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Ciprofol and Remimazolam Preserve Arrhythmia Inducibility Comparable to Propofol During Pediatric Supraventricular Tachycardia Ablation: A Retrospective Comparative Study

Maria Rossi[1]*, Giulia Conti[1]

[1]Department of Phytochemistry, Faculty of Pharmacy, University of Milan, Milan, Italy.

***E-mail** ✉ maria.rossi.it@outlook.com

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ABSTRACT

Propofol remains a widely applied intravenous anesthetic in children. Newer agents, including ciprofol and remimazolam, produce little to no injection discomfort and maintain more consistent hemodynamics. This investigation assessed how these three drugs influence the ability to provoke arrhythmias in pediatric supraventricular tachycardia (SVT). Clinical records of children with SVT who received radiofrequency ablation under general anesthesia between May 2020 and June 2024 were reviewed. After eliminating 28 cases, 173 remained for evaluation. Based on the intravenous anesthetic administered, participants were assigned to a propofol group (Group P), a ciprofol group (Group C), or a remimazolam group (Group R). The primary variable was the inducibility of arrhythmias, while secondary variables included ablation success, extubation duration, bispectral index (BIS), perioperative indicators, and postoperative nausea and vomiting.

The arrhythmia induction rates did not differ significantly among the three groups (97.40% vs 95.35% vs 94.34%) ($P > 0.05$). Similarities were also observed in secondary outcomes such as ablation success ($P > 0.05$), the requirement for isoprenaline ($P > 0.05$), recurrence ($P > 0.05$), and procedure duration ($P > 0.05$). Postoperative nausea and vomiting showed no notable variation. Except for baseline values, BIS readings in Group R exceeded those of Groups P and C at matching intervals ($P < 0.05$). Additionally, Group R demonstrated a shorter extubation time compared with Groups P and C. Ciprofol and remimazolam produced arrhythmia inducibility outcomes similar to propofol in children with supraventricular tachycardia. Both drugs appear suitable for use during radiofrequency ablation of pediatric SVT.

Keywords: Arrhythmia inducibility, Ciprofol, Pediatric, Radiofrequency ablation, Remimazolam, Supraventricular tachycardia

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Introduction

Supraventricular tachycardia (SVT) is the leading reason for performing an electrophysiology study (EPS) in the pediatric population, occurring at a rate of 20 per 100,000 [1, 2]. Atrioventricular reentry tachycardia (AVRT), atrioventricular nodal reentrant tachycardia (AVNRT), and ectopic atrial tachycardia (EAT) constitute the principal SVT subtypes in children [3]. These three entities typically present as narrow-complex, regular tachyarrhythmias and share comparable features [3]. EPS and radiofrequency catheter ablation (RFCA) are usually undertaken under general anesthesia to reduce discomfort and anxiety, prevent movement, and allow the electrophysiology team to conduct precise mapping and ablation. Because accurate diagnosis and treatment require the arrhythmia to be reproduced, dependable SVT induction during EPS is crucial. However, anesthetic drugs can alter conduction properties and sometimes reduce inducibility [4]. Earlier reports show that AVNRT can be provoked in only 74%–89% of pediatric cases under general anesthesia [5, 6]. Thus, pediatric anesthesiologists aim to choose agents that maximize arrhythmia induction during RFCA. Evidence suggests that

induction success rates under inhalational versus intravenous anesthesia are broadly similar [7]. Many institutions, therefore, favor intravenous anesthesia for RFCA. Propofol, the most frequently selected option, minimally affects electrophysiological measurements, assists with accurate localization of arrhythmic foci, and is widely adopted for these procedures [8].

Ciprofol and remimazolam, more recently introduced intravenous sedatives, have shown promising performance in both adults and children across different clinical settings [9–11]. Their onset and recovery profiles resemble those of propofol, but they cause virtually no pain upon injection. Both exhibit milder cardiovascular suppression and steadier hemodynamics, suggesting a more limited impact on the heart [12–14]. Remimazolam is metabolized by tissue esterases rather than hepatic or renal pathways and can be rapidly reversed with flumazenil. Most existing data emphasize perioperative hemodynamic stability for these medications [15–17]. However, no published studies have examined their influence on arrhythmia provocation in pediatric SVT. In this retrospective study, we compared SVT induction during RFCA using ciprofol, remimazolam, and propofol. We anticipated that ciprofol and remimazolam would demonstrate induction rates equivalent to propofol, with potential benefits related to recovery characteristics.

Materials and Methods

Ethical approval

Authorization for this research was granted by the Hospital Ethics Committee (approval number: QFELL-YJ-2024-147), and the project was recorded in the China Clinical Trial Registry (ChiCTR2500109472). All information was maintained within the electronic medical records system. Because this was a retrospective review, informed consent was not required. Data were de-identified, and patient confidentiality was preserved throughout the analysis.

Design and patients

This retrospective review examined pediatric cases of supraventricular tachycardia undergoing RFCA under general anesthesia between May 2020 and June 2024. Eligibility criteria included: American Society of Anesthesiologists (ASA) class I–II; no previous RF ablation; SVT confirmed by symptoms and tachycardia ECG, with recurrent episodes necessitating RFCA; cessation of antiarrhythmic medication for a minimum of 5 half-lives; use of total intravenous anesthesia with tracheal intubation; and administration of the same intravenous anesthetic for induction and maintenance. Patients lacking complete perioperative records were excluded.

Anesthesia method

Upon arrival in the operating room, routine monitoring included ECG, noninvasive arterial pressure, pulse oximetry, BIS, and train-of-four (TOF). All children received total intravenous anesthesia with endotracheal intubation. Drug selection relied solely on clinical judgment and practitioner experience.

Induction: Intravenous sufentanil (0.2–0.3 μg/kg), an induction agent, and rocuronium (0.6 mg/kg) were given. The intravenous anesthetic doses were: propofol 2–2.5 mg/kg for Group P, ciprofol 0.6–0.8 mg/kg for Group C, and remimazolam 0.5–0.8 mg/kg for Group R.

Maintenance: Continuous infusion rates were as follows: propofol 4–8 mg/kg/h in Group P, ciprofol 0.5–0.8 mg/kg/h in Group C, and remimazolam 0.6–1.0 mg/kg/h in Group R. All patients also received remifentanil at 3–6 μg/kg/h. Depth of anesthesia was determined mainly by changes in heart rate and blood pressure, supported by BIS.

At the end of the procedure, anesthetic delivery was discontinued, and the patient was taken to the recovery unit. When TOF was ≥3, neostigmine 0.04 mg/kg with atropine 0.02 mg/kg was administered to reverse neuromuscular blockade. After spontaneous breathing resumed, Group R additionally received flumazenil 0.02 mg/kg. Transfer to the ward occurred once the Aldrete score (5 domains scored 0–2; maximum 10) exceeded 9.

Surgical approach and postoperative management

Electrophysiological testing was completed under general anesthesia. After percutaneous access via the right internal jugular and left femoral veins, a catheter was inserted into the coronary sinus; one tetrode catheter was placed in the right ventricular apex, and another in the high right atrium. Programmed ventricular stimulation plus

an extra stimulus, and incremental atrial pacing—first in the right ventricle and then the right atrium—were performed to assess the accessory pathway and determine Wenckebach's cycle length.

Arrhythmia induction was attempted for diagnostic clarification. Programmed atrial stimulation with up to three extrastimuli was applied, followed by burst pacing at several cycle lengths. If induction still failed, isoproterenol was started at 160–300 μg/h and titrated to raise heart rate, after which stimulation was repeated until tachycardia occurred or a limit of 60 minutes was reached.

For ablation, the endpoint required that within 30 minutes after the lesion, the previously documented tachycardia could no longer be provoked using ventricular or atrial programmed stimulation, with or without isoproterenol.

Data collection

Information was extracted from the hospital database.

① Demographic and diagnostic details were obtained, including age, sex, body mass, the classified form of supraventricular tachycardia, and whether pre-excitation was noted.

② Procedural and monitoring data were recorded: duration of the operation, the interval to extubation, and BIS measurements at designated moments—baseline (T0), 5 minutes after airway intubation (T1), 5 minutes following vascular puncture (T2), midway through the intervention (T3), and at completion (T4).

③ Perioperative outcomes captured included the requirement for isoproterenol, the ability to provoke arrhythmia, ablation outcome, recurrence within 6 months, and the presence of postoperative nausea or vomiting.

Statistical analysis

Data analysis was conducted using SPSS version 26.0. The Shapiro–Wilk procedure evaluated normality for continuous variables. Values consistent with a normal distribution are reported as mean ± SD; skewed data are listed as median (IQR) and compared with the Mann–Whitney U-test. Levene's test assessed equality of variances, guiding the selection of either Welch's t-test or the standard t-test. Categorical variables appear as case counts (%) and were compared by chi-square or Fisher's exact methods.

Results and Discussion

From an initial pool of 201 cases, 28 were excluded, leaving 173 children for the final analysis: 77 assigned to Group P, 43 to Group C, and 53 to Group R **(Figure 1)**. The three cohorts did not differ significantly in age, sex distribution, weight, SVT classification, or the presence of pre-excitation (P > 0.05) **(Table 1)**.

Table 1. Baseline Profile

Variable	Group P (n=77)	Group C (n=43)	Group R (n=53)	P value
Male gender	40 (51.95%)	17 (39.53%)	21 (39.62%)	0.267
Age (years)	10.00 (6.00, 12.00)	8.00 (6.00, 11.00)	10.00 (9.00, 12.00)	0.281
Body weight (kg)	37.90 ± 16.98	37.22 ± 14.91	42.78 ± 16.62	0.251
Type of tachycardia				0.520
AVNRT	17	10	13	
AVRT	47	29	32	
AT	13	4	8	
Pre-excitation	59 (76.62%)	29 (67.44%)	39 (73.58%)	0.551
Duration of procedure (min)	95.01 ± 42.46	83.95 ± 42.62	85.55 ± 34.69	0.254
Extubation time (min)	21.60 ± 5.52	22.12 ± 5.65	17.98 ± 4.69	<0.001

Presented as mean ± SD, median (25th–75th percentile), or n (%).

Abbreviations: AVRT, atrioventricular reentrant tachycardia; AVNRT, atrioventricular nodal reentrant tachycardia; AT, atrial tachycardia.

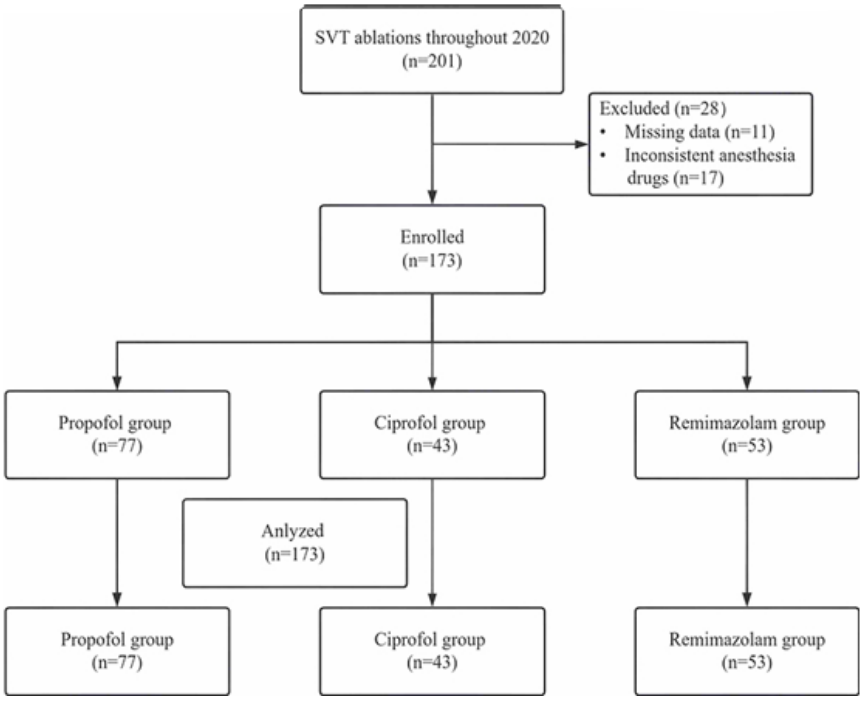


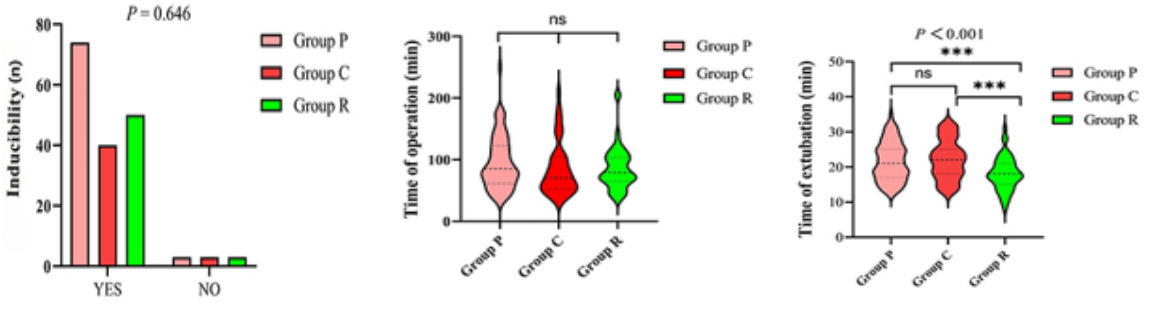
Figure 1. Enrollment pathway.
Abbreviation: SVT, supraventricular tachycardia.

No meaningful variation was seen in arrhythmia-provocation rates among the three anesthetic groups (P > 0.05) **(Figure 2)**. Parameters related to perioperative performance—ablation completion (P > 0.05), isoprenaline use (P > 0.05), recurrence (P > 0.05) **(Table 2)**, and procedural duration **(Figure 2)**—showed comparable results. Rates of nausea and vomiting did not differ by group.

Table 2. Perioperative Outcomes

Variable	Group P (n=77)	Group C (n=43)	Group R (n=53)	P value
Isoprenaline administration	13 (16.88%)	10 (23.26%)	7 (13.46%)	0.450
Arrhythmia inducibility	74 (96.10%)	40 (93.02%)	49 (92.45%)	0.646
Successful ablation	75 (97.40%)	41 (95.35%)	50 (94.34%)	0.149
Recurrence of arrhythmia	2 (2.67%)	1 (2.44%)	1 (2.00%)	0.582
Nausea and vomiting	6 (7.79%)	4 (9.30%)	4 (7.55%)	0.903

Shown as mean ± SD, median (25th–75th percentile), or n (%).



a) b) c)

Figure 2. Comparison of ablation outcome, operative duration, and time to extubation.
(a) Ablation results; (b) operating time; (c) extubation interval. **P < 0.001. Group P: propofol; Group C: ciprofol; Group R: remimazolam.

Marked distinctions in BIS readings were observed. Except for T0, Group R consistently demonstrated higher

BIS values at every measured point than either Group P or Group C ($P < 0.05$) **(Figure 3)**. Group R also exhibited the shortest time to extubation, significantly quicker than both comparator groups.

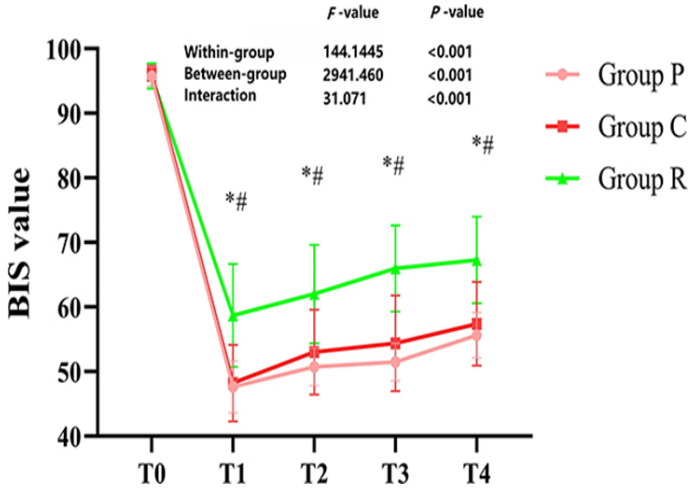


Figure 3. BIS trends at all measurement intervals.
T0: baseline; T1: 5 minutes after intubation; T2: 5 minutes after puncture; T3: midpoint; T4: conclusion.
Asterisks denote $P < 0.001$ for Group P vs Group R; hash marks denote $P < 0.001$ for Group C vs Group R.
Abbreviations: Group P, propofol; Group C, ciprofol; Group R, remimazolam; BIS, bispectral index.

Because general anesthesia offers clear benefits for pediatric patients undergoing EPS and RFCA, the expert consensus released in 2016 by the European Pediatric and Congenital Electrophysiology Society, together with the Heart Rhythm Society, advised its routine use for catheter ablation in children younger than 12 years [18]. Still, the impact of anesthesia on arrhythmia inducibility in this group remains a relevant topic. General anesthesia can, during EPS, decrease sympathetic drive, thereby lowering the probability of triggering reentrant tachyarrhythmias. In addition, specific anesthetic agents may modify cardiac electrophysiology and conduction, altering inducibility and potentially influencing procedural outcomes [4]. Propofol remains the primary intravenous anesthetic for induction and maintenance in children and is known to exert minimal direct influence on sinus node behavior or conduction pathways [19]. Previous retrospective data indicate that SVT can be induced in 83%–88% of propofol-sedated patients [7, 20]. In line with earlier results, the induction rate in the propofol cohort of this study reached 87.01%, increasing to 96.10% when isoproterenol was administered. For children with AVNRT, both inhaled and intravenous anesthetics yield comparable success in provoking tachycardia, while inhalational agents tend to provide slightly better inducibility in EAT. This might be attributable to propofol's ability to dampen AV conduction via enhanced parasympathetic input and baroreflex suppression [21].

Relative to propofol, ciprofol offers several advantages, including less respiratory compromise, improved hemodynamic stability, absence of injection discomfort, reduced lipid exposure, and an overall stronger safety profile [9]. When used in pediatric ambulatory adenoidectomy, a regimen of 0.6 mg·kg−1 ciprofol combined with low-dose rocuronium was shown to allow favorable intubation conditions with stable circulation and BIS values, along with a notably lower incidence of injection-related pain compared with propofol [10]. Continuous infusion of ciprofol leads to limited drug accumulation and enhances safety during pediatric anesthesia [22]. No published clinical data exist regarding its specific influence on cardiac conduction. Animal findings suggest that ciprofol prolongs the corrected QT interval in a dose-dependent fashion within the first hour after administration, yet the frequency of bradycardia and QT prolongation resembles that observed with propofol [23]. In the present study, arrhythmia inducibility showed no meaningful variation between the propofol and ciprofol groups.

In EPS settings, midazolam is frequently used for adult sedation or as an adjunct in children. At therapeutic levels, its effect on cardiac conduction is negligible [19]. Remimazolam, derived from midazolam through the addition of a hydrolytically labile methyl-propionate side chain, is an ultrashort-acting benzodiazepine. In pediatric induction, remimazolam provides a rapid onset, reliable sedation, steady hemodynamics, and improved comfort, resembling the characteristics of propofol [17]. Pharmacokinetic data reveal that its clearance, distribution volume, and half-life are all favorable for tight anesthetic control in children [24]. Case reports indicate that remimazolam only minimally affects myocardial contractility, heart rate modulation, and conduction properties,

offering potential advantages for patients with electrophysiologic abnormalities [25]. Flumazenil, a selective benzodiazepine antagonist, can promptly reverse remimazolam and facilitate faster emergence [26, 27]. Evidence from pediatric strabismus surgery demonstrates that flumazenil reversal shortens anesthesia recovery and enhances emergence quality [28, 29]. Consistent with these findings, recovery time decreased in Group R following flumazenil administration in the current study.

Some experienced electrophysiologists have observed that overly deep anesthesia may suppress arrhythmias or make them harder to provoke. Therefore, keeping the anesthetic depth modest is often essential to allow abnormal conduction pathways to manifest and support effective ablation [30]. However, insufficient monitoring of risk awareness during the procedure can lead to psychological distress, or uncontrolled movements that may endanger young patients. BIS monitoring is extensively used to assess anesthetic depth and is well established among both adult and pediatric practitioners. Existing research shows strong correlations between BIS values and the depth of anesthesia produced by propofol, ciprofol, and remimazolam, indicating that BIS can assist in maintaining an appropriate anesthetic level [31, 32].

In this study, children receiving remimazolam consistently showed higher BIS readings than those in the propofol group, aligning with earlier reports. Prior investigations have also noted that lowering the BIS below 50 with remimazolam is difficult, and in certain cases, values remain above 60 even when substantial doses are used.32 In the analysis by Choi *et al.* involving 1500 individuals anesthetized with remimazolam, 61 patients (4.1%) fulfilled the criteria for inadequate BIS suppression; nonetheless, the modified Brice interview demonstrated that none of these cases involved intraoperative awareness [33]. It has been suggested that remimazolam's strong anterograde amnestic properties may explain the absence of recall despite relatively elevated BIS levels. Although BIS values tend to fluctuate more and skew higher during remimazolam anesthesia, concurrent measurements of neurologic sedation indicators—such as spectral edge frequency and baseline pupil diameter—have confirmed that the depth of sedation remains sufficient [34]. Earlier work showed that resting pupil size during remimazolam anesthesia typically stays under 2 mm, a value comparable to those recorded with sevoflurane, desflurane, and propofol, even though remimazolam may produce intraoperative BIS readings exceeding 60 [34, 35]. Consequently, BIS should not be used to directly compare anesthetic depth between remimazolam and propofol, and these differences likely exert little impact on the main outcomes assessed [16]. No cases of awakening, recall, or intraoperative awareness occurred in the remimazolam cohort. Nevertheless, when the anesthetic depth is intentionally kept light—particularly when BIS surpasses 70—clinicians should remain watchful for signs of consciousness. Persistently high BIS values, even under adequate drug administration, may also prompt concerns about potential overdose. In such situations, perioperative hemodynamic parameters and resting pupil diameter may provide additional guidance on the true depth of anesthesia [16].

This work has several limitations. It was conducted at a single center using a retrospective design. Choices regarding anesthetic type and dosage were not predetermined but instead depended on the clinical judgment and experience of the attending anesthesiologists, based on patient-specific considerations. Because of the retrospective nature of the research, no standardized BIS range was targeted for any of the groups. Furthermore, BIS measurements in the remimazolam group may not accurately represent the true anesthetic depth. The applicability of these findings across pediatric populations and different ethnic groups should be evaluated through large, prospective randomized trials. Future research would benefit from multicenter participation and expanded sample sizes to allow more definitive conclusions.

Conclusion

Overall, ciprofol and remimazolam demonstrated arrhythmia inducibility outcomes in pediatric supraventricular tachycardia that were comparable to those of propofol. A notable observation was the markedly shorter extubation time in the remimazolam group, which may contribute to improved postoperative comfort. Both agents appear suitable for use during radiofrequency ablation procedures in children. Well-designed randomized clinical trials will be valuable for clarifying how various anesthetic agents interact with arrhythmia inducibility.

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Conflict of Interest: None

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Ethics Statement: None

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