The Surgical Patient with Brugada Syndrome: A Four-Case Clinical Experience

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Brugada syndrome is characterized by a distinctive electrocardiographic pattern (right bundle branch block and ST segment elevation in precordial leads) and a high risk of cardiac arrest for malignant dysrhythmia. The genetic basis is a molecular defect of the cardiac sodium channel and the pattern of inheritance is autosomal dominant. Many factors during general anesthesia (medications, bradycardia, temperature changes) could precipitate malignant dysrhythmia in these patients. Because criteria to identify the surgical patient at high risk for developing malignant dysrhythmia are lacking, we can only speculate about the available studies on nonsurgical patients. We describe four patients during general anesthesia and propose intraoperative and postoperative monitoring (the first 36 h).

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In 1992, Brugada and Brugada (1) described eight patients who were resuscitated from cardiac arrest without demonstrable structural heart disease but who presented right bundle branch block and ST segment elevation in leads V1–V2–V3. These cases established this electrocardiographic (ECG) pattern as a distinctive new syndrome associated with augmented risk of sudden death. Since then, the genetic basis of the syndrome has been reported (2): a molecular defect of gene *SCN5A* encoding the cardiac sodium channel mapped to 3p21-p23. Familial occurrence has been described with an autosomal dominant pattern of inheritance. Brugada et al. (3) proposed that asymptomatic patients are at high risk of cardiac arrest (approximately 60% of patients within 1 year from the diagnosis); thus justifying aggressive therapy such as the implantation of a cardioverter-defibrillator. A prospective study (4) reported that in asymptomatic patients the risk of cardiac arrest is infrequent enough to justify postponing implantation of a cardioverter-defibrillator. Many factors (medications, bradycardia, temperature changes) during general anesthesia could precipitate malignant dysrhythmia in these patients.

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Case Reports

Our experience concerns 4 patients with Brugada Syndrome who underwent surgical intervention from September, 2000 to December, 2002. The diagnosis of the syndrome was easily obtained by ECG; all patients presented incomplete right bundle branch block and ST segment elevation ≥0.1 mV in precordial leads. Structural heart disease or coronary artery disease were excluded by noninvasive tests and the absence of creatine phosphokinase elevations. Only one patient had a history of aborted sudden death and syncopes caused by torsades de pointes. The others were asymptomatic.

During general anesthesia, continuos ECG (DI, DII, DIII, aVL, aVF, aVR, V5) with online analysis of dysrhythmia and ST segment, invasive arterial blood pressure by radial artery cannulation, arterial oxygen saturation, end-tidal CO_2, esophageal temperature, and urine output were monitored. Only one patient had an implanted cardioverter-defibrillator at the time of operation. It was turned off for surgery.

Patients received preanesthesia diazepam orally. General anesthesia, after induction with propofol, fentanyl, and cisatracurium, was maintained with sevoflurane, cisatracurium, and fentanyl. Ventilation was controlled and monitored by analysis of arterial blood gases. At awakening we avoided any stimulation and began postoperative analgesia with continue infusion of ketorolac and opioids through an elastomeric pump. An external defibrillator, connected to defibrillation pads placed on the patient, was available in the operating room during surgery.

All patients (Table 1) were males 25 to 43 yr of age; two underwent emergency operation for acute appendicitis and two had elective urologic operations (varicocelectomy and transurethral prostatectomy). One patient, after appendectomy, developed hemoperitoneum. Every patient presented ST segment elevation in precordial leads between 0.1 and 0.2

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Table 1. Demographic Characteristics, Surgical History, and Risk Stratification of the Patients

	Patient 1	Patient 2	Patient 3	Patient 4
Age (yr)	25	36	27	43
Sex	Male	Male	Male	Male
Operation	Appendicitis	Varicocelectomy	Appendicitis	TURP
Symptoms	No	No	No	Yes
ICD (cardioverter-defibrillator)	No	No	No	Yes
ST segment elevation	0,1	0,15	0,15	0,2
Rhythm ECG (electrocardiography) baseline	Sinus	Ventricular ectopy	Sinus	Sinus
Priori et al. risk category	Intermediate	Intermediate	Intermediate	High
Atarashi et al. risk category	Low	High	High	High

TURP = transurethral resection of the prostate.

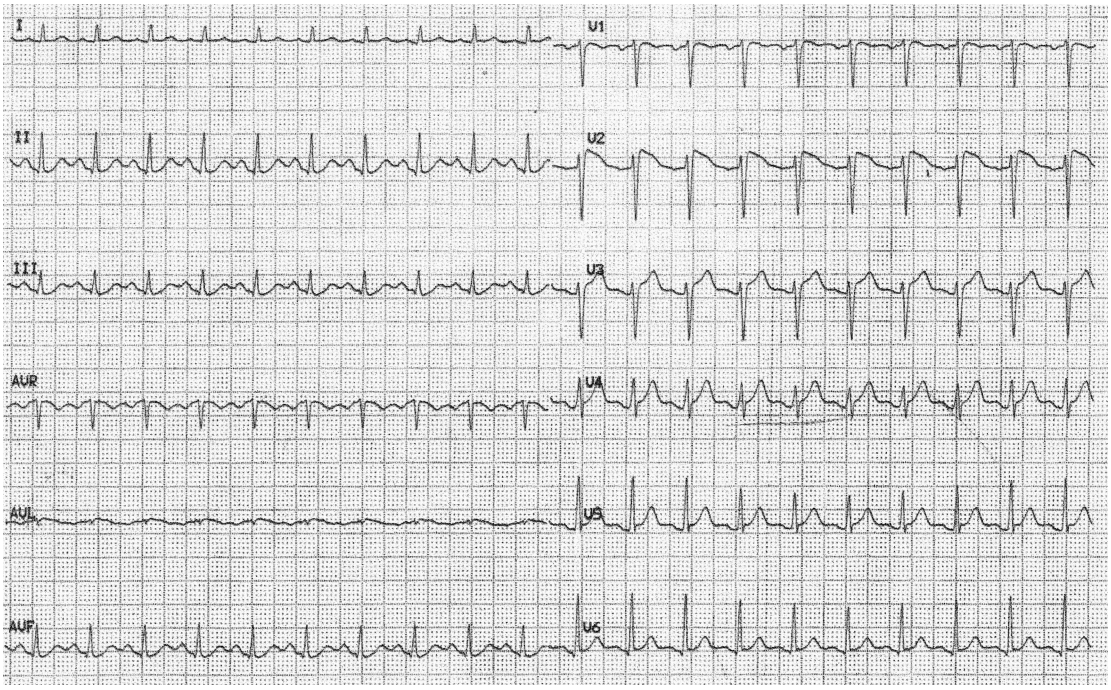

Figure 1. Electrocardiographic (ECG) preoperative pattern of patient number 2. ST segment alteration can be noted in precordial leads V1–V2–V3.

mV (Fig. 1) and incomplete right bundle branch block. During anesthesia, one patient presented rare ectopic beats during ECG monitoring. Neither dysrhythmias nor ST segment elevation were observed. The esophageal temperature was kept ≥35.5°C. The hemodynamic variables were stable and there were no problems with mechanical ventilation or gas exchange.

Every patient was admitted to the cardiac intensive care unit for a postoperative period of at least 36 h; no patient presented worsening in ST segment elevation. The patient who had hemoperitoneum had sinus tachycardia without changes in the ST segment.

Discussion

The prevalence of Brugada syndrome has not been accurately estimated but, according to previous studies, the disease is not uncommon. The incidence may be even more frequent in the younger population and it is the most common cause of sudden death in individuals younger than 50 years without underlying cardiac disease in the Japanese population (5) and in South Asia (6). Roberts and Brugada (7) report an estimated incidence of this form of sudden death between 26 and 38 per 100,000 people per year. Anesthesiologists should be aware of Brugada syndrome because it is not a rare disease; from 20% to 60% of idiopathic ventricular fibrillation could be associated with this syndrome.

Risk stratification in these patients is important for defining treatment: e.g., the choice of cardioverter-defibrillator implantation (4). Current studies only propose risk stratification for nonsurgical patients; the

few reports available did not demonstrate any heart rate instability, electrical storm or other adverse events during surgery, therefore more data are necessary for a better risk evaluation in surgical patients. We can only extrapolate this information from the studies conducted in nonsurgical patients. Priori et al. (4) showed, in a prospective evaluation, that asymptomatic subjects are at less risk for sudden death and that management strategies should be based on risk stratification algorithms. Brugada et al. (8) proposed a risk stratification scheme based on screening with programmed electrical stimulation of asymptomatic patients, but this test is not reproducible and it is useless for risk stratification (4,9,11). Other authors proposed different criteria for risk stratification but they all need to be confirmed: Priori et al. (9) proposed S wave width $\geq$0.08 s in V_1 and ST elevation $\geq$0.18 mV in V_2; Atarashi and Ogawa (10) proposed ST elevation $>$0.15 mV at baseline with pilsicainide-induced additional ST elevation $>$0.1 mV, and Morita et al. (11) proposed the simultaneous presence of syncopes and ST segment elevation at ECG baseline.

All our patients presented an ECG pattern of Brugada syndrome at rest, incomplete right bundle branch block, and different width of ST elevation from V_1 to V_3. Applying the criteria reported above, three of our patients were in a high risk or intermediate risk subgroup for malignant dysrhythmias.

During general anesthesia, many factors could precipitate ventricular fibrillation in these patients. This is only the fifth report about general anesthesia administration in patients with Brugada Syndrome. In a study from Japan (12) concerning a patient without obvious heart disease, and in a study by Brugada et al. (3), it has been suggested that bradycardia could precipitate arrhythmia and that the degree of ST elevation increases with the heart rate. Polymorphic ventricular fibrillation is also inducible with one or two ventricular premature beats during ventricular pacing. For this reason we monitored the ECG trace and used an automated ECG ST segment trending monitor (Datex, Helsinki; Finland) (13) to detect any change. During anesthetic induction with propofol all of our patients had a decrease in heart rate without changes in the ST segment. During anesthesia their heart rates were stable and never $<$60 bpm.

Many drugs can have a proarrhythmic effect. In patients with Brugada syndrome, Class I antiarrhythmic drugs (14) sodium channel blockers (specifically procainamide and ajmaline) can induce ST segment elevation because they interact directly with the receptors affected by the syndrome. The muscarinic and α-adrenergic receptor agonists cause an increase in ST segment elevation (12) in the general population and in many cases of Brugada syndrome (4). Psychotropic (15) drugs also have electrophysiologic effects: amitriptyline induces cardiac sodium channel blockade but also causes the reduction in the inward sodium current and a prominent outward current (several mutations on the *SCN5A* gene produce the same effects); phenotiazines modify the action potential of cardiac myocytes, an effect similar to that reported for quinidine; fluoxetine depresses sodium and calcium channel activation producing a shortening in action potential duration. The final effect of all these drugs is a reduction in action potential duration. Recently it has been reported that epidural bupivacaine administration could induce the ECG characteristic pattern of Brugada syndrome; bupivacaine binds to the sodium channel and produces a depression of the rapid phase of depolarization in Purkinje fibers (16); the patient in this report had a resting ECG showing a right bundle branch block. The authors discussed the potential risk of serious arrhythmias with bupivacaine use. Volatile anesthetics can also interfere with QT interval in patients without Brugada syndrome: a prospective double-blind randomized study (17) found a significant increasing QT interval during induction with isoflurane, no changes with sevoflurane, and significant shortening with halothane. We used sevoflurane in every patient and there were no changes in QT interval.

The ion channel abnormality of Brugada syndrome should be temperature sensitive (18); we therefore monitored esophageal temperature in every patient.

Cardiac arrhythmias, even in the general population, are most likely to occur in the postoperative period (19); therefore it was necessary, during recovery in the intensive care unit, to detect and treat them. Hence, we decided to monitor our patients for 36 postoperative hours.

Brugada syndrome is an increasingly recognized disorder. The ECG pattern should alert the clinician to suspect possible Brugada syndrome. If this finding is confirmed further investigation is justified. However, there is a degree of genetic heterogeneity, and some patients affected by the syndrome do not show the typical ECG pattern. Follow-up data indicate that the risk of ventricular tachyarrhythmia is minimal in the absence of a resting ECG abnormality and the absence of adverse events reported during anesthesia should be reassuring. For these patients many situations that could precipitate ventricular fibrillation happen during anesthesia. Even if the few reports (12,20,21) did not detect any arrhythmic problem, it is difficult to draw a firm conclusion, especially because of the heterogeneous nature of the mutation leading to Brugada syndrome. Risk stratification criteria currently do not allow identification of patients who run the risk of malignant arrhythmias, and surgical patients probably need different criteria for this stratification. It is our opinion that with an adequate anesthetic plan the risk during major or minor procedures

should be the same; during major procedures the risk may be increased for the longer procedure time.

Even if there were no reported problems during surgery, general, regional, or local anesthesia should be carefully managed and should include, at least, monitoring ST segment on ECG, measuring invasive arterial blood pressure and body temperature, keeping an external defibrillator ready in the operating room and, if possible, avoiding drugs that could trigger arrhythmias. We used the necessary intraarterial blood pressure monitoring to readily detect the hemodynamic effects of any dysrhythmia or any drug or other trigger mechanism. Anesthesiologists should consider the risk/benefit ratio of arterial cannulation, especially for short surgery procedures or for regional and local anesthesia.

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General anaesthesia in a patient with Brugada syndrome

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The successful administration of a combined general and epidural anaesthetic to a patient with Brugada syndrome is reported. A review of the literature is presented.

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We describe the successful administration of a combined general and epidural anaesthetic for laparotomy in a patient with Brugada syndrome.[1]

Case report

A 52-yr-old man presented with acute small bowel obstruction for a laparotomy. Eighteen months before admission, the patient had suffered an unheralded episode of a pulseless cardiac arrhythmia (recognized by a relative trained in basic life support) at home. Recovery occurred after basic cardiopulmonary resuscitation, before the arrival of the paramedic ambulance crew. A further episode of monitored ventricular fibrillation (VF) in the ambulance required a single 200 J cardioversion. He had no history of angina or previous syncope and there was no family history of sudden death. His father had suffered a myocardial infarction at the age of 50 and died. The patient had been a smoker until 3 months before admission and had a history of peptic ulcer that had been treated with ranitidine.

On investigation, the patient had a 12-lead ECG showing a partial right bundle branch block with a 'coved' pattern of ST elevation in leads V_1 to V_3 (Fig. 1). Cardiac enzymes were not elevated. Subsequent cardiac catheterization showed normal left ventricular function and coronary arteries. The patient underwent a flecainide challenge with an i.v. bolus of 150 mg. This produced accentuation of the ST elevation, consistent with Brugada syndrome. In view of the documented VF arrest, characteristic ECG features, and the absence of underlying structural heart disease, a diagnosis of Brugada syndrome was made. A single-chamber implantable cardioverter–defibrillator (ICD) was inserted under local anaesthesia and sedation. The patient was discharged home on aspirin, ranitidine, nadolol (subsequently changed to bisoprolol) and amiloride.

Before arrival in the anaesthetic room during this admission, the question of postoperative analgesia was discussed with the patient. Having been informed of the various options and their associated risks, the patient consented to the placement of a thoracic epidural catheter after induction of general anaesthesia. After the patient had arrived in the anaesthetic room, and with the patient fully monitored, the ICD was externally disabled. A right radial arterial cannula and a right internal jugular triple-lumen cannula were inserted under local anaesthetic. The patient underwent rapid sequence induction with thiopental 5 mg kg^{-1} and succinylcholine 100 mg. After intubation of the trachea, the patient was given fentanyl 100 μg and a thoracic epidural catheter was inserted aseptically at the T8/9 space with the patient in the left lateral position. Cefuroxime 1.5 g, metronidazole 500 mg and gentamicin 320 mg were then administered. Anaesthesia was maintained using an oxygen–nitrous oxide–isoflurane mixture with increments of vecuronium 2 mg for neuromuscular block. Epidural analgesia was provided with 0.25% bupivacaine 10 ml and fentanyl 20 μg. An external defibrillator, connected to defibrillation pads placed on the patient, was present in theatre during the laparotomy. At operation, some minor small bowel adhesions were divided. No other abnormality was found. Neostigmine 2.5 mg–glycopyrrolate 0.5 mg solution was used at the end of the procedure to antagonize the neuromuscular block. Continual monitoring of the ECG showed no abnormalities as a result of the anaesthetic or the operation. The internal defibrillator was re-enabled in the recovery room, and the patient went on to recover successfully from the operation.

Discussion

Brugada syndrome is characterized by an ECG pattern of right bundle branch block and ST segment elevation in the

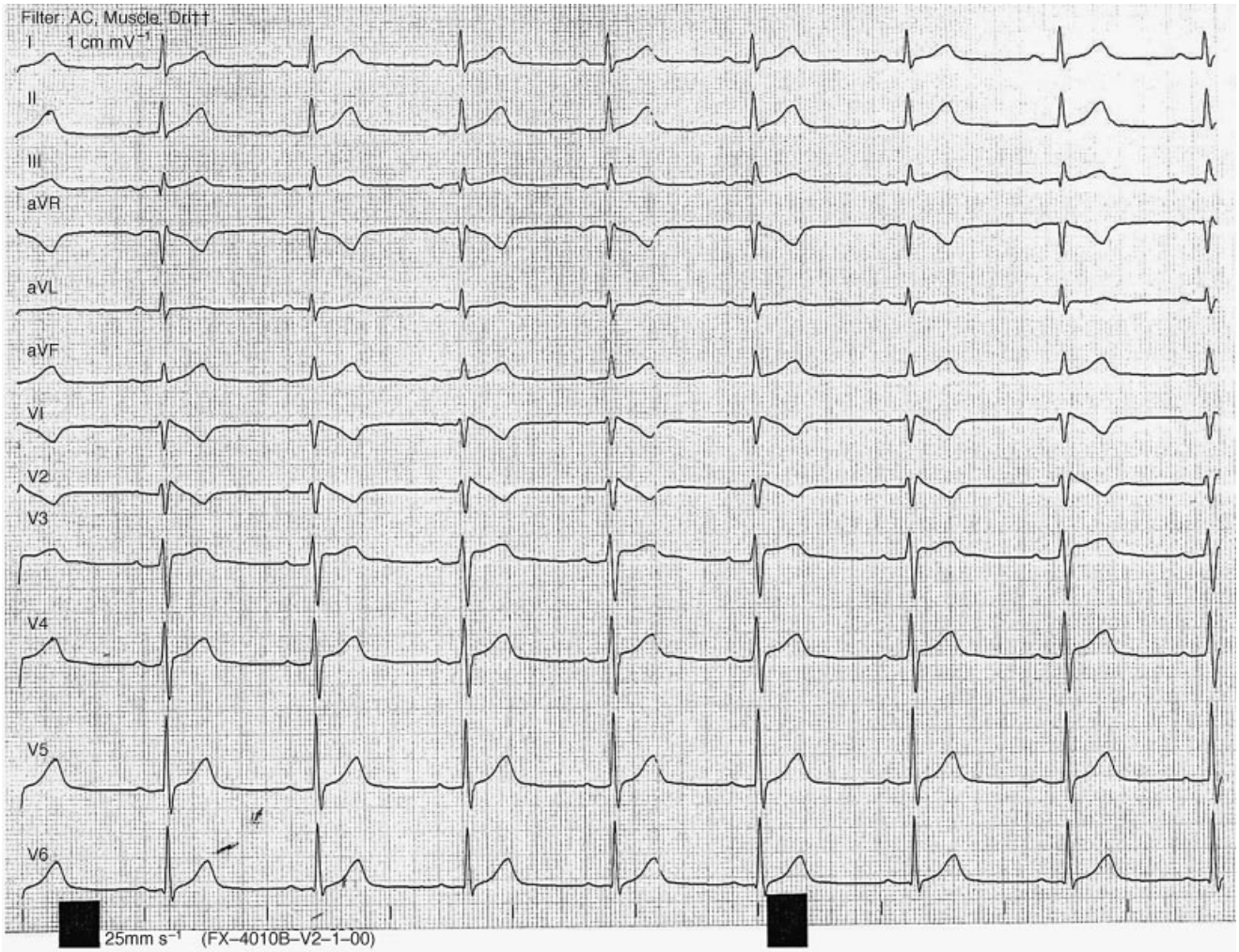

Fig 1 Resting 12-lead ECG showing a characteristic pattern of right bundle branch block with 'coved' ST elevation in leads V_1 to V_3.

right precordial leads (V_1 to V_3), without evidence of underlying structural heart disease. It is associated with a significant risk of ventricular tachyarrhythmias and sudden death. It was first recognized as a distinct clinical entity in 1992.[1] The syndrome is familial (although this was not observed in our patient), with an autosomal dominant mode of transmission and incomplete penetrance. Arrhythmic events are observed at an average age of approximately 40 yr, but have been reported over a wide range of ages from 2 to 77 yr.[2]

Establishing the diagnosis of Brugada syndrome can be difficult. The electrocardiographic signature is concealed in up to 30% of affected individuals[3] and can only be seen after administration of potent sodium channel blockers, such as flecainide, propafenone and procainamide.[4] However, recent follow-up data indicate that the risk of ventricular tachyarrhythmias is low in the absence of a resting ECG abnormality.[5] In patients with an abnormal resting ECG, electrophysiological study incorporating programmed electrical stimulation is recommended to further define the risk of malignant tachyarrhythmia. In the presence of inducible VT/VF, the risk of sudden death is 5–10% per year and ICD implantation is recommended, as it is in any Brugada patient with a history of documented VT/VF or resuscitated cardiac arrest.

The molecular basis for the ventricular arrhythmias remains uncertain. Mutations have been identified in patients with Brugada syndrome in the *SCN5A* gene, which codes for the tetrodotoxin-'insensitive' human cardiac sodium channel (hH1).[6] The functional abnormalities of the expressed mutant channels are opposite to those found in sodium channel mutants associated with long-QT syndrome. In Brugada syndrome, as in some of the other idiopathic ventricular fibrillation syndromes, the sodium channels show loss-of-function features, such as enhanced inactivation.[7] However, it is difficult to see how these features give rise to ventricular arrhythmias. A clue may come from the finding that calmodulin, a ubiquitous calcium-sensing protein, binds to the carboxy-terminal IQ domain of the hH1 channel in a calcium-dependent manner.[8] A naturally occurring mutation (A1924T) in the IQ domain alters hH1 function in a manner characteristic of

the Brugada syndrome, but at the same time inhibits slow inactivation induced by calcium–calmodulin, yielding a clinically benign (arrhythmia-free) phenotype. Further studies will be required to elucidate the precise mechanism(s) by which the other mutations in hH1 give rise to Brugada syndrome.

So far as we can ascertain, this is only the third report of a general anaesthetic having been administered to a patient with Brugada syndrome. The first case report[9] describes a 47-yr-old Japanese male undergoing hemilaminectomy. Anaesthesia was induced with fentanyl 50 μg, droperidol 2.5 mg and propofol 120 mg, and the neuromuscular blocking drug used was vecuronium 8 mg. Maintenance of anaesthesia continued with the use of sevoflurane and further fentanyl 150 μg. Antagonism of the neuromuscular block was accomplished using neostigmine 2.5 mg and atropine 1.0 mg; during antagonism the authors noted an elevation of the ST segments on the ECG.

A second case report[10] describes a 49-yr-old man with Brugada syndrome who had surgery for a polyp on the vocal cords. Despite episodes of vertigo and an ECG showing a right bundle branch block with elevation of the ST segments in leads V_1 and V_2, the cardiologist did not consider that there was an indication for an ICD. The patient was given diazepam 10 mg orally as a premedication and monitored using ECG, a non-invasive blood pressure cuff, pulse oximetry and capnography. Induction of anaesthesia was carried out using fentanyl 0.2 mg, propofol 200 mg, mivacurium 18 mg and glycopyrrolate 0.3 mg. A portable defibrillator was placed in theatre in case ventricular dysrhythmias developed. Anaesthesia was maintained using 1% isoflurane with a nitrous oxide–oxygen gas mixture. After surgery, the patient was transferred to the recovery room and monitored for 2 h. No problems were reported with this anaesthetic.

Both sets of authors in these case reports note that the administration of drugs that block sodium channels, such as procainamide and flecainide, are contraindicated in patients with Brugada syndrome.

Miyazaki and colleagues[11] describe four patients who underwent investigation for Brugada syndrome. They noted that selective α-adrenoceptor stimulation by i.v. norepinephrine in the presence of propranolol or by i.v. methoxamine consistently augmented ST segment elevation whereas α-adrenoceptor block reduced it in three of the patients. Additionally, i.v. neostigmine and class IA antiarrhythmic drugs augmented ST elevation without inducing coronary spasm, but class IB antiarrhythmic drugs had no effect on ST elevation. However, the number of patients was very small and it is difficult to draw firm conclusions from this study, especially in the light of the heterogeneous nature of the mutations leading to Brugada syndrome.

In the case described by Lafuente Martin and colleagues[10] and in our case, isoflurane was administered as an anaesthetic agent. It is perhaps surprising (and illustrates the lack of detailed understanding of the physiology and pharmacology behind Brugada syndrome) that no cardiac arrhythmias were detected during anaesthesia in these cases, in the light of recent evidence suggesting that isoflurane should be avoided in patients with prolonged QT_c syndrome.[12]

Administration of i.v. neostigmine with glycopyrrolate in our patient did not give rise to any detectable cardiac arrhythmia. Likewise, bupivacaine given via the epidural route did not cause problems. However, in view of the fact that drugs that block the sodium channels may cause problems in patients with Brugada syndrome, it may be wise in future to avoid systemic administration of local anaesthetics by routes that cause a rapid increase in serum concentrations of local anaesthetic.

Reported experience of general anaesthesia in Brugada syndrome is limited at present. However, it is an increasingly recognized disorder, and one which many anaesthetists are likely to encounter in their clinical practice in the future. Caution should be exercised when using α-agonists or neostigmine, while class I antiarrhythmic drugs must be avoided. In any patient with an ICD, the device must be disabled immediately before surgery. Close cooperation of the anaesthetist with a cardiologist is essential both before and after surgery. In patients with Brugada syndrome in whom no ICD has been fitted, recovery should take place in either a coronary care unit or a high-dependency unit. This will permit detection and treatment of cardiac arrhythmias, which are most likely to occur in the postoperative period,[13] in a timely manner.

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Respiratory Systolic Variation Test to predict fluid responsiveness

Editor—Priesman and colleagues[1] have published an interesting study showing that the Respiratory Systolic Variation Test (RSVT) is an accurate way of predicting fluid responsiveness. They state that it demands a complex respiratory manoeuvre and off-line measurements and calculations. We note that they use three airway pressures and use linear regression to calculate the slope of a line of best fit. Using linear regression with three points, the middle value has no effect on the slope of the line of best fit. The same accuracy can therefore be obtained using two ventilator pressures, at 10 and 30 cm H_2O. This then makes the respiratory manoeuvre much simpler and a screen capture can be used to measure the two lowest systolic pressures whilst switching from 10 to 30 cm H_2O breaths. The slope is then given by the equation (lowest systolic pressure at 10 cm H_2O)−(lowest systolic pressure at 30 cm H_2O)/20. Using their calculated cut-off value of -0.52 cm/H_2O gives an even easier calculation: if the lowest systolic pressure falls by greater than 10.2 mm Hg when switching from 10 to 30 cm H_2O breaths then fluid responsiveness is implied. This simple modification makes the RSVT a simple bedside test using a standard ventilator and a standard monitor which allows screen capture.

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Editor—We thank Drs Brown and Chappell for their interest in our study. They correctly state that the slope of the line of best fit for the RSVT would not be affected by the addition of a middle value and that the same accuracy may be achieved by a manoeuvre composed of two consecutive breaths. We used three consecutive incremental airway pressures in our study to avoid any erroneous blood pressure measurement resulting from occasional extrasystoles, spontaneous respiratory effort, etc. If the manoeuvre had been of only two breaths, it would have been difficult to identify such abnormalities and discard them from measurement. We did not encounter such a situation in our clinical studies but it did occur in our preliminary animal experiments.

Thus, in our opinion, it is worthwhile to use three breaths with incremental pressures during the RSVT manoeuvre to identify and reject artifacts.

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Anaesthetic management in patients with high-risk Brugada syndrome

Editor—We read with interest the case report from Dr Edge and colleagues,[1] and would like to report the successful management of two cases with Brugada syndrome and focus on risk evaluation of proarrhythmia, postural change and neostigmine administration. During anaesthesia of Brugada syndrome, many factors may precipitate a significant risk of malignant arrhythmias and cardiac arrest.

Both patients were asymptomatic with no medical history of cardiac disease or family history of sudden death. Preoperative echocardiography was normal, and the ECG over the third intercostal space and the ECG following pilsicainide administration revealed obvious augmentation of ST segment elevation in leads V_1–V_4, without QT prolongation. Electrophysiological studies, without prior medication, induced ventricular fibrillation (VF) and systolic pressure <40 mm Hg, and defibrillation restored sinus rhythm. These findings led to a definite diagnosis as high-risk Brugada syndrome.

Before induction of general anaesthesia, the 12-lead ECG was continuously monitored, along with routine monitoring and cardioverter-defibrillator pads. An automated external defibrillator and an i.v. drip infusion of the β-stimulator isoproterenol were prepared, in case ventricular dysrhythmias developed.[2] No pre-anaesthetic medication was

required. General anaesthesia was induced with thiamylal 4 mg kg^{-1}, and tracheal intubation was facilitated by vecuronium 0.1 mg kg^{-1}. Anaesthesia was maintained with isoflurane and nitrous oxide 66% in oxygen.

Case 1. A 51-yr-old man with a left-sided coral-shaped calculus underwent percutaneous nephrolithotripsy twice. During the operations, three types of postural change were required—from supine to lithotomy, lithotomy to prone and prone to supine position.

Case 2. A 56-yr-old man with a mandibular fracture underwent plate fixation and plate removal procedure after 1 yr. Nasotracheal intubation was required because of previous oral surgery.

At the end of the operation, atropine 0.02 mg kg^{-1} and neostigmine 0.02 mg kg^{-1} (half of the normal neostigmine dose), were given slowly to antagonize the neuromuscular block, and the trachea extubated. In both cases, anaesthetic management was uneventful, and no abnormality was detected on the ECGs. During the 24 h postoperative period in the intensive care unit, the patients recovered successfully without any worsening of ST segment elevation on the 12-lead ECG.

Careful preoperative evaluation and anaesthetic management is essential to avoid inducing arrhythmia. The high-risk criteria for patients with Brugada syndrome requiring general anaesthesia are:[3 4] (i) symptomatic cases with syncope or a medical history of VF; (ii) asymptomatic cases showing pathognomonic ST segment elevation on ECG and medication- or EPS-induced VF; and (iii) cases showing coved-type ST elevation on ECGs.

The mechanism of ST-segment elevation with Brugada syndrome is associated with an imbalance in action potential gradients between the right ventricular endocardial and epicardial cells.[2] Many factors during anaesthesia, in particular the autonomic nervous system, influence this imbalance.[1 3–5] Postural change can be regarded as a factor and depth of anaesthesia should be sufficiently controlled before postural change, in order not to disturb autonomic nerve balance.

Neostigmine may augment ST segment elevation in a dose-dependent manner without inducing coronary spasm,[1 3 5] while atropine may reduce elevation.[1 3] Therefore, it may be wise to avoid neostigmine. However, in our cases, neostigmine doses were carefully divided and did not cause any abnormalities. There have been several reports of successful neostigmine administration without problems.[1 5] We feel, neostigmine can be administered safely by careful dose adjustment and by atropine administration before neostigmine.

Most anaesthetics have inhibitory effects on circulation. However, specific differences and safety of the depressant action in each drug at clinical concentrations remain unknown. Further studies are required to clarify the safest anaesthetic management.

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Diffusive pulmonary embolism with bone fragments during spinal surgery

Editor—We would like to report a case of diffusive pulmonary embolism (PE) with bone fragments during spinal surgery. The patient was a 69-yr-old man (height, 174 cm; weight, 75 kg), with ossification of the posterior longitudinal ligament (OPLL) of the thoracic area and he has a history of essential hypertension. Extensive surgery involving resection of the OPLL from T3–T9 was planned. During general anaesthesia his arterial pressure was maintained at 130–140/60–70 mm Hg. In addition to standard monitors, a radial artery catheter was placed percutaneously but a central venous catheter was not inserted. The patient was placed in the prone position onto a Hall's frame and surgery was performed. After laminectomy, the resection of OPLL was initiated by posterior approach using surgical drill. Controlled hypotension by continuous injection of nitroglycerine at 0.5 μg kg^{-1} min^{-1} was performed at a range of 80–90/40–45 mm Hg. The blood gas analysis during the operation revealed progressive oxygen desaturation and carbon dioxide retention (Table 1). Five hours after the start of resection of OPLL, the patient's arterial pressure suddenly decreased from 88/45 to 55/30 mm Hg and the ECG showed sinus rhythm at a rate of 70 beats min^{-1}. Severe hypotension (systolic arterial pressure <35 mm Hg) and bradycadia (30–40 beats min^{-1}) was observed despite the administration of epinephrine and the end-tidal carbon dioxide partial pressure was noted to decrease to 14 mm Hg. The surgical procedure was discontinued and the patient was turned to supine position to carry out a cardiac massage. Despite a cardiac massage the ECG revealed a standstill in electrical activity. Two hours and forty minutes later, resuscitation was discontinued.