Anesthesia in adults with congenital heart disease

Torsten Baehner and Richard K. Ellerkmann

Purpose of review
The current review focuses on patients with congenital heart disease (CHD) with regard to recent trends in global demographics, healthcare provision for noncardiac surgery, as well as anesthetic and perioperative care for these patients.

Recent findings
About 40 years after milestones of surgical innovation in CHD, the number of adults with CHD (ACHD) now surpasses those of children with CHD. This development leads to the fact that even patients with complex CHD managed for noncardiac surgery are not restricted to highly specialized centers. However, preoperative risk assessment for anesthesia in these patients is complex due to underlying cardiac morbidity and substantial CHD-associated noncardiac morbidity. In addition to clinical assessment and echocardiography, biomarker measurement may be a clinically useful tool to estimate severity of heart failure in CHD patients. The high negative predictive value of NT-proBNP makes it particularly valuable as a screening tool. Further, morbidity and mortality in ACHD patients are mainly caused by arrhythmias and therefore are also relevant for perioperative management. Adverse events and perioperative death in ACHD patients in cardiac and noncardiac surgery are frequently related to intraoperative anesthetic care.

Summary
Medical progress in treatment of CHD has shifted morbidity and mortality of these patients largely to adulthood. Future investigations including risk stratification of ACHD patients are necessary to further improve perioperative management, especially for low-risk and high-risk noncardiac management.

Keywords
cardiac anesthesia, congenital heart disease, general anesthesia, pediatric anesthesia

INTRODUCTION

Congenital heart disease (CHD) is the most common birth defect in humans, affecting nearly 1% of live births [1]. There is a great variety of defects, ranging from simple to highly complex defects. Only decades ago, patients who were affected from complex defects died within the first years of life and even patients with moderate defects had very poor prognosis [2]. Over the past decades, surgical and interventional therapies led to remarkable advances in survival of patients with CHD [3▪,4▪▪]. Today, more than 80% of children with CHD survive adolescence and reach adulthood [5]. Investigating quality of life in adults with CHD (ACHD), Apers *et al.* [6▪] found in their recent international study from 15 countries that this may be rated as generally good.

Anesthetic management in CHD varies as much as the variety of heart defects. There are some excellent reviews focusing on anesthetic considerations for specific groups of heart defects to provide an adequate overview of the special features for these different groups [7–9]. In this review, we aimed at recent publications regarding trends in global demographics, healthcare provision for noncardiac surgery, as well as anesthetic and perioperative care in CHD patients.

CHANGING AGE PREVALENCE OF CONGENITAL HEART DISEASES

Increasing survival even in more severe forms of CHD has changed age distribution of CHD patients. The reason for this development has been achieved by crucial advances in surgical treatment of CHD made in the 1970s and 1980s. Certainly, one of the most important improvements was achieved by Fontan and Baudet, pioneers in the field of single

Department of Anesthesiology and Intensive Care, University Hospital Bonn, Bonn, Germany

Correspondence to Torsten Baehner, Department of Anesthesiology and Intensive Care, University Hospital Bonn, Sigmund-Freud-Str. 25, 53105 Bonn, Germany. Tel: +49 228 287 14114; fax: +49 228 287 14125; e-mail: torsten.baehner@ukbonn.de

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KEY POINTS

- We recently met the inversion of CHDs population pyramid as a consequence of the improved surgical treatment in childhood.
- The number of CHD patients consulting nonspecialized hospitals for noncardiac surgery even after complex surgery will increase due to improved survival in childhood.
- Morbidity and mortality in ACHD patients are mainly caused by heart failure and arrhythmias being relevant for perioperative management.
- CHD with simple lesions (such as mild pulmonary valve stenosis, a small uncomplicated atrial or ventricular septal defect, patent ductus arteriosus, a successfully repaired atrial or ventricular septal defect, patent ductus arteriosus, and anomalous pulmonary venous connection without important residua) do not necessarily have to be treated in specialized centers.
- CHD patients with more than simple lesions should be treated in specialized centers, even if surgical risk itself seems to be low.

ventricle palliation. Single ventricle patients were doomed to death until in 1971 Fontan could show that passive perfusion of the lung by directly connecting the right atrium to the pulmonary artery is feasible and improves survival. In a series of cases, Fontan successfully separated systemic and pulmonary circulation, converting parallel circulation into a functionally serial circulation [10]. The subsequent development to the modern Fontan operation with direct cavopulmonary connection nowadays offers a therapeutic option to nearly all previously untreatable and deadly congenital cardiac lesions. Forty years later, Gilboa *et al.* [11▪] recently reported that the number of ACHD now surpasses those of children with CHD and we see an inversion of the *CHD's population pyramid* (Fig. 1). CHD patients aged under 18 years made up to 1 million in the United States in 2010, whereas 1.4 million adults are living with CHD. More than a third of these ACHD patients are currently at least 45 years old. This pronounced increasing adult population with CHD leads to the fact that anesthesiologists in the noncardiac surgery field will now and in the near future have to take care of these adults who may have previously undergone surgery for even complex congenital heart defects.

WHICH HOSPITAL FOR CONGENITAL HEART DISEASE PATIENTS?

Several guidelines and recommendations address which CHD patient should be treated for noncardiac

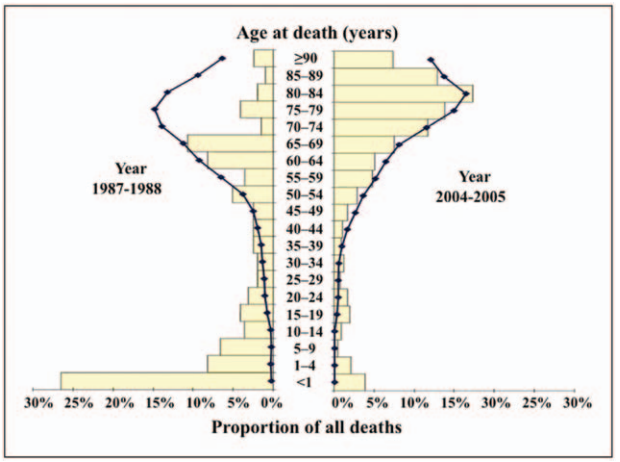

FIGURE 1. Distribution of age at death in patients with congenital heart disease in 1987–1988 and 2004–2005. Age at death is given on the *y*-axis and the proportion of all deaths in the population on the *x*-axis. Solid black curves with diamonds represent the age at death distribution in the general Quebec population during periods of observation (1987–1988; left and 2004–2005; right). Within the first year of life, the proportion of death is close to 0 during both periods of time for the general population. In contrast, the histogram bars represent the cohort of patients with congenital heart disease in the years from 1987 to 1988; left and from 2004 to 2005; right. Although between 1987 and 1988, the proportion of all deaths within the first year of life was more than 25% in the congenital heart disease population, it dropped dramatically below 5% between 2004 and 2005. The distribution of age at death at all other age categories was close to the general population. Reproduced with permission [12].

surgery in highly specialized centers [13–15]. However, the level of evidence for these recommendations is certainly low. The lack of specialized centers and available providers being familiar with CHD is known to be a serious problem in delivery of care to ACHD patients. Moons *et al.* [16] aimed in a survey at the delivery of care for ACHD patients in Europe and chose eight recommendations for the minimal and optimal structure of care from several European recommendations and guidelines. These were the employment of at least one cardiologist specifically trained in the care of ACHD, the provision of care in connection with pediatric cardiology and/or congenital cardiac surgery, treatment of a sufficient number of patients, a minimum of two cardiac surgeons trained in and practicing adult and pediatric cardiac surgery, with a minimum of 50 ACHD operations per year, a fully equipped and staffed electrophysiology laboratory, and a trained and educated nurse in the care of ACHD patients. In addition, general adult cardiac facilities and nonspecialist centers should have a well established

referral system relationship with a specialist center. Moons *et al.* [16] found that only 19% of the specialist centers complied with guideline standards for optimal care structure. However, any noncardiac surgical procedure in patients with CHD carries a greater risk for perioperative adverse events. Maxwell *et al.* [17] analyzed 1191 cases with CHD in noncardiac surgery and observed significantly higher rates of death, perioperative cardiac arrest, myocardial infarction, stroke, respiratory complications, renal failure, sepsis, venous thromboembolism, perioperative transfusion, and reoperation in CHD patients compared with a non-CHD cohort. Faraoni *et al.* [18▪] found that in children scheduled for noncardiac surgery, overall mortality increases more than two-fold in case of severe CHD compared with matched controls. However, in children with minor CHD, no increase in mortality was found [18▪]. It should be clear despite missing high level of evidence that patients with complex CHD should therefore be treated by specialized centers, even if surgical risks of noncardiac procedures may be rated as low. High-risk CHD categories include patients after Fontan procedure, severe pulmonary arterial hypertension, cyanotic CHD, complex CHD, patients with malignant arrhythmias [13,15], and most pregnancies affected from CHD [19] (see below).

WHICH ANESTHESIOLOGIST FOR WHICH CONGENITAL HEART DISEASE PATIENT?

In 2008, American College of Cardiology (ACC) and American heart Association (AHA) published a recommendation that all surgical procedures requiring general anesthesia or conscious sedation in adults with moderate or complex CHD should be performed in a regional ACHD center with an anesthesiologist familiar with these patients [13]. Only patients with simple CHD, as listed in Table 1, can usually be cared for in the general medical community.

However, at present, ACHD receive care for noncardiac surgery in a wide range of settings, often outside of specialized CHD centers. Agarwal *et al.* [20▪] reported in 2016 that 27.1% of ACHD admissions to small-sized hospitals represented complex ACHD. To our knowledge, there is no clear evidence that patients outcome is worse if non-CHD specialized anesthesiologists manage these patients, but knowledge of anesthesia providers for noncardiac surgery in ACHD patients is still an area of development. Maxwell *et al.* [21] conducted a survey in his department under 118 anesthesiologists investigating knowledge and comfort about providing perioperative or obstetric care to ACHD patients. They designed knowledge items to assess lesions that are common in ACHD and found only low levels of knowledge and comfort within this cohort of anesthesiologists. Maxwell *et al.* [22▪] further conducted a structured analysis of the Anesthesia Closed Claims Project database investigating adverse events in CHD patients in cardiac and noncardiac surgery. Factors judged to have major contribution to the adverse event and subsequent death of the patient were in more than half of all cases (55%) intraoperative anesthetic care. The nature of CHD (45%) and preoperative assessment/optimization (40%) also contributed to the adverse event. Brown *et al.* [23▪] recently found that adverse events in pediatric patients with single ventricle physiology undergoing noncardiac surgery are associated with anesthesia in more than 10% of surgical cases. Ramamoorthy *et al.* [24] reported on anesthesia-related cardiac arrest in children with CHD on the basis of data from the Pediatric Perioperative Cardiac Arrest Registry. More cardiac arrests in CHD patients were reported during noncardiac surgery in the general operating room (54%) than during cardiac surgery (26%) and cardiac catheterization (17%). Cardiovascular causes for cardiac arrest were more frequently reported in patients with CHD than in those without (50 vs. 38%; $P = 0.03$), whereas respiratory causes for cardiac arrest were more

Table 1. Diagnoses in adult patients with simple congenital heart disease

Native disease	Repaired conditions
Isolated congenital aortic valve disease	Previously ligated or occluded ductus arteriosus
Isolated congenital mitral valve disease (e.g., except parachute valve and cleft leaflet)	Repaired secundum or sinus venosus atrial septal defect without residua
Small atrial septal defect	Repaired ventricular septal defect without residua
Isolated small ventricular septal defect (no associated lesions)	
Mild pulmonary stenosis	
Small patent ductus arteriosus	

Adapted from [13].

common in patients without CHD (28 vs. 17%; $P = 0.01$).Therefore, a task force of the ACC highlighted the need for creating cohorts of specialists trained to take care of patients with CHD [25].

ANESTHETIC MANAGEMENT

Three groups of ACHD patients may present for noncardiac surgery: uncorrected CHD patients, patients with previous palliative surgery, or patients with previous corrective surgery. Each CHD patient may significantly differ from other ACHD patients regarding anatomy and physiology, even in case of same underlying cardiac lesion. Although anesthetic management in adult patients with a simple acquired valvular lesion, like aortic stenosis, is very similar, anesthetic management in ACHD patients may change completely depending on type of repair, age at repair, associated defects with specific long-term risk factors and complications, and even opposed pathophysiological conditions. For example, after tetralogy of Fallot (TOF) repair, a hemodynamically significant pulmonary regurgitation can be present in one patient, whereas another TOF patient suffers from a significant pulmonary stenosis. Therefore, a careful preoperative risk assessment for anesthesia is necessary.

PREOPERATIVE RISK ASSESSMENT FOR ANESTHESIA

The individual risk of ACHD patients certainly depends on four aspects. At first, there is the underlying nature of CHD. Second, there is the aspect of the individual course of this CHD. It is essential to know that each patient, especially with moderate or complex lesion, must be considered individually. The third point is that anesthesia providers caring for these patients are tasked with substantial CHD-associated noncardiac morbidity. Approximately one-third of CHD patients have additional extracardiac anomalies [26]. In addition, neurologic, pulmonary, hepatic, renal, and endocrine manifestations may arise from CHD, and management is complex [27▪▪]. The following medical comorbidities are particularly common in ACHD: heart failure, arrhythmias, sudden cardiac death, infectious endocarditis, additionally acquired heart diseases, pulmonary hypertension, neurological complications, hematological, and rheological impairments. Some young ACHD patients' also reveal relevant morbidity predominantly only known from elderly patients. Deen *et al.* [28▪] recently reported that patients had a nearly two-fold increased risk for development of a metabolic syndrome. Further, Gurvitz *et al.* [29▪] found that ACHD had a 1.6–2 times higher prevalence of cancer. Breast, colon, and prostate cancers were the most common cancers reported in ACHD.

The last crucial point is certainly the type of the noncardiac surgical procedure. The consequence of this point is that an individual preanesthesiological risk assessment for each CHD patient for every procedure is necessary. This may not be easy in daily routine, especially in case of complex CHD, as additional expert knowledge from other subspecialties, for example, pediatric cardiology or cardiologist with expertise in CHD, might be crucial. Of the abovementioned comorbidities, heart failure and arrhythmias cause most of unplanned hospital admissions in CHD patients. We therefore highlight these issues in context of preoperative evaluation.

HEART FAILURE

Engelings *et al.* [30▪] reported that the leading cause of death in ACHD patients is still CHD-related based on results form a large contemporary cohort study. Heart failure thereby was the leading cause of death in this population. Due to end-stage heart failure, patients with ACHD only constitute a small percentage of the total adult heart transplant population (~3%), but the number of ACHD heart transplant recipients is growing fast with a 40% increase over the last 2 decades [31].

The evaluation of heart failure in ACHD is more difficult compared with the normal population. Patients with complex CHD may differ from the non-CHD population regarding their physical status. A relevant part of the ACHD population may present with good physical performance despite a severe underlying ACHD. Ramamoorthy *et al.* [24] found that in 127 CHD patients with anesthesia-related cardiac arrest, 8% were preoperative classified as American Society of Anesthesiologists physical status I or II.

Clinical assessment of physical status and echocardiography for evaluation of ventricular function are most common in these patients; however, biomarkers like NT-proBNP have been established as a new clinically useful tool. Baggen *et al.* [32▪] recently prospectively enrolled 595 clinically stable ACHD patients in an outpatient setting. Patients were included with a median age of 33(interquartile range 25–41) years, and 90% of patients had New York Heart Association class I. During the follow-up of median 42 months, death or heart failure occurred in 8% of patients. They found that NT-proBNP more than 33.3 pmol/l was strongly associated with cardiovascular events [adjusted hazard ratio (HR) = 9.05 (3.24–25.3), $P < 0.001$] and with

death or heart failure [adjusted HR = 16.0 (2.04–126), $P < 0.001$]. In CHD patients with NT-proBNP levels below the median (<15.2 pmol/l), the cumulative proportion of death and heart failure was below 1%. A comparably powered study was performed by Popelova *et al.* [33]. This longitudinal study had a follow-up of 6 ± 3 years. Popelova described the optimal discrimination value of NT-proBNP for predicting death as more than 74 pmol/l with a 74% sensitivity, 84% specificity, and 98% negative predictive value. This high negative predictive value of NT-proBNP makes it particularly valuable as a screening tool for heart failure in ACHD.

ARRHYTHMIAS AND ANTICOAGULATION

Apart from heart failure, morbidity and mortality in ACHD patients are mainly caused by arrhythmias. Especially, CHDs with preload dependence, for example, Fontan patients, are susceptible for hemodynamic instability during arrhythmias [34].

Supraventricular tachycardia is more frequent than ventricular arrhythmias. Due to the high significance of this morbidity, the ACC/AHA published a guideline in 2016 for the management of ACHD patients with supraventricular tachycardia [35▪]. Atrial arrhythmias in CHD are a common burden, and up to one-third of patients receive antiplatelet therapy and half of patients are on anticoagulants [36▪]. For perioperative management, it is important to know that common scores for thromboembolic risk calculation, like CHADS2 and CHA2DS2-VASc, are not predictive for thromboembolic risk in ACHD patients [36▪]. ACHD patients aged below 55 years revealed a 9–12 times higher age–sex standardized incidence rate of ischemic stroke [37]. Khairy *et al.* [36▪] found that the complexity of CHD was independently associated with thromboembolic events, with rates of 0.00, 0.93, and 1.95% per year in those with simple, moderate, and severe CHDs, respectively. Perioperative management of anticoagulated patients has to be evaluated by a multidisciplinary team, carefully opposing risks of thromboembolic complications vs. hemorrhage. Regarding the need for bridging therapy in patients with anticoagulation, Bouillon *et al.* [38] recently reported for non-CHD patients that bridging therapy in patients with atrial fibrillation is associated with a higher risk of bleeding and a similar risk of arterial thromboembolism compared with no 'bridging therapy'. Whether this can be transferred to patients with CHD should be doubted as these have a higher risk of thromboembolism, but meaningful studies are currently missing.

ANESTHETIC TECHNIQUE

Kloesel *et al.* [39▪▪] recently provided an excellent overview of cardiac embryology and molecular mechanisms of CHD for anesthesiologists. Deeper knowledge of abnormal heart development improves anesthesiologist's understanding of CHDs. Few studies address the issue that anesthetic technique for noncardiac surgery is preferable in ACHD patients. Peripheral regional anesthesia offers high hemodynamic stability. However, a few reasons exist why regional anesthesia is not always applicable in ACHD patients. Typical problems derive from impaired coagulation or allergies. On the other hand, methemoglobinemia after local anesthesia with prilocaine may be fatal in case of low oxygen delivery as present in cyanotic ACHD patients. Neuraxial anesthesia is an established procedure in ACHD patients. Especially, epidural analgesia for labor is common. Typical contraindications regarding coagulation have to be taken into account. The drop of systemic vascular resistance, commonly more pronounced in spinal anesthesia, may be dangerous in patients with left ventricular outflow obstruction or in patients with systemic to pulmonary shunts due to fatal reversal of shunt direction; therefore, especially in these patients, early use of a vasopressor is advantageous [40]. General anesthesia, using either a combination of intravenous and inhalational anesthetics (balanced anesthesia) or total intravenous anesthesia is both common in CHD patients. There are no studies regarding noncardiac surgery in ACHD patients that favor one technique. So, no anesthesia technique is prohibited in ACHD patients, and in principal, all techniques may be applied [41]. However, a profound understanding of anesthesia-induced physiological changes and anticipation of consequences in abnormal circulation in each individual ACHD case is crucial. This might not be trivial under pressure of time in complex lesions like single ventricle, and therefore training is certainly necessary. We would like to add some anesthetic considerations due to special populations.

KEY POINTS OF ANESTHETIC CONSIDERATIONS IN SPECIAL POPULATIONS

Fontan population

Schilling *et al.* [42] reported that at the end of 2014, the living Fontan population of Australia and New Zealand was as high as 4.5 per 100 000 people and will double over the next 20 years. Major long-term problems in Fontan patients are supraventricular arrhythmias, heart failure, Fontan-specific problems like protein-losing enteropathy, pulmonary arteriovenous fistulae, as well as liver

diseases including liver cirrhosis and hepatocellular carcinoma. Gnanappa *et al.* [43] provide an excellent overview dealing with the complex long-term management of Fontan children and adults. During general anesthesia, Fontan patients are at special risk for sustainable hemodynamic instability due to positive pressure ventilation. This is obvious because lung perfusion in these patients is passive. Pulmonary flow depends on the transpulmonary pressure gradient being impaired by a rise of intrathoracic pressure during positive pressure ventilation. Furthermore, Fontan hearts often reveal an impaired ventricular systolic contractile function and a chronotropic incompetence as well as a pronounced preload dependence, which is essential for intraoperative anesthetic management. Tachycardia, bradycardia, hypovolemia, and positive pressure ventilation are therefore undesirable in patients with Fontan circulation.

Shunts and cyanosis in congenital heart disease

Understanding the nature of shunt and cyanosis is essential for anesthetic management. From the hemodynamic point of view, there are three types of shunts. Intracardiac shunts (interatrial and interventricular), vascular (e.g., systemic-to-pulmonary shunt) and complex shunts (e.g., truncus arteriosus, total anomalous pulmonary venous drainage, hypoplastic left heart syndrome, etc.). All shunts are usually left-to-right shunts, causing an increased pulmonary blood flow leading to a chronic burden of right-sided heart structures. Generally, these shunts show no cyanosis but lead to systemic hypoperfusion and pulmonary hyperperfusion. However, every type of shunt may end in shunt reversal and cyanosis if pulmonary perfusion is restricted due to primary reasons, for example, pulmonary hypertension or secondary reasons, for example, right ventricular outflow obstruction as in TOF patients, or decreased systemic vascular resistance, for example, by anesthesia or sepsis. An increased right-to-left shunt due to systemic hypoperfusion accelerates the development of acidosis leading to a further decrease in systemic vascular resistance. Anesthesiologists have to recognize this vicious cycle and treat appropriately to prevent hemodynamic collapse. Hallmarks of anesthesia management are to maintain systemic vascular resistance and to prevent acute increase in pulmonary vascular resistance.

Pregnancy and congenital heart disease

An increasing number of women with complex CHD and good quality of life are currently reaching childbearing age. There is a need to carefully counsel these patients before they decide to become pregnant (see guideline [19,44▪▪]). Elkayam *et al.* [45▪,46▪] provide a detailed review on the state-of-art management of cardiac diseases in pregnancy. Thompson *et al.* [47] found that number of delivery hospitalizations with maternal CHD in the United States is currently 9.0 per 10 000. Today, the leading cause of maternal death is not hemorrhage, sepsis, or thromboembolism but is related to cardiac complications [48]. Van Hagen recently reported data from the registry of pregnancy and cardiac disease, stating that in advanced countries the most prevalent diagnosis in women with cardiac disease is CHD (70%), whereas in emerging countries valvular heart disease is most common (55%) [49]. In these patients, prevalence of cardiac events during pregnancy is as high as 20%.

Table 2. Cardiac Disease in Pregnancy Risk score

Predictors of cardiovascular events	Point
Prior cardiac event (heart failure, transient ischemic attack, and infarction prior to pregnancy) or arrhythmias	1
NYHA functional class at baseline >II or cyanosis	1
Left heart obstruction (mitral valve area $<2.0\,cm^2$, aortic valve area $<1.5\,cm^2$, and LV outflow tract gradient >30 mmHg)	1
Reduced systolic ventricular function (ejection fraction <40%)	1

Zero point confers a 5% risk of cardiac complications during pregnancy, 1 point a 27% risk, and 2 or more points a 75% risk. NYHA, New York Heart Association. Adapted from [51].

Anesthesiologists as well as postoperative intensivists will be faced especially with women having complex CHD. Even women with Fontan circulation have reached childbearing age. However, a high incidence of pregnancy-associated complications has been reported with abortion rates around 43%. Monteiro *et al.* [50] reported that anesthesia techniques for delivery are predominantly neuraxial catheters (86%), whereas general anesthesia is an exception. Most complications in this population were postpartum hemorrhage (50%) and arrhythmias (29%).

For fast preanesthesiological CHD risk estimation, the Cardiac Disease in Pregnancy Risk Score (Table 2) and the modified WHO classification of maternal cardiovascular risk (mWHO) is still up to date [44▪▪,52]. Heart failure is the most common cardiac complication during pregnancy with two peaks for onset. The first peak is between 23 and 30 weeks when most of the important hemodynamic changes have taken place and the second peak around delivery [53]. If heart failure affects a woman with CHD during pregnancy, maternal mortality today is around 4.8%.

CONCLUSION

The pronounced growing population of ACHD leads to the fact that anesthesiologists have to take care for these patients in a wide range of settings. However, any surgical procedure in ACHD patients carries a greater risk than in the normal population. Profound understanding of anesthesia providers regarding the specific cardiopulmonary physiology of different CHDs and the physiological changes induced by anesthesia and anticipation of consequences in abnormal circulation is crucial. Adverse events and subsequent death of CHD patients are often related to intraoperative anesthetic care. Risk evaluation and perioperative management of CHD-associated cardiac and noncardiac morbidity is challenging and calls for a multidisciplinary team approach.

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Conflicts of interest

There are no conflicts of interest.

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