

Original Research



OPEN ACCESS

Received: Aug 19, 2025

Revised: Oct 21, 2025

Accepted: Nov 11, 2025

Published online: Jan 5, 2026

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Comparative Outcomes of Deep Sedation Versus General Anesthesia in Cryoablation for Atrial Fibrillation: Insights From the Korean Heart Rhythm Society Cryoablation Registry

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AUTHOR'S SUMMARY

Although pulsed field ablation has recently emerged, cryoablation remains widely used for atrial fibrillation (AF) ablation due to its practical advantages. However, evidence on the optimal sedation strategy during cryoablation is limited. Using data from the Korean Heart Rhythm Society Cryoablation Registry, we compared the efficacy and safety outcomes of deep sedation (DS) and general anesthesia (GA). After propensity score matching, no significant differences were found in arrhythmia recurrence or major complication rates between the 2 groups. These findings suggest that DS may be a safe and effective alternative to GA in patients undergoing AF cryoablation.

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Funding

This study was supported by a grant from the Korean Heart Rhythm Society (KHRS 2021-3).

Conflict of Interest

The authors have no financial conflicts of interest.

Data Sharing Statement

The data generated in this study is available from the corresponding authors upon reasonable request.

Author Contributions

Conceptualization: Cha MJ, Kwon CH; Formal analysis: Lee JM; Investigation: Lee JM; Methodology: Lee JM; Supervision: Cha MJ, Cho MS, Nam GB, Oh I, Lee S, Kim JY, Lee SH, Park J, Kim K, Yang P, Kim JH, Shim J, Lim HE, Kwon CH; Writing - original draft: Lee JM; Writing - review & editing: Cha MJ, Kwon CH.

ABSTRACT

Background and Objectives: The optimal sedation strategy for cryoablation in atrial fibrillation (AF) remains uncertain. We aimed to compare the safety and efficacy outcomes between deep sedation (DS) and general anesthesia (GA) in patients undergoing cryoablation.

Methods: We analyzed 2,068 patients from the Korean Heart Rhythm Society Cryoablation Registry who underwent cryoablation for AF between 2018 and 2022. Patients were grouped based on anesthesia method: DS (n=1,390) and GA (n=678). Propensity score matching (1:1) was performed to adjust for baseline differences. The primary outcomes included any recurrence of atrial tachyarrhythmias (ATs) after a 3 month blanking period and procedure-related major complications.

Results: The study included 2,068 patients (average age: 61.7±9.7 years; 76.3% male; 57.9% with persistent AF). In the matched cohort, AT recurrence rates were comparable between DS and GA groups (47.1% [n=220] vs. 53.1% [n=225]; p=0.99) during a mean follow-up of 1.2 years. The incidence of major complications was also similar between groups both before (2.8% [n=39] vs. 2.4% [n=16]; p=0.66) and after matching (2.3% [n=15] vs. 2.1% [n=14]; p=1.00). Subgroup analysis based on body mass index (≥30 vs. <30) revealed no significant differences in efficacy and safety outcomes between the DS and GA groups.

Conclusions: DS provides a comparable safety and efficacy profile to GA for cryoablation in patients with AF. These findings support the use of DS as a feasible and practical alternative to GA in routine clinical practice.

Keywords: Anesthesia; Atrial fibrillation; Cryoablation; Deep sedation

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults, and its prevalence continues to rise with an aging population.^{1,3)} Pathophysiologically, AF is a progressive and degenerative disease.⁴⁾ In the early stages, typically paroxysmal AF, focal triggers originating from pulmonary veins (PVs) are the primary mechanism. However, as the disease progresses, structural and functional remodeling leads to the development of reentry substrates, which play a dominant role in persistent and permanent AF.⁴⁾ Despite this evolving pathophysiology, complete PV isolation remains the cornerstone of catheter ablation for AF, regardless of whether the arrhythmia is paroxysmal or persistent.^{2,3,5)}

Radiofrequency catheter ablation (RFCA) has traditionally been the mainstay modality for achieving PV isolation. However, RFCA involves a point-by-point technique to create circumferential antral lesions around the PVs, often resulting in longer procedure times and technical challenges in achieving durable lesion sets. To overcome these limitations, cryoablation was developed as a single-shot technique for PV isolation. Cryoablation has demonstrated non-inferiority to RFCA in maintaining sinus rhythm among patients with drug-refractory paroxysmal AF.⁶⁾ More recently, cryoablation has also shown superiority over antiarrhythmic drug therapy as an initial rhythm control strategy in patients with symptomatic paroxysmal AF.⁷⁾ Furthermore, early use of cryoablation has been associated with a lower risk of progression to persistent AF compared with initial antiarrhythmic drug therapy.⁸⁾

In the RFCA era, the choice of anesthetic strategy - deep sedation (DS) versus general anesthesia (GA) - has been shown to influence procedural outcomes.⁹⁾ However, data

comparing these two approaches in the context of cryoablation are limited.¹⁰⁾ Accordingly, this study aimed to compare the safety and efficacy of DS versus GA in patients undergoing cryoablation for AF, using data from the Korean Heart Rhythm Society Cryoablation Registry.

METHODS

Ethical statement

Data collection was conducted in accordance with the principles of the Declaration of Helsinki (2013) and Good Clinical Practice guidelines. The study protocol was reviewed and approved by the Institutional Review Boards (IRBs) of Asan Medical Center (IRB number, 2022-1495). As the data were retrospectively collected and fully de-identified, the requirement for informed consent was waived.

Study patients

This retrospective analysis utilized data from the Korean Heart Rhythm Society Cryoablation Registry, which includes 12 tertiary centers across South Korea. Between May 2018 and June 2022, a total of 2,689 patients who underwent de novo cryoablation for drug-refractory AF were consecutively enrolled. Patients who received additional concomitant cavo-tricuspid isthmus ablation (n=583) or had missing procedural or outcome data (n=38) were excluded. The final study population comprised 2,068 patients.

The study patients were categorized into 2 groups based on the type of anesthesia used during cryoablation: the DS group (n=1,390) and the GA group (n=678). Among the participating hospitals, 4 centers primarily adopted GA for cryoablation procedures, although DS was also selectively employed in certain cases, while the remaining 8 centers routinely utilized DS (**Supplementary Figure 1**). To adjust for potential baseline differences, propensity score matching (1:1) was conducted. A flow diagram of patient selection is shown in **Figure 1**.

Cryoablation procedure

The cryoablation procedure was generally performed in accordance with established clinical guidelines.¹¹⁾¹²⁾ Procedural techniques and parameters—including cryoenergy delivery duration, imaging guidance (fluoroscopy or intracardiac echocardiography), anesthesia type, and post-ablation testing—were determined at the operator's discretion. In brief, trans-septal access to the left atrium was obtained, and a 15-French steerable sheath (FlexCath Advance; Medtronic, Inc., Minneapolis, MN, USA) was used to deliver a 28-mm cryoablation catheter (Arctic Front Advance; Medtronic, Inc.) into the left atrium. A circular mapping catheter (Achieve; Medtronic, Inc.) was used to guide the balloon to the PV antrum and to record PV potentials before and after ablation. The number and duration of freeze applications were determined by the operator. PV isolation was confirmed by entrance and exit block following cryoablation.

The procedures were performed under either GA or DS. The choice of anesthesia type was determined based on the physician's preference or institutional policy. In general, 4 centers routinely performed the procedure under GA, while the remaining 8 centers used DS. GA was administered by an anesthesiologist with mechanical ventilation support. DS was achieved using continuous intravenous infusions of propofol, dexmedetomidine, or remifentanyl, in combination with intravenous bolus injections of midazolam or fentanyl.

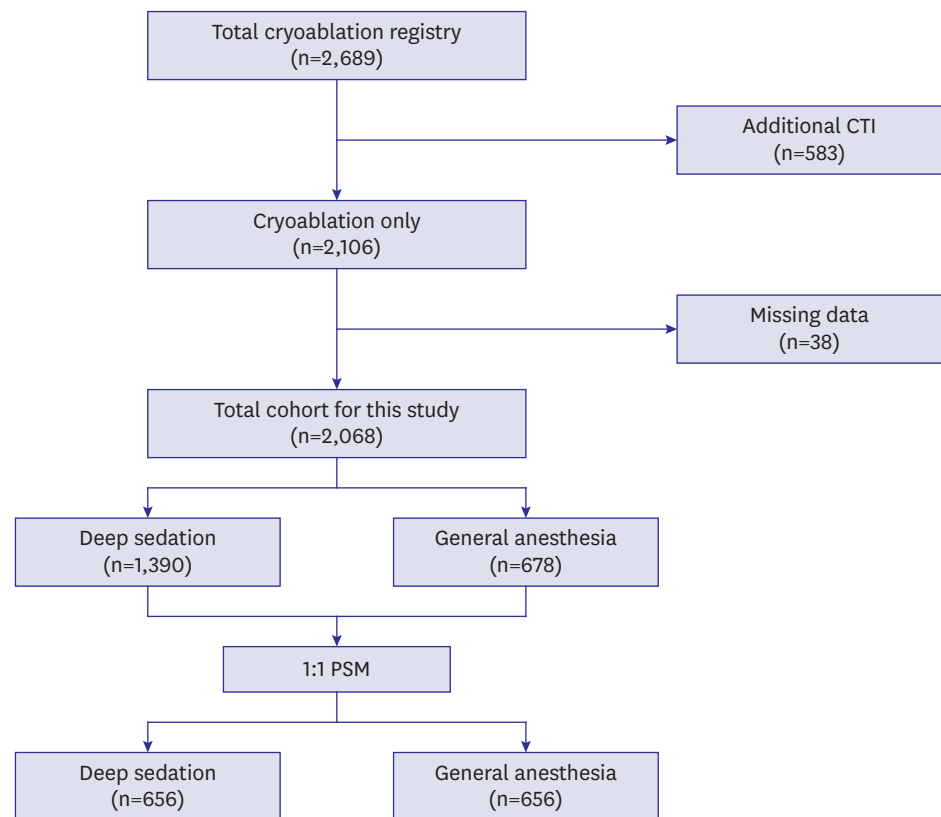


Figure 1. Study flow chart.

CTI = cavo-tricuspid isthmus; PSM = propensity score matching.

Phrenic nerve function was monitored during right-sided PV isolation using pacing of the phrenic nerve via a catheter in the subclavian vein, with diaphragmatic movement assessed by manual palpation and/or additional detection methods. Cryoenergy delivery was terminated immediately upon detection of decreased diaphragmatic excursion. Peri-procedural anticoagulation and antiarrhythmic drug management were conducted in accordance with each institution's standard practice. The initiation or continuation of antiarrhythmic therapy and discharge timing were also determined by treating physicians based on local protocols.

Patient follow-up and study outcomes

Patients were scheduled for in-office follow-up visits every 3 months during the first year after cryoablation, and subsequently at 3- to 6-month intervals in accordance with current guideline and each hospital's standard-of-care protocol.³⁾¹³⁾ Patients were followed at the outpatient clinic at 1, 3, 6, 9, and 12 months and every 3–6 months thereafter. Whenever symptoms occurred after cryoballoon ablation, they were managed using the standard-of-care method of the hospital. Follow-up monitoring was performed according to the standard-of-care practice for each hospital. Rhythm monitoring was performed using any of the following methods, including 12-lead electrocardiogram (ECG), Holter or a single lead ECG patch recording, or an insertable cardiac monitor. Any physician-proven atrial tachyarrhythmias (ATs) including AF, atrial flutter, and atypical atrial flutter in 12-lead ECG or lasting >30 seconds in extended ECG monitoring after the initial 3-month blanking period was defined as clinical recurrence.

The primary efficacy outcome was the recurrence of ATs (AF, atrial flutter, or atrial tachycardia) lasting ≥ 30 seconds, occurring after a 90-day post-procedural blanking period. The primary safety outcome was the occurrence of procedure-related major complications. It was defined as a composite of permanent phrenic nerve injury, symptomatic pericardial effusion, access-site complications requiring intervention, PV stenosis, or complete atrioventricular block that resulted in permanent injury or death, required invasive treatment, or prolonged hospitalization by more than 48 hours.¹⁴⁾ Permanent phrenic nerve injury was defined as persistent phrenic nerve palsy without recovery by the last follow-up.

Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation and were compared using the Student's t-test or Wilcoxon rank-sum test (for non-normally distributed data). Categorical variables were expressed as counts and percentage and were compared using the χ^2 test or Fisher's exact test. Time-to-event outcomes were assessed using Kaplan-Meier analysis, and differences between groups were evaluated using the log-rank test. Predictors of ATs recurrence were analyzed using a Cox proportional hazard model. Variables with $p < 0.1$ in univariable analysis or with clinical relevance were entered into a multivariable Cox proportional hazards model with backward stepwise selection. To minimize selection bias and account for baseline differences between the DS and GA groups, a propensity score matching analysis was performed. We matched each patient in the DS group to those in the GA group at a 1:1 ratio using the nearest method with calipers of width equal to 0.05 of the standard deviation of the logit of the propensity score. Clinically relevant covariates that could influence the choice of sedation strategy, as well as variables with a standardized mean difference greater than 0.1, were included in the propensity score model. Specifically, age, persistent AF, AF duration from diagnosis to ablation, body mass index (BMI) > 30 , and comorbidities including cerebrovascular accident, heart failure, hypertension, diabetes mellitus, coronary artery disease, and chronic kidney disease were incorporated. The balance of baseline characteristics between the DS and the GA groups was evaluated using the standardized mean difference, and a standardized mean difference of < 0.1 indicated a negligible difference (**Supplementary Figure 2**). In addition, we performed subgroup analysis according to BMI threshold of 30 kg/m^2 . All statistical tests were 2-tailed, and a p value < 0.05 was considered statistically significant. Analyses were conducted using R software, version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics of study patients

The baseline characteristics of the study patients stratified by anesthesia type are summarized in **Table 1**. The overall mean age was 61.7 ± 9.7 years, with 1,577 patients (76.3%) being male and 1,197 (57.9%) presenting with persistent AF. Compared to the GA group, patients in the DS group were older (62.2 ± 9.5 vs. 60.6 ± 9.8 , $p < 0.001$) and had a higher prevalence of persistent AF, heart failure, hypertension, diabetes mellitus, and coronary artery disease. The CHA₂DS₂-VASc score was also higher in the DS group. **Table 2** presents the baseline characteristics of the propensity score matched cohort. After 1:1 matching, the mean age of patients was 60.9 ± 9.8 years, 980 patients (74.7%) were male, and 631 (48.1%) had persistent AF. All standardized mean differences were < 0.100 , indicating adequate covariate balance between the groups.

Table 1. Baseline characteristics in total cohort

Total cohort	Overall (n=2,068)	DS (n=1,390)	GA (n=678)	p value	SMD
Age (years)	61.7±9.7	62.2±9.5	60.6±9.8	<0.001	0.165
Age >65 years	835 (40.4)	589 (42.4)	246 (36.3)	0.009	0.061
Age >70 years	424 (20.5)	296 (21.3)	128 (18.9)	0.223	0.024
Male	1,577 (76.3)	1,078 (77.6)	499 (73.6)	0.054	0.040
BMI (kg/m ²)	25.7±3.4	25.7±3.4	25.9±3.4	0.130	0.070
BMI >25 kg/m ²	1,154 (55.8)	768 (55.3)	386 (56.9)	0.500	0.016
BMI >30 kg/m ²	210 (10.2)	132 (9.5)	78 (11.5)	0.180	0.020
Persistent AF	1,197 (57.9)	879 (63.2)	318 (46.9)	<0.001	0.163
AF duration (years)	3.1±3.3	3.4±3.5	2.6±3.0	<0.001	0.280
HF	457 (22.1)	354 (25.5)	103 (15.2)	<0.001	0.103
HTN	1,186 (57.4)	844 (60.7)	342 (50.4)	<0.001	0.103
DM	430 (20.8)	318 (22.9)	112 (16.5)	0.001	0.064
CVA	230 (11.1)	160 (11.5)	70 (10.3)	0.465	0.012
MI	25 (1.2)	13 (0.9)	12 (1.8)	0.157	0.008
CAD	169 (8.2)	130 (9.4)	39 (5.8)	0.007	0.036
PAOD	10 (0.5)	9 (0.6)	1 (0.1)	0.230	0.005
CKD	155 (7.5)	94 (6.8)	61 (9.0)	0.085	0.022
ESRD	51 (2.5)	9 (0.6)	42 (6.2)	<0.001	0.055
SSS	104 (5.0)	79 (5.7)	25 (3.7)	0.065	0.020
MV disease	23 (1.1)	20 (1.4)	3 (0.4)	0.071	0.010
HCMP	44 (2.1)	26 (1.9)	18 (2.7)	0.318	0.008
CHA ₂ DS ₂ -VASc	2.1±1.5	2.2±1.5	1.8±1.4	<0.001	0.280
ICD	10 (0.5)	7 (0.5)	3 (0.4)	1.000	<0.001
PPM	57 (2.8)	46 (3.3)	11 (1.6)	0.040	0.017

The numbers are presented as mean ± standard deviation or number (%).

AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; CVA = cerebrovascular attack; DM = diabetes mellitus; DS = deep sedation; ESRD = end stage renal disease; GA = general anesthesia; HCMP = hypertrophic cardiomyopathy; HF = heart failure; HTN = hypertension; ICD = implantable cardioverter defibrillator; MI = myocardial infarction; MV = mitral valve; PAOD = peripheral arterial disease; PPM = permanent pacemaker; SMD = standardized mean difference; SSS = sick sinus syndrome.

Primary efficacy and safety outcomes according to anesthesia types

During a mean follow-up of 1.2 years, the recurrence rates of ATs were similar between the DS and GA groups in the overall cohort (53.3% [n=501] vs. 48.2% [n=229]; hazard ratio [HR], 0.91; 95% confidence interval [CI], 0.78–1.06; p=0.24; **Figure 2A**). In the matched cohort, the recurrence rates remained comparable (47.1% [n=220] vs. 53.1% [n=225]; HR, 1.00; 95% CI, 0.83–1.20; p=0.99; **Figure 2B**). A summary of procedural complications is provided in **Table 3**. The incidence of major complications was also similar between groups both before (0.6% [n=9] vs. 0.4% [n=3]; p=0.789) and after matching (0.5% [n=3] vs. 0.5% [n=3]; p=1.000). Notably, no cases of permanent phrenic nerve injury were reported in either group.

Predictors of atrial tachyarrhythmias recurrence in propensity score matched cohort

Cox proportional hazards regression analysis for ATs recurrence in matched cohort is shown in **Table 4**. After multivariable adjustment, the following were identified as independent predictors of recurrence: longer AF duration (HR, 1.03; 95% CI, 1.00–1.06; p=0.029), persistent AF (HR, 2.42; 95% CI, 1.98–2.95; p<0.001), and mitral valve disease (HR, 2.35; 95% CI, 1.07–5.16; p=0.033).

Subgroup analysis by body mass index

A subgroup analysis was conducted by stratifying patients in the matched cohort according to a BMI threshold of 30 kg/m². Baseline characteristics of these subgroups are shown in **Supplementary Table 1**. Among 133 patients with a BMI >30, 63 underwent DS and 70 received GA, with no significant baseline difference between the two groups. In contrast,

Table 2. Baseline characteristics in the cohort after PSM*

PSM	Overall (n=1,312)	DS (n=656)	GA (n=656)	SMD
Age (years)	60.9±9.8	60.9±9.9	60.9±9.7	0.065
Age >65 years	483 (36.8)	239 (36.4)	244 (37.2)	0.029
Age >70 years	241 (18.4)	114 (17.4)	127 (19.4)	0.013
Male	980 (74.7)	499 (76.1)	481 (73.3)	0.025
BMI (kg/m ²)	25.7±3.4	25.5±3.3	25.9±3.4	0.070
BMI >25 kg/m ²	716 (54.6)	342 (52.1)	374 (57.0)	0.021
BMI >30 kg/m ²	133 (10.1)	63 (9.6)	70 (10.7)	0.022
Persistent AF	631 (48.1)	313 (47.7)	318 (48.5)	0.013
AF duration (years)	2.7±2.9	2.7±2.8	2.6±3.0	0.019
HF	210 (16.0)	107 (16.3)	103 (15.7)	0.005
HTN	670 (51.1)	332 (50.6)	338 (51.5)	0.011
DM	220 (16.8)	109 (16.6)	111 (16.9)	0.005
CVA	123 (9.4)	55 (8.4)	68 (10.4)	0.005
MI	16 (1.2)	5 (0.8)	11 (1.7)	0.005
CAD	83 (6.3)	44 (6.7)	39 (5.9)	0.005
PAOD	3 (0.2)	2 (0.3)	1 (0.2)	0.002
CKD	96 (7.3)	51 (7.8)	45 (6.9)	0.004
ESRD	30 (2.3)	3 (0.5)	27 (4.1)	<0.001
SSS	64 (4.9)	41 (6.2)	23 (3.5)	0.005
MV disease	8 (0.6)	5 (0.8)	3 (0.5)	<0.001
HCMP	26 (2.0)	8 (1.2)	18 (2.7)	0.004
CHA ₂ DS ₂ -VASc	1.8±1.4	1.8±1.4	1.8±1.4	0.046
ICD	6 (0.5)	3 (0.5)	3 (0.5)	0.002
PPM	35 (2.7)	25 (3.8)	10 (1.5)	0.002

The numbers are presented as mean ± standard deviation or number (%).

AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; CVA = cerebrovascular attack; DM = diabetes mellitus; DS = deep sedation; ESRD = end stage renal disease; GA = general anesthesia; HCMP = hypertrophic cardiomyopathy; HF = heart failure; HTN = hypertension; ICD = implantable cardioverter defibrillator; MI = myocardial infarction; MV = mitral valve; PAOD = peripheral arterial disease; PPM = permanent pacemaker; PSM = propensity score matching; SMD = standardized mean difference; SSS = sick sinus syndrome.

*The variables included in the PSM were age, persistent AF, AF duration from diagnosis to ablation, BMI >30, and comorbidities including cerebrovascular accident, HF, HTN, DM, CAD, and CKD.

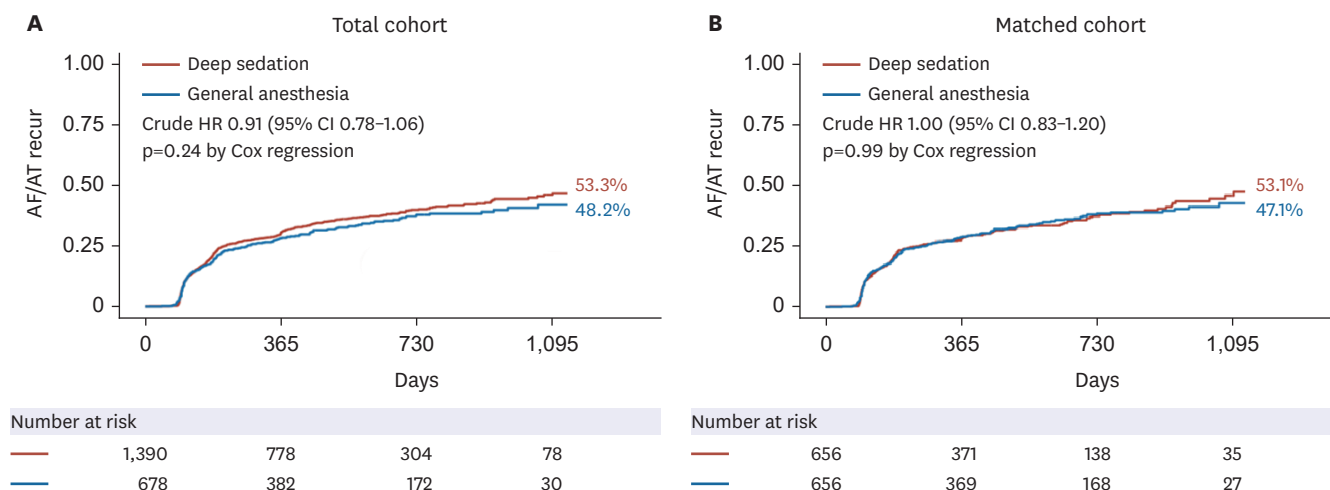


Figure 2. Kaplan-Meier curve of atrial tachyarrhythmias recurrence after cryoablation according to anesthesia strategy. (A) Total cohort; (B) Matched cohort. AF = atrial fibrillation; AT = atrial tachycardia; CI = confidence interval; HR = hazard ratio.

among patients with a BMI ≤30, the GA group had a higher prevalence of end-stage renal disease and hypertrophic cardiomyopathy. As illustrated in **Supplementary Figure 3**, ATs recurrence did not significantly differ by anesthesia strategy in either BMI subgroup.

Table 3. Complications after cryoablation for atrial fibrillation according to sedation strategy

	Total cohort			Propensity score matched cohort*		
	DS (n=1,390)	GA (n=678)	p value	DS (n=656)	GA (n=656)	p value
Major complications	9 (0.6)	3 (0.4)	0.789	3 (0.5)	3 (0.5)	1.000
Pericardial effusion	13 (0.9)	3 (0.4)	0.351	5 (0.8)	3 (0.5)	0.723
Pericardiocentesis	5 (0.4)	0 (0.0)	0.277	2 (0.3)	0 (0.0)	0.479
Atrioesophageal fistula	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Access site complication	12 (0.9)	7 (1.0)	0.894	1 (0.2)	7 (1.0)	0.076
Access site intervention	2 (0.1)	3 (0.4)	0.412	0 (0.0)	3 (0.5)	0.248
Complete atrioventricular block	1 (0.1)	0 (0.0)	1.000	1 (0.2)	0 (0.0)	1.000
Permanent phrenic nerve palsy	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Pneumothorax	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Hemoptysis	3 (0.2)	5 (0.7)	0.157	2 (0.3)	3 (0.5)	1.000
Pulmonary vein stenosis	1 (0.1)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	-
Gastroparesis	7 (0.5)	0 (0.0)	0.148	5 (0.8)	0 (0.0)	0.073
In-hospital cardiac surgery	1 (0.1)	0 (0.0)	1.000	1 (0.2)	0 (0.0)	1.000
In-hospital death	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-

The numbers are presented as number (%).

DS = deep sedation; GA = general anesthesia.

*The variables included in the propensity score matching were persistent atrial fibrillation, atrial fibrillation duration from diagnosis to ablation, body mass index >30, and comorbidities including cerebrovascular accident, heart failure, hypertension, diabetes mellitus, coronary artery disease, and chronic kidney disease.

Table 4. Multivariable analysis for atrial tachyarrhythmias recurrence in matched cohort

	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
Age >65 years	0.90 (0.74–1.09)	0.275	0.97 (0.79–1.18)	0.760
AF duration	1.04 (1.02–1.07)	0.003	1.03 (1.00–1.06)	0.029
Persistent AF	2.44 (2.01–2.97)	<0.001	2.42 (1.98–2.95)	<0.001
BMI >30 kg/m ²	1.11 (0.82–1.50)	0.517	0.98 (0.72–1.34)	0.892
HF	1.10 (0.86–1.41)	0.441		
HTN	0.86 (0.71–1.04)	0.113	0.81 (0.67–0.98)	0.027
DM	0.94 (0.73–1.22)	0.652		
CVA	0.83 (0.59–1.16)	0.277	0.86 (0.61–1.21)	0.382
MI	1.14 (0.51–2.56)	0.747		
CAD	0.94 (0.62–1.40)	0.747		
CKD	1.04 (0.73–1.47)	0.829		
SSS	0.74 (0.45–1.21)	0.230		
MV disease	3.69 (1.75–7.79)	<0.001	2.35 (1.07–5.16)	0.033
HCMP	1.68 (0.99–2.86)	0.056	1.56 (0.91–2.67)	0.106
GA	1.00 (0.83–1.20)	0.985		

AF = atrial fibrillation; BMI = body mass index; CAD = coronary artery disease; CI = confidence interval; CKD = chronic kidney disease; CVA = cerebrovascular attack; DM = diabetes mellitus; GA = general anesthesia; HCMP = hypertrophic cardiomyopathy; HF = heart failure; HR = hazard ratio; HTN = hypertension; MI = myocardial infarction; MV = mitral valve; SSS = sick sinus syndrome.

Additionally, the incidence of major complications was similar between the DS and GA groups across both BMI categories (**Supplementary Table 2**).

DISCUSSION

In this multicenter study comparing DS and GA during cryoablation for AF, several key findings emerged. First, after propensity score matching, the recurrence rates of ATs were comparable between the DS and GA groups, suggesting that the choice of anesthesia strategy does not significantly impact long-term rhythm outcomes. Second, the incidence of major complications was low and similar across both groups, indicating comparable safety profiles for the 2 anesthesia approaches. Third, subgroup analysis by BMI demonstrated no significant interaction between obesity status and anesthesia strategy in terms of arrhythmia recurrence or major complications. Lastly, independent predictors of ATs recurrence

included longer AF duration, persistent AF, hypertension, and mitral valve disease rather than anesthesia type.

In the United States, GA is the predominant anesthesia method for RFCA of AF, while in Europe, clinical practice varies more widely, with GA, conscious sedation, and DS used in relatively equal proportions.¹⁵⁾ Some studies comparing sedation methods have reported no significant differences in respiratory stability or clinical outcomes.¹⁶⁾¹⁷⁾ However, other reports have suggested that GA may provide procedural advantages—particularly in RFCA—by improving catheter stability and enhancing clinical efficacy. These benefits are attributed to more accurate electroanatomical mapping, improved patient immobility, controlled respiratory patterns, and reduced thoracic motion, all of which contribute to more consistent catheter-endocardial contact and lesion formation.⁹⁾¹⁸⁾ These factors may be especially relevant for point-by-point RFCA, where stable contact and controlled energy delivery are crucial for durable lesion creation. However, cryoablation employs a single-shot balloon-based energy delivery system, which may be less dependent on fine catheter manipulation. Consequently, the potential advantages of GA may be less pronounced in the context of cryoablation, as supported by the findings of the present study.

Previous studies that included both RFCA and cryoablation patients have shown no clear superiority of GA over DS in terms of arrhythmia recurrence.¹⁹⁾ Similarly, in trials comparing GA and DS during cryoablation specifically, no significant differences have been reported in acute PV isolation success, 1-year arrhythmia recurrence, or the incidence of major complications.¹⁰⁾²⁰⁾ These findings may reflect the inherent characteristics of cryoablation, a single-shot technique in which the balloon catheter adheres firmly to the PV antrum during cryoenergy delivery. This adherence minimizes the effect of respiratory motion, potentially reducing the advantage of controlled ventilation under GA. This concept is further supported by findings from studies involving pulsed field ablation, another single-shot modality.²¹⁾²²⁾ In these studies, DS demonstrated efficacy and safety outcomes comparable to those of GA. Furthermore, the 2024 AF guidelines notes that although GA has traditionally been used during pulsed field ablation to reduce procedure-related pain and diaphragmatic contraction, recent studies have demonstrated that DS protocols can also be safe and effective in this context.⁵⁾ Given the procedural similarities between cryoablation and pulsed field ablation, it is reasonable to infer that DS might be sufficient and appropriate for single-shot ablation technologies.

In this cohort, the rate of major complications did not differ between the GA and DS groups. Transient phrenic nerve palsy occurred in 2.0% of cases, consistent with findings previously reported using the same registry.²³⁾ Notably, no cases progressed to permanent phrenic nerve injury. This finding is consistent with previous studies, which reported a transient phrenic nerve palsy incidence ranging from 2.7% to 10.7%, with no documented instances of permanent injury.²⁴⁾²⁵⁾

Evidence on the interaction between BMI and anesthesia strategy in AF ablation remains limited. One study reported a higher rate of arrhythmia recurrence in patients with BMI ≥ 40 undergoing RFCA, suggesting that obesity may negatively impact outcomes.²⁶⁾ Conversely, other research has shown that cryoablation can be performed safely and effectively under DS even in patients with BMI ≥ 40 .²⁷⁾ In our study, we performed a stratified analysis using a BMI cutoff of 30 and observed no significant differences in arrhythmia recurrence or major complications between anesthesia strategies in either BMI subgroup. These findings suggest that DS remains a feasible and effective option for cryoablation, even in patients with elevated BMI.

This study has several limitations. First, as a non-randomized, retrospective, registry-based analysis, the findings are subject to potential confounding, including unmeasured variables. Notable limitations are the lack of data regarding the use of antiarrhythmic drugs after cryoablation and detailed cryoablation parameters (such as time to isolation, nadir temperature, and thaw time). In particular, continued use of antiarrhythmic drugs beyond the blanking period may reduce the incidence of late AT recurrence, and the absence of this information may have influenced the observed recurrence rates.²⁸⁾ Nevertheless, all patients were managed post-ablation in accordance with current guidelines and the standard-of-care practices of their respective institutions, which likely mitigates this limitation. Second, the follow-up rhythm monitoring strategy could not be standardized across the 12 participating centers. Moreover, the use of intermittent monitoring is inherently limited by its reduced sensitivity for detecting sporadic arrhythmias, potentially leading to an underestimation of arrhythmia recurrence and an overestimation of arrhythmia-free survival. Furthermore, since AF recurrences are often asymptomatic,²⁹⁾ there is a possibility of under-detection, particularly among patients with paroxysmal AF. Although detailed information on the specific follow-up modalities used for each patient was not available, all institutions involved are tertiary care centers with routine implementation of guideline-based rhythm monitoring protocols.⁵⁾ This likely ensured a reasonably consistent detection of asymptomatic recurrences across the study cohort. Third, because the registry is retrospective in nature, echocardiographic data, including left atrial size, were incomplete, with approximately 300 cases missing. Because of this high rate of data loss, echocardiographic parameters were excluded from the main analyses. However, when left atrial size was incorporated despite missing values, the results in the matched cohort remained consistent, showing that the choice of sedation strategy (GA vs. DS) did not significantly influence AT recurrence (HR, 0.92; 95% CI, 0.77–1.12; $p=0.412$). Thus, although missingness limited the robustness of this analysis, the consistency of the findings supports the reliability of our main results. Fourth, due to the demographic characteristics of the enrolled population, the number of patients with a BMI ≥ 40 (i.e., very severe obesity) was very limited. This restricts the generalizability of our findings to extremely obese patients. However, the overall BMI distribution in this study is representative of the general East Asian population, and thus the findings remain relevant for clinical practice within this demographic context. Fifth, differences in sedation protocols and operator preferences among participating centers may have influenced procedural and clinical outcomes, potentially introducing residual confounding or selection bias that could not be fully adjusted for despite propensity score matching. Finally, since this study was not designed as an equivalence or non-inferiority trial, the comparable outcomes between the DS and GA groups should not be directly interpreted as evidence of equivalence or non-inferiority.

In this large, multicenter registry study, DS demonstrated comparable efficacy and safety to GA for cryoablation in patients with AF. DS is a feasible and effective alternative to GA in contemporary cryoablation practice, including among obese populations.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Baseline characteristics of matched cohort according to anesthesia strategy and BMI

Supplementary Table 2

Complications in matched cohort according to anesthesia strategy and BMI after PSM

Supplementary Figure 1

Volumes of cryoablation according to sedation strategy across participating centers.

Supplementary Figure 2

Distribution of propensity scores for the unmatched and matched cohorts and C-index of the propensity score model. C-index: 0.644. (A) Before matching; (B) After matching.

Supplementary Figure 3

Kaplan-Meier curve of ATs recurrence after cryoablation according to anesthesia strategy and BMI in matched cohort.

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