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Jet Ventilation and Hemodynamic Stability During Pulmonary Vein Isolation: Ventilatory and Hemodynamic Outcomes from A Randomized Controlled Trial (Secondary Analysis under EEG-Guided Total Intravenous Anesthesia)

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Abstract

Background: High-Frequency Jet Ventilation (HFJV) improves catheter stability and shortens procedure time during pulmonary vein isolation (PVI) for atrial fibrillation. This study reports predefined secondary outcomes assessing the ventilatory and hemodynamic safety of HFJV under total intravenous anesthesia (TIVA).

Methods: In this prospective, single-blind randomized controlled trial, 149 adult patients undergoing catheter-based PVI were assigned to HFJV or conventional volume-controlled ventilation. All patients received a standardized TIVA protocol guided by EEG-based depth monitoring. Secondary outcomes included arterial blood gases, hemodynamic tolerance (mean arterial pressure area under the curve <65 mmHg [$AUC_{NIBPM65}$] and root mean square <65 mmHg [$RMS_{NIBPM65}$]), vasopressor use, vasoactive-inotropic score (VIS), and recovery time.

Results: Normocapnia was maintained in both groups, with comparable post-procedural $PaCO_2$ values (p = 0.085). However, $PaCO_2$ >45 mmHg occurred more frequently in the HFJV group (18.7% vs 4.1%, p = 0.01). Oxygenation was preserved, with no desaturation events in either arm ($AUCSpO_2$<90%: 0 %·min in both groups) and no difference in PaO_2 (p = 0.14). HFJV was associated with significantly lower hypotension exposure (AUCNIBP<65: 12,255 vs 46,232 mmHg·min; p = 0.007) and reduced severity (RMSNIBP<65: 0.7 vs 2.2 mmHg; p = 0.011), while vasopressor use (p = 0.077), VIS (p = 0.10), lactate (p = 0.60), and recovery time (53 vs 54 min; p = 0.70) were similar.

Conclusions: Under TIVA with EEG guidance, HFJV was associated with lower cumulative exposure to mild intraoperative hypotension than conventional ventilation during PVI, while maintaining adequate oxygenation and overall normocapnia. The absolute magnitude of the hemodynamic difference was small, and these exploratory, hypothesis-generating findings should be confirmed in trials powered on patient-centered hemodynamic endpoints.

Trial registration: This manuscript is reported in accordance with the CONSORT 2010 statement where applicable. Australian New Zealand Clinical Trials Registry ACTRN12623000982617, registration effective September 8, 2023, retrospective relative to enrollment. https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=385792

Keywords: Electrophysiology, Cardiology Lab, High-Frequency Jet Ventilation, Haemodynamic stability, Hypercapnia, Oxygenation

Background

Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia, affecting an estimated 59 million individuals worldwide[1] and contributing to over 300,000 annual deaths globally[2]. It is associated with significantly increased risks of stroke[3], heart failure[4], myocardial infarction[5], and all-cause mortality. AF has also been associated with cognitive decline and dementia[6], further underscoring the burden of the disease. Early diagnosis and timely intervention can substantially reduce these complications[7].

Catheter ablation within one year of diagnosis has been shown to reduce arrhythmia recurrence[8, 9]. Earlier interventions provide additional benefits: ablation within six months decreases healthcare utilization[10], and when performed within three months in patients on direct oral anticoagulant therapy, it reduces the risk of death, stroke, and major bleeding by up to 50%, with a 55% reduction in all-cause mortality over three years[11].

High-Frequency Jet Ventilation (HFJV) enhances catheter stability during left atrial ablation[12, 13], improving effective lesion delivery and reducing arrhythmia recurrence[12]. It also shortens pulmonary vein isolation (PVI) procedure times[14], which may help alleviate treatment delays. However, widespread adoption of HFJV remains limited due to equipment constraints and safety concerns—such as hypoventilation, barotrauma, and airway dehydration—outlined in expert consensus statements[15].

These concerns stem from outdated or non-representative studies. A 1983 ARDS trial even reported more barotrauma with conventional ventilation than HFJV [16], and evidence from rigid bronchoscopy under HFJV [17] has little relevance to PVI. Importantly, most reported complications occurred in non-intubated patients, whereas AF ablation with HFJV is performed in intubated patients under controlled airway conditions. Endotracheal intubation maintains airway patency, substantially reduces the risk of upper airway barotrauma, and prevents gastric insufflation, as gas is delivered directly into the endotracheal tube. Some electrophysiology studies linked HFJV to longer PACU recovery[18], but these comparisons confounded ventilation with anesthetic technique (propofol vs sevoflurane), limiting their relevance.

When combined with appropriate humidification and ventilatory monitoring, HFJV can reduce complications such as hypoventilation-induced respiratory acidosis and airway dryness[19]. Nevertheless, high-quality prospective data evaluating its anesthetic safety during PVI remain limited.

This randomized controlled trial was originally designed to evaluate cardiac endpoints, including pulmonary vein isolation time, first-pass isolation rate, total radiofrequency duration, average impedance drop, and mean contact force during ablation. The present analysis addresses pre-

specified secondary outcomes related to anesthetic safety, focusing on respiratory and hemodynamic parameters. By applying a strictly standardized propofol-based TIVA protocol and rigorous EEG-guided titration, the study aims to minimize between-group variability in anesthetic depth and drug exposure, while acknowledging that ventilation mode intrinsically affects intrathoracic pressure, venous return, and coronary perfusion pressure, and that these effects cannot be dissociated from the ventilation strategy under investigation[20].

Materials and Methods

Methods

This study was approved by the Ethics Committee of CHU UCL Namur - site Godinne (reference number: B0392022000094; approved December 27, 2022). The study protocol, including all primary and secondary outcomes and the complete statistical analysis plan, was finalized on November 28, 2022, prior to ethics submission and prior to the enrollment of the first patient on January 30, 2023. The trial was submitted to the Australian New Zealand Clinical Trials Registry on June 23, 2023, and registration was effective on September 8, 2023 (ACTRN12623000982617); registration was therefore retrospective relative to enrollment, owing to administrative processing delays. A subset of patients had consequently already been enrolled at the time of submission and at the time of registration confirmation. No database lock, no unblinding, and no interim analysis were performed during this period; no primary or secondary outcome was added, removed, or modified between the ethics-approved protocol and the final analysis; and the independent statistician was blinded to group allocation throughout. Written informed consent was obtained from all participants prior to enrollment. Patients and members of the public were not involved in the design, conduct, or reporting of the trial.

Recruitment

A parallel-group, single-blind, randomized controlled trial was conducted at CHU UCL Namur in Yvoir, Belgium, a tertiary university teaching hospital. All catheter ablation procedures were performed in a dedicated cardiac catheterization laboratory specialized in interventional electrophysiology.

Eligible participants were adult patients (≥18 years) with documented paroxysmal or persistent atrial fibrillation scheduled for PVI via radiofrequency catheter ablation. Exclusion criteria included prior AF ablation, severe chronic obstructive pulmonary disease (COPD GOLD stage 4), previous lung transplantation, cystic fibrosis, primary ciliary dyskinesia, or any other condition associated with mucociliary dysfunction. Additional exclusion criteria comprised corrected complex congenital heart disease, morbid obesity (body mass index > 40 kg/m^2), and known soy allergy, which contraindicates the use of propofol.

Data Management

Study data were collected and managed using REDCap® (Research Electronic Data Capture, Vanderbilt University, Nashville, Tennessee, USA), a secure, web-based platform hosted at CHU UCL Namur[21, 22]. REDCap® provides a user-friendly interface for validated data entry, audit trails for

tracking modifications and exports, automated procedures for data export to standard statistical software, and functionalities for integration with external sources.

Randomization and Blinding

After obtaining written informed consent, eligible patients were enrolled by one of the two interventional cardiologists (BR or OX). Patients were then randomized in a 1:1 ratio to either the HFJV or volume-controlled ventilation (VCV) group using a REDCap®-generated allocation sequence. Randomization was stratified by operator (BR or OX), atrial fibrillation type (paroxysmal or persistent), and left atrial volume on CT scan (<75 mL, 75–100 mL, >100 mL).

The trial followed a parallel-group, single-blind design with blinded outcome analysis. Allocation concealment was maintained until after induction of anesthesia and confirmation of complete neuromuscular blockade. Participants were blinded to group allocation; however, blinding of anesthesiologists and interventional cardiologists was not feasible due to inherent differences in ventilation management and the distinct acoustic signatures of the techniques. All statistical analyses were performed by an independent statistician who remained blinded to group assignment.

Anesthetic Management

To minimize variability, all patients received a standardized anesthetic protocol with sufentanil, propofol TIVA (Schnider model), and rocuronium. Depth of anesthesia was continuously titrated using processed-EEG monitoring (NeuroSENSE®), ensuring adequate hypnosis (slow/alpha activity, BIS-equivalent 40–60) while minimizing hemodynamic impact. Hemodynamic management targeted a mean arterial pressure >65 mmHg (ephedrine first-line, phenylephrine or norepinephrine if required). Non-invasive blood pressure was measured automatically at a fixed 2.5-minute cycling interval in all patients and throughout the entire procedure; invasive arterial monitoring is not part of the standard of care for elective PVI in hemodynamically stable patients at our institution and was not used. Ephedrine was administered exclusively as intravenous boluses (3–9 mg). Although the written protocol permitted continuous phenylephrine infusion at the anesthesiologist's discretion, no patient actually received phenylephrine as an infusion; phenylephrine was administered exclusively as intravenous boluses. Norepinephrine, when required, was administered as a continuous infusion. Intraoperative fluid administration was not protocolized and was left to the attending anesthesiologist's discretion. After intubation and initial VCV (7 mL/kg IBW, PEEP 5 cmH_2O), patients were randomized after transseptal puncture to continue VCV (control) or receive HFJV (intervention). Full protocol details are provided in Appendix 1.

Study Outcomes

All primary and secondary endpoints were pre-specified in the registered study protocol before the initiation of patient enrollment, ensuring consistency in data collection and analysis throughout the trial. There were no changes to trial outcomes after the trial commenced.

Primary outcomes

The primary outcomes focused on procedural metrics related to PVI, including: (1) total ablation time; (2) time required to achieve complete isolation of all four pulmonary veins; and (3) acute procedural success, defined as confirmed electrical isolation of all pulmonary veins.

These primary outcomes are presented in a separate manuscript.

Secondary outcomes

The present article reports exclusively on pre-specified secondary outcomes related to anesthetic management. These included intraoperative respiratory and hemodynamic parameters, assessed by ABG analyses obtained immediately after transseptal puncture and just before catheter removal, as well as continuous monitoring data extracted from anesthesia records. All secondary endpoints were defined a priori in the study protocol.

Data were documented immediately after the procedure using a standardized form completed jointly by the cardiologist and the anesthesiologist, and cross-validated against the anesthesia records and electrophysiology system logs. The comparison of ventilation strategies was strictly limited to the PVI phase, defined as the interval between transseptal puncture and withdrawal of the ablation catheter from the left atrium.

Assessment of Ventilatory Mode Impact on Gas Exchange

To assess the impact of ventilation mode on gas exchange, ABG samples were collected from the left atrium at two standardized time points: immediately after transseptal access and just before catheter withdrawal at the end of the ablation procedure. Hypercapnia was evaluated based on changes in $PaCO_2$ between these two time points. Oxygenation was assessed by comparing PaO_2 values and by calculating the area under the curve (AUC) for peripheral oxygen saturation (SpO_2) < 90% (AUC_{SpO2_90}). Desaturation was defined as any recorded SpO_2 value below 90% during the procedure.

Assessment of Hemodynamic Impact

Hemodynamic impact was assessed using two complementary metrics: (1) The area under the curve ($AUC_{NIBPM65}$) for mean arterial pressure (MAP) values below 65 mmHg, which reflects the cumulative exposure to hypotension, taking into account both how long and how far the MAP remained under the threshold; (2) The root mean square ($RMS_{NIBPM65}$) of MAP values below 65 mmHg, which captures the average severity of hypotension episodes, regardless of their duration. Specifically, $RMS_{NIBPM65}$

was calculated as the square root of the mean squared difference between 65 mmHg and all MAP values falling below this threshold. Unlike $AUC_{NIBPM65}$, which increases with both time and depth of hypotension, $RMS_{NIBPM65}$ provides a normalized index of the average severity of hypotension, independently of time. It reflects how low the pressure dropped, on average, during hypotensive episodes. For instance, an $RMS_{NIBPM65}$ of 3 mmHg means that, during periods when MAP was <65 mmHg, values were on average 3 mmHg below that threshold — regardless of how long the hypotension lasted. Clinically, this helps distinguish between a brief drop to 50 mmHg and a sustained plateau at 63 mmHg: both might yield similar AUCs but would be clearly differentiated by $RMS_{NIBPM65}$.

Vasopressor use was analyzed both as a binary variable (presence or absence of administration) and as a continuous variable using the vasoactive inotropic score (VIS)[23]. Finally, arterial lactate levels were measured from left atrial blood samples obtained immediately after transseptal access and at the end of the ablation procedure.

Assessment of Ventilatory Mode Impact on recovery room length of stay

To evaluate the impact of the ventilation mode on recovery time, recovery room length of stay was defined as the interval between patient admission to the post-anesthesia care unit (PACU) and the anesthesiologist's authorization for discharge to the ward. This authorization was granted once the patient had achieved an Aldrete score of 14 or higher and reported no significant postoperative pain.

Harms

Adverse event ascertainment was not systematic. The trial was designed around procedural (cardiological) endpoints and the case report form did not include a formal, graded, structured adverse event capture framework (CTCAE or MedDRA). Clinical events were captured only when they became apparent during the intraoperative or immediate postoperative period, without pre-specified definitions or severity grading, and were cross-validated against the anesthesia record and the electrophysiology system log. This approach does not meet the CONSORT Harms extension standard, and the present analysis is therefore not designed to support formal claims of safety. The harms section reports descriptive observations only.

Statistical Analysis

Based on prior estimates of procedural duration, a 15-minute reduction was anticipated with HFJV. The calculated sample size of 150 patients, equally randomized between groups, yielded a statistical power of 63% to detect this anticipated difference in the primary cardiologic endpoint. Although adequate for the original objective, this power is limited for secondary analyses focused on anesthetic and hemodynamic outcomes. All analyses were conducted according to the intention-to-treat principle, and no protocol deviations or crossovers occurred during the study.

Arterial oxygen and carbon dioxide tensions (Pa_{O_2} and Pa_{CO_2}) were expressed in mmHg; peripheral oxygen saturation (Sp_{O_2}) was expressed as a percentage. The time-weighted AUC for SpO_2 < 90% was reported as a % · min. Lactate values were expressed in mmol/L. Hemodynamic parameters were evaluated through the time-weighted AUC for mean arterial pressure (MAP) < 65 mmHg, expressed in mmHg·min, and the root mean square (RMS) of MAP < 65 mmHg.

To normalize vasopressor usage across anesthesiologists, ephedrine administration was converted into phenylephrine equivalents using a validated conversion factor (1 mg ephedrine = 81.2 µg phenylephrine)[24].

Between-group comparisons were performed using the Wilcoxon rank-sum test for continuous variables and chi-square or Fisher's exact test for categorical variables, as appropriate. Post-procedural values adjusted for baseline were analyzed using analysis of covariance (ANCOVA), including the baseline (pre-PVI) value as a covariate and ventilation group as the main predictor.

The vasoactive-inotropic score was calculated per Gaies et al. [23] from continuous infusions only. Bolus ephedrine and bolus phenylephrine were not included in the VIS, consistent with the original score specification, which applies to continuous infusions of dopamine, dobutamine, epinephrine, norepinephrine, milrinone, and vasopressin. In this trial, phenylephrine was administered exclusively as intravenous boluses; although the written protocol permitted continuous phenylephrine infusion at the anesthesiologist's discretion, no patient received it as an infusion. For the descriptive comparison of cumulative vasopressor exposure, ephedrine doses were converted to phenylephrine equivalents using a validated factor (1 mg ephedrine = 81.2 µg phenylephrine [24]), but this conversion was not used in the VIS calculation.

The time-course analyses of Sp_{O_2} and non-invasive MAP (NIBPM) were performed using generalized least squares (GLS) regression models with a first-order autoregressive correlation structure and restricted cubic splines (with 3 knots for Sp_{O_2} and 5 knots for MAP). The number of knots was selected based on minimization of the Akaike Information Criterion.

All analyses were conducted using R software version 4.4.1 (The R Foundation for Statistical Computing, Vienna, Austria, 2024). Data visualization was performed with the *ggplot2* package; group comparisons with *gtsummary*; and GLS modeling with restricted splines using the *rms* package.

A nominal two-sided p-value below 0.05 was considered statistically significant for each individual test. All between-group comparisons of secondary anesthetic endpoints are reported as exploratory and hypothesis-generating; no single secondary endpoint was designated as confirmatory, and no formal hierarchy of outcomes was pre-specified. In accordance with the CONSORT 2025 statement and the ICH E9(R1) guideline on multiplicity in clinical trials, a formal false discovery rate sensitivity analysis was applied to the nine interpretable between-group comparisons of secondary anesthetic outcomes (the AUC SpO_2 <90 % endpoint was excluded because the outcome was constant in both arms and no valid p-value is computable); adjusted values are reported in Supplementary Table S1.

No a priori power calculation was performed for the anesthetic endpoints: the trial was powered on the primary cardiological endpoint, and the present analysis is under-powered for detecting clinically meaningful differences in anesthetic and hemodynamic outcomes.

No interim analyses were conducted.

Missing data

Missing data were minimal and occurred in a small number of arterial blood gas variables. Out of 149 patients analyzed, the following pre- and post-procedural measurements were missing:

$PaCO_2$ Pre-PVI: 1/149 (VCV group: 1/74)

$PaCO_2$ Post-PVI: 1/149 (VCV group: 1/74)

PaO_2 Pre-PVI: 1/149 (VCV group: 1/74)

PaO_2 Post-PVI: 2/149 (VCV group: 1/74; HFJV group: 1/75)

Lactate Pre-PVI: 1/149 (VCV group: 1/74)

Lactate Post-PVI: 1/149 (VCV group: 1/74)

Given the very low frequency of missing values, no imputation method was applied, and complete case analysis was performed. The small number of missing observations is unlikely to have introduced significant bias.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT® (OpenAI, San Francisco, California, USA) and Claude (Anthropic, San Francisco, California, USA) to enhance the quality of the English scientific writing, terminological consistency, and the preparation of the point-by-point response to reviewers. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Results

Participant flow

Between January 30, 2023, and September 17, 2024, a total of 150 adult patients (≥18 years) were enrolled in this parallel-group randomized controlled trial (Figure 1). Participants were allocated in a 1:1 ratio to either the HFJV group (intervention) or VCV group (control). One patient in the control arm withdrew consent after randomization, leaving 149 patients available for analysis. Baseline characteristics of the patients are presented in Table 1. No significant differences were observed between groups at baseline. No protocol deviations were observed throughout the study. Mean procedure duration time was 79 minutes in the HFJV arm and 90 minutes in the VCV arm.

Anesthetic outcomes are presented in Table 2, while Table 3 provides adjusted comparisons based on ANCOVA analyses.

Assessment of Ventilatory Mode Impact on CO_2 Gas Exchange

Pre-PVI $PaCO_2$ values were similar between the HFJV and VCV groups: 37 mmHg [34–43] vs 38 mmHg [36–41], respectively (p = 0.40). Post-PVI $PaCO_2$ values also showed no significant difference: 38 mmHg [34–45] in the HFJV group vs 38 mmHg [35–40] in the VCV group (p = 0.30). In the ANCOVA, pre-PVI $PaCO_2$ was a significant predictor of post-PVI $PaCO_2$ (β = 0.46; 95% CI [0.30–0.63]; p < 0.001). After adjustment, post-PVI $PaCO_2$ was 1.6 mmHg higher on average in the HFJV group compared to VCV, but this difference was not statistically significant (β = 1.6; 95% CI [–0.21 to 3.3]; p = 0.085). However, when applying a clinical threshold ($PaCO_2$ >45 mmHg), hypercapnia occurred more frequently in the HFJV group than in the VCV group (18.7% vs 4.1%, p = 0.011).

Assessment of Ventilatory Mode Impact on O2 Gas Exchange

Pre-PVI PaO_2 values were comparable between the HFJV and VCV groups: 138 mmHg [97 to 230] vs 154 mmHg [112 to 193], respectively (p > 0.90). Post-PVI PaO_2 values were also similar: 190 mmHg [133 to 238] in the HFJV group vs 175 mmHg [123 to 207] in the VCV group (p = 0.20). In ANCOVA, pre-PVI PaO_2 was significantly associated with post-PVI PaO_2 (β = 0.39; 95% CI [0.27–0.50]; p < 0.001). After adjustment, the HFJV group had a 15 mmHg higher post-PVI PaO_2 compared to VCV, although the difference was not statistically significant (β = 15; 95% CI [–4.9 to 35]; p = 0.14). The $AUC_{SpO2\_}90$ was 0 %·min in both groups; no episode of peripheral oxygen desaturation below 90 % was observed in either arm (no p-value is reported because the outcome was constant in both groups).

Baseline lactate levels were similar between groups: 0.70 mmol/L [0.60 to 0.90] in the HFJV group vs 0.70 mmol/L [0.60 to 0.80] in the VCV group (p = 0.90). Post-PVI lactate values also did not differ significantly: 0.70 mmol/L [0.50 to 0.90] in HFJV vs 0.60 mmol/L [0.60 to 0.70] in VCV (p > 0.90). In ANCOVA, pre-PVI lactate levels were strongly associated with post-PVI values (β = 0.64; 95% CI [0.51–

0.76]; p < 0.001), but no significant intergroup difference was observed after adjustment (β = –0.01; 95% CI [–0.04 to 0.07]; p = 0.60).

Figure 2 displays heatmaps of all individual SpO_2 values over time for the HFJV (A) and VCV (B) groups. Smoothed saturation trends with 95% confidence intervals (C) were derived from the same dataset. The widening of the confidence bands near the end reflects a reduced number of observations due to variable procedural durations.

Assessment of Ventilatory Mode Impact on Hemodynamic Stability

Exposure to hypotension, measured by the $AUC_{NIBPM65}$, was significantly lower in the HFJV group than in the VCV group: 12,255 mmHg·min [0 to 61,806] vs 46,232 mmHg·min [0 to 130,239], respectively (p = 0.007). Severity of hypotension, evaluated using $RMS_{NIBPM65}$, was also significantly reduced in the HFJV group: 0.7 mmHg [0.0 to 3.6] compared to 2.2 mmHg [0.0 to 7.6] in the VCV group (p = 0.011).

The proportion of patients requiring vasopressors was not significantly different: 22/75 (29%) in the HFJV group vs 32/74 (43%) in the VCV group (p = 0.077). Similarly, Vasoactive inotropic scores (VIS) remained low in both groups, with no statistically significant difference: 0.00 [0.00 to 0.02] in the HFJV group vs 0.00 [0.00 to 0.03] in the VCV group (p = 0.10). Importantly, no patient in the HFJV group required conversion to conventional ventilation due to hemodynamic instability.

Figure 3 displays heatmaps of all individual NIBPM values over time for the HFJV (A) and VCV (B) groups. Smoothed NIBPM trends with 95% confidence intervals (C) were derived from the same dataset. The widening of the confidence bands near the end reflects a reduced number of observations due to variable procedural durations.

Assessment of Ventilatory Mode Impact on recovery room length of stay

Recovery room stay duration was similar between groups: 53 minutes [44 to 71] in the HFJV group versus 54 minutes [45 to 70] in the VCV group, with no statistically significant difference (p = 0.70).

Harms

Adverse event ascertainment was not systematic. Clinical events were captured only when they became apparent during the intraoperative or immediate postoperative period, without pre-specified definitions or severity grading, and were cross-validated against the anesthesia record and the electrophysiology system log. Within these limitations, no intraoperative conversion from HFJV to conventional ventilation for hemodynamic, respiratory, or airway reasons was performed, no pericardial effusion requiring drainage or cardiopulmonary resuscitation was recorded, and no immediately apparent postoperative complication leading to unplanned intensive care admission or to delayed hospital discharge was documented. These observations are descriptive and should not be interpreted as formal safety evidence.

Discussion

Atrial fibrillation, the most common supraventricular tachyarrhythmia, carries substantial cardiovascular risk[1]. Early detection and intervention help mitigate these risks[7], yet procedural delays often reduce the efficacy of such approaches. HFJV has been shown to improve catheter stability[12, 13], reduce recurrence[12], and shorten procedural time[14]. Despite these benefits, its broader use remains limited by equipment constraints and safety concerns[15], largely derived from older, non-representative studies and settings unrelated to PVI[16, 17]. This study compared HFJV and VCV during PVI under a standardized anesthesia protocol, ensuring ventilation mode was the only variable.

HFJV maintained overall $PaCO_2$ stability, with occasional hypercapnia exceeding 45 mmHg

Pre- and post-PVI $PaCO_2$ levels were comparable between groups, with no statistically significant differences. ANCOVA showed a mean $PaCO_2$ increase of 0.46 mmHg, with no significant difference between ventilation modes after baseline adjustment. The use of predefined HFJV settings, combined with standardized end-tidal carbon dioxide ($EtCO_2$) maneuvers every 30 minutes, ensured that $PaCO_2$ remained within clinically acceptable limits—despite the absence of continuous ABG or transcutaneous carbon dioxide ($PtCO_2$) monitoring. Nevertheless, when applying a clinical threshold of $PaCO_2$ >45 mmHg, hypercapnia occurred more frequently in the HFJV group than in the VCV group, suggesting that although average levels were comparable, a subset of patients exposed to HFJV may be more prone to exceed conventional safety thresholds.

An additional consideration supports cautious interpretation of the dichotomized $PaCO_2$ analysis. Pre-PVI $PaCO_2$ >45 mmHg was already numerically higher in the HFJV arm at baseline (13.3% versus 6.8%, p = 0.29), reflecting a non-significant but directional imbalance. When post-PVI $PaCO_2$ was analyzed as a continuous variable with ANCOVA adjustment for pre-PVI values (Table 3), the between-group difference was not statistically significant (β = 1.6 mmHg, 95% CI –0.21 to 3.3, p = 0.085). This suggests that part of the signal captured by the dichotomized analysis is attributable to the pre-existing baseline asymmetry rather than to a HFJV-specific incremental effect.

The dichotomized result should therefore be interpreted as a clinically-oriented, secondary, hypothesis-generating observation. More generally, dichotomization of a continuous variable reduces statistical efficiency and introduces an arbitrary threshold[25]; it is reported here only because the 45 mmHg cutoff has a specific clinical alert function in our institutional HFJV protocol.

The dichotomized result should therefore be interpreted as a clinically-oriented, secondary, hypothesis-generating observation rather than as confirmatory evidence.

Previous reports of hypercapnia during HFJV were mainly drawn from longer procedures or from different clinical settings [12, 26]. In our study, mean procedure duration was 79 minutes in the HFJV arm and 90 minutes in the VCV arm, which is comparable to durations reported in high-volume electrophysiology centers [27, 28] and in interventional radiology, where HFJV is routinely employed [29-31]. Our findings therefore support the feasibility and overall respiratory safety of HFJV in procedures of approximately 1.5 hours—representative of moderate duration in this context—particularly in high-throughput centers [27, 28].

CO_2 monitoring during HFJV remains challenging, as $EtCO_2$ underestimates $PaCO_2$ due to incomplete washout and the open-circuit configuration of the system [32, 33]. Although $PtCO_2$ monitoring has been shown to correlate more closely with $PaCO_2$ and to detect earlier rises in carbon dioxide levels [34, 35], it was not available in our study. Instead, $EtCO_2$ was assessed every 30 minutes after a standardized maneuver [36], providing reliable trends but limited temporal resolution. The observation of occasional hypercapnia in the HFJV group underscores the potential value of more frequent or continuous monitoring, ideally using $PtCO_2$, to detect early deviations and further optimize ventilation strategies in this context [34].

HFJV preserved adequate oxygenation throughout the procedure.

Oxygenation parameters remained high and stable throughout the procedure in both ventilation groups. Post-procedural PaO_2 was 15 mmHg higher with HFJV after baseline adjustment, but not statistically significant. The AUC_{SpO2_90} remained null in both groups, indicating the absence of desaturation events and confirming adequate oxygenation control with both ventilation strategies. These findings are consistent with previous studies conducted in interventional radiology settings[30, 31, 37].

The time-course analysis of oxygen saturation (Figure 2) further supports this stability: both groups consistently maintained values above 90%.

Lactate levels, a surrogate marker of tissue perfusion and metabolic stress, also remained low and stable throughout the procedure. No significant difference was found between groups at baseline or post-ablation. As expected, baseline lactate strongly predicted post-procedural values, but the type of ventilation did not significantly influence lactate dynamics.

Taken together, these findings suggest that despite the use of a moderate inspired oxygen fraction (FiO_2 50%), systemic oxygen delivery and metabolic homeostasis were effectively preserved under both ventilation strategies.

HFJV was associated with lower cumulative exposure to mild intraoperative hypotension than volume-controlled ventilation.

HFJV was associated with a more favorable hemodynamic profile compared to VCV. Exposure to intraoperative hypotension, assessed by the AUCNIBPM65 was nearly four times lower in the HFJV group. Similarly the RMSNIBPM65, reflecting the integrated severity of hypotension over time, was approximately three times lower in the HFJV group than in the VCV group. These findings are consistent with a directionally lower exposure to mild intraoperative hypotension under HFJV. However, the absolute magnitude of the between-group difference in average severity (RMS<65: 0.7 versus 2.2 mmHg) was small. The highly skewed distributions with near-zero medians in both arms suggest that the between-group difference in AUC<65 is largely driven by a subset of patients with prolonged or severe hypotensive exposure, rather than reflecting a uniform group-level difference (HFJV: range 0–262,771 mmHg·min; VCV: range 0–279,969 mmHg·min). No statistically significant difference was observed in vasoactive-inotropic score (VIS) or in the proportion of patients receiving vasopressors (29% HFJV vs 43% VCV, p = 0.077). These findings should therefore be interpreted as associations, not as confirmatory evidence of a clinical benefit. The AUC MAP <65 mmHg and RMS MAP <65 mmHg comparisons also survived the formal multiplicity correction applied as a sensitivity analysis (Supplementary Table S1).

The apparent discordance between higher hypotension exposure in the VCV group and the absence of a statistically significant difference in vasopressor use or VIS warrants careful interpretation. Several non-mutually exclusive mechanisms likely contribute. First, the trial was not powered for vasopressor-based endpoints; the 14-percentage-point absolute difference in vasopressor administration is directionally consistent with the AUC signal but did not reach statistical significance. Second, the binary nature of the vasopressor-use variable (one observation per patient, regardless of the number of hypotensive episodes) inherently limits its sensitivity relative to AUC-based metrics, which integrate every MAP excursion below threshold across the entire procedural window. This difference in measurement granularity rather than a true contradiction between endpoints likely underlies the apparent discordance. Consistent with this interpretation, the proportion of patients experiencing at least one MAP < 65 mmHg episode (derived from AUC<65 > 0) was 52% in the HFJV group versus 74% in the VCV group, a directional pattern congruent with both the AUC signal and the vasopressor-use trend, and further supporting the hypothesis that the non-significant vasopressor result reflects insufficient power rather than a true null effect. Third, the VIS as defined by Gaies et al. was validated for continuous infusions[23]; bolus ephedrine and bolus phenylephrine, which dominated vasopressor use in this cohort, are not captured by this score. Finally, although we cannot formally exclude under-treatment of hypotension in the VCV arm, identical hemodynamic targets and an identical escalation sequence applied in both arms. Taken together, AUC and RMS metrics reflect cumulative physiological exposure, whereas VIS and the binary vasopressor-use variable reflect pharmacological intervention for sustained hypotension; the two should be viewed as complementary rather than contradictory.

Time-course analysis of NIBPM further supports these observations. The heatmap (Figure 3) shows a dense cluster of pressure measurements between 70 and 90 mmHg in both groups. However, the

smoothed trajectories (Figure 3) reveal consistently higher MAP values in the HFJV group from approximately 20 minutes onward, suggesting more sustained arterial pressure.

This comparison was made possible by the strict standardization of anesthetic management. The use of processed EEG-guided titration has been shown to reduce anesthetic drug consumption[38], thereby minimizing the hemodynamic impact of total intravenous anesthesia with propofol.

When delivered at appropriate working pressures to ensure adequate oxygenation while maintaining normocapnia, distal HFJV, administered just proximal to the carina, may produce lower mean intrathoracic pressures than conventional ventilation[39, 40]. This physiological characteristic facilitates venous return, increases left ventricular stroke volume, and reduces left ventricular filling pressures[41]—an especially relevant advantage in atrial fibrillation, where preload is already compromised by the absence of coordinated atrial contraction. These mechanisms may partly explain the improved hemodynamic tolerance observed in our study.

Our results contrast with the limited existing literature, which reports higher rates of hypotension under HFJV compared to conventional ventilation[18, 42]. However, those two studies were retrospective, involved longer procedures, and used heterogeneous anesthetic protocols (e.g., sevoflurane vs. TIVA), limiting direct comparison[42]. In our trial, anesthesia was strictly standardized using EEG-guided TIVA, ensuring balanced depth and minimizing the hemodynamic impact of propofol. This methodological rigor likely accounts for the improved hemodynamic stability observed and suggests that previously reported hypotension associated with HFJV may reflect suboptimal anesthetic management rather than a ventilation-related effect.

Taken together, our results suggest that HFJV may contribute to improved hemodynamic stability during left atrial ablation. This reduced hypotension exposure may benefit vulnerable patients and warrants confirmation in larger trials.

HFJV did not prolong recovery room stay.

Recovery room stay duration was comparable between groups, with no significant difference observed between HFJV and VCV.

A large retrospective study published in 2024 reported prolonged recovery time associated with HFJV[18]. However, such findings have not been consistently reproduced in short-duration procedures—particularly those comparable in length to ours[43-45]—especially when anesthetic depth is rigorously controlled using processed electroencephalographic monitoring[38]. In our study, recovery room stay duration appeared unaffected by the ventilation strategy alone.

Implications of the whole study together for the field

In this prospective randomized trial conducted under rigorously EEG-guided total intravenous anesthesia and $EtCO_2$-monitored ventilation, HFJV was associated with lower cumulative exposure to mild intraoperative hypotension and preserved gas exchange compared with conventional VCV. These ventilatory and hemodynamic observations are exploratory and hypothesis-generating. Because adverse event ascertainment was not systematic, our findings do not establish safety in a formal sense, but they support the feasibility of HFJV as an alternative ventilation strategy for PVI when integrated with a standardized anesthetic protocol.

Limitations of our study

This study has several methodological limitations. First, its single-center design may limit the generalizability of the findings. However, strict adherence to the predefined protocol and analysis according to the intention-to-treat principle helped preserve internal validity. Second, blinding of cardiologists and anesthesiologists to group allocation was not feasible, but the use of a rigorously standardized anesthetic and procedural protocol minimized the risk of performance or detection bias.

Most importantly, this analysis reports exclusively on pre-specified secondary outcomes. The original sample size calculation was based on cardiological endpoints rather than anesthetic parameters, and randomization was stratified according to cardiological criteria. As a result, potential imbalances in anesthetic-related factors cannot be entirely ruled out, although no differences were observed between groups regarding major patient comorbidities likely to influence hemodynamics or gas exchange. In addition, although a written anesthesia protocol was applied, minor deviations related to individual anesthesiologist practice may have occurred. Together, these factors limit the statistical robustness and external validity of findings related to hemodynamic and respiratory endpoints.

The trial was submitted to the ANZCTR after enrollment had begun, reflecting an administrative delay rather than a protocol modification; the study protocol and statistical analysis plan were finalized and approved by the Ethics Committee prior to the first inclusion. We acknowledge this as a formal limitation relative to the CONSORT recommendation for prospective public registration, while noting that the scientific integrity of the pre-specified outcomes was ensured by the prior ethics approval process.

Adverse event ascertainment was non-systematic and did not use a formal graded framework (CTCAE or MedDRA). Our observations therefore do not meet the requirements of the CONSORT Harms extension and should not be cited as confirmatory safety evidence for HFJV. A future trial powered on anesthetic endpoints should incorporate prospective, structured adverse event capture with pre-specified definitions and severity grading.

The comparison involved nine interpretable between-group tests of secondary anesthetic endpoints, and no a priori hierarchy was pre-specified. All comparisons are therefore reported as exploratory

and hypothesis-generating. A formal false discovery rate sensitivity analysis, conducted in accordance with CONSORT 2010 and ICH E9(R1) recommendations, is provided in Supplementary Table S1; only the AUC MAP <65 mmHg, RMS MAP <65 mmHg, and dichotomized $PaCO_2$ >45 mmHg comparisons remained below the conventional threshold after correction.

Hemodynamic monitoring relied on non-invasive blood pressure cycling every 2.5 minutes rather than on beat-to-beat invasive arterial measurement. This sampling frequency limits the temporal resolution of our hemodynamic endpoints and may under-capture transient, rapidly corrected hypotensive events. Because the cycling interval was identical across arms, this limitation is not expected to systematically favor either group but may reduce overall sensitivity. Intraoperative fluid administration was not protocolized and was left to the attending anesthesiologist's discretion. Although the procedural context makes major between-group imbalances unlikely, we cannot formally exclude differences in crystalloid loading that may have contributed to the hemodynamic findings. Similarly, mode-intrinsic physiological effects of HFJV (lower mean intrathoracic pressure, altered venous return) cannot be dissociated by design from the ventilation strategy itself. Finally, the vasoactive-inotropic score was validated for continuous infusions and does not capture bolus ephedrine or bolus phenylephrine, which dominated vasopressor support in this cohort; the VIS therefore under-represents the pharmacological rescue of mild transient hypotension in our dataset, which may explain the discordance between AUC/RMS signals and VIS/vasopressor-use comparisons. Lastly, mode-intrinsic physiological effects of HFJV (lower mean intrathoracic pressure, altered venous return, coronary perfusion pressure) cannot be dissociated by design from the ventilation strategy itself.

Ideas for future research

Future investigations could explore comparisons with high-frequency low-tidal volume ventilation (HFLTV), a strategy typically implemented using respiratory rates of 25–30 breaths per minute and tidal volumes of 3–3.5 mL/kg[46]. HFLTV appears to be gaining preference in centers without access to jet ventilation devices and may represent a viable alternative for procedures requiring minimal thoracic excursion and stable respiratory conditions. However, its effects on intrathoracic pressure and hemodynamic stability in the specific context of left atrial ablation remain insufficiently documented and warrant further investigation.

Importantly, the hemodynamic trends observed, particularly the marked reduction in hypotension exposure in the HFJV group, suggest a potential hemodynamic advantage. These findings merit further investigation. Prospective multicenter trials with adequate statistical power and a primary focus on anesthetic and hemodynamic outcomes are warranted to confirm and extend these observations.

Conclusions

In this randomized controlled trial, HFJV during left atrial ablation under EEG-guided TIVA was associated with lower cumulative exposure to mild intraoperative hypotension than VCV, with preserved oxygenation, overall normocapnia, and a comparable recovery room length of stay. The absolute magnitude of the hemodynamic difference was small, and the proportion of patients requiring vasopressors did not differ significantly between arms. These findings derive from pre-specified secondary endpoints in a trial powered on cardiological outcomes, with non-systematic adverse event ascertainment; they are therefore exploratory and hypothesis-generating and do not constitute confirmatory safety evidence. Prospective trials powered on patient-centered anesthetic endpoints, with structured adverse event capture and direct comparison with emerging alternatives such as HFLTV, are warranted.

List of abbreviations

ABG, arterial blood gas

AF, atrial fibrillation

ANCOVA, Analysis of covariance

AUC, area under the curve

HFJV, high-frequency jet ventilation

IBW, ideal body weight

MAP, mean arterial pressure

PVI, pulmonary vein isolation

RMS, root mean square

TIVA, total intravenous anesthesia

VCV, volume-controlled ventilation

VIS, Vasoactive-Inotropic Score

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

Ethics approval and consent to participate :

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of CHU UCL Namur - site Godinne (reference number: B0392022000094). The trial was registered retrospectively in the Australian New Zealand Clinical Trials Registry on September 8, 2023 (ACTRN12623000982617); see Methods for the full protocol chronology. Written informed consent was obtained from all participants prior to enrollment. This manuscript is reported in accordance with the CONSORT 2010 statement where applicable.

Consent for publication

Not applicable

Availability of data and materials

The individual participant data (IPD) generated and/or analyzed during the current study are not publicly available due to privacy considerations but are available from the corresponding author upon reasonable request.
De-identified IPD may be shared with researchers who submit a methodologically sound proposal and whose aims are consistent with the approved scientific objectives of the study. Access will be possible from 6 months to 5 years after publication of the main results and is subject to prior approval by the Principal Investigator.

Conflicts of Interest

The authors declare that they have no competing interests.

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Author contributions: CRediT

Adrien Maseri: Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing. **Laurent Bairy:** Data curation, Formal analysis, Investigation, Software, Writing – review & editing. **Benoît Bihin:** Formal analysis, Resources, Visualization, Writing – original draft. **Fabien Dormal:** Data curation. **Benoît Collet:** Data curation, Investigation. **Michaël Hardy:** Investigation, Writing – review & editing. **Quentin Delhez:** Investigation, Writing – review & editing. **Philippe Dubois:** Writing – review & editing. **Olivier Xhaët:** Investigation. **Benoît Robaye:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – review & editing.

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Declaration of generative AI in scientific writing

During the preparation of this work, the authors used ChatGPT® (OpenAI, San Francisco, California, USA) and Claude (Anthropic, San Francisco, California, USA) to enhance the quality of the English scientific writing, terminological consistency, and the preparation of the point-by-point response to reviewers. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Figures, tables and additional files

Figure 1. CONSORT Flow Diagram

Figure 2. Heatmap of individual peripheral oxygen saturation (SpO_2) values over time for (A) the High Frequency Jet Ventilation (HFJV) and (B) Volume Controlled Ventilation (VCV) groups. The blue and red lines represent the mean SpO_2 values in both groups, respectively. (**C**) Smoothed time-course of peripheral oxygen saturation (SpO_2) for High Frequency Jet Ventilation (blue) and Volume Controlled Ventilation (red) groups, with 95% confidence intervals.

Figure 3. Heatmap of individual non-invasive mean arterial pressure (NIBPM) values over time for (A) the High Frequency Jet Ventilation (HFJV) and (B) Volume Controlled Ventilation (VCV) groups. The blue and red lines represent the mean NIBPM values in both groups, respectively. (C) Smoothed evolution of non-invasive mean arterial pressure (NIBPM) over time for HFJV (blue) and VCV (red) groups, with 95% confidence intervals.

Table 1. Participants characteristics

Table 2. Main results

Table 3. ANCOVA

Appendix 1. Intervention protocol

Supplementary Table S1. Benjamini–Hochberg false discovery rate correction applied to the nine interpretable between-group comparisons of secondary anesthetic endpoints.