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REVIEW ARTICLE

Perioperative management of patients with pre-excitation syndromes

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Abstract

Patients with pre-excitation abnormalities are at a high risk for life-threatening perioperative arrhythmias. In Wolff-Parkinson-White syndrome, the anaesthetics used for invasive diagnostic testing/ablation, should not affect cardiac electrophysiology; propofol, sevoflurane, fentanyl, sufentanil , alfentanil are suitable. In non-ablative surgery, propofol, sevoflurane, isoflurane, fentanyl, alfentanil, sufentanil have been used safely. Among neuromuscular blockers, cis-atracurium, rocuronium and vecuronium are good choices. Ketamine, pancuronium and pethidine should be avoided because of their sympathomimetic actions. Anticholinergic/ anticholinesterase combinations for neuromuscular block reversal should preferably be omitted, while sugammadex seems more attractive. In regional anaesthesia, addition of epinephrine and high sympathetic blocks should be avoided. Hypotension should be treated with pure alpha-adrenergic agonists. Other pre-excitation abnormalities associated with different accessory pathways are the Mahaim Fiber and Lown-Ganong-Levine syndrome. Sympathetic activation should be avoided. Total intravenous anaesthesia with propofol probably represents the safest option. A careful anaesthetic plan and close cooperation with cardiologists are mandatory for successful management.

Keywords: Pre-excitation; Wolff-Parkinson-White syndrome; Mahaim fiber syndrome; Lown-Ganong-Levine syndrome; anaesthesia

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Introduction

In 1893, the physiologist S. Kent reported the existence of atrio-ventricular (AV) pathways in mammalian hearts [1], while in 1930, the cardiologists Wolff, Parkinson and White described an "unusual cardiac mechanism" manifested as paroxysmal tachycardia or atrial fibrillation (AF) and characterised by a bundle-branch block and a short PR interval on the electrocardiogram (ECG) [2]. Since then, this electrophysiological abnormality has attracted the interest of investigators [3, 4], while the term "pre-excitation" was first used by Öhnell in 1944 [5].

Normally, the cardiac electrical impulses are generated in the sino-atrial (SA) node and then are spread to the right and left atrium. After passing through the AV node and His bundle, the stimuli reach the Purkinje fibers and propagate across the ventricular myocardium. The action potential of the AV node depends on slow inward calcium current which delays AV conduction as the heart rate (HR) increases, thus preventing fast supraventricular rhythms to reach the ventricles. However, abnormal AV muscular connections may serve as accessory pathways (APs) allowing atrial impulses to bypass the critical delay in the AV node. In most APs, the action potential relies on rapid inward

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sodium currents. As a result, the stimuli travel towards the ventricles faster than usual, causing early depolarisation of the ventricular myocardium, a condition named "pre-excitation" [5]. The quick transmission of cardiac impulses combined with fast HRs may predispose to detrimental ventricular tachycardias (VTs), even ventricular fibrillation (VF) [6-8].

More than one APs may exist in the same patient, located almost anywhere in the AV groove [5]. The AP conduction is usually bidirectional, but rarely it may be only retrograde (ventriculo-atrial). In this case, the pathways are called "concealed" due to the absence of electrocardiographic signs of pre-excitation [3, 5].

In the past, the term "pre-excitation" was exclusively used for the Wolff-Parkinson-White (WPW) syndrome. Today, other pre-excitation mechanisms due to different APs have also been identified. Specifically, Mahaim Fiber and Lown-Ganong-Levine syndrome represent pre-excitation conditions which are encountered more rarely than the well known WPW.

Perioperative management of patients with pre-excitation may become quite challenging, especially if there is no time for adequate preoperative investigation and clinical optimisation – as in emergencies –, or even worse, in undiagnosed cases. It is possible that the poorly controlled or unknown underlying electrophysiological abnormality will become unmasked during anaesthesia and surgery, giving rise to potentially life-threatening arrhythmias.

In the literature, pre-excitation syndromes have been mainly approached from the view of the disease (i.e. presentation, diagnosis, treatment), while anaesthetic data are scarce. The present review aims to focus on the perioperative management of patients with WPW and two other, less known pre-excitation syndromes.

We conducted a Pubmed® literature search for all types of published articles (up to February 2018) using the terms: "Preexcitation", "Pre-excitation", "Wolff-Parkinson-White syndrome", "WPW syndrome" "Mahaim pre-excitation", "Mahaim fibers", "Lown-Ganong-Levine syndrome" and "anaesthesia" or "perioperative management " or "perioperative care" in all possible combinations. Articles in languages other than English were used, if they had a detailed English abstract containing specific and relevant information. We identified 75 suitable articles. Additionally, seven publications were found by manual searching. Since the number of randomised controlled trials (RCTs) was small, the articles we considered were mostly observational studies, retrospective studies, case series and case reports. We also used articles providing information on genetics, clinical presentation, diagnostic and therapeutic approach of the disorders. In total 119 articles were included in the present review.

The WPW syndrome

Pathophysiology and clinical features of WPW syndrome

The main pathophysiological characteristic of the syndrome is the existence of an accessory AV pathway, named "bundle of Kent". It represents an abnormal fibro-muscular connection which ends up directly into the ventricular myocardium and has remained after incomplete AV separation [9, 10]. It may connect the left atrium and ventricle (type A), or the right atrium and ventricle (type B), and can conduct the stimuli bi-directionally [5, 10]. The prevalence of WPW syndrome is 0.1-3.1‰ in general population, higher in men [10]. Most cases are sporadic, while the more rare familial form is characterised by autosomal dominant inheritance and has been linked to chromosome 7q34-q36 and mutations in the gamma-2 regulatory subunit of AMP-activated protein kinase gene (PRKAG2) [11].

The ECG pattern consists of a short PQ interval (< 120 ms), a slurred upstroke at the beginning of QRS (delta wave) and a broad QRS complex (> 120 ms). This characteristic "WPW pattern" represents an exclusively ECG feature, found 10-100 times more frequently than the actual "WPW syndrome" which refers to the combination of the ECG pattern with symptomatology [9, 12]. While many individuals with a WPW-pattern will remain asymptomatic for life, patients with WPW-syndrome usually develop arrhythmias between the ages 20-40 years [10]. The commonest symptom is palpitations, while dizziness, lightheadedness, chest pain, shortness of breath and syncopal episodes may also occur. Rarely, the first manifestation of the disorder is cardiac arrest [10].

The most common arrhythmias are atrioventricular reentrant tachycardias (AVRTs) [10], usually orthodromic. In orthodromic tachycardias, the stimuli travel down the AV node and return back via the AP, producing narrow QRS complexes on the ECG [9]. Less often, the conduction proceeds down the AP and retrogradely up the AV node, causing antidromic tachycardias with a wide QRS [9]. Finally, AF or atrial flutter may develop; both rhythms can be dangerous if rapid anterograde conduction occurs through an AP with a short refractory period. In this case, many atrial impulses may travel towards ventricles, causing extremely fast ventricular responses, VF and sudden cardiac death [12]. Risk factors for life-threatening arrhythmias are APs with short anterograde effective refractory period, short RR interval in pre-excited AF, inducible AVRT during electrophysiology studies (EPS), multiple APs, male gender and young age [13, 14]. Sometimes, pre-excitation may imitate acute myocar-

dial infarction, while negative delta waves can also be confused with pathological Q waves [15, 16]. Further investigation for definite diagnosis includes cardiac troponin I levels or echocardiographic assessment of myocardial wall movement [15, 16].

The initial diagnosis of WPW syndrome is based on the ECG pattern combined with symptomatology. More specific examination includes Holter monitoring and exercise or pharmacological testing with ajmaline or procainamide [12]. Finally, EPS may be required to elucidate the abnormality and identify the exact AP location and its characteristics.

Treatment, conservative or invasive, is case-specific, since both long-term antiarrhythmic therapy and AP catheter ablation are not without risks, namely drug-side effects, or heart injury, ischaemia and thrombo-embolism due to catheterisation [10]. The decision depends on the risk/benefit ratio, according to the type, severity and frequency of symptoms [10].

Anaesthetic considerations in WPW syndrome

Patients with WPW syndrome may require anaesthesia for EPS/ablation or for non-ablative procedures. In diagnostic/therapeutic interventions, anaesthetics should not interfere with cardiac electrophysiology, while in non-ablative surgery, drugs should ideally prevent – or at least not facilitate – the generation of arrhythmias associated with APs.

Anaesthesia and surgery may unmask an undiagnosed syndrome, and suspicious cases should be referred for further investigation before elective surgery. A detailed cardiac history during pre-anaesthetic evaluation is the corner stone of not missing undiagnosed patients [12]. Apart from a 12-lead ECG, Holter monitoring may be useful, especially in intermittent WPW. Echocardiography can reveal congenital cardiac abnormalities that coexist in 7-20% of patients, such as Ebstein's anomaly, valve lesions, cardiac hypertrophy, atrial aneurysms and septal defects [10, 11, 17]. An EPS may also be needed; the benefit of postponing an elective surgery for EPS testing should be examined. The capability of rapid anterograde AP conduction increases the risk of sudden death and is an indication for radiofrequency catheter ablation (RFCA) to precede surgery [17]. Diagnosed patients should be carefully assessed preoperatively regarding their symptoms and current treatment, and should be clinically optimised. Cardiological consultation and close cooperation are mandatory for a safe management plan.

Anaesthesia for electrophysiologic investigation and ablation

Although cardiac complications during EPS are usually not related to the anaesthetic technique [18, 19], accurate diagnostic mapping and successful ablation may be impaired by anaesthetic drugs that alter the conduction in the normal and accessory pathways [20]. Thus, agents with minimal effects on cardiac electrophysiology should be preferred [19].

Among general anaesthetics, propofol is considered appropriate for use in EPS/ablations, as it does not impede the generation of diagnostic supraventricular tachycardias (SVTs) [20]. Despite reports about bradycardia, AV block, even asystole [21], Sharpe and colleagues suggest that propofol per se has no direct effects on SA or AV node or intra-atrial conduction [22]. Moreover, propofol did not affect the refractory periods of normal and accessory pathways and did not interfere with EPS/ablation in a study with adult WPW patients [22]. Also, in children, propofol-based anaesthesia did not cause problems during EPS/RFCA [23, 24]. Two randomised studies in youngsters undergoing RFCA, showed that propofol was similarly suitable with isoflurane, both leaving unaffected the SA and AV node function [25, 26]. Nevertheless, the findings about isoflurane are not consistent; experimental research has shown that it may depress the SA node discharge, and prolong the AV and ventricular conduction [21]. Similarly, in adults undergoing surgical cryoablation, isoflurane at 1 MAC was associated with slower conduction in normal and aberrant systems [27]. Also, a retrospective study of children showed that isoflurane prolongs the atrial, ventricular and AP anterograde effective refractory period [28]. Notably, not only isoflurane [29], but also enflurane [29, 30], and halothane [29] are considered rather unsuitable agents for EPS/ablations, since they prolong the refractory period and slow the conduction in normal and accessory pathways, thus interfering with interpretation of tests and determination of ablation success. In patients receiving halothane anaesthesia, persistent delta waves and difficulty with AP localisation have also been reported [31]. Conversely, experimental studies have shown that sevoflurane exerts only moderate effects on cardiac electrophysiology [21]. Additionally, clinical data suggest that sevoflurane has a favorable profile for use in EPS/ablations [32, 33]. In adults, it did not affect the function of SA node or AV and AP conduction, and did not prevent diagnostic reciprocating tachycardias [32]. Also in children, when given after propofol, sevoflurane caused only moderate prolongation of the AP antegrade effective refractory period, without interfering with the ablative procedure [33]. On the other hand, desflurane at 1 MAC prolonged the AP effective refractory period and impaired the induction of diagnostic SVTs in paediatric patients [24]. The authors considered it unsuitable for EPS/ablative procedures [24].

Regarding opioids, animal studies have shown that morphine may exert a direct negative action on SA

and AV nodes, while fentanyl may decrease the SR, but this action is not clinically significant [21]. In WPW patients, fentanyl was found to exert no effect on AP refractory period or SA conduction [34, 35], but it may increase the cardiac vagal tone causing prolongation of the sinus node recovery time, especially when combined with propofol [35]. More pronounced effects have been reported for remifentanil: both experimental and clinical studies have shown that it may depress sinus node automaticity and delay SA and AV conduction [21, 36-38]. These properties render remifentanil less attractive for use in EPS, as it may interfere with testing and results. On the contrary, sufentanil is devoid of significant direct actions on the normal intracardiac or AP conduction [21, 29]. Also, an alfentanil/midazolam-based anaesthesia has been suggested as suitable, because it leaves unaffected both the AV node and aberrant bundle [39].

Among adjuvants, dexmedetomidine has been studied in EPS/ablative procedures. A prospective trial in children receiving thiopental/ketamine anaesthesia showed that i.v. dexmedetomidine (1 μg/kg followed by 0.7 μg/kg/h infusion), given after successful ablation caused significant sinus and AV node depression, without affecting the atrial or ventricular refractoriness [40]. The authors consider that the drug may interfere with the generation of tachycardias and interpretation of measurements [40]. Different findings were reported by a retrospective study of children receiving propofol or sevoflurane: dexmedetomidine (0.5-1 μg/kg followed by 0.5-1 μg/kg/h infusion) given during EPS/ablation was associated with increased need for isoproterenol for SVT induction, but did not affect the electrophysiological parameters or the interventions and their success [41]. Regarding other factors, controlled ventilation in patients subjected to RFCA under GA was found to facilitate the procedure and increase the ablation success [42].

The published clinical trials on the use of anaesthetics for EPS/ablation are presented in Table 1.

Anaesthesia for non-ablative surgical procedures

In patients with WPW syndrome undergoing non-ablative surgery, antiarrhythmic treatment should be continued perioperatively. Additionally, sympathetic stimulation should be avoided, because it may shorten the AP refractory period and facilitate life-threatening arrhythmias [43-47]. Anaesthetics and adjuvants that increase AP refractoriness should be preferred.

Regarding volatiles, early research demonstrated that enflurane was advantageous over both halothane and isoflurane, because it increased the AP refractoriness more than the other two agents, while it was the only volatile that did not prolong the coupling interval, thus the vulnerable time for SVT generation [29]. Also, in two older case reports enflurane was described as a safe agent for WPW patients [48, 49]. Conversely, Dobkowski and colleagues suggested that enflurane may trigger arrhythmias and should not be used in WPW syndrome [30]. In a more recent report, isoflurane was preferred among other volatiles due to its property to prolong the AP refractory period and decrease the likelihood of tachycardias [50]. Similarly, most investigators consider isoflurane as a safe choice for patients with WPW [45, 51-53]. Although halothane could be preferred for its bronchodilatory properties in selected cases [52], its potential to sensitize myocardium to catecholamines is a major drawback. Sevoflurane seems less advantageous than isoflurane, since it does not prolong the AP refractory period [32]. Nevertheless, it has been used safely for the maintenance of anaesthesia in a number of cases [54-57]. Also, no adverse effects have been reported for nitrous oxide [34, 48-49, 54, 58]. Finally, desflurane has been found to prolong the refractory period of AP, without affecting the electrophysiology of sinoartrial node and normal pathways [24], but the available data are limited [59].

Among intravenous anaesthetics, propofol does not affect the AP refractory period [22]. Induction or maintenance of anaesthesia with propofol combined with fentanyl has been associated with cardiovascular stability in WPW patients [44, 50, 54, 55, 58-63]. Moreover, it was reported that delta waves disappeared after propofol administration and reappeared after its discontinuation [58]. Similarly, a decrease of QRS duration and return of PR interval into normal ranges were observed when propofol infusion (25 μg/kg/min) was added to isoflurane anaesthesia [63]. Thiopental has been used in several cases, and small (50 mg) to moderate doses (4 mg/kg) did not cause conduction problems [18, 45, 48, 51, 53, 64, 65]. Nevertheless, in the early 70's its safety had been questioned due to observed ECG changes after anaesthesia induction; the ECG signs of acute myocardial infarction were attributed to enhanced conduction in the AP caused by thiopental [66-68]. Experimental data suggest that etomidate in high plasma concentrations may decrease the SR and prolong AV conduction [21]. Nevertheless, in common clinical doses it offers significant cardiovascular stability, quite desirable in patients with WPW, although specific data are rather limited [49]. Ketamine should better be avoided due to its sympathomimetic effects.

Most opioids are suitable for patients at risk for tachyarrhythmias, since they maintain haemodynamic stability with a mild reduction of HR [21]. Additionally, alfentanil/midazolam anaesthesia produces no significant effects on AP conduction and the refractory period [39], while the sufentanil/lorazepam combination may even cause a mild prolongation of the AP effective

Table 1. Clinical studies on the anaesthetic management of patients with Wolff Parkinson White syndrome undergoing electrophysiological studies and/or ablation of accessory pathways

Author / study	Patients	Type of anaesthesia / Drugs used	Findings / Suggestions
Irish (1988)[18], retrospective	Children, adolescents, adults with AV APs n = 181 (197 procedures)	GA with various drugs: diazepam, fentanyl, scopolamine, droperidol, thiopental, halothane, enflurane, isoflurane, N_2O, pancuronium, succinylcholine, tubocurarine	•Incidence of arrhythmias not related to anaesthetic agent •Standard anaesthetic methods and drugs can be used in most cases
Joung (2006)[19], retrospective	Children, adolescents n = 131 (47 WPW)	Various anaesthetic techniques: No sedation, conscious sedation, deep sedation, GA (midazolam, fentanyl, ketamine, propofol)	•Complication incidence did not differ and was not related to anaesthetic method
Moore (2011)[20], retrospective	Children, adolescents n = 151	GA: propofol infusion	• GA may interfere with risk stratification / Propofol is a good choice
Sharpe (1995)[22], prospective	Adults, n = 12	GA: alfentanil, midazolam, vecuronium / ± propofol for maintenance	• Propofol: no effect on AV and AP conduction / suitable for EPS / ablation
Pappone (2004)[23], RCT	Children, n = 47 (20 received intervention)	GA: propofol	•Propofol: no significant complications
Hino (2017)[24], randomized crossover study	Children, n = 36	GA with propofol or desflurane at 0.5 or 1 MAC	• Desflurane 1 MAC: ↑ AP refractory period, no effect on normal pathways, impaired SVT induction. •Desflurane: unsuitable for EPS/ablation •Propofol: suitable for EPS/ablation
Lavoie (1995)25, RCT	Children, adolescents n = 20 (9 WPW)	GA: alfentanil, thiopental, pancuronium, N_2O, propofol or isoflurane	•Neither propofol nor isoflurane had significant effects on SA or AV node
Erb (2002)[26], RCT	Children, adolescents n = 60	GA: midazolam, sevoflurane, pancuronium, fentanyl, N_2O, isoflurane or propofol	•SVT induction independent of propofol or isoflurane administration •Isoflurane and propofol equally suitable
Dobkowski (1990)[27], prospective*	Adults, n = 7	GA: lorazepam, morphine, sufentanil, vecuronium, isoflurane	•Isoflurane 1 MAC: prolonged the conduction in both normal pathways and AP
Chang (1996)[28], retrospective	Infants, children, adolescents n = 51	Sedation (pethidine, promethazine, chloropromazine) versus GA with isoflurane	•Compared to sedatives, isoflurane prolonged the refractory periods in AP (antegrade), atria and ventricles. •Isoflurane: interfered with EPS
Sharpe (1994)[29], RCT	Adults, n = 21	GA: lorazepam, sufentanil, vecuronium, volatiles (halothane or isoflurane or enflurane)	• Lorazepam / sufentanil: no effect on AP •Volatiles: ↑ in AV and AP refractoriness (mostly enflurane)
Dobkowski (1991)[30], prospective*	Adults, n = 7	GA: lorazepam, morphine, sufentanil, vecuronium, enflurane	•Enflurane: ↓ AV and AP conduction / should not be used in WPW patients
Tempe (1997)[31], retrospective	Adults, n = 13	GA: morphine, halothane, pancuronium	•Halothane: interferes with EPS/ablation
Sharpe (1999)[32], prospective	Adults, n = 15	GA: midazolam, alfentanil, vecuronium, sevoflurane	•Sevoflurane: no effect on AV or AP conduction/ suitable for ablations
Pérez (2008)[33], prospective	Children, n = 15	GA: fentanyl, vecuronium, propofol replaced by sevoflurane	•Sevoflurane: moderate changes in AP properties/suitable for ablations
Gómez-Arnau (1983)[34], prospective	Adults, n = 18	GA: Morphine, thiopental, fentanyl, diazepam, N_2O, pancuronium, droperidol	•Droperidol: dose-dependent ?of AP conduction, ↑ antegrade & retrograde refractory period •Induction agents, fentanyl, diazepam: no effect on AP refractory period
Fujii (2009)[35], prospective	Children, n = 27 (9 WPW)	GA: propofol, fentanyl, vecuronium	•Fentanyl/propofol combination: ↓ SN automaticity
Fujii (2011)[37], RCT	Children, n = 60 (29 completed study)	GA: propofol, remifentanil, vecuronium	•Remifentanil: ↓ SN automaticity, ↓ SA conduction
Niksch (2010)[38], RCT	Children, adolescents n = 15 (5 WPW)	GA: propofol ± remifentanil	•Remifentanil: ↓ SN & AV function – may affect EPS findings
Sharpe (1992)[39], prospective	Adults, n = 8	GA: lorazepam, alfentanil, midazolam, vecuronium	•Alfentanil/midazolam anaesthesia: no effect on AV node or AP conduction

AP: accessory pathway, AV: atrio-ventricular, EPS: electrophysiological study, GA: general anaesthesia, MAC: minimum alveolar concentration, n: number of patients, RCT: randomised controlled trial, SA: sino-atrial, SN: sinus node, SVT: supraventricular tachycardia, WPW: Wolff-Parkinson-White

* study published in the form of abstract

refractory period [21]. Fentanyl at doses 30-50 μg/kg was found to exert no effect on the anterograde effective refractory period of the AP [34]. It is the most popular opioid, used in the majority of reported cases, and is described as very safe [44, 49, 50, 53, 54, 56, 58, 60, 62-64]. Conversely, the atropine-like effect of pethidine renders it less appropriate for WPW patients [12].

Regarding neuromuscular blockers (NMBs), succinylcholine may act on muscarinic or adrenergic receptors of the sinus node, with bradycardia presenting more often [21]. These effects make the drug less attractive compared to modern non-depolarising NMBs, even though it has been used uneventfully in several cases [18, 48, 53, 64, 69, 70]. Among non-depolarising agents, pancuronium may not exert significant direct effects on APs [34], but enhances AV conduction, increases HR and has triggered SVT in a couple of cases; thus it is suggested to be avoided [44, 45]. Atracurium may cause histamine release and possible autonomic instability [71], while cis-atracurium is devoid of cardiovascular effects and represents a safer choice [21]. Rocuronium has mild vagolytic properties, while vecuronium may cause HR reduction [21]; both have been used safely in WPW patients [53-55, 57].

The reversal of NMB may cause problems, since neostigmine can induce serious tachyarrhythmias by depressing the AV while facilitating AP conduction; Kadoya and collagues reported that 1mg of neostigmine converted a narrow complex AF to haemodynamically unstable wide complex tachycardia [54]. Additionally, the anticholinergic actions of atropine and glycopyrrolate are undesirable in WPW patients [49-51]. Especially atropine accelerates the conduction and shortens the anterograde and retrograde effective refractory period in the AP [72]. Thus, it seems that the standard anticholinergic/anticholinesterase combination should preferably be omitted [53, 71]. Alternatively, sugammadex could be used for rocuronium or vecuronium reversal; it seems to exert no significant actions on cholinesterase, nicotinic and muscarinic receptors [73]. Two case reports describe its uneventful use [55, 57].

Sedation with a benzodiazepine/opioid combination can be administered alone or as supplement to local anaesthesia for minor surgical procedures [46]. Among benzodiazepines, diazepam is cardiovascularly stable, without effects on the AP refractory period [34]. Nevertheless, its long duration of action (half life: 43 h) is a disadvantage, especially for outpatient cases. The intermediate acting lorazepam (half life: 14 h) or the short acting midazolam (half life: 2 h) have also been found to exert no significant effects on AP conduction, and represent more attractive choices [32, 39]. They can be safely used in conjunction with fentanyl, alfentanil or sufentanil [21, 39, 46]. Also, droperidol (200-600 μg/kg) was found to depress the antegrade and retrograde conduction of the AP in a dose-dependent manner and a fentanyl/droperidol combination was suggested as a useful regimen [34].

When GA is provided, adequate doses of anesthetics and opioids should be given to suppress the sympathetic response to laryngoscopy/tracheal intubation. Supraglottic airway devices should be preferred whenever possible, since their insertion causes less sympathetic stimulation [74], but care should be taken to avoid hypercarbia during spontaneous ventilation. Intraoperatively, deep anaesthesia and sufficient analgesia reduce the stress response to surgical noxious stimuli.

Regional anaesthesia (RA) may be advantageous over GA in terms of avoiding airway manipulation and patient's exposure to multiple drugs with possible proarrhythmic properties. Additionally, RA techniques provide high quality intraoperative and also postoperative analgesia via central neuraxial and peripheral nerve catheters. Nevertheless, caution is needed with the height of sympathetic blockade, because sinus bradycardia and intra-cardiac conduction defects may develop if the thoracic (T1 to T4) cardio-accelerator fibers are blocked. The AV conduction time and functional refractory period may become prolonged and AP conduction facilitated due to unopposed parasympathetic tone [75, 76]. Cases of WPW syndrome unmasked due to high levels of spinal blocks are not rare, especially if combined with other vagal stimulants [17, 76, 77]. Thoracic epidural and single shot spinal anaesthesia are more likely to cause cardiac sympathectomy, thus careful dosing and increased vigilance for a high blockade are required. The spinal dose of local anaesthesia should ideally produce the minimum level of sensory block required for the surgery. Addition of opioids allows a reduction in local anaesthetic doses [78, 79], while selective spinal opioid analgesia may be used in some cases (i.e. labor), thus minimising haemodynamic fluctuations [78, 80].

Dose titration and gradual elevation of the block can be achieved with lumbar epidural and combined low-dose-spinal/epidural anaesthesia. These modalities offer more haemodynamic stability and should probably be preferred over single-shot spinal anaesthesia [81]. There are several reports of operations (caesarean deliveries included) performed safely under a simple epidural [64, 82-84] or a combined spinal/epidural anaesthesia [81, 85-88]. In selected cases, combined general/regional anaesthesia may be used; successful thoracotomy under propofol anaesthesia together with thoracic epidural analgesia has been reported [61].

Reduced venous return and atrial filling due to an extensive sympathetic blockade may precipitate arrhythmias. Adequate fluid loading should be con-

sidered in order to reduce – as possible – the risk and magnitude of hypotension, subsequent sympathetic activation or need for sympathomimetic drugs [88, 89]. If hypotension occurs, a pure alpha-adrenergic agonist (i.e. phenylephrine) is the vasopressor of choice [88, 90, 91]. The addition of epinephrine to local anaesthetics should be avoided, as it may shorten the AP refractory period and facilitate arrhythmias [43]. Finally, supplementation of any regional technique with adequate sedation in order to reduce anxiety and sympathetic stimulation is advisable [16].

In pregnant patients with WPW, physiological adaptation and emotional factors increase the risk of arrhythmias; estrogens, intravascular volume expansion, haemodynamic changes, pain, stress and oxytocin given during labor may all trigger SVTs, especially when an extended subarachnoid sympathetic block is established [87, 92, 93]. In this regard, a simple epidural or a combined spinal/epidural are the modalities of choice for caesarean delivery. Vaginal delivery has also been accomplished safely in WPW parturients, even in cases with severe co-morbidities, under a carefully managed labor epidural analgesia with local anaesthetic/opioid combination [83, 84]. Regarding oxytocin, it should be omitted if possible [71, 88], since it has been associated with paroxysmal SVT, even in common clinical doses [90].

Management of perioperative arrhythmias

Orthodromic AVRTs are regular narrow-complex tachycardias (constant R-R intervals, QRS < 120 ms) that should be treated as any other paroxysmal SVT with vagal maneuvers, such as carotid sinus massage, Valsalva or Valsalva-like maneuver in case of mechanical ventilation, along with 100% oxygen [94]. If these measures fail, adenosine IV boluses should be given, starting with 6 mg, followed by 12 mg and further 12 mg, if tachycardia persists. Adenosine suppresses both sinus automaticity and AV conductivity, and usually converts an SVT to normal SR [90, 95]. It should be given as a rapid push, because of its very fast elimination. Its ultra-short duration of action also renders adenosine suitable for parturients [87, 92], even though it may cause temporary bradycardia to the fetus; thus, fetal HR monitoring is suggested during administration [90].

Beta blockers or more rarely calcium channel blockers have been used to treat WPW-related SVTs [44, 51, 91-94]. Beta blockers can also be given preventively before laryngoscopy [96]. The very short acting esmolol is preferred over long acting agents [44], especially in parturients, even though the risk of causing fetal distress still exists [92].

Both ephedrine and phenylephrine have been used to treat hypotension [18, 81, 86, 90]. Moreover, phenylephrine was reported to resolve a paroxysmal SVT resistance to various other measures and drugs [91].

Antidromic AVRT presents as regular wide-complex tachycardia (QRS > 120 ms), sometimes difficult to differentiate from VT [9]. Amiodarone or procainamide can be used to restore the rhythm in haemodynamically stable patients. If there is doubt about the type of arrhythmia, it should be treated as VT [97].

Pre-excited AF presents as irregular wide complex tachycardia, often resembling VF or Torsades de Pointes [97]. Amiodarone (300 mg i.v. in 20 min) can be given, while digoxin and verapamil are contraindicated, and also adenosine and diltiazem should be avoided, since they block the AV node while concomitantly facilitating AP conduction, thus increasing the risk of VF [90, 97]. Procainamide and propranolol can be useful because they prolong the AP refractory period [57]. Expert cardiologic consultation is required in such high risk situations.

Electrical synchronised cardioversion is indicated for SVT or AF resistant to antiarrhythmic drugs or in cases with extreme tachycardia and/or hypotension/shock, myocardial ischaemia, heart failure/pulmonary oedema or syncope [17, 59, 81, 97, 98]. Immediate defibrillation should be performed in VF or pulseless VT [97]. Antiarrhythmic drugs and a defibrillator should be prepared before anaesthesia induction [57, 81].

Sympathetic stimulation should be avoided: alleviation of anxiety, adequate intraoperative anaesthesia/analgesia, suppression of response to intubation, avoidance of anticholinergic/sympathomimetic drugs are mandatory [96]. The patient should be kept warm, normovolaemic, normocarbic and balanced regarding the acid base and electrolyte status [51]. Smooth recovery from anaesthesia, sufficient postoperative analgesia, prevention of nausea/vomiting that may cause stress and tachycardia are also important.

A concealed WPW syndrome should be considered in the differential diagnosis of paroxysmal SVTs occurring during anaesthesia. If the syndrome is suspected, cardiological consultation and postoperative ECG Holter should be requested [99]. Appearance of the electrocardiographic WPW pattern after induction of anaesthesia should not necessarily lead to surgery cancellation, especially if the patient has no history of suspicious symptoms and is haemodynamically stable [100, 101]. Nevertheless, in such cases the anaesthesiologist should be fully prepared to treat any arrhythmias that may arise [99]. It is also important to note that asymptomatic patients with intermittent WPW do not receive antiarrhythmic treatment and generally carry a low risk for tachyarrhythmias [47, 100, 102, 103]. Adequate preparation, invasive blood pressure monitoring, and a high level of vigilance are of paramount importance.

The identified publications on the anaesthetic management of patients with WPW-syndrome undergoing non-ablative surgical procedures are presented in Table 2.

Other Pre-Excitation Syndromes with different Accessory Pathways

Mahaim Fibers

In 1938, I. Mahaim described anatomic connections between the AV node and ventricles [104]. These "Mahaim Fibers" were initially considered to connect the AV node or the His bundle/fascicles with the right ventricle (nodo- or fasciculo-ventricular fibers) [104], but later, it was demonstrated that they usually originated in the right atrium and terminated in the right ventricular wall (atrio-ventricular) or near the right bundle branch (atrio-fascicular) [105]. Mahaim Fibers (MFs) are found in 0.5-1:10 000 of the general population, comprising about the 3% of APs [106, 107], and may coexist with other cardiovascular pathology, such as Ebstein's anomaly [107].

The MF pathways exhibit longer conduction times compared to the bundle of Kent, while they share some of the AV properties, such as similar conduction velocity, conduction delay at high atrial rates and sensitivity to adenosine [107]. They allow only antegrade conduction and may be part of a circuit with retrograde conduction through the AV node; these antidromic AVRTs are characterized by a wide QRS complex and may be difficult to differentiate from ventricular arrhythmias [107, 108]. Tachycardia with a left bundle brunch block pattern may be seen as the result of right ventricle pre-excitation (stimulated before LV) via MFs [106]. The ECG may have features of pre-excitation, but usually it has a normal PQ interval and minimal or no delta wave [106, 107]. An rS pattern in lead III is found in about 60% of the patients, while an additional suspicious finding is the absence of q wave in lead I [106]. The combination of such an ECG with young age and history of tachyarrhythmias strongly suggests the existence of MFs, but certain diagnosis requires an EPS.

Beta-blockers, class IA and IC antiarrhythmics are used to prevent tachycardias [107], but definite treatment with AP ablation is preferred in many cases [107, 108]. Anaesthetic data on the management of patients with MFs are limited. Conditions and drugs causing sympathetic activation and catecholamine release should be avoided; Zweifler and colleagues suggested that perioperative stress and pain were possibly the triggering factors of a wide complex tachycardia (MF pathway conduction with AV nodal reentry) in a woman with undiagnosed MFs (Table 3) [108].

Lown- Ganong-Levine syndrome

The Lown-Ganong-Levine (LGL) syndrome is another rare pre-excitation condition first described in 1952 [109]. Its ECG pattern is characterised by a short PQ interval (< 120 ms), a normal or inverted P wave, and a QRS complex of normal morphology and duration [109, 110]. The combination of the above features with paroxysmal SVTs is suggestive of LGL syndrome, which comprises the 17% of cases with short PQ interval [109]. Compared to WPW, it has shorter PJ and PQ intervals which remain constant over the years, while the QRS complex usually has a duration of 80 ms or less, without the characteristic slurring (i.e. no delta wave) [109].

The short PQ interval reflects a fast conduction of the action potential from atria to ventricles, without the normal delay in the AV node. The involved mechanisms are not quite clear: enhanced AV conduction may be caused by a congenitally hypoplastic and malfunctioning AV node, which allows atrial impulses to be rapidly conducted to the ventricles [111]. Another possible mechanism is the presence of James or Brechenmacher fibers which bypass – partially or completely – a normal AV node: James fibers connect the upper part of the AV node with its lower part or with the His bundle [112], while the Brechenmacher fibers form a route between the atrium and bundle of His, thus completely bypassing the AV node [113]. In both cases, the avoidance of normal AV delay results in short PQ intervals, while the normal stimulation of ventricles through the His-Purkinje fibers gives normal QRS complexes. The normal and the bypass tract form a circuit for reentry arrhythmias. Atrial flutter, AF and VT may develop, while the deterioration of a paroxysmal AF into VF can cause sudden cardiac death [109, 114, 115].

The syndrome is mainly diagnosed in women who develop tachyarrhythmias usually in their fourth decade of life [109, 110, 116]. Sympathetic stimulation, changes in cardiac automaticity/conduction, and pregnancy-associated physiologic adaptations may trigger or facilitate SVTs [109, 117].

As in WPW, perioperative management of patients with LGL should first aim to minimise possible triggering factors of arrhythmias. Benzodiazepines, such as midazolam or diazepam [110, 116], could relieve preoperative anxiety, while drugs with sympathomimetic properties, such as ketamine or pancuromium, should be avoided [65]. Patients should continue their antiarrhythmic medication perioperatively, while beta blockers – especially short acting ones, such as esmolol – could be useful [116]. Episodes of SVT should be managed with vagal maneuvers and adenosine [110].

As shown in Table 3, anaesthetic data are rather limited; thiopental and propofol have been used without

Table 2. Case reports and series describing the perioperative management, complications and outcome of patients with WPW syndrome undergoing non-ablative procedures

First author (year)	Syndrome	No of pts-gender/ age	Surgery/ procedure	Anaesthesia	Complications & Management (*)	Outcome / Remarks
Lustik[15] (1999)	WPW†	1F/34y	Uterus dilation / evacuation (17w)	RA SA (no further details)	•Reported palpitations / chest pain •ECG: inferior Q waves *Cardiologic consultation	•Uneventful course •Postop EPS/ RFCA
Le Manach[16] (2006)	WPW†	1M/67y	Abdominal aortic aneurysm repair	GA Premed: midazolam. IN & MNT: propofol, sufentanil, atracurium, N_2O, morphine.	•Post-op ECG changes mimicking inferior MI *Daily ECG follow-up, Troponin I measurements	•Uncomplicated course •ECG returned to normal
Garg[17] (2011)	WPW	1M/32y	Urological surgery	Spinal: bupivacaine + fentanyl. Upper sensory level: T8 Other drugs: diazepam, midazolam	Intermittent WPW - intraop rhythm changes (HR:70-90) *none	•Uneventful course / pt haemodynamic stable •Vigilance for level of neuraxial block
Naço[44] (2009)	WPW	1F/17y	Thyroidectomy	GA IN: Midazolam, fentanyl, propofol, pancuronium MNT: halothane	•SVT after pancuronium / tracheal intubation *Adenosine, esmolol	•Uneventful course •Pancuronium may trigger SVT
Richmond[45] (1988)	WPW	1M/ 36w‡, 40w‡	1) IPPV for pneumonia 2) Pyloromyotomy	1) Pancuronium for IPPV 2) GA with thiopental, vecuronium, isoflurane, N_2O •Wound infiltration: bupivacaine	1) Prolonged SVT episode (289 bpm) *Sync cardioversion 2) None	Uneventful course
Schmitz[46] (1997)	WPW	1F/26y	Teeth surgical removal	•Premed: midazolam / Sedation: fentanyl, midazolam, N_2O •Local anaesthesia (bupivacaine)	•None / Sedation associated with ECG normalization	Uneventful course
Wakita[47] (2007)	Intermittent WPW†	1F/49y	Tooth extraction	IV sedation: propofol Local anaesthesia: lidocaine (± epinephrine)	Repeated appearance of δ-waves	•Uneventful course •Epinephrine and autonomic imbalance implicated in δ-waves
Okada[48] (1990)	WPW	1M/29y	Maxillary cyst operation	GA (premed: atropine, hydroxyzine, pethilorfan) IN: thiopental, succinylcholine MNT: enflurane, N_2O	None	Uneventful course
Janes[49] (1989)	WPW	1F/35y	Laparoscopic sterilisation	GA (premed: temazepam) IN: etomidate, fentanyl, atracurium MNT: enflurane, N_2O RV: glycopyrrolate/neostigmine	Postop retrosternal discomfort + ECG changes: Glycopyrrolate suspected	•Uneventful course •Sympathetic stimulation should be avoided
Sinha[50] (2010)	WPW/ Ebstein's anomaly/ MVS	1F/23y	Danielson's repair & MVR	GA (premed: diazepam, morphine) IN: propofol, fentanyl, midazolam, vecuronium MNT: isoflurane	•SVT (↓ BP) *Adenosine, amiodarone, IV fluids	Pt discharged with persistent pre-excitation on ECG
Goldhill[51] (1988)	WPW	1M/46w‡	3 surgeries for VPS and hydroceles / 1 CT	GA (± premed with atropine) Thiopental, atracurium, isoflurane, N_2O	•SVTs *Vagal stimulation, propranolol or verapamil	Uneventful course
Laloyaux[52] (1998)	WPW/ Cantrell's pentalogy	1M/42w‡ & 48w‡	1) Inguinal hernia repair 2) Blalock-Taussig shunt	1) GA: halothane / RA: Caudal with mepivacaine, bupivacaine 2) GA: sufentanil, pancuronium, lidocaine, diazepam	•SVT preop / transient tachycardia intraop *no extra drugs (already on digoxin, amiodarone)	•Uneventful recovery/ Infant died few weeks later due to unrelated reason
Kumar[53] (1986)	WPW	1M/30y	Lumbar laminectomy	GA (premed: papaveretum, hyoscine) IN: thiopental, succinylcholine MNT: isoflurane, N_2O, fentanyl, vecuronium	None	•Uneventful course •Isoflurane + fentanyl: safe choice •Vecuronium: safe choice
Kadoya[54] (1999)	Intermittent WPW	1M/67y	Laryngeal microsurgery	GA IN: propofol, fentanyl, vecuronium MNT: sevoflurane, N_2O RV: Neostigmine without atropine	•AF with narrow QRS after sevoflurane/N_2O discontinuation *none •AF 110-180 bpm (wide QRS) with ↓ BP after neostigmine *Sync cardioversion	•Extubation → ICU transfer → recovery uncomplicated •Avoidance of anti-cholinesterases

Şahin[55] (2015)	WPW	1M/51y	Inguinal hernia repair	GA (premed: midazolam) IN: tramadol, propofol, rocuronium MNT: sevoflurane 1 MAC, air RV: sugammadex 2 mg/kg	↑ HR (108 bpm) after intubation *i.v. remifentanil	•Uneventful recovery •Sugammadex: may be a safe choice
Nakamura[56] (2009)	WPW/ Ebstein's anomaly	n = 3 1M/34y 1M/5m 1F/5y	Valvuloplasty/ AP ablation	GA with sevoflurane, fentanyl, midazolam	None	Successful procedures
Sengul[57] (2016)	WPW	1F/23y	CD	GA (parturient denied RA) IN: fentanyl, propofol, rocuronium MNT: sevoflurane, O_2/air RV: sugammadex 2 mg/kg	None	•Uneventful course •Sugammadex under NMT monitoring may be safe in WPW
Seki[58] (1999)	WPW	1F/29y	Uterus dilation & curettage (missed abortion)	GA Premed: midazolam IN & MNT: propofol, fentanyl	WPW pattern on ECG/ Propofol caused ECG normalization / δ-wave returned after propofol discontinuation	•Postop ECG: WPW pattern •Propofol: possible favourable profile
Sato[59] (2014)	WPW†	1M/59y	Video-assisted thoracoscopic lobectomy	GA & TEA (catheter insertion) IN: propofol MNT: desflurane, remifentanil	3 SVT episodes *Antiarrhythmics: no effect *Sync cardioversion	•Uneventful course •Postop EPS revealed concealed WPW
Yamaguchi[60] (1998)	WPW	1M/62y	Microsurgery of larynx	GA Premed: atropine, hydroxyzine IN & MNT: propofol, fentanyl	↑ BP after surgical laryngoscope inserted-stable thereafter *none	Uneventful course
Kajikawa[61] (2001)	WPW	1M/57y	Thoracic surgery	GA & TEA IN: propofol, fentanyl MNT: propofol (+ TEA)	Severe hypercapnia during one lung ventilation	Hypercarbia did not cause tachyarrhythmias
Takayama[62] (2000)	WPW	1M/55y	Minimally invasive direct CAB	GA IN: midazolam, fentanyl, vecuronium MNT: propofol, fentanyl, O_2/air (+ diltiazem infusion)	None	•Uneventful procedure •Propofol/fentanyl useful and safe •Intraop diltiazem may prevent paroxysmal SVT
Gupta[63] (2013)	WPW	1F/30y	Laparoscopic cholecystectomy	GA Premed: alprazolam, ranitidine IN: fentanyl, propofol MNT: isoflurane, propofol	•Post-intubation: ?HR, ↑ BP, WPW pattern •Propofol caused ECG normalization	•Uneventful course •Propofol: possilble favorable profile
Klepper[64] (1981)	WPW	1F/28y, pregnant	•Cardioversion (35^w, 40^w) •CD (40^w)	•GA with fentanyl, thiopental, succinylcholine, N_2O •RA: EA for CD (+ oxytocin)	•No complications associated with GA / EA	•Uneventful course
Sadowski[65] (1979)	n = 13 11 WPW	3½y -64y	•7 bundle division •4 non-ablative surgeries	GA Thiopental, halothane or enflurane, N_2O, morphine, pancuronium or d-tubocurarine ± diazepam	•Arrhythmias in 2 cases after skin incision and during cardiac manipulation *Sync cardioversion	•Thiopental 1-3 mg/kg: did not affect cardiac conduction •Pancuronium: may cause tachyarrhythmias
Hannington-Kiff[66] (1968)	WPW†	1F/16y	•Auditory meatus enlargement / tonsillectomy •Surgical pack change	•GA (premed: hyoscine) IN: thiopental 4 mg/kg, succinylcholine MNT: halothane, N_2O, tubocurarine RV: atropine/neostigmine	•Soon after induction: T-wave inversion, ST depression in II, III, aVF *no specific measures	•Constant WPW pattern •Family investigation: father with latent WPW •Hyoscine: better than atropine for premed due to less tachycardia
Campkin[67] (1969)	WPW†	1M/34y	Craniotomy & clipping of aneurysm	•GA with thiopental, succinylcholine, halothane, N_2O (surgery cancelled) •GA Premed: promazine, atropine IN: thiopental, succinylcholine MNT: halothane, N_2O, tubocurarine	•Post-induction ECG changes: MI suspected *pt awakening, surgery postponed, investigation •Hypotension enhanced ECG changes *BP elevation: ECG changes resolved	•Clinical course uneventful •ECG changes persisted for > 5 months
Van der Starre[69] (1978)	WPW†	1M/22y	Knee arthroscopy	GA Premed: atropine, promethazine IN: clemastine, propanidid, succinylcholine MNT: halothane, N_2O	Episodes of sinus tachycardia *Discontiuation of halothane / lidocaine i.v. / postop transfer to ICU	Avoid drugs that produce tachycardia or negative inotropic effects
Suppan[70] (1979)	WPW	1F/45y	Laparoscopic ligation of the Fallopian tubes	GA IN: atropine, althesin, diazepam, succinylcholine, tubocurarine, pentazocine MNT: althesin, tubocurarine	None	•Uneventful / no ECG changes •Althesin: a possible alternative to thiopental

Rahul[71] (2006)	WPW	n = 2 1M/42y 1M/26y	•Lower limb fracture •Nephrectomy	1) RA: CSE SA: hyperbaric bupivacaine 0.5% + fentanyl EA: plain bupivacaine 0.375% infusion + fentanyl bolus 2) GA (premed: glycopyrrolate) IN: midazolam, fentanyl, propofol, vecuronium MNT: propofol, N_2O, vecuronium RV: glycopyrrolate/neostigmine	•In case 2 (GA): T-wave inversion in leads I-II-III without hemodynamic instability *No treatment	•Uneventful recovery •ECG normalised (at 24 h postop) •Probably RA preferable to GA
Shiroyama[76] (1994)	Intermittent WPW†	1 pt / no further details	No further details	RA Spinal, upper sensory level: C6	WPW pattern on ECG	•ECG normalized in 3d •High spinal block may cause ↓ AV & ↑ AP conduction and unmask intermittent WPW
Lubarsky[77] (1989)	WPW †	n = 2 1M/73y 1M/14y	1) Transurethral resection of prostate 2) Circumcision	1) RA Premed: pethidine, pento-barbital, cefazolin SA with tetracaine (i.v. diazepam, ephedrine, phenylephrine as needed) 2) GA Diazepam, isoflurane, N_2O	•Postop wide QRS complexes (T6 block, low Na^+, hypothermia, nausea) *furosemide/warm saline •Wide QRS complexes after physostigmine for gagging *no treatment	•ECG normalized •WPW unmasked due to ↑ vagal tone (nausea, hypothermia, spinal block, gagging, physostigmine)
Deviseti[79] (2016)	WPW	1F/20y	Evacuation of molar pregnancy	•RA: SA with hyperbaric bupivacaine 0.5% + fentanyl Level of sensory block: T8 •Other drugs: midazolam, fentanyl, oxytocin	None	Postop transfer to HDU for monitoring
Brizgys[80] (1984)	WPW	1F/19y	VD	RA SA: morphine Pudendal nerve block (lidocaine)	Transient sinus tachycardia (130 bpm) during delivery *Monitoring of vital signs	•Uneventful course •Intrathecal opioids for labour analgesia do not induce sympathetic block: useful in WPW
Namshikar[81] (2013)	WPW	n = 2 1F/30y 1F/28y	Elective CDs	CSE SA: hyperbaric bupivacaine 0.5% (1.7-2 mL) Postop analgesia: epidural bupivacaine 0.1-0.125% ± fentanyl 50 µg Other drugs: diclofenac, oxytocin (20 IU infusion)	None	•Uneventful course •CSE useful and safe
Ruiz-Castro[82] (1996)	WPW/ MV prolapse	1F/22y	CD	RA: EA	↓ BP 45 min after block *Methoxamine	No further incidents
Robinson[83] (2000)	WPW/ FHPP	1F/29y	Forceps assisted VD	RA: EA with bupivacaine/epinephrine, fentanyl, morphine	None	•Uneventful course •Discharge on 2nd postnatal day
Misa[84] (2007)	WPW/ Ebstein's anomaly	1F/25y	Forceps assisted VD	RA: EA with bupivacaine, fentanyl, chloroprocaine, lidocaine	Mild ↓ BP after delivery *Phenylephrine	•Uneventful course •Discharge after 48 h
Tachikawa[85] (2008)	WPW/ Ebstein's anomaly	Not available	Ankle joint fracture repair	RA: CSE (no further details)	None	Uneventful course
Sahu[86] (2011)	WPW	1F/45y	Abdominal hysterectomy	RA: CSE with bupivacaine, fentanyl Postop PCEA	↓ BP after initial epidural bolus *Phenylephrine	Postop ICU for 24 h monitoring
Palaria[87] (2013)	WPW	1F/30y	Emergency CD	RA (CSE) •SA with hyperbaric bupivacaine •Postop EA: bupivacaine •Other drugs: oxytocin	None	Uneventful course
Kaur[88] (2012)	WPW	1F/30y	CD	RA (CSE) •SA: hyperbaric bupivacaine 0.5% (1.8 ml) - block up to T8 •EA: bupivacaine 0.5% - level T5 •Postop EA: bupivacaine 0.125%	None	•Oxytocin was withheld •Postop transfer to ICU for 24 h observation
Kabade[89] (2011)	WPW	1F/48y	Abdominal hysterectomy	•RA: EA with bupivacaine, lidocaine •Other drugs: alprazolam, ranitidine, ondansetron, midazolam	None	•Uneventful course •Epidural preferred for haemodynamic stability *Prepare defibrillator / antiarrhythmics

Shora[90] (2007)	WPW	n = 2 1F/28y 1F/25y	CDs	RA in both cases •SA: hyperbaric bupivacaine (12.5 mg) •Other drugs: oxytocin	1. SVT with hypotension after oxytocin 5 IU *Vagal manoeuvres no effect, phenylephrine for hypotension, adenosine terminated SVT 2. None	•Uneventful course •Adenosine - under fetal HR monitoring- is the first choice in parturients
Jacobson[91] (1985)	WPW	1M/17y	Eye surgery	GA (premed: diazepam) IN: thiopental, fentanyl, tubocurarine, lidocaine 100 mg, MNT: halothane, fentanyl, N_2O RV: edrophonium	2 SVT episodes with ↓ BP (at induction and postop) *O_2, carotid sinus massage, verapamil, head down position, edrophonium, procainamide, sync cardioversion: no effect Phenylephrine: effective	•Uneventful course •Possible triggering factors of SVT: ↓ BP & reflex ↑ HR (at induction), lidocaine, postop retching, MVP *Phenylephrine may be useful in terminating paroxysmal SVT
Van Zijl[92] (2001)	WPW†	1F/27y	Emergency CD	RA: SA with hyperbaric bupivacaine, fentanyl	SVT (220 bpm) with ?BP *Fluids, Valsalva maneuvre, carotid sinus massage: no effect Verapamil: effective	•Pt transferred to ICU •EPS / RFCA in 2 m •Neonate died due to unrelated reason •Caution with SA
Okamoto[93] (2003)	WPW	1F/36y	CD	RA: EA with mepivacaine	4 SVT episodes *Valsalva maneuvre, carotid massage: no effect Verapamil,dysopyramide: effective	•Verapamil, dysopyramide: effective •Oxytocin, pain, anxiety, may trigger SVT
Bronheim[95] (1992)	WPW	1M/51y	Surgical ablation	GA (premed: morphine, scopolamine) IN: fentanyl, midazolam, pancuronium, metocurine. MNT: enflurane	Paroxysmal SVT after pericardium manipulation *Adenosine: effective	•Further procedure uneventful •Adenosine is effective in WPW syndrome
Jones[96] (1984)	WPW	n = 3 (1WPW) 1F/72y	Cholecystectomy	Propranolol before anaesthesia IN: thiopental, fentanyl, alcuronium MNT: enflurane, N_2O RV: glycopyrrolate / neostigmine	None	•Uneventful course •Prophylactic propranolol before laryngoscopy may be helpful
Wheeler[98] (2002)	WPW†	1M/72y	CABG	GA	Postop wide / narrow QRS tachy *Adenosine, amiodarone: no effect Sync cardioversion: effective, then sotalol	•Hospitalized for 16 days •Tachy episodes after discharge •EPS / ablation 3 months later
Nishikawa[99] (1993)	WPW†	1M/50y	Transurethral resection of bladder tumor	RA •Premed: secobarbitone •SA: tetracaine •Obturator nerve block with lidocaine	•Electrical stimulation for block triggered paroxysmal tachycardia *spontaneous resolution •2 similar episodes without haemodynamic instability *midazolam	•Uncomplicated course • Postop Holter suggested for possible concealed WPW
Chhabra[100] (2003)	WPW†	1M/15	Modified radical mastoidectomy	GA IN: pethidine, thiopental, vecuronium MNT: halothane, N_2O RV: glycopyrrolate / neostigmine	WPW pattern, but haemodynamically stable *Switch to isoflurane, lidocaine i.v. (no effect)	•Surgery continued and completed uneventfully •Normal SR after extubation / discharge after cardiac evaluation
Esenther[101] (2015)	Intermittent WPW†	1M/4y	Elective bronchoscopy	GA Sevoflurane, N_2O	Intermittent tachy-arrhythmia haemodynamically stable *None	•Uneventful course •ECG diagnosis of intermittent WPW
Braun[103] (1996)	Intermittent WPW/ isorhythmic AV dissociation (after modified Fontan operation)	1F/30y	CD	GA (RA not preferred because pt was receiving heparin SC) IN: etomidate, succinylcholine MNT: halothane, fentanyl, midazolam, N_2O	None	•Uneventful course (Main focus of paper on the management of post-Fontan parturients)

AF: atrial fibrillation, AP: accessory pathway, AV: atrio-ventricular, BP: blood pressure, bpm: beats per minute, CA(B)G: coronary artery (bypass) graft, CD: caesarean delivery, CSE: combined spinal-epidural anaesthesia, CT: computerized tomography, EA: epidural anaesthesia/ analgesia, ECG: electrocardiogram, EPS: electrophysiological study, F: female, FHPP: familial hypokalaemic periodic paralysis, GA: general anesthesia, HR: heart rate, HDU: high dependency unit, ICU: intensive care unit, IPPV: intermittent positive-pressure ventilation, IN:

induction, M: male gender, m: months, MAC: minimum alveolar concentration, MI: myocardial infarction, MNT: maintenance, MVS: mitral valve stenosis, MVR: mitral valve repair, NMT: neuromuscular transmission monitoring, PC(E)A: patient controlled (epidural) analgesia, Premed: premedication, Preop: preoperatively, Postop: postoperatively, pt(s): patient(s), RA: regional anaesthesia, RFCA: radiofrequency catheter ablation, RV: reversal of neuromuscular blockade, SA: spinal anaesthesia, SC: subcutaneously, SR: sinus rhythm, SVT: supraventricular tachycardia, Sync cardioversion: synchronized electrical cardioversion, TEA: thoracic epidural anaesthesia/analgesia, †: undiagnosed, VD: vaginal delivery, VPS: ventriculo-peritoneal shunting, w‡: weeks (post-conceptual age), WPW: Wolff-Parkinson-White, y: years

Table 3. Publications on perioperative management, complications and outcome of patients with rare pre-excitation syndromes: Mahaim fiber and Lown-Ganong-Levine syndrome

First author (publication year)	Syndrome - clinical description	No of pts - Sex/ Age	Type of surgery	Type of anaesthesia / Drugs used	Complications / *Management	Outcome / Points of interest
Sadowski[65] (1979)	In total: n = 13 LGL: n = 2 1 case LGL†	•31y •51y†	1) bundle division 2) 2 other operations	1) GA: enflurane, N_2O, d-tubocurarine 2) GA: morphine, N_2O, pancuronium or d-tubocurarine	1) None 2) Arrhythmia in first surgery → diagnosis of LGL *Sync cardioversion	•Uneventful course •Pancuronium: may cause tachyarrhythmias
Zweifler[108] (2011)	Mahaim fiber†	1F/ 38y	Spinal surgery	Plan for GA Premed in OR: midazolam, fentanyl	After premed: ↑ HR (180 bpm) - wide QRS - varying morphology *Lidocaine: SR restoration	•12-lead ECG: T-wave inversion •Surgery postponed / EPS & AP ablation / surgery: 2w later
Sharma[110] (2011)	LGL	1F/ 42y	Cholecystec-tomy	GA & EA (lumbar) for postop analgesia IN: midazolam, propofol, fentanyl, vecuronium MNT: TIVA with propofol RV: glycopyrrolate/neostigmine	1 episode of SVT *carotid sinus massage	•Uneventful course •TIVA with propofol & adequate postop analgesia may be useful
Jones[116] (1984)	In total: n = 3 LGL: n = 1	1F/ 36y	Mastectomy	GA / premed: diazepam, continuation of medication (verapamil) + propranolol IN: thiopental, fentanyl, alcuronium MNT: enflurane, N_2O RV: glycopyrrolate/neostigmine	None	•Propranolol may be useful for prophylaxis, but caution when combined with drugs like verapamil (enhanced effect)

AP: accessory pathway, bpm: beats per minute, EA: epidural anaesthesia/analgesia, ECG: electrocardiogram, EPS: electrophysiological study, F: female, GA: general anaesthesia, HR: heart rate, IN: induction, intraop: intraoperatively, LGL: Lown-Ganong-Levine, M: male, MNT: maintenance, No of pts: number of patients, OR: operating room, Premed: premedication, Preop: preoperatively, Postop: postoperatively, Pts: patients, RV: reversal of neuromuscular blockade, SR: sinus rhythm, SVT: supraventricular tachycardia, Sync cardioversion: synchronised electrical cardioversion, TIVA: total intravenous anaesthesia
No of pts: number of patients, †: disease undiagnosed, *: management of complication

problems for anaesthesia induction in two cases [110, 116]. Total i.v. anaesthesia with propofol may reduce the risk of tachyarrhythmias throughout surgery; furthermore, propofol has been reported to successfully terminate paroxysmal SVTs [110, 118]. Additionally, since a short PQ interval may be found in conditions such as Duschenne muscular dystrophy [119], the risk of malignant hyperthermia (MH) should probably be considered, especially in children. In this regard, succinylcholine or inhalational agents should be avoided, although a couple of reports do not describe problems with enflurane administration in adults with LGL syndromes [65, 116]. Modern non-depolarising NMBs exhibit a safe profile, while reversal with gycopyrrolate/ neostigmine was uneventful in two cases [110, 116].

Limitations. In the present review, we mainly used information from retrospective and observational studies, case series and reports, while – as expected – data from RTCs were limited. Different study designs and populations may account for some contradictory findings, although we consider that safe conclusions could be drawn for most anaesthetics used in WPW. For the more rare pre-excitation conditions, data were rather limited, since only a small number of case reports were identified. Nonetheless, we think that the present review may contribute to a better understanding of pre-excitation syndromes and provide useful information for their perioperative management.

Conclusion

Anaesthesia and perioperative care of patients with pre-excitation syndromes may be difficult, especially if they are undiagnosed, under-treated or if there is no adequate time for clinical optimisation, as in emergencies. These patients are at a high risk of developing life-threatening arrhythmias perioperatively. Close cooperation with a cardiologist is mandatory,

while increased vigilance and postoperative cardiovascular monitoring will allow prompt therapeutic intervention in cases of arrhythmias.

Conflict of interest

Nothing to declare

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