

## REVIEW ARTICLES

# Paediatric cardiomyopathy and anaesthesia

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### Editor's key points

- Paediatric cardiomyopathy (CM) is rare but carries significant perioperative risks.
- Of the various forms, dilatational (60%) and hypertrophic (25%) CM are the most common.
- Response to anaesthetic and cardiovascular drugs varies with the type of CM.
- A history or findings suggestive of CM require thorough assessment of cardiac function before operation.

**Summary.** 'Cardiomyopathy' (CM) is defined by the World Health Organization as 'a disease of the myocardium associated with cardiac dysfunction'. In a child, it is associated with a significant risk for anaesthesia. In addition, cardiac arrest under anaesthesia has been attributed to an undiagnosed CM. Care of these patients is complicated by the fact that there are several different forms of CM that have differing anaesthesia management goals, aimed at maintaining the patient's baseline haemodynamic variables of preload, heart rate, contractility, and afterload. With the emergence of new diagnostic tools, together with advances in cardiac imaging and improved treatment modalities (such as ventricular assist devices), the anaesthetic management of a child with a CM is evolving. This review describes the different forms of the disease in terms of pathology, aetiology, and clinical presentation. Dilated, hypertrophic, and restrictive CM are the most common forms. We examine recent advances in therapy, including the management of severe end-stage disease, while highlighting the specific anaesthetic considerations for children with each type of CM.

**Keywords:** anaesthesia; cardiomyopathies; child

'Cardiomyopathy' (CM) is defined by the World Health Organization (WHO) as 'a disease of the myocardium associated with cardiac dysfunction' and is either: dilated, hypertrophic, restrictive, arrhythmogenic right ventricular, or unclassified.<sup>1</sup> This WHO definition is considered by some to inadequately emphasize the complexity of this disease.<sup>2–3</sup> The American Heart Association (AHA) issued a consensus statement and revised classification based on genetics, heart structural changes, cellular events, and multi-organ involvement.<sup>4</sup> The European Society of Cardiology adopted an alternative classification which, although aligns more closely with the WHO, is more clinically orientated.<sup>5</sup>

The practicing anaesthetist should be aware of the evolving CM classification since formerly unknown aetiologies of CM are now being identified at the genetic, molecular, and cell structural level.<sup>3</sup> However, for the purpose of this review, the WHO definition of CM is adopted.<sup>1</sup> Since with this classification, certain pathophysiological features common to dilated, hypertrophic, restrictive, arrhythmogenic right ventricular, or unclassified CM permit discussion and recommendations of general principles for safe anaesthetic management in these children.

The aim of this review is to provide an updated analysis of CM in children. We collected material from standard textbooks and from searches of the electronic databases (MEDLINE and PUBMED) where the search terms included

the individual subgroups, along with 'genetics', 'anaesthesia', and 'paediatric'. Additional reports were obtained from reference lists of cited papers. Abstracts were screened for relevance and full articles obtained.

A practicing anaesthetist may encounter paediatric patients with a known CM and be asked to provide anaesthesia care. Broadly speaking, the management goals are to optimize myocardial function by maintaining the patient's baseline haemodynamic variables of preload, heart rate, contractility, and afterload. There is no ideal anaesthetic agent for all children, for all CMs. Therefore, the choice of anaesthetic agent is determined in part by therapeutic goals of maintaining the baseline haemodynamics. A greater concern is that in a seemingly healthy child, anaesthesia and surgery may unmask occult cardiac disease that may result in a sudden unexpected cardiovascular event, including death. This review will focus on the various types of CM and highlight the anaesthetic precautions and implications for this complex group of patients (Table 1).

The incidence of paediatric CM is 4.8 per 100 000 infants and 1.3 per 100 000 children under 10 yr.<sup>6</sup> Dilated CM (DCM) is most typical and accounts for 60% of affected children. Hypertrophic CM (HCM) represents 25% of cases, followed by ventricular non-compaction (9%) and restrictive CM (RCM) (2.5%). Arrhythmogenic right ventricular dysplasia and the unclassified group including endomyocardial

fibroelastosis are less common.<sup>6</sup> CM may present soon after birth, although RCM tends to present at ~2 yr of age.

The prognosis for children with symptomatic CM is poor. Around 40% of children presenting with symptomatic CM in the USA either receive a heart transplant or die within 2 years,<sup>7</sup> and 50% of all paediatric heart transplants are for CM and up to 12% of all heart transplants are performed in children.<sup>8</sup> In the developing world, therapeutic options for children with a significant CM are severely limited. Children with either symptomatic or asymptomatic CM remain at significant risk of perioperative arrhythmia, cardiac arrest, and death.

In a review of 1700 forensic autopsies in France, 50 cases (3%) were evaluated for unexpected cardiac death in asymptomatic patients during anaesthesia. Cardiac lesions were found in almost all of these cases and of note, nine of these unexpected deaths occurred in children. In six of these nine children, a diagnosis of CM was confirmed histologically.<sup>9</sup> In another review of sudden unexplained death, gene mutations resulting in a predisposition for long QT syndrome and ventricular tachycardia were identified in more than one-third of cases. Finally, in a large analysis of sudden infant death syndrome, mutations in cardiac calcium channels were found in 5–10% of cases.<sup>10</sup> These studies highlight the need for rigorous histological, biochemical, and genetic analysis after an unanticipated intraoperative cardiac arrest or death to exclude cardiac disease in family members.<sup>9–13</sup>

## CM subtypes

### Dilated cardiomyopathy

DCM, also called congestive CM, is characterized by dilatation and impaired contractility of one or both ventricles. The estimated annual incidence of DCM is 0.58 per 100 000 children<sup>14–15</sup> and is associated with a 14% mortality rate in the 2 years after diagnosis.<sup>14–17</sup> Recently, genetic testing in related family members at risk for sudden cardiac death (SCD) has revealed the long arm of chromosome 10 as being a particularly important site for possible mutations causing some forms of DCM.<sup>10</sup> Unfortunately, the natural progression of DCM reported in children has not improved dramatically, despite advances in diagnosis and therapy. A 5 yr mortality rate after time of diagnosis of 35–70% is still reported.<sup>14</sup>

DCM may be congenital or the result of infection, inflammation, metabolic or endocrine disease, and malnutrition. It can also be the result of longstanding supraventricular tachycardia or simply idiopathic. In a series of 1426 children with DCM from the USA and Canada, 66% were idiopathic. The most common *known* causes were myocarditis (46%) and those associated with metabolic neuromuscular disease (26%).<sup>15</sup>

There are very few clinical signs until DCM is severe. In smaller children, any history of cough, decreased effort tolerance, poor feeding, failure to thrive, syncopal episodes, or chest pain should result in a thorough examination looking

for cardiomegaly and clinical signs of cardiac failure. Thrombi may occur in the dilated ventricle, and so an embolic event can be the presenting scenario. An ECG may reveal bundle branch block and ST-T wave abnormalities, but the diagnosis is confirmed with echocardiography.

The common pathophysiological features of DCM include biventricular dilatation, systolic and diastolic myocardial dysfunction, decreased ejection fraction (EF), and decreased cardiac output (CO). Atrial filling pressure and left ventricular end-diastolic pressure (LVEDP) are usually elevated. Often there is associated mitral valve regurgitation, tricuspid valve regurgitation, or both. The dilated myocardium is potentially arrhythmogenic, but the arrhythmias associated with DCM may be primary or secondary.

In children, potentially treatable causes of DCM should always be considered. These include anomalous origin of the left coronary artery arising from the pulmonary artery and critical coarctation of the aorta.<sup>17–18</sup> With early surgical correction, these children may have full recovery and reversal of their ventricular dysfunction.

It has been found that nearly 7% of children who sustain burn injuries >70% may develop a reversible DCM.<sup>19–20</sup> This often presents >100 days after the injury. It should be suspected and managed early since this CM is reversible after recovery of the burn. The cause is unknown, although inflammatory mediators may play an aetiological role.

### Anaesthetic considerations

The preoperative assessment includes a mandatory echocardiogram to determine ventricular function. Consultation with a paediatric cardiologist is essential.

In addition, more detailed information can be obtained from advanced radiological and interventional tools, but often a simple chest X-ray can be invaluable. For example, the enlarged heart may cause extrinsic airway compression at the origin of the left main bronchus. Often, the addition of carefully adjusted PEEP is all that is needed to overcome the obstruction. Intubation of the trachea *per se* may not always ensure that the extrinsic compression is overcome as the obstruction may be distal to the trachea.<sup>21</sup>

Review of the concurrent medications is important. Most children have a degree of myocardial dysfunction and require ongoing cardiac anti-failure therapy, including after-load reduction with angiotensin-converting enzyme (ACE) inhibitors and  $\beta$ -adrenergic blockade. Potassium level should be evaluated as these patients may be receiving diuretics or digoxin and hypokalaemia corrected before operation. Although controversial, if the patient is prescribed ACE inhibitors, these should be continued including the day of surgery, even with the possibility of intraoperative hypotension.<sup>22</sup> Biventricular pacing may be part of the medical therapy in DCM.<sup>23</sup> Therefore, a preoperative functional assessment of the pacemaker may be required.

Anaesthetic principles for DCM include maintenance of normal diastolic arterial pressure to optimize coronary perfusion, maintenance of preload, avoidance of tachycardia,

**Table 1** CM subtypes and anaesthesia implications

Classification	Pathophysiology, echocardiography recognition	Anaesthetic implications
Dilated	Four heart chamber dilatation Predominantly left ventricular dilatation Mitral or tricuspid regurgitation Poor EF	Consider neuromuscular co-morbidities Maintain adequate preload, normal heart rate Avoid increased SVR Invasive monitoring Inotropes may be required
Hypertrophic	Dynamic LVOTO Ventricular cavity obliteration Poor diastolic myocardial relaxation Normal EF may be recorded despite poor function Increased two-dimensional left ventricular mass in $\text{g m}^{-2}$	Maintain relatively slow heart rate Prevent hypovolaemia Normal to increased SVR Phenylephrine bolus if ECG ST segment depression Avoid propofol as the sole anaesthetic agent
Restrictive	Near-normal ventricles Dilated atria and pulmonary veins Poor diastolic ventricular relaxation Intra-ventricular thrombi	Consider associated metabolic, genetic disease states Maintain preload, contractility Avoid bradycardia Avoid any further increase in PVR
Arrhythmogenic right ventricular dysplasia	Fibro-fatty infiltration of right ventricle  Arrhythmias/abnormal EKG findings Right ventricular failure	Avoid exogenous catecholamine/drugs with a sympatheticomimetic effect External defibrillation pads
Left ventricular hypertrabeculation/non-compaction	Deep myocardial trabeculations  Varying degrees of myocardial hypokinesis Intraventricular thrombi possible	Consider associated neuromuscular disorders

avoidance of decreased myocardial contractility, and ensuring that the systemic vascular resistance (SVR) is not elevated. A poorly contracting left ventricle will not maintain CO in the presence of a high SVR. If inotropic support is required, dilating agents such as milrinone, dobutamine, or low-dose epinephrine may be titrated to clinical effect. In fact, many children are currently successfully managed on long-term milrinone and other inotropic support in the hospital ward and at home while awaiting transplantation.<sup>24</sup> However, for the anaesthetist, it is important to consider that at end stage, a fibrotic-dilated cardiomyopathic heart may not be able to increase contractility with the addition of an inotrope.

In general, children do not cooperate, as well as adults, and therefore require deeper sedation or general anaesthesia for almost all diagnostic or surgical therapeutic procedures. The myocardial depressant effect of general anaesthetic agents in paediatric patients with severe ventricular dysfunction is poorly described. Intraoperative monitoring of cardiac function with transoesophageal echocardiography (TOE) may be helpful.<sup>25</sup> In the only specific review to date of children with DCM undergoing anaesthesia, certain observations were made. Significantly, complications were greater in procedures of longer duration and it was therefore recommended that cardiovascular support, invasive monitoring, and postoperative intensive care monitoring

should strongly be considered for patients with severe DCM undergoing subjectively longer anaesthetic procedures.<sup>26</sup>

### Hypertrophic cardiomyopathy

HCM is defined as an abnormal, inappropriate thickening of cardiac muscle, occurring in the absence of an obvious inciting stimulus. More common in adults, the incidence is low in children (3–5 cases per million). As patients can be asymptomatic, unfortunately the diagnosis is often made post-mortem. In fact, HCM is the most common cause of SCD in children.<sup>27–29</sup> Most HCM are idiopathic in origin, but less common causes include inborn errors of metabolism, malformation syndromes, and neuromuscular disorders. Overall, children with idiopathic HCM who survive beyond 1 yr of age have an annual mortality rate of 1%.<sup>30</sup> Mutations in one of at least 12 sarcomeric or non-sarcomeric genes are now implicated in the aetiology of HCM. Mutations in the  $\beta$ -myosin heavy chain and myosin-binding protein C genes comprise almost 50% of the patients genotyped so far. Six other sarcomere genes each account for a small number of cases, that is, cardiac troponin T, cardiac troponin I,  $\alpha$ -tropomyosin, cardiac  $\alpha$ -actin myosin regulatory light chain, and myosin essential light chain.<sup>27–31</sup>

The hypertrophy may be uniform and diffuse or asymmetrical and focal. The classic variety is that which causes dynamic outflow tract obstruction typically of the left

ventricle. However, a focal area of hypertrophy may also incorporate and surround a coronary vessel, so-called myocardial bridging.<sup>32</sup> An incidence of myocardial bridging of 28% has been found at the time of cardiac catheterization in children with HCM.<sup>33</sup> Associated with this myocardial bridging is the finding of a 'diastolic time lag' in which the previously compressed coronary vessel remains under-filled (for 30–75% of diastole). Diastole is when the greatest proportion of coronary blood flow normally occurs. Therefore, children with HCM and a myocardial bridge are at increased risk of sudden death during a period of shortened diastole (such as tachycardia). Surgical resection of the bridge in these forms of HCM may be a therapeutic consideration.<sup>33 34</sup> As mentioned, the presenting scenario can be catastrophic with SCD for patients who were previously asymptomatic.

### Anaesthetic considerations

A preoperative echocardiogram is again invaluable, but unlike patients with DCM where the EF is a variable used to assess myocardial function, in children with HCM, two-dimensional left ventricular mass (2DLVmass) index expressed as  $\text{g m}^{-2}$  may be more useful in assessing myocardial reserve before operation.<sup>35</sup> In one series, infants with severe HCM and a 2DLVmass index  $>150 \text{ g m}^{-2}$  (normal for infants around  $60 \text{ g m}^{-2}$ ) were predisposed to perioperative arrhythmias and the risk of myocardial ischaemia in the presence of an intraoperative tachycardia and low diastolic arterial pressure.<sup>35 36</sup>

The anaesthetic management of patients with HCM aims to minimize any increase in systolic left ventricular outflow tract obstruction (LVOTO). This is achieved by maintaining a normal to slightly elevated SVR, preventing hypovolaemia, and avoiding a state of increased myocardial contractility (either through endogenous or exogenous catecholamine stimulation). Heart rate is usually kept at a normal to low rate, aimed at optimization of diastolic filling time and enhanced stroke volume. Sinus rhythm is essential. As a disease of diastolic dysfunction, these patients rely on atrial contraction to fill a non-compliant ventricle. Atrial fibrillation or supraventricular arrhythmias are, therefore, poorly tolerated.

The volatile anaesthetic agents may be used in HCM judiciously. Isoflurane may increase heart rate; however, sevoflurane appears to be well tolerated in all but the most severe forms of HCM.<sup>27</sup> As the sole anaesthetic agent in severe forms of infantile HCM, propofol may not offer the safest anaesthetic option since it significantly decreases preload and SVR is reduced by as much as 20%.<sup>35–37</sup> Children with HCM are very sensitive to an adequate ventricular filling pressure. The use of a diuretic that decreases intravascular volume has been shown to increase LVOTO.<sup>35</sup>

Inotropes should be used only with great caution. In fact, they may decrease CO due to ventricular cavity obliteration leading to a decrease in diastolic filling time and worsen LVOTO. Hypotension, if not due to hypovolaemia, but possibly due to low coronary perfusion pressure from low diastolic

arterial pressure, may be alleviated with low-dose phenylephrine boluses and  $\beta$ -adrenergic blockers used for control of heart rate and reduction in systolic cavity obliteration.

The clinical dilemma as to which anaesthesia agents are safe in patients with HCM is intriguing as it is postulated that it is not so much the medication used, but how it is administered that determines anaesthetic outcomes in HCM.<sup>38</sup> Ketamine may be a reasonable choice in certain circumstances due to its ability to preserve spontaneous breathing and diastolic arterial pressure. However, caution should be exercised with ketamine and any associated tachycardia that results in ECG ST-segment depression should be treated promptly with  $\beta$ -adrenergic blockade.

Significantly, patients with HCM due to certain inborn errors of metabolism involving lipid oxidation may be at risk of accumulation of free fatty acids, even after a minor procedure with an inhalation anaesthetic agent.<sup>39 40</sup> I.V. propofol anaesthesia should also be avoided in this group of patients since it may cause a condition similar to that seen in the propofol infusion syndrome.<sup>41</sup> A combination of opioid, benzodiazepine, and barbiturate has been shown to be acceptable in patients with lipid oxidation metabolic disorders.<sup>41</sup>

The risk of SCD with arrhythmias is a major consideration in patients with HCM. Risk markers for SCD in this group of patients include:<sup>42</sup>

- (i) family history of SCD,
- (ii) unexplained syncope,
- (iii) abnormal arterial pressure response during upright exercise,
- (iv) non-sustained ventricular tachycardia,
- (v) severe left ventricular hypertrophy ( $\geq 30 \text{ mm}$ ).

Patients with previous cardiac arrest or with two or more risk factors should be considered for an implantable cardiac defibrillator (ICD). Infection risk after implantation of the device and psychological counselling remain two other important considerations in children with an ICD.<sup>43</sup>

### Restrictive cardiomyopathy

RCM is defined as cardiac muscle disease resulting in impaired ventricular filling with normal or decreased diastolic volume of either or both ventricles. The condition usually results from increased stiffness of the myocardium that causes pressure within the ventricle to rise precipitously with only small increases in volume. It accounts for only 2–5% of all paediatric cardiomyopathies and unfortunately presents late in the disease process due to physiological adaptation. However, progressive increase in pulmonary vascular resistance, from restricted forward blood flow through the non-compliant left ventricle, results in early mortality. RCM has a 2 yr survival, once diagnosed, of  $<50\%$ .<sup>6 7 44 45</sup>

In the early stage of the disease, systolic function is maintained, however as restriction (endomyocardial fibrosis) progresses with time, LVEDP increases because of the poor compliance of the fibrotic left ventricle. Stroke volume significantly decreases and CO decreases. The severity of the



disease on presentation determines the anaesthetic challenges in these patients.<sup>44</sup> Recently, cardiac sarcomere gene mutations have been identified in four out of 12 (33%) patients with a mean age of 5.1 yr diagnosed with RCM.<sup>45</sup> One of the distinguishing features of RCM is the relentless progression of an elevated LVEDP and resultant increase in pulmonary vascular resistance (PVR). By the time, many children with an RCM present with exercise intolerance, PVR is already  $>10\text{--}15$  Woods units  $\text{m}^{-2}$  (normal  $<2$ ). This often prohibits them from being a recipient of a heart transplant alone and a heart-lung transplant is the only alternative.<sup>46</sup>

Again the most common aetiology for RCM in children is idiopathic. Known causes include amyloidosis, haemosiderosis, hypereosinophilia (Löffler's disease), and endocardial fibroelastosis.<sup>47</sup> Radiation therapy may also cause an RCM.<sup>48</sup>

LVOTO in RCM is rare.<sup>49</sup> The diagnosis of RCM is often made by echocardiography. Small ventricles, massively dilated atria, and rarely a pericardial effusion are seen.<sup>46</sup> The jugular venous pressure is often raised and can show a paradoxical increase in height during spontaneous inspiration. This is due to increased venous return into a non-compliant ventricle.

### Anaesthetic considerations

A preoperative echocardiogram is mandatory to assess the extent of the disease, evaluate right heart pressures, and evaluate for potential intra-ventricular thrombi. Systolic and diastolic dysfunction is present simultaneously, and CO remains predominantly dependent on heart rate and preload. Arrhythmias should be anticipated. Anaesthetic agents that induce a bradycardia, such as alfentanil, sufentanil, or fentanyl, may cause a significant decrease in CO.<sup>50</sup> Ketamine exerts its inotropic effect on ventricular muscle in some mammalian species by indirectly inhibiting neuronal catecholamine uptake. Therefore, in children with DCM in severe congestive cardiac failure who are catecholamine deplete, ketamine should be used with caution.<sup>51</sup> Milrinone, dobutamine, and amrinone have been used successfully as inotropic agents in RCM patients waiting for cardiac transplantation.<sup>52</sup> It is important to avoid any iatrogenic increase in PVR (such as high airway pressures, hypercarbia, or hypoxia). An elevated PVR in the presence of a low CO in these patients may cause rapid haemodynamic deterioration. Rarely, in severe cases from equatorial regions (e.g. Africa, North East Brazil, or Southern India), surgery has been attempted to remove endomyocardial fibrosis if found to be the cause of the RCM.<sup>53</sup>

### Arrhythmogenic right ventricular dysplasia/CM

Characterized by the gradual replacement of myocytes by adipose and fibrous tissue, it usually presents between the ages of 10–50 yr.<sup>54–56</sup> Arrhythmogenic right ventricular dysplasia/CM (ARVD/C) and long QT syndrome are the most common primary arrhythmic causes of SCD.<sup>57</sup> The inheritance of this disorder is autosomal-dominant with variable

penetrance in ~50% of patients. Despite the increased understanding of the gene loci for this disease, to date no specific gene marker has been entirely useful in determining relative risk in family members.<sup>58</sup> At least 11 different ARVD/C gene loci mostly involved with cardiac cell attachment desmosomes have been identified. Desmosomal disruption is thought to be unmasked by exercise-induced arrhythmias in ARVD/C-susceptible individuals.<sup>54 59</sup> Two extra-desmosomal gene loci may be responsible for cardiac arrhythmias and explain exaggerated fibrosis that is part of the pathophysiology of this form of CM.<sup>54 60 61</sup>

Pathologically, the free wall of the right ventricle is replaced by fibro-fatty infiltration. Recent evidence indicates that the left ventricle is often involved in this disease process.<sup>62</sup> This myocardial infiltration is thought to be the locus for spontaneous arrhythmias. Symptoms including palpitations, syncope, atypical chest pain, or dyspnoea are typical, but SCD may be the initial manifestation of the disease without any antecedent symptomatology.<sup>54 55</sup> Patients are thought to pass through four stages of the disease. A concealed phase, an overt arrhythmogenic phase, then isolated right heart failure, and finally biventricular failure. Initial presentation can be in any of the four stages.<sup>63</sup> Approximately 50% of patients have an abnormal ECG.<sup>64</sup> The ECG changes include: complete or incomplete right bundle branch block (RBBB), QRS prolongation without RBBB, epsilon wave immediately after the QRS in leads  $V_1\text{--}V_2$ ,<sup>65</sup> and T-wave inversion in  $V_1\text{--}V_3$ , or delayed ( $>55$  ms) S-wave upstroke in  $V_1\text{--}V_3$ .<sup>64</sup> Diagnosis may be confirmed echocardiographically (regional or global right ventricular hypokinesis with or without dilatation), or by angiography (demonstrating right ventricular wall anomalies in the absence of other structural heart defects) and histologically after an endomyocardial biopsy.<sup>66</sup> Ultra-fast magnetic resonance imaging (MRI) with ECG gating is useful in confirming the diagnosis of fibro-fatty myocardial infiltration.<sup>67</sup>

Therapeutic interventions consist of insertion of an ICD, and radiofrequency catheter ablation for arrhythmias to prevent cardiac death after sudden ventricular tachycardia or fibrillation. The antiarrhythmics sotalol and amiodarone are often prescribed to these patients. These medications may predispose the vulnerable heart to the ventricular tachy-dysrhythmia *torsade de pointes*.<sup>68 69</sup> Should overt cardiac failure progress, it is often treated with diuretics,  $\beta$ -adrenergic blockers, ACE inhibitors, and anticoagulants.

### Anaesthetic considerations

Care in avoiding catecholamine-induced arrhythmias needs to be exercised when anaesthetizing these patients.<sup>38</sup> In a recent review of 50 autopsies performed for perioperative death, ARVD/C was detected in 18 (36%). Four of the patients in this series died on induction, nine during surgery, and five within 2 h after surgery. Unfortunately, no indication of the anaesthetic agents used is made in this report.<sup>9</sup>

Specifically, agents such as epinephrine in local anaesthetics should probably be avoided. During regional

anaesthesia, the use of a smaller dose of bupivacaine is also recommended.<sup>54</sup> A lower threshold to insert an arterial cannula for invasive arterial pressure monitoring and central venous pressure monitoring together with the use of intraoperative TOE should strongly be considered for major surgery. Propofol has been safely used for induction and maintenance of anaesthesia in ARVD/C.<sup>70</sup> The newer neuromuscular blocking agents such as vecuronium, atracurium, and rocuronium can be used, but pancuronium increases sympathetic activity and is best avoided. It is also important to avoid inducing a tachycardia during reversal of neuromuscular block. In a recent case discussion, halothane was not recommended because of its potent negative inotropic effect.<sup>54</sup> It is considered prudent to place external cardioversion/defibrillation pads on the chest before operation in select cases where the risk of intraoperative arrhythmia is high. If cardioversion/defibrillation pads are not available, an external stand-alone defibrillator with patient appropriate sized external paddles should be readily available in the operating theatre. Antiarrhythmic medication should be continued for all surgical procedures except when radiofrequency catheter ablation is undertaken.<sup>71</sup>

### Left ventricular hypertrabeculation/non-compaction

Left ventricular hypertrabeculation (LVHT) or non-compaction is a rare form of CM thought to be due to an embryological failure of myocardial development. Certain sections of the myocardial wall show deep trabeculations with various degrees of myocardial dysfunction. Cardiac failure may be improved with long-term i.v. inotropic support and poor cardiac function due to ventricular dyssynchrony may resolve with biventricular pacing.<sup>72</sup> Some patients with intractable systolic dysfunction may require heart transplantation even in the neonatal period.<sup>73</sup>

As LVHT is rare, it is an infrequent differential diagnosis in a patient presenting with cardiac failure. Diagnosis by echocardiography alone is not always possible.<sup>74–76</sup> Arrhythmias and ECG changes, including tall QRS complexes (43%), ST-T wave abnormalities (37%), and left bundle branch block (20%), have all been variously reported. Only 10% of LVHT patients have a normal ECG. Diagnosis may be confirmed by MRI.<sup>77</sup>

Whether LVHT is associated with an increased risk of thromboembolism is debatable. In one study, the frequency of thromboembolism was not increased in 62 LVHT patients compared with controls matched for age, sex, and ventricular function.<sup>78</sup> It is still a theoretical risk and should remain a consideration for the anaesthetist.

Up to 80% of patients with LVHT have an associated neuromuscular disorder.<sup>76</sup> These include Duchenne and Becker muscular dystrophy, dystrobrevinopathy, myotonic dystrophy, myoadenylate-deaminase deficiency, glycogenosis, zaspopathy, mitochondriopathy, Friedreich ataxia, Charcot-Marie-Tooth disease, and Barth syndrome.<sup>76 79 80</sup>

Barth syndrome is a rare X-linked mitochondrial cardioskeletal myopathy, presenting in infancy with CM, growth delay,

and hypotonia.<sup>79</sup> Genetic testing and early diagnosis improve survival and such tests are now commercially available.<sup>79 80</sup>

### Anaesthetic considerations

The anaesthetic implications in these children include assessing the degree of myocardial reserve and screening for neuromuscular disease, particularly in the presence of failure to thrive or delayed developmental milestones. The potential hyperpyrexia or hyperkalaemia/rhabdomyolysis risks with anaesthesia in certain neuromuscular disorders should also be borne in mind. Attention to any muscular weakness at the time of tracheal extubation is required and neuromuscular blocking agents should be used with caution.

### Special considerations in severe CM

Anaesthesia in children with severe CM typically includes an early cardiac catheterization measuring CO and PVR to determine suitability for heart transplantation if myocardial function fails to recover. Newer medications that might help bridge to transplant or recovery in severe CM include nesiritide and levosimendan. A recent prospective randomized trial in 20 children with DCM found that nesiritide significantly decreased mean PVR and capillary wedge pressure compared with placebo. Nesiritide is a recombinant human B-type natriuretic peptide (rh-BNP); it activates guanylate cyclase invoking vascular smooth relaxation.<sup>16</sup> Levosimendan has a similar beneficial effect but binds to cardiac troponin C increasing the sensitivity of the myocardial contractile apparatus to calcium.<sup>81 82</sup>

If the CO remains low and there is evidence of multi-organ dysfunction, mechanical circulatory support with a ventricular assist device (VAD) may be indicated. VADs function as a bridge to recovery or heart transplantation. The Berlin Heart or EXCOR™ Pediatric, a paracorporeal pneumatically driven pulsatile VAD for children more than 2 kg, is one example of a device being used more frequently.<sup>83–86</sup>

### Anaesthetic considerations in patients with a VAD

The current outcomes and anaesthetic implications for children with VADs have recently been well reviewed.<sup>84–87</sup> Clinically avoiding hypotension is the main goal as it has been reported with all induction and maintenance techniques.<sup>84</sup> In a recent series of patients with the Berlin Heart EXCOR™, hypotension was responsive to i.v. fluid therapy and  $\alpha$ -receptor agonist administration.<sup>84</sup> Haemodynamically, ketamine is well tolerated as an anaesthetic induction agent in these patients.<sup>84</sup> It is vital during cardiac arrest or severe dysrhythmias that external cardiac compressions should not be initiated when the device is *in situ*, since cannulae disruption and myocardial trauma may occur.<sup>85</sup> If the CO is inadequate under anaesthesia, troubleshooting includes consideration of medications administered, pericardial tamponade or cannula thrombosis or kinking.<sup>88</sup> These devices do require attention to detail but herald an exciting era in the management of children suffering from severe CM and

are therefore likely to become more prevalent in paediatric anaesthesia practice.

In conclusion, this review has focused on the pathophysiological presentation of the various types of CM. The safe administration of anaesthesia to these children requires an understanding of the different CM subtypes. Children whose clinical history or physical findings suggest a possible diagnosis of CM should have an in-depth assessment of cardiac function before undergoing anaesthesia.

## Declaration of interests

None declared.

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