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REVIEW ARTICLE

Perioperative management of hereditary arrhythmogenic syndromes

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Editor's key points

- Patients with inherited cardiac channel disorders are at high risk of severe perioperative arrhythmias.
- Agents used for treatment or to be avoided vary in the various syndromes and their subtypes.
- Understanding of the potential autonomic actions of anaesthetic agents on the different conditions is required.
- Preoperative optimization and preparation of the appropriate emergency drugs is essential.

Summary. Patients with inherited cardiac channel disorders are at high risk of perioperative lethal arrhythmias. Preoperative control of symptoms and a multidisciplinary approach are required for a well-planned management. Good haemodynamic monitoring, adequate anaesthesia and analgesia, perioperative maintenance of normocarbia, normothermia, and normovolaemia are important. In congenital long QT syndrome, torsades de pointes should be prevented with magnesium sulphate infusion and avoidance of drugs such as droperidol, succinylcholine, ketamine, and ondansetron. Propofol and epidural anaesthesia represent safe choices, while caution is needed with volatile agents. In Brugada syndrome, β-blockers, α-agonists, and cholinergic drugs should be avoided, while isoproterenol reverses the ECG changes. Propofol, thiopental, and volatiles have been used uneventfully. In congenital sick sinus syndrome, severe bradycardia resistant to atropine may require isoproterenol or epinephrine. Anaesthetics with vagolytic properties are preferable, while propofol and vecuronium should be given with caution due to risk of inducing bradyarrhythmias. Neuraxial anaesthesia should produce the least autonomic imbalance. Arrhythmogenic right ventricular dysplasia/cardiomyopathy induces ventricular tachyarrhythmias, which should be treated with β-blockers. Generally, β-adrenergic stimulation and catecholamine release should be avoided. Halothane and pancuronium are contraindicated, while large doses of local anaesthetics and epinephrine should be avoided in neuraxial blocks. In catecholaminergic polymorphic ventricular tachycardia, β-blocker treatment should be continued perioperatively. Catecholamine release and β-agonists, such as isoproterenol, should be avoided. Propofol and remifentanil are probably safe, while halothane and pancuronium are contraindicated. Regional anaesthesia, without epinephrine, is relatively safe. In suspicious cardiac deaths, postmortem examination and familial screening are recommended.

Keywords: anaesthesia; arrhythmogenic right ventricular dysplasia; Brugada syndrome; channelopathies; congenital long QT syndrome; congenital sick sinus syndrome; polymorphic catecholaminergic ventricular tachycardia

Hereditary arrhythmias comprise a heterogeneous group of cardiac channel disorders occurring in patients with apparently normal hearts.[1] Subtype 3 of congenital long QT syndrome (LQTS), Brugada syndrome, and congenital sick sinus syndrome (SSS) are associated with sodium channel dysfunction.[1] The cardiac ryanodine receptor-2/calcium release channel is involved in arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) and in catecholaminergic polymorphic ventricular tachycardia (CPVT).[1–3] The loss of function of L-type calcium channels is implicated in Brugada/short QT syndrome and potassium channel defects in subtypes of LQTS.[1] A phenotypic overlap and clinical combinations[1] of some channelopathies possibly indicate a relation or overlap between underlying genetic pathways and molecular mechanisms.

Inherited arrhythmogenic syndromes are underdiagnosed, as they may remain asymptomatic for a long time. Nevertheless, they represent the most common cause of sudden cardiac death in a young population.[1 3] Anaesthesia and surgery may unmask these syndromes, which usually present as life-threatening arrhythmias in patients with an unremarkable medical history.[4] A retrospective analysis of 1700 sudden cardiac deaths showed that 50 of them had occurred perioperatively, in young patients without a history of cardiac disease.[4] In the case of death due to a hereditary channelopathy, further investigation and familial genetic screening should be performed.[5]

The specific anaesthetic implications and prompt therapeutic interventions required in these cases make the perioperative management of these patients a challenge for the anaesthetist. This review analyses the clinical profile of hereditary arrhythmogenic syndromes and focuses on the anaesthetic management and perioperative care of patients with a diagnosed or suspected hereditary arrhythmia.

We conducted a PubMed® literature search for all types of published articles combining the free text and MeSH thesaurus terms: 'congenital long QT syndrome', 'Brugada syndrome', 'congenital sick sinus syndrome', 'arrhythmogenic right ventricular dysplasia', 'catecholaminergic polymorphic ventricular tachycardia', 'hereditary arrhythmias', 'inherited cardiac channelopathies', and 'inherited cardiac arrhythmias', with 'anaesthetic management', 'perioperative management', 'anaesthesia', 'general anaesthesia', 'epidural anaesthesia', or 'neuraxial anaesthesia'. A total of 248 articles, published up to November 2011, were retrieved; 114 of which were found to be relevant. There were no randomized prospective studies and the articles were mostly case reports, case series, and retrospective studies. Additional relevant studies were also sought by manual searching of the bibliographies found in the electronically identified articles. We also used articles that provided information on genetics, clinical features, diagnostic, and therapeutic approach of the syndromes. In total, 146 articles were found suitable to be included in the present review.

Congenital long QT syndrome

LQTS is a congenital (c-LQTS) or acquired disorder of cardiac ion channels characterized by heterogeneity of cellular repolarization and precipitation of tachyarrhythmias.[6 7] Jervell–Lange-Nielson and Romano-Ward syndromes were the first congenital LQT disorders described.[6 8] Six genotypes have been identified with six subgroups of c-LQTS (LQT1–LQT6), respectively.[8] The prevalence of c-LQTS is estimated to be $<$1:5000, even close to 1:2000–2500 in white infants.[9] The syndrome is characterized by autosomal-dominant transmission, while rarely the inheritance pattern may be autosomal-recessive, as in Jervell–Lange-Nielson syndrome.[6]

The subtypes of c-LQTS, as determined by genetic testing, are associated with different channel dysfunctions and variable clinical profiles. In c-LQT1 and c-LQT2, the potassium currents are affected, while c-LQT3 affects sodium channels.[1] Patients with c-LQT1 are prone to dysrhythmias after sympathetic activation such as exercise, while in patients with c-LQT2, dysrhythmias can be triggered by auditory stimuli, such as telephone ringing[10] or monitor alarm.[11] In contrast, patients with c-LQT3 are prone to cardiac events at rest or sleeping, due to polymorphic ventricular tachycardia (torsades des pointes) induced by bradyarrhythmias.[10]

The diagnosis of c-LQTS may be difficult, as 40% of genetically proven cases have no clinical symptoms when diagnosed and have a normal or borderline lengthened QT interval on their resting ECG.[8] As QT interval varies with heart rate, calculation of the corrected QT interval (QTc) is a more reliable marker. The ECG may be a useful diagnostic tool for c-LQT subcategory determination; in LQT1, T-waves are broad-based, with normal to high amplitude and indistinct onset; in LQT2, T-waves are usually bifid with low amplitude; while in LQT3, T-waves are peaked with late onset and ST segment is long.[12] A prolonged QTc ($\geq$430 ms), suspicious clinical symptoms, and a family history of sudden death are specific characteristics of the syndrome. Affected individuals are at risk of developing torsades des pointes, which may be followed by ventricular fibrillation and sudden death.

Treatment of c-LQTS includes a permanent pacemaker and/or an implanted cardioverter-defibrillator (ICD) and left cardiac sympathetic denervation.[6 8 10] β-Blockers may be useful in patients with LQT1 and LQT2.[8 10] In patients with c-LQT3, sodium channel blockers are beneficial and β-blockade is contraindicated.[8 10] Left stellate ganglion block has been reported to shorten temporarily the QT interval in patients with Romano-Ward syndrome, and could possibly be considered in emergency cases.[13]

In patients with c-LQTS, reducing the risk of torsades des pointes is mandatory, as the haemodynamic compromise is severe, even though the episodes are usually short-lived and self-terminating. Magnesium sulphate (initial bolus dose of 30 mg kg^{-1}, followed by an infusion of 2–4 mg kg^{-1}) is the drug of choice for prevention and treatment of torsades des pointes.[6 14] Asynchronous defibrillation and cardiopulmonary resuscitation may be necessary if ventricular fibrillation occurs. A rapid and short-acting β-blocker, such as esmolol, should be considered in LQT1 and LQT2, while cardiac pacing may be beneficial in LQT3 patients.[12] Lidocaine 1.5 mg kg^{-1} i.v., with repeated doses of 0.5–0.75 mg kg^{-1} every 5 min up to a maximum dose of 3 mg kg^{-1}, may be useful.[15] Amiodarone should not be given as it prolongs the QT interval.[8]

Anaesthetic considerations

Since clinical and electrophysiological heterogeneity of c-LQTS render the effects of different drugs unpredictable, the available data are inconclusive.[7] Patients on β-blockers should continue their treatment perioperatively.[6] Preoperative preparation of the patient should be performed in a quiet and comfortable environment to avoid triggering torsades des pointes.[6] Midazolam and fentanyl have been used for anxiolysis without complications in adults[6 8] and children[16] with c-LQTS.

Several drugs that are commonly used perioperatively prolong the QT interval and should be avoided: droperidol, ondansetron, dolasetron, chlorpromazine, amiodarone, ephedrine, epinephrine, norepinephrine, dobutamine, dopamine, isoproterenol, phenylephrine, midodrine, diphenhydramine, oxytocin, and certain antibiotics. Among cardiovascular drugs, atropine, glycopyrronium, etilefrine, and metaraminol, have not been associated with QT prolongation and are not contraindicated in patients with c-LQT syndrome (www.QTdrugs.org, Arizona Center for Education and Research on Therapeutics). Perioperative infusion of magnesium sulphate (30 mg kg^{-1}) is recommended as a prophylaxis against torsades des pointes.[6] A defibrillator and transvenous pacing wires and leads should be ready for prompt use.[11 12]

Both general and neuraxial anaesthesia have been advocated in patients with c-LQTS (Table 1). Hypothermia should be avoided since it prolongs the QT interval, possibly

Table 1 Reported cases of perioperative management, complications, and outcome of patients with hereditary arrhythmogenic syndromes—congenital Long QT syndrome. No. of pts, number of patients; CSE, combined spinal–epidural; c-LQTS, congenital long QT syndrome; CPVT, catecholaminergic polymorphic ventricular tachycardia; GA, general anaesthesia; PVCs, premature ventricular contractions; VF, ventricular fibrillation; Tdp, torsade de pointes. *Analgesia for labour. †Outcome 'well' indicates that the patient was discharged from hospital

First author	Syndrome	No. of pts	Age/ sex	Type of anaesthesia	Patient at presentation	Drugs used	Complications	Complication management	Time of complication	Outcome†
Behl[11]	c-LQTS	1	22/F	CSE*	Diagnosed	Racemic bupivacaine/ diamorphine; levobupivacaine/ alfentanil	Uneventful	—	—	Well
McKechnie[15]	c-LQTS	1	11/F	GA	Undiagnosed	Sevoflurane/N_2O; remifentanil/ rocuronium; ondansetron	Polymorphic PVCs	Lidocaine i.v. 1 mg kg^{-1}	Intraoperatively, after ondansetron administration	Well
Saussine[16]	c-LQTS	1	8/M	GA	Diagnosed	Sevoflurane/midazolam; fentanyl/rocuronium	PVCs; TdP	Chest compressions. Stop sevoflurane administration	Intraoperatively	Well
Johnston[21]	c-LQTS	1	24/F	GA	Diagnosed	Thiopental/rocuronium; isoflurane/remifentanil; morphine	Uneventful	—	—	Well
Kubo[17]	c-LQTS	1	25/F	Subarachnoid	Diagnosed	Bupivacaine; fentanyl	QT prolongation	Landiolol i.v.; 0.04 mg kg^{-1} min^{-1}	After subarachnoid injection	Well
Ganta[19]	c-LQTS	1	25/F	Epidural	Diagnosed	Lidocaine	Uneventful	—	—	Well
Al-Refai[20]	c-LQTS	1	31/F	Subarachnoid	Diagnosed	Bupivacaine; fentanyl/ morphine	Uneventful	—	—	Well
Kenyon[22]	c-LQTS; CPVT	22	2–14; M/F	GA	All diagnosed	Sevoflurane/isoflurane; propofol/remifentanil; fentanyl/rocuronium; vecuronium, e.a.	Uneventful			Well (for all)
Pleym[35]	c-LQTS	1	27/F	GA	Undiagnosed	Thiopental/succinylcholine; fentanyl/rocuronium; glycopyrronium/neostigmine	PVC; VF	CPR	After glycopyrronium/ neostigmine administration	Well

through delayed recovery of the inactivated sodium channels.[6 8 15]

Neuraxial anaesthesia is considered to be advantageous, as it reduces the stress response and provides effective analgesia.[8] Combined spinal–epidural anaesthesia has been used safely,[11 17] but prolongation of the QTc interval during spinal anaesthesia in patients without cardiovascular disease has been reported.[18] Epidural anaesthesia with gradual establishment of the sympathetic block and lower risk of hypotension and vasopressor drugs is better than single-shot spinal anaesthesia.[19] Ephedrine and phenylephrine are included in the list of drugs that prolong QT, but both have been used without adverse effects in c-LQT parturients for treatment of hypotension after combined spinal–epidural anaesthesia for Caesarean delivery.[17 20] The addition of epinephrine to local anaesthetics in neuraxial techniques is best avoided as sympathetic stimulation and catecholamines may trigger torsades des pointes.[6 8 19] Nevertheless, the addition of 1:200 000 epinephrine to 2 ml of 0.5% racemic bupivacaine for a test dose in combined spinal–epidural labour analgesia has been used without complications.[11] Bupivacaine,[17 20] levobupivacaine,[11] and lidocaine[19] have all been safely used for neuraxial block in patients with c-LQTS.

In general anaesthesia, catecholamine release should also be avoided. Thiopental prolongs the QT interval,[6 8] but has been used safely for Caesarean section in two cases.[8 21] Ketamine should be avoided due to sympathetic stimulation[6 12 22] and QT interval prolongation.[23] In contrast, propofol is considered safe[6 8 22] and is recommended for patients with LQTS.[7] In patients without QT prolongation, anaesthesia induction and maintenance with propofol may shorten the QT interval.[24 25]

Inhalation anaesthetics prolong the QTc interval,[26 27] and reports about their safety are conflicting.[6–8 21 22 24 28] Isoflurane has been safely used in patients with QT prolongation.[6 21 22] Sevoflurane produced significant arrhythmias in a paediatric patient with c-LQTS when used for induction and maintenance of anaesthesia.[16] In children[29] and adults with normal QT, sevoflurane was found to significantly prolong both QT and QTc intervals.[24] The induction and maintenance of anaesthesia with desflurane in healthy populations is also associated with immediate QTc prolongation.[26] The clinical significance of these findings in patients with LQTS is not clear, but some authors recommend avoiding these agents.[7 12] Nitrous oxide has not been associated with adverse effects in patients with c-LQTS,[15] while data regarding its impact on cardiac conduction are lacking.[30] It should probably be used with caution because of its sympathomimetic properties.[30]

The Valsalva manoeuvre lengthens the average QTc interval in healthy volunteers and in LQTS patients,[31] suggesting that high positive airway pressures are best avoided.[8]

Succinylcholine should also be avoided, since it may prolong the QTc interval or provoke vagal stimulation and has resulted in asystole after pacemaker inhibition by fasciculations.[21 22 32] Rocuronium, vecuronium, atracurium, and cisatracuriun do not prolong the QTc interval and are considered safe.[6 8 16 21]

Adequate analgesia attenuates catecholamine release; fentanyl,[16 17 20 22] remifentanil,[15 21 22] alfentanil,[11] morphine, and diamorphine have been successfully used during induction of anaesthesia to reduce the sympathetic response and subsequent QT prolongation during laryngoscopy.[6 11 16 21] Esmolol 3 mg kg^{-1} and alfentanil 0.03 mg kg^{-1} prevented the prolongation of QTc interval after thiopental and succinylcholine, but only alfentanil obtunded the sympathetic response to laryngoscopy.[33] Centrally acting α-2 agonists such as clonidine and dexmedetomidine may also suppress the sympathetic response to tracheal intubation and are not considered to affect the QT interval (www.QTdrugs.org). Topical anaesthesia to the vocal cords may be beneficial.

Anticholinsterase–anticholinergic drug combinations (neostigmine or edrophonium with atropine or glycopyrronium) prolong QTc interval,[34] and dysrhythmias have been reported after their administration.[35 36] However, another report found that the combination of neostigmine and glycopyrronium did not cause any complications.[21] These agents should be administered with caution to avoid profound changes in heart rate. Morphine, diamorphine, paracetamol, and diclofenac may be used for postoperative analgesia.[11 21] The antiemetics droperidol, domperidone, and several 5-HT$_3$ antagonists (ondansetron, dolasetron, granisetron) prolong the QT interval and should be avoided in patients with diagnosed or suspected c-LQTS (www.QTdrugs.org). Nevertheless, ondansetron has been used without adverse effects.[22] Metoclopramide is not contraindicated, but an antiemetic regimen based on dexamethasone probably represents the safest choice.[22]

Brugada syndrome

Brugada syndrome is a hereditary arrhythmia characterized by autosomal-dominant transmission with incomplete penetrance.[37] It mostly affects male adult patients from South-East Asia and presents with syncope and/or sudden death caused by ventricular fibrillation in apparently healthy subjects.[38–40]

The pathophysiology and molecular basis of Brugada syndrome is not clear. Mutations in the SCN5A gene of cardiac sodium channels have been identified in 20–30% of patients with Brugada syndrome and are also related to LQTS.[38 39] The development of extrasystoles and polymorphic ventricular tachycardia is thought to result from an action potential imbalance between the epicardium and the endocardium. Dispersion of repolarization produces local pre-excitation, as different parts of the myocardium are predisposed to reactivation at different times.[41]

Diagnostic criteria for Brugada syndrome include specific ECG characteristics, such as ST elevation $\geq$0.1 mV, coved or saddleback in V_1–V_3 leads, with or without right bundle branch block.[38 40] In the presence of inducible malignant tachyarrhythmias, the risk of sudden death is 5–10% per year.[37] The characteristic ECG findings are often intermittent and occur during sleep, when parasympathetic tone is increased.[39 42] Class IA antiarrhythmic drugs, such as

ajmaline and procainamide,[42] and class IC antiarrhythmics, such as pilsicainide,[40] are used for a pharmacological provocation test, as they induce the characteristic ST changes.

Currently, there is no pharmacological treatment for the prevention or cure of Brugada syndrome and patients at risk of arrhythmia are treated with placement of an ICD.[37 42]

Anaesthetic considerations

Pharmacological interactions during anaesthesia and autonomic imbalance may facilitate ECG changes in Brugada syndrome. β-Blockers and α-agonists should be avoided, as they may exacerbate ST elevation.[43] ECG changes are usually resolved when the triggering drugs are discontinued.[42] Class IA and Class IC antiarrhythmics and also cholinergic drugs, such as neostigmine, should be avoided.[42–44] Although specific data are lacking, α-2 agonists, such as clonidine and dexmedetomidine, should also probably be avoided as they may produce sympathetic suppression and increased vagal stimulation of the heart.[45] In contrast, β-agonists or α-blockers should be considered if ST-changes appear in the absence of arrhythmias.[42 43] Isoproterenol is the β-agonist of choice and has been reported to restore successfully elevated ST segments to the pretreatment level in patients undergoing a challenge test with pilsicainide.[40] Atropine and ephedrine have been used for the treatment of bradycardia and hypotension, respectively, without complications.[40]

Most anaesthetic agents have been used uneventfully in patients with Brugada syndrome (Table 2). Propofol,[39 40 42 46–52] thiopental,[37 44 53] and midazolam[39 40 47] have been given without complications. Fentanyl has also been used uneventfully.[37 39 40 42 44 46 47 50 51 53] The data on the use of remifentanil are limited,[52] but it is not contraindicated and it may be of use in short procedures, such as cardioverter defibrillator insertion. Nitrous oxide has been used without complications in patients with Brugada syndrome, in combination with propofol or a volatile agent.[39 40 48 49 53 54] Isoflurane[37 44 54] and sevoflurane[40 46 48–50 52 53] have also been used without any adverse effects. Nevertheless, the use of volatile anaesthetics has raised some concerns, since mutations in the SCN5A gene may be linked to both Brugada syndrome and LQTS and there may a risk of producing QT prolongation.[42 55]

Neuraxial techniques have also been used in patients with Brugada syndrome[37 44 47 50 56] (Table 2). Bupivacaine epidurally has been implicated in the evolution of a Brugada-type ECG.[47] However, other authors report the use of bupivacaine for epidural and intrathecal anaesthesia without adverse effects.[37 44] Bupivacaine should be used with caution, since there is no clear evidence of its safety.

I.V. administration of lidocaine (class IB antiarrhythmic), although a sodium channel blocker, did not induce ST-segment elevation[43] and has been used uneventfully to attenuate intubation-related haemodynamic changes.[40]

Mivacurium,[40] succinylcholine,[37 39] atracurium,[39] cisatracurium,[46] and vecuronium[37 40 44 54] have all been used without adverse effects. Some authors suggest avoiding neostigmine for reversal of neuromuscular block, as it may trigger the characteristic ECG pattern,[40 46] but others have used neostigmine combined with atropine[39 54] or glycopyrronium[37] without complications.

Fentanyl, ketorolac, and meperidine have been successfully used for postoperative analgesia in patients with Brugada syndrome.[44 46 47] Droperidol and 5-HT_3 receptor antagonists are not contraindicated as antiemetics in Brugada syndrome (www.QTdrugs.org), but the possible link between long QT and Brugada syndrome should be kept in mind. Metoclopramide and dimenhydrinate are preferably avoided (www.QTdrugs.org) and should be used with caution.

Sick sinus syndrome

SSS includes a number of abnormalities originating from sinus node dysfunction. Although more cases have been reported in the elderly, the incidence in infants, children, and young adults is significant, and SSS is one of the main causes of sudden death in this population.[57] The disease is usually sporadic, but familial and congenital cases have also been described.[57] The familial forms are characterized by autosomal-dominant transmission with variable penetrance.[57] Congenital forms, even though associated with sudden death syndrome in infants, are considered to be less severe than sporadic types.[57] There is a possible relationship between hereditary SSS and polymorphism of β-adrenoreceptor gene, specifically the variant Ser49gly.[58] In some cases, histological examination has shown a small node or extensive fibrous replacement in the atrial node.[59] Sinus node dysfunction progresses gradually and patients are often asymptomatic, especially at early stages of the disease. Symptoms, if present, are usually non-specific and result from vital organ hypoperfusion during hypotensive episodes.[59] They include dizzy spells, fatigue, impaired memory, syncope, paresis, and pulmonary oedema.[59] The ECG appearance of SSS includes sinus bradycardia, sinus arrest without an escape rhythm, episodes of exit block, sino-atrial block, or alternation of supraventricular tachycardia and sinus bradycardia, known as tachycardia–bradycardia syndrome.[60] ECG, Holter ECG (12–24 h), and assessment of the response to exercise may detect the disorder. Provocation testing with atropine or isoproterenol may also help in the differential diagnosis between SSS and excessive vagal tone; the heart rate in SSS rarely increases above 90–100 beats min^{-1}, being less responsive to atropine. Another diagnostic test is the increased sinus node suppression after atrial pacing at 150 beats min^{-1}.[61] Electrophysiological assessment of direct sinus node activity and tests before and after administration of atropine and propranolol may reveal the underlying abnormality, which may be an intrinsic sinus node dysfunction or disturbed autonomic regulation.[57 62]

A permanent atrial or dual-chamber pacemaker[60] is required if clinical symptoms are present and in bradycardia–tachycardia syndrome.[63 64] Treatment of severe bradyarrhythmias with pharmacological agents is not always

Table 2 Reported cases of perioperative management, complications, and outcome of patients with hereditary arrhythmogenic syndromes—Brugada syndrome. No. of pts, number of patients; CSE, combined spinal–epidural; GA, general anaesthesia. †Outcome 'well' indicates that the patient was discharged from hospital. ‡Diagnosed at preanaesthetic evaluation

First author	Syndrome	No. of pts	Age/sex	Type of anaesthesia	Patient at presentation	Drugs used	Complications	Complication management	Time of complication	Outcome†
Edge[37]	Brugada	1	53/M	GA; epidural	Diagnosed	Thiopental/succinylcholine; isoflurane/vecuronium; bupivacaine/fentanyl	Uneventful	—	—	Well
Vaccarella[39]	Brugada	1	69/F	GA	Diagnosed	Atenolol/midazolam; propofol/succinylcholine; fentanyl/atracurium	Uneventful	—	—	Well
Inamura[40]	Brugada	6	51–63; M	GA	All diagnosed	Diazepam/midazolam; propofol/vecuronium; sevoflurane/N_2O; fentanyl	Uneventful	—	—	Well (for all)
Cordery[42]	Brugada	1	16/M	GA	Undiagnosed	Propofol/atracurium; fentanyl	Uneventful	—	—	Well
Kim[44]	Brugada	2	33, 56; M	Subarachnoid/GA	Both diagnosed	Bupivacaine; thiopental/vecuronium; fentanyl/isoflurane	Uneventful	—	—	Well
Santambrogio[46]	Brugada	4	25–43; M	GA	All diagnosed	Diazepam/propofol; fentanyl/cisatracurium; sevoflurane	Uneventful	—	—	Well (for all)
Phillips[47]	Brugada	1	77/M	Epidural; GA	Undiagnosed	Midazolam/propofol; fentanyl/rocuronium; bupivacaine	ST elevation in V_1-V_3	—	Postoperatively, after epidural bupivacaine	Well
Hayashida[54]	Brugada	2	51, 56; M	GA	Both diagnosed	Thiamylal/vecuronium; isoflurane/N_2O	Uneventful	—	—	Well
Theodotou[48]	Brugada	1	55/M	GA	Diagnosed	Propofol/succinylcholine; sevoflurane/N_2O	Uneventful	—	—	Well
Canbay[53]	Brugada	1	3.5/M	GA	Diagnosed	Thiopental/vecuronium/fentanyl; sevoflurane/N_2O	Uneventful	—	—	Well
Candiotti[49]	Brugada	1	25/M	GA	Diagnosed‡	Propofol/rocuronium; sevoflurane/N_2O	Uneventful	—	—	Well
Fujiwara[50]	Brugada	1	68/M	GA; thoracic paravertebral block	Diagnosed	Propofol/fentanyl/vecuronium; sevoflurane; ropivacaine	Uneventful	—	—	Well
Bramall[56]	Brugada	1	40/F	Subarachnoid	Diagnosed	Hyperbaric bupivacaine	Uneventful	—	—	Well
Goraksha[51]	Brugada	1	14/M	GA	Diagnosed	Propofol/fentanyl; atracurium	Uneventful	—	—	Well
Brunetti[52]	Brugada	1	38/M	GA	Suspected	Propofol/remifentanil; cisatracurium/sevoflurane	ECG changes	—	After operation	Well

Table 3 Reported cases of perioperative management, complications, and outcome of patients with hereditary arrhythmogenic syndromes—sick sinus syndrome. No. of pts, number of patients; CSE, combined spinal–epidural; GA, general anaesthesia; SSS, sick sinus syndrome; NA, not available. †Outcome 'well' indicates that the patient was discharged from hospital

First author	Syndrome	No. of pts	Age/sex	Type of anaesthesia	Patient at presentation	Drugs used	Complications	Complication management	Time of complication	Outcome†
Burt[59]	SSS	1	76/M	GA	Undiagnosed	Papaveretum; thiopental/halothane; N_2O	Asystole	Chest compressions	Intraoperatively	Well
Ishida[63]	SSS	1	40/F	Epidural; GA	Undiagnosed	Propofol/fentanyl; vecuronium; ropivacaine	Asystole	Atropine 0.5 mg; chest compressions	Intraoperatively	Well
Nakamura[64]	SSS	1	67/M	GA	Undiagnosed	Thiopental/fentanyl; vecuronium/isoflurane	Bradycardia	Postpone surgery; temporary cardiac pacemaker placement	Before operation	Well
Cohen[65]	SSS	1	79/M	Subarachnoid	Diagnosed	Lidocaine/epinephrine	Bradycardia, sinus pause; asystole	Atropine i.v. 1 mg; chest compressions	Intraoperatively	Well
Murakawa[66]	SSS	1	59/F	GA	Diagnosed	Propofol/fentanyl; ketamine/vecuronium	Bradycardia	Atropine; temporary cardiac pacing	Intraoperatively	Well
Kabutan[67]	SSS	1	NA	GA	Undiagnosed	Isoflurane	Cardiac arrest	Temporary cardiac pacing	Intraoperatively	Well
Ishiyama[68]	SSS	1	53/F	Epidural; GA	Undiagnosed	Lidocaine; propofol/ vecuronium; isoflurane/ N_2O	Repeated; asystole	Atropine 0.5 mg; temporary i.v. cardiac pacing	Intraoperatively	Well; permanent pacemaker; placed
Underwood[69]	SSS	1	46/F	Subarachnoid	Undiagnosed	Midazolam; heavy bupivacaine	Asystole	Chest blows	Intraoperatively	Well
Kawaguchi[70]	SSS	1	75/F	GA; Neuroleptanesthesia	Undiagnosed	NA	Bradycardia; asystole	Resolved spontaneously	Intraoperatively	Well
Hirata[71]	SSS	1	50/M	GA	Undiagnosed	NA	Bradycardia	Atropine; isoproterenol	Intraoperatively	Well
Levy[74]	SSS	1	83/F	GA	Undiagnosed	Alfentanil/ glycopyrronium; propofol/vecuronium	Bradycardia	Methoxamine; isoprenaline	Intraoperatively	Well
Iinuma[75]	SSS	1	79/M	Epidural; GA	Diagnosed	Thiamylal/vecuronium; fentanyl; sevoflurane/ N_2O; mepivacaine/ morphine	Complete AV block; bradycardia	Atropine; transcutaneous pacing (ineffective); isoproterenol	Intraoperatively	Well
Nishio[79]	SSS	1	66/F	GA	Diagnosed	Propofol/sevoflurane; remifentanil	Uneventful	—	—	Well
Kim[84]	SSS	1	69/M	GA	Undiagnosed	Lidocaine 1% 30 mg i.v.	Bradycardia; sinus arrest	Postponed surgery	Before operation	Well
Corr[88]	SSS	1	83/F	Subarachnoid	Undiagnosed	Heavy bupivacaine; Midazolam	Bradycardia	Glycopyrronium	Intraoperatively	Well

Table 4 Reported cases of perioperative management, complications and outcome of patients with hereditary arrhythmogenic syndromes—arrhythmogenic right ventricular dysplasia and catecholaminergic polymorphic ventricular tachycardia. No. of pts, number of patients; CSE, combined spinal–epidural; CPVT, catecholaminergic polymorphic ventricular tachycardia; ARVD, arrhythmogenic right ventricular dysplasia; GA, general anaesthesia; PVCs, premature ventricular contractions; SVTs, supraventricular tachycardia; VT, ventricular tachycardia; ALS, advanced life support; NA, not available. *Severe head injury, patient transferred to operating theatre from the intensive care unit. †Outcome 'well' indicates that the patient was discharged from hospital

First author	Syndrome	No. of pts	Age/sex	Type of anaesthesia	Patient at presentation	Drugs used	Complications	Complication management	Time of complication	Outcome†
Houfani[96]	ARVD	2	13, 16/F	GA	Both undiagnosed	Thioopental, sufentanil, vecuronium, isoflurane	VT; cardiac arrest	ALS	After operation	Death (for both)
Bastien[105]	ARVD	1	82/M	GA	Undiagnosed	Thiopental/phenoperidine; midazolam/isoflurane	SVT; asystole	ALS; internal cardiac compressions	Intraoperatively	Death
Martinez Torrente[106]	ARVD	1	43/M	Epidural; GA	Diagnosed	Fentanyl/thiopental; cisatracurium; isoflurane/N_2O; fentanyl epidurally	Uneventful	—	—	Well
Bonnet[107]	ARVD	1	19/M	GA*	Diagnosed	Midazolam; fentanyl; isoflurane	VT	Resolved spontaneously	Intraoperatively and after operation	Death (not related to ARVD)
Massen[108]	ARVD	1	27/F	GA	Undiagnosed	Alfadione; pancuronium	PVCs; SVTs; bigeminy	Resolved spontaneously; Patient transfer to ICU	Intraoperatively	Well
Toh[109]	ARVD	1	59/F	Epidural; GA	Undiagnosed	Bupivacaine; propofol/ succinylcholine; atracurium; isoflurane/N_2O	Acute heart failure; cardiogenic shock	Fluid administration; norepinephrine i.v.; epinephrine i.v.	Intraoperatively	Death
Bauce[111]	ARVD	4	18–35/F	Epidural	All diagnosed	NA	Uneventful	—	—	Well (for all)
Dornan[118]	CPVT	1	18/F	GA	Diagnosed	Propofol/remifentanil	Uneventful	—	—	Well
Chan[120]	CPVT	1	27/F	CSE	Diagnosed	Ropivacaine/fentanyl	Uneventful	—	—	Well

effective. Although atropine is reported to have successfully restored the heart rate in SSS-related excessive bradycardia or asystole,[63 65] it is usually ineffective[66–70] or only transiently effective.[71] Therefore, prompt treatment with isoproterenol,[71] and if not effective, with epinephrine along with chest compressions is required in patients with suspected SSS-related severe bradycardia.[59 68] On the other hand, aggressive treatment of tachyarrhythmias may result in excessive bradycardia.[59] In either case, temporary, external, or transvenous cardiac pacing is required for haemodynamic stabilization and to minimize the risk of arrhythmia recurrence perioperatively.[59 66 67]

Anaesthetic considerations

Although anaesthesia may unveil undiagnosed cases of SSS,[66 67 70 71] a previous uneventful anaesthetic is of limited significance, since symptoms may be mild, non-specific, or absent.[68 69] Preoperative 24 h Holter ECG, evaluation of responses to β-agonists or electrical atrial pacing and an exaggerated response to carotid sinus massage may reveal a suspected SSS.[61 72 73] Nevertheless, SSS has been uncovered after induction of general anaesthesia in a patient with a normal preoperative Holter ECG.[71] Unexpected severe bradycardia resistant to atropine is a common feature of SSS[64 66 67 69 70 74] and possibly a warning sign that should alert the physician. If the syndrome is suspected during anaesthesia, β-agonists, such as isoproterenol, and an external cardiac pacemaker should be ready for prompt use.[63]

Anaesthesia-related autonomic imbalance may cause serious conduction abnormalities, even in patients with a functioning implanted pacemaker. Complete atrioventricular block has been reported in a patient with SSS and single-chamber atrial pacing, after epidural administration of mepivacaine and subsequent sympathetic block.[75]

In diagnosed asymptomatic patients without an implanted pacemaker, preoperative insertion of a transvenous temporary pacemaker has been recommended, because anaesthesia *per se* or surgical manoeuvres[63] may induce serious dysrhythmias, resistant to conventional pharmacological treatment.[61 64] On the other hand, it has been suggested that such prophylactic measures are not indicated in patients for spinal anaesthesia, especially if they have not undergone electrophysiological testing for SSS subcategory determination, and if the neuraxial block is not extended to upper thoracic dermatomes.[65]

Perioperatively, SSS usually manifests as refractory, severe bradycardia, or unexpected asystole.[63–69 71] Complications during general anaesthesia have been reported in patients who received volatile or i.v. anaesthetics (Table 3). Unexpected long sinus pauses or sudden asystole have been reported in undiagnosed patients receiving halothane,[59] enflurane, and isoflurane.[68] Older volatiles such as halothane,[76 77] methoxyflurane,[76]enflurane,[77] and isoflurane[77] have been found to depress the automaticity of sinoatrial nodal cells. Nitrous oxide has not been implicated in arrhythmias reported in patients with SSS.[59 68 75] Nevertheless, atrioventricular junctional rhythms may be facilitated, when N_2O is combined with older volatiles.[30] Sevoflurane probably does not impair the sinoatrial rate.[78] In combination with remifentanil, it has been used uneventfully in a patient with SSS presenting with sinoatrial block.[79] However, remifentanil causes bradyarrhythmias and has been found to significantly depress sinus node function and prolong sinoatrial conduction time.[80] Propofol has also been associated with bradyarrhythmias and unexpected asystole-related deaths.[81] In dogs with autonomic block, propofol did not directly affect the sinus node and cardiac conduction system,[82] but other investigators have found that propofol causes a dose-related depression of sinoatrial node activity and His-Purkinje conductivity in normal pig hearts.[83] In patients with SSS, sinus arrest with atrio/nodal escape beats has been reported after induction of anaesthesia with propofol, ketamine, and fentanyl.[66] Profound bradycardia was also observed when a small dose of lidocaine was administered i.v. before propofol for pain reduction.[84] α-2 adrenoreceptor agonists are better avoided, as they may induce sinus arrest, junctional bradycardia, and atrioventricular block.[44 85]

In most of the case reports of SSS-related complications, vecuronium was used for neuromuscular block.[63 66 74 75] Vecuronium has been associated with a higher incidence of severe (<40 beats min^{-1}) and symptomatic bradycardia than atracurium.[86] A comparison of vecuronium and rocuronium showed that profound bradycardia occurred in the vecuronium group only and that 5% of the vecuronium group patients had periods of transient asystole.[87] This suggests that neuromuscular blocking agents with vagolytic properties, such as rocuronium, should be used in patients with SSS.

Severe bradyarrhythmias have also been reported in patients with unsuspected SSS receiving general combined with epidural anaesthesia.[63 68 75] Cervical epidural injection of lidocaine 1.5% has been implicated in recurrent episodes of sinus arrest under isoflurane anaesthesia.[68] Recurrent bradycardia and asystole have been reported in a patient during propofol/fentanyl/vecuronium general anaesthesia combined with epidural administration of ropivacaine 0.75%.[63] Similar episodes were observed during or even hours after spinal anaesthesia with bupivacaine 0.5% or lidocaine 5% and blocks up to T_8–T_{10}.[65 69 88] Neuraxial anaesthesia may produce hypotension due to block of the sympathetic vasomotor fibres (T_5–L_1) and subsequent vasodilation. It is possible that patients with SSS cannot develop a tachycardic response to compensate. Spinal and epidural anaesthesia may also directly impair the heart rate, if the cardio-accelerator sympathetic fibres (T_1–T_4) are blocked. In SSS, the autonomic nervous system plays a major role, either as enhanced basal parasympathetic activity or as increased sympathetic tone masking sinus node dysfunction.[62] In these patients, sympathetic block results in unopposed parasympathetic tone and may induce bradyarrhythmias and cardiovascular collapse.

Vagal responses to surgical manoeuvres may also precipitate life-threatening bradycardia in patients with SSS.[63] Successful treatment of nausea/vomiting reduces the risk of bradycardia due to manoeuvres associated with vagal tone enhancement. Metoclopramide may induce serious bradyarrhythmias, possibly by action on muscarinic cholinergic and 5-HT_3 receptors.[89 90] Ondansetron is probably preferable, although it may also impair the cardiac rhythm—by blocking the 5-HT_3 receptors serotonergic activity on the autonomic nervous system.[90 91]

Arrhythmogenic right ventricular dysplasia/cardiomyopathy

ARVD/C is a genetic myocardial disorder mainly characterized by structural abnormalities and electrical instability of the right ventricle, although progression to right and left heart failure is also possible.[92–95] The prevalence of ARVD/C is 1:5000–10 000.[96 97] It is a major cause of ventricular tachyarrhythmias and possibly the most common cause of sudden cardiac death in young, apparently healthy adults.[4] The disease is inherited in up to 50% of cases, characterized by autosomal-dominant transmission with variable penetration.[95] There are also autosomal-recessive patterns of inheritance, as in 'Naxos disease' and in 'Carvajal syndrome'.[98] Genetic studies have identified mutations in genes responsible for plakoglobin, desmoplakin, plakophilin-2,[92 98] desmoglein-2, desmocollin-2,[95] and also in cardiac ryanodine receptor-2 gene.[2 95]

Pathophysiological features include thinning of the right ventricular wall, with consequent dilatation and aneurysm formation, along with depolarization/repolarization changes.[92 93 99] The disease may be symptomless for a long time or may present as palpitations, dyspnoea, syncopal episodes, life-threatening arrhythmias, or sudden cardiac death, usually during exercise/physical effort.[92 93 99]

Diagnosis of ARVD is based on the Task Force Criteria for ARVD[100 101] (www.arvd.com/diagnosis_crit.html), and may be difficult in mild forms and early stages of the disease.[93] Since symptoms are mainly induced by exercise, physical examination tests may be normal at rest. In 50% of affected cases, ECG abnormalities may be identified; usually a right bundle branch block and/or T wave inversion in V_1–V_3 leads,[99 100] QRS prolongation or epsilon waves, a terminal notch in the QRS complex due to slow intraventricular conduction, may be present in V_1–V_3 leads. ECG and Holter ECG may reveal frequent ventricular extrasystoles or ventricular tachycardia with left bundle branch block morphology.[100 101] Echocardiography and magnetic resonance imaging may reveal dyssynchronous contraction, dyskinetic, or akinetic areas or aneurysms in the right ventricle.[100 101] Electrophysiological studies may be needed, while familial history is a significant diagnostic criterion.[92 100 101] Right ventricular angiography is the diagnostic gold standard, even though the definite diagnostic finding is the presence of fibrofatty replacement of myocardium in right ventricular endomyocardial biopsy.[100] However, the patchy pattern of lesions render this technique unreliable due to false-negative results.

Mortality is estimated at 2–4% per year despite treatment,[95] which include permanent ICD placement, catheter/radiofrequency ablation, and pharmacological agents.[92 93 102] Competitive sports and strenuous exercise should be avoided.[103] ICDs are recommended in symptomatic patients with a history of syncopal episodes, sustained ventricular arrhythmias, or sudden cardiac arrest, when drugs are ineffective and also when a family history of sudden death exists.[92] Ablation is an alternative to ICD for intractable ventricular tachycardia, despite pharmacological treatment.[102] Antiarrhythmic agents, such as sotalol, amiodarone, and β-blockers (metoprolol), are used to suppress the ventricular tachycardic episodes,[103 104] while angiotensin-converting enzyme inhibitors and diuretics may also be helpful.[93 99] Cardiomyoplasty and cardiac transplantation are an option in cases that are unresponsive to other therapies.

Anaesthetic considerations

Patients with undiagnosed ARVD/C are at high risk of perioperative sudden death.[96] A retrospective analysis found that 18 of 50 sudden perioperative cardiac deaths in patients without a history of cardiac disease were caused by ARVD/C.[4] Uneventful anaesthetic history is of little prognostic significance,[96 105] while the presence of T-wave inversion in V_1–V_3 leads in young patients' ECG should be further investigated by echocardiography.[96]

In high-risk patients with ARVD/C, preoperative suppression of tachycardias is essential.[96 106] All patients should continue to receive their antiarrhythmic drugs perioperatively.[107] Premedication with a benzodiazepine is appropriate.[107]

Transoesophageal echocardiography should also be considered for monitoring during major and prolonged surgical procedures.[99] Pulmonary artery catheterization should probably be avoided due to high risk of ventricular arrhythmias and right ventricular wall perforation.[99 107] Most reports of ARVD/C (Table 4) describe undiagnosed cases which were unmasked perioperatively.[93 105 108 109] Thiopental,[96 105 106] propofol,[109] and isoflurane[105 106 109] have all been given to patients with ARVD/C without being specifically implicated in any of the observed complications. Isoflurane has been used in critically ill ARVD/C patients.[94] Nitrous oxide was not associated with adverse effects when used in two patients with ARVD/C,[106 109] but the clinical significance of its sympathomimetic effects[30] in ARCD/C is not known. Fentanyl[94 107] and sufentanil[96] have been used safely. There are no data on the use of remifentanil. No adverse effects have been reported with vecuronium[96] and atracurium.[109] Succinylcholine and volatile agents do not trigger malignant hyperthermia in patients with mutations in cardiac ryanodine receptor-calcium release channel, so they are not contraindicated in patients with ARVD/C.[109 110]

In contrast, halothane[96] and pancuronium are best avoided[108] because of possible arrhythmogenicity.

Epidural analgesia has not been related to perioperative complications in patients with ARVD/C.[109] High doses of local anaesthetics should be avoided due to the possibility of cardiotoxicity, as is the addition of epinephrine.[99] Caution is needed if vasopressors are required for treatment of hypotension. α-Adrenergic agonists, such as phenylephrine or norepinephrine, are preferable as β-adrenergic stimulation may result in arrhythmias.[107 109] A β-blocker such as esmolol should be available for suppression of ventricular tachycardias, if they occur.[107]

Metoclopramide, ondansetron, and other drugs which may produce prolongation of ventricular depolarization (QRS) due to 5-HT_3 receptor antagonism should be used with caution.[90 91] Droperidol has been found to prevent epinephrine–halothane-induced ventricular tachyarrhythmias,[30] and may be useful in patients with ARVD/C.

Six cases of pregnancy and delivery in women with ARVD/C receiving antiarrhythmic treatment have been reported.[111] In all cases, the pregnancy-induced physical changes were well tolerated, without worsening of symptoms. In four cases, Caesarean section was performed under epidural anaesthesia without complications, but details regarding the anaesthetic technique were not reported. Close clinical observation is required during the peripartum period, due to the high risk of life-threatening ventricular arrhythmias.[111]

In patients with right heart failure undergoing surgical treatment for congenital ARVD/C, pulmonary vascular vasodilators such as prostaglandin E1, nitroglycerin, and dobutamine are of use and optimal oxygenation, mild hyperventilation, and early extubation are important.[94]

Cardiovascular collapse in patients with ARVD/C may be unresponsive to resuscitation with fluids and inotropes,[96 99 109] due to apoptosis of cardiac myocytes.[99] Most reported perioperative deaths have occurred in undiagnosed patients.[96 105 109] The drugs used for general or regional anaesthesia were not implicated in these deaths.[107 109] Major fluid shifts, haemorrhage, and metabolic acidosis were associated with most complications and deaths in ARVD/C patients.[107 109] In two undiagnosed cases, postoperative sudden death, unresponsive to resuscitation, occurred without obvious cause.[96] Postmortem examination revealed cardiac structure abnormalities diagnostic of ARVD/C.[96]

Catecholaminergic polymorphic ventricular tachycardia

CPVT is a rare malignant hereditary disease characterized by adrenergic-dependent, potentially lethal tachyarrhythmias in individuals with structurally normal hearts.[112 113] The inheritance pattern is autosomal-dominant and mutations in the cardiac ryanodine receptor gene-2 have been identified.[2 114 115] A family history of syncope or sudden death is positive in up to 30% of patients with CPVT.[112 115] The disease typically presents as syncopal episodes after physical effort or acute emotional stress.[112 116] The syncope may be accompanied by loss of continence, leading to a misdiagnosis of epilepsy.[112 116]

Diagnosis is based on ECG changes during exercise, as the resting ECG is usually normal. During exercise, the ECG shows isolated monomorphic ventricular premature beats which increase in number as the physical effort continues, eventually becoming polymorphic bursts with bidirectional salvoes.[112] These changes are reproducible with isoproterenol infusion.[117]

As the syndrome is adrenaline-dependent, all patients are instructed to abstain from competitive athletics and effortful activities.[112 114] Emotional stress should also be avoided. The pharmacological treatment of CPVT is β-blockers,[112 117] while amiodarone is ineffective.[112] Nadolol (40–80 mg day^{-1}) is the preferred β-blocker, because of its prolonged half-life.[112 118] It is crucial to emphasize the necessity of not interrupting β-blocker therapy perioperatively. A syncopal episode has been reported in a patient treated with nadolol after one missed dose.[112] An ICD may be necessary in patients with recurrent life-threatening arrhythmias or episode of cardiac arrest.[114] Positive results have been reported by addition of a selective serotonin re-uptake inhibitor in a patient with CPVT refractory to both β-blockers and ICD.[119]

Anaesthetic considerations

There are only few reports on the anaesthetic management of patients with CPVT[118 120] (Table 4). Perioperative continuation of β-blocker treatment is important.[112 118 120] Preoperative stress and anxiety with subsequent tachycardia should be avoided by giving an anxiolytic, such as temazepam.[118]

Propofol and remifentanil have been used as induction and maintenance agents in a patient with CPVT, without complications.[118] Centrally acting sympatholytic drugs, such as clonidine and dexmedetomidine, may be useful in an adrenergic-dependent syndrome, such as CPVT. Neuromuscular blocking agents, with the exception of pancuronium, can be safely administered to this group of patients. Patients with CPVT and mutations in the cardiac ryanodine receptor gene (RyR2) are not susceptible to developing malignant hyperthermia with succinylcholine or volatiles.[108] Halothane should generally be avoided because of possible arrhythmogenic effects on these patients. Hypotension, caused by β-blocker treatment, may be accentuated by positive-pressure ventilation which should be modified accordingly.[118]

Uneventful combined spinal–epidural anaesthesia for Caesarean section has been reported in a parturient with CPVT.[120] Bupivacaine 0.5% was administered spinally and epidurally, while fentanyl was injected spinally.[120] The addition of epinephrine to local anaesthetics is contraindicated.

Perioperatively, regardless of the anaesthetic technique, the aim should be the avoidance of adrenergic stimulation/catecholamine release that may provoke arrhythmias. β-Adrenergic agonists, such as isoproterenol, are

contraindicated for the same reason.[112 118] Intraoperative tachycardia should be treated promptly with a β-blocker such as esmolol[118] or labetalol[120] i.v. If hypotension occurs, a vasopressor with a pure α-agonist action is preferable.[118]

Adequate postoperative analgesia is mandatory and antiemesis should also be provided, since nausea/vomiting may result in significant stress. I.V. ondansetron has been successfully used in patients with CPVT.[118]

General management principles

Patients diagnosed with a hereditary arrhythmogenic syndrome should be carefully evaluated before operation, regarding the severity/frequency of symptoms and effectiveness of current treatment. Before elective surgery, patients should be clinically optimized with pharmacological or invasive treatment, aiming for suppression of arrhythmias and control of symptoms.[12 96] A multidisciplinary approach, including cardiological consultation, is recommended for a well-planed perioperative management tailored to individual patient's needs. The effects of commonly used anaesthetic agents on cardiac electrophysiology are summarized in Supplementary Table S1.

Before operation, pacemakers should be programmed in a non-sensing mode (e.g. VOO or DOO) and ICDs should be inactivated in order to avoid any electromagnetic and diathermy interference.[37 42 44 64 75 106] Intraoperatively, external defibrillator pads can be applied, while a five-lead ECG and invasive arterial pressure monitoring are mandatory.[8 40 44 46] Alleviation of anxiety,[108] adequate anaesthetic depth and analgesia, maintenance of normocarbia, normothermia, and normovolaemia, smooth recovery, and sufficient postoperative analgesia are extremely important, especially when sympathetic stimulation should be avoided.[5 96 105] Also, electrolyte and acid–base disorders should be promptly corrected. After operation, the implanted devices should be reactivated and reset at their preoperative mode.[6 8 20–22 42] Continuous haemodynamic monitoring in a high dependency unit for at least 24 h is strongly recommended.[42 46] Postmortem examination should be performed in every case of perioperative sudden cardiac death, and if a hereditary cardiac channelopathy is suspected, familial phenotypic and genetic screening is recommended.[5]

Perioperative management of patients with inherited cardiac channelopathies is often difficult, especially if they are not diagnosed or treated properly. These patients are at high risk of perioperative life-threatening arrhythmias and sudden cardiac arrest. The risk is not reduced in patients with previous uneventful anaesthetics. A hereditary arrhythmogenic syndrome should be suspected in patients with a history of severe arrhythmias, syncopal episodes, arrest, or when sudden cardiac death of a family member has occurred. A carefully planned anaesthetic management is pivotal. Cooperation between the specialities involved, good haemodynamic monitoring, and a high level of awareness for prompt pharmacological or invasive intervention are of paramount importance. In suspicious perioperative cardiac deaths, postmortem examination and familial screening should be performed.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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