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REVIEWS

Anaesthesia management for non-cardiac surgery in children with congenital heart disease

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Abstract

Congenital heart disease (CHD) is the most common form of congenital abnormality and occurs in over 1% of new-borns. Approximately 30% of children with CHD have other extra-cardiac anomalies, which significantly increases mortality in CHD patients. It is expected that the number of CHD patients who consult non-specialized hospitals for non-cardiac surgery after palliative or corrective operations will increase because of the extraordinary progression of treatments, such as surgical procedures, interventional procedures, and intensive care medicine, as well as diagnosis. The aim of this article is to enable anaesthesiologists who are not usually engaged in the anaesthesia management of CHD patients to provide perioperative management for CHD patients safely and with confidence by having basic and advanced knowledge about CHD patients and their pathophysiological characteristics.

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Key words: anaesthesia, children, congenital heart diseases, extra-cardiac anomalies, Fontan and hemi-Fontan circulation, Ohm's law, pulmonary vascular resistance

Congenital heart disease (CHD) is the most common form of congenital abnormality and occurs in over 1% of newborns [1]. This frequency is much higher than expected and is still constant regardless of the continuous progression of prenatal diagnosis [2, 3]. In addition to the diagnosis, treatments such as surgical procedures [4–7], interventional procedures [8, 9], and intensive care medicine [10] have made extraordinary progress in the past several decades. CHD patients tend to have palliative or corrective operations younger than before [11], and the prognoses, especially in the patients with more complicated CHD, have improved markedly [12, 13]. Therefore, it is expected that the number of CHD patients who consult non-specialized hospitals for non-cardiac surgery after palliative or corrective operations will increase. Indeed, it has been reported that the risk of perioperative cardiac arrest is higher in CHD children [14]. Although the frequency of perioperative complications for non-cardiac surgery in CHD patients who have no preoperative complications such as pulmonary hypertension, congestive heart failure, or cyanosis, has been reported to be as low as the frequency in non-CHD patients [15], recent cohort studies have reported that CHD patients who were undergoing non-cardiac surgery exhibited increased perioperative morbidity and mortality [16, 17]. The aim of this article is to enable anaesthesiologists who are not usually engaged in anaesthesia management for CHD patients to provide perioperative management for CHD patients safely and with confidence by having basic and advanced knowledge about CHD patients and their pathophysiological characteristics [18].

SPECIAL ASPECTS OF THE MEDICAL EXAMINATION AND ANAMNESIS IN CHD PATIENTS

Anaesthesiologists who examine CHD patients and inform them and their parents about the perioperative anaesthesia management need to have at least basic knowledge about CHD patients and their pathophysiological characteristics. Usually, the parents are very well informed about CHD in their children and are familiar with their past medical history, including the therapies and operations that the patients have undergone. Therefore, the interview from the parents gives us much information. In addition, the latest medical summary by the cardiologist or cardiac surgeon must be checked to summarize

the actual status of the patient and the anatomy of their circulatory system.

Approximately 30% of children with CHD have other extra-cardiac anomalies, which is significantly higher than the prevalence in children without CHD [19]. The presence of an extra-cardiac anomaly significantly increases mortality in CHD patients because extra-cardiac malformations are also associated with chromosomal abnormalities [20, 21]. In addition, the premature birth rate and the mortality rate of premature babies with CHD are more than double of those of children without CHD [22]. Therefore, a detailed anamnesis, particularly by younger children, is extremely helpful to be able to predict the presence of extra-cardiac malformations and to estimate the degree of heart insufficiency: Does the baby sweat when drinking from the bottle? Does the child fatigue easily when playing? In this way, the contents of the questions also change according to the age of the patient. The New York Heart Association (NYHA) functional classification is also helpful in estimating the patients' abilities (Table 1) [23]. These questions about activity in daily life are also useful in the estimation of the degree of heart insufficiency in patients.

It is also very important to evaluate the possibility that a patient has a difficult airway. Laryngotracheal stenosis can be a cause of a difficult airway [24]. The duration of artificial ventilation management after heart surgery is one of the most important questions because laryngotracheal stenosis can be present after long-term artificial ventilation management with intubation. Indeed, it has been reported

that the major aetiology of acquired laryngotracheal stenosis is related to intubation [25, 26], and the symptoms of laryngotracheal stenosis can be confused with asthma or other airway diseases that are not responsive to therapy [27, 28]. On the other hand, most patients do not require additional special laboratory or other diagnostic tests after undergoing a simple corrective operation for CHD with an otherwise empty anamnesis without parallel medications.

PREVENTION OF ENDOCARDITIS

Infectious endocarditis is a life-threatening illness and is difficult to treat so that it may have serious consequences for the patients. Therefore, a generous antibiotic treatment for all patients with heart disease was recommended and was performed for a long time. However, it is now recommended that only patients with a defined high risk of endocarditis are to receive endocarditis preventive antibiotic treatment, which is a drastic change from the recommendations from the American Heart Association in 2007 [29]. Table 2 shows an example of endocarditis protective antibiotic treatment for non-cardiac intervention [30].

The endocarditis high-risk patient characteristics are listed below (Table 3). With the exception of the conditions listed in Table 3, antibiotic prophylaxis is no longer recommended for any other form of CHDs [29]:
— cardiac valve repair (mechanical valve or biological valve)
— previous endocarditis
— unrepaired cyanotic CHD

Table 1. New York Heart Association (NYHA) functional classification

NYHA class	Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases

Table 2. An example of endocarditis protective antibiotic treatment for non-cardiac intervention in high risk patients [30]

Situation	Antibiotics	Dose per administration	
		Small patients	Elder patients
Oral administration (*p.o.*)	Amoxicillin	50 mg kg^{-1} *p.o.*	2 g *p.o.*
Intravenous administration (*i.v.*) (when oral administration is impossible)	Ampicillin	50 mg kg^{-1} *i.v.*	2 g *i.v.*
In case of penicillin-/amoxicillin allergy oral administration (*p.o.*)	Clindamycin	20 mg kg^{-1} *p.o.*	600 mg *p.o.*
In case of penicillin-/amoxicillin allergy intravenous administration (*i.v.*) (when oral administration is impossible)	Clindamycin	20 mg kg^{-1} *i.v.*	600 mg *i.v.*

Table 3. The defined endocarditis high risk patients [29]

Cardiac valve repair (mechanical valve or biological valve)	
Previous endocarditis	
Congenital heart diseases (CHDs)	Unrepaired cyanotic CHD
	During the first 6 months after palliative or corrective operations using prosthetic material or catheter intervention
	Repaired CHD with residual defects at the prosthetic material
Cardiac transplantation recipients who develop cardiac valvulopathy	

Except for the conditions listed in Table 3, antibiotic prophylaxis is no longer recommended for any other form of CHD

— CHD during the first 6 months after a palliative or corrective operation that used prosthetic material or a catheter intervention

— repaired CHD with residual defects in the prosthetic material

— cardiac transplantation recipients who develop cardiac valvulopathy

CONSEQUENCES OF CHRONIC HYPOXIA

Patients who have not yet undergone surgery or patients who have received only a palliative operation require detailed laboratory tests to be performed. In particular, haemoglobin/haematocrit (Hb/Ht), parameters of blood coagulation and electrolyte status should be determined [31]. Patients with cyanotic CHD frequently have very high Hb/Ht levels as a consequence of chronic hypoxia. Hb >20 g dL^{-1} or Ht > 65% are associated with hyperviscosity and decreased capillary blood velocity and perfusion, which may thus lead to a decreased oxygen supply in the peripheral tissue [32] or a high risk of thromboembolism [33]. When Ht is > 60%, cardiac output decreases due to the increased viscosity as described above, and the theoretical danger of renal or cerebral thromboembolism complications could increase [34]. A Ht of > 70% could induce coagulopathy, which is assumed to be associated with an increased risk of cerebral stroke [35–37]. However, phlebotomy is not warranted to reduce this assumed risk of stroke [35, 36]. The hyperviscosity can worsen as a result of a too long fasting period or as a result of insufficient intraoperative infusion therapy. Secondary polycythaemia is also connected with coagulopathy [38]. For this reason, patients with cyanotic CHD should receive adequate infusion during the preoperative fasting period.

The goal of the management of chronically cyanotic patients is to increase pulmonary blood flow to increase the arterial oxygen saturation. The targeted Ht level should be a maximum of approximately 60% via controlled infusion therapy [39–44]. Chronic liver congestion can restrain the production of coagulation factors, for example, in patients with Fontan circulation [45, 46].

APPLICATION OF OHM'S LAW TO HAEMODYNAMICS

Ohm's law can be applied to estimate the haemodynamic status and to evaluate the effect of treatment. The formula of the original "Ohm's Law" is as follows:

$$V = R \times I$$

V, R, and I represent the voltage, the resistance, and the current, respectively. In the application of "Ohm's law" to haemodynamics in the human body, V is equal to the blood pressure (BP), I is equal to the cardiac output (CO), and R indicates the systemic vascular resistance (SVR). CO is the product of the systolic volume of the ventricle (SV) multiplied by the heart rate (HR). Thus, "Ohm's law for haemodynamics in the human body" can be expressed in the following formula:

$$BP = SVR \times SV \times HR$$

This formula indicates that the change in BP is a result of the changes on the right side of the formula. During massive bleeding, for example, SV decreases because of a reduction in the filling of the ventricle, which will be compensated by an increase in HR and SVR for a certain amount of time to maintain the left side of the formula (BP), which is a result of the changes in the right side of the formula. Considering this "Ohm's law for haemodynamics in the human body", it can be easily understood that volume therapy via infusion or transfusion to compensate for the preload is an adequate therapy in such situations. As another example, the cause of hypotension after anaesthesia introduction or during anaesthesia maintenance is a decline in HR and/or SVR via the suppression of the sympathetic system. Therefore, treatments to increase HR and/or SVR such as the administration of atropine, ephedrine, phenylephrine, or other catecholamines are adequate in such situations. However, it should be noted that HR may decrease more via monotherapy with α-adrenergic agonists such as phenylephrine as a compensatory reaction to the rise in SVR, and when atropine is administered to increase HR in such a situation, BP may rise more

than expected due to a combination of elevations in both SVR and HR. In particular, in small paediatric patients or babies, the increase in SV cannot compensate for BP due to the small capacity of the ventricle. Thus, the increase in HR upon the administration of atropine, for example, is an adequate therapy when HR is extremely low for the patient's age. In this matter, the "Ohm's law for haemodynamics in the human body" is a very simple but very helpful method to understand the causes of the changes in blood pressure and circulation status, and thus to determine the adequate choice of therapy and medications. This knowledge is applicable to all patients as well as to CHD patients.

PREMEDICATION IN CHD PATIENTS FOR NON-CARDIAC SURGERY

Premedication is also important for CHD patients, especially cyanotic CHD patients, because haemodynamic balance may collapse because of stress such as crying due to the separation from parents or due to anaesthesia induction. Some parents may have undergone cardiac surgeries or other operations repeatedly; therefore, some of them may have unpleasant memories or negative impressions about anaesthesia. Premedication is given to address this point. However, excessive sedation, including respiratory suppression, must be avoided because a rise in $PaCO_2$ due to respiratory suppression leads to a rise in pulmonary artery resistance and worsening hypoxemia. It is particularly important in pulmonary hypertension (PHT) patients to perform moderate sedation without excessive respiratory suppression.

For example, the oral administration of 0.5 mg kg^{-1} of midazolam 15–30 minutes before anaesthesia induction is simple and adequate. This treatment makes the patients more cooperative and reduces their anxiety due to their separation from the parents and due to the anaesthesia induction with minimal effects on recovery times, and its amnesic effect is also a great advantage [47, 48]. For elder patients, oral administration of 7.5 mg or 15 mg midazolam is adequate. Oral midazolam as a premedication is also safe and effective in cyanotic CHD children [49].

ANAESTHETICS FOR ANAESTHESIA MANAGEMENT

Hemodynamic monitoring during anaesthesia management is indispensable because anaesthetics have negative inotropic effects [50–52]. However, no anaesthetics are absolutely contraindicated for CHD patients.

The cyanotic CHD patients with decreased pulmonary blood flow because of the presence of an R-L shunt need higher minimum alveolar concentration (MAC) values of sevoflurane, and their inhalational anaesthesia introduction time is prolonged compared to patients without CHD. On the other hand, MAC level and inhalational anaesthesia induction time in the acyanotic CHD patient with increased pulmonary blood flow because of the presence of an L-R shunt are not different [53]. In contrast, it is assumed that intravenously administered anaesthetics reach the systemic circulation faster in the cyanotic CHD patients with an R-L shunt, and their effects may appear faster and be stronger.

Bradycardia during anaesthesia management can usually be treated with the administration of 0.01 mg kg^{-1} atropine. However, the effect of routine pretreatment with atropine for vagal reflex bradycardia prior to tracheal intubation in paediatric patients is still controversial [54–57].

For anaesthesia induction in CHD patients with insufficient ventricular function, a single high dose of fentanyl (25–30 µg kg^{-1}) can stabilize the haemodynamics because opioids have relatively few cardiovascular side effects [58, 59]. If ventricular function is better, an additional titration dose of a hypnotics, 0.1 mg kg^{-1} midazolam or 1–3 mg kg^{-1} propofol, for example, is also possible. This high dose fentanyl anaesthesia induction is also acceptable in patients with insufficient ventricular function for non-cardiac operations because these patients should receive artificial respiration management by the intensive care unit (ICU) postoperatively.

Muscle relaxants can be chosen according to the predicted length of the operation. Pancuronium is often used during paediatric heart surgery because an increase in heart rate (HR) is expected. Rocuronium, vecuronium, cisatracurium, and mivacurium are the muscle relaxants that are frequently used for non-cardiac surgery. Rocuronium can be neutralized completely by sugammadex (4 mg kg^{-1} intravenous administration) without brady- or tachycardia induced by the combination of neostigmine and atropine, and 16 mg kg^{-1} sugammadex can neutralize the effect of rocuronium completely even directly after the high dose administration of rocuronium (1 mg kg^{-1}) in an emergency [60–62].

It is not recommended to administer remifentanil via the same IV line as the blood products such as fresh frozen plasma (FFP) or platelet concentrates (PC) that include blood plasma because the degradation of remifentanil, whose context sensitive half-time (CSHT) is 3–4 minutes [63, 64], begins organ-independently due to the presence of a nonspecific esterase in the blood plasma [63–65] in the IV line. In other words, it is probable that remifentanil is already partly degraded in the IV line; therefore, its blood concentration falls before the medication reaches the patients.

A frequent question concerns the use of regional anaesthesia procedures in CHD patients after corrected or palliative operations. It is reported that spinal anaesthesia and epidural anaesthesia in CHD patients can be performed as safely as in patients without CHD, as long as a drastic drop in peripheral vascular resistance is avoided [66–68]. The method by which the change in circulation status should be evaluated and treated has already been mentioned above in the section "APPLICATION OF OHM'S

Table 4. Factors which affect the pulmonary vascular resistance (PVR)

Factor to increase the PVR	Factors to decrease the PVR
Low FiO_2, hypoxemia	High FiO_2
High $PaCO_2$, hypoventilation	Low $PaCO_2$, hyperventilation
Acidosis	Alkalosis
High airway pressure, high PEEP, atelectasis	Spontaneous breathing, low PEEP
Hypothermia	Nitric oxide (NO)
Vasopressor	Vasodepressor (Nitroglycerine, PGE1: prostaglandin E1, etc.)
High Hb/Ht	Low Hb/Ht
Insufficient anaesthesia/analgesia	Sufficient anaesthesia/analgesia

LAW TO HAEMODYNAMICS". Patients with a high Ht level (Ht > 70%) due to chronic hypoxemia may have coagulopathy as mentioned above in the section "CONSEQUENCES OF CHRONIC HYPOXIA" [35–38]. The indication and safety of regional anaesthesia procedures should be considered in conjunction with the patient's clinical status and the blood coagulation examination.

ANAESTHESIA MANAGEMENT AND HAEMODYNAMICS IN PATIENTS WITH "FONTAN CIRCULATION"

Patients with so-called "Fontan circulation" present with a special characteristic of circulation physiology. The blood flow from the superior vena cava (SVC) and the inferior vena cava (IVC) in Fontan circulation flows directly into the systemic circulation via the pulmonary artery without the assistance of the right ventricle [69]. In other words, the pulmonary blood flow, which is at the same time the preload for the cardiac output, is determined by the pressure gradient between the central venous pressure and pulmonary vascular resistance in patients with Fontan or hemi-Fontan (Glenn) circulation.

Once the Fontan circulation has become imbalanced, patients experience a vicious cycle as follows: SpO_2 drops; as a result, the myocardial pump function worsens, the pressure of the common atrium rises, and the pressure gradient for the pulmonary circulation decreases. Then, the blood flow to the lung decreases, which leads to the more aggravation of SpO_2 and cardiac output.

The "recruitment manoeuver" is performed to improve atelectasis (for example, high respiratory pressure at approximately 20 cm H_2O on high PEEP at approximately 20 cm H_2O for 15–30 seconds) [70, 71] and is reported to reduce the preload and cardiac output in haemodynamically stable patients following cardiac surgery because of a rise in the intra-thoracal pressure [68]. This negative effect on the circulation is supposed to be more significant in the patient with Fontan circulation because of a rise in the afterload for the venous return.

Laparoscopic operations may affect Fontan circulation; the venous return to the heart may be compromised because of the increased intra-abdominal pressure that results from the insufflation of carbon dioxide into the abdomen [67]. As a consequence, blood oxygen saturation and cardiac output may decrease. However, it is also reported that a laparoscopic operation can be performed uneventfully when the anaesthesia is managed appropriately [72], and a laparoscopic operation is not contraindicated for patients with Fontan circulation.

A sufficient volume of administration and an adequate ventilation setting are the keys to maintaining the pressure gradient between the central venous pressure and the pulmonary vascular resistance for lung circulation in patients with Fontan or hemi-Fontan (Glenn) circulation. Table 4 shows factors that affect the pulmonary vascular resistance (PVR). Figure 1 shows that Fontan circulation is affected by positive pressure artificial ventilation; therefore, an early cessation of artificial ventilation is desirable in patients with Fontan and hemi-Fontan (Glenn) circulation.

This recommendation seems to be a bit paradoxical in light of the data presented in Table 4; however, newer investigations indicate that a high-normal $PaCO_2$ increases the blood flow to the pulmonary artery because of an increase in the venous return via cerebral circulation in the patients with hemi-Fontan (Glenn) circulation [73].

MONITORING

Anaesthesia management in CHD patients for non-cardiac surgery requires only normal monitoring, such as the use of an electrocardiogram (ECG), pulse oximetry, non-invasive blood pressure (NIBP), and capnometry as in patients without CHD. Central venous catheter or arterial blood pressure monitoring are not necessary in most cases. In the patient with a Blalock-Taussig shunt (BT shunt: a connection between the subclavian artery and the pulmonary artery), the blood pressure measured in the arm on the same side shows a significantly lower value than on the opposite side because of a stenosis at the anastomosis of the BT shunt.
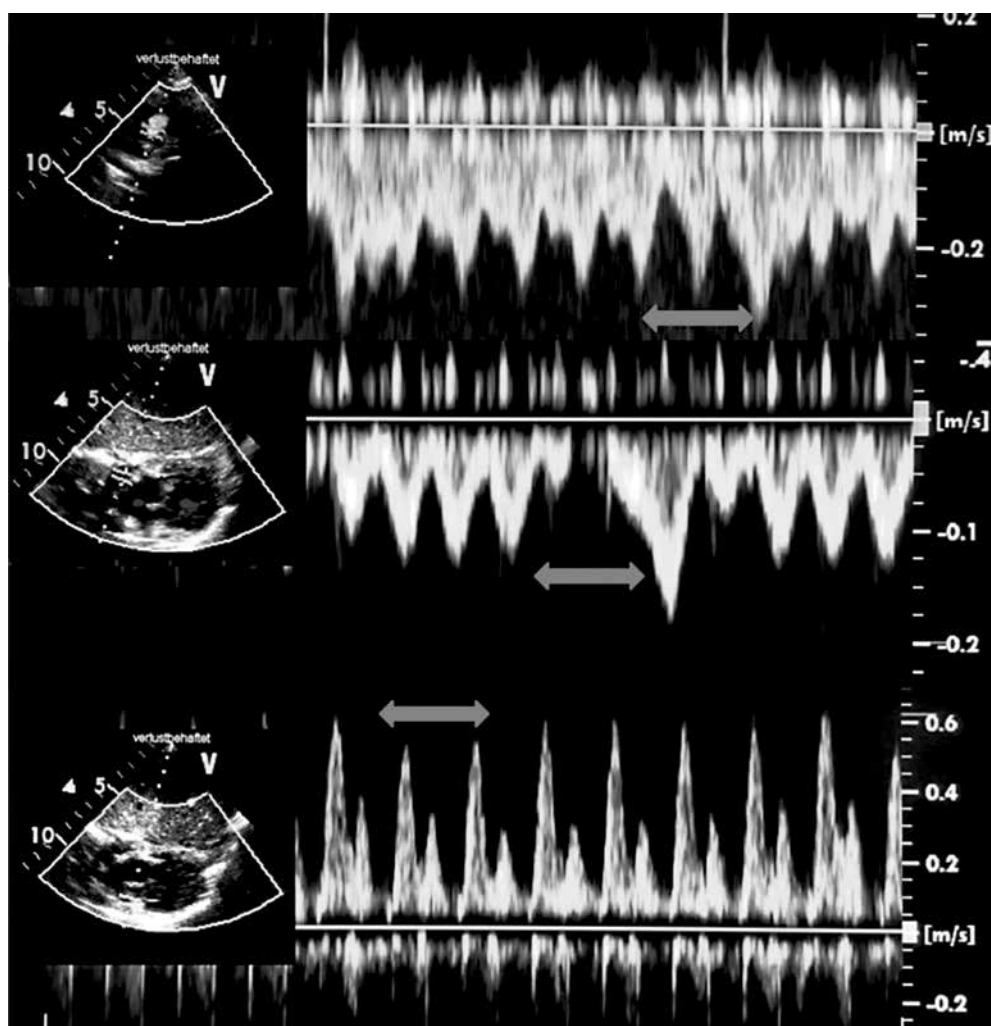
Figure 1. Effects of the positive artificial ventilation on the blood flow profiles in the patients with Fontan circulation . **A** — Glenn flow, **B** — Fontan flow, **C** — pulmonary venous return decrease in the inspiratory phase because of a rise in the airway pressure (⇔ arrow)

Table 5. Examples of the harmful phenomena due to perioperative hypothermia

Postoperative respiratory complications due to aspiration and respiratory infectious disease
Shivering increasing oxygen consumptions and causing oxygenation disorder
Cardiopulmonary complications due to the changes of cardiac output and rhythmus
Hyperglycemia through decreasing insulin secretion
Hypovolemia and electrolytes abnormality
Intestinal tract problems and following delay of oral intake
Anesthesia awakening delay because of the extend of action time of drugs
Infection of the operation wound
Increase in amount of bleeding and transfusion

Therefore, the blood pressure should be measured on the opposite side of a BT shunt.

Perioperative temperature monitoring and management is very important because hypothermia leads to several complications that can affect the morbidity and mortality of the patients (Table 5) [74–80]. The body temperature of the patient under general anaesthesia decreases remarkably because the function of the temperature centre in the hypothalamus is depressed; additionally, the peripheral vessels are expanded, and the core body temperature is
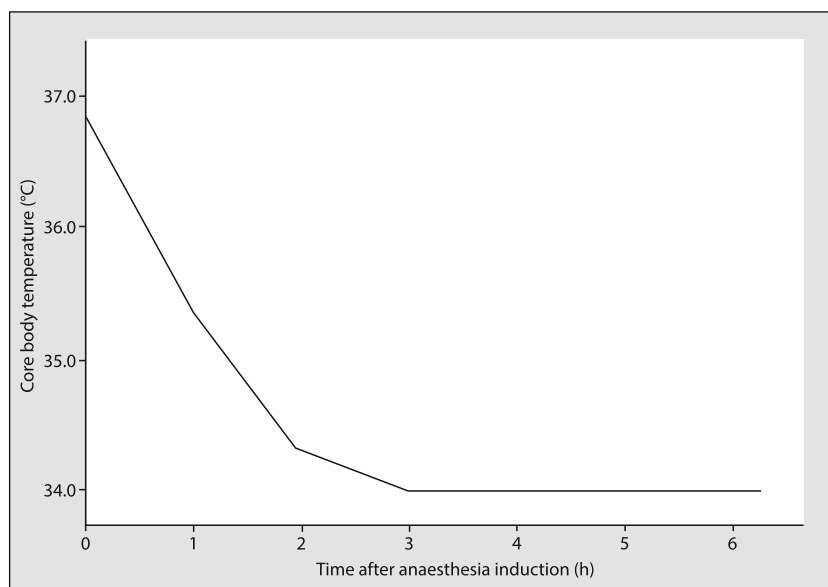
Figure 2. The time course of the core body temperature after anaesthesia induction. The core body temperature decreases rapidly in the first one or two hours after the anaesthesia induction and stays stable at around 34 degrees

redistributed. The core body temperature decreases rapidly within the first one or two hours after anaesthesia induction and stays stable at approximately 34 degrees (Fig. 2) [81]. The younger the patient is, the swifter the body temperature decreases. Therefore, it is incorrect to judge that the core body temperature remains warm, even if the body surface of the patient is still warm. In patients with polycythaemia, hypothermia worsens peripheral perfusion and leads to a metabolic acidosis.

In cases, in which a central venous catheter is necessary, the use of a real-time ultrasound-guided technique is recommended [82, 83] because the central veins are so often punctured that they may be occluded by a thrombus, and the coagulation status may have not yet normalized because of daily anticoagulant therapy in CHD patients.

WHICH PATIENTS FOR NON-CARDIAC SURGERY SHOULD BE REFERRED TO SPECIALIZED CENTRES?

The American Heart Association (AHA) and the American College of Cardiology (ACC) together published a guideline for the management of patients with congenital heart disease in 2008 [84, 85]. This guideline describes the answers to the question very well. For example, patients with Fontan circulation, severe pulmonary hypertension, cyanosis, clinically relevant symptoms such as heart insufficiency, cardiac valvulopathy, chronic anticoagulation therapy, and an arrhythmia that requires therapy are categorized into "high risk" patients and should be referred to a specialized heart centre [84, 85]. This guideline lists the types of patients with CHD who do not need to be referred to specialized heart centres for non-cardiac surgery and can be treated in non-specialized centres (Table 6) [84, 85].

CONCLUSION

The aim of this article is to enable anaesthesiologists who are not usually engaged in the anaesthesia management of CHD patients to provide perioperative management for CHD patients safely and with confidence by having basic and advanced knowledge about CHD patients and their pathophysiological characteristics. It is necessary to acquire

Table 6. Patients with CHD, who need not to be referred to specialized heart centers for non-cardiac surgery [84, 85]

Not corrected CHDs	Operative/interventional corrected CHDs
Isolated congenital aortic valvulapathy	Closed/occluded patent ductus arteriosus (PDA)
Isolated congenital mitral valvulopathy (excluding "parachute valve", cleft leaflet)	Closed/occluded atrial septal defect (ASD) without rest shunt
Isolated patent foramen ovale (PFO) or atrial septal defect (ASD)	Corrected sinus venosus ASD without rest shunt
Isolated ventricular septal defect (VSD)	Closed/occluded ventricular septal defect (VSD) without rest shunt
Small patent ductus arteriosus (PDA)	
Mild pulmonary stenosis	

basic knowledge of the characteristics of circulation physiology in patients with CHD. A careful and detailed anamnesis is the most important key to understand the actual anatomy and to evaluate the actual status of CHD parents correctly, and this becomes the basis of safe perioperative anaesthesia management in CHD patients.

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