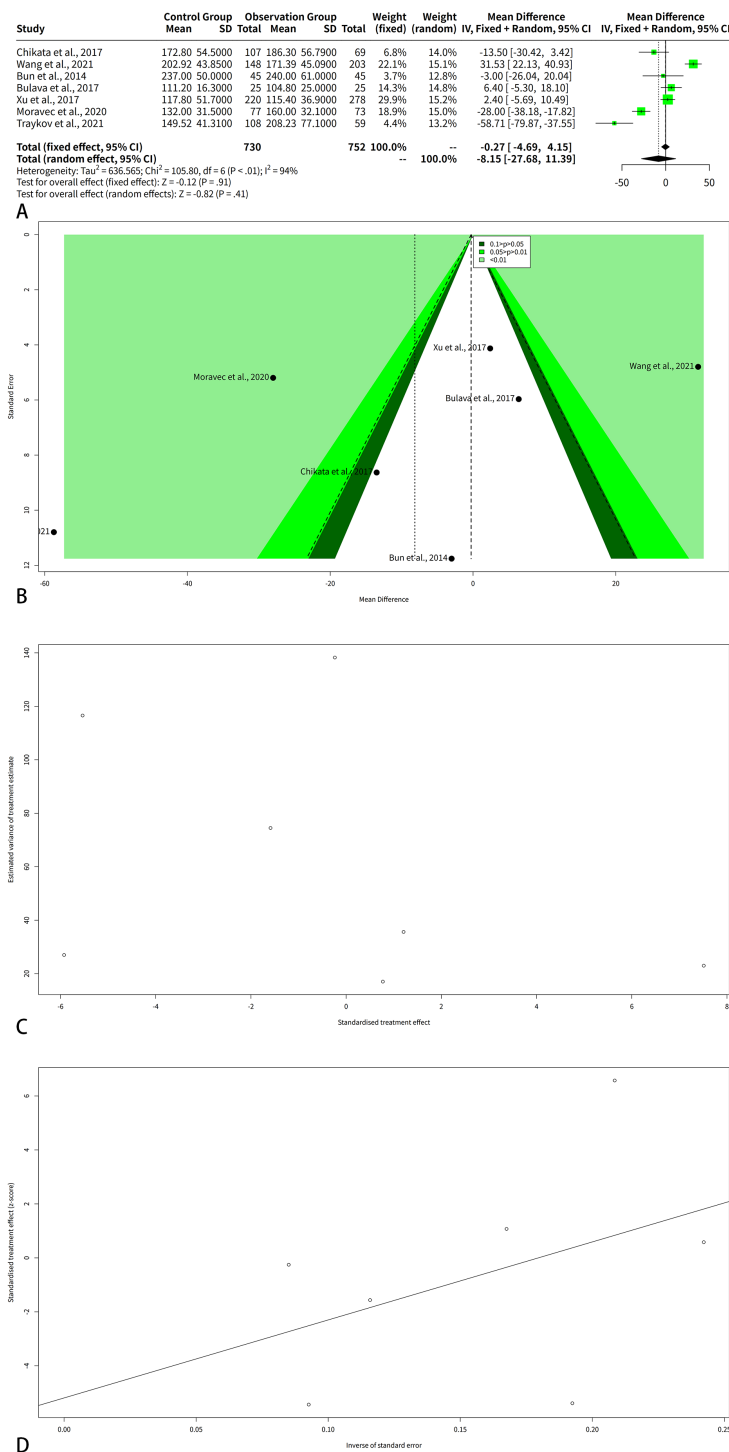


Fig. 3. Comparing procedural time under different sedation methods. (A) Forest plot of mean difference in procedural time between general anesthesia and deep sedation groups. (B) Funnel plot of effect estimates and standard errors for procedural time. (C) Begg's test for funnel plot asymmetry. (D) Egger's test for funnel plot asymmetry. SD, Standard Deviation; CI, Confidence Interval; IV, inverse-variance weighting.

regression test in Fig. 3D shows that $t = -1.13$, $df = 5$, and $p = 0.31$, indicating that the intercept was not significantly different from zero, which implied no publication bias.

The influence analysis results, presented in Table 2 (Ref. [15–19,26]) and corresponding to Fig. 4B, provide

insights into the effect of individual studies on the meta-analysis of procedural time for the two groups. The results showed that four studies had negative r student values, indicating lower effect sizes than the pooled effect size, and three studies had positive r student values, indicating higher

Table 1. Summary of included studies.

Study	Region	Study type	Sample size	Mean age	Anesthesia strategy
Chikata <i>et al.</i> [15], 2017	Japan	Retrospective study	176	66.2	General anesthesia Conscious sedation
Wang <i>et al.</i> [16], 2021	China	Retrospective study	351	62.4	General anesthesia Conscious sedation
Xu <i>et al.</i> [17], 2017	China	Retrospective study	498	60.6	General anesthesia Conscious sedation
Moravec <i>et al.</i> [18], 2021	Czech	RCT	150	56.6	General anesthesia Conscious sedation
Traykov <i>et al.</i> [19], 2021	Bulgaria	Retrospective study	167	57.5	General anesthesia Conscious sedation
Wutzler <i>et al.</i> [13], 2013	Germany	Retrospective study	316	59.0	Deep sedation
Grimaldi <i>et al.</i> [12], 2022	USA	Retrospective study	401	61.4	Deep sedation
Iacopino <i>et al.</i> [20], 2023	Italy	Retrospective study	29	55.0	Deep sedation
Kottkamp <i>et al.</i> [21], 2011	Greece	Retrospective study	650	60.0	Deep sedation
Foerschner <i>et al.</i> [22], 2022	Germany	Retrospective study	3211	65.8	Deep sedation
Narui <i>et al.</i> [23], 2017	Japan	Retrospective study	255	56.5	Deep sedation Conscious sedation
Bun <i>et al.</i> [24], 2015	Monaco	Retrospective study	90	60.5	General anesthesia Local anesthesia
Martin <i>et al.</i> [25], 2018	UK	Retrospective study	292	59.2	General anesthesia Conscious sedation
Hama <i>et al.</i> [26], 2017	Japan	Retrospective study	389	67.0	General anesthesia Conscious sedation Deep sedation
Stašková <i>et al.</i> [27], 2017	Czech	RCT	50	59.8	General anesthesia Conscious sedation

RCT, randomized controlled trial.

Table 2. Influence diagnostics of procedural time for general anesthesia and deep sedation groups.

Study	Labels	rstudent	dffits	cook.d	cov.r	QE.del	hat	weight	infl
Chikata <i>et al.</i> , 2017 [15]	CS versus GA	-6.692	-2.317	5.370	1.120	256.646	0.107	10.709	*
Wang <i>et al.</i> , 2021 [16]	CS versus GA.1	2.227	0.781	0.609	1.123	296.465	0.109	10.941	*
Hama <i>et al.</i> , 2017 [26]	AS versus GA	-5.295	-1.378	1.898	1.068	273.384	0.063	6.340	*
Xu <i>et al.</i> , 2017 [17]	CS versus GA.2	15.674	13.444	180.74	1.736	55.763	0.424	42.387	*
Moravec <i>et al.</i> , 2021 [18]	CS versus GA.3	-5.774	-2.294	5.264	1.158	268.086	0.136	13.637	*
Traykov <i>et al.</i> , 2021 [19]	CS versus GA.4	-7.402	-2.921	8.531	1.156	246.640	0.135	13.474	*

Abbreviation: rstudent, studentized residual, measuring the effect of omitting a specific study on the overall results; dffits, DFFITS statistic, assessing the influence of individual studies on the overall fit; cook.d, Cook's distance, evaluating the influence of each study on the model; cov.r, The covariance ratio, comparing the covariance matrix with and without the specific study; QE.del, change in Q statistic when the study is omitted; hat, Hat value, assessing the leverage of individual studies; infl, influence statistic, providing an overall assessment of the study's effect; CS, conscious sedation; GA, general anesthesia; AS, analgo-sedation. *: It indicates that the impact of the study's results on the overall outcome is significant.

Table 3. Leave-one-out analysis (sorted by I^2) of procedural time for general anesthesia and deep sedation groups.

Study	Labels	Effect	LLCI	ULCI	I^2
Xu <i>et al.</i> , 2017 [17]	CS versus GA.2	47.619	33.072	62.166	0.910
Traykov <i>et al.</i> , 2021 [19]	CS versus GA.4	139.812	127.941	151.682	0.980
Chikata <i>et al.</i> , 2017 [15]	CS versus GA	136.412	124.727	148.097	0.981
Moravec <i>et al.</i> , 2021 [18]	CS versus GA.3	136.283	124.401	148.164	0.981
Hama <i>et al.</i> , 2017 [26]	AS versus GA	131.119	119.709	142.528	0.982
Wang <i>et al.</i> , 2021 [16]	CS versus GA.1	118.960	107.259	130.660	0.983
Bun <i>et al.</i> , 2015 [24]	LA versus GA	126.664	115.481	137.847	0.983

Abbreviation: LA, local anesthetics. LLCI stands for the lower limit of the confidence interval. It is the lower bound of the confidence interval for the pooled effect size. ULCI stands for the upper limit of the confidence interval. It is the upper bound of the confidence interval for the pooled effect size. I^2 stands for heterogeneity index.

effect sizes than the pooled effect size. The results also showed that six studies had large absolute values of dffits and cook.d, suggesting their large effect on the pooled effect size and its CI, and one study had small absolute values of dffits and cook.d, indicating its small effect on the pooled effect size and its CI. Meanwhile, six studies had infl flags,

indicating that they are influential according to some criteria. The study of Bun *et al.* [24], 2015 did not show any infl flag, indicating that it is not influential according to some criteria.

Leave-one-out analysis was conducted to assess the influence of each study on the pooled effect size and hetero-

Table 4. Baujat diagnostics (sorted by heterogeneity contribution) of procedural time for general anesthesia and deep sedation groups.

Study	Labels	HetContrib	InfluenceEffectSize
Xu <i>et al.</i> , 2017 [17]	CS versus GA.2	141.532	104.129
Traykov <i>et al.</i> , 2021 [19]	CS versus GA.4	47.402	7.381
Chikata <i>et al.</i> , 2017 [15]	CS versus GA	39.983	4.795
Moravec <i>et al.</i> , 2021 [18]	CS versus GA.3	28.792	4.546
Hama <i>et al.</i> , 2017 [26]	AS versus GA	26.262	1.778
Bun <i>et al.</i> , 2015 [24]	LA versus GA	13.037	0.336
Wang <i>et al.</i> , 2021 [16]	CS versus GA.1	4.416	0.543

Abbreviation: HetContrib stands for heterogeneity contribution. It is a measure of the extent to which a study contributes to the overall heterogeneity in a meta-analysis. InfluenceEffectSize stands for influence effect size. It is a measure of the extent to which a study affects the pooled effect size in a meta-analysis.

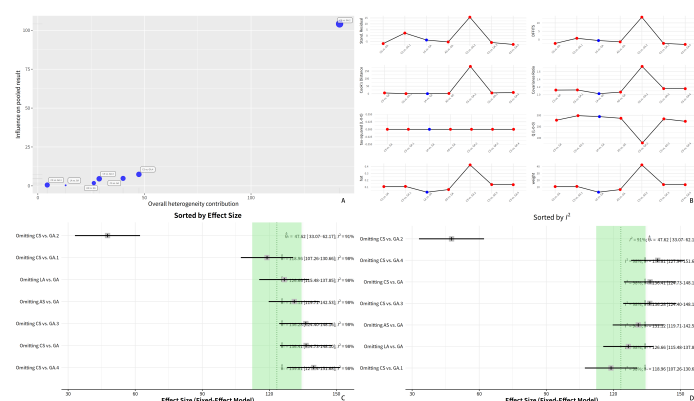


Fig. 4. Insights into influence, leave-one-out analysis, effect size, and heterogeneity. (A) Leave-one-out analysis results. (B) Influence analysis results. (C) Baujat diagnostics for effect size. (D) Baujat diagnostics for heterogeneity.

genicity of the meta-analysis, as shown in Table 3 (Ref. [15–19,24,26]) and Fig. 4A. The results showed that the pooled effect size and its CI varied depending on which study was excluded. The effect size ranged from 47.619 minutes to 139.812 minutes, and the CI ranged from 28.094 minutes to 23.741 minutes. The heterogeneity among the remaining studies similarly varied depending on which study was excluded. The heterogeneity index (I^2) ranged from 0.910 to 0.983, indicating high to very high heterogeneity. The study by Xu *et al.* [17], 2017 had the lowest effect size and the lowest heterogeneity when excluded, suggesting its large influence on the overall results and contribution to the heterogeneity among the studies. The study by Traykov *et al.* [19], 2021 had the highest effect size and the second highest heterogeneity when excluded, suggesting its large influence on the overall results and contribution to the heterogeneity among the studies.

Baujat diagnostics was performed to assess the influence of each study on the heterogeneity and the effect size of the meta-analysis, as shown in Table 4 (Ref. [15–19,24,26]) and Fig. 4C (sorted by effect size) and Fig. 4D (sorted by heterogeneity). The study by Xu *et al.* [17], 2017 had the highest heterogeneity contribution and the highest influence

effect size, indicating its largest effect on the heterogeneity and pooled effect size in the meta-analysis. The study by Traykov *et al.* [19], 2021 had the second-highest heterogeneity contribution and the third-highest influence effect size, suggesting its large effect on the heterogeneity and pooled effect size. The studies by Chikata *et al.* [15], 2017 and Moravec *et al.* [18], 2021 demonstrated moderate heterogeneity contributions and influence effect sizes, indicating some effect on the heterogeneity and pooled effect size. The studies by Hama *et al.* [26], 2017, Bun *et al.* [24], 2015, and Wang *et al.* [16], 2021 exhibited low heterogeneity contributions and influence effect sizes, indicating their slight effect on the heterogeneity and pooled effect size in the meta-analysis.

We performed a p -curve analysis to assess the evidential value and statistical power of the meta-analysis as shown in Fig. 5A shows the summary statistics of the p -curve analysis. The total number of studies provided for the meta-analysis was seven, but only three of them were statistically significant ($p < 0.05$) and included in the p -curve analysis. The right-skewness test had a p Binomial = 0.125, which means that the proportion of studies with $p < 0.025$ was not significantly higher than expected by

chance ($p > 0.05$). The right-skewness test had a $z_{Full} = -9.604$ and a $p_{Full} = 0$, indicating that the distribution of p -values was significantly right skewed ($p < 0.001$). The right-skewness test had a $z_{Half} = -9.223$ and a $p_{Half} = 0$, suggesting that the distribution of half p -values was significantly right skewed ($p < 0.001$). These results demonstrated the evidential value present in the studies, meaning that they were not likely to be false positives or due to selective reporting. The flatness test had a $p_{Binomial} = 1.000$, indicating that the proportion of studies with $p < 0.025$ was not significantly lower than expected by chance ($p > 0.05$). The flatness test had a $z_{Full} = 9.346$ and a $p_{Full} = 1$, demonstrating that the distribution of p -values was not significantly different from flat ($p > 0.05$). The flatness test had a $z_{Half} = 9.744$ and a $p_{Half} = 1$, exhibiting that the distribution of half p -values was not significantly different from flat ($p > 0.05$). These results indicated inadequate or no evidential value in the studies, meaning that they were not likely to be underpowered or due to p -hacking. The power estimate was 99%, indicating that the studies had a high probability of detecting a true effect if it exists.

GOSH diagnostics was performed to assess the heterogeneity and clustering of the studies in the meta-analysis. The results are shown in Fig. 5B for the K-means model, Fig. 5C for the DBSCAN model, and Fig. 5D for the Gaussian mixture model. The K-means, DBSCAN, and GMM algorithms identified two potential outliers: Xu *et al.* [17], 2017 and Wang *et al.* [16], 2021. They also identified two potential outliers: Study 2 (Wang *et al.* [16], 2021) and Study 5 (Xu *et al.* [17], 2017). These results indicated that some studies had more heterogeneity and influence than the others on the meta-analysis results and that removing them may change the pooled effect size and its CI remarkable.

The studies were divided into three subgroups on the basis of comparison among general anesthesia (GA), conscious sedation (CS), local anesthesia (LA), and analgo-sedation (AS). The results showed that in the CS versus GA subgroup, the pooled MD = -12.3103 minutes, the 95% CI [-38.6095; -13.9889], $Q = 104.33$, and $I^2 = 96\%$. This finding demonstrated no significant difference between the CS and GA groups in procedural time across the five studies ($p > 0.05$), but a very high heterogeneity was present among the studies. Therefore, different methods of sedation or anesthesia for catheter ablation of AF had similar effects on procedural time, but variation was found among the studies that compared CS and GA (shown in Fig. 6A).

The studies were divided into two subgroups on the basis of whether they were outliers or non-outliers according to GOSH diagnostics. The results showed that in the non-outlier subgroup, the pooled MD was -18.9129 minutes, the 95% CI [-39.4534; -1.6277], $Q = 36.34$, and $I^2 = 89\%$. This finding indicated a marginally significant difference between the groups in procedural time across the five studies ($p = 0.06$) and a high heterogeneity among the studies. In the outlier subgroup, the pooled MD was 16.8627

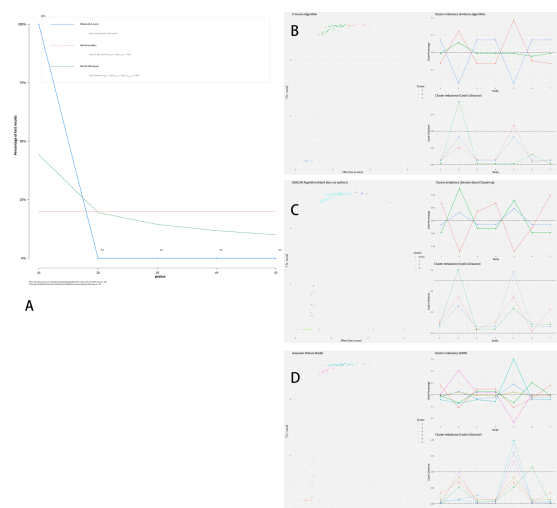


Fig. 5. P-curve analysis and GOSH diagnostics with K-means, DBSCAN, and Gaussian mixture models. (A) P-curve analysis. (B) GOSH Diagnostics - K-means Model. (C) GOSH Diagnostics - DBSCAN Model. (D) GOSH Diagnostics - Gaussian Mixture Model.

minutes, the 95% CI [-11.6835; -45.4089], $Q = 21.18$, and $I^2 = 95\%$. This finding demonstrated no significant difference between the groups in procedural time across the two studies ($p > 0.05$) and a very high heterogeneity among the studies. In conclusion, different methods of sedation or anesthesia for catheter ablation of AF had different effects on procedural time depending on whether they were outliers or not, and that variation existed among the studies in both subgroups (shown in Fig. 6B).

Serious Intraprocedural Complications for Deep Sedation for Catheter Ablation of AF

A meta-analysis was conducted on the rate of serious intraprocedural complications for deep sedation for catheter ablation of AF, as shown in Fig. 7A. The meta-analysis included seven studies with a total of 4713 patients, of whom 72 had serious intraprocedural complications. The results showed that the pooled proportion of serious intraprocedural complications for deep sedation was 0.0153, indicating that about 1.5% of the patients had serious intraprocedural complications. The 95% CI of the pooled proportion was [0.0121; 0.0192], indicating a 95% chance that the true proportion of serious intraprocedural complications was between 1.2% and 1.9%. The fixed- and random-effect models showed the same results, suggesting no significant difference between them. The heterogeneity among the studies was very low, as indicated by $\tau^2 = 0$, $\tau = 0$, $I^2 = 0\%$, and $Q = 2.37$ ($p = 0.8826$). Therefore, the studies had similar effect sizes and no evidence of inconsistency nor variation among them was found. The serious intraprocedural complications included cardiac tamponade, severe allergic reaction, coronary air embolism, transient ischemic attack,

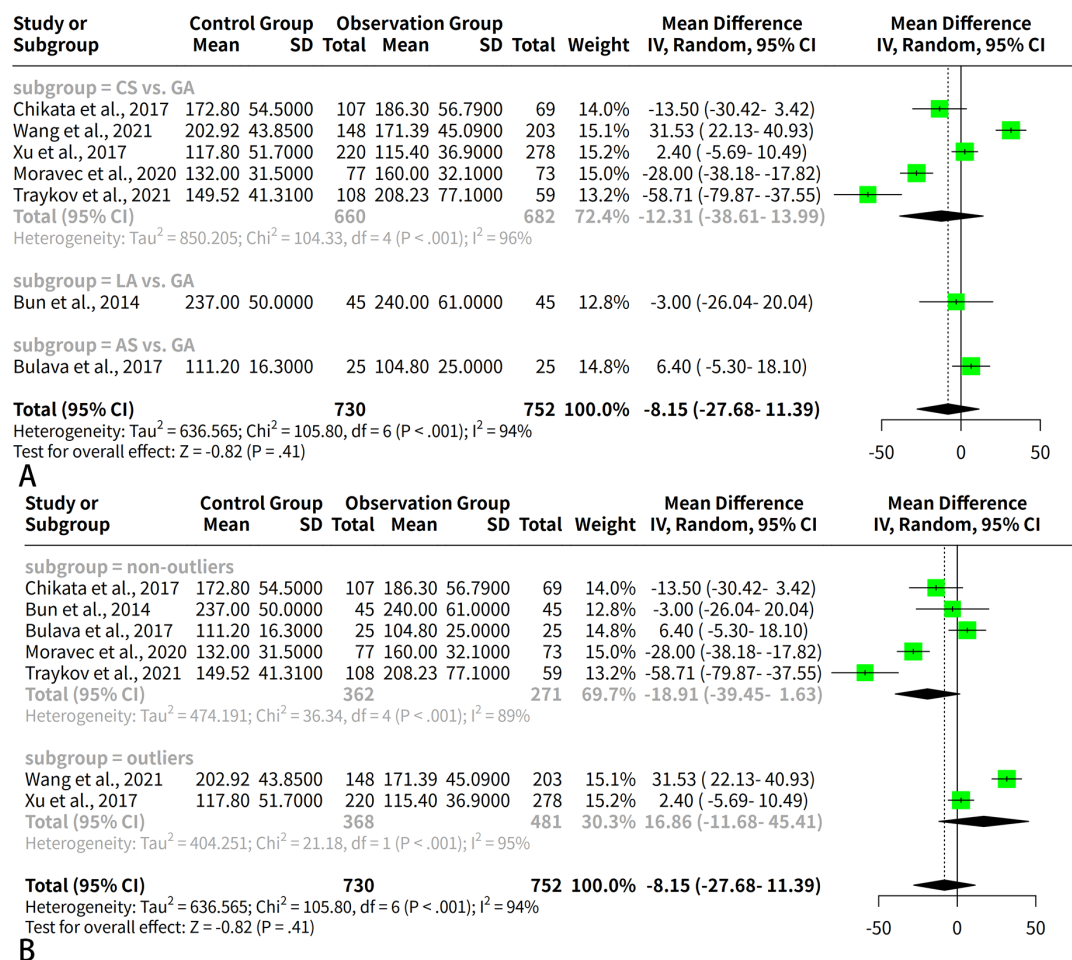


Fig. 6. Subgroup analysis of mean difference in sedation methods. (A) Forest plot of the mean difference between general anesthesia and conscious sedation/analgesedation groups by a subgroup of non-outlier and outlier. (B) Forest plot of the mean difference between general anesthesia and conscious sedation/analgesedation groups by a subgroup of general anesthesia (GA) and conscious sedation (CS), local anesthesia (LA), or analgesedation (AS).

myocardial infarction, pericardial effusion, pericardial tamponade, endotracheal intubation, and noninvasive ventilation. The most common complication was cardiac tamponade, which occurred in six patients in one study. The most severe complication was endotracheal intubation, which occurred in one patient in one study. No procedural complications were documented in one study. The funnel plot in Fig. 7B shows that the studies were roughly distributed in an inverted funnel shape, with a symmetrical pattern on both sides. This finding suggested no significant publication bias nor heterogeneity among the studies.

Meta-Analysis of the Effect of Sedation or Anesthesia Methods on Total Perioperative Complications for Catheter Ablation of AF

A meta-analysis was conducted on the rate of total perioperative complications for conscious/analgesedation and general anesthesia for catheter ablation of AF, as shown in Fig. 8A. The meta-analysis included nine studies with

a total of 2221 patients, of whom 567 had total perioperative complications. The results demonstrated that the fixed-effect model showed a significant difference between the groups in the rate of total perioperative complications across nine studies ($p = 0.0266$). The pooled OR = 1.2622, indicating that the patients who received conscious/analgesedation had 26% higher odds of having total perioperative complications than those who received general anesthesia. The 95% CI of the pooled OR was [1.0273; 1.5507], which indicated a 95% chance that the true OR was between 1.03 and 1.55. The random-effect model showed a marginally significant difference between the groups in the rate of total perioperative complications across the nine studies ($p = 0.0730$). The pooled OR = 1.2887, indicating that the patients who received conscious sedation/analgesedation had 29% higher odds of having total perioperative complications than those who received general anesthesia. The 95% CI of the pooled OR was [0.9766; 1.7006], indicating a 95% chance that the true OR

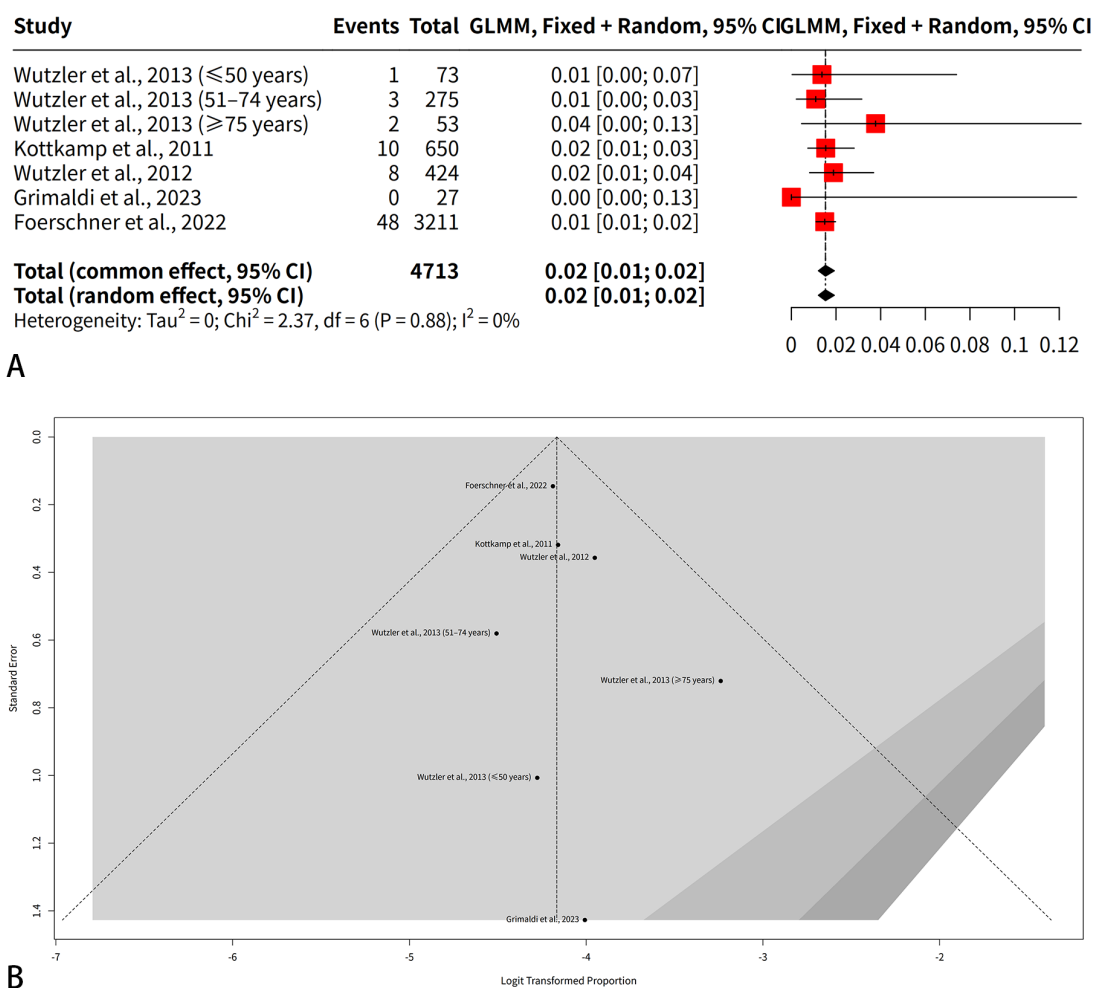


Fig. 7. Adverse events in deep sedation. (A) Forest plot of the pooled proportion of adverse events for deep sedation with fixed- and random-effect models. (B) Funnel plot of the effect size and standard error of the studies included in the meta-analysis. GLMM, Generalized Linear Mixed Model.

was between 0.98 and 1.70. The heterogeneity among the studies was moderate, as indicated by $\tau^2 = 0.0678$, $\tau = 0.2604$, $I^2 = 40.3\%$, and $Q = 13.41$ ($p = 0.0986$). Therefore, the studies had some variation in their effect sizes and some evidence of inconsistency or diversity was observed among them.

The funnel plot in Fig. 8B shows that the studies were roughly distributed in an inverted funnel shape, with a symmetrical pattern on both sides, suggesting no significant publication bias nor heterogeneity among the studies. The studies were mainly concentrated at the top of the inverted funnel, indicating small standard errors and high precision. The studies at the bottom of the inverted funnel had larger standard errors and lower precision, and they were more likely to be affected by random sampling errors or other sources of variation.

Begg's rank correlation test of the funnel plot asymmetry was conducted for the meta-analysis of the effect of different methods of sedation or anesthesia on the procedural time for catheter ablation of AF. The results showed

that the $ks = 1.0000$, indicating a perfect positive correlation between the effect size and its variance. The $ks = 9.5917$, showing a large standard error of the ks value. The z value = 0.10, indicating a very small difference between the observed ks value and the expected ks value under the null hypothesis of no correlation. The $p = 0.9170$, which indicated a very high probability of obtaining the observed ks value or more extreme by chance if the null hypothesis was true. These results exhibited no significant evidence of funnel plot asymmetry nor publication bias among the studies included in the meta-analysis ($p > 0.05$, Fig. 8C).

The meta-analysis used two graphical methods to explore the heterogeneity and influence of the studies included: the Baujat plot (Fig. 8D) and the Galbraith plot (Fig. 8E). The results showed that in the Baujat plot, the study of Martin *et al.* [25], 2018 was located at the top right corner, which indicating that it had a high contribution to heterogeneity and a high influence on the pooled estimate. The study of Martin *et al.* [25], 2018 exhibited the highest $1/SE$ value, indicating its smallest standard error and the

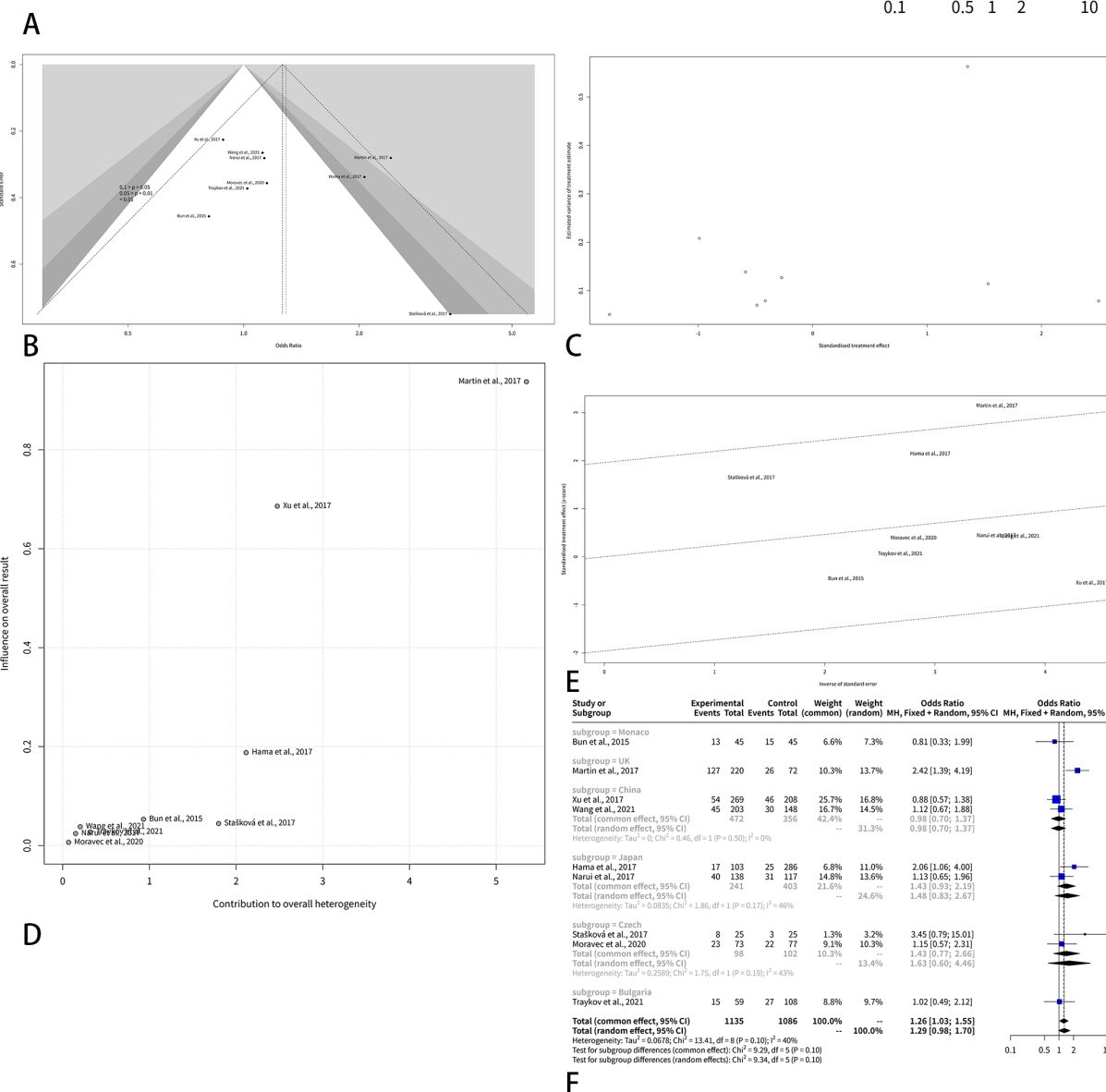
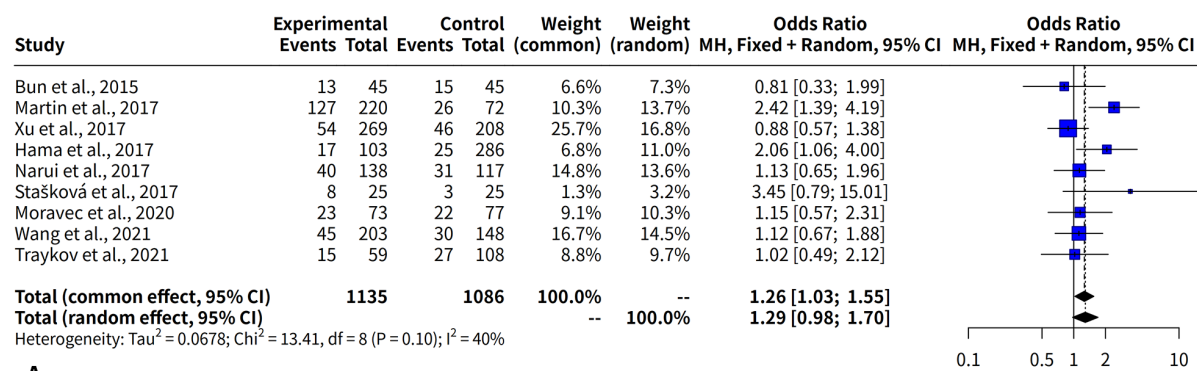


Fig. 8. Comparative analysis of sedation/anesthesia methods and perioperative complications. (A) Forest plot of the odds ratios and 95% confidence intervals for total perioperative complications by sedation or anesthesia methods. (B) Funnel plot of the standard error versus the log odds ratio for total perioperative complications by sedation or anesthesia methods. (C) Begg's rank correlation test for funnel plot asymmetry. (D) Baujat plot of the contribution to heterogeneity and influence on the pooled estimate by study. (E) Galbraith plot of z-statistic versus the standard normal deviate by study. (F) Forest plot of the odds ratios and 95% confidence intervals for total perioperative complications by region/country. MH, Mantel-Haenszel.

highest precision among all studies. In the Galbraith plot, all studies were distributed in four quadrants, suggesting that they had different directions and magnitudes of deviation from the pooled estimate. The study of Martin *et al.* [25], 2018 was located at the upper quadrant, suggesting its positive deviation and large z-statistic. No study was located at the lower quadrant, indicating that no study had a negative deviation and a large z-statistic. The other studies were located in the middle quadrants. Thus, they had either a positive or a negative deviation but a small z-statistic. These results indicated that the study of Martin *et al.* [25], 2018 was an outlier and an influential study in both plots, and that it may have caused some heterogeneity and bias in the meta-analysis. The other studies were more consistent and less influential in both plots.

The meta-analysis results for each subgroup are shown in Fig. 8F, suggesting some variation in the ORs across different regions, but none of them were significantly different from one another or the overall effect size.

Discussion

This meta-analysis compared general anesthesia, deep sedation, and conscious sedation for catheter ablation of AF. The results showed no significant difference in procedural time between the general anesthesia and conscious/analgo sedation groups across seven studies, despite the high heterogeneity ($I^2 = 94\%$). This discovery was substantiated by a study conducted by Stašková *et al.* [27], 2017 in a randomized trial involving 50 patients, revealing no significant difference in procedural time between patients subjected to general anesthesia and those undergoing conscious sedation. The significant heterogeneity observed in the seven studies may be attributed to the varying study designs and the wide range of sample sizes used in each study. Factors, such as gender and the original health status of the patients, may have contributed to this heterogeneity. Deep sedation was associated with longer procedural time than conscious sedation based on eight studies, although the heterogeneity was moderate ($I^2 = 43\%$). This finding contrasts with those of Narui *et al.* [23], 2017, who found no difference in procedural time between deep and conscious sedation groups among 255 patients. The heterogeneity observed in these eight studies was likely a result of the wide variation in sample sizes, with the largest sample size differing from the smallest by nearly a factor of 100. A notable detail that all eight studies were conducted in different regions of the country, and the differences in the level of healthcare provided in each region may have contributed to the observed heterogeneity. The rate of serious intraprocedural complications with deep sedation was 1.5% based on seven studies, consistent with prior reports of major complication rates around 1%–3%. Conscious sedation/analgo sedation had 26%–29% higher

odds of perioperative complications than general anesthesia across nine studies, although the heterogeneity was moderate ($I^2 = 40\%$). This finding contrasts with those of Wutzler *et al.* [13], 2013, who found no difference in complication rates between deep sedation and general anesthesia groups among 316 ablation procedures. In these nine studies, where the differences in sample size were relatively small, a noticeable reduction in heterogeneity was observed. However, the remaining heterogeneity in the study results may have arisen from differences in study design, variations in participant age, and variances in the level of healthcare across the countries/regions where the studies were conducted.

Deep sedation may lead to longer operative times due to increased monitoring and regulation requirements, possibly attributed to the effects of anesthetic drugs and stricter control over the patient's physiological state [28]. By contrast, conscious sedation showed no significant difference compared with general anesthesia, likely because it still offers sufficient sedation and comfort while avoiding additional risks and costs associated with general anesthesia [29]. However, conscious sedation is linked to a higher risk of postoperative complications, possibly attributed to its unique characteristics such as increased psychological stress from the patient's awareness during the procedure and a heightened vulnerability to postoperative side effects of sedatives [30].

The limitations of this meta-analysis should be acknowledged. First, the significant heterogeneity observed in some of the outcomes, particularly procedural time and complication rates, may have introduced uncertainty into the findings. This heterogeneity may have arisen from variations in patient populations, ablation techniques, and operator expertise across the included studies. Second, most studies in this meta-analysis were retrospective, which could introduce selection bias and potential confounding variables that were not controlled for. Third, publication bias may be a concern, because studies with negative or null findings may be less likely to be published. Additionally, the relatively small sample sizes in some of the included studies may limit the generalizability of the findings to broader populations. Ultimately, as a result of the variability in the description of relevant study characteristics within the original articles, challenges in effectively distilling these attributes as grouping variables were encountered. This inconsistency in the content of the original articles limited the utilization of these characteristics for the purpose of grouping variables in the analysis.

Despite these limitations, this meta-analysis provides valuable insights into the comparative effectiveness of different sedation methods for catheter ablation of AF. However, caution should be exercised when interpreting and applying these findings in clinical practice, and individual patient factors and local expertise should continue to guide sedation or anesthesia choices for these procedures. Future

well-designed prospective studies with larger sample sizes and standardized protocols are warranted to further elucidate these issues and refine our understanding of the optimal sedation approach for AF ablation.

Conclusions

This meta-analysis found no significant difference in procedural time between general anesthesia and conscious sedation for AF ablation. However, deep sedation was associated with longer procedural time. The rate of complications was low with deep sedation. Conscious sedation had a higher risk of perioperative complications than general anesthesia. Significant heterogeneity was observed among the studies. Additional randomized controlled trials are warranted to clarify the optimal anesthesia strategy during AF ablation.

Availability of Data and Materials

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding authors.

Author Contributions

TY: conception, design, materials, data collection, analysis, literature review, and writing. YF: design, materials, data collection, analysis, literature review, and writing. JS: supervision, materials, data collection, analysis, literature review, and writing. QW: materials, data collection, analysis, literature review, and writing. TW: supervision, materials, data collection, analysis, writing, and critical review. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.59958/hsf.7153>.

References

- [1] Penela D, Cappato R. How effective is cryoablation in the treatment of atrial fibrillation? *European Heart Journal Supplements*. 2021; 23: E51–E54.
- [2] Gorantla A, Alsaqali M, Francois J, Sivakumar S, Freytes-Santiago L, Jallad A, *et al*. Comparative Effectiveness of Various Radiofrequency Ablation Catheters in the Ablation of Typical Atrial Flutter. *Cardiology and Therapy*. 2023; 12: 741–747.
- [3] Andrade JG, Khairy P, Dubuc M. Catheter cryoablation: biology and clinical uses. *Circulation. Arrhythmia and Electrophysiology*. 2013; 6: 218–227.
- [4] Yu K, Yamashita T, Shingyochi S, Matsumoto K, Ohta M. Radiofrequency ablation with a vibrating catheter: A new method for electrode cooling. *Medical Engineering & Physics*. 2016; 38: 458–467.
- [5] Eick OJ. Factors influencing lesion formation during radiofrequency catheter ablation. *Indian Pacing and Electrophysiology Journal*. 2003; 3: 117–128.
- [6] Zambouri A. Preoperative evaluation and preparation for anesthesia and surgery. *Hippokratia*. 2007; 11: 13–21.
- [7] Zhao J, Tan X, Wu X, Li J, Wang S, Qu R, *et al*. The efficacy and safety of general anesthesia vs. conscious sedation for endovascular treatment in patients with acute ischemic stroke: a systematic review and meta-analysis. *Frontiers in Neurology*. 2023; 14: 1291730.
- [8] Dobson G, Chow L, Filteau L, Hurdle H, McIntyre I, Milne A, *et al*. Guidelines to the Practice of Anesthesia - Revised Edition 2021. *Canadian Journal of Anaesthesia*. 2021; 68: 92–129.
- [9] Hara T, Ozawa A, Shibutani K, Tsujino K, Miyauchi Y, Kawano T, *et al*. Practical guide for safe sedation. *Journal of Anesthesia*. 2023; 37: 340–356.
- [10] Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018: A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. *Anesthesiology*. 2018; 128: 437–479.
- [11] Pang N, Gao J, Zhang N, Zhang B, Wang R. Comparison of the Different Anesthesia Strategies for Atrial Fibrillation Catheter Ablation: A Systematic Review and Meta-Analysis. *Cardiology Research and Practice*. 2022; 2022: 1124372.
- [12] Grimaldi M, Di Monaco A, Gomez T, Berman D, Datta K,

- Sharma T, *et al.* Time Course of Irreversible Electroporation Lesion Development Through Short- and Long-Term Follow-Up in Pulsed-Field Ablation-Treated Hearts. *Circulation. Arrhythmia and Electrophysiology*. 2022; 15: e010661.
- [13] Wutzler A, Loehr L, Huemer M, Parwani AS, Steinhagen-Thiessen E, Boldt LH, *et al.* Deep sedation during catheter ablation for atrial fibrillation in elderly patients. *Journal of Interventional Cardiac Electrophysiology*. 2013; 38: 115–121.
- [14] Lortie CJ, Filazzola A. A contrast of meta and metafor packages for meta-analyses in R. *Ecology and Evolution*. 2020; 10: 10916–10921.
- [15] Chikata A, Kato T, Yaegashi T, Sakagami S, Kato C, Saeki T, *et al.* General anesthesia improves contact force and reduces gap formation in pulmonary vein isolation: a comparison with conscious sedation. *Heart and Vessels*. 2017; 32: 997–1005.
- [16] Wang Z, Jia L, Shi T, Liu C. General anesthesia is not superior to sedation in clinical outcome and cost-effectiveness for ablation of persistent atrial fibrillation. *Clinical Cardiology*. 2021; 44: 218–221.
- [17] Xu JJ, Gao LJ, Chang D, Xiao XJ, Zhang RF, Lin J, *et al.* Clinical characteristics and outcome comparison between atrial fibrillation patients underwent catheter ablation under general anesthesia or local anesthesia and sedation. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2017; 24: 935–939. (In Chinese)
- [18] Moravec O, Skala T, Klementova O, Skalova J, Hutyra M, Precek J, *et al.* General anesthesia or conscious sedation in paroxysmal atrial fibrillation catheter ablation. *Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc, Czechoslovakia*. 2021; 165: 162–168.
- [19] Traykov V, Marchov D, Marinov M, Boychev D, Gelev V. General anaesthesia during radiofrequency ablation of atrial fibrillation is associated with improved procedural characteristics but with similar long-term outcomes: a single center study. *EP Europace*. 2021; 23: euab116.243.
- [20] Iacopino S, Colella J, Dini D, Mantovani L, Sorrenti PF, Malacrida M, *et al.* Sedation strategies for pulsed-field ablation of atrial fibrillation: focus on deep sedation with intravenous ketamine in spontaneous respiration. *EP Europace*. 2023; 25: euad230.
- [21] Kottkamp H, Hindricks G, Eitel C, Müller K, Siedziako A, Koch J, *et al.* Deep sedation for catheter ablation of atrial fibrillation: a prospective study in 650 consecutive patients. *Journal of Cardiovascular Electrophysiology*. 2011; 22: 1339–1343.
- [22] Foerschner L, Harfoush N, Thoma M, Spitzbauer L, Popa M, Bourier F, *et al.* Deep sedation with propofol in patients undergoing left atrial ablation procedures-Is it safe? *Heart Rhythm O2*. 2022; 3: 288–294.
- [23] Narui R, Matsuo S, Isogai R, Tokutake K, Yokoyama K, Kato M, *et al.* Impact of deep sedation on the electrophysiological behavior of pulmonary vein and non-PV firing during catheter ablation for atrial fibrillation. *Journal of Interventional Cardiac Electrophysiology*. 2017; 49: 51–57.
- [24] Bun SS, Latcu DG, Allouche E, Errahmouni A, Saoudi N. General anesthesia is not superior to local anesthesia for remote magnetic ablation of atrial fibrillation. *Pacing and Clinical Electrophysiology*. 2015; 38: 391–397.
- [25] Martin CA, Curtain JP, Gajendragadkar PR, Begley DA, Fynn SP, Grace AA, *et al.* Improved outcome and cost effectiveness in ablation of persistent atrial fibrillation under general anaesthetic. *Europace*. 2018; 20: 935–942.
- [26] Hama Y, Ishimura M, Yamamoto M, Himi T. P313 General anesthesia improves the success rate of catheter ablation of paroxysmal atrial fibrillation. *EP Europace*. 2017; 19.
- [27] Stašková K, Bulava A, Tesařík R, Toušek F. Radiofrequency catheter ablation of atrial fibrillation performed under general anesthesia: results of a unicentric randomized trial. *Vnitřní Lekarství*. 2017; 63: 163–169. (In Czech)
- [28] Braga A, Martins S, Ferreira AR, Fernandes J, Vieira T, Fontes L, *et al.* Influence of Deep Sedation in Intensive Care Medicine Memories of Critical COVID-19 Survivors. *Journal of Intensive Care Medicine*. 2023; 38: 657–667.
- [29] Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, *et al.* General Anesthesia Versus Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke: The AnStroke Trial (Anesthesia During Stroke). *Stroke*. 2017; 48: 1601–1607.
- [30] Kent CD, Mashour GA, Metzger NA, Posner KL, Domino KB. Psychological impact of unexpected explicit recall of events occurring during surgery performed under sedation, regional anaesthesia, and general anaesthesia: data from the Anesthesia Awareness Registry. *British Journal of Anaesthesia*. 2013; 110: 381–387.