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Comparison of Electrophysiologic Effects of Propofol and Isoflurane-based Anesthetics in Children Undergoing Radiofrequency Catheter Ablation for Supraventricular Tachycardia

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Background: **Radiofrequency catheter ablation (RFCA), which is typically performed with general anesthesia in children, is an interventional therapy for tachyarrhythmia. Although the electrophysiologic (EP) effects of isoflurane- and propofol-based anesthetics have been shown to be similar, a retrospective analysis reported significantly longer RFCA procedural duration with the use of isoflurane. It remains unclear whether the ability to successfully perform RFCA differs between these drugs.**

Methods: **Patients were randomly assigned to receive either an isoflurane- or propofol-maintained anesthetic. Drug administration was titrated according to the pharmacodynamic endpoint of depth of sedation using bispectral index score. The ability to induce sustained tachycardia (using a scoring system), procedural durations, and effects on cardiac electrophysiologic properties were evaluated and compared between the groups.**

Results: **Sixty subjects were included in this study. Sustained supraventricular tachycardia (SVT) was inducible with the assigned drug in all but four subjects. In three of these four subjects, SVT was also not inducible with the alternative study drug. Ability to induce the first sustained SVT was similar between the groups ($P = 0.83$). Total procedural durations were similar (isoflurane 224 ± 84 min *vs.* propofol 221 ± 86 min, mean ± SD, $P = 0.88$). Atrioventricular nodal conduction was slower with propofol compared with isoflurane, but this result did not appear to be clinically relevant. Finally, ventricular repolarization was prolonged by isoflurane *versus* propofol, the clinical significance of which was not demonstrated.**

Conclusion: **Isoflurane- and propofol-based anesthesia were equally suitable in children and adolescents undergoing RFCA.**

RADIOFREQUENCY catheter ablation (RFCA) is a highly effective therapy for supraventricular tachycardia (SVT) in children.[1,2] In this patient population, general anesthesia is required to ensure comfort during the prolonged procedure and to assure immobility, the latter facilitating accurate mapping and subsequent ablation of the accessory pathway or arrhythmogenic focus, which may increase safety for pediatric patients undergoing RFCA.

The electrophysiologic effects on the normal or aberrant conduction system of various anesthetic drugs such as propofol, isoflurane, sevoflurane, and alfentanil–midazolam have been investigated in subjects undergoing ablative procedures.[3–9] For all these drugs, the observed electrophysiologic alterations were either absent or minimal. However, the relevance of either the lack or presence of changed electrophysiologic parameters for the successful performance of the RFCA procedure remains unclear. Successful management of anesthesia in patients undergoing RFCA requires that the pathologic tachycardia remains inducible. Still, it is well known that certain forms of SVT can be difficult to induce with anesthesia, particularly in the pediatric population.[8] Further, in a recent retrospective analysis in children undergoing RFCA, procedural duration lasted significantly longer, and induction of SVT was more difficult in patients receiving isoflurane- compared with propofol-based anesthesia.[10] This finding suggests that the ease with which RFCA is performed may be different between anesthetic drugs. To evaluate this observational information, we performed a randomized trial wherein the electrophysiologist was blinded as to whether the patient received propofol- or isoflurane-based anesthesia, and we tested the hypothesis that the time for successful arrhythmia characterization and ablation of the arrhythmogenic substrate is independent of the hypnotic drug used.

Materials and Methods

Patients

All children and adolescent patients aged 4–18 yr and scheduled to undergo RFCA for SVT were invited to participate in the study. Patients were offered RFCA in the following circumstances: SVT incompletely responsive to antiarrhythmic drugs; SVT in children who had contraindications to take safe antiarrhythmic drugs; SVT in children who had side effects from safe antiarrhythmic drugs; SVT in children whose families chose not to use antiarrhythmic drugs; incessant SVT; or Wolff-Parkinson-White syndrome in children with a history of documented SVT, palpitations, syncope, or who wanted to participate in competitive sports. Except in patients having Wolff-Parkinson-White syndrome, SVT was always documented before catheter ablation during a previous

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emergency room evaluation, by ambulatory rhythm monitoring, or by provocative outpatient esophageal electrophysiologic study. Subjects with contraindications to undergo an inhalational induction or to the use of either propofol or isoflurane were excluded. Patients were randomly allocated to receive propofol (group PRO) or isoflurane (group ISO). Blocked randomization was generated using a computer random number. To ensure blinding of the electrophysiologist, the drug infusion pump was hidden in a box, and opaque tubing was used. In group PRO, an empty sham isoflurane vaporizer was installed, and in group ISO, an infusion pump delivering normal saline was used. Dose adjustments were always performed simultaneously on the infusion pump and on the vaporizer, and all changes were recorded. The anesthesiologist was not blinded. Before initiation, this study was approved by the Duke University Medical Center Institutional Review Board; written informed consent was obtained from a parent or legal guardian of each subject, and, when appropriate, the patient's assent was also obtained.

Anesthesia

Preanesthetic medication consisted of midazolam given either orally (0.5 mg/kg up to a maximum of 10 mg) or intravenously (2 mg) when intravenous access was established before induction of anesthesia. Routine monitoring included electrocardiography, noninvasive blood pressure measurements, invasive blood pressure monitoring by indwelling arterial catheters, and pulse oximetry. In all patients, anesthesia was induced by inhaling sevoflurane in 66% nitrous oxide and 33% oxygen *via* a face mask. Pancuronium (0.1 mg/kg) was used to facilitate tracheal intubation, and fentanyl (2–4 μg/kg) was administered before laryngoscopy. After tracheal intubation, the fresh gas flow was set to 0.5 l/min O_2 and 1 l/min N_2O for the remainder of the procedure, and sevoflurane was discontinued. Thereafter, anesthesia was maintained with the assigned study drug**:** isoflurane was started with an inspiratory fraction of 1%, and propofol infusion was started with 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Real-time bispectral index (BIS) data were obtained *via* electroencephalogram (EEG) electrodes applied in a frontotemporal montage (BIS sensor, Aspect Medical Systems, Newton, MA). The EEG activity was recorded using an Aspect 1050, version 3.3 (Aspect Medical Systems, Newton, MA), and averaged values were recorded every 5 s using a computerized data logging system. Dosage of the study drugs was adjusted to maintain the BIS within a range of 50–60. When BIS persisted more than 60 or less than 50 under stable hemodynamic conditions, adjustments were performed as follows: Group ISO, increase by increments of 0.2% or decrease by decrements of 0.1%; Group PRO, increase with a bolus dose of 0.25 mg/kg and increase infusion rate by 20%, or decrease infusion rate by 20%.

Electrophysiologic Procedures

All electrophysiologic procedures were performed with the guidance of the same operator (R.J.K.). After stable anesthesia was established, venous access was obtained in standard fashion, using both femoral veins and the right internal jugular vein. Electrode catheters were positioned in the high lateral right atrium, right ventricular apex, His bundle region, and within the coronary sinus, whenever possible. Variations existed because of abnormal cardiac anatomy. A diagnostic electrophysiologic study was performed using a standard protocol and varied only in the presence of repaired congenital heart disease or if the patient entered the laboratory with incessant SVT. Programmed stimulation was performed using a Bloom stimulator (model DTU 215-A; Bloom Electrophysiology/Fischer Imaging Corporation; Denver, CO), and data were displayed, recorded, and analyzed using a computerized multichannel system (PrukaART; Pruka Engineering Inc; Houston, TX). Sometimes, in addition, a computerized electroanatomic mapping system (Carto-Biosense; Biosense Webster; Diamond Bar, CA) was used. The baseline protocol was completed in all patients, even if the clinically relevant tachycardia was induced early in the protocol. The only exception was a patient with incessant SVT, which could not be terminated for more than a few beats. All electrophysiologic indices were measured and recorded at the conclusion of each pacing run within the baseline (and subsequent) protocol(s). If the clinically suspected SVT was not induced during the baseline protocol, isoproterenol (0.03–0.07 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was infused, and the protocol repeated until SVT was induced. If it still was not inducible, atropine (0.02 mg/kg) was added, or epinephrine (0.05–0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$) infusion was substituted. Failing these maneuvers, the patient was switched to the alternate anesthetic study drug. After an interim of 30 min, the diagnostic electrophysiologic study was repeated. If SVT was still not inducible, the anesthetic was discontinued, and the patient extubated. At the discretion of the cardiologist, the procedure was then abandoned or pursued with the patient receiving conscious sedation (*e.g.*, midazolam, fentanyl).

All pacing was performed using a 2-ms square wave at twice the diastolic threshold. For purposes of this study, two types of pacing procedures were used. (1) Extrastimulus testing (EST) involved an eight-beat drive-train at a cycle length of 400–600 ms (the slowest allowable by the prevailing sinus rate), followed by a premature stimulus, which was introduced progressively earlier in subsequent drive-trains, until a propagated response no longer occurred. When this procedure was performed at two different drive-train cycle lengths, data from the longer drive-train cycle length were always used. This procedure was performed in the atrium (AEST) and in the ventricle (VEST). (2) Incremental pacing (IP) involved pacing at the slowest rate allowable by the pre-

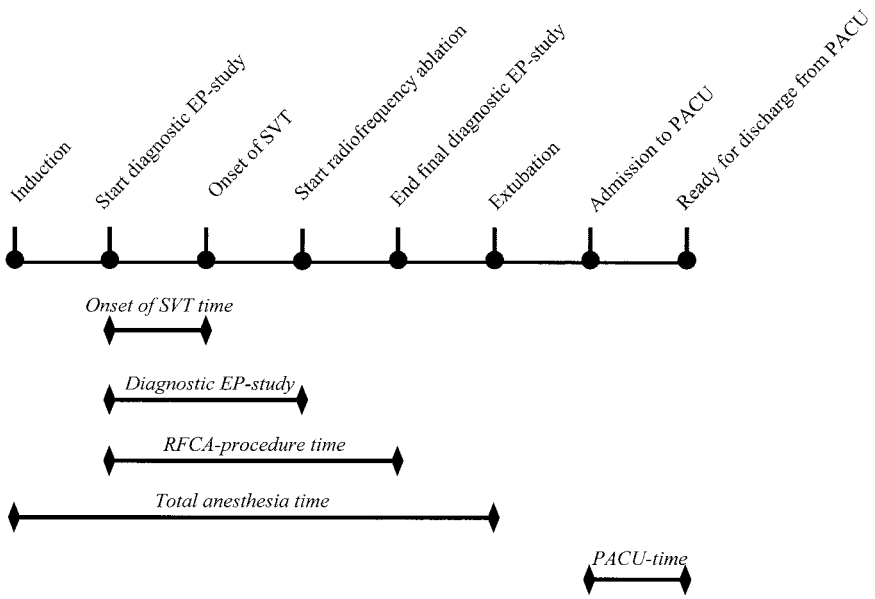

Fig. 1. Flow chart of events and corresponding time intervals. EP = electrophysiologic; SVT = supraventricular tachycardia; RFCA = radiofrequency catheter ablation; PACU = postanesthesia care unit.

vailing sinus rate and reducing the paced cycle length (increasing the rate) by 10–20 ms after every eighth beat. This procedure was continued until the conduction phenomenon of interest was observed and was also performed from the atrium (AIP) and the ventricle (VIP).

After conclusion of the diagnostic study, ablation of the abnormal substrate(s) was (were) performed using a commercial radiofrequency generator (EPT-1000 TC; Electrophysiology Technologies/Boston Scientific; San Jose, CA), and muscle relaxation was reestablished using pancuronium to allow the ablation be performed during apnea to avoid respiration-related intrathoracic movement. This approach permits application of radiofrequency energy near vital structures, such as the atrioventricular node, with reduced concern of potentially dangerous catheter dislodgement. The patient was then observed for 30–60 min for the return of SVT substrate before a final diagnostic electrophysiologic study was repeated at baseline and with isoproterenol ($0.03–0.07\ \mu g \cdot kg^{-1} \cdot min^{-1}$).

Postprocedural Care

Endotracheal extubation was performed after the patient was awake. Postprocedural care was then provided in the recovery room, and patients were ready for transfer to a ward room when the following criteria were met: Patient was hemodynamically stable; patient was fully conscious and able to protect the airway; pain was controlled; there was absence of severe nausea or active vomiting; and the skin was warm and dry.

Time Analyses

The following time intervals were analyzed (fig. 1): Onset of SVT time (start of first diagnostic electrophysiologic study until induction of first SVT), diagnostic electrophysiologic study time (start of first diagnostic electrophysiologic study until start of ablation), RFCA procedure time (start of first diagnostic electrophysiologic study until end of final diagnostic electrophysiologic study), total anesthesia time (anesthesia induction until tracheal extubation), postanesthesia care unit (PACU) time (admission to PACU until ready for transfer to ward). Analyses were performed by using an intention to treat approach. If a patient entered the laboratory in SVT or if SVT was induced by initial catheter placement, the "onset of SVT time" was designated "0 min."

Inducibility of Supraventricular Tachycardia

An arbitrary scoring system was devised to compare the conditions required to initiate SVT during the diagnostic electrophysiologic study (table 1).

Electrophysiologic Parameter Analyses

All measurements were taken by the same electrophysiologist (R.J.K.), who was blinded to the patients' group assignment. For purposes of this study, data were only analyzed from the initial electrophysiologic study (*i.e.*, in the absence of cardioactive drugs). Electrocardiographic measurements of interest included the PR interval (PR), the QRS duration (QRS), the sinus cycle length (CL), and the QT interval corrected for rate using the Bazett formula (QTc). Intracardiac conduction intervals of interest, how they were measured, and their clinical relevance are shown in table 2. The actual electrophysiologic parameters of interest, their definitions, the pacing procedures used to determine them, and their clinical relevance are shown in table 3. Data from patients who had undergone surgery for congenital heart disease were excluded from electrocardiographic and electrophysiologic data analyses. In patients with an accessory pathway, accessory pathway function sometimes rendered determination of the underlying normal

Table 1. Inducibility of First Sustained Supraventricular Tachycardia (SVT)

	SVT Score	Group Isoflurane (n)	Group Propofol (n)
SVT Induced without pharmacologic intervention	1	15	16
SVT Incessant upon entry to the laboratory		1	0
SVT Induced by catheter placement		5	3
SVT Induced during baseline study		9	13
SVT Induced during isoproterenol administration	2	11	10
SVT Induced during isoproterenol and atropin or epinephrine administration	3	2	2
SVT Not inducible under the general anesthetic assigned	4	2	2

conduction system impossible. The corresponding measurements were excluded from analyses. This variably included the PR, QRS, QTc, AH, HV, AVNFRP, AVBCL, and VABCL. See tables 2 and 3 for explanations of abbreviations.

Statistical Analyses

Sample size calculation in this study was based on detecting equivalence between therapies (*i.e.*, conservative character).[11] The α error was set at 0.05, and the β error at 0.15. Based on previous data from our laboratory, it was estimated that the RFCA procedure time would last 240 min, with a variance of 60 min. A difference of 45 min (about 20% of the RFCA procedure time) was considered a reasonable limit for "equal" time. Using these indices, it was calculated that 26 patients were needed in each group. To further compensate for nonadherence in about 10% of cases (*i.e.*, sustained tachycardia that was not inducible with the assigned study drug, no ablation performed), a sample size of 30 patients per group was needed.

Procedural duration data were analyzed by Student *t* test. In addition, the time to complete the RFCA procedure was analyzed using the log-rank test, and regression techniques were used to control for potential confounding variables induced by an imbalance in diagnoses between treatment groups. All electrophysiologic parameters were analyzed for normal distribution by the Shapiro-Wilk test; accordingly, data with a normal distribution were analyzed by Student *t* test, and data not having a normal distribution were analyzed by Wilcoxon rank sum test. All analyses were performed using SAS System for Windows v6.12 (SAS Institute, Cary, NC). A *P* value less than 0.05 was considered statistically significant.

Results

Patients

Sixty of 63 eligible patients agreed to participate and were consequently included in the study. Two patients were excluded from the analysis: one patient had ventricular tachycardia and not SVT, and in a second patient, ablation was not attempted because of procedure-induced congestive heart failure. Demographic data and diagnoses are shown in table 4. The baseline characteristics were similar with a predominance of male subjects in both groups. In four patients (table 5), sustained SVT could not be induced with the assigned study drug. However, sustained SVT could be induced with the alternative anesthetic treatment in only one of the four subjects. In one of these patients, the procedure was also pursued with conscious sedation; again, sustained SVT was not inducible.

Time Analyses

The RFCA procedure time, the onset of SVT time, the diagnostic electrophysiologic study time, the anesthesia time, and the time until ready for discharge from the PACU were not significantly different between the groups (table 6). The upper limit of the 95% confidence interval (CI) for the difference in RFCA procedure time was 42 min. Survival curves for the two treatment groups were similar ($P = 0.89$, log-rank test; fig. 2). Regression modeling of the RFCA procedure time showed an imbalance: the variable "diagnosis: multiple substrates" was significant as the major contributor ($P = 0.002$). After adjustment for this variable, the upper limit of the 95% CI of the RFCA procedure time was reduced to 31 min. A plot of RFCA procedure time by diagnosis and groups showed clusters for patients with atrioven-

Table 2. Intracardiac Conduction Intervals of Interest

Conduction Interval	Method of Measurement	Clinical Relevance
P Wave-to-atrial interval in ms (PA)	Onset of surface *P* wave to local atrial electrogram from His bundle catheter	Measure of right atrial conduction velocity
Atriohisian interval in ms (AH)	Local atrial electrogram from His bundle catheter to onset of His bundle electrogram	Measure of AV nodal conduction velocity
Hisioventricular interval in ms (HV)	Onset of His bundle electrogram to onset of earliest ventricular activation (from surface QRS or intracardiac ventricular electrogram)	Measure of combined His bundle, bundle branch, and Purkinje fiber conduction velocity

AV = atrioventricular.

Table 3. Electrophysiologic Parameters of Interest

Electrophysiologic Parameter	Definition	Pacing Procedure Used for Determination	Clinical Relevance
Atrial effective refractory period (AERP)	The longest atrial stimulus-to-atrial stimulus interval not resulting in a propagated response by the premature stimulus	AEST	A measure of atrial muscle refractoriness
Atrial functional refractory period (AFRP)	The shortest atrial electrogram-to-atrial electrogram interval obtainable	AEST	A measure of both atrial muscle refractoriness and conduction velocity
Anterograde AV nodal functional refractory period (AVNFRP)	The shortest His electrogram-to-His electrogram interval obtainable	AEST	A measure of both AV node refractoriness and conduction velocity
Atrioventricular block cycle length (AVBCL)	The longest atrial electrogram-to-atrial electrogram interval not followed by a His electrogram	AIP	A measure of AV nodal refractoriness (anterograde)
Ventriculoatrial block cycle length (VABCL)	The longest ventricular electrogram-to-ventricular electrogram interval not followed by an atrial electrogram	VIP	A measure of AV nodal refractoriness (retrograde)
Ventricular effective refractory period (VERP)	The longest ventricular pacing stimulus-to-ventricular pacing stimulus interval not resulting in a propagated response by the premature stimulus	VEST	A measure of ventricular muscle refractoriness
Ventricular functional refractory period (VFRP)	The shortest ventricular electrogram-to-ventricular electrogram interval obtainable	VEST	A measure of both ventricular muscle refractoriness and conduction velocity

AV = atrioventricular; AEST = atrial extrastimulus testing; AIP = atrial incremental pacing; VIP = ventricular incremental pacing; VEST = ventricular extrastimulus testing.

tricular reentry tachycardia and atrioventricular node reentry tachycardia. However, a large variability in patients undergoing RFCA with the diagnosis "multiple substrates" was observed (fig. 3).

Inducibility of Supraventricular Tachycardia

The condition required to initiate the first SVT during the diagnostic electrophysiologic study was similar between the groups ($P = 0.83$; fig. 4). The BIS level when SVT was first induced was also similar between the groups: group PRO = 55 ± 8; group ISO = 54 ± 6; $P = 0.21$.

Electrophysiologic Parameters

The effects of isoflurane and propofol on cardiac electrocardiographic and electrophysiologic properties are shown in table 7. The parameters were compared between the groups and are represented according to the distribution of resulting values. Resulting values that were normally distributed are presented as the mean ± SD, and those that were not normally distributed are presented as the median (quartiles). Five patients (two in group ISO and three in group PRO) had undergone congenital heart surgery, and 11 patients (five in group ISO and six in group PRO) had accessory pathway function, rendering analysis of some aspects of the underlying normal conduction system impossible. The longest atrial and ventricular drive-drain cycle lengths within each pacing protocol were similar between the two groups (table 7), allowing for a comparison of the reported parameters.

Discussion

The results provided by the present study supported our hypothesis that the time required for successful RFCA in children is not different between patients undergoing propofol- or isoflurane-based anesthesia. Sustained SVT was inducible in 93% of the patients, independent of the type of anesthesia. Of note, in three of

Table 4. Diagnoses, Demographic Data, and Administered Drugs

	Group Isoflurane	Group Propofol
Arrhythmia Diagnosis (n):		
Atrioventricular node reentery tachycardia	9	9
Atrioventricular reciprocating tachycardia	7	14
Atrial ectopic tachycardia	2	0
Atrial reentery tachycardia	2	1
Ventricular tachycardia	1	0
Multiple substrates	8	6
No tachycardia	1	0
Demographic data		
Age (yr)	13.0 (9.7, 15.2)	12.6 (8.3, 15.8)
Gender (% woman/% man)*	45/55	30/70
Height (cm)	153 (139, 170)	152 (128, 170)
Weight (kg)	55 (39, 62)	55 (38, 70)
Administered drugs		
Fentanyl (mg)	187 (100, 200)	171 (125, 200)
Pancuronium (mg)	8.8 (8, 10)	10.3 (7, 12)
Propofol (mg)		1600 (1088, 1820)
Isoflurane (MAC · h)	3.8 (2.8, 4.9)	

Data presented as mean (twenty-fifth, seventy-fifth percentile) or * = %.

Table 5. Characteristics of Patients with Noninducible Sustained SVT

Age (y)	Gender	Initial Group Assignment	Diagnosis	Remarks
10	Men	Isoflurane	AVNRT (atypical); AET	AVNRT: sustained SVT not inducible using either ISO or PRO AET inducible only during PRO using ventricular burst pacing
6	Women	Propofol	AVNRT (atypical)	No ablation; SVT in PACU; ablation performed during ventricular pacing in a second session
5	Men	Propofol	AVNRT (atypical); accessory pathway (slow conducting)	No ablation
14	Men	Isoflurane	None	Diagnosis of ventricular tachycardia made by subsequent event recorder

AVNRT = atrioventricular node reentery tachycardia; AET = atrial ectopic tachycardia; ISO = isoflurane; PRO = propofol; SVT = supraventricular tachycardia; PACU = postanesthesia care unit.

four patients in whom SVT was not inducible with the assigned drug, sustained SVT was also not inducible after the patients were switched to the alternative study drug. Procedural duration (table 6, fig. 2) and the use of catecholamine required to initiate the first SVT (table 1) were similar between the study groups.

The few patients with certain arrhythmia types make definitive statements about a relationship between RFCA procedure duration and arrhythmia type speculative. However, the results showed that the time to successfully complete RFCA might be influenced by the technical difficulty in ablating the lesion (*e.g.*, single *vs.* multiple substrates; fig. 3). After adjusting the RFCA procedure time for the variable "diagnosis: multiple substrates," the upper limit of the CI for the difference between the treatment groups was substantially reduced.

Several studies have concluded that isoflurane-based anesthesia might make RFCA in children difficult. In a retrospective analysis, Cohen *et al.*[10] found that the induction of SVT was more difficult and procedural duration was prolonged in children undergoing RFCA with isoflurane-based anesthesia compared with propofol-based anesthesia. In addition, based on observed alterations in accessory pathway conduction in children undergoing RFCA with isoflurane-based anesthesia, Chang *et al.*[9] speculated that electrophysiologic mapping might be more difficult in patients receiving isoflurane. The findings of these studies[9,10] contrast with the results of our present study. However, various factors, such as lack of randomization, lack of control over depth of anesthesia, and differences in operator experience and practice, are confounding factors in those previous studies and may account for the discrepancy between their findings and those in this randomized, controlled study.

Previous studies have examined the effects of isoflurane and propofol on cardiac conduction in children undergoing RFCA. Lavoie *et al.*[7] compared the electrophysiologic effects of propofol and isoflurane with a preceding "baseline" anesthesia using alfentanil, midazolam, nitrous oxide, and pancuronium. Analyzing 10 patients in each group, there was reported unaltered sinuatrial and atrioventricular node function for both drugs compared with the "baseline" anesthesia. In a case-control study, Chang *et al.*[9] matched 12 children with Wolff-Parkinson-White syndrome undergoing RFCA with isoflurane-based general anesthesia with control subjects (children receiving an intramuscular mixture of meperidine, promethazine, and chlorpromazine); isoflurane prolonged the anterograde effective refractory period of the accessory pathway and the effective refractory periods of the atrial and ventricular muscle.

The present study showed intracardiac evidence for slower atrioventricular node conduction with the influence of propofol compared with isoflurane; PR and AH intervals and AVNFRP were longer in the PRO group (table 7). These parameters are either specific measures (AH) of or nonspecific surrogate markers (PR, AVNFRP) for atrioventricular nodal conduction velocity (table 3). The mechanism could be autonomic reflexes or direct drug effect. For example, propofol alters the balance

Table 6. Times

	Group Isoflurane	Group Propofol	*P* Value	Upper Limit 95% CI
RFCA procedure time (min)	224 ± 84	221 ± 86	0.88	42
Onset of SVT time (min)	32 ± 27	37 ± 25	0.52	7
Diagnostic EP study time (min)	93 ± 25	89 ± 28	0.60	16
Anesthesia time (min)	317 ± 88	319 ± 97	0.92	40
PACU time (min)	114 ± 40	106 ± 44	0.54	27

Values are mean ± SD; *P* value, Student *t* test; CI = confidence interval for the difference of isoflurane minus propofol; RFCA = radiofrequency catheter ablation; SVT = supraventricular tachycardia; EP = electrophysiologic; PACU = postanesthetic care unit.

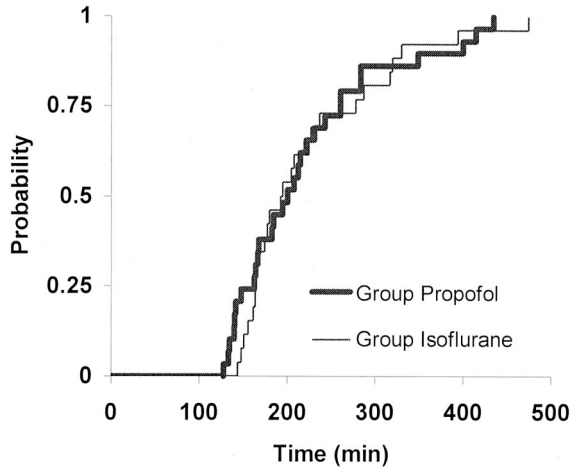

Fig. 2. Survival curves for radiofrequency catheter ablation procedure time in group ISO (isoflurane) and group PRO (propofol). Probability refers to the fractional probability of completion of radiofrequency catheter ablation.

between parasympathetic and sympathetic tone[12] and baroreflex regulatory responses.[13] Thus, if the dose of propofol used in the present study had less vasodilatory properties than isoflurane, there is expected to be less baroreflex inhibition from propofol and higher parasympathetic tone. Conversely, the present results could be explained by improved atrioventricular nodal conduction by isoflurane. Supporting this possibility, the negative dromotropic effect of adenosine is blunted by isoflurane.[14] Sharpe *et al.*[5] did not find a direct effect on atrioventricular conduction with propofol. Whatever the mechanism, the influence on atrioventricular nodal function was not clinically important. Neither the AVBCL and VABCL parameters (table 6), associated with atrioventricular nodal refractoriness, nor the ease of induction of SVTs that depend on atrioventricular nodal function were different between the groups. The best measure of atrioventricular nodal refractoriness is the AVNERP. An *a priori* decision to not use this parameter was made

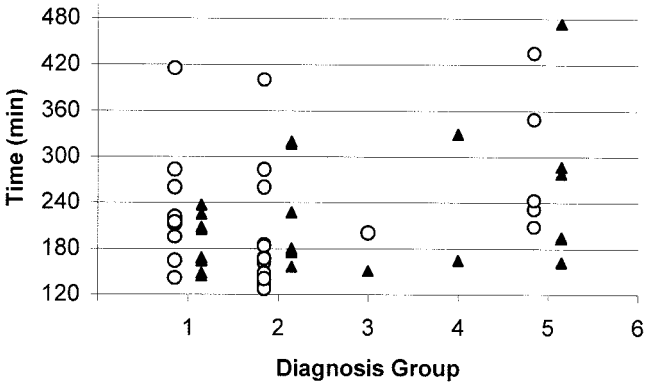

Fig. 3. Radiofrequency catheter ablation procedure time by diagnosis. ▲ = group ISO, ○ = group propofol. Diagnosis groups: 1 = atrioventricular reciprocating tachycardia; 2 = atrioventricular node reentry tachycardia; 3 = atrial reentry tachycardia; 4 = atrial ectopic tachycardia; 5 = multiple substrates.

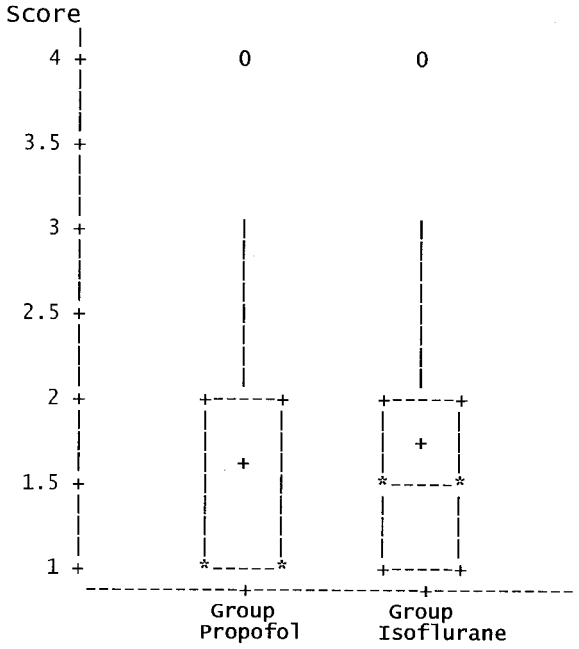

Fig. 4. Box plots of SVT inducibility score. SVT = supraventricular tachycardia. The boxes represent the median (*), 25th–75th percentiles, and range, including extremes (○).

based on the nearly constant observation in children that the AVNERP is less than the AFRP, making the former not obtainable.

There is, however, evidence that propofol can have pronounced negative dromotropic effects, as it has been rarely associated with cardiovascular collapse, lactic acidosis, severe bradycardia, and third degree atrioventricular block in children.[15–18] It has also been reported in adults to cause isolated third degree atrioventricular block, which can be reversed with anticholinergic drugs.[19]

In accordance with the results by Chang *et al.*[9], VERP was also prolonged in our study in group ISO (table 6). Further, the QTc was significantly prolonged in group ISO, corroborating previous findings in children[20] and in healthy adult patients[21] that isoflurane lengthens the QTc and propofol has minimal effects on QTc.[22] Taken together, these findings suggest that isoflurane affects cardiac repolarizing currents. This complex phenomenon involves the orderly function of multiple voltage-gated ventricular myocardial sodium, calcium, and potassium channels and energy-dependent sarcolemmal and plasmalemmal ion pumps. The precise mechanism by which isoflurane influences ventricular repolarization is unknown. Although torsade de pointes ventricular tachycardia has been reported in a young woman with bulimia and hypokalemia while receiving isoflurane anesthesia,[23] other reports have noted the safety of this agent in patients having known long QT syndrome.[24,25]

The BIS, a value derived from the processed EEG, is capable of monitoring the level of sedation for isoflurane and propofol.[26] In patients undergoing RFCA, BIS mon-

Table 7. Electrophysiologic Parameters from Initial Baseline Testing

	Group Isoflurane	Group Propofol	*P* Value
Longest drivedrain cycle lengths			
Atrial (ms)	600 (600, 500) n = 25	600 (600, 500) n = 27	0.18
Ventricular (ms)	600 (600, 500) n = 25	550 (600, 500) n = 26	0.14
Sinus node automaticity			
CL (ms)	654 ± 108 n = 28	687 ± 116 n = 27	0.29
Atrial muscle properties			
PA (ms)	34 ± 9 n = 27	36 ± 10 n = 27	0.43
AERP (ms)	227 ± 31 n = 26	227 ± 41 n = 26	0.94
AFRP (ms)	263 ± 30 n = 26	256 ± 36 n = 26	0.42
AV node properties			
AH (ms)	51 (60, 39) n = 27	56 (73, 47) n = 26	0.04
PR (ms)	124 ± 17 n = 22	135 ± 18 n = 25	0.04
AVNFRP (ms)	367 (400, 345) n = 24	400 (454, 376) n = 25	0.07
AVBCL (ms)	320 (350, 280) n = 22	310 (400, 290) n = 17	0.91
VABCL (ms)	280 (340, 220) n = 9	280 (340, 260) n = 17	0.87
His-Purkinje properties			
HV (ms)	43 ± 8 n = 22	40 ± 9 n = 22	0.36
Ventricular muscle properties			
QRS (ms)	90 (94, 83) n = 22	85 (100, 80) n = 22	0.78
QTc (ms)	457 ± 27 n = 22	428 ± 25 n = 22	0.001
VERP (ms)	246 ± 20 n = 25	233 ± 24 n = 26	0.04
VFRP (ms)	270 ± 18 n = 25	260 ± 22 n = 26	0.1

For a given parameter, results having a normal distribution are presented as the mean ± SD and *P* value determined from the Student's *t*-test. Results not having a normal distribution are presented as the median (25^{th}, 75^{th} percentile) and p value determined from the Wilcoxon Rank Sum test. AERP = atrial effective refractory period; AFRP = atrial functional refractory period; AH = atriohisian interval; AVBCL = atrioventricular block cycle length; AVNFRP = atrioventricular nodal functional refractory period; CL = sinus cycle length; HV = Hisioventricular interval; PA = *P* wave-to-atrial interval; PR = PR interval; QRS = QRS duration; QTc = rate-corrected QT interval; VABCL = ventriculoatrial block cycle length; VERP = ventricular effective refractory period; VFRP = ventricular functional refractory period.

itoring may be especially useful because hemodynamic parameters such as heart rate and blood pressure, typically used to assess depth of sedation in paralyzed patients, are altered because of the use of cardiac pacing and drugs, which have chronotropic effects. The present report is the first to use BIS monitoring in patients undergoing RFCA with general anesthesia. This pharmacodynamic endpoint provided a basis for rational clinical comparisons between propofol and isoflurane administration. The similar BIS levels obtained during the first induction of SVT suggested that depth of sedation was equal in the study groups. Thus, the depth of sedation is not considered to have affected the comparison of ease of induction of the first sustained SVT.

There are several limitations to the present study. First, as mentioned previously, the atrioventricular nodal effective refractory period, the most widely recognized clinical measure of atrioventricular nodal refractoriness, was not used because of limitations in our ability to derive this parameter on a regular basis. Second, we did not attempt to compare anesthetic effects on accessory pathway function. Because patients in this study did not serve as their own control subjects and because the range of electrophysiologic characteristics of accessory pathways is broad, there were insufficient numbers of patients having accessory pathways to derive meaningful data. Nonetheless, accessory pathways were identified and successfully ablated in all patients participating in this study, thus suggesting that potentially measurable effects on the accessory pathway were not clinically relevant. Third, although the sedative effect of isoflurane and propofol can be continuously measured using BIS analysis,[26] it is unknown whether the interactions of nitrous oxide with isoflurane or propofol are differently

reflected in such monitoring. However, nitrous oxide, as used in this study, has been shown to induce loss of consciousness without causing a change in the BIS level.[27]

In conclusion, isoflurane and propofol were equally suitable anesthetic agents in children and adolescents undergoing RFCA when applied under the BIS-controlled conditions of this study.

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References

1. Kugler JD, Danford DA, Houston K, Felix G: Radiofrequency catheter ablation for paroxysmal supraventricular tachycardia in children and adolescents without structural heart disease. Pediatric EP Society, Radiofrequency Catheter Ablation Registry. Am J Cardiol 1997; 80:1438–43

2. Wren C: Catheter ablation in paediatric arrhythmias. Arch Dis Child 1999; 81:102–4

3. Sharpe MD, Dobkowski WB, Murkin JM, Klein G, Guiraudon G, Yee R: Alfentanil-midazolam anaesthesia has no electrophysiological effects upon the normal conduction system or accessory pathways in patients with Wolff-Parkinson-White syndrome. Can J Anaesth 1992; 39:816–21

4. Sharpe MD, Dobkowski WB, Murkin JM, Klein G, Guiraudon G, Yee R: The electrophysiologic effects of volatile anesthetics and sufentanil on the normal atrioventricular conduction system and accessory pathways in Wolff-Parkinson-White syndrome. ANESTHESIOLOGY 1994; 80:63–70

5. Sharpe MD, Dobkowski WB, Murkin JM, Klein G, Yee R: Propofol has no direct effect on sinoatrial node function or on normal atrioventricular and accessory pathway conduction in Wolff-Parkinson-White syndrome during alfentanil/midazolam anesthesia. ANESTHESIOLOGY 1995; 82:888–95

6. Sharpe MD, Cuillerier DJ, Lee JK, Basta M, Krahn AD, Klein GJ, Yee R: Sevoflurane has no effect on sinoatrial node function or on normal atrioventricular and accessory pathway conduction in Wolff-Parkinson-White syndrome during alfentanil/midazolam anesthesia. ANESTHESIOLOGY 1999; 90:60–5

7. Lavoie J, Walsh EP, Burrows FA, Laussen P, Lulu JA, Hansen DD: Effects of propofol or isoflurane anesthesia on cardiac conduction in children undergoing radiofrequency catheter ablation for tachydysrhythmias. ANESTHESIOLOGY 1995; 82:884–7

8. Lai LP, Lin JL, Wu MH, Wang MJ, Huang CH, Yeh HM, Tseng YZ, Lien WP, Huang SK: Usefulness of intravenous propofol anesthesia for radiofrequency catheter ablation in patients with tachyarrhythmias: Infeasibility for pediatric patients with ectopic atrial tachycardia. Pacing Clin Electrophysiol 1999; 22: 1358–64

9. Chang RK, Stevenson WG, Wetzel GT, Shannon K, Baum VC, Klitzner TS: Effects of isoflurane on electrophysiological measurements in children with the Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol 1996; 19:1082–8

10. Cohen IT, Furbush N, Moak J: Propofol infusions for radiofrequency catheter ablation for supraventricular tachycardia in children (abstract). Anesth Anal 1999; 88:S291

11. Makuch R, Simon R: Sample size requirements for evaluationg a conservative therapy. Cancer Treat Rep 1978; 62:1037–40

12. Deutschman CS, Harris AP, Fleisher LA: Changes in heart rate variability under propofol anesthesia: A possible explanation for propofol induced bradycardia. Anesth Analg 1994; 79:373–7

13. Ebert TJ, Muzi M, Berens R, Goff D, Kampine JP: Sympathetic responses to induction of anesthesia in humans with propofol or etomidate. ANESTHESIOLOGY 1992; 76:725–33

14. Morgan-Huges NJ, Sherry KM: Effect of anaesthesia on the cardiac response to intravenous adenosine. Br J Anaesth 2000; 84:633–5

15. Cray SH, Robinson BH, Cox PN: Lactic acidemia and bradyarrhythmia in a child sedated with propofol. Crit Care Med 1998; 26:2087–92

16. Strickland RA, Murray MJ: Fatal metabolic acidosis in a pediatric patient receiving an infusion of propofol in the intensive care unit. Crit Care Med 1995; 23:405–9

17. Bray RJ: Fatal myocardial failure associated with a propofol infusion in a child (letter). Anaesthesia 1995; 50:94

18. Parke TJ, Stevens JE, Rice AS, Greenaway CL, Bray RJ, Smith PJ, Waldmann CS, Verghese C: Metabolic acidosis and fatal myocardial failure after propofol infusions in children: five case reports. BMJ 1992; 305:613–6

19. James MF, Reyneke CJ, Whiffler K: Heart block following propofol: A case report. Br J Anaesth 1989; 213–5

20. Michaloudis D, Fraidakis O, Petrou A, Gigourtis C, Parthenakis F: Anaesthesia and the QT interval. Anaesthesia 1998; 53:435–9

21. Michaloudis D, Fraidakis O, Lefaki T, Dede I, Kanakoudes F, Askitopoulou H, Pollard J: Anesthesia and the QT interval in humans. Anaesthesia 1996; 51:219–24

22. McConachie I, Keaveny JP, Healy TE, Vohra S, Million L: Effect of anaesthesia on the QT interval. Br J Anaesth 1989; 63:558–60

23. Suri R, Poist ES, Hager WD, Gross JB: Unrecognized bulimia nervosa: A potential cause of perioperative cardiac dysrhythmias. Can J Anaesth 1999; 46:1048–52

24. Carlock FJ, Brown M, Brown EM: Isoflurane anaesthesia for a patient with long QT syndrome. Can Anaesth Soc J 1984; 31:83–5

25. Medak R, Benumof JL: Perioperative management of the prolonged QT interval syndrome. Br J Anaesth 1983; 55:361–4

26. Glass PS, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P: Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. ANESTHESIOLOGY 1997; 86:836–47

27. Barr G, Jakobson JG, Oewall A, Anderson RE: Nitrous oxide does not alter bispectral index: Study with nitrous oxide as sole agent and as an adjunct to i.v. anaesthesia. Br J Anaesth 1999; 82:827–30