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## ORIGINAL ARTICLE

## Favorable Safety Experience of Local Dental Anesthesia in ICD Recipients with Cardiac Channelopathies

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### Abstract

**Background:** Dental anesthetic management in implantable cardioverter defibrillator (ICD) recipients with cardiac channelopathies (CCh) can be challenging due to the potential risk of life-threatening arrhythmias and appropriate ICD therapies during procedural time.

**Objectives:** The present study assessed the hypothesis that the use of local dental anesthesia with 2% lidocaine with 1:100,000 epinephrine or without a vasoconstrictor can be safe in selected ICD and CCh patients, not resulting in life-threatening events (LTE).

**Methods:** Restorative dental treatment under local dental anesthesia was made in two sessions, with a wash-out period of 7 days (cross-over trial), conducting with a 28h - Holter monitoring, and 12-lead electrocardiography, digital sphygmomanometry, and anxiety scale assessments in 3 time periods. Statistical analysis carried out the paired Student's t test and the Wilcoxon signed-rank test. In all cases, a *significance level* of 5% was adopted. All patients were in stable condition with no recent events before dental care.

**Results:** Twenty-four consecutive procedures were performed in 12 patients (9 women, 3 men) with CCh and ICD: 7 (58.3%) had long QT syndrome (LQTS), 4 (33.3%) Brugada syndrome (BrS), and 1 (8.3%) Catecholaminergic polymorphic ventricular tachycardia (CPVT). Holter analysis showed no increased heart rate (HR) or sustained arrhythmias. Blood pressure (BP), electrocardiographic changes and anxiety measurement showed no statistically significant differences. No LTE occurred during dental treatment, regardless of the type of anesthesia.

**Conclusion:** Lidocaine administration, with or without epinephrine, can be safely used in selected CCh-ICD patients without LTE. These preliminary findings need to be confirmed in a larger population with ICD and CCh.

**Keywords:** Anesthesia, Dental/methods; Defibrillators, Implantable; Channelopathies, Epinephrine; Lidocaine.

### Introduction

Implantable cardioverter defibrillator (ICD) remains an effective therapeutic option to prevent sudden death, with a favorable profile in the natural history of cardiac channelopathies (CCh),<sup>1</sup> which are inherited cardiac ion channels disorders associated with potential ventricular arrhythmias and sudden death in the presence of a

structurally normal heart.<sup>2,3</sup> The most prevalent CCh are congenital long QT syndrome (LQTS), Brugada syndrome (BrS), and catecholaminergic polymorphic ventricular tachycardia (CPVT), which account for approximately one-third of unexplained sudden deaths.<sup>4,5</sup>

The treatment goal of CCh is to avoid arrhythmias and sudden death, which still remains a challenge. In cases of

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syncope, torsade de pointes or cardiac arrest requiring cardiopulmonary resuscitation, ICD and/or cardiac sympathetic denervation are often the treatment choices.<sup>6</sup>

The vast majority of devices employ bipolar leads, resulting in less susceptibility to electromagnetic interference (EMI).<sup>7</sup> Many studies assessed if magnetic electrical and electromagnetic fields from dental devices could affect cardiovascular implantable electronic devices (CIEDs).<sup>8-13</sup>

However, dental anesthetic management of patients with ICD are limited to case reports.<sup>14, 15</sup> These patients demand adequate care and analgesia because of the potential risk of life-threatening events (LTE), such as sustained ventricular tachycardias, as well as ICD therapies during the intervention and arrhythmic syncope.<sup>16</sup> It is crucial to provide a wary dental treatment environment in order to avert triggers for arrhythmic events, such as emotional stress, auditory stimuli, or increased vagal tone.<sup>17, 18</sup> Dentists, preferably with a cardiologist background, should obtain a detailed medical history of patients with ICD.<sup>19</sup>

It is important to emphasize that the use of local dental anesthesia in ICD recipients requires basic knowledge in order to avoid eminent complications in patients with risk of sudden cardiac death. In our previous study,<sup>20</sup> the use of local dental anesthesia with and without epinephrine in selected stable patients with LQTS and BrS did not result in life-threatening arrhythmias, though the maximum HR increased after the use of vasoconstrictors during the anesthesia period. Thus, we decided to perform a sub-analysis in cases with CCh and ICD recipients.

The present study aimed to determine the safety of lidocaine 2% with and without epinephrine 1:100,000 in patients with CCh and ICD.

## Methods

### Population

This study consisted of consecutive patients treated at the Heart Institute of Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo with inherited CChs (LQTS, BrS, or CPVT) and ICD, who were receiving optimal drug therapy. The inclusion criteria were patients with dental caries, unsatisfactory restorations in the mandible, and a recommendation for restorative dental treatment. The exclusion criteria were the following: allergy to lidocaine, sodium metabisulfite, or methylparaben; patients with recurrent syncope or

sustained arrhythmias documented for at least 3 months, including appropriate and inappropriate ICD shocks; patients who had received epinephrine in the previous 24 hours; and patients with a body weight <20 kg (a child  $\approx$  6 years of age because of the maximum safe dose of lidocaine, 4.4 mg/kg, used in 2 anesthetic cartridges).<sup>21</sup>

All patients were included after reading and signing the written informed consent form. This study was approved by the Ethics Committee of Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo (18221913.5.0000.0068), was previously registered at ClinicalTrials.gov (ID: NCT03182777), and can be accessed at <https://clinicaltrials.gov/ct2/show/NCT03182777?term=NCT03182777&rank=1>

### Monitoring

We compared the use of a mandibular nerve block with 2 cartridges (3.6 mL) of 2% lidocaine (72,000  $\mu$ g of lidocaine) without a vasoconstrictor and 2 cartridges of 2% lidocaine with 1:100,000 epinephrine (36  $\mu$ g of epinephrine) in all patients resulting in 2 conditions, verifying the occurrence of life-threatening arrhythmias (hemodynamically unstable arrhythmias, sustained ventricular tachycardia, or appropriate device shocks) in selected patients with CChs and ICD.

All patients were submitted to two sessions of restorative dental treatment with a washout period of 7 days (crossover trial), and the same patients were subsequently used as their own controls.

The procedure was blinded to the patient and the dentist performing to the presence or absence of epinephrine, and the carpule syringe was then covered with a sterile aluminum foil by one member of our research team. Next, our research team developed a randomization program in Excel (Microsoft Office), accomplished through the randomization of the application of an anesthetic solution.

The cardiac electrical activity was registered and analyzed during the two sessions in all patients for 28 hours by a Holter monitor (SEER Light Extend; GE Healthcare Brazil) with 3-channels (V1, V3, and V5 equivalent leads), starting 1 hour before the procedure. The occurrence and frequency of ventricular and supraventricular arrhythmias, identified on a minute-by-minute basis over the 28-hour study period (basal period, anesthesia period, procedure period, and post-procedure period), and the minimum, medium, and maximum heart rates (HRs) were included as electrocardiographic variables.

Specific records were also conducted at three time points during the dental treatment (at the beginning of the basal period, 15 minutes after the application of anesthesia, and at the end of the procedure) by the 12-lead electrocardiography (higher leads in BrS patients), digital sphygmomanometry for blood pressure (BP), and assessment of the Facial Image Scale for anxiety.

Corrected QT (QTc) interval in LQTS patients was calculated using Bazett's formula ( $QTc = QT \text{ interval} / RR \text{ interval}$ ), preferably in lead II, or V2 and V5. QTc values  $>460$  ms for women were considered abnormal.<sup>22</sup> The QT interval was manually measured from the beginning of the QRS complex to the end of the T wave from all 12 leads, using the tangent method. Whenever the end of the T wave could not be determined in any given lead, this lead was excluded from the analysis. The same cardiologist (NQSO) made all measurements, later confirmed by a second cardiologist (FCCD), both blinded to the patients' data. Occasional disagreements were resolved by consensus. Changes in QTc (categorized in  $>10\%$  of shortening or lengthening of QTc) were also analyzed.

For patients with BrS, an additional high right precordial lead was included to observe the possible occurrence of dynamic changes during the phases of the dental procedure.

Possible device shocks or ICD therapies were scheduled to be analyzed in all patients by the medical team, regardless of any therapies. The morphological pattern of dynamic changes was also analyzed in the right precordial leads in patients with BrS, as previously described.<sup>20</sup>

### Statistical Analysis

Due to the exploratory nature of this small cohort pilot study, there was no calculation in sample size. It was not possible to estimate the real incidence of arrhythmias with the use of local dental anesthetics in patients with CCh and ICD, since the literature is limited due to the absence of studies in this population.

The Kolmogorov-Smirnov test was used to verify the normality of the data. Continuous variables presenting normal distribution were described using mean and standard deviation, and those that did not show normal distribution were presented as median and interquartile range (IQR). All qualitative variables were calculated with absolute and relative frequencies. For comparison between 2 groups in relation to the means, the paired Student's t

test was applied. The Wilcoxon signed-rank test was used when the normality assumption was rejected.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 20.0 (SPSS, Inc, Chicago, IL). All tests were two tailed and the level of significance was set at 5%.

### Results

Twenty-four procedures were performed in 12 patients (9 women, 3 men) with CCh and ICD: 7 (58.3%) had LQTS, 4 (33.3%) BrS, and 1 (8.3%) CPVT. Ages ranged from 17 to 67 years, with a mean age of  $42.5 \pm 14$ , and 8 patients (66.6%) were white. All patients were in stable condition, with no recent events before the dental care and were receiving antiarrhythmic drug treatment (if indicated) according to the medical decision (Table 1).

There were no symptoms or ICD therapy (anti-tachycardia pacing therapy [ATP] and shocks triggered). No complications occurred during the dental procedure requiring interruption. After the administration of 2 cartridges of anesthetics, no patients complained of pain in either session, which lasted from 32 to 93 minutes, with an average of  $55 \pm 15$  minutes.

Holter monitoring registered the HR and numbers of supraventricular and ventricular premature beats per hour in both conditions (with and without epinephrine) during the study periods, with no significant difference between them ( $P > 0.05$ ) (Table 2).

No LTE occurred during dental treatment, regardless of the type of anesthesia. No patient with ICD received device shocks during the procedures and no sustained arrhythmias were observed.

Patients with LQTS and ICD presented no LTE, and the QTc measurements showed no statistically significant differences (Table 3). After the administration of anesthesia, changes in QTc (categorized in  $>10\%$  of shortening or lengthening of QTc) occurred in 2 patients, shortening this interval (Table 4; Figure 1 - A, B, C).

The four patients with BrS presented no changes in ECG morphology in either condition, with and without epinephrine, during the 3 moments of this study, and had no LTE.

The patient with CPVT showed no occurrence or documentation of ventricular arrhythmia in the electrocardiographic tracings.

At the recording time points, with and without epinephrine, there were no significant differences

Table 1 – Data from ICD recipients with CCh

CCh	Patient random number	Sex	Age	ICD Prevention	Symptoms	FH	Gene variants	ICD model
LQTS	12	F	67	secondary	ACA	yes	KCNH2	Lumax 640 VR-T (BT)
	21	F	41	secondary	ACA	no	KCNH2	Lumax 340 DR-T (BT)
	22	F	36	primary	asymptomatic	yes	KCNQ1	Lincox SD 65/16 (BT)
	23	M	28	primary	syncope	no	KCNH2	Lumax 340 DR-T (BT)
	26	M	17	secondary	ACA	no	KCNH2	AnalyST DR CD (SJ)
	27	F	53	secondary	ACA	yes	NI	Fortify ST DR (SJ)
	29	F	41	secondary	ACA	yes	KCNH2	Protecta XT DR (MD)
BrS	5	M	51	secondary	ACA	no	NI	Fortify ST DR (SJ)
	11	M	39	primary	syncope	yes	NI	Fortify ST VR (SJ)
	13	F	62	primary	palpitations	yes	NI	Dynagen EL DR (BS)
	15	M	41	primary	palpitations	yes	NI	Virtuoso VR (MD)
CPVT	16	F	34	secondary	ACA	no	NI	Protecta XT DR (MD)

CCh: cardiac channelopathy; Sex - M: male / F: female; ICD: implantable cardioverter defibrillator; ACA: Aborted cardiac arrest; SCD: sudden cardiac death; FH: Family history (SCD or channelopathy); NI: not identified; BT: Biotronik; SJ: ST Jude/ Abbott; MD: Medtronic; BS: Boston Scientific; LQTS: long QT syndrome; BrS: Brugada syndrome; CPVT: catecholaminergic polymorphic ventricular tachycardia.

Table 2 – Medium HR, density of ventricular arrhythmias and ICD therapy of the sample during study periods

	Without Epinephrine	With Epinephrine	p-value
28h Period	<b>medium HR (bpm)</b>		0.401
	mean ± SD	81.4 ± 9.2	80.3 ± 8
	<b>VPB</b>		0.541*
	median (IQR)	0.1 (0–6.4)	0.1 (0–8.7)
	<b>ICD therapy</b>	0	0
Basal Period	<b>medium HR (bpm)</b>		0.645
	mean ± SD	76.1 ± 8.3	76.6 ± 6.9
	<b>VPB</b>		0.752*
	median (IQR)	0 (0–0)	0,5 (0–7)
	<b>ICD therapy</b>	0	0
Anesthesia Period	<b>medium HR (bpm)</b>		0.261
	mean ± SD	72.5 ± 7.9	73.9 ± 7.6
	<b>VPB</b>		0.465*
	median (IQR)	0 (0–0)	0 (0–18)
	<b>ICD therapy</b>	0	0

Paired Student's *t* test; \* Wilcoxon signed-rank test. VPB: ventricular premature beats; ICD: implantable cardioverter defibrillator; HR: heart rate; IQR: interquartile range; SD: standard deviation.

**Table 3 – Mean and standard deviation QTc and average QTc at three study moments in the conditions without vasoconstrictor and with epinephrine in LQTS patients**

	Without vasoconstrictor	With epinephrine	p-value
<b>Basal period</b>			
QTc			0.911
mean ± SD	482.1 ± 42.7	484.4 ± 28.1	
<b>End of anesthesia</b>			
QTc			0.053
mean ± SD	456 ± 25.5	478 ± 23.4	
<b>End of procedure</b>			
QTc			0.306
mean ± SD	461.9 ± 34.6	473.7 ± 33	
<b>Average QTc</b>			
mean ± SD	466.7 ± 30.8	478.7 ± 25.8	0.362

*Paired Student's t test; QTc: Corrected QT; SD: standard deviation.*

in systolic and diastolic BP values and in anxiety measures.

## Discussion

In our study protocol, no patient received ICD therapy (ATP or appropriate/inappropriate discharges) during the dental treatment under local anesthesia regardless of the use of a vasoconstrictor. No sustained arrhythmias were observed, indicating that stable or treated patients with CCh and ICD can even be sheltered when epinephrine at pattern doses is used with lidocaine.

The safety of these anesthetics could be observed in our study protocol when QTc shortened in 2 LQTS patients, suggesting a possible protective effect of lidocaine. No LTE occurred in patients with LQTS, and no significant prolongation of the QT interval was observed.

Patients with BrS preserved the same electrocardiographic pattern during the three-time points in both conditions, with and without epinephrine, and no dynamic changes occurred in the high precordial leads.

No procedure-related complication was found in the patient with CPVT, nor was ventricular arrhythmia documented, even under epinephrine use. These results could also be explained, in part, by the possible protective

**Table 4 – Changes in the QTc interval (categorized in more than 10% of shortening or lengthening of QTc) after administration of local anesthesia when compared to the basal period, using lidocaine without vasoconstrictor and with epinephrine in LQTS patients**

Patient	Condition (random)	LQTS type	Changes in QTc interval
12	without epinephrine	2	no
	with vasoconstrictor		no
21	with epinephrine	2	no
	without vasoconstrictor		no
22	without vasoconstrictor	1	no
	with epinephrine		no
23	with vasoconstrictor	2	yes (shortening)
	without epinephrine		no
26	with vasoconstrictor	2	no
	without epinephrine		no
27	with epinephrine	1	no
	without vasoconstrictor		no
29	with epinephrine	2	no
	without vasoconstrictor		yes (shortening)

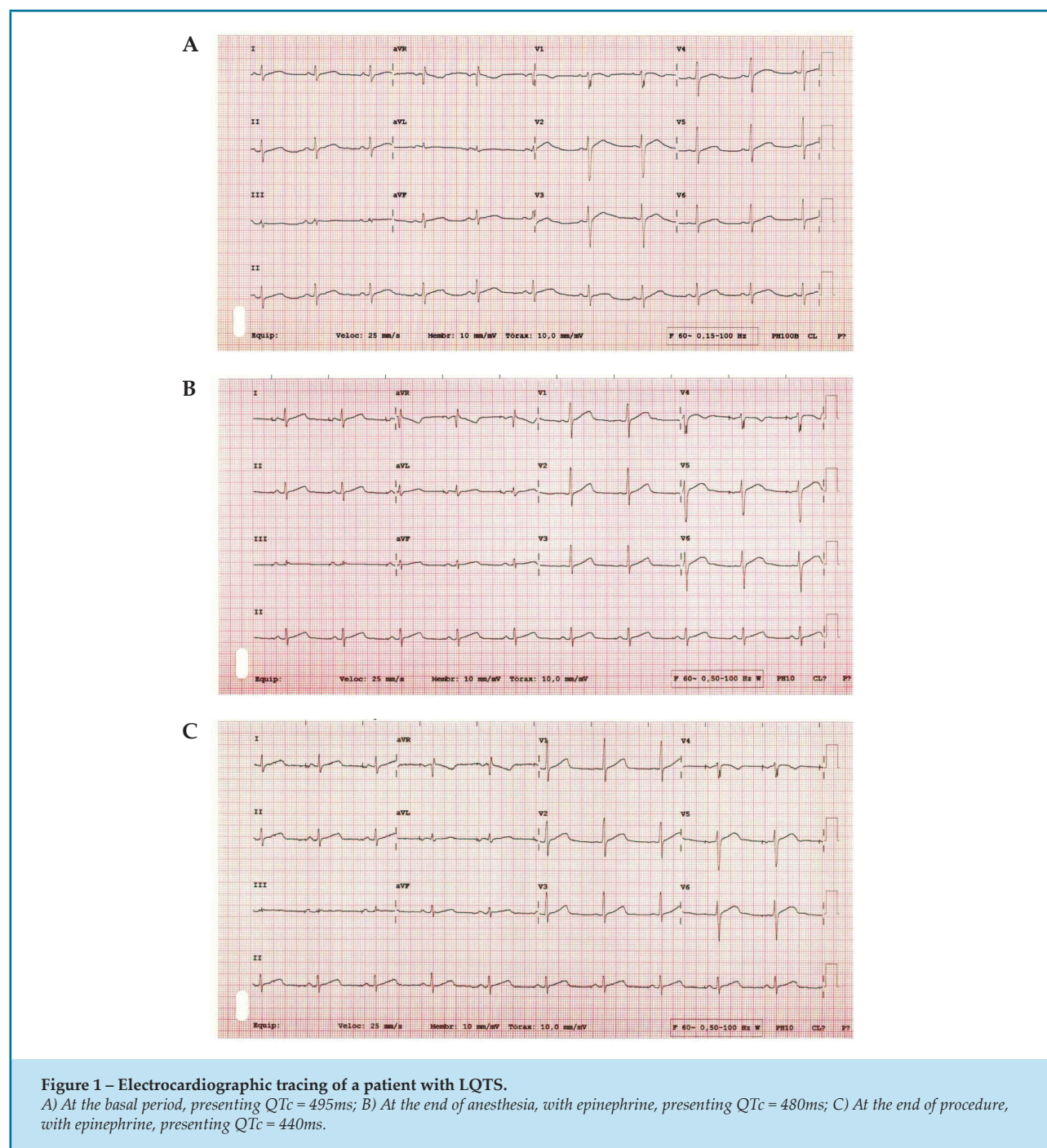
*QTc: Corrected QT; LQTS: long QT syndrome.*

effect of lidocaine in both periods, as well as by our strict inclusion criteria (only stable patients).

In a previous study, the use of local dental anesthesia with and without epinephrine in selected stable patients with LQTS and BrS did not result in life-threatening arrhythmias, though the maximum HR increased after the use of vasoconstrictors during the anesthesia period.<sup>23</sup>

According to American Society of Anesthesiologists Task Force,<sup>24</sup> anesthetic techniques do not influence the function of cardiac rhythm management devices (CRMD). However, anesthetic-induced physiologic changes (*i.e.*, cardiac rate, rhythm, or ischemia) in the patient may induce unexpected CRMD responses or adversely affect CRMD-patient interaction.

Anesthetic drugs have not been proven to affect pacing thresholds, though the physiologic consequences



of anesthetic management may. Myocardial ischemia and high blood levels of local anesthetics may increase electrophysiologic thresholds, but one hardly needs to be cautioned in these areas. It is also important to avoid hyperventilation in these patients, which could abruptly lower serum potassium levels.<sup>7</sup>

Vital parameters could be influenced by the use of vasoconstrictors added to the stress of the dental

procedure.<sup>25</sup> The findings of the present study showed no significant changes in BP and anxiety when compared to the conditions with and without epinephrine in patients with LQTS, BrS, and CPVT.

However, Tom<sup>26</sup> pointed out that anesthetics with epinephrine used in dentistry may have considerable effects upon the sensing and function of CIED. These can promote tachyarrhythmias and trigger ICD events

if there is no prior modification of anesthetic techniques, particularly with higher doses.

The insertion of an ICD can be performed under local anesthesia with sedation during induction of VF, testing of the defibrillator, and placement in the subpectoral pocket, thus avoiding general anesthesia. The total dose of local anesthesia should be minimized, and systemic absorption limited by the use of lidocaine with epinephrine. Local anesthesia, because of its sodium channel blockade, may exacerbate Brugada ECG changes. However, the class IB drugs, mexilitine and lidocaine, have not proven to cause ST-segment elevation<sup>27</sup> which, in the final analysis, also suggests protective and safety effects.

Theodotou and Cillo<sup>14</sup> described a case report using local anesthesia for dental treatment in a 55-year-old patient with ICD, BrS, and valvular heart disease. He was subjected to exodontia and abscess drainage under general anesthesia, along with 15 milligrams of lidocaine, with 1:100,000 epinephrine applied in the intraoral region for local anesthesia of the operated area. The patient presented no adverse cardiac events or intraoperative complications.

The dental care of a seven-year-old boy with a medical history of LQTS using ICD was described by Karp and Ganoza.<sup>28</sup> After a syncope episode with development of torsades de pointes, he suffered dental trauma and had no complications in his tooth extraction under general anesthesia.

In our casuistry, it was noted that 5 out of 7 patients with LQTS were carriers of type 2 LQTS, which could characteristically involve events triggered by noise and emotions.<sup>29</sup> The dental environment needs to be as calm and quiet as possible, but device noise is inevitable. Fortunately, none of the patients with LQTS had LTE, provided that the exclusion criteria were respected.

One case report described a 13-year-old CPVT patient, who had already undergone previous dental treatment under general anesthesia. Due to the recurrence of carious lesions and the need for further intervention, the cardiologist did not contraindicate the use of local anesthesia with epinephrine. However, the dentist considered it prudent to use 3% mepivacaine for local anesthesia in the amount of 3 cartridges, along with the administration of nitrous oxide to perform dental restorations in the dental chair in a hospital setting.<sup>30</sup> Our study also observed a favorable experience with one CPVT patient using lidocaine with and without epinephrine.

It is crucial to comprehend the perioperative management of these patients to avoid preventable complications, as the EMI sources should be kept as far from CIEDs as possible.<sup>7</sup> It is also important to be aware of inadvertent intravascular administration of local anesthesia.<sup>31</sup> Our protocol did not use sources that could interfere with sensing and pacing activity.

One of our limitations is the fact that this protocol can be applied only to stable patients, as mentioned in the methods section. Our small sample of patients also limits a strong statistical power of efficacy. However, this protocol can be used for exploratory data for future large studies or meta-analyses.

To the best of our knowledge, this is the first study of its kind (although small) to investigate the use of local dental anesthesia in consecutive patients with CCh and ICD, with no detectable adverse clinical impact.

## Conclusion

The use of lidocaine with and without epinephrine in CCh and ICD recipients did not result in LTE and had no clinical impact on patient safety. These preliminary findings need to be confirmed in a larger population with CCh and ICD.

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## Author Contributions

Conception and design of the research and analysis and interpretation of the data: Oliveira ACG, Neves ILI, Sacilotto L, Olivetti NQS, Bueno ACP, Pessente GD, Paul MAS, Montano TCP, de Carvalho CMA, Grupi CJ, Barbosa SA, Pastore CA, Samesima N, Wu TC, Hachul DT, Scanavacca MI, Neves RS, Darrieux FCC; acquisition of data: Oliveira ACG, Sacilotto L; obtaining financing: Neves ILI, Darrieux FCC; writing of the manuscript and critical revision of the manuscript for intellectual content: Oliveira ACG, Darrieux FCC.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

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## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Comissão de Ética para Análise de Projetos de Pesquisa (CAPPesq) under the protocol number 18221913.5.0000.0068. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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