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CLINICAL RESEARCH

Comparative analysis of anaesthesia modalities in pulmonary vein isolation: insights from a prospective multicentre registry

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Aims

Atrial fibrillation (AF), the most common sustained arrhythmia in adults, is increasing in prevalence globally. Catheter ablation (CA), particularly pulmonary vein isolation (PVI), is a key treatment option. Pulmonary vein isolation can be performed using different energy sources, including cryoballoon ablation (CBA), radiofrequency ablation (RFA), or pulse field ablation. Anaesthesia modalities for these procedures include general anaesthesia (GA), deep sedation (DS), and conscious sedation (CS). However, the optimal anaesthesia modality remains unclear, as previous studies have shown mixed outcomes. This study aims to compare the safety and efficacy of different anaesthesia modalities in PVI.

Methods and results

This prospective, multicentre study, based on the Israeli Catheter Ablation Registry, evaluated the impact of different anaesthesia modalities on procedural outcomes and safety in AF ablation. Data from 1002 patients who underwent PVI between January 2019 and December 2021 across 14 centres were analysed. Patients were stratified by anaesthesia modality—CS vs. GA, with the latter encompassing DS. Key outcomes, including AF recurrence, procedural complications, and success rates, were evaluated over a 24-month follow-up period. Additionally, a sensitivity analysis was performed for the subgroup of patients who underwent CBA. Of the 1002 patients, 53% received GA, 6.3% DS, and 40% CS, with CBA used in 84% of cases. Complete PVI was achieved in 91% of patients, with comparable success rates observed between CS and GA groups. No significant differences were found between CS and GA modalities in terms of AF recurrence rates at 12 months (15% vs. 16%) and 24 months (19.5% vs. 21.2%), or in 12-month rehospitalization rates (19.8% vs. 16.5%). Sensitivity analysis of the CBA subgroup yielded similar results, with no significant differences in AF recurrence, complications, or procedural duration between CS and GA modalities.

Conclusion

Conscious sedation is as safe and effective as general anaesthesia in AF ablation, particularly with cryoablation. The choice of anaesthesia appears to be driven by patient characteristics and institutional factors without affecting long-term outcomes such as AF recurrence or complication rates.

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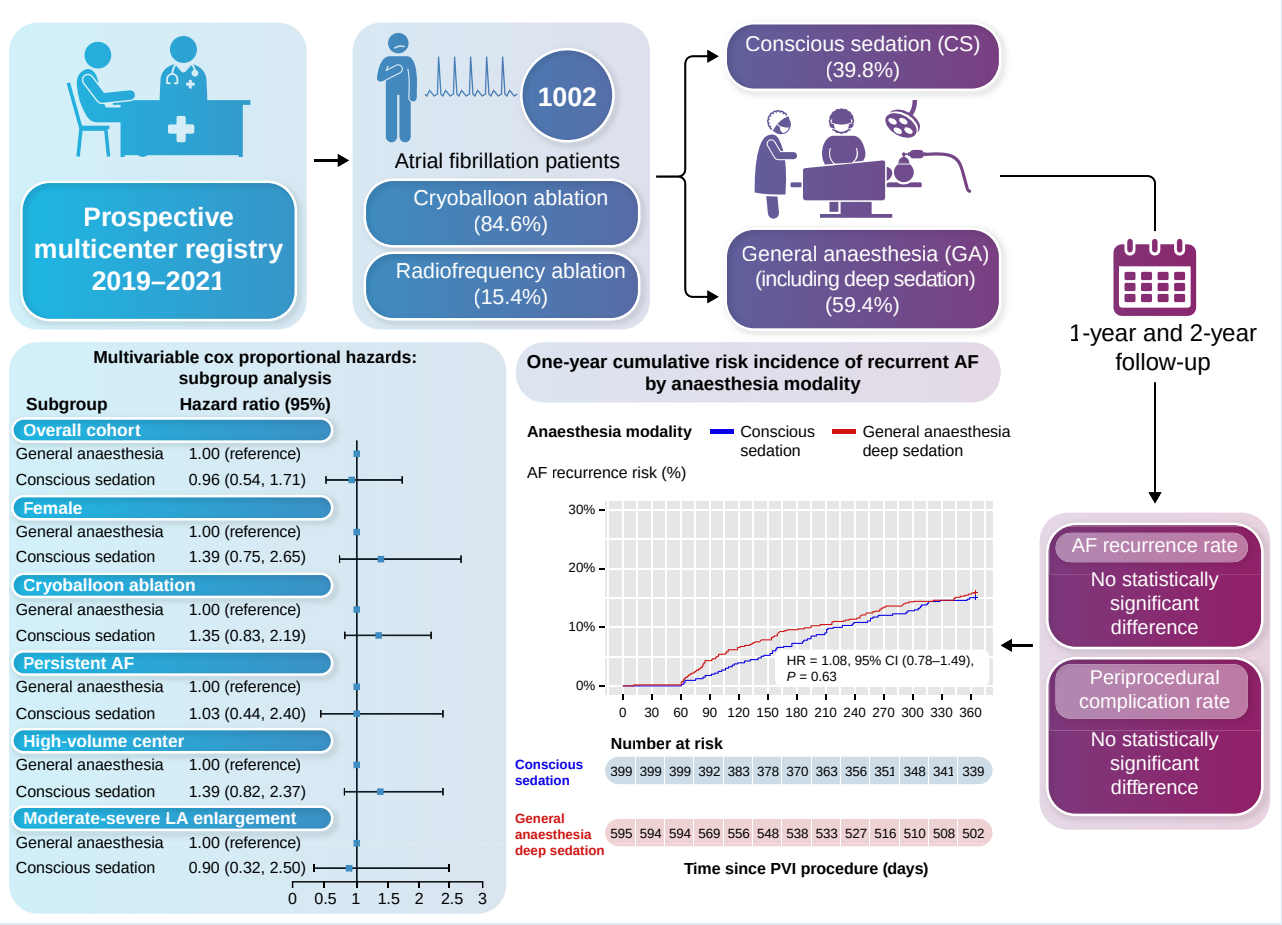
Graphical Abstract



Keywords Pulmonary vein isolation • Cryoballoon ablation • Radiofrequency ablation • General anaesthesia • Conscious sedation • AF recurrence

What's new?

- The decision-making process for selecting an anaesthesia modality in catheter ablation is not well established and is influenced by various factors, including patient characteristics, preferences, operator expertise, and resource availability. Previous studies have largely been retrospective, limited by small sample sizes, or focused primarily on radiofrequency energy procedures.
- Our prospective, multicentre study found no significant differences in procedural outcomes or complications between conscious sedation and general anaesthesia (including deep sedation), particularly in cases utilizing cryoballoon ablation.
- The selection of anaesthesia modality is influenced more by centre-specific and patient-specific characteristics rather than inherent procedural advantages.

Introduction

The incidence of atrial fibrillation (AF), the most frequently sustained cardiac arrhythmia in adults, is steadily increasing globally.[1–4] Several risk factors contributing to the development of AF have been identified.[5,6]

Catheter ablation (CA) has become a central component of AF treatment, leading to a substantial rise in AF ablation procedures over the past decade.[7–9] Pulmonary vein isolation (PVI), a technique that electrically isolates the left atrium (LA) from the pulmonary veins (PVs) to prevent AF triggers, is a key procedure. The two most commonly used energy sources for PVI are radiofrequency ablation (RFA) and cryoballoon ablation (CBA).[9,10] Recently, pulse field ablation (PFA) has emerged as an innovative technique, though its adoption remains less widespread compared to RFA and CBA.[11,12] Radiofrequency ablation delivers thermal ablation in a point-by-point fashion, typically using power levels ranging from 20 to 50 W, with the precision and depth of ablation points being critical for the success. In contrast, CBA involves placing a balloon at the PV antrum to create a circular ablation lesion using cryoenergy.[10]

Pulmonary vein isolation procedures can be conducted under general anaesthesia (GA), deep sedation (DS), or conscious sedation (CS). General anaesthesia has historically been favoured for its benefits, such as enhanced catheter stability during ablation and reduced patient mobility, discomfort, and anxiety.[10,13,14] As CBA for CA became widespread, several studies suggested that CS could be a viable alternative to GA, offering comparable efficacy and procedural complication rates while significantly reducing procedure time and eliminating anaesthesia complications. Nevertheless, the results have been inconsistent.[15–18]

Table 1 Baseline characteristics stratified by anaesthesia modality

Characteristic	Overall (*n* = 1002)	Conscious sedation (*n* = 399)	General anaesthesia[a] (*n* = 595)	*P*-value
Demographics				
Age, mean ± SD (yrs)	64.1 ± 11.3	64.24 ± 10.57	63.92 ± 11.79	0.66
Female sex, *n* (%)	374 (37.3)	153 (38.3)	221 (37.1)	0.75
BMI, mean ± SD (kg/m^2)	29.32 ± 5.39	29.47 ± 5.13	29.25 ± 5.56	0.55
Comorbidities				
Ischaemic heart disease, *n* (%)	172 (17.2)	68 (17.1)	104 (17.5)	0.94
Clinical HF (NYHA 2–4), *n* (%)	122 (12.3)	46 (11.6)	76 (12.9)	0.62
Ischaemic CM, *n* (%)	40 (4)	13 (3.3)	27 (4.5)	0.40
Non-ischaemic CM, *n* (%)	110 (11)	51 (12.8)	59 (9.9)	0.19
Hypertension, *n* (%)	629 (62.8)	260 (65.3)	369 (62.1)	0.33
Dyslipidaemia, *n* (%)	508 (50.7)	214 (53.6)	294 (49.4)	0.21
Diabetes mellitus, *n* (%)	257 (25.6)	111 (27.8)	146 (24.5)	0.28
Cerebrovascular accident, *n* (%)	90 (9)	21 (5.3)	69 (11.6)	<0.01
Thromboembolic event, *n* (%)	32 (3.2)	7 (1.8)	25 (4.2)	0.05
PVD, *n* (%)	38 (3.8)	17 (4.3)	21 (3.5)	0.67
Chronic obstructive pulmonary disease, *n* (%)	81 (8.1)	24 (6)	57 (9.6)	0.06
Obstructive sleep apnoea, *n* (%)	187 (18.7)	79 (20.1)	108 (18.2)	0.53
Atrial fibrillation characteristics				
AF type, paroxysmal, *n* (%)	644 (64.3)	270 (67.8)	374 (63.2)	0.15
Atrial flutter, *n* (%)	214 (21.4)	75 (19.4)	139 (23.6)	0.14
AF duration, mean ± SD (yrs)	4.11 ± 4.13	4.38 ± 4.41	3.94 ± 3.95	0.12
Prior cardioversion, *n* (%)	545 (54.4)	205 (51.4)	340 (57.1)	<0.01
Prior AF ablation, *n* (%)	70 (7)	28 (7.1)	42 (7.1)	>0.99
Chronic OAC, *n* (%)	872 (87)	353 (88.5)	519 (87.2)	0.46
Antiplatelet therapy, *n* (%)	66 (6.6)	27 (6.8)	39 (6.6)	0.99
Rate control medication, *n* (%)	662 (66.1)	290 (72.7)	372 (62.5)	<0.01
Pre-procedure AAD, *n* (%)	656 (65.5)	257 (64.4)	399 (67.1)	0.34
Failure of one AAD, *n* (%)	635 (63.4)	238 (59.6)	397 (66.7)	0.03
Failure of two AADs, *n* (%)	263 (26.2)	87 (21.8)	176 (29.6)	<0.01

AAD, antiarrhythmic drug; AF, atrial fibrillation; BMI, body mass index; CM, cardiomyopathy; HF, heart failure; IQR, interquartile range; kg, kilogram; NYHA, New York Heart Association; OAC, oral anticoagulant; PVD, peripheral vascular disease; SD, standard deviation; yrs, years.
[a]The general anaesthesia cohort includes the deep sedation subgroup.

The decision-making process for selecting an anaesthesia modality remains inadequately defined, with factors such as patient characteristics, preferences, operator expertise, and resource availability playing a role.[4,10,13,19] Most previous research has been retrospective or limited by small sample sizes.[15,16,20–22] To address these limitations, we conducted a prospective, multicentre study to evaluate procedural and outcome differences, focusing on safety and efficacy among the various anaesthesia modalities.

Methods

Study population

The Israeli Catheter Ablation Registry is a prospective, multicentre registry encompassing all patients who underwent AF ablation from January 2019 to December 2021 across 14 electrophysiology centres nationwide. This registry is a collaborative effort by the cardiac electrophysiology community and is managed by the Israeli Center for Cardiovascular Research. Ethical approval was obtained from the ethics committees of all participating institutions, and patients provided written consent. The registry collects demographic information, clinical characteristics, imaging reports, specific procedural data, and outcomes for each patient.

Data acquisition

All data were collected prospectively during the patient's initial hospital admission for ablation. The managing electrophysiologist entered the information into a secure, web-based electronic case report form using REDCap software, protected by a firewall and password. Collected variables included baseline patient characteristics (demographics, comorbidities, vital signs, lab results, and imaging reports), procedural history, and concurrent and prior medical therapy [including antiarrhythmic drugs (AADs), rate control, anticoagulation, and antiplatelet drugs]. Procedural specifics included ablation methodology, duration from skin to skin, PV anatomy, PV occlusion, nadir temperature, time to isolation, fluoroscopy duration, and immediate complications. Echocardiographic indices, such as left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD),

Table 2 Laboratory, electrocardiographic, echocardiographic, and procedural indices

Characteristic	Overall ($n = 1002$)	Conscious sedation ($n = 399$)	General anaesthesia[a] ($n = 595$)	*P*-value
Laboratory characteristics				
Creatinine, median [IQR] (mg/dL)	0.9 [0.8–1.06]	0.9 [0.8–1.05]	0.91 [0.8–1.06]	0.12
Haemoglobin, median [IQR] (g/dL)	13.8 [12.6–14.7]	13.6 [12.6–14.7]	13.80 [12.7–14.6]	0.57
Echocardiographic and electrocardiographic characteristics				
Bundle branch block, *n* (%)	86 (8.6)	29 (7.3)	57 (9.6)	0.19
LVEF, mean ± SD (%)	54.71 ± 10.43	56.14 ± 10.29	53.73 ± 10.44	<0.01
Left ventricular hypertrophy, *n* (%)	203 (20.3)	103 (25.8)	100 (16.8)	<0.01
Left atrial enlargement, *n* (%)	198 (19.8)	94 (23.6)	104 (17.5)	0.06
Left atrial size, mean ± SD (mm)	42.68 ± 8.81	42.68 ± 7.24	42.53 ± 9.63	0.83
sPAP, mean ± SD (mmHg)	32.69 ± 10.62	35.18 ± 10.54	31.12 ± 10.42	<0.01
Significant mitral regurgitation, *n* (%)	119 (11.9)	60 (15.0)	59 (9.9)	0.02
Significant mitral stenosis, *n* (%)	23 (2.3)	9 (2.4)	14 (2.5)	>0.99
Significant tricuspid regurgitation, *n* (%)	36 (3.6)	18 (4.5)	18 (3.0)	0.29
Procedural characteristics				
Energy source, n (%)				
Cryoballoon ablation, *n* (%)	841 (83.9)	352 (88.2)	489 (82.2)	0.01
Radiofrequency ablation, *n* (%)	153 (15.3)	47 (11.8)	106 (17.8)	0.01
Procedure duration, median [IQR] (min)	90 [60–120]	85 [60–120]	90 [60–125]	0.57
Sinus rhythm at admission, *n* (%)	666 (66.5)	281 (70.4)	385 (64.7)	0.07
High-volume centre, *n* (%)	582 (58.1)	90 (22.6)	492 (82.7)	<0.01

dL, decilitre; IQR, interquartile range; LVEF, left ventricular ejection fraction; mg, milligram; min, minutes; MR, mitral regurgitation; MS, mitral stenosis; sPAP, systolic pulmonary artery pressure; SD, standard deviation.
[a]The general anaesthesia cohort includes the deep sedation subgroup.

LA diameter, systolic pulmonary arterial pressure (sPAP), left ventricular hypertrophy (LVH), mitral regurgitation (MR), and tricuspid regurgitation (TR), were collected throughout the study.

Anaesthesia definitions and protocol

Mild or moderate sedation, also known as 'conscious sedation', refers to a state of reduced consciousness induced by anaesthetic drugs where patients can intentionally respond to verbal commands, either independently or with minimal tactile stimulation while maintaining spontaneous breathing and a patent airway. In contrast, deep sedation (DS) represents a deeper level of reduced consciousness, where patients are not easily aroused but still exhibit purposeful responses to painful stimuli. These patients may require ventilatory support or assistance in maintaining a patent airway, though endotracheal intubation is generally not necessary. General anaesthesia (GA), however, induces a state of complete unresponsiveness, even to painful stimuli. It is typically associated with impaired independent ventilatory function, often requiring positive pressure ventilation and assistance to maintain a patent airway, most commonly through the use of an endotracheal tube or a laryngeal mask.[23–25]

The study sedation protocol required obtaining informed consent for the selected anaesthesia modality and included an assessment of the patient's pre-procedural risk based on the American Society of Anesthesiologists classification system.[26]

As commonly accepted and based on the preceding definitions, GA and DS were grouped together due to their shared procedural characteristics, particularly regarding sedation depth and airway management, distinguishing them from CS.

In the GA group, the presence of an anaesthesiologist was required throughout the procedure. Anaesthetic management typically involves combinations of fentanyl, propofol, and midazolam. Muscle relaxants, such as rocuronium, and inhaled anaesthetics, including sevoflurane, were administered at the anaesthesiologist's discretion. In contrast, procedures under CS primarily relied on fentanyl, with low-dose midazolam added when necessary. These medications were administered by the electrophysiologist or trained cardiology nursing staff.

Follow-up protocol

Patients received prescriptions for oral anticoagulants for a minimum of 3 months post-ablation, with the continuation or discontinuation of anticoagulation and AADs determined by the treating physician. Follow-up care involved directly engaging patients and reviewing their clinical and hospital records upon readmission. Standard follow-up included outpatient visits at 3 to 6 months and then annually or earlier if symptoms suggestive of arrhythmia recurrence were observed. Patients underwent electrocardiograms (ECGs) and 48 h Holter monitoring during these visits. Documentation covered all occurrences of direct current (DC) cardioversions, repeat procedures, AAD usage, and both acute and chronic complications. Documented complications encompassed tamponade, thromboembolism, stroke, transient ischaemic attack, phrenic nerve paralysis, heart block, pericarditis, significant vascular issues requiring medical intervention or prolonged hospital stays, atrio-oesophageal fistulas, and mortality.

Outcomes

The primary efficacy endpoint was the confirmed AF recurrence lasting at least 30 s after the 8 weeks post-procedure blanking period.[10] Atrial fibrillation recurrences were verified through a clinical 12-lead ECG or an ambulatory monitor. Atrial fibrillation recurrences within the initial 8 weeks post-ablation were not considered when determining primary clinical recurrence. As previously mentioned, the cohort was divided into two groups based on the anaesthesia modality used: the CS group and the GA group, which also included DS.

Table 3 Procedural complications and outcomes stratified by anaesthesia modality

Characteristic	Overall ($n = 1002$)	Conscious sedation ($n = 399$)	General anaesthesia[a] ($n = 595$)	*P*-value
Peri-procedural outcomes/complications				
Isolation of all pulmonary veins, *n* (%)	915 (91.3)	363 (91)	552 (92.8)	0.36
Phrenic nerve palsy/injury, *n* (%)	70 (7)	26 (6.5)	44 (7.4)	0.69
Intra-procedural cardioversion, *n* (%)	305 (30.4)	130 (32.6)	175 (29.4)	0.54
Peripheral vascular events, *n* (%)	14 (1.4)	10 (2.5)	4 (0.7)	0.03
Neurologic events, *n* (%)	6 (0.6)	1 (0.3)	5 (0.8)	0.45
Pulmonary events, *n* (%)	2 (0.2)	0 (0)	2 (0.3)	0.66
Pericardial tamponade, *n* (%)	1 (0.1)	0 (0.0)	1 (0.2)	1
Combined peri-procedural complications, *n* (%)[b]	93 (9.3)	39 (9.8)	54 (9.1)	0.79
Sinus rhythm at discharge, *n* (%)	973 (97.1)	394 (98.7)	579 (97.3)	0.19
Anticoagulant therapy at discharge, *n* (%)	970 (96.8)	390 (97.7)	580 (97.5)	0.95
Rate control therapy at discharge, *n* (%)	595 (59.4)	251 (62.9)	344 (57.8)	0.27
Antiarrhythmic therapy at discharge, *n* (%)	704 (70.3)	281 (70.4)	423 (71.1)	0.22
Long-term outcomes				
Deceased within 12 months, *n* (%)	7 (0.7)	2 (0.5)	5 (0.8)	0.81
AF recurrence during blanking period, *n* (%)	83 (8.3)	34 (8.5)	49 (8.2)	0.97
AF recurrence within 12 months, *n* (%)	155 (15.5)	60 (15)	95 (16)	0.76
AF recurrence within 24 months, *n* (%)	204 (20.4)	78 (19.5)	126 (21.2)	0.59
Re-ablation within 12 months, *n* (%)	53 (5.3)	17 (4.3)	36 (6.1)	0.28
Rehospitalization within 12 months, *n* (%)	177 (17.7)	79 (19.8)	98 (16.5)	0.21
Cardiac-related, *n* (%)	132/177 (74.6)	61/79 (77.2)	71/98 (72.4)	0.29

AF, atrial fibrillation.
[a]The general anaesthesia cohort includes the deep sedation subgroup.
[b]Including phrenic nerve palsy/injury, neurologic events, pulmonary events, peripheral vascular events, and pericardial tamponade.

Statistical analysis

Statistical analyses were performed using two-tailed tests with a significance threshold set at a $P < 0.05$. Variables were characterized based on their attributes. Categorical variables were expressed as frequencies and percentages, with the χ^2 test or Fisher's exact test used to determine the significance of differences between groups.

The conformity of all variables to a normal distribution was assessed using the Kolmogorov–Smirnov test, QQ-plot visualization, and analysis of distribution and variance in residuals. Variables that followed a normal distribution were represented using means and standard deviations (SDs), and differences between groups were analysed using Student's *t*-test. In contrast, continuous variables that did not follow a normal distribution were described using medians and interquartile ranges (IQRs), covering the 25th to the 75th percentiles, with the Mann–Whitney *U* test used to assess significance.

We utilized a binomial multivariable regression model to identify specific predictors of the chosen anaesthesia modality. A multivariable Cox proportional hazards analysis was utilized to evaluate the relationship between anaesthesia modality and the primary endpoint of AF recurrence. Results were expressed as hazard ratios (HRs) with corresponding 95% confidence intervals (95% CIs). The model was adjusted for key clinically relevant variables, including demographic characteristics, comorbidities, and procedural factors. Additionally, subgroup analyses were conducted to further explore potential outcome variations across distinct patient groups.

A sensitivity analysis was conducted to assess the consistency of outcomes within the subgroup of patients who underwent CBA, which represented the majority of the cohort. Statistical analyses were conducted using SPSS statistical software version 27.0.0 (IBM, Armonk, NY, USA) and R software version 4.3.1 (The R Foundation).

Ethics and patient consent

Ethical approval was obtained from the ethics committees of all participating institutions, and patients provided written consent.

Results

Baseline cohort characteristics

The study cohort consisted of 1002 patients who underwent PVI between January 2019 and December 2021. Among them, 84.6% received CBA, while 15.4% underwent RFA. Regarding anaesthesia modality, 532 patients (53%) were administered GA, 63 (6.3%) received DS, and 399 (40%) were under CS, with the anaesthesia modality undocumented in eight patients (0.7%).

The mean age of participants was 64.1 ± 11.3 years, with females comprising 37.3% of the cohort. Approximately two-thirds of the patients had paroxysmal AF, with no statistically significant difference between the CS and GA groups (67.8% vs. 63.2%; $P = 0.15$). Chronic anticoagulation therapy was administered to 87% of the patients (in accordance with their thrombotic risk), and approximately two-thirds of the cohort was on AADs without significant differences among groups (64.4% vs. 67.1%; $P = 0.34$) (*Table 1*).

Comorbidities were generally consistent across the CS and GA groups, with a few notable differences. Patients in the GA group were more likely to have a history of cerebrovascular accident (CVA)

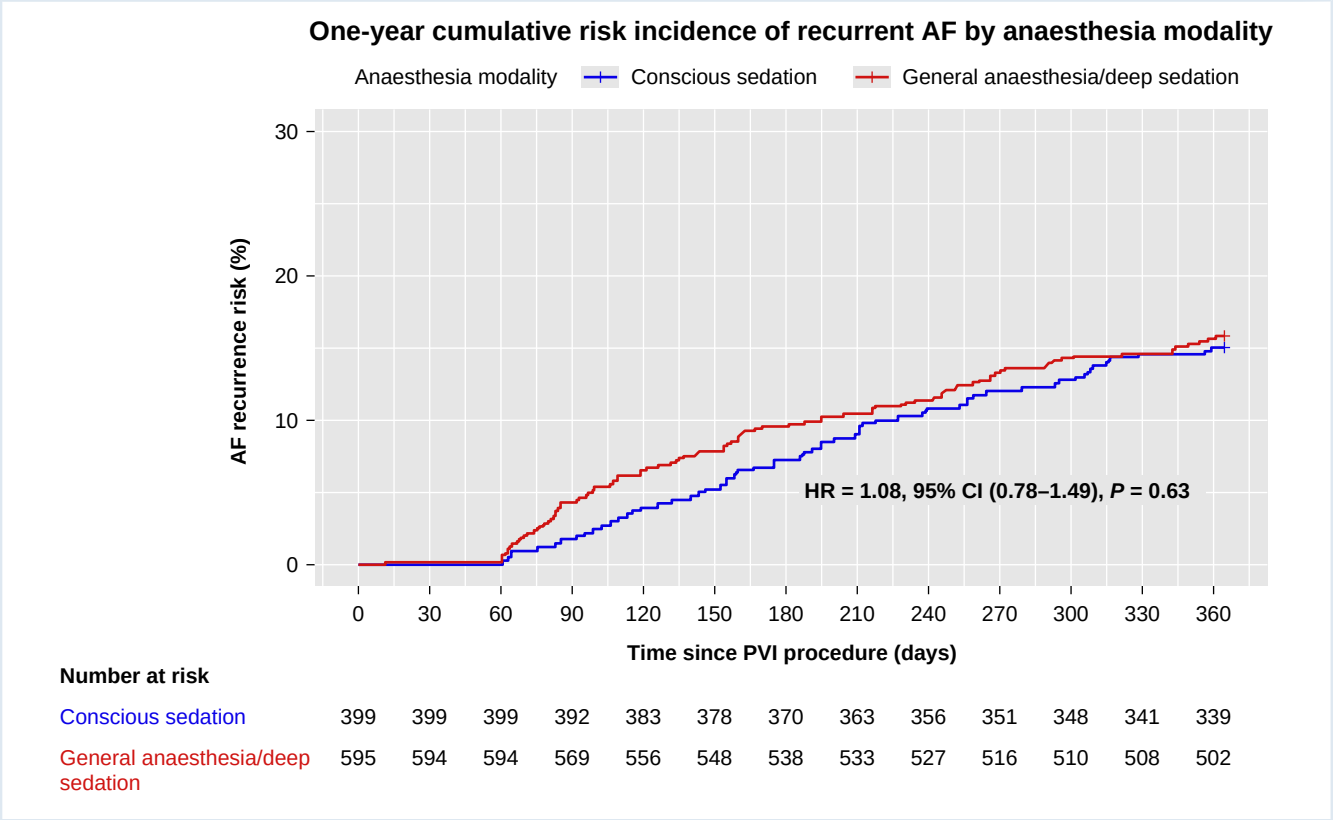


Figure 1 One-year cumulative risk incidence of atrial fibrillation recurrence stratified by anaesthesia modality. Kaplan–Meier survival curves depicting the 1-year cumulative risk of AF recurrence following PVI, stratified by anaesthesia modality. The upper curve represents general anaesthesia/deep sedation (GA/DS), while the lower curve shows conscious sedation (CS). The HR comparing GA to CS is 1.08 (95% CI: 0.78–1.49), with a *P*-value of 0.63, indicating no statistically significant difference in the risk of AF recurrence between the two groups. The lower panel shows the number of patients at risk over time for each group.

(11.6% vs. 5.3%; $P < 0.01$) and chronic obstructive pulmonary disease (9.6% vs. 6%; $P = 0.06$). Additionally, the GA group had a higher incidence of failure of AAD (66.7% vs. 59.6%; $P = 0.03$) (*Table 1*).

Pulmonary vein isolation procedures utilizing RFA were more likely to be performed using a GA strategy in comparison with CBA (69.3% vs. 58.1%; $P = 0.01$). The GA group typically included patients with lower LVEF (53.7 ± 10.4 vs. 56.1 ± 10.3; $P < 0.01$) and lower sPAP (31.1 ± 10.4 vs. 35.1 ± 10.5 mmHg; $P < 0.01$ (*Table 2*).

Procedural outcomes and complications

Isolation of all PVs was achieved in most of the patients (91.3%), with no statistically significant difference observed between the CS and GA groups (91% vs. 92.8%; $P = 0.36$) (*Table 3*). Vascular, neurological, and pulmonary complications were notably low overall (*Table 3*). Specifically, phrenic nerve palsy, primarily transient, occurred in 70 patients (7%), with no significant difference in incidence between the CS and the GA groups (7.4% vs. 6.5%, $P = 0.69$). The vast majority of patients (97.1%) were discharged in sinus rhythm and were prescribed anticoagulant therapy (96.8%) (*Table 3*).

Notably, the AF recurrence rate at 12 (15% vs. 16%, $P = 0.76$) and 24 months (19.5% vs. 21.2%, $P = 0.58$) did not differ significantly between both groups. Furthermore, the 12-month post-procedural rehospitalization rates were similar (19.8% vs. 16.5%; $P = 0.21$) (*Table 3*).

A cumulative risk analysis of AF-free survival demonstrated that GA had no significant impact on AF recurrence risk between the groups, with a crude HR of 1.08 (95% CI: 0.78–1.49; $P = 0.63$) (*Figure 1*). To account for potential baseline differences between both groups, a multivariate Cox proportional hazards regression analysis was performed to estimate the adjusted HR for AF recurrence. The model accounted for key variables, including age, female sex, clinical heart failure (HF), chronic obstructive pulmonary disease, prior CVA, LVEF, sPAP, AF duration, centre volume, and energy source. The analysis yielded an adjusted HR of 0.96 (95% CI: 0.54–1.71; $P = 0.89$), indicating no significant association between GA and AF recurrence.

Subgroup analysis

To ensure the consistency of the results across specific subgroups, an exploratory subgroup analysis was conducted using adjusted multivariable Cox hazards regression models. Subgroups analysed included females, CBA procedures, persistent AF, high-volume centres, and moderate-to-severe LA enlargement. The results indicate no significant differences in AF recurrence between anaesthesia modalities across the subgroups (*Figure 2*). For instance, in the CBA subgroup, the HR for CS was 1.35 (95% CI; 0.83–2.19), while in the persistent AF subgroup, the HR was 1.03 (95% CI: 0.44–2.40) (*Figure 2*).

Predictors of general anaesthesia selection

A binomial logistic regression model was employed to identify factors associated with the use of GA. The results, detailed in *Table 4*, indicate that GA selection was strongly influenced by the use of RFA as the procedural energy source and by procedures conducted at high-volume centres, with odds ratios (ORs) of 2.77 (95% CI: 1.72–4.35, $P < 0.01$) and 22.08 (95% CI: 15.5–31.9, $P < 0.01$), respectively. Additionally,

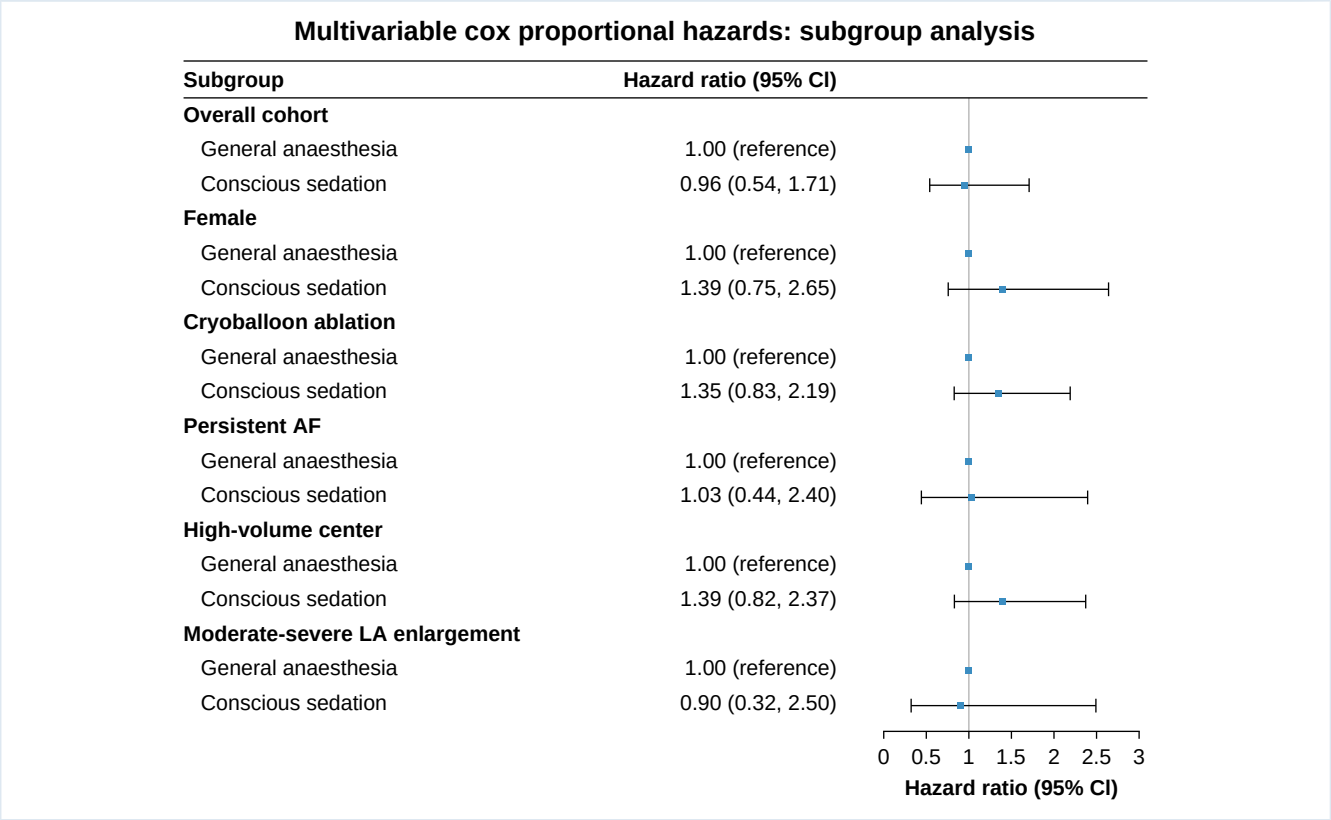


Figure 2 Subgroup analysis using multivariable cox proportional hazards model. Forest plot demonstrating the association between anaesthesia modality and AF recurrence for the entire cohort and separately for the subgroups: female sex, CBA, persistent AF, high-volume centre, and moderate-to-severe LA enlargement. The *x*-axis depicts HR with 95% CIs, while the *y*-axis represents the anaesthesia type across various subgroups. The analysis was adjusted for age, female sex, clinical HF, chronic obstructive pulmonary disease, prior CVA, LVEF, sPAP, AF duration, centre volume, and energy source. AF, atrial fibrillation; CVA, cerebrovascular accident; HR, hazard ratio; LA, left atrial; LVEF, left ventricular ejection fraction; sPAP, systolic pulmonary artery pressure.

Table 4 Predictors of GA/DS selection

Characteristic	OR	95% CI	*P*-value
Age	0.99	0.98–1.01	0.45
Female sex	1.35	0.94–1.94	0.11
Hypertension	0.86	0.58–1.28	0.47
Clinical heart failure	1.01	0.62–1.65	0.97
Ischaemic heart disease	1.36	0.85–2.19	0.20
Diabetes mellitus	0.98	0.66–1.45	0.90
Previous CVA	2.41	1.28–4.69	<0.01
Obstructive sleep apnoea	0.78	0.50–1.19	0.24
Chronic obstructive pulmonary disease	1.96	1.05–3.76	0.04
Persistent AF	2.08	1.42–3.03	<0.01
Radiofrequency ablation	2.77	1.72–4.35	<0.01
High-volume centre	22.08	15.51–31.95	<0.01

AF, atrial fibrillation; CI, confidence interval; CVA, cerebrovascular accident; DS, deep sedation; GA, general anaesthesia; OR, odds ratio.

the presence of persistent AF and a history of CVA were significantly associated with GA use, with ORs of 2.08 (95% CI: 1.42–3.03, $P < 0.01$) and 2.41 (95% CI: 1.28–4.69, $P < 0.01$), respectively.

Sensitivity analysis of procedural outcomes in the cryoballoon ablation group

In a sensitivity analysis that included patients who underwent CBA, the results were generally consistent with those observed in the overall cohort analysis (*Table 4*). Notably, there was no significant difference in complete PVI between the two groups (90.3% vs. 91.2%, $P = 0.76$). General anaesthesia did not offer any advantage in terms of procedural duration (median 80 min [IQR: 60–102] vs. 75 min [IQR: 60–120]; $P = 0.25$), peri-procedural complications (10.2% vs. 9.8%; $P = 0.93$) or 1-year AF recurrence rates (13.4% vs. 16%; $P = 0.34$) (*Table 5*).

Discussion

This prospective, multicentre study offers valuable insights into the anaesthetic modality used during PVI, supported by a large and diverse cohort that mirrors current real-world clinical practices. Our findings highlight the complex relationship between anaesthesia modality, patient

Table 5 Sensitivity analysis of patient characteristics and procedural outcomes in the CBA group

Characteristic	Overall (*n* = 848)	Conscious sedation (*n* = 352)	General anaesthesia[a] (*n* = 489)	*P*-value
Baseline characteristics				
Age, mean ± SD (yrs)	64.09 ± 11.4	64.02 ± 10.80	64.06 ± 11.88	0.96
Female sex, *n* (%)	317 (37.4)	133 (37.8)	184 (37.6)	>0.99
Clinical heart failure (NYHA 2–4), *n* (%)	97 (11.4)	33 (9.5)	64 (13.2)	0.12
Ischaemic cardiomyopathy, *n* (%)	38 (4.5)	11 (3.1)	27 (5.5)	0.14
Cerebrovascular accident, *n* (%)	76 (9)	20 (5.7)	56 (11.5)	<0.01
Chronic obstructive pulmonary disease, *n* (%)	67 (8)	21 (6)	46 (9.4)	0.09
Low volume centre, *n* (%)	338 (40)	269 (76.4)	69 (14.1)	<0.01
AF duration, median [IQR] (yrs)	3 [1–5]	3 [1–5]	2 [1–5]	0.17
Procedure duration, median [IQR] (min)	78 [60–112.75]	80 [60–102]	75 [60–120]	0.25
LVEF, mean ± SD (%)	54.85 ± 10.5	56.55 ± 10.08	53.61 ± 10.65	<0.01
sPAP, mean ± SD (mmHg)	32.3 ± 10.29	34.12 ± 9.57	31.04 ± 10.63	<0.01
Outcomes/complications				
Isolation of all pulmonary veins, *n* (%)	764 (90.1)	318 (90.3)	446 (91.2)	0.76
Phrenic nerve palsy/injury, *n* (%)	65 (7.6)	25 (7.1)	40 (8.2)	0.65
Combined peri-procedural complications, *n* (%)	84 (10)	36 (10.2)	48 (9.8)	0.93
AF recurrence within 12 months, *n* (%)	125 (14.7)	47 (13.4)	78 (16)	0.34
AF recurrence within 24 months, *n* (%)	169 (19.9)	62 (17.6)	105 (21.5)	0.19

AF, atrial fibrillation; CBA, cryoballoon ablation; IHD, ischaemic heart disease; IQR, interquartile range; min, minutes; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OSA, obstructive sleep apnoea; SD, standard deviation; sPAP, systolic pulmonary artery pressure; yrs, years.
[a]The general anaesthesia cohort includes the deep sedation subgroup.

characteristics, and procedural outcomes, revealing no significant difference in post-PVI AF recurrence rates between CS and GA or DS modalities.

The traditional preferential use of GA in patients undergoing PVI is particularly notable, mainly due to its benefits of greater stability during ablation, as well as reduced pain and anxiety.[10,21] However, recent reports indicate a growing trend towards adopting CS in recent years.[14] Several studies found that patients undergoing AF ablation using GA were more likely to achieve freedom from AF recurrence and had shorter procedure times.[16,21] Nonetheless, other studies have shown conflicting results regarding outcomes.[15,27–29]

In the current study, no significant differences were observed between the anaesthesia modalities regarding complete PVI, procedural complications, AF recurrence, or rehospitalization rates. While patients in the GA group appeared to have a higher comorbidity than those in the CS group, a multivariable adjustment showed no significant difference in the AF recurrence rate. Furthermore, a subgroup analysis demonstrated no outcome differences across various subgroups, reinforcing the overall reliability of the results.

Notably, CBA was the predominant energy source modality in our cohort, and within this sub-population, the rates of complete PVI, procedural complications, and AF recurrence were comparable. A recent multivariate analysis conducted by Mahmoodi *et al.*,[15] which included 300 patients with AF treated with CBA, also showed no association between anaesthesia modality and AF recurrence rate.

Conversely, most studies utilizing RFA have highlighted the benefits of using GA. Di Biase *et al.*[16] randomized 257 patients undergoing *de novo* RFA for paroxysmal AF to receive either CS or GA, with results showing GA to be associated with a higher likelihood of freedom from AF recurrence and shorter procedure times. Similarly, Stašková *et al.*[20] randomized 50 patients, reporting a higher success rate and shorter procedure times under GA. Conversely, Moravec *et al.*[22] conducted a small randomized controlled trial with RFA, demonstrating the non-inferiority of CS in AF recurrence, though it came at the expense of longer fluoroscopy times and increased radiofrequency energy. Additionally, Wang *et al.*[30] performed a retrospective analysis of 351 patients undergoing their first RFA and found no significant difference in freedom from atrial arrhythmia at 1 year between the CS and GA groups.

A recent retrospective analysis by Da Riis-Vestergaard *et al.*,[21] involving 7959 patients who underwent PVI between 2010 and 2018, demonstrated a reduction in AF recurrences in patients treated with GA. However, as the majority of patients underwent RFA, the generalizability of these results to those undergoing CBA remains uncertain. Finally, a meta-analysis conducted by Li *et al.*,[31] including some of these mentioned studies, found no significant differences between GA and CS concerning AF recurrence and complication rates.

The current study did not include patients treated with pulsed-field ablation due to its limited adoption during the study period. Pulsed-field ablation, a novel non-thermal technique based on irreversible electroporation, has gained prominence for its improved safety and efficiency in AF ablation.[32–34] Traditionally, GA has been the preferred sedation method for PFA to address procedural challenges such as diaphragm contractions and transient cough, as highlighted in the inspIRE trial, where GA was used in 73% of cases.[35] Emerging evidence suggests that optimized sedation protocols could also serve as a safe and effective alternative to GA.[11,12,36]

Our study shows that the selection between GA and CS is primarily driven by patient- and centre-specific factors. Patients with chronic obstructive pulmonary disease or persistent AF were more frequently administered GA, likely due to concerns about airway management,

maintaining catheter stability during ventilation, and the need for a more controlled procedural environment. Additionally, the most significant factors favouring the use of GA were the employment of RFA and procedures performed at high-volume centres, likely due to the availability of anaesthesiologists and the complexity of the procedures.

Limitations

Despite the numerous strengths of our study, including the integration of the latest updates to the blanking period definition and the AF ablation consensus document in our statistical analysis,[10] several limitations must be acknowledged. First, as a registry-based study rather than a randomized controlled trial, variations in patient care across different centres may have introduced biases. Second, although the cohort only included procedures using both CBA and RFA procedures, it was predominantly composed of patients undergoing CBA, limiting the generalizability of the findings to RFA-treated patients. Third patients treated with PFA were not included, as this modality had not yet been widely adopted in clinical practice during the study period. Fourth, the study's follow-up period was limited to 24 months, which may have overlooked late recurrences or complications.

Conclusion

The current study demonstrates that CS during AF CA is as safe and effective as GA, particularly when using CBA for PVI. These findings offer valuable insights into the use of tailored sedation approaches in catheter-based PVI procedures.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL *et al.* Heart Disease and Stroke Statistics-2023 Update: a report from the American Heart Association. *Circulation* 2023;**147**:e93–621.
2. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM *et al.* 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation. *J Am Coll Cardiol* 2024;**83**:109–279.
3. Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nat Rev Cardiol* 2014;**11**:639–54.
4. Van Gelder IC, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, Crijns HJGM *et al.* 2024 ESC guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2024; **45**:ehae17636.
5. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. *JAMA* 1994;**271**:840–4.
6. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. *Circulation* 2017;**136**:583–96.
7. Poole JE, Bahnson TD, Monahan KH, Johnson G, Rostami H, Silverstein AP *et al.* Recurrence of atrial fibrillation after catheter ablation or antiarrhythmic drug therapy in the CABANA trial. *J Am Coll Cardiol* 2020;**75**:3105–18.
8. Ngo L, Ali A, Ganesan A, Woodman R, Adams R, Ranasinghe I. Ten-year trends in mortality and complications following catheter ablation of atrial fibrillation. *Eur Heart J Qual Care Clin Outcomes* 2022;**8**:398–408.
9. Boersma L, Andrade JG, Betts T, Duytschaever M, Pürerfellner H, Santoro F *et al.* Progress in atrial fibrillation ablation during 25 years of europace journal. *Europace* 2023;**25**:euad244.
10. Tzeis S, Gerstenfeld EP, Kalman J, Saad EB, Sepehri Shamloo A, Andrade JG *et al.* 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol* 2024;**26**: euae043.
11. 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. *Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol* 2023;**25**: euad230.
12. Grimaldi M, Quadrini F, Caporusso N, Troisi F, Vitulano N, Delmonte V *et al.* Deep sedation protocol during atrial fibrillation ablation using a novel variable-loop biphasic pulsed field ablation catheter. *Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol* 2023;**25**:euad222.
13. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L *et al.* 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace* 2018;**20**:e1–160.
14. Garcia R, Waldmann V, Vanduynhoven P, Nesti M, Jansen De Oliveira Figueiredo M, Narayanan K *et al.* Worldwide sedation strategies for atrial fibrillation ablation: current status and evolution over the last decade. *Europace* 2021;**23**:2039–45.
15. Mahmoodi E, Leitch J, Davies A, Leigh L, Oldmeadow C, Dwivedi J *et al.* The importance of anaesthesia in atrial fibrillation ablation: comparing conscious sedation with general anaesthesia. *Indian Pacing Electrophysiol J* 2023;**23**:47–52.
16. Di Biase L, Conti S, Mohanty P, Bai R, Sanchez J, Walton D *et al.* General anesthesia reduces the prevalence of pulmonary vein reconnection during repeat ablation when compared with conscious sedation: results from a randomized study. *Heart Rhythm* 2011;**8**:368–72.
17. Weinmann K, Heudorfer R, Lenz A, Aktolga D, Rattka M, Bothner C *et al.* Safety of conscious sedation in electroanatomical mapping procedures and cryoballoon pulmonary vein isolation. *Heart Vessels* 2021;**36**:561–7.
18. Tohoku S, Schmidt B, Bordignon S, Chen S, Bologna F, Chun JKR. Initial clinical experience of pulmonary vein isolation using the ultra-low temperature cryoablation catheter for patients with atrial fibrillation. *J Cardiovasc Electrophysiol* 2022;**33**:1371–9.
19. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C *et al.* 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2021;**42**:373–498.
20. Stašková K, Bulava A, Tesařík R, Toušek F. Radiofrequency catheter ablation of atrial fibrillation performed under general anesthesia: results of a unicentric randomized trial. *Vnitr Lek* 2017;**63**:163–9.
21. Da Riis-Vestergaard L, Tønnesen J, Ruwald MH, Zörner CR, Middelfart C, Hein R *et al.* General anaesthesia compared to conscious sedation for first time atrial fibrillation catheter ablation—a Danish nationwide cohort study. *Europace* 2024;**26**:euae203.
22. 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. *Biomed Pap Med Fac Univ Palacky Olomouc Czechoslov* 2021;**165**:162–8.
23. An Updated Report by the American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 2002;**96**:1004–17.
24. Statement on Continuum of Depth of Sedation: Definition of General Anesthesia and Levels of Sedation/Analgesia [Internet]. [cited 2024 Nov 24]. Available from: https://www.asahq.org/standards-and-practice-parameters/statement-on-continuum-of-depth-of-sedation-definition-of-general-anesthesia-and-levels-of-sedation-analgesia
25. Green SM, Irwin MG, Mason KP. The international committee for the advancement of procedural sedation. Procedural sedation: providing the missing definition. *Anaesthesia* 2021;**76**:598–601.
26. Doyle DJ, Hendrix JM, Garmon EH. American society of anesthesiologists classification In: *Statpearls [internet]*. Treasure Island (FL): StatPearls Publishing; 2024. Available from: http://www.ncbi.nlm.nih.gov/books/NBK441940/
27. 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 Vessels* 2017;**32**:997–1005.
28. 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**:935–42.
29. Li A, Chen Y, Wang W, Su L, Ling Z. Association of clinical predictors with recurrence of atrial fibrillation after catheter ablation. *Ann Noninvasive Electrocardiol* 2020;**25**:e12787.
30. 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. *Clin Cardiol* 2021; **44**:218–21.
31. Li KHC, Sang T, Chan C, Gong M, Liu Y, Jesuthasan A *et al.* Anaesthesia use in catheter ablation for atrial fibrillation: a systematic review and meta-analysis of observational studies. *Heart Asia* 2019;**11**:e011155.
32. Reddy VY, Gerstenfeld EP, Natale A, Whang W, Cuoco FA, Patel C *et al.* Pulsed field or conventional thermal ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2023;**389**: 1660–71.
33. Di Monaco A, Vitulano N, Troisi F, Quadrini F, Romanazzi I, Calvi V *et al.* Pulsed field ablation to treat atrial fibrillation: a review of the literature. *J Cardiovasc Dev Dis* 2022;**9**:94.

34. Reddy VY, Neuzil P, Koruth JS, Petru J, Funosako M, Cochet H *et al.* Pulsed field ablation for pulmonary vein isolation in atrial fibrillation. *J Am Coll Cardiol* 2019;**74**: 315–26.
35. Duytschaever M, De Potter T, Grimaldi M, Anic A, Vijgen J, Neuzil P *et al.* Paroxysmal atrial fibrillation ablation using a novel variable-loop biphasic pulsed field ablation catheter integrated with a 3-dimensional mapping system: 1-year outcomes of the multicenter inspIRE study. *Circ Arrhythm Electrophysiol* 2023;**16**:e011780.
36. Rillig A, Hirokami J, Moser F, Bordignon S, Rottner L, Shota T *et al.* General anaesthesia and deep sedation for monopolar pulsed field ablation using a lattice-tip catheter combined with a novel three-dimensional mapping system. *Europace* 2024;**26**:euae270.