

# orphananesthesia

## Anaesthesia recommendations for patients suffering from **Brugada syndrome**

**Disease name:** Brugada syndrome

**ICD 10:** I47.2

**Synonyms:** SUNDS - Sudden unexplained nocturnal death syndrome, Idiopathic ventricular fibrillation, Pokkuri (Japanese), Bangungut, Lai Tai (Philippines and Southeastern Asia).

Brugada syndrome is an arrhythmogenic cardiopathy defined both by the presence of ECG alterations at rest and by the occurrence of malignant tachyarrhythmias. Patients usually display complete or incomplete right bundle branch block pattern in more than one right precordial lead (V1-V3) at ECG, in association with variable ST segment elevation (more or less than 2 mm, coved-type or saddle-back type). Clinical presentation includes syncope, typically occurring at rest or during sleep, and it is caused by fast polymorphic ventricular tachycardia. In some cases ventricular fibrillation may occur, leading to cardiac arrest and sudden death. The prevalence of the disease ranges from 5/10000 (Caucasians) to 14/10000 (Japanese), and it is considered a major cause of sudden death among young males of Asian origin without cardiopathy background.

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Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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### Disease summary

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Although de novo mutations are possible, the syndrome shows an autosomal dominant inheritance with incomplete penetrance. Thus far, only loss of function mutations in the gene encoding for cardiac sodium channel (SCN5A on chromosome 3p21-23) are certainly linked to the syndrome, but they are identified just in 20% of patients. Therefore, other ionic channel disturbances may have a role in the disease (e.g. calcium channel CACNA1c and CACNB2b alterations). Average age of diagnosis is 40 years, and implantable cardioverter-defibrillator (ICD) is the only effective therapeutic option for symptomatic patients with spontaneous or pharmacologic-induced ECG pattern. Local anaesthetics (especially bupivacaine), as well as increased vagal tone, fever, inadequate analgesia and electrolyte imbalances, may trigger malignant arrhythmias in these patients.

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### Typical surgery

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Patients with a definitive diagnosis may turn to anaesthetists for insertion of an ICD just like unknown patients do for non-related surgery.

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### Type of anaesthesia

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At present time, there is a definite recommendation neither for general nor for regional anaesthesia.

General anaesthesia can be performed safely, both as inhalational and as balanced with opiates. To date, the clinical effects of halogenated agents on the ECG and QTc interval are controversial. Several authors have reported variable patterns of QTc prolongation (or shortening) with almost every volatile anaesthetic available. This may raise safety concerns because of the patients' proarrhythmic condition. The body of evidence to recommend a specific agent is quite little and is based on seminal studies or case reports. However, in most of the cases, sevoflurane has been used with no intraoperative complications.

According to experimental animal models, propofol may affect cardiac calcium channel function, promoting the alterations of cardiac depolarization underlying ST segment elevation in Brugada patients. While propofol boluses are considered safe, there are conflicting reports on the safety of propofol-based continuous infusions. Although some authors conducted propofol TIVA uneventfully, maintenance of general anaesthesia with propofol is recommended for the shortest period of time and with the lowest infusion rates as possible. In the late phases of Propofol Infusion Syndrome (PRIS), the development of a Brugada-like ECG has been reported. To date, it remains unclear whether PRIS and Brugada syndrome share a common pathophysiology. Propofol-based general anaesthesia should be performed carefully with coexisting sepsis, impaired microcirculation, increased endogenous or exogenous catecholamine levels.

Regional anaesthesia and neuroaxial blockade may be performed with caution. Since local anaesthetics affect myocardial sodium channels, their use may precipitate ECG alterations and cardiac arrhythmias. Local anaesthetics with slow dissociation properties (e.g. bupivacaine and ropivacaine) should be avoided as long as several complications have been reported, mainly when performing epidural infusions. Lignocaine is considered safe when combined with adrenaline and used in low dose. Rapid absorption into the systemic circulation and the use of large amounts of local anaesthetics should be avoided. Whenever

feasible, ultrasound-guided peripheral nerve blocks should be preferred over neuroaxial/central blockade. When needed, longer-lasting analgesia could be produced by repeated boluses through a continuous nerve catheter.

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#### **Necessary additional diagnostic procedures (preoperative)**

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Despite being very characteristic (ST segment elevation  $\geq 2$  mm, coved-type with no isoelectric tract and with negative T-wave from V1 to V3 precordial leads), Brugada-like ECG is not an exclusive feature of the syndrome, and other primary heart diseases underlying this pattern should be ruled out (e.g. ischaemic heart disease, myopericarditis, pulmonary embolism, aortic dissecting aneurysm, hyperkalemia or hypercalcemia, dystrophinopathies, left bundle branch block). Once these conditions have been excluded, all patients with diagnostic type 1 ECG pattern and/or personal history of syncope, dizziness, vertigo, nocturnal agonal respiration or seizures of unknown origin should be referred to a cardiologist for risk stratification. Asymptomatic patients with an uncertain ECG pattern (ST segment elevation  $< 2$  mm, either coved or saddle-back type) are at lower risk of arrhythmias. However, they should be asked if sudden death at a young age already occurred in their families and should subsequently be referred to a cardiologist. As soon as a patient with Brugada syndrome is identified preoperatively, first-degree relatives should be screened for the disease. In case a patient already has an ICD, the model should be noted, and further intraoperative management of the device should be performed under the supervision of a trained physician. Preoperative beta-blockade should be adopted after weighing up benefits and potential risks with regards to intraoperative bradycardia, which may be increased by the interaction with anaesthetic agents.

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#### **Particular preparation for airway management**

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Not reported.

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#### **Particular preparation for transfusion or administration of blood products**

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Not reported. Promptly correct calcemia or kaliemia imbalances following repeated transfusion, as they may provide a substrate for arrhythmia triggering.

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#### **Particular preparation for anticoagulation**

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Not reported.

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#### **Particular precautions for positioning, transport or mobilisation**

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Ventricular tachycardia in Brugada syndrome usually occurs during periods of bradycardia and increased vagal tone. Anaesthetists should be careful during intraoperative position changes to avoid unintentional parasympathetic stimulation and reflexes.

### **Probable interaction between anaesthetic agents and patient's long term medication**

Not reported. Quinidine may be used in patients with ICD and multiple shocks, in cases with contraindication to ICD implantation and in children as a bridge to ICD or as an alternative to it. Careful monitoring of QTc should be performed, and QT-prolonging drugs should be avoided.

### **Anaesthesiologic procedure**

Since they have resulted in Brugada ECG patterns, droperidol and phenothiazines are recommended neither as sedative premedication nor as antiemetic prophylaxis.

Benzodiazepines have been used uneventfully as preoperative premedication.

The choice of induction agent is not critical. Thiopental sodium has been used as induction agent with no problems reported. Despite a few reports of adverse events (ST segment elevation), propofol boluses as well as etomidate are probably safe. To date, ketamine has been reported to develop Brugada-like ECG in case of acute intoxication with far higher plasma levels than those reached in clinical practice. Nonetheless, once ketamine has been chosen, careful cardiac monitoring is necessary, particularly with concomitant use of propofol.

Although it has been used for neuromuscular blockade at intubation, succinylcholine raises concerns about the risk of bradycardia and hyperkalemia and it is not recommended. Non-depolarizing agents have been used without any reported complication.

Volatile anaesthetics may be used for induction or maintenance of anaesthesia, both in O<sub>2</sub>-air and in O<sub>2</sub>-N<sub>2</sub>O mixture. In the majority of clinical reports, sevoflurane was the most common chosen agent.

Among cardiovasoactive drugs, alpha-receptor agonists (e.g. norepinephrine, methoxamine, phenylephrine) have been reported to worsen ST segment elevation or unmasking Brugada ECG pattern in affected patients. Clonidine and dexmedetomidine have raised concerns as well, as they may induce bradycardia. Vasopressors with dual alpha- and beta-agonist action (dopamine) have unpredictable effects. Ephedrine has been used uneventfully to treat intraoperative hypotension. Beta-adrenergic agents (e.g. isoproterenol, orciprenaline and dobutamine) may have beneficial effects as antiarrhythmic drugs. Worth of mentioning, low-dose isoproterenol infusion has been used successfully to restore persistent ST-segment elevation and to treat electrical storm. Class IC sodium channel blockers (e.g. flecainide, propafenone) and class III amiodarone are contraindicated, as they precipitate cardiac arrhythmias.

Intraoperatively, factors known to affect autonomic tone such as light/too deep anaesthesia and inadequate analgesia should be minimised. Bradycardia as a result of increased surgical stimulation should be avoided. Fever and hypertermia are known to worsen ECG manifestations of Brugada syndrome, and they should be prevented, both during the surgical procedure and postoperatively. Hyperkalemia, hypokalemia, hypercalcemia and metabolic acidosis may induce electrical instability. Therefore electrolyte homeostasis should be pursued.

Neuromuscular blockade (NMB) antagonisation is a matter of debate. Neostigmine and pyridostigmine may increase parasympathetic drive and induce bradycardia. Furthermore, while some authors have used neostigmine without complications, some others report

accidents at awakening and recommend NMB to wear off spontaneously. To date, avoiding cholinergic agents seems to be prudent, even though likelihood of complications is reduced by simultaneous administration of atropine or glycopyrrolate. When using steroidal nondepolarizing agents to achieve NMB, i.v. sugammadex would be the reversal agent of choice. Up to 4 mg/Kg sugammadex have been used with no ECG alterations reported.

Nausea and vomiting are concomitant with increased parasympathetic tone, and they should be prevented. Intravenous antiserotonergic agents (ondansetron, granisetron) and dexamethasone are safe.

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### Particular or additional monitoring

Standard monitoring should include: 5-lead ECG with continuous right precordial ST-tracing, pulse-oximetry and arterial cannulation. The last one allows the detection of a cardiac arrhythmia even in case of concomitant electrocautery disturbances. External defibrillation pads should be applied before starting anaesthesia. If already present, ICD should be turned off to prevent inappropriate discharge due to monopolar surgical diathermy. In pacemaker-dependent patients, the pacemaker/ICD should be switched to a non-sensing mode (VOO or DOO). Nonetheless, time spent in VOO or DOO should be limited to prevent a potential R-on-T phenomenon. The pacemaker/ICD should be turned on and reprogrammed soon after the end of the surgical procedure. The presence of a trained physician in the operating theatre is recommended. Defibrillation pads should remain on site until the time ICD is turned on again.

Body temperature monitoring is strongly recommended to avoid fever or hyperthermia. Furthermore, NMB monitoring is necessary for appropriate reversal or antagonisation at emergence from anaesthesia. To minimize autonomic imbalances due to inadequate anaesthesia, some authors recommend BIS or Spectral Entropy use.

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### Possible complications

ST segment elevation or increase, life-threatening arrhythmias such as rapid polymorphic VT and VF with cardiac arrest may develop as a consequence of bradycardia, hyperthermia, hyperkalaemia, neuro-mediated surgical reflexes, vomiting, interaction between the above mentioned drugs, or as a combination of them all. Notice that arrhythmias are more likely under these conditions, but they may occur even in their absence. Where persistent ST-segment elevation or worsening of an already elevated ST-segment are observed, low-rate isoproterenol infusion (0.15 mcg/min) has been reported to be effective in restoring the previous ECG.

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### Postoperative care

As for any other procedure, the degree of postoperative assistance and monitoring depends on the specific surgical procedure, on intraoperative complications and preoperative conditions of the patient. ICU admission is not mandatory. However, postoperative monitoring of every patient (including those with an ICD) should include continuous ECG tracing for at least 24-36 hours. Thus, a short stay in a cardiology ward or a coronary care unit has been suggested by some authors.

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### Information about emergency-like situations / Differential diagnostics

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*caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease*

Emergency situations caused by the illness have been described previously.

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### Ambulatory anaesthesia

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Ambulatory anaesthesia is recommended only for low-risk surgery and in case potentially arrhythmogenic drugs have not been administered.

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### Obstetrical anaesthesia

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Brugada syndrome is 8 times more frequent among young males than in females. Thus, few data about anaesthesia practice in the obstetrical field are available. Spontaneous delivery seems to be safe in patients with Brugada syndrome. Opioids may be used with confidence, both for intrathecal administration and for epidural infusion. Bupivacaine and ropivacaine should be avoided whenever possible. Nonetheless, subarachnoid use of 0,5% bupivacaine for caesarean section with no complications has been described. Due to the large amounts of local anaesthetic that should be used and to the risk of systemic absorption, bupivacaine and ropivacaine epidural infusions should rather be avoided. In this case, lidocaine (with or without opioids) would be the drug of choice. While ergonovine alkaloids as uterotonic agents are not recommended, oxytocin use is considered safe. Intraoperative hypotension should be managed by i.v. fluid administration and ephedrine, although phenylephrine has been used without complications, too.

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