

Ethanol Infusion into the Vein of Marshall Enhances Mitral Isthmus Block and Reduces Atrial Fibrillation Recurrence: A Comprehensive Meta- Analysis

Marshall Toplardamarına Etanol İnfüzyonu Mitral İstmus
Blokajını Artırır ve Atriyal Fibrilasyon Nüksünü Azaltır:
Kapsamlı Bir Meta-Analiz

ABSTRACT

Adjunctive vein of Marshall ethanol infusion (EIVOM) during atrial fibrillation (AF) ablation has emerged as a promising technique with the potential to significantly improve procedural outcomes. Despite the existing body of evidence, a comprehensive evaluation focusing on mitral isthmus block, AF recurrence, and procedural duration has not yet been conducted. This meta-analysis aims to rigorously assess the benefits of EIVOM combined with radiofrequency ablation (EIVOM-RF) compared with radiofrequency ablation alone (RF-only) in patients undergoing catheter ablation for AF or related arrhythmias. We systematically reviewed both randomized controlled trials and observational studies that compared EIVOM-RF with RF-only approaches, encompassing a total of 1,406 patients in the EIVOM-RF group and 1,849 in the RF-only group. The primary outcomes assessed included the rate of successful mitral isthmus ablation, recurrence of atrial arrhythmias, and overall procedure time. Patients treated with EIVOM-RF demonstrated a significantly lower likelihood of atrial arrhythmia recurrence compared to those receiving RF-only treatment. Furthermore, EIVOM-RF was associated with an impressive increase in the success rate of achieving mitral isthmus block. While total procedure time tended to be longer with EIVOM-RF, this difference was statistically significant and showed considerable variability. These findings compellingly indicate that EIVOM enhances procedural efficacy, albeit at the cost of increased procedural duration. In conclusion, EIVOM combined with RF ablation represents a transformative approach that markedly improves procedural success rates and significantly reduces arrhythmia recurrence in patients undergoing ablation for AF.

Keywords: Atrial fibrillation, catheter ablation, ethanol infusion, meta-analysis, mitral isthmus block, recurrence, vein of Marshall

ÖZET

Atriyal fibrilasyon (AF) ablasyonu sırasında ek olarak Marshall toplardamarına etanol infüzyonu, prosedür sonuçlarını önemli ölçüde iyileştirme potansiyeli olan umut verici bir teknik olarak ortaya çıkmıştır. Mevcut kanıtlara rağmen, mitral istmus bloğu, AF nüksü ve prosedür süresine odaklanan kapsamlı bir değerlendirme henüz yapılmamıştır. Bu meta-analiz, AF veya ilgili aritmiler için kateter ablasyonu geçiren hastalarda, radyofrekans ablasyonu (sadece RF) ile karşılaştırıldığında, radyofrekans ablasyonu ile kombine EIVOM'un (EIVOM-RF) faydalarını titizlikle değerlendirmeyi amaçlamaktadır. EIVOM-RF ile sadece RF yaklaşımlarını karşılaştıran randomize kontrollü çalışmalar ve gözlemsel çalışmaları sistematik olarak inceledik; EIVOM-RF grubunda toplam 1.406 hasta, sadece RF grubunda ise 1.849 hasta yer almaktaydı. Değerlendirilen birincil sonuçlar arasında başarılı mitral istmus ablasyon oranı, atriyal aritmilerin nüks etme oranı ve toplam prosedür süresi yer almaktaydı. EIVOM-RF ile tedavi edilen hastalar, sadece RF tedavisi alanlara kıyasla atriyal aritmi nüksü yaşama olasılığının önemli ölçüde daha düşük olduğunu göstermiştir. Ayrıca, EIVOM-RF, mitral istmus blokajının başarı oranında etkileyici bir artışla ilişkilendirilmiştir. EIVOM-RF ile toplam işlem süresi daha uzun olma eğilimindedir, bu fark istatistiksel olarak anlamlıdır ve belirgin değişkenlik göstermiştir. Bu bulgular, EIVOM'un işlem süresini arttırmasına rağmen işlem etkinliğini arttırdığını kesin olarak göstermektedir. Sonuç olarak, RF ablasyon ile birlikte uygulanan EIVOM, AF için ablasyon uygulanan hastalarda işlem başarı oranlarını belirgin şekilde arttıran ve aritmi nüksünü önemli ölçüde azaltan dönüşüme neden olacak bir yaklaşımdır.

Anahtar Kelimeler: Atriyal fibrilasyon, kateter ablasyonu, etanol infüzyonu, meta-analiz, mitral istmus bloğu, nüks, Marshall veni

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Atrial fibrillation (AF) is the most prevalent sustained arrhythmia encountered in clinical practice and is associated with substantial morbidity, including increased risks of stroke, heart failure, and reduced quality of life. Catheter ablation (CA), particularly through pulmonary vein isolation (PVI), is a well-established treatment for AF, especially in its paroxysmal form.¹ However, its efficacy in managing persistent and long-standing AF is often inadequate, primarily due to the intricate substrate and challenges in achieving lasting linear lesions, especially across the mitral isthmus (MI).² The vein of Marshall (VOM)—a vestigial structure involved in arrhythmogenic conduction and autonomic modulation—has emerged as an innovative therapeutic target with the potential to enhance ablation strategies.

Recent investigations have highlighted the use of ethanol infusion into the vein of Marshall (EIVOM) as a powerful adjunct to CA.³ This approach aims to achieve robust mitral isthmus block, suppress arrhythmogenic activity, and facilitate autonomic denervation, ultimately improving long-term rhythm outcomes. Initial observational studies and the VENUS randomized trial (the Vein of Marshall Ethanol Infusion for Persistent Atrial Fibrillation) have shown promising results; however, considerable variability remains across studies in terms of patient demographics, procedural techniques, and reported outcomes.²

The latest meta-analysis by Ge et al.⁴ synthesized data from nine studies, revealing that the combination of EIVOM with CA significantly enhances rates of mitral isthmus block and markedly reduces the recurrence of AF and atrial tachycardia (AT), while maintaining a stable profile of periprocedural complications. However, as highlighted in their findings, discrepancies in study design and methodology, limited subgroup analyses, and inconsistent reporting hinder the broader applicability and mechanistic understanding of these conclusions. Critical outcome measures, including procedural duration and subgroup performance in specific arrhythmia phenotypes (e.g., peri-mitral atrial flutter), remain inadequately explored. In the present meta-analysis, we aim to build upon prior findings by incorporating newly published studies from 2023 to 2025 and focusing on three pivotal procedural and clinical endpoints: (1) the success rate of mitral isthmus ablation, (2) the recurrence of atrial arrhythmias following the blanking period, and (3) procedure time. This comprehensive synthesis of the evolving evidence surrounding EIVOM aims to further clarify its vital role in advancing modern electrophysiology.

Materials and Methods

Study Selection and Data Sources

A systematic review and meta-analysis were conducted to evaluate the efficacy and procedural outcomes of ethanol infusion into the vein of Marshall combined with radiofrequency ablation (EIVOM-RF) compared with radiofrequency (RF) ablation alone for the treatment of atrial arrhythmias. The study protocol was registered with PROSPERO (International Prospective Register of Systematic Reviews) (CRD420251062338). Included in the analysis were 12 multi-center and single-center retrospective studies, two prospective single-center observational studies, one prospective single-center randomized controlled trial (RCT), and one multi-center RCT (Figure 1). Follow-up durations varied, with some studies reporting no follow-up and others extending

ABBREVIATIONS

AAD	Antiarrhythmic drug
AF	Atrial fibrillation
AT	Atrial tachycardia
BMI	Body mass index
CA	Catheter ablation
CAD	Coronary artery disease
DM	Diabetes mellitus
EIVOM-RF	Ethanol infusion into the vein of Marshall combined with radiofrequency ablation
HF	Heart failure
HTN	Hypertension
LA	Left atrial
LVEF	Left ventricular ejection fraction
MI	Mitral isthmus
PVI	Pulmonary vein isolation
RCT	Randomized controlled trial
RF-only	Radiofrequency ablation alone
VOM	Vein of Marshall

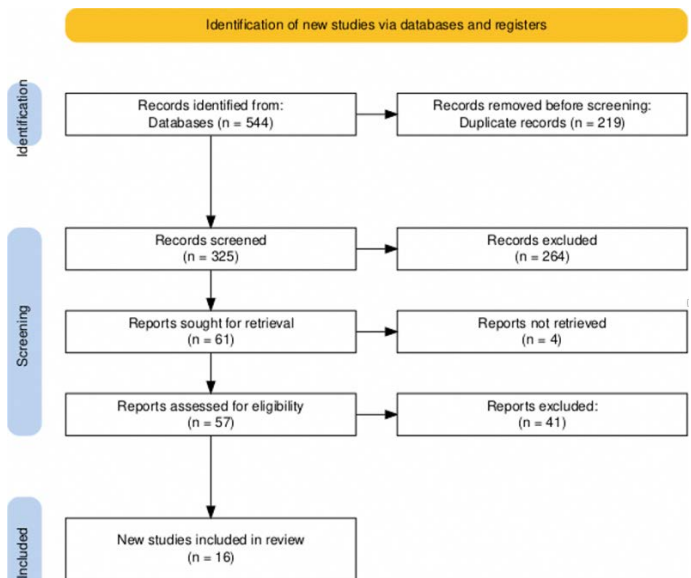


Figure 1. Flowchart of the study selection process for the meta-analysis.

up to 70 months; however, the majority (13 studies) reported a 12-month follow-up period. The atrial tachycardia subtypes investigated included persistent AF, paroxysmal AF, non-paroxysmal/paroxysmal AF, peri-mitral atrial tachycardia, and peri-mitral flutter. In total, 3,255 patients were included across all studies, with 1,406 in the EIVOM-RF group and 1,849 in the RF-only group.

Data Extraction and Outcomes

Data extraction was conducted by two independent researchers to ensure a thorough and unbiased approach. Any disagreements were resolved through collaborative discussions to reach a unanimous consensus. Baseline characteristics extracted included critical factors such as age, sex, hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), history

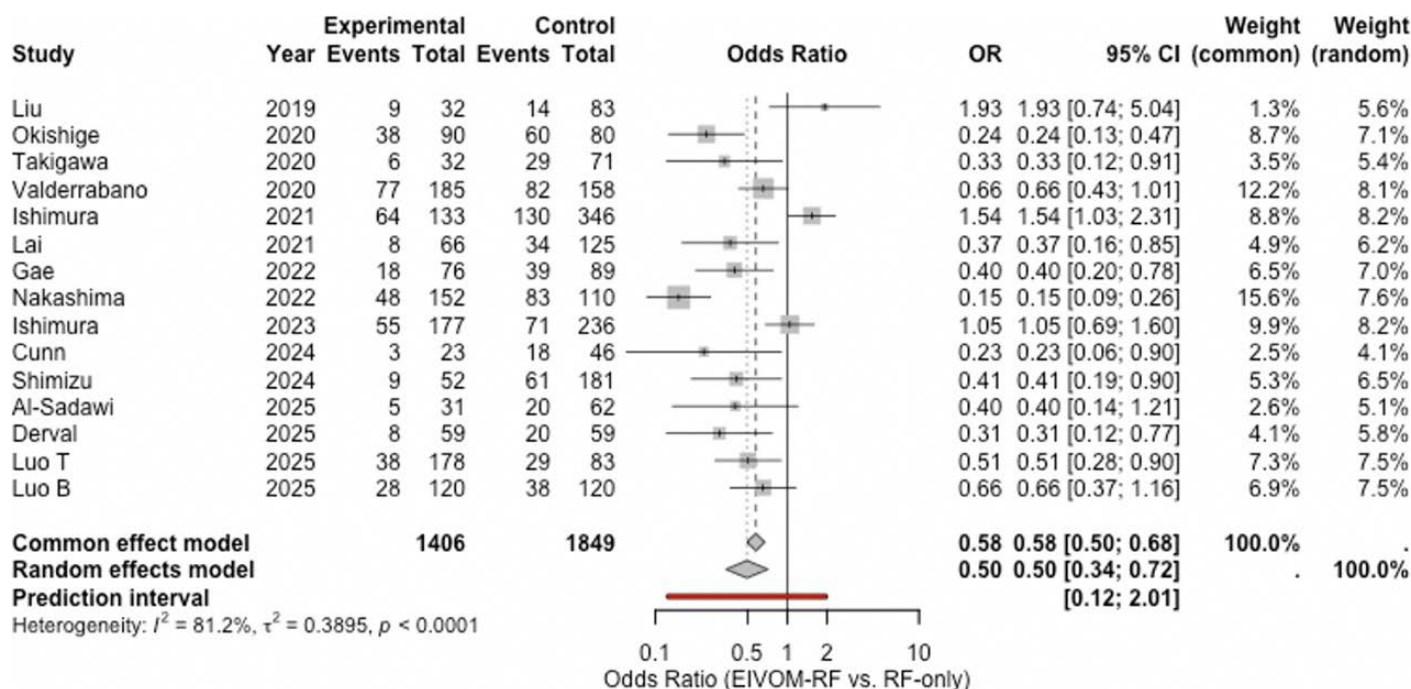


Figure 2. Forest plot of pooled effect sizes comparing vein of Marshall ethanol infusion combined with radiofrequency ablation versus radiofrequency ablation alone for atrial arrhythmia recurrence.

of stroke, heart failure (HF), CHA₂DS₂-VASc score (Congestive Heart Failure, Hypertension, Age ≥ 75 years (doubled), Diabetes Mellitus, prior Stroke or TIA (doubled), Vascular disease, Age 65–74 years, and Sex category (female)), left ventricular ejection fraction (LVEF), left atrial (LA) diameter, LA volume index, body mass index (BMI), and prior use of antiarrhythmic drugs (AADs). Key outcome measures assessed included recurrence of atrial arrhythmias (15 studies), total procedure time (12 studies), and ablation success (11 studies). Comprehensive data collection included both the EIVOM-RF and RF-only groups, with continuous variables reported as means and standard deviations (or ranges when available), while binary outcomes were presented as event counts.

Risk of Bias Assessment

Risk of bias was evaluated using the Ottawa risk of bias tool, adapted to assess the quality of both observational studies and RCTs. The domains assessed included selection bias, performance bias, detection bias, attrition bias, and reporting bias. Each study was rated as low, moderate, or high risk, with results summarized narratively to inform interpretation of the meta-analysis findings.

Statistical Analysis

Meta-analyses were performed using R statistical software (version 4.3.3; R Foundation for Statistical Computing) with the 'meta' and 'metafor' packages. For recurrence of atrial arrhythmias and MI ablation, binary outcomes were analyzed using the Mantel-Haenszel method for the common-effect model and the inverse variance method for the random-effects model, with odds ratios (OR) and 95% confidence intervals (CI) reported. Total procedure time, a continuous outcome, was analyzed using the inverse variance method for both models, with mean differences (MD) and 95% CI reported. The restricted

maximum-likelihood estimator was used to estimate between-study variance (τ^2), with Q-profile methods applied to obtain confidence intervals of τ^2 and τ . Heterogeneity was assessed using the I^2 statistic (low < 25%, moderate 25–75%, high > 75%) and Cochran's Q test, with a p-value < 0.10 indicating significant heterogeneity. Prediction intervals were calculated using the t-distribution to estimate the range of true effects in future studies. A continuity correction of 0.5 was applied in studies with zero cell frequencies for MI ablation. Forest plots were generated to visualize effect sizes, with weights reported for both fixed- and random-effects models.

Results

Study Characteristics

This meta-analysis integrates findings from 16 studies conducted between 2019 and 2025, encompassing data from a total of 3,255 patients (1,406 treated with EIVOM-RF and 1,849 with RF-only). The studies demonstrated considerable diversity in design, including 12 retrospective analyses (eight multi-center and four single-center), two prospective observational studies (one single-center), and both a prospective single-center RCT and a multi-center RCT. Follow-up durations varied from 0 to 70 months, with 13 studies reporting a 12-month follow-up period. AT subtypes investigated included persistent AF (the focus of 12 studies), paroxysmal AF (one study), non-paroxysmal/paroxysmal AF (two studies), peri-mitral AT (one study), and peri-mitral atrial flutter (one study). Baseline characteristics showed significant variability: patient ages ranged from 56.0 to 68.0 years, the proportion of male participants ranged from 57.3% to 90.6%, and comorbidities varied considerably, with hypertension affecting 22.4% to 87.5% of patients and diabetes mellitus affecting 4.2% to 35.0% (Appendix 1).^{2,3,5-18}

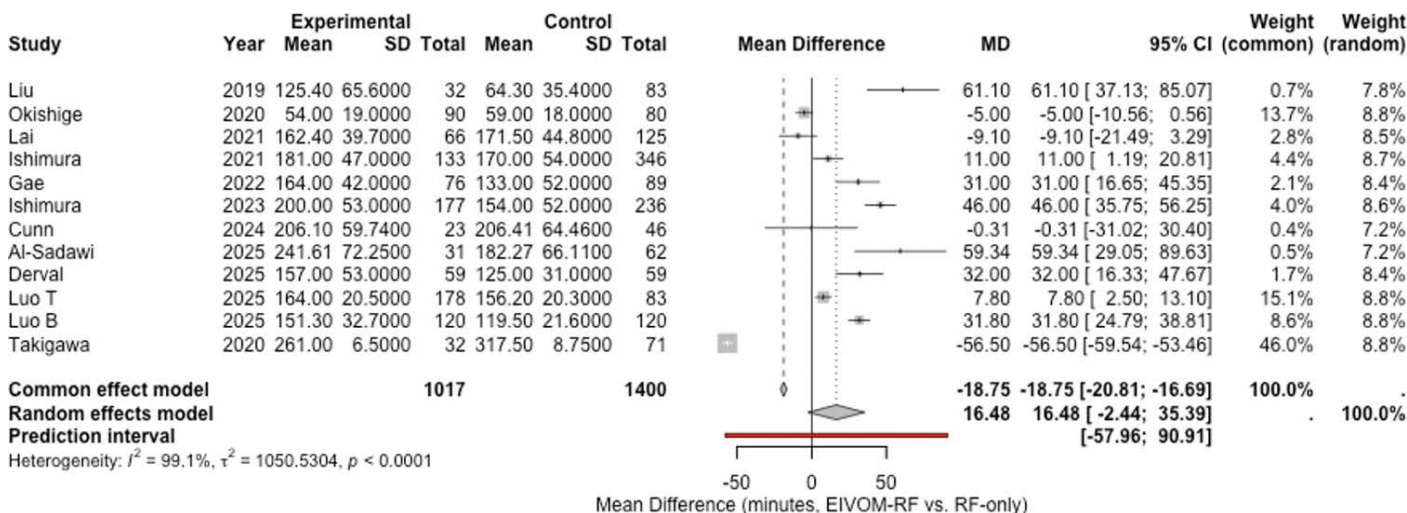


Figure 3. Forest plot of pooled effect sizes comparing vein of Marshall ethanol infusion combined with radiofrequency ablation versus radiofrequency ablation alone for total procedure time.

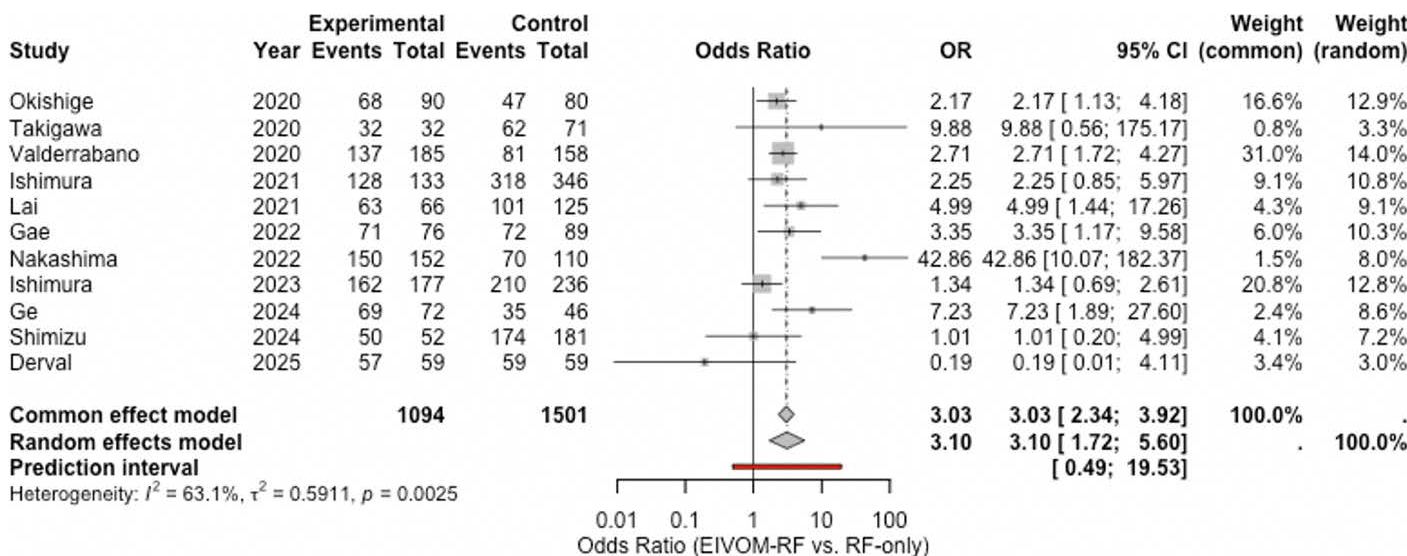


Figure 4. Forest plot of pooled effect sizes comparing vein of Marshall ethanol infusion combined with radiofrequency ablation versus radiofrequency ablation alone for mitral isthmus ablation.

Recurrence of Atrial Arrhythmias

A comprehensive analysis of 15 studies reporting recurrence of atrial arrhythmias revealed notable findings (Figure 2). The fixed-effects models demonstrated an OR of 0.5789 [95% CI: 0.4953, 0.6765], with a z-score of -6.88 and a p-value < 0.0001, indicating a significant reduction in recurrence with EIVOM-RF. The random-effects model showed an OR of 0.4954 [95% CI: 0.3423, 0.7169], with a z-score of -3.72 and a p-value of 0.0002, along a prediction interval of [0.1224, 2.0055]. High heterogeneity was observed ($I^2 = 81.2\%$ [70.1%, 88.2%], $Q = 74.63$, $df = 14$, $P < 0.0001$; $\tau^2 = 0.3895$), indicating considerable variability among studies. Individual study ORs ranged from 0.1501 (Nakashima et al.⁹ in 2022) to 1.9286 (Liu et al.¹⁵ in 2019), with model weights varying significantly (common: 1.3%–15.6%, random: 4.1%–8.2%).

Total Procedure Time

Twelve studies evaluated total procedure time (Figure 3). The fixed-effects model revealed a mean difference (MD) of -18.7509 [95% CI: -20.8096, -16.6923], with a z-score of -17.85 and a highly significant p-value of < 0.0001, favoring RF-only procedures. In contrast, the random-effects model indicated a mean difference of 16.4778 [95% CI: -2.4362, 35.3919], with a z-score of 1.71 and a p-value of 0.0877, along with a wide prediction interval [-57.9551, 90.9107]. Heterogeneity among studies was extremely high ($I^2 = 99.1\%$ [98.9%, 99.3%], $Q = 1,260.57$, $df = 11$, $P < 0.0001$; $\tau^2 = 1,050.5304$), underscoring the variability in the findings. Individual mean differences ranged widely, from -56.5000 in Takigawa et al.¹¹ in 2020 to 61.1000 in Liu et al.¹⁵ in 2019, with study weights demonstrating variability (common: 0.4%–46.0%, random: 7.2%–8.8%).

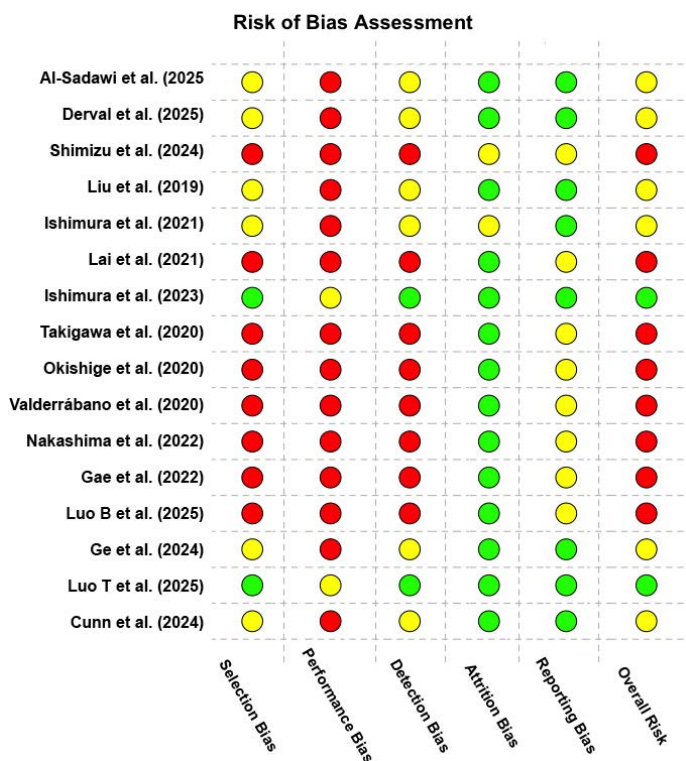


Figure 5. Risk of bias assessment using the Ottawa risk of bias tool, tailored to evaluate the quality of observational studies and randomized controlled trials.

Mitral Isthmus Ablation

A comprehensive analysis of 11 studies (k = 11, o = 2,595; o.e = 1,094, o.c = 1,501; e = 2,216) evaluated the success of MI ablation, as illustrated in Figure 4. The fixed-effects model revealed an OR of 3.0306 [95% CI: 2.3433, 3.9196], with a z-value of 8.45 and P < 0.0001, strongly favoring EIVOM-RF. Similarly, the random-effects model demonstrated an OR of 3.1020 [95% CI: 1.7198, 5.5951], with a z-value of 3.76 and P = 0.0002, underscoring the robustness of these findings, with a prediction interval of [0.4928, 19.5255]. The level of heterogeneity was moderate (I² = 63.1% [29.2%, 80.7%], Q = 27.07, df = 10, P = 0.0025; tau² = 0.5911), indicating some variability among the studies. Individual ORs ranged from 0.1933 (Derval et al.¹⁷ in 2025) to 42.8571 (Nakashima et al.⁹ in 2022), with corresponding weights varying accordingly (common: 0.8%–31.0%, random: 3.0%–14.0%).

Risk of Bias

The risk of bias assessment using the Ottawa tool showed considerable variability across the studies (Figure 5). While most retrospective studies demonstrated a moderate to high risk due to potential selection and reporting biases, the RCTs by Valderrábano² in 2020 and Derval et al.¹⁷ in 2025 showed a lower risk profile. However, concerns regarding performance bias persist due to inadequate blinding. Detailed ratings and supporting information are provided in the supplementary materials.

Discussion

In clinical electrophysiology, improving outcomes for patients with non-paroxysmal AF remains a significant challenge. Despite

advancements in ablation techniques, recurrence rates are still high. While PVI is foundational in AF treatment, it often proves insufficient for patients with persistent arrhythmias driven by non-pulmonary triggers and macro re-entrant circuits. One critical area that requires intervention is the mitral isthmus, where achieving a durable linear block is often technically complex.¹⁹ Incomplete block in this region frequently leads to recurrence of arrhythmias, especially peri-mitral flutter. A promising solution to the anatomical and electrophysiological challenges encountered in standard ablation is ethanol infusion into the VOM.²⁰ Ethanol has the ability to reach the epicardial area of the mitral isthmus, which is typically inaccessible using endocardial radiofrequency energy. Its infusion results in chemical ablation of myocardial fibers and autonomic ganglia, facilitating substrate modification and autonomic denervation. These effects enhance lesion durability and reduce the likelihood of conduction recovery, thereby lowering the risk of arrhythmia recurrence.²¹

This meta-analysis compiles data from 16 pivotal studies involving more than 3,200 patients, providing strong evidence for the effectiveness of EIVOM as a valuable adjunct to catheter ablation for AF. Patients who received EIVOM during their ablation procedures demonstrated consistently higher rates of complete mitral isthmus block—an outcome that emerged across multiple studies. This finding suggests that the addition of ethanol effectively addresses structural barriers that hinder successful treatment. Moreover, the notable reduction in arrhythmia recurrence further underscores the clinical advantages of this innovative approach. The improved rhythm outcomes are especially significant for patients with persistent AF, for whom traditional ablation often falls short. Although a moderate increase in procedural duration was noted with EIVOM, this can be attributed to the additional steps required for cannulation and ethanol delivery. Importantly, this slight prolongation does not compromise procedural safety or overall outcomes. This trade-off appears worthwhile given the substantial improvements in lesion quality and sustained arrhythmia control. Embracing EIVOM not only enriches the ablation process but also holds the potential to transform patient outcomes in the management of atrial fibrillation.

Autonomic modulation is an important mechanism through which EIVOM enhances procedural success. The vein of Marshall contains autonomic innervation that can affect atrial refractoriness and promote AF.²² Ablating this area not only aids in creating structural changes but also mitigates the effects of vagal triggers, helping to stabilize rhythm.²² This dual approach highlights the growing significance of EIVOM in comprehensive substrate modification.

Mitral isthmus block is technically challenging with traditional RF ablation. In this analysis, incorporating EIVOM significantly increased the likelihood of achieving a successful mitral isthmus block by more than three times (OR = 3.10, 95% CI: 1.72–5.60), suggesting that ethanol infusion enhances lesion formation efficiency in the mitral isthmus. This improvement may stem from both mechanical and neuro-autonomic factors, including fibrotic alterations in the epicardial musculature, autonomic denervation, and better transmuralty of ablation lesions. Moreover, the occurrence of atrial arrhythmias after the

blanking period was significantly lower in the EIVOM–RF group (OR = 0.50, 95% CI: 0.34–0.72), highlighting lasting rhythm control benefits. This effect persisted across different follow-up durations and arrhythmia types, affirming the strength of the outcome. However, there was considerable heterogeneity ($I^2 = 81.2\%$), likely resulting from variations in study designs, patient characteristics, and the ablation techniques employed across studies. One concern regarding the implementation of EIVOM in ablation workflows is the potential increase in procedural burden. As expected, EIVOM–RF was associated with a trend toward longer total procedure times, with a mean difference of 16.48 minutes (95% CI: –2.44 to 35.39), although this was not statistically significant ($P = 0.0877$). The substantial heterogeneity in this measure ($I^2 = 99.1\%$) could result from differences in operator experience, procedural workflow, and the technical difficulty of accessing the VOM. Nonetheless, it is crucial to consider this additional time alongside the long-term benefits of reduced recurrence rates and decreased need for repeat ablation procedures.

Our findings build on previous meta-analyses, including that by Ge et al.,⁴ by incorporating more recent studies and broadening the scope of analysis. While earlier studies demonstrated the advantages of EIVOM for achieving mitral isthmus block and managing arrhythmia, our work adds further detail by including subgroup analyses and evaluating procedure time as a key endpoint. The inclusion of two RCTs, specifically the VENUS trial and the study by Derval et al.,¹⁷ further strengthens the evidence and helps clarify causal relationships.^{2,17} Notably, although the Derval et al.¹⁷ trial did not show a benefit for mitral isthmus block, it did not significantly alter the overall effect size due to the larger supportive dataset.

The observed heterogeneity across outcomes necessitates cautious interpretation. For recurrence and procedure time, variability among studies was considerable, highlighting the influence of study design, patient demographics, and procedural techniques. The observed heterogeneity across outcomes necessitates cautious interpretation. For recurrence and procedure time, the variability among studies was considerable, underscoring the impact of study design, patient characteristics, and ablation techniques. Several of the included studies were retrospective and single-center, which may introduce selection bias and limit the applicability of the findings. Risk assessments indicated a higher risk of bias in non-randomized studies, primarily due to performance and reporting inconsistencies. However, the persistent trends across diverse studies enhance the reliability of the primary findings. Another limitation relates to inconsistencies in reporting. Not all studies uniformly detailed follow-up durations, definitions of mitral isthmus block, or methods for assessing recurrence, potentially affecting pooled estimates. Additionally, variations in post-ablation antiarrhythmic drug usage, operator expertise, and center-specific protocols could skew outcomes. The learning curve associated with EIVOM, which requires specialized skills and equipment, may also impact both success rates and procedural duration. Limited prospective data and differing follow-up methods introduce further bias. Rare complications from ethanol infusion, such as damage to the coronary sinus or surrounding structures, should also be considered. It is also important to acknowledge that the current evidence base is limited by the

lack of standardized criteria for patient selection and variations in procedural techniques among studies. These methodological differences likely contribute to the observed heterogeneity and may affect the generalizability of our results. Therefore, interpretation of the present findings should remain cautious, and future investigations should focus on defining clear patient selection strategies and procedural standardization to ensure consistent outcomes. Future randomized trials with standardized methodologies are needed to refine patient selection, optimize procedural workflows, and confirm long-term safety.

Conclusion

This comprehensive and updated meta-analysis suggests that EIVOM is associated with a higher success rate of mitral isthmus ablation and a lower recurrence of atrial arrhythmias in patients undergoing CA. Although these findings indicate a potential clinical benefit, they should be interpreted with caution due to study heterogeneity and differences in patient selection and procedural strategies. Even though there is a slight increase in procedure time, the substantial benefits of enhanced rhythm control and long-lasting lesion formation make a strong case for its integration into standard clinical practice, particularly for patients with persistent AF or complex substrate. These results not only advocate for the broader adoption of EIVOM within tailored ablation strategies but also highlight the urgent need for ongoing improvements in procedural techniques and the generation of robust evidence through well-designed clinical trials.

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Appendix 1. Each study listed reports demographic variables including Age, Male (%), and comorbidity prevalence, as well as relevant echocardiographic or procedural indices essential for interpreting study heterogeneity and patient clinical profiles

Study	Year	Study type	Follow-up (months)	Total number of patients	Group	Age	Male (%)	HTN (%)	DM (%)	CAD (%)	Stroke (%)	HF (%)	CHA ₂ DS ₂ -VASc score	LA diameter (mm)	BMI
Cunn et al. ⁵	2024	Multi-center, retrospective	12	69	EIVOM-RF	67 (7.4)	73.9	87	21.7	13	8.7	N/A	2.61 (0.24)	N/A	35.1 (9.0)
					RF only	66.2 (10.9)	63	84.8	15.2	21.7	6.5	N/A	2.56 (0.23)	N/A	30.9 (5.7)
Luo T et al. ⁶	2025	Multi-center, retrospective	12	261	EIVOM-RF	61.3 (7.5)	70.8	60.1	15.2	N/A	11.2	18.1	N/A	48.9 (2.3)	26.8 (2.8)
					RF only	61.5 (8.7)	77.1	53	18.1	N/A	7.2	14.5	N/A	48.5 (2.5)	26.9 (2.7)
Ge et al. ⁷	2024	Single-center, retrospective	N/A	118	EIVOM-RF	64.3 (8.3)	66.6	87.5	11.1	2.8	0	0	1.65 (1.26)	43.6 (5.2)	25.1 (3.4)
					RF only	62.7 (8.7)	65.2	54.3	8.7	2.2	0	0	1.48 (1.07)	43.6 (5.6)	24.9 (2.8)
Luo B et al. ³	2025	Multi-center, retrospective	36	240	EIVOM-RF	57.4 (6.8)	81.7	58.3	31.7	23.3	15.8	10.8	3 (2-5)	45.1 (4.2)	24.8 (7.3)
					RF only	56.4 (7.2)	80.8	54.2	35	22.5	14.2	13.3	3 (2-4)	43.5 (3.8)	25.6 (6.6)
Gao et al. ⁸	2022	Prospective, single-center, observational	6	165	EIVOM-RF	63.3 (9.5)	68.4	63.2	11.8	13.2	14.5	10.5	2.2 (1.6)	42.9 (6.4)	N/A
					RF only	63.1 (11.0)	57.3	58.3	19.1	15.7	7.9	15.7	2.3 (1.8)	43.0 (5.6)	N/A
Nakashima et al. ⁹	2022	Single-center, retrospective	12	262	EIVOM-RF	63.8 (9.4)	75.7	N/A	N/A	N/A	N/A	N/A	2.0 (1.0-3.0)	N/A	28.3 (5.0)
					RF only	60.9 (9.2)	81.8	N/A	N/A	N/A	N/A	N/A	2.0 (1.0-3.0)	N/A	28.1 (4.2)
Valderrábano et al. ²	2020	Multi-center, randomized controlled trial (RCT)	12	343	EIVOM-RF	66.6 (9.6)	74.1	77.8	28.1	28.1	10.3	25.9	2.9 (1.6)	44.8 (7.9)	31.2 (6.6)
					RF only	66.4 (9.9)	78.5	65.8	19.6	25.9	12	26.6	2.6 (1.6)	47.0 (7.5)	31.9 (6.5)
Okishige et al. ¹⁰	2020	Single-center, retrospective	12	342	EIVOM-RF	63.5 (10.0)	63.3	27.8	6.7	N/A	5.6	4.4	0.76 (0.83)	38.7 (7.3)	23.8 (3.5)
					RF only	62.2 (9.6)	76.3	23.8	13.8	N/A	6.3	2.5	0.87 (0.66)	41.1 (4.3)	22.7 (2.9)
Takigawa et al. ¹¹	2020	Single-center, retrospective	12	103	EIVOM-RF	63 (59-70)	78.1	59.4	21.9	28.1	3.1	9.4	2 (1-2)	N/A	N/A
					RF only	63 (57-67)	74.6	40.9	4.2	21.1	5.6	16.9	2 (0-3)	N/A	N/A
Ishimura et al. ¹²	2023	Single-center, retrospective	13	413	EIVOM-RF	69 (8.6)	75.7	62.1	29.9	3.4	N/A	0	2.1 (1.2)	49 (5.8)	N/A
					RF only	69 (7.8)	66.1	66.1	25.8	5.9	N/A	0.4	1.8 (1.1)	48 (5.4)	N/A
Lai et al. ¹³	2021	Single-center, retrospective	12	191	EIVOM-RF	61.0 (10.9)	71.2	48.5	16.7	18.2	9.1	29.2	N/A	43.6 (5.5)	N/A
					RF only	61.1 (10.3)	67.2	22.4	22.4	16	13.6	22.4	N/A	42.7 (4.7)	N/A
Ishimura et al. ¹⁴	2021	Single-center, retrospective	12	479	EIVOM-RF	67 (8.0)	78.2	66.2	27.8	2.3	N/A	0	1.6 (0.95)	49 (5.0)	N/A
					RF only	68 (8.9)	72.8	65	24.3	6.6	N/A	0.6	1.6 (0.85)	49 (6.1)	N/A
Liu et al. ¹⁵	2019	Multi-center, retrospective	12	115	EIVOM-RF	56.4 (9.4)	90.6	59.4	15.6	18.8	15.6	12.5	1.7 (1.3)	42.3 (7.3)	N/A
					RF only	56.0 (10.1)	83.1	45.8	13.3	15.7	6	15.7	1.1 (1.1)	40.5 (5.8)	N/A
Shimizu et al. ¹⁶	2024	Single-center, retrospective	70	233	EIVOM-RF	66.8 (1.3)	74	62	20	N/A	14	48	N/A	46.1 (0.9)	25.5 (0.6)
					RF only	68.4 (0.7)	60.9	66.7	22.4	N/A	11.5	47.7	N/A	45.0 (0.5)	25.4 (0.3)
Derval et al. ¹⁷	2025	Prospective, single-center, RCT	12	118	EIVOM-RF	66 (8)	81.4	61	15.3	N/A	8.5	N/A	2 (1)	N/A	N/A
					RF only	65 (8)	86.4	42.4	5.1	N/A	3.4	N/A	2 (1)	N/A	N/A
Al-Sadawi et al. ¹⁸	2025	Retrospective, single-center	60	93	EIVOM-RF	68.0 (9.2)	61.3	64.5	12.9	22.6	6.5	35.5	2.73 (1.51)	48.5 (7.2)	34.1 (6.5)
					RF only	65.8 (9.5)	64.5	75.8	32.3	22.6	8.1	35.5	3.00 (1.54)	48.8 (6.7)	34.9 (6.7)

HTN, Hypertension; DM, Diabetes mellitus; CAD, Coronary artery disease; HF, Heart failure; LA, Left atrial; BMI, Body mass index; EIVOM-RF, Ethanol infusion into the vein of Marshall combined with radiofrequency ablation; RF-only, Radiofrequency ablation without adjunctive ethanol infusion.