

Impact of Anesthetics on the ST Segment Among Patients with Brugada Syndrome: Case Series

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Mignanelli G, Goncalves S, Trillat B, Dumans V, and Guen ML, all authors are equally contributed to this work.

1. Abstract

1.1. Aim: Brugada syndrome is a canalopathy causing rhythmic sudden death. The use of many drugs such as anesthetics but also many analgesics are contraindicated or not recommended in this pathology. The literature shows a low-level evidence while clinical experience may bring additional knowledge.

1.2. Methods: we conducted a retrospective cohort of 6 patients planned for elective surgery under general anesthesia with the aim to evaluate the EKG pattern of people with Brugada syndrome according to the hypnotic agent used. A continuous monitoring of heart rate and ST segment in the right precordial lead from induction to discharge of the room was retrospectively analyzed with concomitant drugs.

1.3. Results: this study did not show any conductive or rhythmic event after the use of propofol in daily practice whether in bolus or continuous administration. No related-effect by analgesic was documented.

1.4. Conclusion: under continuous monitoring, propofol administration remains possible in case of Brugada syndrome. Other agents used in daily practice, such as opioids, seem safe for these patients as it does not show any conductive or rhythmic event.

2. Introduction

Brugada syndrome, or "Sudden Unexpected Nocturnal Death

Syndrome" (SUNDS), is a canalopathy causing rhythmic sudden death by early inactivation of myocardial sodium channels [1, 2, 3, 4]. Described for the first time by Josep and Pedro Brugada in 1992 [5], the diagnosis of Brugada syndrome is mainly based on electrocardiogram (EKG) with two presentations: type I and II. Patients with type I Brugada syndrome (typical elevation of ST in the precordial derivations) are more likely to have rhythmic complications than the others [2, 6, 7]. All of these patients have no myocardial structural abnormalities [2]. The overall prevalence of this disease occurring at any age is 0.05% and is responsible for 4% of all sudden deaths and to 20% of sudden deaths in patients with structurally normal hearts [8]. Furthermore, this pathology is an important cause of sudden deaths in young subjects [9].

The use of many molecules such as anesthetics including propofol in the first place, but also many analgesics such as tramadol, fentanyl and sufentanil are contraindicated or at least not recommended in this pathology and this emphasizes the anesthesia challenge for such patients [10, 11]. Nevertheless, the rationale for these recommendations is based either on in vitro studies [12, 13, 14, 15, 16, 17] or in case reports and small series with a low-level of evidence [18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36].

The literature highlights that in patients with Brugada syndrome,

the occurrence of typical EKG changes must catch physicians' attention. The most specific change is a significant ST-elevation in right precordial leads. It is a predictive but reversible factor for ventricular rhythm disorders [1, 4, 8]. As a result, a continuous EKG monitoring helps to an early detection of abnormalities and the immediate suspension of triggering factors usually normalizes EKG with a risk regression for serious rhythm disorders and sudden death [37, 38, 39]. It is therefore reasonable to consider that the absence of significant ST elevation in right precordial leads during anesthesia in subjects with Brugada syndrome is a serious argument of safety of anesthetics, with a limited risk of severe ventricular rhythm disorders.

This cohort aims to evaluate the EKG pattern of patients with Brugada syndrome according to the main hypnotic used (propofol bolus followed by sevoflurane versus maintenance of anesthesia).

3. Methods

In 2016, the anesthesia department of Foch Hospital (tertiary hospital) created a database collecting complex medical cases. This database has been registered within the french authority (CNIL n°. 2034822) and we extracted from this database patients carrying a Brugada syndrome by specific keywords (Brugada and SUNDS).

Among these patients, demographic data were retrospectively collected. In addition, we were able to retrieve medical records about anesthetic management and monitoring in the operating theater and in the post-anesthesia care unit (PACU) (Centricity High Acuity Anesthesia, General Electric, Buc, France). It resulted in a minute-by-minute hemodynamic (arterial blood pressure, heart rate, SpO₂) and ST-segment measuring (Monitor B850, General Electric, Buc, France). A ST-segment significant change was defined as an elevation of more than two millimeters (0.2mV) in the right precordial leads [2]. Moreover, any rhythm disturbance during the recording period could be detected through any paroxysmal changes of heart rate. The occurrence of a paroxysmal heart rhythm disorder was defined as the increase in heart rate to more than 100 beats per minute in the absence of chronic impregnation by an anti-arrhythmic or chronotropic-negative effects drugs [40]. This continuous monitoring was used to put in perspective the variations of the ST segment in the right precordial leads and/or rhythm disorder according to the agents used during anesthesia: propofol and other drugs.

The primary endpoint was defined as the absence of significant elevation of the ST segment in the right precordial leads during patients' with Brugada syndrome anesthesia, from induction to the discharge from PACU. A specific follow-up during the length of stay was performed with the patients' medical file.

Patient's demographic data were presented as median and interquartile range for quantitative data, or absolute value, percentage for qualitative ones. The primary endpoint review was obtained by performing a non-parametric regression by smoothing the V1

segment elevation values recorded each minute (R software). The occurrence of rhythm disorders consideration was carried out on the Excel software after reporting the heart rate reading every minute and converted into graphs in curves for each patient.

4. Results

Six patients were retrospectively included between 2016 and 2019 as described on (Table 1).

Table 1: Demographic characteristics of patients with Brugada Syndrome

Population (n=6)	
Demographic data :	
Age (years)	65 [63;71,5]
Male (%)	4 (67)
Female (%)	2 (23)
ASA Score :	
ASA 2 (%)	2(33)
ASA 3 (%)	4(67)
Type of syndrome :	
Brugada syndrome type I (%)	4(67)
Brugada syndrome type II (%)	2(33)
Annual incidence ⁺ :	
2016 (%)	1(17)
2017 (%)	2(33)
2018 (%)	0(0)
2019 (%)	3(50)
Global incidence	6(100)
Genetic mutation identified* (%)	1 (17)
Treatment of Brugada syndrome (%)	
High blood pressure (%)	2 (33)
Anesthesia procedures :	
Induction :	
Propofol (%)	3(50)
Etomidate or Thiopental (%)	3(50)
Maintenance :	
Propofol (%)	3(50)
Sevoflurane (%)	3(50)
Airway management :	
Intubation (%)	3 (50)
Laryngeal mask (%)	3(50)
Duration of general anesthesia (minutes)	88.5 [78.5;151]

ASA: American Society of Anesthesiology

+ Annual incidence, all interventions included outside maternity

* SCN5A mutation

Qualitative variables are presented as numbers or percentages. Quantitative variables are presented as median [Q1-Q3].

The EKG pattern continuous monitoring showed no significant elevation of the ST segment in V1 derivation from the induction to the end of the anesthesia, regardless of the drugs used, in all patients included [Figure 1]. Particularly, no significant change in the ST segment was observed in patients who received propofol at induction with similar doses than usually (2 to 3 mg.kg⁻¹) [41]. There, were also no ST segment elevation in patients with maintenance of general anesthesia by a continuous administration of propofol (TCI administration). The remaining patients received either etomidate or thiopental at induction, with no elevation of the right precordial ST segment. In this case, maintenance of the anesthesia was performed either by sevoflurane or propofol with no modification in the ST segment.

Regarding the secondary endpoints, three patients received neu-

romuscular blocking agents: one with atracurium and then antagonized with neostigmine, two with rocuronium, one of which was antagonized with sugammadex. These patients did not show any significant ST segment variation in V1 lead over time. Many other agents suspected to cause rhythmic or hemodynamic disorders in patients with Brugada syndrome were administrated without any complication. Tramadol was used in two of our patients at a dosage of 100mg. Two patients received analgesia with remifentanyl and

four with sufentanyl. At last, one patient in our cohort received three 9 mg boluses of ephedrine and one 50 µg bolus of neosynephrine with no detectable event [10]. And more importantly, no paroxysmal tachycardia was observed during anesthesia [Figure 2]. The postoperative follow-up of these patients show no cardiac complication: no episode of palpitations or syncope during LOS occurred. No serious rhythm disorder has been reported after general anesthesia.

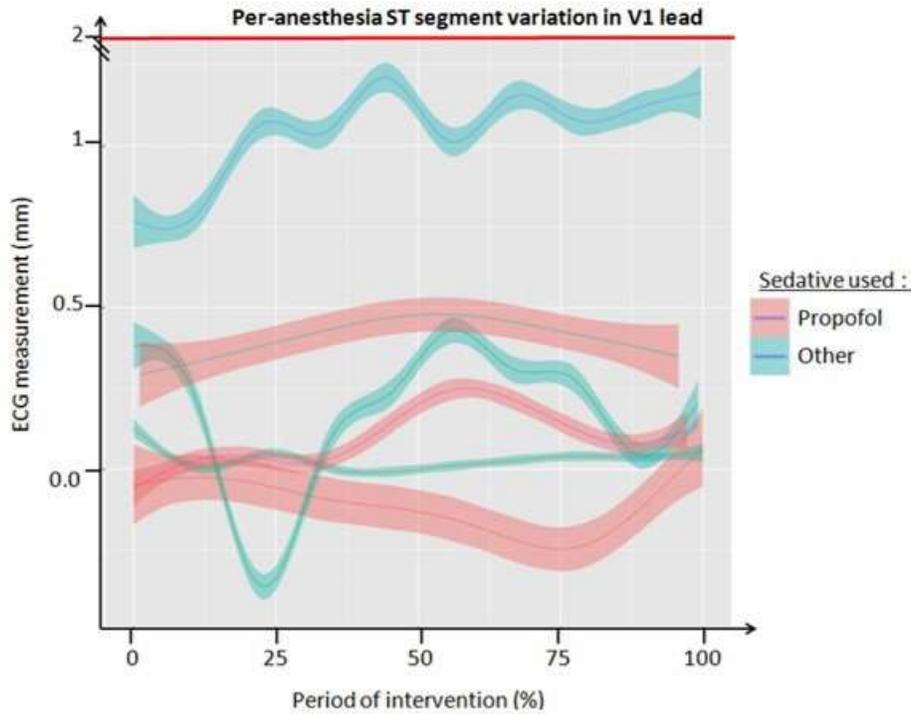


Figure 1: Individual curves obtained by performing a non-parametric regression by smoothing the V1 segment variation values recorded each minute during anesthesia (R software)

ECG: electrocardiographic; mm: millimeter

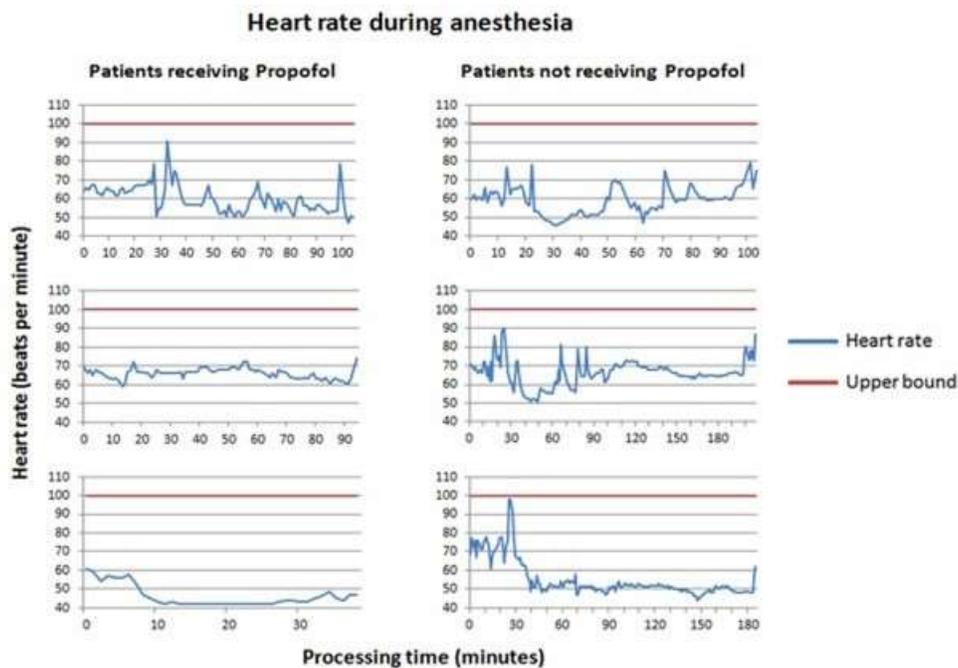


Figure 2: Individual heart rate per minute monitored during anesthesia

5. Discussion

Since 1992 with the original description of Brugada syndrome, many drugs have been incriminated as triggers of rhythm disorders with a high risk of sudden death. Among these drugs, many are used in the anesthesia field in daily practice and substitution by another drugs may be really challenging in most situations. In a formal description, Brugada syndrome is a rare disease and the literature is mostly made up of case reports. The resulting recommendations are therefore of low rank, with low levels of evidence, and do not allow a clear determination of safety for the use of these medications in patients with Brugada syndrome. Consequently, practices are very heterogeneous and subject of matter.

A recent controlled and randomized trial involving eighty patients conducted in 2019 by Flamée and al. [42] led to significant advances in knowledge. It was established that propofol induction compared with etomidate did not affect the QRS complexes and ST segments on the EKG performed at different stages of the surgical course: before induction, short recording of three minutes after induction once patients became unresponsiveness. In all the cases, maintenance of the anesthesia was performed by sevoflurane without monitoring the depth of anesthesia. Our study is therefore of particular importance because for the first time, a continuous monitoring of the ST segment and of the heart rate during anesthesia procedure is carried out in patients with Brugada syndrome, including in patients receiving propofol maintenance.

The interest of a continuous electrocardiographic monitoring, in addition to looking for a possible delayed effect of propofol on the myocardial sodium channels, is to be able to collect a possible ST elevation in right precordial leads or rhythm disorder with the injection of another drug suspected for decompensating Brugada syndrome such as analgesics, neuromuscular blocking agents or agents having a hemodynamic effect primarily. However, there is no ST segment elevation in V1 leads or paroxysmal rhythm disorders in this cohort. These results are compatible and complementary with the conclusions of recent studies, including the one of Flamée and al. [18, 42]. Furthermore, the use of propofol and remifentanyl in TCI-anesthesia is rarely described in the literature focusing on patients with Brugada syndrome. The use of this technique, correlated with the use of the scope and a bispectral index monitor allows to optimize sedatives and analgesics use by reaching the minimum effective dose, particularly justified with these patients. Finally, heart rate monitoring is used to diagnose the occurrence of rhythm disorders that might have occurred without any ST segment elevation, which did not occur in this cohort.

The second major point is the absence of delayed event after surgery which is partially related to the suppression of any significant trigger like anesthetics.

Some limitations can still be highlighted. First, the number of patients, although consistent for a rare disease, remains low with the

inclusion of only six patients over four years in a retrospective cohort. Second, there may be an interest in keeping them under monitoring over a long time to identify hemodynamic or cardiac events occurring later, particularly in patients with kidney or liver dysfunction that modifies pharmacokinetics. At last, this cohort is heterogeneous as the type of surgery and the type of anesthesia. But this is a representation of the real life with a remarkable accommodation to the recommendation in this specific identified situation.

In conclusion, this study analyzing specifically and continuously the ST segment variations in a right precordial lead during anesthesia does not show any conductive or rhythmic event after the use of anesthetic drugs in daily practice whether in bolus or continuous administration. Its interpretation remains difficult due to a small cohort and the variety of anesthesia procedures studied. It would be useful to create an international registry for the follow-up of patients with Brugada syndrome, allowing the often mentioned precautions to be updated while obtaining more solid and reliable knowledge. This approach would provide the opportunity to formulate recommendations with a high level of evidence to homogenize practices and increase the safety of care for these patients.

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Reference

1. Antzelevitch C, Yan GX. Cellular and ionic mechanisms responsible for the Brugada syndrome. *J Electrocardiol.* 2000; 33: 33-9.
2. Bayés de Luna A, Brugada J, Baranchuk A, Borggrefe M, Breithardt G, Goldwasser D, et al., Current electrocardiographic criteria for diagnosis of Brugada pattern: a consensus report. *Journal of Electrocardiology.* 2012; 45: 433-42.
3. Chen Q, Kirsch GE, Zhang D, Brugada R, Brugada J, Brugada P, et al., Genetic basis and molecular mechanism for idiopathic ventricular fibrillation. *Nature.* 1998; 392: 293-6.
4. Romero J, Li DL, Avendano R, Diaz JC, Tung R, Di Biase L. Brugada Syndrome: Progress in Genetics, Risk Stratification and Management. *Arrhythm Electrophysiol Rev.* 2019; 8: 19-27.
5. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. *J Am Coll Cardiol.* 1992; 20: 1391-6.
6. Babai Bigi MA, Aslani A, Shahrzad S. aVR sign as a risk factor for life-threatening arrhythmic events in patients with Brugada syndrome. *Heart Rhythm.* 2007; 4: 1009-12.
7. Priori SG, Napolitano C, Gasparini M, Pappone C, Della Bella P, Giordano U, et al., Natural history of Brugada syndrome: insights for

- risk stratification and management. *Circulation*. 2002; 105: 1342-7.
8. Antzelevitch C, Brugada P, Brugada J, Brugada R, Shimizu W, Gussak I, et al., Brugada syndrome: a decade of progress. *Circ Res*. 2002; 91: 1114-8.
 9. Antzelevitch C, Brugada P, Borggrefe M, Brugada J, Brugada R, Corrado D, et al., Brugada Syndrome: Report of the Second Consensus Conference. *Circulation*. 2005; 111: 659-70.
 10. <https://pubmed.ncbi.nlm.nih.gov/19716089/>
 11. Kloesel B, Ackerman MJ, Sprung J, Narr BJ, Weingarten TN. Anesthetic management of patients with Brugada syndrome: a case series and literature review. *Can J Anaesth*. 2011; 58: 824-36.
 12. Saint DA. The effects of propofol on macroscopic and single channel sodium currents in rat ventricular myocytes. *Br J Pharmacol*. 1998; 124: 655-62.
 13. Berman MF, Lipka LJ. Relative sodium current block by bupivacaine and lidocaine in neonatal rat myocytes. *Anesth Analg*. 1994; 79: 350-6.
 14. de La Coussaye JE, Brugada J, Allessie MA. Electrophysiologic and arrhythmogenic effects of bupivacaine. A study with high-resolution ventricular epicardial mapping in rabbit hearts. *Anesthesiology*. 1992; 77: 132-41.
 15. Haeseler G, Foadi N, Ahrens J, Dengler R, Hecker H, Leuwer M. Tramadol, fentanyl and sufentanil but not morphine block voltage-operated sodium channels. *Pain*. 2006; 126: 234-44.
 16. Hara Y, Chugun A, Nakaya H, Kondo H. Tonic block of the sodium and calcium currents by ketamine in isolated guinea pig ventricular myocytes. *J Vet Med Sci*. 1998; 60: 479-83.
 17. Wu YJ, Fang DC. Computer simulation of metoclopramide block of cardiac sodium channels. *Journal of Tongji Medical University*. 1992; 12: 94-7.
 18. Dendramis G, Baranchuk A, Brugada P. Anaesthetic management of patients with Brugada syndrome. *Indian J Anaesth*. 2018; 62: 154.
 19. Vernooy K, Delhaas T, Cremer OL, Di Diego JM, Oliva A, Timmermans C, et al., Electrocardiographic changes predicting sudden death in propofol-related infusion syndrome. *Heart Rhythm*. 2006; 3: 131-7.
 20. Tsutsumi YM, Tomiyama Y, Horikawa YT, Sakai Y, Ohshita N, Tanaka K, et al., General anesthesia for electroconvulsive therapy with Brugada electrocardiograph pattern. *J Med Invest*. 2011; 58: 273-6.
 21. Konishi J, Suzuki T, Kondo Y, Baba M, Ogawa S. Rocuronium and sugammadex used effectively for electroconvulsive therapy in a patient with Brugada syndrome. *J ECT*. 2012; 28: e21-2.
 22. Ferreira MN, Fontes S, Machado H. Interscalene plexus block and general anesthesia in Brugada syndrome. *Saudi J Anaesth*. 2019; 13: 371-3.
 23. Biricik E, Hatipoğlu Z, Küçükbingöz Ç. Sugammadex in a Patient with Brugada Syndrome. *Turk J Anaesthesiol Reanim*. 2016; 44: 99-101.
 24. Phillips N, Priestley M, Denniss AR, Uther JB. Brugada-type electrocardiographic pattern induced by epidural bupivacaine. *Anesth Analg*. 2003; 97: 264-7.
 25. Vernooy K, Sicouri S, Dumaine R, Hong K, Oliva A, Burashnikov E, et al., Genetic and biophysical basis for bupivacaine-induced ST segment elevation and VT/VF. *Anesthesia unmasked Brugada syndrome*. *Heart Rhythm*. 2006; 3: 1074-8.
 26. Corey SA, Varkey S, Phillips DR, Gay GL. Brugada Syndrome Induced by an Interscalene Block: A Case Report. *JBJS Case Connect*. 2017; 7: e96.
 27. Barajas-Martínez HM, Hu D, Cordeiro JM, Wu Y, Kovacs RJ, Meltser H, et al., Lidocaine-induced Brugada syndrome phenotype linked to a novel double mutation in the cardiac sodium channel. *Circ Res*. 2008; 103: 396-404.
 28. Clancy CE, Wehrens XHT. Mutation-specific effects of lidocaine in Brugada syndrome. *Int J Cardiol*. 2007; 121: 249-52.
 29. Arumugam D, Atherton JJ, Martin PT. A lethal injection? *The Lancet*. 2012; 379: 492.
 30. Bramall J, Combeer A, Springett J, Wendler R. Caesarean section for twin pregnancy in a parturient with Brugada syndrome. *International Journal of Obstetric Anesthesia*. 2011; 20: 181-4.
 31. Cole JB, Sattiraju S, Bilden EF, Asinger RW, Bertog SC. Isolated tramadol overdose associated with Brugada ECG pattern. *Pacing Clin Electrophysiol*. 2012; 35: e219-21.
 32. Rollin A, Maury P, Guilbeau-Frugier C, Brugada J. Transient ST elevation after ketamine intoxication: a new cause of acquired brugada ECG pattern. *J Cardiovasc Electrophysiol*. 2011; 22: 91-4.
 33. Bonilla-Palomas JL, López-López JM, Moreno-Conde M, Gallego de la Sacristana A, Gámez-López AL, Villar-Ráez A. Type I Brugada electrocardiogram pattern induced by metoclopramide. *Europace*. 2011; 13: 1353-4.
 34. Dash S, Pragathee S. Anaesthetic Management in Brugada Syndrome - A Case Report. *J Clin Diagn Res*. 2017; 11: UD03-4.
 35. Joshi S, Raiszadeh F, Pierce W, Steinberg JS. Antiarrhythmic induced electrical storm in Brugada syndrome: a case report. *Ann Noninvasive Electrocardiol*. 2007; 12: 274-8.
 36. Duque M, Santos L, Ribeiro S, Catré D. Anesthesia and Brugada syndrome: a 12-year case series. *J Clin Anesth*. 2017; 36: 168-73.
 37. Delinière A, Baranchuk A, Gai J, Bessiere F, Maucort-Boulch D, Defaye P, et al., Prediction of ventricular arrhythmias in patients with a spontaneous Brugada type 1 pattern: the key is in the electrocardiogram. *Europace*. 2019; 21: 1400-9.
 38. Brugada R, Campuzano O, Sarquella-Brugada G, Brugada P, Brugada J, Hong K. Brugada Syndrome. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJ, Stephens K, et al., éditeurs. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993.
 39. Junttila MJ, Gonzalez M, Lizotte E, Benito B, Vernooy K, Sarkozy A, et al., Induced Brugada-Type Electrocardiogram, a Sign for Imminent Malignant Arrhythmias. *Circulation*. 2008; 117: 1890-3.
 40. Al-Khatib Sana M, Stevenson William G, Ackerman Michael J,

Bryant William J, Callans David J, Curtis Anne B., et al. 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary. *Circulation*. 2018; 15: e190-252.

41. Sédation et analgésie en structure d'urgence (Réactualisation de la Conférence d'experts de la Sfar de 1999) - La SFAR [Internet]. Société Française d'Anesthésie et de Réanimation. 2016 [cité 26 sept 2020]. Disponible sur: <https://sfar.org/sedation-analgesie-structure-urgence/>
42. Flamée P, Varnavas V, Dewals W, Carvalho H, Cools W, Bhutia JT, et al., Electrocardiographic Effects of Propofol versus Etomidate in Patients with Brugada Syndrome. *Anesthesiology*. 2020; 132: 440-51.