Peri-operative Anesthetic Innovations During Pediatric Cardiac Surgery

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General introduction

CONGENITAL HEART DISEASE: A SHORT NOTE OF HISTORY

Congenital heart disease (CHD) refers to a series of birth defects that affect the heart and thoracic vessels, affecting 6 to 8 out of 1,000 babies being born. In 40% of these children no treatment is indicated because of minimal effect on hemodynamics and outcome. In 60% treatment will be required; about half of them will require urgent surgery after birth, while the other half will probably require surgery or medication at some point during childhood. Due to advances in heart surgery, 85% of children with congenital heart disease will survive into adulthood (1).

Although CHD has been recognized for centuries, therapeutic options were not available until the 20th century (2). Until the late 1930s little advances were made in cardiac surgery due to a lack of refinement in anesthesia and problems related to now routine perioperative support techniques, such as blood transfusion and mechanical ventilation (3). After the first successful ligation of a patent ductus arteriosus in 1938 (4), a lot of new operations found their origin. In 1949 perioperative mortality, approached 14.5% (5). In the 1950s extracorporeal circulation made its entry. The introduction of new anesthetic drugs and the use of prostaglandins to maintain ductal patency and pulmonary blood flow was one of the most important advances of the 1970s (6). In the late 1970s cardioplegia solutions were introduced. During the 1980s sufentanil and midazolam offered alternatives to potent volatile anesthetics, although hospital mortality was still 6% (7). From the 1990s miniaturizing components of the cardiopulmonary bypass circuit reduced priming volumes, producing less coagulation factor dilution and further improvement in patient outcome.

During the past two decades, mortality after surgery for congenital cardiac disease has decreased dramatically and is now reported to be 4% in the European Association for Cardio-thoracic Surgery and the Society of Thoracic Surgeons Congenital Heart Surgery Database (8), the focus of clinical research and efforts to improve quality has now shifted to that of the minimization of morbidity (9).

ASPECTS OF QUALITY

Although quality management is a major strategic issue in health care organizations, there is little agreement on the precise definition and content of quality and quality management (10). Most often concepts and tools regard organizational quality and originate from industry. For instance, the Netherlands implemented into the governmental medical safety design policy, a report from a Royal Dutch Shell director, "In this organisation you work safely, otherwise you don't work here at all", plays a key-role (11).

The Orde van Medische Specialisten (organisation for medical specialists in the Netherlands) reports that professional medical practice quality is seen as interplay between product-quality, process-quality, and structure-quality (12). Product-quality has aspects of Good Clinical Practice like: efficiency, expertise, making adequate indications for medical care, capability, safety and carefulness. Process-quality has aspects of attitude like: respectful treatment, willingness to give adequate information, trustful relationship, cooperation and accountability. Structure-quality has aspects of organisational management like: continuity of care, availability of care, functionalism and integrated care.

From the point of view of the medical professional, however, quality directly relates to the delivery of medical care. One should approach each patient asking not only "How can I provide the best care in this case?" but also "How can I improve the care I provide?". This opens the way to innovative care.

Although, efficacy and cost-effectiveness are important aspects, innovative care may at some point introduce less efficiency and may initially seem to increase costs. When however the medical professional results improve, a new reality for the organization is constructed.

According to Deming a quality improvement cycle consists of planning, doing, checking and acting (13). This fits elegantly for improving patient care i.e. for application of innovative care.

This thesis concerns aspects of innovative care and quality improvement in the operative treatment of pediatric patients with congenital heart disease.

LATEST IMPROVEMENTS OF TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) AND ITS APPLICATION IN CLINICAL PRACTICE OF CHILDREN WITH CHD

Until 1990, intraoperative evaluation of infants and children undergoing congenital heart surgery was not feasible with TEE because probe sizes were too large (14). The development of miniaturized single- and bi-plane probes demonstrated that TEE could be performed safely in the pediatric population (15). A multiplane TEE probe which obtains images in several planes is an obvious advantage, certainly considering the complexity of the intracardiac defects. Until 2007, the use of mini-multiplane TEE probe (10.7 – 8.0 mm diameter tip with a 7.4 mm diameter shaft) was still limited to children above the weight of 5 kg (16).

In Chapter 1 we describe the physical characteristics and the acoustic properties of the Oldelft microMulti TEE probe (8.2 – 7 mm diameter tip with a 5.2 mm diameter shaft), a new technology that was developed at the Thoraxcentre to study neonates and small children.

In Chapter 2 we evaluated the clinical and diagnostic ability of this new technology in 42 neonates and infants (as small as 2.5 kg) undergoing cardiac surgery to provide data on safety and feasibility. Chapter 3 describes the limitations, loss of image quality in larger children (>25 kg) of the Oldelft micromultiplane TEE probe.

In Chapter 4 we highlight an aspect of clinical necessity of intraoperative TEE. Mechanical circulatory support with a left ventricle assist device (LVAD) is used in an increasing number of children for treatment of advanced heart failure as bridge to transplant. In adult patient care, intra-operative TEE plays a key-role in evaluating LVAD cannula positioning, haemodynamic stabilisation and the effect of device settings on right and left heart function. No data were available and no studies defined the role of intra-operative TEE for haemodynamic stabilisation during LVAD implantation in children. Therefore, we studied the utility of intra-operative TEE in pediatric patients undergoing centrifugal LVAD placement.

Aortic coarctation should be considered as a complex cardiovascular syndrome (17,18,19). There is controversy about the accurate assessment of the haemodynamic significance of blood flow obstruction caused by re-stenosis after aortic coarctation repair, for as the arm-leg blood pressure difference may not necessarily represent the haemodynamic significance of re-stenosis (20). Although an exact assessment of the aortic anatomy is required for an optimal surgical repair, no feasible intra-operative visualisation of a possible residual stenosis of the aorta exists. Till today, a brachial-ankle blood pressure difference of > 20 mmHg (18) or > 30 mmHg (21) is the only intra-operative indication for residual stenosis. Therefore, we decided to assess the feasibility of 3D echocardiography by assessing intra-operative morphological details of aortic coarctation and its repair in children. By this way three-dimensional echocardiography made its **very first** clinical entrance in pediatric cardiac anesthesia and surgery (Chapter 5).

Chapters 4 and 5 show how innovation improves medical professional result and becomes a new reality.

END-EXPIRATORY LUNG VOLUME AND MECHANICAL VENTILATION

With regard to reducing morbidity after congenital heart surgery, pulmonary complications and central airway problems are a frequent cause for delayed recovery following cardiac surgery in infants and small children (22).

Ventilation can profoundly alter cardiovascular function via complex processes (9), due to the location of lungs and heart in the thoracic cavity. These processes reflect the interaction between many factors like: Ventricular function, Circulating blood volume, Distribution of the flow of blood, Autonomic tone, Volume of air in the lungs, or pulmonary volume, and Intrathoracic pressure (23).

Changes in pulmonary volume alter autonomic tone and pulmonary vascular resistance, and at high pulmonary volumes compress the heart. Hyperinflation increases pulmonary vascular resistance and the pressure in the pulmonary arteries, impeding right ventricular ejection. Decreases in pulmonary volume induce alveolar collapse and hypoxia, stimulating an increased pulmonary vasomotor tone by the process of hypoxic pulmonary vasoconstriction. Maneuvers of alveolar recruitment, positive end-expiratory pressure, and continuous positive airway pressure may reverse hypoxic pulmonary vasoconstriction and reduce the pressure in the pulmonary arteries (9).

General anaesthesia is known to promote lung volume reduction, which prompts atelectasis, lung compliance and arterial oxygenation (24). In children, decreased lung volume is of special importance because of the lower elastic retraction forces and a lower relaxation volume, which makes them more prone to airway collapse (25). Monitoring end-expiratory lung volume (EELV) is a valuable tool to optimise respiratory settings that could be of importance in mechanically ventilated pediatric patients (26). We evaluated the feasibility and precision of an ICU ventilator with an inbuilt nitrogen wash-out/wash-in technique in mechanically ventilated pediatric patients. In Chapter 6 the results of EELV measurements in pediatric post-operative cardiac surgery patients are given. Optimising alveolar recruitment by alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP) would allow preventing ventilator-induced lung injury (VILI). In Chapter 7 we describe the effect of ARS and PEEP on variables like oxygenation and compliance of the respiratory system in paediatric patients undergoing cardiac surgery for CHD. Here again we see how innovation improves medical professional result and can become a new reality in common clinical practice.

INTRAOPERATIVE GLYCEMIC CONTROL DURING PEDIATRIC CARDIAC SURGERY.

Several studies report that the occurrence of hyperglycemia in the postoperative period is associated with increased morbidity and mortality rates in children after cardiac surgery for congenital heart disease (27-30). However, an association with intraoperative management or complexity of congenital heart disease has not yet been assessed.

Lately there is concern that glycemic control in the peri-operative period, aiming at avoiding hyperglycemia while maintaining a strict euglycemic target, could place patients at risk for hypoglycemia and hereby enhance the risk for adverse outcome (27, 28, 31-33).

In the light of this controversy we report on our pediatric cardiac anesthesiological management and the blood glucose levels during open cardiac surgery for congenital heart disease in Chapter 8. Amongst other items, this chapter reflects the aspects of quality management in a research setting: Plan (clinical research planning), Do (collect data), Check (data analysis) and Act (implementation).

AIM OF THE THESIS

The aim of this thesis is to study actual aspects of perioperative care in pediatric cardiac surgery by applying innovative techniques and concepts in order to improve the quality of care.

Quality of care in pediatric cardiac anesthesia is clearly an evolving work in progress. Good surgical team behaviour (34), process improvements, structural improvements, and increases in expertise have diminished overall mortality rates.

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Chapter 1

A new transesophageal probe for new borns

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Ultrasound Med Biol. 2009 Oct;35(10):1686-9.

ABSTRACT

Current transesophageal probes are designed for adults and are used both in the operating theatre for monitoring as well as in the outpatient clinic for patient with specific indications, like obesitas, artificial valves etc. For newborns (< 5 Kg) TEE imaging is not possible because the current probes are too big for introducing them in the esophagus. There is a clear need for a small probe in newborns that are scheduled for complicated cardiac surgery and catheterization.

We present the design and realization of a small TEE phased array probe with a tube diameter of 5.2 mm and head size of only 8.2 - 7 mm. The number of elements is 48 and the centre frequency of the probe 7.5 MHz. A separate clinical evaluation study was carried out on 42 patients (Scohy et al. 2007).

INTRODUCTION

The clinical application of transesophageal echocardiography (TEE) technology continues to progress, with various indications and diagnostic uses (Milani et al. 2003). The most common indications for TEE in pediatric patients with congenital heart disease (CHD) are for assessment during cardiac surgery and interventional cardiac catheterization procedures (Ayres et al. 2005). Another indication for TEE in pediatric patients is in situations in which the transthoracic technology is diagnostically inadequate because of poor quality or limited echocardiographic windows, which is frequently encountered in patients receiving mechanical ventilation, and other critically ill patients in an intensive care unit. Other indications for TEE are pediatric patients with intracardiac conduits or patients with suspicion of CHD, but where transthoracic echocardiography is nondiagnostic (Ayres et al. 2005). Until 1990, TEE evaluation in infants and children was not possible because probes were too large (Muhiudeen et al. 1998). The development of miniaturized single- and biplane probes (from 3.3 to 9 mm diameter) generated a number of studies, which demonstrated that TEE can be performed safely in the pediatric population (Bruce et al. 2002; Andropoulus et al. 2000; Yumoto et al. 2002). A multiplane TEE probe is an obvious advantage, certainly considering the complexity of the intracardiac defects in neonates (Shiota et al.1999; Tardif et al. 1994; Yvorchuk et al. 1995). Until recently, a safe investigation with the multiplane technique was limited to children of $5 kg (Sloth 1996). Recently, we demonstrated that a new Oldelft micromultiplane TEE probe (8.2 to 7-mm tip diameter, 5.2-mm shaft diameter) connected to a Philips iE33 ultrasound system (Philips, Andover, MA, USA) provided excellent intraoperative TEE assessment in neonates as small as 2.5 kg without major complications (Scohy et al. 2007). In this study, we describe the physical characteristics and the acoustic properties of the Oldelft/Philips micromultiplane TEE probe.

MEASUREMENTS AND METHODS

Transducer

The TEE transducer consists of 48 elements. The element width is 70 mm and the kerf 30 µm. The center 32 elements measure 7.5 mm in the elevation, whereas eight elements at both ends of the transducer are tapered from 7.5 to 3.75 mm (size of element 1 and 48), resulting in an octagonal shape. The transducer center frequency is 7.5 MHz, which is higher than the standard 5-MHz frequency of an adult TEE probe. The probe was connected to a Philips IE33 scanner for the clinical evaluation and to a dedicated phased array system (Lecoeur E´ lectronique, Chuelles, France) for acoustic in vitro measurements. A photograph of the transducer is shown in Fig. 1.

Figure 1: Photograph of the new probe (micro-multi) together with 2 commercially available TEE probes. Top: Adult probe. Middle: mini multiplane probe. Bottom: micro multiplane probe.

Acoustic measurements

The probe was connected to an experimental phased array system (Lecoeur E´ lectronique), enabling optimal control in transmission. The acoustic field was measured with a calibrated hydrophone of 0.2-mm diameter (Precision Acoustics, Teddington Middlesex, UK), of which the position was controlled by a computer-controlled X-Y-Z system (6K4, Parker Hannifin Corporation, Rohnert Park, CA, USA). For beam profile measurements, the scanner operated in a single-line mode steering at 0° and focused at an axial distance of 2 cm. The profiles were measured using a transmit pulse of two periods and a center frequency of 7.5 MHz. The generated peak pressure at the focal point was kept low (240 kPa).

Simulations

Simulations were done using Field II (Jensen and Svendsen 1992; Jensen 1996). For the simulations, the same settings were used as for the measurements (lateral focus at 2 cm, elevation focus at 6 cm, steering 0 degrees, acoustic pressure 240 kPascal).

RESULTS

Figure 2 shows the beam profiles in lateral and elevation at a distance of 2 cm. The lateral and elevation –3 dB beamwidths (one way) were, respectively, 0.5 mm and 1 mm. The dotted line in the figure denotes the result of the simulation, which is in agreement with the measurements. Figure 3 shows the acoustic pulse in focus (left) and the corresponding frequency spectrum (right). The maximum in the frequency spectrum is at 7.5 MHz, as seen in the figure. By considering this value as the center frequency, the relative bandwidth at –6 dB is 53%.

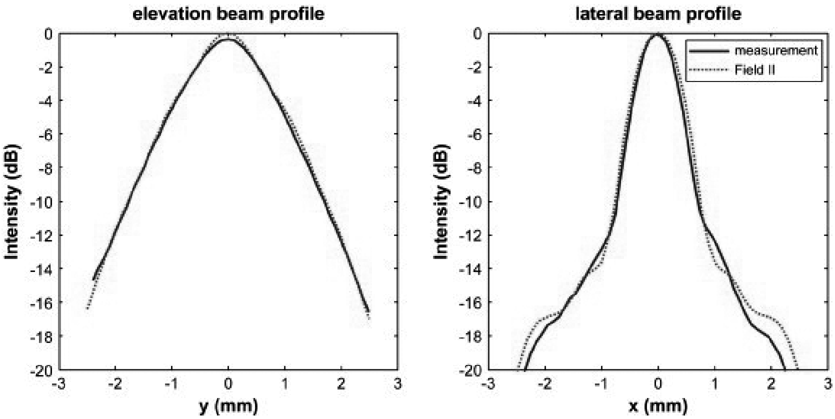

Figure 2: Lateral (right) and elevation (left) beam profile at an axial distance of 2 cm

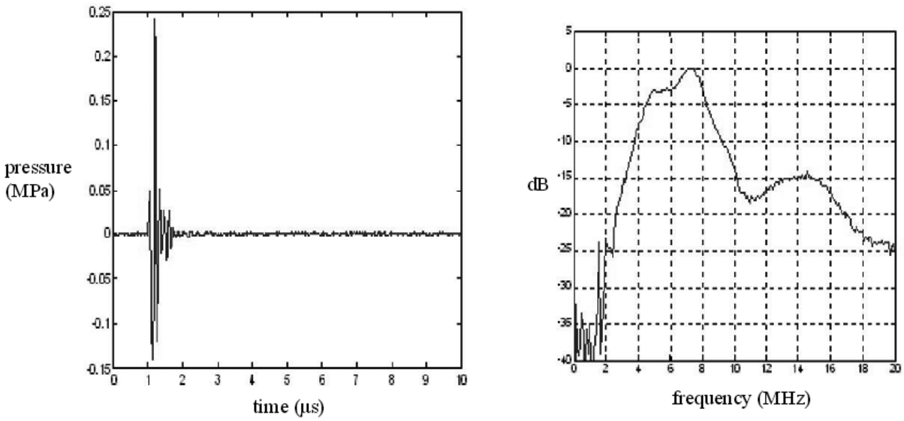

Figure 3: Acoustic pulse (left) and corresponding frequency spectrum at an axial distance of 2 cm.

Clinical examples

Figures 4, 5 and 6 have been acquired as part of a routine intraoperative TEE examination in a 1-week-old neonate weighing 2.6 kg, with transposition of the great arteries, and who was scheduled for arterial switch procedure. Institutional review board approval/ consent was waived. Figure 4 shows the aorta and the pulmonary artery before the arterial switch procedure for transposition of the great arteries; this image could only be visualized in a 113_ multiplane angle. In Fig. 5 we measured the velocity of the septal site of the mitral valve annulus with pulsed-wave tissue Doppler imaging, which can be used to evaluate left ventricular function. Figure 6 shows the post-repair patency of the coronary artery after implantation in the aorta with color Doppler. We also distinguish the bifurcation of the mainstem into the left anterior descending and the circumflex coronary arteries.

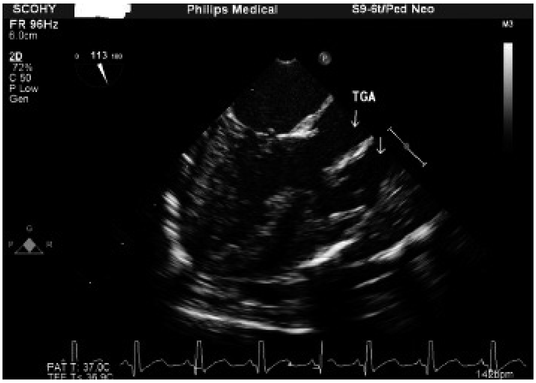

Figure 4: Aorta and Pulmonary artery in Transposition of the Great Arteries in a 2.6 kg neonate in a multiplane angle of 113°.

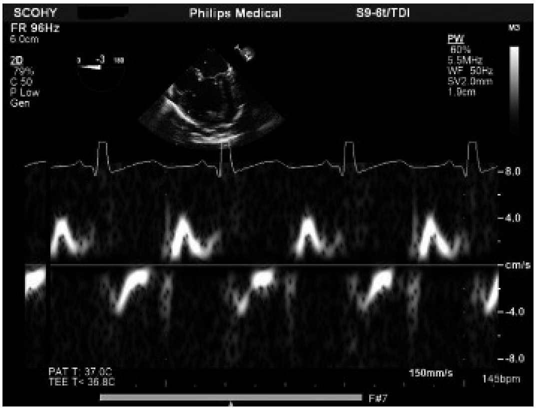

Figure 5: Pulsed-wave Tissue Doppler Imaging at the septal site of mitral valve annulus in a 2.6 kg neonate.

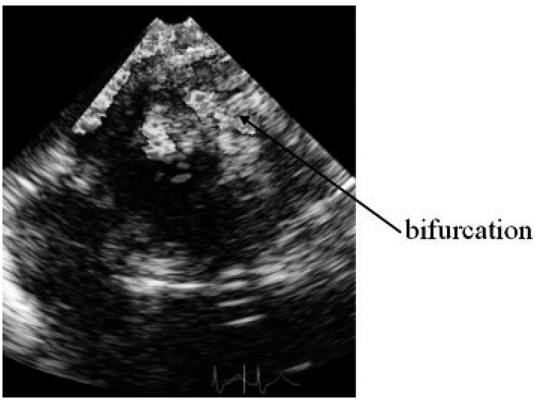

Figure 6: Color Doppler of the mainstem coronary artery re-implantation in the aorta.

CONCLUSION

We present the design and realization of a small TEE phased array probe with a tube diameter of 5.2 mm. The image quality of the probe is good and the probe has a clear diagnostic value for neonates.

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Chapter 2

Intraoperative evaluation of micromultiplane transesophageal echocardiographic probe in surgery for congenital heart disease

Scohy TV, Gommers D, ten Harkel DJ, Deryck Y, McGhie J, Bogers AJ.

Eur J Echocardiogr. 2007 Aug;8(4):241-6.

ABSTRACT

Introduction: In the last years, transesophageal transducers for multiplane Doppler echocardiography have demonstrated their superior imaging performance in pediatric patients undergoing cardiac surgery. To date, the size of these probes has limited their use in neonates and small children. New technologies allowing to perform TEE in smaller patients are therefore promising.

Methods: We report our clinical experience with the Oldelft microMultiplane TEE probe (8.2 -7 mm diameter tip with a 5.2 mm diameter shaft) specifically meant for use in neonates.

Results: Forty-two patients were examined intra-operatively using the microMulti TEE harmonic transducer. Patients examined ranged in age from 4 days to 6 years and ranged in weight from 2.5 to 23.8 kg. In two patients we had to adapt ventilatory settings because of increased airway resistance after probe insertion. In 3 patients surgical re-intervention was performed due to TEE assessment immediately after weaning from bypass. In two patients significant obstruction of the right ventricular outflow tract was still present after Fallot correction, and one patient had an additional muscular ventricular septal defect still present after VSD closure.

Conclusions: The MicroMulti TEE harmonic transducer provided excellent diagnostic intra-operative TEE in neonates and small children without major complications, special attention should be taken for ventilatory parameters in neonates less than 3 kg.

INTRODUCTION

The role of transesophageal echocardiography (TEE) during surgery for congenital cardiac disease to define complex anatomical structures, functional abnormalities, and to monitor hemodynamics is well established (1,2). Until 1990, intraoperative evaluation of infants and children undergoing congenital heart surgery was not feasible with TEE because probe sizes were too large (1). It is not surprising that inability to pass the TEE probe and complications as esophageal trauma, airway compromise, and aortic compression occur predominantly in smaller children (3). The subsequent development of miniaturized single- and bi-plane probes (from 9 mm down to 3.3 mm diameter) has generated a number of studies, which have demonstrated that TEE can be performed safely in the pediatric population (4,5,6). However, the use of a mini multiplane TEE probe (10.7 – 8.0 mm diameter tip with a 7.4 mm diameter shaft) is still limited to children above the weight of 5 kg (7). A multiplane TEE probe for neonates and small children, which obtains images in several planes, is an obvious advantage, certainly considering the complexity of the intracardiac defects (8,9,10). In this study we evaluated the clinical and diagnostic ability of the Oldelft microMulti TEE probe (8.2 – 7 mm diameter tip with a 5.2 mm diameter shaft) in neonates and infants undergoing cardiac surgery to provide data on safety and visibility.

METHODS

Forty-two consecutive neonates and infants undergoing surgery for congenital cardiac defects at the ErasmusMC Thoraxcentrum were included. All patients undergo routinely TEE during cardiac surgery. Since the availability of the Oldelft microMultiplane TEE probe the weight limit has dropped to 2.5 kg.

Before induction of anesthesia, all patients were monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. After the insertion of a peripheral venous line, general anesthesia was induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg. Patients were nasotracheally intubated and pressure controlled ventilated (PCV) using a Siemens 900C ventilator. Anesthesia was maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. Invasive monitoring via a femoral arterial line and an internal jugular central venous catheter was performed, and a Foley bladder catheter and rectal temperature probe were inserted. The lubricated Oldelft MicroMultiplane TEE probe was inserted blindly with or without a jaw thrust of the mandible or under direct laryngoscopic view. During insertion of the TEE probe special attention was payed to tidal volume and dampening of the arterial waveform (3). TEE examinations were performed using Philips iE 33 ultrasound system (Philips, Andover, MA. USA) equipped with 2D, pulsed, continuous, and color Doppler capabilities. All TEE examinations were conducted by the same anaesthesiologist in presence of a second anaesthesiologist who was responsible for the care of the patient.

TEE PROBE

The microMulti TEE Transducer is a miniature, phased array ultrasound (center frequency 7.5 MHz / bandwidth > 40% / 48 elements / 0.1mm pitch) multiplane TEE probe, developed for neonates and small children. The microMultiplane TEE transducer consists of an octagonal 48-element array, 5.0 mm elevation , 4.77 mm lateral aperture, rotatable through 180° mounted on the distal end of a gastroscope. The microMulti TEE Transducer uses a flexible shaft with a thickness of max 5.2 mm, with a length of 70 cm, with a bending neck capable of articulating in the anterior and posterior directions (120° +/- 10° upward anterior, 90° +/- 10° backward posterior). The bending neck has a diameter of 5.6 mm and a length of 40 mm. The bead on the transition to the shaft has a diameter of 6.2 mm. The tip is 8.2 mm wide, 7.0 mm thick and has a length of 24.0 mm. Figure 1 shows a comparison of an adult, the mini multiplane and the micro multiplane TEE probe tips.

Complete TEE examination took place before cardiopulmonary bypass(CPB). After the initial examination, the probe was advanced into the stomach and left in an unlocked position during the procedure; the ultrasound emission was turned off during bypass. The TEE assessment of the surgical repair occurred immediately after weaning from CPB.

Figure 1: Adult, miniMulti and microMulti TEE probe.

RESULTS

Demographic data are summarized in Table 1. Patients examined ranged in age from 4 days to 6 years and ranged in weight from 2.5 to 23.8 kg. Table 1 also lists the diagnostic information concerning patients who were evaluated before, during and after surgery.

Table 1: Patients Characteristics

	Weight (kg)	Age	Diagnosis	Procedure
1	2,5	2w2d	AS	Autograft procedure
2	2,5	4d	TGA / PDA / ASD	Switch
3	2,5	2m	PDA / PA	Atrioseptectomy, closure PDA, central shunt
4	2,6	5d	TGA	Switch
5	2,8	8d	TAPVC / PDA / DORV / TGA	Reimplant Pulm Ven, atrioseptectomie,VP shunt
6	2,9	3w	HLHS	Norwood
7	3	6w	VSD	Closure
8	3,3	3w	DORV / TGA / PS / PDA	Central shunt
9	3,4	1m3w	VSD / ASD	Closure
10	3,5	7w	VSD / ASD	Closure
11	3,6	12d	HLHS	Norwood
12	3,6	2w	CoA / VSD / ASD	repair
13	3,8	16d	TOF (Spells)	Correction + transannular patch
14	4,3	1m3w	residual VSD after TOF	closure VSD
15	4,5	2w5d	Coa / VSD	Single stage repair
16	4,8	4m	residual VSD after TOF	Closure VSD
17	4,9	3m2w	VSD	Closure
18	5,3	4m	TOF	Correction + transannular patch
19	5,4	3m2w	TOF	Correction + transannular patch
20	5,9	3m	ALCAPA	reimplant LCA
21	6	9m	TOF	Correction + transannular patch
22	6,1	11m	Multiple muscular VSDs	Banding AP
23	6,4	7m	DORV / TGA / PS	PCPC
24	7,3	5m	VSD / PS / ODB	Correction + transannular patch
25	7,7	9m	AVSD	repair
26	8	6m	ASD	closure
27	9	1y	TGA / PA / DORV / MBT	PCPC, closure MBT
28	9	8m	Sinus Venosus Defect	Closure
29	9	1y	VSD	Closure
30	9,8	11m	HLHS / TGA / Cor triatriatrum / obstruction left LV	atrioseptectomy, deobstruction left LV
31	10	16m	TOF (Spells)	Correction + transannular patch
32	10	2y	HLHS	TCPC
33	10,8	3y	ASD	Closure
34	11	24m	ASD / PS	Closure
35	13,4	4Y	ASD / ODB	Closure
36	13,3	2y6m	HLHS	TCPC
37	13	2y10m	ASD	Closure
38	15	3y	Sinus Venosus Defect	Closure
39	15	4y	Reop TOF / DCRV	Valvulo+infundibulotomie
40	20	6y	CoA / VSD	repair
41	20	5y	DSAS	Membrane resection
42	23,8	6y	TR + TS of prosthetic valve	New valve

AS=aortic stenosis; ASD=atrial septal defect; ALCAPA=abnormal left coronary artery from the pulmonary artery; CAVSD=complete atrioventricular septal defect; CoA=aortic coarctation; DORV=double outlet right ventricle; HLHS=hypoplastic left heart syndrome; LCA=left coronary artery; PA=pulmonary atresia; PDA=patent ductus arteriosus; PS=pulmonary stenosis; PV=pulmonary veins; TAPVC= total anomalous pulmonary venous connection; TGA=transposition great arteries; TR=tricuspid regurgitation; TS=tricuspid stenosis; TOF=tetralogy of Fallot; VSD=ventricular septal defect; VPshunt=ventricular pulmonary shunt.

None of the patients was excluded beforehand. There were two patients with complications related to introduction of the probe or its use during the surgical procedure. Patient 1 had an increased airway resistance with increased air leak after introduction of the microMulti TEE probe, the problem was solved by increasing PEEP level from 4 to 6 cm H_2O and increasing peak inspiratory pressure from 10 to 14 cm H_2O above PEEP. Patient 6 had increased airway resistance after introducing the probe, withdrawal of the nasal endotracheal tube for 0.5 cm, and PEEP increase from 4 to 8 cm H_2O and peak pressure increase from 10 to 18 cm H_2O solved the problem. In both patients we noticed no further difficulties during TEE examination.

In three patients surgical re-intervention during the continued procedure was decided after intra-operative TEE assessment of the initial repair. Case 21 and 31 had significant RVOT obstruction (continuous-wave Doppler velocities of 4.0 m/s) after correction , therefore widening of the RVOT (CW velocities 1.4 m/s and 2.0 m/s) was performed. Case 14 showed an additional muscular VSD after VSD correction, which was closed subsequently. This reintervention rate is comparable to the 5-10% as reported earlier in pediatric cardiac surgery after TEE assessment.

In two of the larger patients (case 40 and 42, body weight 20 and 24 kg) we had poor quality images.

DISCUSSION

TEE has become the standard of care in many institutions performing pediatric cardiac surgery, to evaluate the surgical repair after weaning from cardiopulmonary bypass. The cardiac performance can be assessed and possible residual lesions can be immediately corrected (11). As surgical techniques have improved, greater numbers of neonatal and small patients are referred for repair of complex intracardiac defects. TEE is frequently used in this population. Due to the relatively large size and rigid nature of TEE probes, airway complications, inadvertent extubation, and insertion failures have been reported to occur predominantly in smaller patients (3). Until recently a safe investigation with multiplane technique in neonates and infants was limited to children of 5 kg or more (7). The Oldelft MicroMultiplane TEE probe provided excellent diagnostic intra-operative TEE in neonates and small children without major complications, this probe allows multiplane imaging in neonates and smaller children and provides additional and clear information, with less manipulation than would be required for biplane visualization. This is illustrated in Figures 2-7. In Figure 2 we measured a flow velocity of 4 m/s with continuous wave (CW) doppler in the pulmonary artery after surgical repair, with the simplified modification of the Bernoulli equation ($\Delta P = 4 \times \Delta V^2$) the estimated instantaneous systolic gradient would be 64 mmHg. Figure 3 shows an overriding aorta and VSD in TOF. Figure 4 shows the RVOT and the pulmonary artery. In Figure 5 we measured the velocity time integral (VTI) with CW Doppler in a transgastric long-axis view of the aortic valve. Figure 6 shows color Doppler flow in the left coronary artery (LCA) and figure 7 shows a transgastric long-axis view of the aortic valve.

In this study we were able to acquire useful images in children down to a weight of 2.5 kg, however in two of the larger children (case 40 and 42) we noticed poor quality images. Although in two children ventilatory problems occur they could be resolved by changing ventilatory settings.

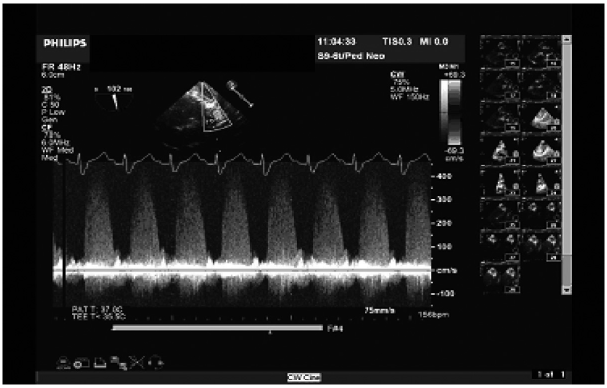

Figure 2: Continuous Wave flow velocity measurement in pulmonary artery in a multiplane angle of 102°

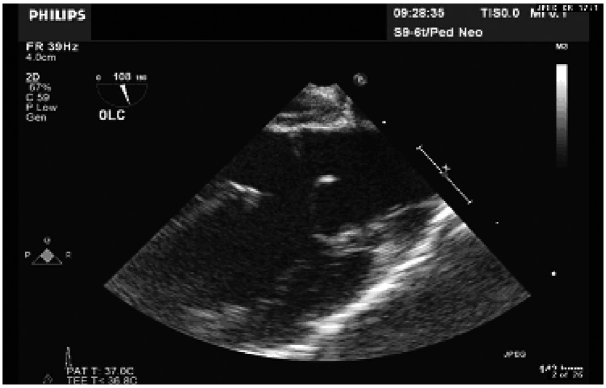

Figure 3: Ventricular Septal Defect and overriding aorta in Tetralogy of Fallot in a multiplane angle of 108°

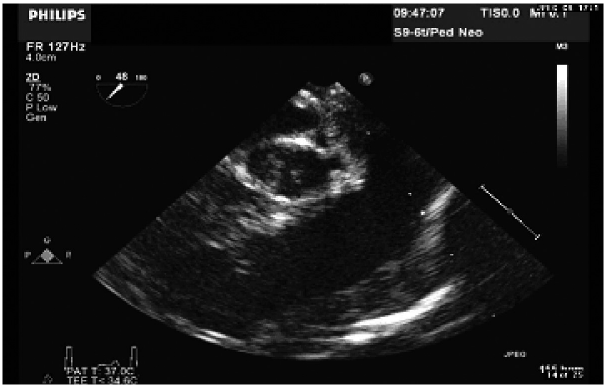

Figure 4: Pulmonary artery in a multiplane angle of 48°.

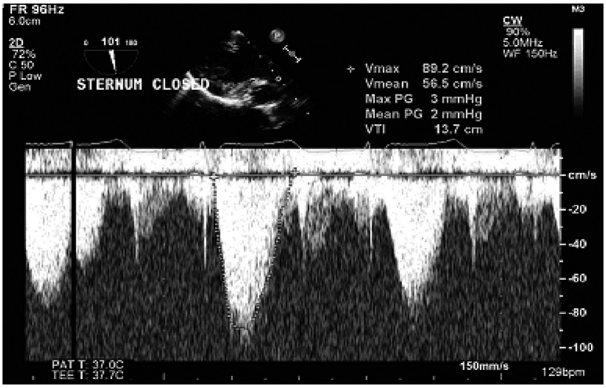

Figure 5: CW Doppler VTI measurement through a normal aortic valve in a transgastric long-axis view; multiplane angle 101°.

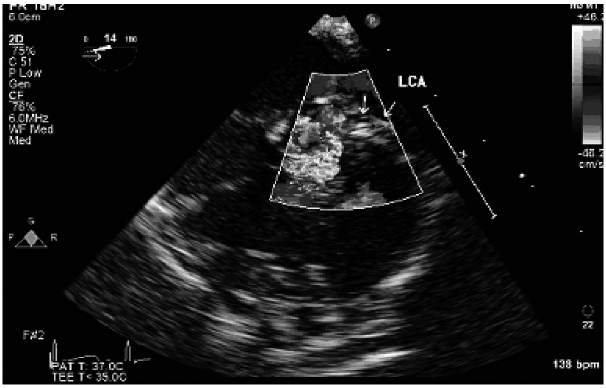

Figure 6: Color Doppler flow in Left Coronary Artery in a multiplane angle 14°

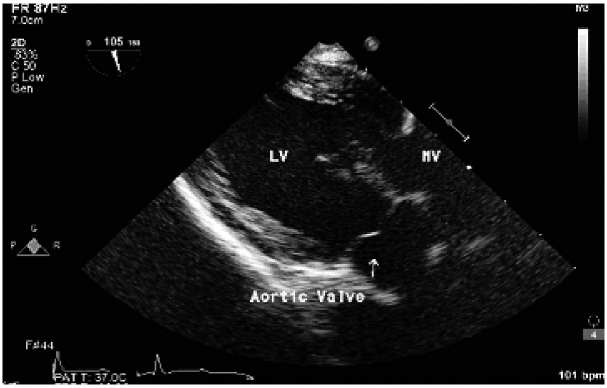

Figure 7: Transgastric long-axis view of the aortic valve in a multiplane angle 105°.

In conclusion the Oldelft microMultiplane TEE probe examinations provided excellent diagnostic intraoperative TEE assessment in neonates as small as 2.5 kg without major complications. In larger children (>20kg) however we noticed poor image quality, further investigation will have to confirm this.

Immediate TEE assessment of the surgical repair after weaning from bypass may prevent unplanned reoperations in the early and late post operative period. In the smallest infants attention should be payed to ventilatory settings during and after introduction of the microMulti TEE probe. Furthermore intra-operative TEE assessment also provided additional information concerning cardiac performance. This information assisted in taking the appropriate decisions for optimal pharmacologic treatment during weaning of bypass. Intraoperative TEE monitoring is recommended in all cases.

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Chapter 3

Image quality using a micromultiplane transesophageal echocardiographic probe in older children during cardiac surgery

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CORRESPONDENCE

Transesophageal echocardiography (TEE) is a standard procedure both for the intraoperative evaluation and monitoring of adult and paediatric patients undergoing cardiac surgery (1-5). Cardiac performance can be assessed and residual lesions are immediately corrected (3), thus avoiding re-operations and reducing morbidity, mortality, and costs (1). We recently showed that the micromultiplane TEE probe (8.2 – 7 mm diameter, 24mm length tip, with a 5.2 mm diameter shaft ; Oldelft, Delft, The Netherlands) allows diagnostic intra-operative TEE assessment of children and neonates as small as 2.5 kg without major complications (3). However, in two heavier children (> 20kg), we noticed poor quality images. TEE is a semi-invasive procedure and although complications are rare (local trauma to the oropharynx and the oesophagus), the use of the smallest probe available with acceptable image quality should be preferred (4). The purpose of the current study is to define the upper weight of patients in which the micromultiplane TEE probe provides diagnostic images.

All patients weighing less than 50 kg and above 15 kg undergoing cardiac surgery at the Thoraxcentre of the Erasmus MC Rotterdam between January 2006 and December 2007 were included. All patients at our centre routinely undergo TEE examination during cardiac surgery. Institutional Review Approval/Consent was waived. Before induction of anaesthesia, all patients are monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. After the insertion of a peripheral venous line, general anaesthesia was induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg.

Patients were tracheally intubated and pressure controlled ventilated (PCV) using a Siemens 900C ventilator (Siemens, Lund, Sweden). Anaesthesia was maintained with midazolam 0.1 mg/kg per hour and sufentanil 1 mcg/kg per hour. Invasive monitoring via a radial arterial line and an internal jugular central venous catheter was performed, and a Foley bladder catheter with an integrated temperature probe was inserted. After putting a Latex free micro paediatric ultrasound transducer probe cover (Palmedic, Lichtenvoorde, The Netherlands) the micromultiplane TEE probe was inserted blindly with or without a jaw thrust of the mandible or under direct laryngoscopic view. All TEE examinations were performed using Philips iE 33 ultrasound system (Philips, Andover, Massachusetts, USA) equipped with 2D, pulsed, continuous, and color Doppler capabilities. All TEE examinations were conducted and digitally recorded by the same cardiac anaesthesiologist in presence of a second anaesthesiologist who was responsible for the care of the patient. Afterwards an experienced echocardiographer and cardiac anaesthesiologist reviewed and scored all images separately. Images were divided in mid-oesophageal (MOE) and transgastric (TG) views. All images were evaluated as following: 1 = "Excellent", 2 = "Good", 3 = "Poor" and 4 = "Not interpretable".

Table 1: Patient characteristics and evaluation.

					Image	Quality	Score	*
patient	**weight (kg)**	**age**	**diagnosis**	**surgical procedure**	**MOE views 1**	**TG views 1**	**MOE views 2**	**TG views 2**
1	15	4	TOF DCRV	Valvulo + infundibulotomy	1	1	1	1
2	15	3	ASD	closure	1	1	1	1
3	15	7	cardiomyopathy	levitronix LVAD	1	1	1	1
4	15	4	ASD	closure	1	1	1	1
5	17	4	SVD	closure	1	1	1	1
6	17	6	ASD	closure	1	1	1	1
7	17.1	4	ASD	closure	1	1	1	1
8	17.3	4	ASD	closure	1	1	1	1
9	17.7	4	VSD,RVH,DCRV	resection fibromusculair edge	1	1	1	1
10	20	5	DSAS	Membrane resection	1	1	1	1
11	20	6	CoA, VSD	repair	1	2	1	2
12	21	6	ASD reop	closure	1	2	1	2
13	24	6	TI, TS	TVR	1	2	1	2
14	25	8	VSD	closure	2	2	1	2
15	26	8	TI, TS, Endocarditis	TVR	2	3	2	3
16	27	10	SVD	closure	2	3	2	3
17	33	9	CoA	Repair	3	4	4	4
18	36	11	cardiomyopathy	HTX	4	4	4	4
19	37	11	VSD	closure	4	4	4	4
20	50	13	DCRV	Membrane resection	4	4	4	4

ASD, aortic stenosis; CoA, aortic coartation; DCRV, double chambered right ventricle; DSAS, dynamic subaortic stenosis; HTX, transplantation of the heart; LVAD, left ventricle assist device; MOE, mid-oesophageal; RVH, right ventricular hypertrophy; SVD, sinus venosus defect; TOF, tetralogy of fallot; TG, transgastric; TR, tricuspid regurgitation; TS, tricuspid stenosis; TVR, tricuspid valve replacement; VSD, ventricle septum defect; *Image Quality Score: 1=excellent; 2=good image quality; 3=Poor image quality; 4="Not interpretable" image quality. MOE=mid-oesophageal, TG=transgastric.

The micromultiplane TEE probe was developed at the Thoraxcentre to study neonates and small children and consists of a rotational phased array ultrasound multiplane transducer (center frequency ~7.5 MHz / bandwidth >40% / 48 elements / 0.1 mm pitch), mounted at the tip of a flexible gastroscope. The transducer is an octagonal 48-element array, 5.0 mm elevation, 4.7 mm lateral aperture, rotatable through 180°. The gastroscope has a thickness of max 5.2 mm, a length of 70 cm and a bending neck capable of articulating in the anterior and posterior directions (120° ± 10° upward anterior, 90° ± 10° backward posterior). The bending neck has a diameter of 5.6 mm and a length of 40 mm. The bead on the transition to the shaft has a diameter of 6.2 mm. The tip is 8.2 mm wide, 7.0 mm thick and has a length of 24.0 mm (Figure 1) (6).

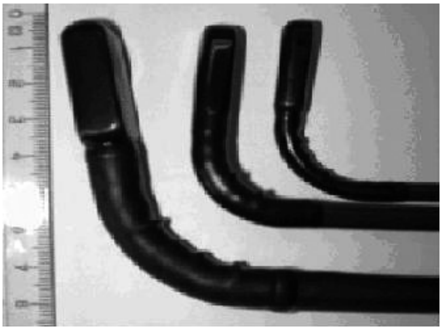

Figure 1: An adult multiplane, minimultiplane and a micromultiplane TEE probe are shown.

The demographic, diagnostic and evaluation data are summarized in Table 1. The patients ranged in age from 3 to 13 years and in weight from 15 kg to 50 kg. The images up to a body weight of 20 kg were evaluated "excellent" in all views. From a body weight of 20 to 25 kg images were evaluated "excellent" in the MOE views and "good" in the TG views, from 25 to 27 kg images were considered "good" at the MOE level and "poor" at the TG level. In the patients weighing 33 kg and more all images were assessed "poor" and we had to use an adult TEE probe, providing excellent image quality.

TEE is a semi-invasive procedure for cardiac imaging and although complications are rare the smallest probe providing diagnostic images should be used. It is not surprising that inability to insert the TEE probe, oesophageal trauma, airway compromise, and aortic compression occur predominantly with thicker TEE probes (7).

There are several reasons why there is an upper weight limit for the micromultiplane TEE probe. First, because the centre frequency of the micromultiplane TEE transducer is 7.5 MHz, which gives an optimal image to a depth of 6–7 cm (8). This explains why the image quality in the far field becomes "poor", in heavier patients.

Second, during TEE examination of heavier patients (>25 kg) it was impossible to acquire deep TG longaxis and TG longaxis views. This can be explained by the shorter bending neck (length of only 40 mm) of the micromultiplane TEE probe, as compared to that of an adult TEE probe, which is approximately 80 mm long (Figure 1). This makes it impossible to reach the apex of the left ventricle.

A third explanation for the quality getting less within heavier patients is the fact that the micromultiplane-phased array has less elements as compared to the standard adult TEE probe (48 vs. 64). This results in a lower resolution and consequently a lower image quality (4). Finally a small probe within larger patients may have less-than-optimal acoustic coupling with the heart (4).

In conclusion; the micromultiplane TEE probe provides image of "excellent" and "good" quality in patients up to a weight of 25 kg. In patients above 25 kg, an adult TEE probe, providing excellent image quality, can be used.

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Chapter 4

Intraoperative transesophageal echocardiography is beneficial for haemodynamic stabilisation during left ventricular assist device implantation in children

Scohy TV, Gommers D, Maat AP, Dejong PL, Bogers AJ, Hofland J.

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ABSTRACT

Background: Mechanical circulatory support, with a Left Ventricular Assist Device (LVAD) is used in an increasing number of children for treatment of advanced heart failure as bridge-to-transplant. To date no data are available and no studies have defined the role of intraoperative transesophageal echocardiography (TEE) for haemodynamic stabilisation during Centrimag Levitronix centrifugal pump implantation in children.

Methods: Children with therapy resistant heart failure, undergoing LVAD implantation using Berlin Heart Excor pediatric cannula connected to a Levitronix Centrifumag pump, are intraoperatively monitored using an Oldelft micromultiplane TEE. Intraoperative TEE is specially used to monitor right ventricular (RV) and left ventricular (LV) function, correct position of the cannulas and response to pharmacological treatment.

Results: In 5 consecutive patients RV function was assessed by TEE after starting LVAD Levitronix centrifugal pump. Initial RV failure presents with RV dilation and LV collapse. After titration of vasopressor and inotropic agents, RV contractility improved and thereby the filling of the LV. In one child, despite those measures the RV showed no improvement by TEE and a Levitronix right ventricular assist device (RVAD) to support the RV function was implanted as well. All patients could haemodynamically be stabilised before transport to the Intensive Care Unit.

Conclusion: The complex interaction of the right- and left ventricular function and correct positioning of the cannula, during LVAD implantation in children with end-stage cardiac failure is improved by simultaneous visualisation of cardiac performance of both ventricles and cannula positioning by means of intraoperative multiplane TEE.

Implication statement

Intraoperative TEE is beneficial for haemodynamic stabilisation and evaluation of cannula positioning during LVAD implantation in children.

INTRODUCTION

Mechanical circulatory support, with a LVAD is used in an increasing number of children for treatment of advanced heart failure as bridge-to-transplant. To date no data are available and no studies have defined the role of intraoperative TEE for haemodynamic stabilisation during LVAD implantation in children. Intraoperative TEE plays a fundamental role in evaluating LVAD cannula positioning, haemodynamic stabilisation and the effect of device settings on right and left heart function.

This manuscript describes the utility of intraoperative TEE in pediatric patients undergoing centrifugal LVAD placement.

METHODS

At the Erasmus MC Thorax centre all pediatric patients undergo routinely TEE during cardiac surgery. Institutional Review Approval/consent was waived. Thus children with therapy resistant heart failure, undergoing Berlin Heart Excor pediatric cannula implantation connected to a Levitronix Centrifumag pump (Levitronix, Zurich, Switzerland), are all intraoperatively monitored by TEE.

A LVAD centrifugal pump assists the left ventricle (LV) by drainage of blood from the LV apex and pushes the blood via a pump into the ascending aorta. For drainage an inflow cannula is connected to the LV apex and the LVAD and for delivery an outflow cannula is placed into the ascending aorta (Fig 1).

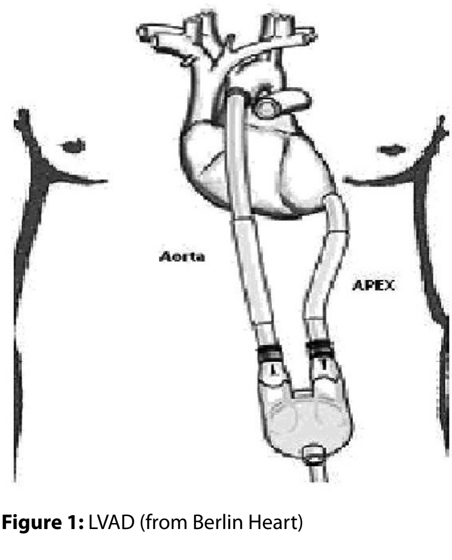

Figure 1: LVAD (from Berlin Heart)

Before induction of anaesthesia, all children are monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. After the insertion of a peripheral venous line, general anaesthesia is induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg.

Patients are tracheally intubated and pressure controlled ventilated (PCV) using a Siemens 900C ventilator (Siemens, Lund, Sweden). Anaesthesia is maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. Invasive monitoring is performed via a cannula into a radial artery and a central venous catheter placed into an internal jugular vein. A Foley bladder catheter with an integrated temperature probe is inserted also into all patients.

All TEE examinations are performed with an Oldelft micromultiplane TEE transducer (Oldelft, Delft, The Netherlands) (1) covered with a Latex free micro paediatric ultrasound probe cover (Palmedic, Lichtenvoorde, The Netherlands) connected to a Philips iE33 ultrasound system (Philips, Andover, MA, USA).

Before the procedure starts, cardiac output (CO) is calculated according the body surface (CO = 2.4 $l/min/m^2$) in order to give us a target cardiac output for the optimal output settings of the LVAD centrifugal pump (cardiac index cannot be measured with the pump). The body surface area (BSA) is calculated according to the Dubois formula: BSA (m^2) = 0.20247 x Height (m) $^{0.725}$ x Weight (kg) $^{0.425}$ (2).

The Erasmus MC Rotterdam intraoperative TEE examination protocol for LVAD implantations consists of a general echocardiographic examination and the specific pre-LVAD and post-LVAD considerations. Pre-LVAD recommended views are Mid Oesophageal (MOE) 4-chamber view for evaluation of LV and right ventricular (RV) function, Tricuspid insufficiency (TI), Mitral valve stenosis (MS) and Right-Left (RL) shunts (atrial and ventricular). MOE Aortic Valve (AV) Long-Axis (LA) view to evaluate Aortic Insufficiency (AI) and ventricular RL shunt. The MOE RV inflow – outflow view is used to evaluate Pulmonic insufficiency (PI) in case of RVAD. Post-LVAD recommended views are MOE 4-chamber view for evaluation of de-airing, RL shunting, inflow cannula flow pattern (pulsed wave (PW), continuous wave (CW) and colour Doppler) and alignment in LV, LV unloading, RV function. In the MOE AV LA view we evaluate AI and outflow cannula flow pattern (PW, CW and colour Doppler). Evaluation of ascending and descending aorta for aortic dissection is also done (3).

After going on cardiopulmonary bypass (CPB) inflow cannula is inserted in the LV apex and the outflow cannula is connected to the ascending aorta. Before weaning from CPB all patients received dobutamine 4 mcg/kg/min IV. After stopping CPB, Levitronix pump was started by increasing the rotations/min under echocardiographic guidance in MOE 4 chamber view. The Levitronix pump rotations/min were increased until calculated CO was reached. We desided not to place a left atrial pressure catheter. If during this process RV dilated and LV collapsed, CPB was restarted and additional medication to support RV was started according to our protocol for additional RV support. This protocol consists in dobutamine, enoximone and inhaled nitric oxide (NO). The whole process was repeated until Levitronix pump output reached the calculated CO.

RESULTS

Five consecutive children with therapy resistant heart failure undergoing LVAD implantation were studied. Patient characteristics are shown in Table 1. All patients received dobutamine 4 mcg/kg/min iv before weaning from CPB and starting of the LVAD centrifugal pump. In the first attempt of weaning from CPB and starting LVAD, RV failure was seen in all patients by dilation of the RV and collapse of the LV (Fig 2) when LVAD output was set above half of the calculated CO. After going back on CPB, echographic evaluation of cannula positioning, starting inhaled nitric oxide (NO) and titration of vasopressor and inotropic agents (Table 1) RV contractility improved, emptying of the RV improved and thereby the filling of the LV. On the second attempt of weaning from CPB with starting LVAD centrifugal pump in patients 1, three to five a haemodynamic stable condition was achieved. Pump settings and some haemodynamic data are given in Table 2.

In patient 2, weaning from CPB was also not successful after starting the LVAD centrifugal pump. TEE examination showed collapse of the LV and dilatation of the RV. Therefore, dobutamine 7.5 mcg/kg/min iv, enoximone 0.2 mg/kg iv bolus injection, noradrenalin 0.1 mcg/kg/min iv and inhaled nitric oxide 20 ppm was started to improve RV function. Despite these inotropic agents the maximal RV output was just 0.5 L/min (LVAD pump output just before RV dilation and LV collapse), being less than 30% of the calculated necessary value (1.7 L/min). Therefore, we decided to implant a RVAD for support of the RV function. After this biventricular assist device (BiVAD) implantation weaning from CPB was successful. The patient showed a mean arterial pressure (MAP) of 80 mmHg, iv noradrenalin could be stopped and nitro-glycerine 1 mcg/kg/min iv was started (Table 2).

Table 1: Patients characteristics

Nr	Age	Weight (kg)	Diagnosis and time to LVAD	cause	other diseases
1	11m	9	DCM 5 w	virale	Sick Euthyroid syndrome
2	7y	15	DCM 8 m	idiopathic	Asthma
3	10y	23	DCM 16 m	idiopathic	
4	12 m	8	DCM	idiopathic	
5	4y	11	DCM 2 y	idiopathic	congenital hypothyroid
					PDA: catheter closure

Table 2: Pump settings when successfully weaning from CPB

Nr	Pharmaco support needed for successful weaning of CPB	LVAD Levitronix	Cardiac Output	mean arterial pressure	RVAD Levitronix	right atrial pressure	Blood gases (kPa)	Calcutated CO	Flow velocity PW Doppler m/s outflow cannula
1	Dobu 9 mcg/kg/min	1900 rot/min	0,8 l/min	70 mmHg	--	12 mmHg	pH 7,40	1.0 l/min	1.8
	Milrinone 0.55mcg/kg/min						pCO2 4,7		
	NA 0,6 mcg/kg/min						pO2 20,2		
	Inhaled NO 15 ppm								
2	Dobu 7,5 mcg/kg/min	2200 rot/min	2,2 l/min	80 mmHg	2,0 l/min	16 mmHg	pH 7.41	1.7 l/min	1.6
	Nitroglycerin 1 mcg/kg/min						pCO2 4.84		
	Inhaled NO 20 ppm						pO2 30		
3	Dobu 10 mcg/kg/min	2000 rot/min	1,6 l/min	60 mmHg	--	15 mmHg	pH 7,35	2.2 l/min	1.4
	Milrinone 1,0 mcg/kg/min						pCO2 5,3		
	NA 0,08 mcg/kg/min						pO2 30,1		
	Inhaled NO 15 ppm								
4	Dobu 3 mcg/kg/min	2100 rot/min	1,0 l/min	70 mmHg	--	12 mmHg	pH 7,41	1.0 l/min	1
	NA 0.02 mcg/kg/min						pCO2 4,17		
	Inhaled NO 20 ppm						pO2 43,8		
5	Dobu 5 mcg/kg/min	1700 rot/min	1.6 l/min	60 mmHg	--	10 mmHg	pH 7,38	1.3 l/min	1.2
	Inhaled NO 10 ppm						pCO2 5,6		
							pO2 12,8		

In all patients cannula were orientated correctly. Flow into the apical cannula was laminar and unidirectional by means of colour, PW (Fig 3) and CW Doppler. The MOE AV LA view (Fig 3) was used to assess the positioning of the outflow cannula, by means of color, PW and CW Doppler. PW Doppler flow velocities are given in Table 2.

None of the patients had RL shunt with concomitant systemic desaturation (4). Also none of them had AI or MS, which could have worsened the emptying of the LV and the latter also limiting filling of the LV. We observed no air entering from the sewing ring around the apex cannula when the Levitronix pump kept pumping after LV collapse (4).

All patients maintained a haemodynamically stable condition during transport to the Intensive Care Unit. Four patients remained haemodynamically stabilised with the Levitronix pump and could later on be switched to a definitive Berlin Heart Excor ventricle between two and six days. Unfortunately patient 2 died after six days due to intractable pulmonary haemorrhage in severely damaged lungs.

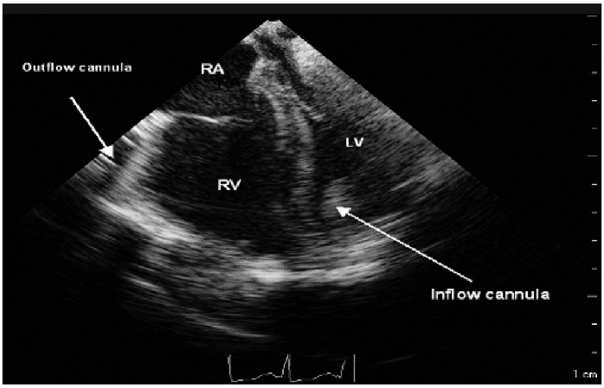

Figure 2: MOE 4-chamber view of dilated RV, collapsed LV and outflow cannula in the LV apex.

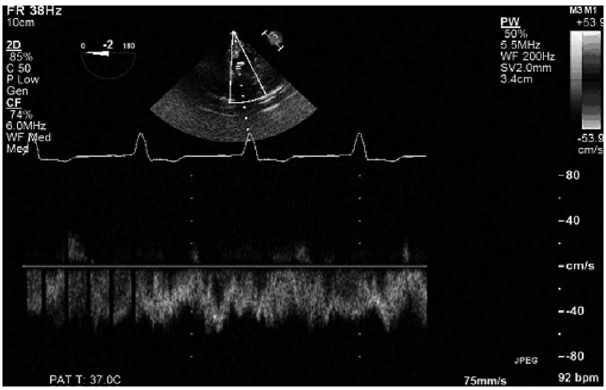

Figure 3: PW Doppler of the inflow cannula in the LV apex.

DISCUSSION

In our center a Levitronix Centrimag pump is used as an intermediate LVAD device for haemodynamic stabilisation in children with therapy resistant heart failure. The Berlin Heart Excor LV inflow cannula is implanted in the left ventricular apex while a Berlin Heart Excor outflow cannula is anastomosed with the ascending aorta. Both cannulae are connected to a LVAD centrifugal pump, which provides continuous flow. The use of a LVAD centrifugal pump, connected to Berlin Heart Excor cannulae, is reported as an attractive combination as bridge to bridge, for three main reasons. First for financial reasons: for a pediatric LVAD programme a range of different sized Berlin Heart systems should be readily available on the shelf, the initial investment is easily between € 350 000 and € 400 000, on the other hand by connecting the cannulae of the Berlin Heart Excor System to a Levitronix pump only the cannulae and one size of Levitronix pump have to be available minimising the investment (5).

The switch from Levitronix to the Berlin Heart Excor System (stop-clamp-disconnect-connect-start) took less then one minute. Secondly as bridge to decision for severely sick patients (5) and finally because of reduced bleeding complications: we start anti-coagulation when bleeding is less then 1 ml/kg/min for three hours with heparin to target activated clotting time (ACT) level (140-160 sec), while in the Deutches Herz-centrum in Berlin heparin is started 8-12 hours post-operative. When a patient is still bleeding, surgical intervention is considered (6). Besides the hemorrhage from the right lung, which we considered as an intrinsic pulmonary problem, we did not face bleeding problems during six days of support.

In all patients we were able to evaluate de-airing of the LV, in- and outflow cannula orientation, pharmacological support of RV function and LVAD settings, guided by in-traoperative TEE.

TEE is beneficial for the assessment of ventricular preload and function (7,8). In Table 2 right atrial pressures (RAP) are listed when weaning from CPB was successful. The varia-tion in RAP makes it difficult to use a predefined RAP as a target for optimal preload.

We chose not to use Left Atrial Pressure (LAP) catheter. Although LAP can be useful, we prefer echocardiography (Trans Thoracic Echocardiography at ICU) because of the additional information concerning cannulae positioning and because of the avoidance of the small bleeding risk when removing LAP catheter.

RV function is a critical factor in LVAD function because adequate LVAD support must be warrented by adequate transpulmonary blood flow (9). Because the ventricles are in-series the output of one ventricle is the input of the other (9), maximal RV output could be measured with the LVAD Levitronix pump and TEE. When the LVAD Levitronix pump output was set too high the RV dilated because right ventricular function then was unable to drain the venous return and subsequently LV collapsed, because of the misbalance between input and output. In all cases TI occurred during RV failure and RV dilation. An estimate of RV and pulmonary artery pressures (PAP) can be obtained from tricuspid velocity measurements, but unfortunately in all 5 patients the angle between the regurgitation jet and the Doppler signal was > 30º, which makes PAP estimation unreliable. Intraoperative multiplane TEE is usefull to distinguish between RV failure and mechanical problems due to the position of the in- or outflow cannula (table 3).

Table 3: Echocardiographic checklist in case of LVAD problems.

Echocardiographic checklist in case of LVAD problems
1. Cannulae malpositioning
2. RV failure
3. Pulmonary Hypertension
4. Underfilling

Inflow obstructions are described in adults during circulatory support; echo shows aliased flow at the cannula orifice with high velocities (>2.3 m/s in adults) (4). Cannula kinking causes the loss of Doppler signal in any echo views (9). A laminar flow through inflow and outflow cannulae of the LVAD is essential for its function. The outflow cannula in the ascending aorta can be visualized with TEE, in a MOE AV LA view at a multiplane angle of 120° (Figure 3), which gives a perfect alignment from the outflow cannula and the Doppler signal. In contrast with adults the deep transgastric AV long axis view was not needed in children to evaluate the outflow cannula orientation. The inflow cannula placed in the LV apex can be visualised in the MOE 4-chambre view (Figure 4), also providing a perfect alignment between inflow cannula and Doppler signal. Correctly orientated cannulas are assessed by color, PW and CW Doppler. A continuous unidirectional low-velocity flow is considered to be related with a correct orientation of the cannula.

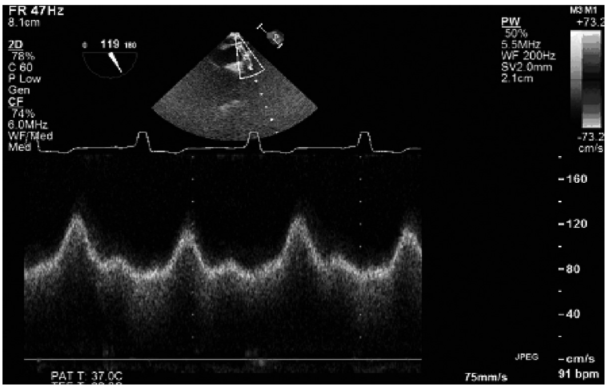

Figure 4: PW Doppler in the outflow cannula in the Ascending Aortic in a MOE long-axis view at a multiplane angle of 120°.

Transesophageal echocardiographic examination includes also checking for RL shunts, which lead to concomitant systemic desaturation. AI, which limits the emptying of the LV and MS limiting LV filling, are also examined by TEE. At the Erasmus MC we use an Oldelft micromultiplane probe for intraoperative TEE in children (1). With this probe complete TEE examinations are feasible in paediatric patients above 2.5 kg. Therefore we were able to do an intraoperative TEE assessment in LVAD and RVAD procedures in children.

We conclude that intraoperative multiplane TEE is clearly beneficial for the simultaneous visualisation of the complex interaction of the right- and LV function, correct positioning of the cannulae and the effect of device settings on right and left heart function during LVAD implantation in children with end-stage cardiac failure.

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Chapter 5

Rapid method for intraoperative assessment of aortic coarctation using three-dimensional echocardiography

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ABSTRACT

Background: The availability of three-dimensional (3D) echography with its multiplanar review analysis software on board now allows detailed examination in assessing morphological details. We evaluated the feasibility of 3D echography in assessing intraoperative morphological details of aortic coarctation (CoA) and its repair.

Methods and Results: Nine consecutive children scheduled for surgery of aortic coarctation were intraoperatively evaluated. Intra-operative 3D data sets were taken and analyzed online before resection of the coarctation, showing the cross sectional area (CSA) of the proximal aorta, coarctation and the distal descending aorta. After resection of the coarctation and extended end-to-end anastomosis, a 3D dataset was recorded to analyze the CSA of the anastomosis.

In nine out of nine consecutive procedures, intraoperative 3D echography permitted comprehensive viewing and measuring of aortic CoA and its repair. In three out of nine surgical procedures, intraoperative 3D echography provided additional information to support surgical decision-making.

Conclusion: Intraoperative 3D echography is a feasible noninvasive imaging modality for intraoperative assessment of CoA and its repair, which provides useful additional information.

INTRODUCTION

Several recent studies have shown that CoA should be considered as a complex cardiovascular syndrome rather than an isolated narrowing at the aortic isthmus (1-3). In their long-term assessment of 404 patients with CoA after surgical repair Hagar et al. (2) showed that repair of the CoA should not only consent of removal of the stenosis properly but also of preservation of the compliance of the aorta by end-to-end anastomosis as first choice of reconstruction (4) and secondly even residual gradients of 20 mm Hg or less should be treated as they significantly contribute to hypertension. The actual recommendation in the European Society of Cardiology guidelines for removal of restenosis is, however, a residual systolic blood pressure (BP) gradient at the coarctation site of greater than 30mm Hg (5).

There is controversy about the accurate assessment of the haemodynamic significance of blood flow obstruction caused by restenosis after CoA repair (6). It has been shown that after CoA repair, the arm–leg BP difference may not represent the haemodynamic significance of restenosis. At one end of the spectrum, the arm–leg BP difference may be increased by residual changes in the sympathetic regulation of BP after CoA repair (7). This may create a BP gradient in the absence of restenosis. At the other end of the spectrum, the arm–leg BP difference may be decreased by collateral circulation (6). This may eliminate a BP gradient in the presence of restenosis (6).

Till today a brachial-ankle BP difference greater than 20 mmHg (2) or 30 mmHg (5) is the only intraoperative indication for residual stenosis. No feasible intraoperative visualization of a possible residual stenosis of the aorta exits, while an exact assessment of the aortic anatomy is required for an optimal surgical repair (8).

The availability of three-dimensional (3D) echography allows an intraoperative comprehensive analysis of datasets in infinite planes, and detailed examination of anatomy (figure 1) (9,10). In this report we evaluated the feasibility of 3D echography in assessing intraoperative morphological details of aorta coarctation (CoA) and its repair.

MATERIALS AND METHODS

Nine consecutive children scheduled for resection of CoA and reconstruction with extended end-to-end anastomosis were intraoperatively evaluated. Before induction of anaesthesia, all patients were monitored with right brachial non-invasive BP (NIBP) measurement. After the insertion of a peripheral venous line, general anesthesia was induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg. Patients were nasotracheally intubated and pressure controlled ventilated. Anesthesia was maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. Invasive monitoring was applied via a 20G arterial line in the femoral artery and a Foley bladder catheter.

After performing a left thoracotomy and gently holding the lung aside, the left thorax was filled with warm saline. The x7-2 matrix-array transducer (Philips, Andover, MA, USA) was placed into a sterile Latex-free transducer probe cover and then placed into the warm saline to obtain the optimal image of the aorta isthmus. An intrathoracic 3D echography of the CoA was performed with the transducer connected to an iE33 ultrasound system (Philips).

The biplane mode ensured that our transducer position was optimal. A full volume data set made up of seven sub volumes was acquired during a 10 s mechanical ventilation hold to avoid motion artifacts during acquisition. Images are analyzed on the online workstation Philips Qlab 3D quantification (3DQ) (Philips).

Intra-operative 3D data sets before resection of the CoA were analyzed with regard to the cross sectional area (CSA) of the distal transverse aortic arch, CoA, and the descending aorta. After reconstruction of the aorta an analysis was made of the CSA of the end-to-end anastomosis.

Statistical analysis

Descriptive statistics were performed with Graphpad 4.0 software package (Graphpad software Inc. San Diego, USA).

RESULTS

Nine consecutive infants scheduled for surgical CoA repair were evaluated. Patient's characteristics are reported in Table 1. In all patients, 3D echographic data sets were taken and analyzed intraoperatively before and after surgical repair. None of the patients were excluded. In three out of the nine surgical procedures 3D echography provided additional information to support decision-making.

In one patient with a coarctation CSA of 0.1 cm^2 (figure 2) and a brachial-ankle BP difference of 35 mmHg, a postcorrection anastomosis CSA of 0.05 cm^2 and the brachial-ankle BP difference of only 30 mmHg were found in relation to a thrombus in the descending aorta. After thrombectomy and additional resection of 1.5 mm both proximaly and distally the anastomosis CSA was 0.16 cm^2 and brachial-ankle BP difference was 19 mmHg.

In a second patient the brachial-ankle systolic BP difference was 60 mmHg after end-to-end anastomosis, which was confirmed by a 3D echo CSA measurement of the anastomosis of 0.07 cm^2. After reanostomosis the CSA was 0.18 cm^2 and brachial-ankle pressure gradient (PG) was 15 mmHG.

In a third patient with a pre-operative brachial-ankle systolic PG of 70 mmHg an invasive arterial line was placed in the right femoral artery (no pulsations, good oxygenated blood aspiration) after induction of general anesthesia. Indeed the brachial NIBP was 92/45 mmHg and invasive femoral artery systolic BP was 20mmHg. Because of easy aspiration of oxygenated blood we assumed a correct positioning of the femoral artery line. After resection of the coarctation (CSA 0.05 cm^2) and extended end-to-end anastomosis femoral arterial BP was still pulse less and 20 mmHg, but 3D echography showed an adequate anastomosis with a CSA of 0.44 cm^2. Relying on the 3D echographic measurements surgery was completed. After surgery the femoral artery pulsations were good (right leg NIBP = 96/48 mmHg) and the femoral artery line was removed.

Descriptive statistics of CSA of aortic coarctation, proximal aorta, anastomosis and the distal aorta are shown in figure 3.

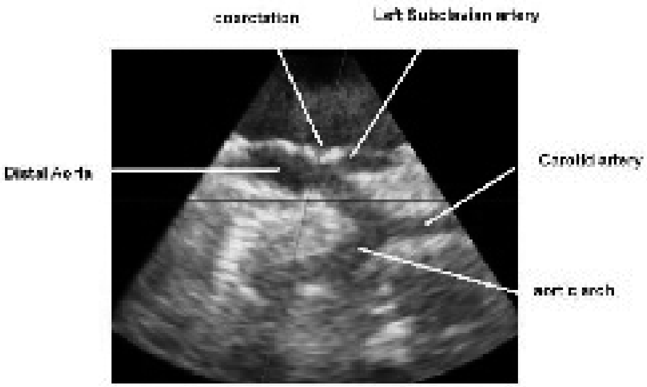

Figure 1: Multiplanar review slice plane: aortic arch.

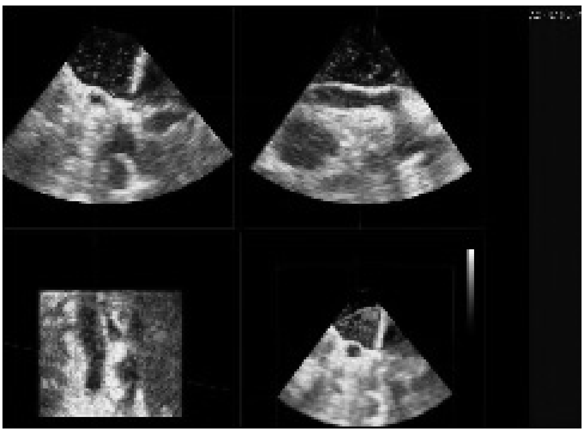

Figure 2: Three-dimensional echo cross-sectional area measurement of aortic coarcatation

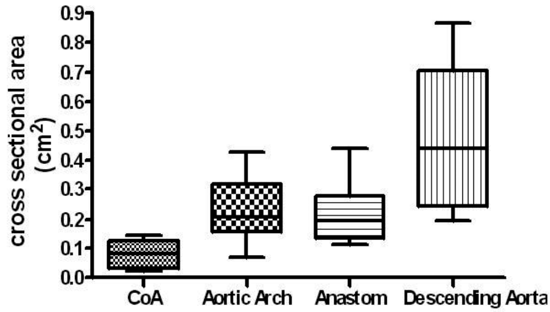

Figure 3: Three-dimensional measurement of cross-sectional area of coarctation, proximal aorta, end-to-end anastomosis and distal aorta

Table 1: Patient's characteristics

nr	assoc patho	gender	age	weight (kg)
1		f	3w	4
2	bicuspid AV	m	3w	3.7
3	Turner, bicuspid AV	f	6m	6.5
4		f	12d	3.1
5		m	2y	13
6		m	2y	12.8
7		m	6w	4
8	bicuspid AV	f	3.5y	14.5
9		f	3.5y	14.5

DISCUSSION

Multiplanar review (MPR) analysis of 3D data sets is a sensitive and accurate mode for delineation of morphological details, providing additional information to 2D echography (9). The MPR mode allows the operator to view the moving 3D data set in three orthogonal planes simultaneously and to review the image in infinite planes by moving each of the three planes through the data set. Each plane is referenced in each of the other two planes being simultaneously viewed, allowing anatomical structures to be examined in their entirety in 3D. This has an advantage over 2D echocardiography, in that the anatomical structure is not examined in fixed single planes, with detail missing between the planes viewed, but can be examined completely by moving each plane gradually throughout the data set (9). Acquiring and analyzing a 3D data set in the MPR mode took no more than 2 min. Position and CSA of CoA and its repair were clearly visualized and measured by MPR in all nine patients.

Till today, the difference in systolic pressure between arm and ankle has been widely used clinically to predict the central aortic pressure difference, with an intraoperative brachial-ankle BP difference greater than 20 mmHg (2) or 30 mmHg (5) giving an indication of residual stenosis. However, realizing that the pressure difference across a constriction is related to flow the accuracy of this test has been debated, because aortic blood flow depends on cardiac output (11). Evaluations of CoA repair should preferably contain not only haemodynamic (11) but also anatomical information (8) to achieve the highest possible diagnostic accuracy, given a re-intervention rate of up to 16.6% (3). In our series, in nine out of nine surgical procedures intraoperative 3D echography permitted comprehensive viewing and measuring of CoA and its repair and in three out of nine surgical procedures, intraoperative 3D echography provided additional information to support intraoperative decision-making.

CONCLUSION

Intraoperative 3D echography permitted comprehensive 3D viewing and measuring of CoA, aorta arch, anastomosis and descending aorta, revealing their exact CSA. In our opinion, 3D echography is a feasible and non-invasive imaging modality for intraoperative assessment of coarctation repair, providing useful additional information to support intraoperative decision-making. Further investigation for defining the exact clinical value of 3D echography during aortic CoA repair is mandatory.

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Chapter 6

Measurement of end-expiratory lung volume in intubated children without interruption of mechanical ventilation

Bikker IG, Scohy TV, Ad J J C Bogers, Bakker J, Gommers D.

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ABSTRACT

Purpose: Monitoring end-expiratory lung volume (EELV) is a valuable tool to optimize respiratory settings that could be of particular importance in mechanically ventilated pediatric patients. We evaluated the feasibility and precision of an intensive care unit (ICU) ventilator with an in-built nitrogen washout/washin technique in mechanically ventilated pediatric patients.

Methods: Duplicate EELV measurements were performed in 30 patients between 5 and 43 kg after cardiac surgery (age, median + range: 26, 3-141 months). All measurements were taken during pressure-controlled ventilation at 0 cm H_2O of positive end-expiratory pressure (PEEP).

Results: Linear regression between duplicate measurements was excellent (R^2 = 0.99). Also, there was good agreement between duplicate measurements, bias ± SD: -0.3% (-1.5 mL) ± 5.9% (19.2 mL). Mean EELV ± SD was 19.6±5.1 mL/kg at 0 cm H_2O PEEP. EELV correlated with age (p<0.001, r 0.92, R^2 0.78), body weight (p<0.001, r 0.91, R^2 0.82) and height (p<0.001, r 0.94, R^2 0.75).

Conclusion: This ICU ventilator with an in-built nitrogen washout/washin EELV technique can measure EELV with precision, and can easily be used for mechanically ventilated pediatric patients.

INTRODUCTION

Monitoring end-expiratory lung volume (EELV) might be a valuable tool to optimize respiratory settings in anesthetized ventilated patients [1]. General anesthesia is known to promote lung volume reduction, which promotes atelectasis, lung compliance, and arterial oxygenation [2]. In children, decreased lung volume is of special importance due to the lower elastic retraction forces and a lower relaxation volume, which makes them more prone to airway collapse [3,4] . Furthermore, EELV has been described as one of the variables known to adequately assess mechanical characteristics of the ventilated lung [5].

However, determining EELV in ventilated patients is not without difficulty. EELV can be measured with computer tomography [6,7], but this technique is not available for routine measurements. Traditionally, EELV measurement techniques are based on dilution of tracer gases, like sulfur hexafluoride washout [8,9], closed circuit helium dilution [10], or open-circuit multibreath nitrogen washout [11-13]. All these techniques require expensive and/or complex instrumentation, and are generally not suitable for routine EELV measurements during surgery and in the intensive care unit (ICU). An alternative is the simplified helium dilution method, using a re-breathing bag with a helium mixture. However, an important disadvantage of this latter technique is the interruption of mechanical ventilation for a short period of time [14].

Recently, Stenqvist et al. [15] introduced a novel method to measure EELV without interruption of mechanical ventilation, based on a simplified and modified Multiple Breath Nitrogen Washout (MBNW) technique, which is integrated within a mechanical ventilator. This method requires a step change in the inspired oxygen fraction (FiO_2), without the need for supplementary tracer gases or specialized additional monitoring equipment [15]. Although this method has been successfully applied in adult ventilated patients at the ICU and whilst undergoing surgery [15-17], no data regarding feasibility and precision exist for mechanically ventilated pediatric patients.

Therefore, we evaluated the feasibility and precision of this MBNW device to measure EELV during mechanical ventilation of pediatric patients after cardiac surgery.

METHODS

After approval of the local institutional human investigations committee, 30 mechanically ventilated children were enrolled in the study. All patients underwent cardiac surgery for congenital heart repair, and received postoperative mechanical ventilatory support in the ICU. Exclusion criteria were: severe cardiovascular instability, thoracic deformations, and residual intracardiac shunt postoperatively evaluated by transesophageal echocardiography (TEE).

EELV measurements were carried out with the COVX module (GE Healthcare, Helsinki, Finland) integrated within the ventilator. This module has been described in detail earlier [15]. Briefly, O_2 and CO_2 are measured with standard clinical sensors and the residual N_2 as remaining ventilator air is calculated. A step change in the N_2 concentration is induced by changing FiO_2. The N_2 volume change and N_2 fraction change is measured with the COVX module integrated in the Engström Carestation ventilator and EELV is calculated.

Patients were nasotracheally intubated with a cuffed Hi-Contour pediatric endotracheal tube (Mallinckrodt) and anesthesia was maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. During the operation, patients were ventilated in pressure-controlled mode at the following settings: tidal volume of 6-8 mL/kg, frequency adjusted to maintain a $PaCO_2$ level between 4.5 and 5.5 kPa, positive end-expiratory pressure (PEEP) of 8 cm H_2O, I/E ratio of 1:1 and FiO_2 of 0.5. After weaning from cardiopulmonary bypass (CPB), the lungs were routinely re-expanded by a recruitment maneuver (RCM) and mechanical ventilation was continued with the same settings as before CPB. Once admitted to the ICU, mechanical ventilation was continued with the same settings as before transportation except for the FiO_2, which was set at 0.40 or 0.45. FiO_2 was decreased because the measurement requires a FiO_2 step change and becomes less precise at a FiO_2 above 0.65, according to manufacturer's specifications. Patients were sedated by midazolam intravenously (0.1 mg/kg/h) and morphine (10 mcg/kg/h).

After stabilization at the ICU, EELV was measured twice (washout and washin) with the COVX module by nitrogen washout/washin with first an incremental and second a decremental FiO_2 step of 0.2 at a PEEP of 0 cm H_2O. This measurement was repeated after 10 min. Before measurements, hemodynamic and ventilatory parameters were recorded and arterial blood gas analysis was performed.

Statistical analysis

Statistical analysis was performed with Graphpad software package (version 5.0, Graphpad Software Inc., San Diego, USA). Results are expressed as mean ± SD for normally distributed data and median and interquartile range (IQR) for not normally distributed data. The Shapiro-Wilk normality test was used to evaluate the distribution of all data. Agreement between duplicate measurements was analyzed using Spearman correlation and Bland-Altman's analysis [18]. For all comparisons, $p < 0.05$ was considered significant.

RESULTS

In the present study, 30 mechanically ventilated patients were examined; Table 1 presents demographic data and main physiologic characteristics. All patients were studied after congenital cardiothoracic surgery and tolerated the procedure well. Repairs included closure of ventricular septal defect (7), closure of atrial septal defect (8), correction of tetralogy of Fallot (3), repair of subpulmonary stenosis (3) and subaortal stenosis (2), pacemaker implantation (1) and total cavopulmonary connection (6). The hemodynamic and ventilatory parameters before the measurements at 0 cm H_2O PEEP are provided in table 2.

Linear regression between duplicate EELV measurements (as average of washin/washout) measured with the nitrogen washin/washout technique was performed. Duplicate measurements were highly correlated (p<0.001, r = 0.99, R^2 = 0.99). To assess the difference between the duplicate measurements a Bland-Altmann analysis was performed (Fig. 1). Bias ± SD was -0.3% (-1.5 mL) ± 5.9% (19.2 mL).

Mean EELV ± SD was 19.6±5.1 mL/kg at a PEEP level of 0 cm H_2O. Figure 2 shows the relation between EELV and patient characteristics. EELV was highly correlated with age (p<0.001, r 0.92, R^2 = 0.78), body weight (p<0.001, r = 0.91, R^2 = 0.82) and height (p<0.001, r = 0.94, R^2 = 0.75).

Table 1: Characteristics of the patient population

N	30
Gender, female/male	9/21
Age in months, (range)	26 (3-141)
Weight, kg	10.9 (8.5)
Height, m	0.87 (0.35)

Data are presented as median with interquartile range unless stated otherwise

Table 2: Hemodynamic and ventilatory parameters before EELV measurement

Heart rate (bpm)	124 (22)
Mean arterial pressure (mmHg)	65 (11)
FiO_2 (%)	41 (2)
Tidal volume (mL/kg)	7.7 (1.0)
pH	7.41 (0.05)
PaO_2 (kPa)	20.7 (7.3)
$PaCO_2$ (kPa)	4.38 (0.46)
SaO_2, (%)	98.4 (2.4)

Data are presented as mean with standard deviation unless stated otherwise

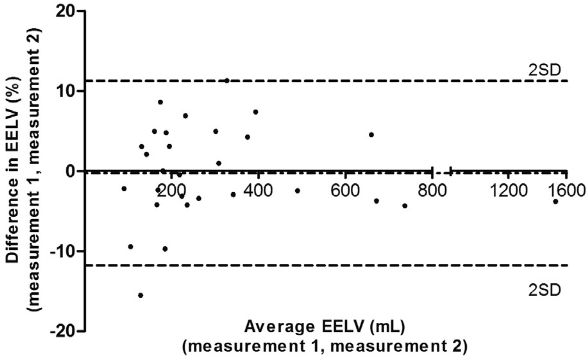

Figure 1: Bland-Altman analysis. Comparison of duplicate end-expiratory lung volume (EELV) measurements with the multibreath nitrogen washout technique. Measurements were performed in the supine position at 0 cm H2O positive end-expiratory pressure (PEEP) in mechanically ventilated pediatric patients after cardiac surgery.

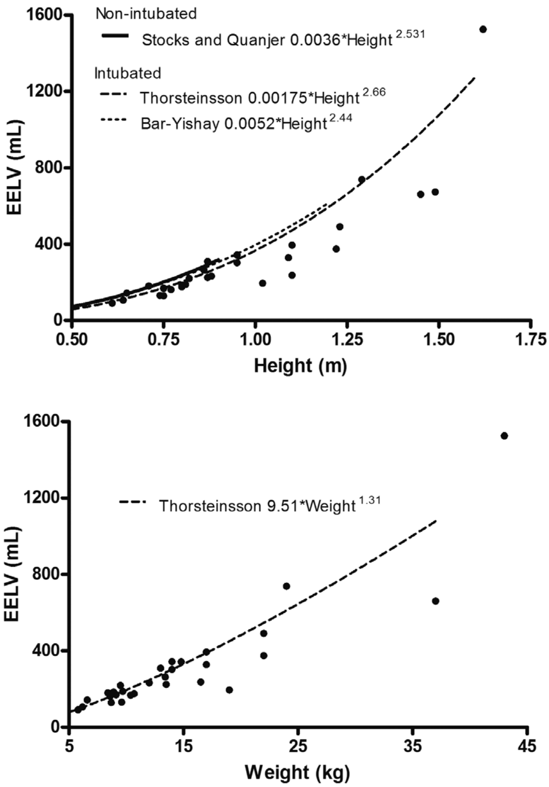

Figure 2: Relation between EELV (average of duplicates) and height or body weight. Measurements were performed in the supine position at 0 cm H2O PEEP in mechanically ventilated pediatric patients after cardiac surgery. The lines represent non-linear regression equations from non-intubated children, Stocks and Quanjer [26] and intubated children at 0 cm H2O PEEP, Thorsteinsson et al. [23] and Bar-Yishay et al. [21].

DISCUSSION

The present study shows that, in sedated mechanically ventilated pediatric patients, this non-invasive MBNW technique can easily measure EELV with good precision. We confirmed that EELV is highly correlated with the patient's height and body weight (Fig. 2).

Precise and easily performable measurements of EELV are essential in order to use this parameter to optimize respiratory settings. Although accurate and precise methods to measure EELV are available for ventilated pediatric patients, these older methods require complex equipment or tracer gases that limit their use in clinical practice [8,19]. In this study, we used an ICU ventilator with an in-built MBNW technique to measure EELV during mechanical ventilation; a good agreement was found between duplicate measurements with this device. Chiumello et al. [20] recently compared this technique with computed tomography and helium dilution in adult ICU patients and described high reproducibility between duplicate measurements (bias ± SD: 48 ± 165 mL). In our pediatric patients an even better level of precision was found: bias ± SD 1.0 % (-1.7 mL) ± 5.7% (15.5 mL).

Although accuracy was not evaluated in the present study, measured EELV was comparable to that reported in other studies [21-24]. Ungern-Sternberg et al. [24] described the effect of cardiopulmonary bypass and aortic clamping on EELV in children during mechanical ventilation with 3 cm H_2O PEEP; in their study EELV increased from 22 ± 5 to 27 ± 6 mL/kg after opening of the chest and decreased markedly to 16±5 mL/kg after closing the chest and was still reduced to 18 ± 5 mL/kg during the following 90 min. These values are comparable with our measured EELV (mean ± SD) of 19.6 ± 5.1 mL/kg. Moreover, our values are similar to those of pediatric patients during nitrous-oxide-halothane anesthesia, in which an EELV (mean ± SD) of 19 ± 6 mL/kg was found during mechanical ventilation and 22 ± 7 mL/kg during spontaneous breathing [22].

Schibler et al. [25] investigated the effect of different levels of PEEP on EELV in 22 mechanically ventilated children. At 0 cm H_2O PEEP, EELV was 20 ± 7 mL/kg, which is comparable to our results. At a PEEP of 5 and 10 EELV increased to 24 ± 8 and 28 ± 6 mL/kg, respectively. In the present study, we did not use PEEP during the measurements to allow comparison to studies in which EELV was measured without PEEP [21,23,26]. The application of PEEP is known to increase EELV and to prevent the formation of atelectasis. If higher PEEP levels were used, the EELV could be restored to above the normal values displayed in figure 2.

Among our patients, characteristics such as age, height, and body weight were highly correlated with measured EELV (Fig. 2). Our data are comparable with data from two previous studies [21,23] in which children were ventilated without the application of PEEP. Below 1 m of height or below 15 kg body weight, the agreement was excellent, but above 1 m of height most of our values were slightly below their regression equations. The reason for this is unknown. Thorsteinsson et al. [23], measured EELV directly after induction of anesthesia in healthy children and in children with cardiac anomalies, whereas we measured EELV after cardiac surgery with CPB. It is known that cardiac surgery and CBP may lower EELV [24,27]. Bar-Yishay et al. [21], measured EELV in awake children in the supine position or during ketamine anesthesia. Ketamine anesthesia is known to preserve lung function [28].

A potential limitation of the present study is that accuracy was not evaluated. However, measured values with this technique were close to those of previous studies. Another potential limitation of the used technique is the measurement of EELV in patients requiring a $FiO_2 > 65\%$. It has been suggested in the manufacturer's specifications that the accuracy error increases from 10% to 15% at a $FiO_2 > 0.65$ in adult patients. However, in the present study we only measured at a $FiO_2 < 65$. An important advantage of this method is that no tracer gases and no expensive or specialized equipment are required, bringing this parameter closer to clinical practice.

Therefore, we conclude that this nitrogen washout EELV technique can measure EELV with good precision. Especially below a height of 1 m or 15 kg body weight, our data are in good agreement with earlier comparable studies. Furthermore, this device can easily be used in mechanically ventilated pediatric patients without a tracer gas and without interruption of mechanical ventilation.

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Conflict of interest statement

The department of Intensive Care, Erasmus MC, received an unrestricted grant from GE Healthcare.

Abbreviations

CPB	Cardiopulmonary bypass
EELV	End-Expiratory Lung Volume
FiO_2	Fraction of inspired oxygen
ICU	Intensive Care Unit
NMBW	Nitrogen Multiple Breath Washout
PEEP	Positive End-Expiratory Pressure
RCM	Recruitment Manuever
TEE	Transesophageal echocardiography

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Chapter 7

Alveolar recruitment strategy and peep improves oxygenation, dynamic compliance of respiratory system and end expiratory lung volume in paediatric patients undergoing cardiac surgery for congenital heart disease.

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SUMMARY

Objective: Optimizing alveolar recruitment by alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP) allows preventing ventilator induced lung injury (VILI). Knowing that PEEP has its most beneficial effects when dynamic compliance of respiratory system (Crs) is maximized, we hypothesize that the use of 8 cm H_2O PEEP with ARS results in an increase of Crs and end expiratory lung volume (EELV) compared to 8 cm H_2O PEEP without ARS and to zero PEEP in paediatric patients undergoing cardiac surgery for congenital heart disease.

Methods: Twenty consecutive children were studied. Three different ventilation strategies were applied to each patient in the following order: 0 cm H_2O PEEP, 8 cm H_2O PEEP without an ARS and 8 cm H_2O PEEP with a standardized ARS. At the end of each ventilation strategy, Crs, EELV and arterial blood gases were measured.

Results: EELV, Crs and PaO_2 / FiO_2 ratio changed significantly ($p < 0.001$) with application of 8 cm H2O + ARS. Mean $PaCO_2$ - $PETCO_2$ difference between 0 PEEP and 8 cm H2O PEEP + ARS was also significant ($p < 0.05$).

Conclusion: An Alveolar Recruitment Strategy with relative high PEEP significantly improves Crs, oxygenation, $PaCO_2$ - $PETCO_2$ difference and EELV in pediatric patients undergoing cardiac surgery for congenital heart disease.

Implication statement

The use of 8 cm H_2O PEEP with alveolar recruitment strategy (ARS) would result in an increase of dynamic compliance of respiratory system (Crs), EELV and oxygenation compared to 8 cm H_2O PEEP without ARS and to 0 cm H_2O PEEP (ZEEP), in pediatric patients undergoing cardiac surgery for congenital heart disease.

BACKGROUND

General anaesthesia is known to promote atelectasis, which leads to reductions in lung volume, lung compliance and arterial oxygenation [1]. The goal of mechanical ventilation is to establish an acceptable level of gas exchange, while preventing ventilator induced lung injury (VILI). VILI are prevented by preventing repetitive re-opening of atelectatic lung areas and thus by decreasing alveolar stress [2]. Optimizing alveolar recruitment by alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP) allow to prevent lung injury by decreasing alveolar stress [3-5].

In infants and children there we found only two studies reporting on ARS on normal lungs [4,6]. Tusman et al. used ARS to open up the lung and used PEEP of 5 cm H_2O to keep the lung open showing less atelectasis on magnetic resonance imaging [4]. Marcus et al. used only ARS (no PEEP) and showed an increase in compliance for 7 minutes [6]. In their animal (Adult New-Zealand Rabbits) study (lung lavage model), Rimensberger et al [7,8] showed that ventilation after ARS of 30 cm H_2O boosted ventilatory cycle onto the deflation limb of the pressure/volume (PV) curve, when a PEEP of 8 cm H_2O was used. This ARS resulted in a significant increase in end-expiratory lung volume (EELV), oxygenation and dynamic compliance despite equal PEEP levels used before and after ARS.

Knowing that PEEP has its most beneficial effects when dynamic compliance is maximized [9], we hypothesize that the use of 8 cm H_2O PEEP with ARS would result in an increase of Crs, EELV and oxygenation compared to 8 cm H_2O PEEP without ARS and to zero cm H_2O PEEP (ZEEP), in pediatric patients undergoing cardiac surgery for congenital heart disease.

METHODS

After obtaining approval from the local ethics committee and obtaining parental informed consent, 20 consecutive children scheduled for cardiac surgery for congenital heart disease were included. We included infants after cardiac surgery for congenital heart disease, infants without any residual intracardiac shunt, who needed post-operative mechanical ventilatory support at the ICU. The exclusion criteria included: a) residual intracardiac shunting evaluated by transesophageal echocardiography (TEE), b) hemodynamic instability defined by > 5mcg/kg/min dobutamine, c) rhythm other than sinus rhythm, d) valve regurgitation evaluated by TEE and e) respiratory failure defined by a FiO2 > 0.8.

Before induction of anesthesia, all patients were monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. After the insertion of a peripheral venous line, general anesthesia was induced with midazolam 0.2 mg/kg, sufentanil 2 mcg/kg and pancuronium 0.15 mg/kg. Patients were nasotracheally intubated with a cuffed Hi-Contour paediatric endotracheal tube (Mallinckrodt, Athlone, Ireland) and pressure controlled ventilated (PCV) using a Engstrom Carestation ventilator (GE Healthcare, Helsinki, Finland). Anesthesia was maintained with midazolam 0.1 mg/kg/h and sufentanil 1 mcg/kg/h. Invasive monitoring via 20G arterial line in the femoral artery, an internal jugular central venous catheter, a Foley bladder catheter, a rectal temperature probe and the Oldelft MicroMultiplane TEE probe (Oldelft, Delft, The Netherlands) connected to a iE33 (Philips, Andover, MA, USA) were routinely inserted [10]. Mechanical ventilation was performed at the following settings (tidal volume of 8 ml/kg, frequency adjusted to maintain a $PaCO_2$ level between 4.5 and 5.5 kPa, PEEP of 8 cm H_2O and I/E ratio 1/1). No additional catheters were inserted. During CPB, CPAP was applied at a level of 8 cm H_2O. After weaning from CPB, the lungs were re-expanded by an ARS: peak airway pressure of 40 cm H_2O, PEEP of 8 cm H_2O for 5 consecutive mechanical breaths with I/E ratio 1/1, which was sufficient to recruit all of the visible atelectasis before closure of the thorax. Mechanical ventilation was continued with the same settings as before cardiopulmonary bypass. The existence of any residual intra-cardiac shunt was ruled out by TEE [10]. At the end of the operation the patients were disconnected from the ventilator and ventilated by hand bagging during transport to the ICU. Once admitted at the ICU, an ARS as used intraoperatively was performed and mechanical ventilation was continued with the same settings as before transportation. Patients were sedated by midazolam intravenously (0.1 mg/kg/h) and morphine (10 mcg/kg/h).

After arrival at the ICU, 3 different ventilation strategies were applied to each patient in the following order: 0 cm H_2O PEEP, 8 cm H_2O PEEP without an ARS and 8 cm H_2O PEEP with a standardized ARS. The ARS was performed as intraoperatively [4]. Each ventilation strategy commenced after disconnection from the ventilator for 15 seconds, which has been shown to result in immediate lung collapse [4], and was applied for 20 minutes. At the end of each ventilation strategy: Crs (ml/kg/cm H_2O), EELV as determined with a COVX module integrated in the ventilator (GE Healthcare, Helsinki, Finland) and arterial blood gases were measured. Measurements of EELV were obtained by multiple breath nitrogen washout technique. This equipment has been described in detail earlier [11].

Fluid management during the study was guided clinically, if right atrial pressure (RAP) and blood pressure (BP) raises while compressing the liver manually the patients were considered hypovolemic. Hypovolemia was treated with gelofusine bolus 5 ml/kg. This action was repeated until BP stayed stable and only RAP raised during manual liver compression.

After each ventilator setting we specially looked for air leakage in the thoracic drainage systems.

Statistical analysis

Statistical analysis was performed with Graphpad 5.0 software package (Graphpad software Inc. San Diego, CA, USA). Results are expressed as mean ± SD for normal distributed data and median + interquartile range (IQR) for not normally distributed data. The Shapiro-Wilk normality test was used to evaluate the distribution of all data. To compare EELV, compliance and PaO_2 / FiO_2 ratio, values were normalized to 0 cm H_2O PEEP. Repeated measures ANOVA with Bonferroni's post hoc analysis was used to test whether the normalized: EELV, compliance and PaO_2 / FiO_2 ratio were different at the used PEEP levels. A $p < 0.05$ was considered to represent a significant difference.

RESULTS

Twenty consecutive mechanically ventilated pediatric patients after cardiac surgery were studied. None of the patients met any exclusion criteria. The main demographic data are reported in Table 1. Surgery included the correction of ASD (5), VSD (4), Subvalvular PS after TOF (3), TOF (2), SVD (2), Subvalvular AS (1), aortic coarctation (1), DCRV (1) and PM implantation (1). In all patients EELV, Crs and blood gases were collected. None of the patients were excluded.

Table 1: Patients demographics

N	20
Gender, female/male	6/14
Age, months (median + range)	34 (3 - 132)
Weight, kg (median + range)	10.1 (8.8 – 15.5)
Length, m (median + range)	0.85 (0.75 – 1.07)

Descriptive statistics of EELV/kg (Figure 1), Crs (Figure 2) and PaO_2 / FiO_2 ratio (Figure 3) are shown for the three measured PEEP levels: 0 cm H_2O (0), 8 cm H_2O (8) and 8 cm H_2O + ARS (8+ARS). Data are normalized to values at 0 cm H_2O PEEP (0 PEEP = 100%).

Median EELV/kg increased from 18.65 ml (IQR 15.95 – 21.45) to 28.55 ml (IQR 23.40 – 31.45) while increasing PEEP from 0 to 8 cm H_2O and with the application of an ARS, median EELV/kg increased to 34.95 ml (IQR 28.60 – 39.85). The changes from 0 to 8 ($p < 0.001$; 99 % CI –12.11 to – 6.86), from 8 to 8+ARS ($p < 0.001$; 99 % CI – 8.04 to – 2.79) and from 0 to 8+ARS ($p < 0.001$; 99 % CI –17.53 to – 12.22) were significant (Table 2).

Table 2:

	0 cm H_2O	8 cm H_2O	ARS + 8 cm H_2O
EELV (ml/kg)	18.65	28.55*	34.95*
Crs (ml/kg/cm H2O)	0.67	0.78*	0.91*
P/F ratio (kPa)	53.4	56.8	65.8*
PaCo2 - PETCO2	0.24	0.22	0.12*

* = Significant compared to 0 cm H_2O

We also found a significant increase in median Crs that increased from 0.67 ml/kg/cm H_2O (IQR 0.59 – 0.75) to 0.78 ml/kg/cm H_2O (IQR 0.65 – 0.87) while increasing PEEP from 0 to 8 cm H_2O ($p<0.01$; 95 % CI –22.48 to –2.92) and with the application of an ARS, median Crs increased to 0.91 ml/kg/cm H_2O (IQR 0.77 –1.06) (between 8 and 8+ARS: $p < 0.001$; 95 % CI –31.43 to –11.87). Between 0 and 8 +ARS $p < 0.001$ (95 % CI –44.13 to –24.57) (Table 2).

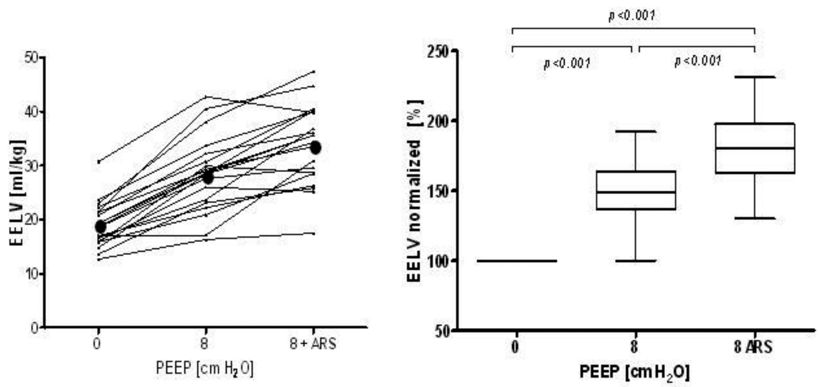

Figure 1: EELV/kg versus PEEP

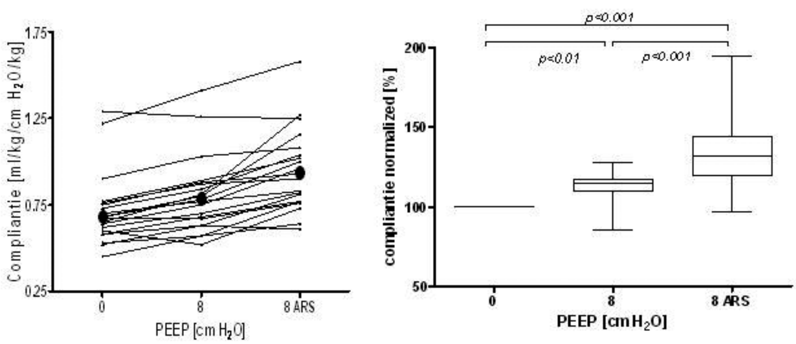

Figure 2: Crs versus PEEP

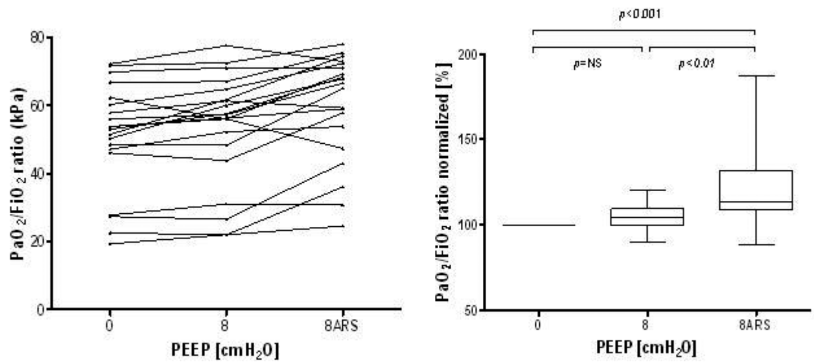

Figure 3: PaO2/FiO2 ratio versus PEEP

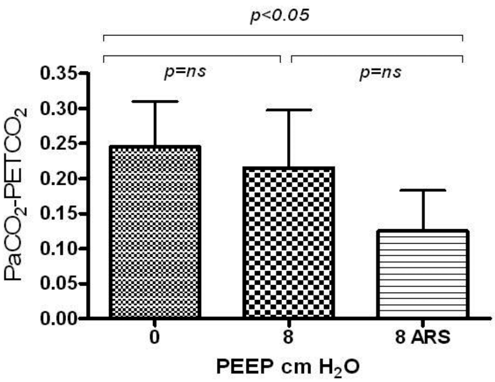

Figure 4: PaCO2 – PETCO2

Median PaO_2 / FiO_2 ratio increased from 53.4 kPa (IQR 46.5 – 61.3) to 56.8 kPa (IQR 46.5 – 63.3) while increasing PEEP from 0 to 8 cm H_2O (p = NS) and with the application of an ARS, median PaO_2 / FiO_2 ratio increased to 65.8 kPa (IQR 50.5 – 71.70)($p < 0.01$, 95 % CI −26.73 to −5.96). Between 0 and 8 +ARS $p < 0.001$ (95 % CI −31.58 to −10.82) (Table 2).

Mean $PaCO_2$ - $PETCO_2$ differences (Figure 4) decrease from 0.24 kPa (SD 0.29) to 0.22 kPa (SD 0.37) while increasing PEEP from 0 to 8 cm H_2O (p = NS) and to 0.12 kPa (SD 0.26) with an ARS (p=NS) (Figure 4), the difference between 0 and 8+ARS was significant (p = 0.014; 95 % CI 0.026 to 0.213) (Table 2).

We found no significant differences in heart rate (HR), mean arterial pressure (MAP) and right atrial pressure (RAP) between the three strategies. Mean HR, RAP and MAP in the 0 cm H_2O group were 123 beats/min (SD 21.2), 9.64 mmHg (SD 4.16) and 64.3 mmHg (SD 10.3). In the 8 cm H_2O group mean HR, RAP and MAP were respectively 123 beats/min (SD 21.5), 11.1 mmHg (SD 4.2) and 66.5 mmHg (SD 9.6). In the 8+ARS group, mean HR, RAP and MAP were respectively 123 beats/min (SD 22.8), 10.8 mmHg (SD 4.2) and

69.2 mmHg (SD 13.3). Eleven patients received 1 fluid bolus and 9 patients received 2 fluid boluses when applying 8 cm H_2O. After ARS + 8 cm H_2O, 8 patients received 1 fluid bolus.

None of the patients had air leakage on any moment.

DISCUSSION

We applied ARS and 8 cm H_2O PEEP in 20 infants without apparent lung disease after cardiac surgery for congenital heart disease and obtained significantly improved dynamic compliance of respiratory system (Crs), EELV, and oxygenation compared to 8 cm H_2O PEEP without ARS and compared to zero PEEP. There were no statistical significant changes in any of the other hemodynamic measurements.

The principal objective of the ventilatory management of acute lung injury is to maintain an acceptable gas exchange without inflicting additional lung damage [8]. The key elements of such a lung protective approach are to limit lung over-distention and to maintain sufficient EELV to prevent alveolar collapse [8].

The significant simultaneous increase of EELV and Crs observed during ARS + PEEP compared to PEEP alone are due to the extra recruitment of collapsed alveoli. If ARS + PEEP would preferentially over-distend aerated alveolar units before expanding collapsed areas, it would cause only an increase of EELV and Crs would remain unchanged or even decrease. An increase of EELV after enhancing the total airway pressure is to be expected and carries the risk of hyperinflating the lungs, but an increase of both, Crs and EELV, indicates that there is no over-distention.

The significant ($p < 0.05$) decrease in $PaCO_2 - PETCO_2$ difference (Figure 4) and the significant increase in PaO_2 / FiO_2 ratio ($p < 0.001$), although clinically not relevant, indicates that there is less ventilation perfusion mismatch, shunting or both, in the 8 cm H_2O PEEP + ARS group compared to 0 cm H_2O PEEP group. Less ventilation perfusion mismatch means less atelectasis.

We optimized alveolar recruitment by ARS and maintained lung volume with adequate PEEP, hereby decreasing low volume trauma by decreasing shear stress of repetitive closing and reopening of small airways and thus preventing for VILI [3-5]. We also showed that Crs and EELV improved after 8 cm H_2O PEEP + ARS, indicating that there is no alveolar stress or over-distention which would cause large volume trauma.

Because mechanical ventilation should maximize oxygenation and minimize VILI while having the least detrimental effect on hemodynamics [9], further investigation is needed to clarify the optimal PEEP level with an ARS in children without apparent lung disease under general anaesthesia, because it is possible that a lower or higher PEEP might result in an even bigger efficacy.

CONCLUSION

Our study provides strong evidence to conclude that ARS + PEEP of 8 cm H2O significantly decreases ventilation perfusion mismatch, shunting or both and improves dynamic compliance of the respiratory system (Crs), oxygenation, and EELV. Such changes likely reduce alveolar stress and may thereby reduce the potential risk for VILI in children recovering from heart surgery.

Conflict of interest

There is no conflict of interests

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Chapter 8

Intraoperative glycemic control without insulin infusion during pediatric cardiac surgery for congenital heart disease

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Paediatr Anaesth. 2011 Apr 4. (Epub ahead of print)

ABSTRACT

Background: Many studies are reporting that the occurrence of hyperglycemia in the postoperative period is associated with increased morbidity and mortality rates in children after cardiac surgery for congenital heart disease. This study sought to determine blood glucose levels in standard pediatric cardiac anesthesiological management without insulin infusions.

Methods: The study population consisted of 204 consecutive pediatric patients aged from 3 days to 15.4 years undergoing open cardiac surgery for congenital heart disease between June 2007 and January 2009. Glucose containing fluids were not administrated intraoperatively, all patients received high dose of opioids (sufentanil 10mcg/kg) and steroids (30mg/kg methylprednisolone) iv. Glucose levels were measured before CPB, 10 minutes after initiation of CPB, every hour on CPB, post CPB and on arrival at Intensive Care Unit (ICU).

Results: Intraoperatively only 1 patient had a glucose level < 50 mg/dl (=34.2 mg/dl), 57/204 patients (27.9%) had at least one intraoperative glucose > 180 mg/dl, but only 12 patients (5.8%) had a glucose level > 180 mg/dl at ICU arrival. 30 days mortality was 1.5% (3/204).

Younger age, lower body weight and lower CPB temperature were associated with hyperglycemia at ICU arrival, as were higher RACHS and Aristotle severity scores.

Conclusion: A conventional (no insulin, no glucose) anesthetic management seems sufficient in the vast majority of patients (96.5%). Special attention should be paid to small neonates with complex congenital heart surgery, in whom insulin treatment may be contemplated

BACKGROUND

Several studies report that the occurrence of hyperglycemia in the postoperative period is associated with increased morbidity and mortality rates in children after cardiac surgery for congenital heart disease [1-4]. However, no association with intraoperative management or complexity of congenital heart disease has yet been assessed.

Lately there is concern that glycemic control in the peri-operative period, aiming at avoiding hyperglycemia while maintaining a strict euglycemic target, could place patients at risk for hypoglycemia and hereby enhance the risk for adverse outcome [1,2,5-7]. In addition, the NICE-sugar Study [6] found that postoperative intensive glucose control (81 to 108 mg/dl; 4.5 to 6.0 mmol/l) increased mortality and a moderate blood glucose target <180mg/dl (<10mmol/l) resulted in lower mortality in adults.

Infants often have reduced glycogen reserve, especially in the setting of physiological stress, and insulin therapy in this setting may place them at risk for developing hypoglycemia [8]. To our knowledge there is only one published report on adverse outcome and intraoperative glucose levels during complex congenital heart surgery in children [2].

In this light we report on our pediatric cardiac anesthesiological management and the blood glucose levels in 204 consecutive children during open cardiac surgery for congenital heart disease, exploring the association between blood glucose and complexity of congenital heart disease patient and preoperative characteristics.

METHODS

The study population consisted of 204 consecutive pediatric patients aged from 3 days to 15.4 years undergoing open cardiac surgery for congenital heart disease between June 2007 and January 2009. The Erasmus MC internal review board approved the retrospective study and the need for informed consent was waived. Pre-operatively children were not allowed any food at least four hours before induction of anesthesia, but were allowed glucose containing clear liquids until two hours before anesthesia. None of the patients received premedication. Before induction of anesthesia, all patients were monitored with a five-lead, two-channel electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. All patients without a peripheral intravenous (iv) access had an inhalation induction with sevoflurane 8%. After insertion of iv catheter, midazolam 0.3 mg/kg, sufentanil 2 mcg/kg, pancuronium 0.15 mg/kg and 40mg/kg cefazoline were administrated and sevoflurane was stopped. Patients were nasotracheally intubated and pressure controlled ventilated after an alveolar recruitment strategy [9]. Anesthesia was maintained with midazolam 0.1 mg/kg/h. Invasive monitoring via 20G arterial line in the femoral artery, an internal jugular central venous catheter, a Foley bladder catheter, a rectal temperature probe and the Oldelft MicroMultiplane TEE probe (Oldelft, Delft, The Netherlands) were routinely inserted [10].

Before incision we administered another 0.2mg/kg midazolam, 2mcg/kg sufentanil together with 30mg/kg magnesium sulfate, 30mg/kg methylprednisolone, 1 mg/kg ranitidine and 1mg/kg furosemide. All patients received a continuous infusion of NaCl 0.9% during the pre-incision period. Glucose containing fluids were not administrated intraoperatively. In case of normovolemic hypotension we administered 1 mcg/kg phenylephrine, in case of hypertension sevoflurane was used. Before initiation of CPB we administered 2mcg/kg sufentanil, 0.1 mg/kg midazolam, 300 IU heparine and 20mg/kg cefazoline,. Another bolus of 2mcg/kg sufentanil and 0.1 mg/kg midazolam was administrated during rewarming phase of CPB and dobutamine 4 mcg/kg/min was started. After declamping of the aorta enoximone 0.2mg/kg was administrated.

Pediatric CPB circuits consisted always of hollow-fiber oxygenator with hard-shell reservoir, a roller pump and arterial filter. The circuits were phosphorylcholine coated. Prime volumes varied depending on patient's body weight; for neonates and infants up to 10 kg - 300 ml, for patients up to 25 kg - 450 ml and for patients up to 45 kg – 850 ml. Prime was composed of homologous red blood cells (RBCs), fresh-frozen plasma (FFP) and Gelofusine (B.Braun, Melsungen, Germany) and was always completed with 0.5 g/kg BW mannitol, 0.5 g/kg BW human albumin 20% solution (Sanquin, Amsterdam, The Netherlands), 4.2 IU heparine / mL priming volume and 2-5 ml $NaHCO_3$ 8.4%.

Administration of RBCs, FFP, crystalloids or colloids during CPB was based upon the system working volumes and target values for hematocrit during the CPB (not lower than 0.28 L/L for acyanotic as well as cyanotic patients). Human albumin was added to maintain the COP ≥15 mmHg. In accordance with protocol no modified ultrafiltration and no antifibrinolitic medication was used.

Activated clotting time was monitored during the bypass and maintained above 480 sec. Nonpulsatile CPB, with mild hypothermia of 28 °C to 32° C, was performed with blood flow rates between 1.8 L/min/m^2 to 3.2 L/min/m^2 to maintain venous oxygen saturation above 70% and mean arterial pressure between 40 to 60 mmHg. In case of a deep hypothermic circulatory arrest (DHCA) patients were cooled till 18 ° C nasopharyngeal and 21 ° C rectal temperature. Anterograde cerebral perfusion was utilized when appropriate. During CPB α – stat regulation was employed together with target value for arterial oxygen tension of 20 kPa. Myocardial protection was achieved with non-glucose containing crystalloid cardioplegia. Cardioplegic solution was preferably sucked into the cell-saving device (CS). Perioperative blood loss was collected and processed by CS device, together with residual volume of the CPB circuit. The CS product was always considered first line blood replacement therapy.

After weaning from CPB another 2 mcg/kg sufentanil and 0.1 mg/kg midazolam was administered. All patients received a total of 10 mcg/kg of sufentanil throughout the whole surgical procedure.

Glucose levels were measured before CPB, 10 minutes after initiation of CPB, every hour on CPB, 10 minutes after administrating 4 mg/kg Protamine and on arrival at Intensive Care Unit (ICU).

In line with previous publications, we defined the following blood glucose categories: severe hypoglycemia (< 30mg/dl; 1.7 mmol/l), moderate hypoglycemia (30-60mg/dl; 1.7-3.3 mmol/l)), euglycemia (60-125 mg/dl; 3.3-6.9 mmol/l), mild hyperglycemia (126-139 mg/dl; 6.9-7.7 mmol/l), moderate hyperglycemia (140-179 mg/dl; 7.7-9.9 mmol/L), or severe hyperglycemia (>180 mg/dl, >9.9 mmol/l) [2-5,11].

For reasons of safety a 2 ml/kg glucose 10% solution was given when blood glucose level dropped under 50 mg/dl (2.8 mmol/l).

Statistical analyses

All statistical analyses were performed with SPSS 15.0 (SPSS Inc, Chicago, IL, USA).

Continuous variables are displayed as mean (SD), or median and interquartile range, categorical variables are displayed as proportions. The One-Sample Kolmorogov-Smirnov Test was used to analyse distribution of continuous variables. In case of a normal distribution comparison of continuous variables was done using the independent samples T-test, otherwise the Mann-Whitney U-test was used.

The Spearman Correlation test was applied to assess correlation between blood glucose level on arrival at ICU, Length of stay in the hospital (LOS), ICU days, highest intraoperative blood glucose against age, weight, Aristotle complex score, RACHS score, CPB time, aortic cross clamp time (AoX), lowest intraoperative body temperature, and cyanotic/acyanotic CHD.

Univariable linear regression was applied to assess influence of cyanotic/acyanotic CHD, age, weight, Aristotle complex score, RACHS score, CPB time, aortic cross clamp time (AoX), lowest intraoperative body temperature, intraoperative blood glucose levels (<60 mg/dl), intraoperative blood glucose levels (<75 mg/dl), moderate intraoperative blood glucose levels (>140 mg/dl) and severe intraoperative blood glucose levels (>180 mg/dl) as independent variables on LOS, ICU days, extubation time and mortality as dependent variables.

Univariable binary logistic regression analysis was used to study potential determinants of blood glucose level > 180 mg/dl on arrival at ICU. The following factors were considered as potential determinants: patient age, weight, Aristotle score, RACHS score, CPB time, AoX time, lowest intraoperative body temperature, blood glucose level before CPB as covariates was used.

Graphs were constructed with Graphpad software package (version 4.0, Graphpad Software Inc.,San Diego, USA).

RESULTS

204 consecutive pediatric patients from 2.4 kg to 45 kg (130 male/ 74 female) (cyanotic versus acyanotic lesions 95/109) operated for congenital heart disease on CPB at the Thoraxcenter Rotterdam The Netherlands were included. Patients demographics, surgical procedure code by Aristotle Complexity Score [12], RACHS (risk adjustment for surgery for congenital heart disease) [13], CPB time, AoX time and lowest body temperature, blood glucose levels, LOS, IC stay are listed in Table 1. According to the Kolmogorov-Smirnov Test all groups of Table 1 are not normally distributed except for blood glucose level on arrival at ICU. Operations by RACHS-1 category are shown in table 2.

Box plots of per-operative and on arrival at ICU blood glucose levels are displayed in figure 1.

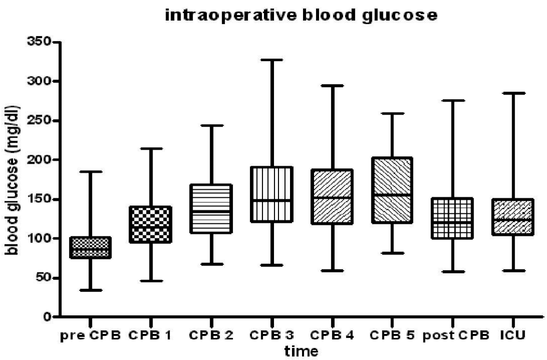

Figure 1: Intraoperative and ICU arrival blood glucose levels.

No patients received insulin during surgery.

Fifty-seven of the two-hunderd-four patients (27.9%) had at least one intraoperative glucose level > 180 mg/dl (10 mmol/l), 132/204 patients (64%) had at least one intraoperative glucose level > 140 mg/dl (7.7 mmol/l), but only 12 patients (5.8%) had a glucose level > 180 mg/dl (10 mmol/l) on arrival at ICU (table 3), 59 patients (28.9%) had a glucose level > 140 mg/dl (7.7 mmol/l) on arrival at ICU.

Intraoperatively only 1 patient (a 2 year old boy with ASD) had a blood glucose level < 50 mg/dl (2.8 mmol/l). We measured 34.2 mg/dl and after administration of 2ml/kg glucose 10% blood glucose level rose to 48.6 mg/dl where after another glucose bolus was administrated and blood glucose level rose to 120 mg/dl.

Nine out of 204 patients had Deep Hypothermic Cardiac Arrest (DHCA), of which 5/9 (56%) had blood glucose levels > 180 mg/dl (10 mmol/l) on arrival at ICU, while only 7

Table 1: Patients demographics and operative details

Age: n=204	
Median (IQR)	221 (81-965)
< 30 days (n)	22
>30 days < 1 year (n)	101
>1 year	81
Weight (kg): n=204	
Median (IQR)	8 (4.5-13.3)
<5kg (n)	59
>5kg (n)	145
Aristotle score: n=204	
Median (IQR)	8 (6-9)
|RACHS score: n=204	
Median (IQR)	2 (2-3)
Cyanotic lesions/ acyanotic lesions	95/109
CPB (min): n=204	
Median (IQR)	82 (52.5-107)
AOX (min): n=204	
Median (IQR)	47 (26-67.5)
DHCA (min): n=9	
Median (IQR)	53 (21.5-70.5)
CPB temp (Celsius): n=204	
Median (IQR)	30.3 (28.7-33.5)
Extubation (hours): n=142	
Median (IQR)	7.1 (4.9-10.18)
LOS (days); n=201	
Median (IQR)	8 (7-15)
IC stay (days): n=201	
Median (IQR)	1 (1-4)
Blood glucose pre CPB (mg/dl): n=204	
Median (IQR)	86 (75-103)
Highest blood glc intraoperative (mg/dl): n=204	
Median (IQR)	160 (129-194)
Blood glucose ICU (mg/dl): n=204	
Median (IQR)	126 (106-151)

SD= standard deviation; IQR= Interquartile range; RACHS= risk adjustment for surgery for congenital heart disease; CPB= cardiopulmonary bypass; AoX= aortic cross clamp time; DHCA= deep hypothermic cardiac arrest; ICU= intensive care unit, LOS= length of stay in hospital , IC= intensive care.

Table 2: Individual procedures by RACHS-1 category

Risk Category 1

- ASD closure (29)
- Coarctation repair with left-left shunt at age > 30d (1)
- Partially anomalous pulmonary venous return repair (2)
- Sinus venosus atrial septal defect closue (2)

Risk Category 2

- Aortic-pulmonary window repair and ASD closure (1)
- Aortic valvuloplasty at age > 30d (1)
- Partial cavo-pulmonary connection (16)
- Pulmonary valvuloplasty (5)
- Pulmonary valve replacement (1)
- Total repair of TOF (21)
- VSD closure (29)
- VSD and ASD closure (9)
- VSD closure and pulmonary valvuloplasty (2)
- VSD closure and right vemtricle infundibulectomy (5)
- VSD closure and subaortic stenosis (3)

Risk Category 3

- Anomalous left coronary artery from pulmonary artery reimplantation (1)
- Aortic- and mitral valvuloplasty (1)
- Aortic-pulmonary window (2)
- Arterial switch operation (3)
- CAVSD repair (19)
- Coarctation repair and VSD closure (2)
- Heart transplantation (2)
- Intracardiac tumor excision (1)
- Left Ventricular Assist Device (1)
- Mitral valvuloplasty (1)
- Pulmonary artery banding and VSD closure (1)
- Pulmonary valve replacement and VSD closure (1)
- Ross procedure (1)
- Tricuspid valvuloplasty (1)
- TOF repair with pulmonary atresia (1)
- Total cavo-pulmonary connection (16)
- Tricuspid valve repositioning for Ebstein anomaly at age > 30d (1)

Risk Category 4

- Atrial septectomy (1)
- Arterial switch operation and VSD closure (6)
- Hypoplastic aortic arch repair and VSD closure (2)

Table 2: continued

Interrupted aortic arch repair (1)
TAPVR repair at age < 30d (5)
TAPVR, CAVSD and TGA repair (1)
Risk Category 5
Damus-Kaye-Stansel procedure (1)
Norwood operation (5)

ASD=atrial septal defct, CAVSD=complete atrioventricular septal defect, TAPVR=Total anomalous pulmonary venous return, TGA=transposition of great arteries, TOF=tetralogy of Fallot, VSD=ventricular septal defect.

Table 3: Data of patients with hyperglycemia > 180mg/dl at ICU arrival.

gender	Age	Weight (kg)	sort	Aristotle Score	RACHS score	CPB time (min)	AOX (min)	CPB temp	DHCA/ ACP (min)	glc IC (mg/ dl)
M	1m3d	13.4	ASD	3	1	45	20	35.1		181.8
F	4d	2.5	Switch+ASD	13	4	148	93	26.2	4/0	196.2
M	3m3d	5.9	ALCAPA	10	3	224	156	25.8		185.4
M	14d	3.8	VSD,ASD,CoA,PDA	15	3	104	53	26.1	21/0	199.8
M	2m	2.5	PDA, AP-window, Atrial Septal Fenestartion.	9.8	2	65	30	28.4		201.6
M	1m16d	4.3	TOF	8	2	156	94	28.6		219.6
M	5m2d	5.2	TOF	8	2	85	45	30.7		190.8
M	6d	3.8	VSD+corr. Ao Arch	13	4	126	56	22.1		187.2
M	4d	3.4	Norwood	14.5	6	197	110	17.2	82/59	275.4
F	3m11d	5.4	TOF+corr. Ao Arch	14	5	111	66	21.5	24/0	181.8
M	7d	3	Norwood	14.5	6	162	100	25.5	54/34	286.2
M	13d	3.1	ASD+PDA	6	1	102	45	29.3		196.2

ASD=atrial septal defect; Switch= arterial switch operation; ALCAPA= abnormal left coronary artery from the pulmonary artery; VSD= ventricular septal defect; CoA=aortic coarctation; PDA= patent ductus arteriosus; AP-window=aortic pulmonary window; TOF= tetralogy of Fallot; corr. Ao Arch= correction aortic arch, RACHS= risk adjustment for surgery for congenital heart disease, CPB= cardiopulmonary bypass, AoX= Aortic crossclamping, DHCA= deep hypothermic cardiac arrest, ACP= antegrade cerebral perfusion, glc IC= blood glucose on Intensive Care arrival.

of 195 (3.5%) of the patients who did not undergo DHCA had blood glucose levels > 180 mg/dl on arrival at ICU.

Of the 204 patients 142 had representative extubation times (table 1), the other 62 patients received supplemental sedation for early transportation to the children ICU (logistic problem), or needed supplemental sedation because of their actual clinical condition or both.

Thirty-day mortality was 1.5% (3/204); one sudden death 23 days postoperative after good recovery from TOF repair, one death a week after Norwood procedure due to respiratory infections complicated with necrotic enterocolitis and 1 death due to a mediastinale hemorrhage after Norwood procedure which needed postoperative ECMO support.

Factors potentially associated with hyperglycemia (blood glucose level > 180 mg/dl) on arrival at ICU are shown in table 4. Patients age < 30 days had higher glucose levels on ICU arrival compared to patients age > 30 days (156.1 $\pm$ 54.1 versus 126.2 $\pm$ 30.5; p=0.001). Patients weighing 5 kilos or less had higher glucose levels on ICU arrival compared to patients weighing more than 5 kilos (139.0 $\pm$ 44.1 versus 125.5 $\pm$ 29.8; p=0.008).

Table 4: Logistic regression analysis (blood glucose >180 mg/dl at ICU arrival as dependent variable)

	B	S.E.	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Weight	-0.358	0.144	**0.013**	0.699	0.527	0.927
Age_days	-0.018	0.007	**0.008**	0.982	0.969	0.995
Aristotle_Score	0.317	0.101	**0.002**	1.373	1.126	1.675
RACHS_score	0.633	0.223	**0.004**	1.884	1.217	2.916
CPB_time	0.006	0.003	0.07	1.006	1	1.012
AoXmin	0.12	0.006	0.068	1.012	0.999	1.024
gluc_pre	0.028	0.01	**0.004**	1.028	1.009	1.048
CPB temp	-0.296	0.066	**0.000**	0.744	0.654	0.846
DHCA	0.4	0.014	**0.004**	0.5	1.012	1.069

RACHS= risk adjustment for surgery for congenital heart disease, CPB= cardiopulmonary bypass, AoX= Aortic crossclamping, DHCA= deep hypothermic cardiac arrest, ACP= antegrade cerebral perfusion, glc IC= blood glucose on Intensive Care arrival. B=sample regression coefficient, S.E.= standard error, Sig.= two-sided P value or observed significance level, Exp(B)= exponentiation of the B coefficient, C.I.=confidence interval.

Table 5 displays the correlation results between intraoperative blood glucose levels and LOS, ICU days, extubation time and mortality. All correlations were either nonsignificant or at the most very weak (Spearman´s Rho ‹ 0.30).

Linear regression suggested that neither lower intraoperative blood glucose levels (<60 or <75 mg/dl) nor higher intraoperative blood glucose levels (>140 or >180mg/dl) had influence on LOS, ICU stay, mortality or extubation time (Table 6).

Blood glucose levels at ICU arrival were associated with longer ICU stay (p=0.04) (Figure 2).

Table 5: Correlation analysis results of intraoperative blood glucose versus LOS, ICU days, extubation time and mortality.

Correlation	Spearman's rho	Significance (2-tailed)
Highest intraop Glc / ICU days	0.199	0.005
Highest intraop Glc / LOS	0.197	0.005
Highest intraop Glc / ICU glc	0.284	0.0001
Highest intraop Glc / Extubation time	0.259	0.0001
Highest intraop Glc / mortality	0.132	NS
> 140 mg/dl intraop glc / LOS	0.14	NS
> 140 mg/dl intraop glc / ICU days	0.102	NS
> 140 mg/dl intraop glc / extubation time	0.143	NS
> 140 mg/dl intraop glc / mortality	0.09	NS
> 180 mg/dl intraop glc / LOS	0.137	NS
> 180 mg/dl intraop glc / ICU days	0.147	0.038
> 180 mg/dl intraop glc / extubation time	0.203	0.015
> 180 mg/dl intraop glc / mortality	0.175	0.012

Table 6: Linear regression analysis results: Lower (<60 and <75mg/dl) and higher intraoperative blood glucose levels (>140 and >180mg/dl) versus LOS, ICU stay, mortality or extubation time.

					95%	C.I.
Linear Regression	**B**	**Std Error**	**Beta**	**Sign.**	**lower**	**higher**
<60mg/dl intraop glc / LOS	-1.949	4.285	-0.035	**0.65**	-10.399	6.501
<60mg/dl intraop glc / ICU days	0.154	1.863	0.006	**0.934**	-3.519	3.828
<60mg/dl intraop glc / extubation	1.715	2.2	0.071	**0.437**	-2.635	6.066
<60mg/dl intraop glc / mortality	-0.004	0.038	-0.009	**0.91**	-0.08	0.071
<75mg/dl intraop glc / LOS	1.884	2.711	0.063	**0.488**	-3.461	7.23
<75mg/dl intraop glc / ICU days	0.795	1.178	0.06	**0.501**	-1.529	3.118
<75mg/dl intraop glc / extubation	0.741	1.169	0.667	**0.528**	-1.572	3.053
<75mg/dl intraop glc / mortality	-0.025	0.024	-0.089	**0.325**	-0.072	0.024
>140mg/dl intraop glc / LOS	2.492	1.991	0.088	**0.212**	-1.435	6.418
>140mg/dl intraop glc / ICU days	-0.943	1.214	-0.77	**0.438**	-3.337	1.45
>140mg/dl intraop glc / extubation	1.258	0.852	0.124	**0.142**	-0.426	2.942
>140mg/dl intraop glc / mortality	0.023	0.018	0.9	**0.199**	-0.12	0.58
>180mg/dl intraop glc / LOS	2.45	2.05	0.84	**0.233**	-1.593	6.493
>180mg/dl intraop glc / ICU days	0.015	0.01	0.118	**0.126**	-0.004	0.062
>180mg/dl intraop glc / extubation	1.319	0.877	0.126	**0.135**	-0.414	3.053
>180mg/dl intraop glc / mortality	0.027	0.17	0.106	**0.11**	-0.006	0.06

B=sample regression coefficient, S.E.= standard error, Sig.= two-sided P value or observed significance level, Beta=standardized coefficient, C.I.=confidence interval.

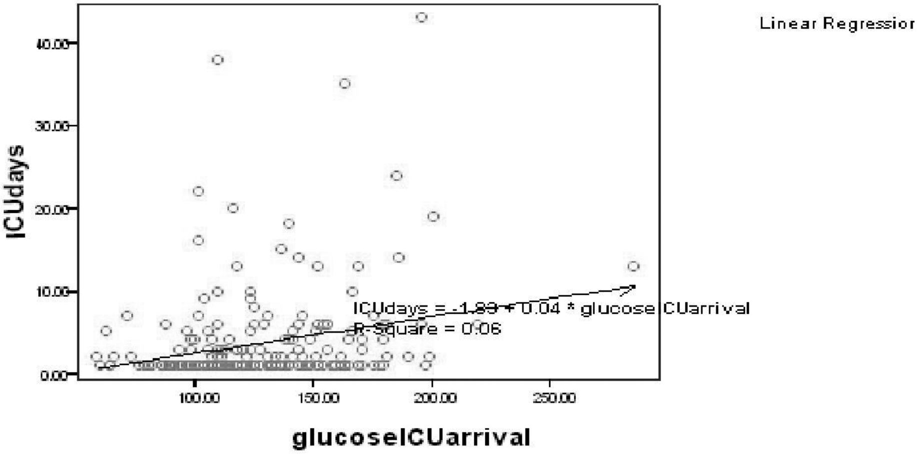

Figure 2: Blood glucose levels at ICU arrival versus ICU days.

DISCUSSION

Stress, steroids and administration of glucose are conditions that are associated with hyperglycemia in the neonate. High circulating levels of cortisol and catecholamines (adrenaline and noradrenaline) have the reverse action to insulin, rendering the baby insulin resistant and catabolic, and in addition the latter directly suppress insulin release.

The study shows that with a conventional (no insulin, no glucose) pediatric cardiac anesthetic approach there is little risk for intraoperative hypoglycaemia during pediatric cardiac surgery for congenital heart disease. However, frequent blood glucose monitoring is appropriate. Since all patients received 30mg/kg methylprednisolone iv before going on CPB and since steroids use in pediatric cardiac surgery is still controversial [20,21], additional benefit in preventing hyperglycemia might be achieved by withholding steroids in pediatric cardiac surgery. In addition, severe hyperglycemia on ICU arrival was uncommon, but comparable with the paper of DeCampli et al. [14], younger patients (< 30 days) and lower weights (< 5 kilos) were associated with a higher risk for hyperglycemia on ICU arrival.

High doses of opioids (sufentanil 10mcg/kg) attenuate the physiologic response to stress in infants undergoing cardiac surgery [16-18]. On the other hand there is concern that high dose opioids may influence extubation time and ICU stay. But, even with high dose opioids, all our 142 pediatric patients, that did not received additional sedations, were extubated within 21.1 hours after arrival at ICU. High doses of sufentanil together with non-glucose iv fluids contributed to the high percentage (95%) of our patients that had glucose level < 180 mg/dl (10 mmol/l) on arrival at ICU. These findings together with the NICE-SUGAR study [6] results, which showed that a blood glucose target of < 180 mg/dl (<10 mmol/l) resulted in lower mortality in adult patients than did a more strict blood glucose target. Endorse the belief that a conventional (no insulin, no glucose) anesthetic management seems sufficient in the vast majority of patients [6].

Special attention should be paid to neonates who need DHCA for surgical repair and are at an increased risk of postoperative hyperglycemia (5 out of 9 DHCA patients had blood glucose levels > 180 mg/dl at ICU arrival). In these patients a more strict intraoperative glycemic target ((90-140 mg/dl; 5-7.7 mmol/l) [5], (110-126 mg/dl; 6.1-7 mmol/l) [2]) might be useful, requiring insulin infusions and Real-Time continuous glucose monitoring [8].

Balancing between perioperative hypoglycemia and hyperglycemia

Our study did not support the hypothesis that lower- or higher intraoperative blood glucose levels would be associated with a longer duration of postoperative hospitalisation.

According to the results of Polito et al.[2] 23% of our patients are at greater risk for adverse outcome (mortality and composite morbidity variable) because of an intraoperative glucose level < 75 mg/dl (4.1 mmol/l). Our results do not support this, patients whose minimum intraoperative glucose level was < 75 mg/dl or even < 60 mg/dl did not show any association with LOS, ICU stay, extubation time or mortality. Avoiding lower glucose levels (< 75 mg/dl) can only be achieved by administrating glucose containing fluids in the pre CPB period, which will increase the occurrence of hyperglycemic periods [15].

Twenty-eight percent of our patients had at least one intraoperative glucose level > 180 mg/dl (10 mmol/l) and 64% had at least one episode of blood glucose levels > 140 mg/dl which, in accordance to the results of Polito et al.[2], is not associated with adverse events. We only found a weak association between blood glucose levels at ICU arrival and ICU days.

On the other hand various other reports have shown an association between postoperative hyperglycemia and enhanced extubation times, LOS and mortality [1,3,4].

Finally in our study we observed an overall 30 days postoperative mortality of 1.5% (3/204), if we only take into account the patients $\leq$ 10 kg then mortality would be 3/131 (2.3%), were the now reported mortality in the European Association for Cardio-thoracic Surgery and the Society of Thoracic Surgeons Congenital Heart Surgery Database is 4% [19] .

Limitations

This is a non-blinded retrospective study. Because of logistic problems at our ICU 30% of our patients had to be transported to another department for which they received additional sedation, the reason for additional sedation whether it was for transportation or for medical reasons was not traceable.

Conclusions and recommendations

Since the optimal intraoperative blood glucose target range in pediatric patients during cardiac surgery for congenital heart disease remains unclear: "Conventional intraoperative high dose opioids and withholding glucose in intravenous fluids permits for a safe and moderate glucose control during pediatric cardiac surgery for congenital heart disease".

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General discussion

Although professional medical practice quality is seen as interplay between product-quality, process-quality and structure-quality (1), from the point of view of the medical professional, however, quality directly relates to the delivery of medical care. A medical professional should not only deliver the best care in each patient, but should also be involved in improving the care to be delivered, thus opening the way to innovative care.

Efficacy and cost-effectiveness are important aspects in this regard, but innovative care may at some point introduce less efficiency and may initially seem to increase costs. When however the medical professional results improve, a new reality for the organization is constructed.

This thesis concerns different aspects of innovative care and quality improvement in the operative treatment of pediatric patients with congenital heart disease.

2D TRANSESOPHAGEAL ECHOCARDIOGRAPHY

In this work we described the physical characteristics and the acoustic properties of the Oldelft micromultiplane transesophageal echocardiography (TEE) probe that was developed at the Thorax centre. This new technology allows performing TEE in neonates as small as 2.5 kg to patients up to a weight of 25 kg, and provided excellent image quality. In patients above 25 kg bodyweight an "adult-size" TEE probe can be used. The use of intraoperative TEE monitoring for left ventricular assist device (LVAD) implantation in children with therapy resistant heart failure highlights an aspect of clinical necessity of intraoperative TEE.

Perioperative conditioning with TEE in pediatric cardiac surgery is an obvious quality improvement, which should be regarded as standard of care and we strongly believe that the pediatric cardiac surgical team responsible for managing the patient intraoperatively (anesthesiologist and surgeon) should be able to interpret TEE, for cardiac performance and judge the adequacy of the surgical repair.

Since a micromultiplane TEE probe for neonates is recently available on the market, we can concentrate on different aspects regarding intraoperative TEE during pediatric cardiac surgery for congenital heart disease. So far little is known about the influences of medication on the contractility of the neonate's heart. Due to stringent lack of medication that is labelled for pediatric use most knowledge comes from research in the adult population, large part of the medication used in pediatric practise is prescribed off-label. Since TEE has been proven to be a valid tool for measuring contractility of the heart, we can now focus on the influence of specific medication on contractility of the heart of neonates and young children.

3D ECHOCARDIOGRAPHY

We presented the **very first** clinical introduction of intraoperative three-dimensional echocardiography in pediatric cardiac anesthesia and surgery, which permitted comprehensive 3D viewing and measuring of the morphology of aortic coarctation revealing the exact cross sectional area, hereby providing useful additional information and helping to prevent unplanned reoperations in the early or late post-operative period.

Epicardial and intrathoracic echocardiography have the inconvenience of interfering in the surgeons work field, while intra-operative 3D TEE is feasible without having this objection.. Therefore we challenge engineers, bio- engineers and developing companies for the development of a micro 3D TEE probe for neonates, which will undoubtedly add an incremental value in the assessment of morphology and surgical repair of congenital heart diseases.

MECHANICAL VENTILATION

Lung Protective Ventilation (LPV) has been introduced to avoid atelectasis. This is achieved by short periods of high inspiratory pressures to open up collapsed alveoli (alveolar recruitment strategy (ARS)) followed by a relatively high level of positive end-expiratory pressure (PEEP) to keep the alveoli open. In addition, low tidal volume ventilation is used, further minimizing over-distention.

We described that monitoring end-expiratory lung volume (EELV) is a valuable tool in mechanically ventilated pediatric patients and that optimization of EELV by an alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP) significantly improved dynamic compliance of respiratory system (Crs), oxygenation, $P_aCO_2 - P_{et}CO_2$ difference, and EELV in pediatric patients undergoing cardiac surgery for congenital heart disease.

LPV, because of the relatively high PEEP, leads to frequent concern about its effect on right ventricular (RV) afterload. Especially in patients with Fontan circulation (univentricular heart, caval veins connected to the pulmonary artery and thus central venous pressure as the driving pressure for the pulmonary circulation) the influence of mechanical ventilation on RV afterload is of great concern. Until today LPV for Fontan patients is considered inappropriate because of the assumed negative influence of high PEEP on RV afterload. Our preliminary data indeed show that the application of PEEP without ARS enhances RV afterload, but show no difference in RV afterload between zero PEEP ventilation and our ventilatory settings (ARS and high PEEP) in patients with biventricular repair after pediatric cardiac surgery, using echo Doppler obtained by TEE to assess the effect of ARS and PEEP on the RV afterload. If this also is applicable for the influence of mechanical ventilation on the patients with a Glenn shunt or a Fontan circulation, LPV will not deteriorate pulmonary circulation and since LPV causes less VILI, the patient with a Glenn shunt or a Fontan circulation may benefit most of such a "lung protective ventilation strategy".

Further studies in this regard should provide not only support of our data but also widespread application of these techniques. Ideally further research will provide us an easy and practical way to assess the ideal PEEP for every individual patient.

From our present findings we conclude that mechanical ventilation in pediatric patients undergoing cardiac surgery with biventricular repair is feasible using the described lung protective ventilatory management.

BLOOD GLUCOSE LEVELS

After evaluating the effect of our anesthetic management on intraoperative blood glucose levels we conclude that, until the optimal intraoperative blood glucose target range in pediatric patients during cardiac surgery for congenital heart disease remains unclear, a conventional (no insulin, no glucose) anesthetic management seems sufficient in the vast majority of patients.

Frequent glucose monitoring is the corner stone of all kinds of glucose management. Special attention should be paid to small neonates with complex congenital heart surgery who are at an increased risk of postoperative hyperglycemia. In these patients a more strict intraoperative glycemic target might be useful, requiring insulin infusions and Real-Time continuous glucose monitoring.

THE INTRODUCTION OF INNOVATIVE TECHNIQUES FOR IMPROVEMENT OF QUALITY OF CARE

The efforts by both pediatric cardiac anesthesiologists and congenital cardiac surgeons, to improve quality of care seem to yield reward. In our hospital we notified a mortality of approximately 2 % in the pediatric cardiac surgery patients where the now reported mortality in the European Association for Cardio-thoracic Surgery and the Society of Thoracic Surgeons Congenital Heart Surgery Database is 4%.

This provides an adequate setting to study actual aspects of perioperative care in pediatric cardiac surgery by applying innovative techniques and concepts in order to improve the quality of care. Quality of care in peri-operative treatment and pediatric cardiac anesthesia is clearly an evolving work in progress. Good surgical team behaviour (2), process improvements, structural improvements, and increases in expertise have diminished overall mortality rates. Diligent research has brought us to the present state of pediatric cardiac anaesthesia, and diligent research will enable the pediatric cardiac team to further improve knowledge in the benefit of children with congenital heart disease.

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SUMMARY

In **Chapter 1** we describe the physical characteristics and the acoustic properties of the Oldelft micromultiplane transesophageal echocardiography (TEE) probe that was developed at the Thorax centre. Because of the complexity of the intracardiac defects and their repair, there is a clear need for a small multiplane probe in newborns that are scheduled for cardiac surgery and catheterization. We present the design and realization of a small TEE phased array probe with a tube diameter of 5.2 mm and head size of only 8.2–7 mm. The number of elements is 48 and the center frequency of the probe is 7.5 MHz.

In **Chapter 2** we report our clinical experience with the Oldelft micromultiplane TEE probe (8.2-7 mm diameter tip with a 5.2 mm diameter shaft) specifically meant for use in neonates.

This new technology allows performing TEE in neonates as small as 2.5 kg, and provides excellent diagnostic intraoperative TEE assessment without major complications. A complete TEE examination should be undertaken, to screen for unsuspected or previously undetected defects. Hemodynamic evaluation with TEE of ventricular function at the time of discontinuation of cardiopulmonary bypass (CPB) assists in taking the appropriate decision for optimal pharmacological treatment. Both global and regional ventricular function can be monitored continuously by TEE. Postbypass TEE screening for pooled air is facilitated. TEE assessment of the surgical repair may prevent unplanned reoperations. In this aspect intraoperative TEE is an inexpensive, accurate, valuable and safe addition to the perioperative care of patients and should be mandatory during all corrective surgical procedures for congenital heart disease.

In **Chapter 3** we report on the limitations of the micromultiplane TEE probe. This new technology provides image of “excellent” and “good” quality in patients up to a weight of 25 kg. In patients above 25 kg the image quality decreased but an adult TEE probe, providing excellent image quality, can be used in these children.

Chapter 4 highlights an aspect of clinical necessity of intraoperative transesophageal echocardiography. Five consecutive children with therapy resistant heart failure, undergoing left ventricular assist device (LVAD) implantation are intraoperatively monitored using the Oldelft micromultiplane TEE. Intraoperative TEE is specially used to monitor right ventricular (RV) and left ventricular (LV) function, correct position of the cannulas and response to pharmacological treatment. Mechanical circulatory support, with a LVAD is used in an increasing number of children for treatment of advanced heart failure as bridge-to-transplant. To date no data were available and no studies had defined

the role of intraoperative transesophageal echocardiography (TEE) for hemodynamic stabilization during LVAD implantation in children. The complex interaction of the RV and LV function and correct positioning of the cannula, during LVAD implantation in children with end-stage cardiac failure is improved by simultaneous visualization of cardiac performance of both ventricles and cannula positioning by means of intraoperative multiplane TEE.

Chapter 5 presents the **very first** clinical introduction of perioperative three-dimensional echocardiography in pediatric cardiac anesthesia and surgery. The availability of three-dimensional (3D) echocardiography with its multiplanar review (MPR) analysis software on board now allows detailed examination in assessing morphological details. We evaluated the feasibility of 3D echography in assessing intraoperative morphological details of aortic coarctation (CoA) and its repair. Intraoperative 3D echography is a feasible noninvasive imaging modality for intraoperative assessment of aortic coarctation and its repair, which provides useful additional information and may prevent unplanned reoperations in the early or late post-operative period.

In **Chapter 6** we describe that monitoring end-expiratory lung volume (EELV) is a valuable tool to optimize respiratory settings that could be of particular importance in mechanically ventilated pediatric patients. EELV is the Functional Residual Capacity (FRC) of the mechanically ventilated patient. We evaluated the feasibility and precision of an intensive care unit (ICU) ventilator with an in-built nitrogen washout/wash in technique in mechanically ventilated pediatric patients.

This ICU ventilator with an in-built nitrogen washout/wash in EELV technique can measure EELV with precision, and can easily be used for mechanically ventilated pediatric patients, without disconnecting from the ventilator.

In **Chapter 7** we studied optimization of EELV by an alveolar recruitment strategy (ARS) and maintaining lung volume with adequate positive end-expiratory pressure (PEEP), which allows preventing ventilator-induced lung injury (VILI). Mechanical ventilation in children is known to decrease pulmonary blood flow and cardiac output. A progressive fall in cardiac index occurs with increasing PEEP, and the fall becomes significant at PEEP higher than 6 cm H_2O. This might be explained by over-distention of aerated lung areas in the presence of atelectatic lung areas, mediated by a significant rise in pulmonary vascular resistance or as a result of a decrease in venous return. In this regard, Lung Protective Ventilation (LPV) has been introduced to avoid atelectasis. This is achieved by short periods of high inspiratory pressures to open up collapsed alveoli (recruitment) followed by a relatively high level of PEEP to keep the alveoli open. In addition, low tidal volume ventilation is used, further minimizing over-distention. Knowing that PEEP has its most beneficial effects on hemodynamics when dynamic compliance of respiratory system (C_{rs}) is maximized, we hypothesize that the use of 8 cm H_2O PEEP with ARS results in an increase in C_{rs} and end-expiratory lung volume (EELV) compared to 8 cm H_2O PEEP without ARS and to zero PEEP in pediatric patients undergoing cardiac surgery for congenital heart disease.

We conclude that an alveolar recruitment strategy with relatively high PEEP significantly improves C_{rs}, oxygenation, P_aCO_2 – $P_{ET}CO2$ difference, and EELV in pediatric patients undergoing cardiac surgery for congenital heart disease.

In **chapter 8** we evaluated the effect of our anesthetic management on intraoperative blood glucose levels.

Until the optimal intraoperative blood glucose target range in pediatric patients during cardiac surgery for congenital heart disease remains unclear, a conventional (no insulin, no glucose) anesthetic management seems sufficient in the vast majority of patients (95%) [6]. Special attention should be paid to small neonates with complex congenital heart surgery who are at an increased risk of postoperative hyperglycemia. In these patients a more strict intraoperative glycemic target ((90-140 mg/dl; 5-7.7 mmol/l) [5], (110-126 mg/dl; 6.1-7 mmol/l) [2]) might be useful, requiring insulin infusions and real-time continuous glucose monitoring [8].

Conventional intraoperative high dose opioids (sufentanil 10mcg/kg) and withholding glucose in intravenous fluids permits for a save and moderate glucose control (< 180 mg/dl; < 10 mmol/l) during pediatric cardiac surgery for congenital heart disease.

SAMENVATTING

In **hoofdstuk 1** beschrijven we de fysische en akoestische eigenschappen van de Oldelft micromultiplane transesophageal echocardiography (TEE) probe, ontwikkeld in het Thoraxcentrum. Gezien de complexiteit van zowel de aangeboren hartafwijkingen als hun chirurgisch herstel, is er grote behoefte aan een multiplane TEE probe aangepast voor kinderen. We presenteren de ontwikkeling en realisatie van een kleine TEE probe met een buis diameter van 5.2 mm en een tip afmeting van slechts 8.2 bij 7 mm. De probe bevat 48 elementen met een gemiddelde frequentie van 7.5 MHz.

In **hoofdstuk 2** beschrijven we onze klinische ervaring met de Oldelft micromultiplane TEE probe bij pasgeborenen en kinderen. Deze nieuwe technologie laat ons toe TEE onderzoek te verrichten bij pasgeborenen vanaf 2.5 kg, en laat ons tevens toe om een excellente diagnostische intra-operatieve TEE beoordeling te maken, zonder majeure complicaties. Na de inleiding van de narcose wordt een volledig TEE onderzoek verricht, om de patiënt nogmaals te screenen voor onverwachte, nog niet gediagnosticeerde defecten. Hemodynamische monitoring van de kamerfuncties met TEE net voor het stoppen van de hart-longmachine helpt bij het nemen van de juiste beslissing voor het opstarten van de meest geschikte farmacologische behandeling. Zowel de gehele als de regionale kamerfunctie kan continu worden opgevolgd doormiddel van TEE. Het screenen voor achtergebleven lucht tijdens de ontluchting van het hart wordt mogelijk. TEE beoordeling van de uitgevoerde heelkundige ingreep kan ongeplande heringrepen voorkomen. Omwille van al deze aspecten is intra-operatieve TEE een goedkoop, accuraat, waardevol en veilig hulpmiddel tijdens de peri-operatieve behandeling van de patiënt. TEE zou verplicht moeten zijn voor alle hart chirurgische ingrepen bij kinderen met aangeboren hartafwijkingen.

Hoofdstuk 3 beschrijft de beperkingen van de micromultiplane TEE probe. Deze nieuwe technologie verschaft kwalitatief goede beelden in patiënten tot 25 kg lichaamsgewicht. Bij kinderen boven de 25 kg vermindert de kwaliteit aanzienlijk, maar in deze gevallen kan men reeds gebruik maken van een volwassen, al dan niet, 3 dimensionale TEE probe.

Hoofdstuk 4 beschrijft de klinische noodzaak van intra-operatieve TEE. Vijf opeenvolgende kinderen met therapie resistent hartfalen, die een left ventricular assist device (LVAD = pomp die de linker hartkamer ondersteunt) krijgen ingeplant worden intra-operatief gemonitord met de Oldelft micromultiplane TEE. De inra-operatieve TEE wordt voornamelijk gebruikt om de rechter- en de linker hartkamer functie te volgen, de correcte positie van de geïmplanteerde canules te controleren en het effect van de farmacologische behandeling te beoordelen.

Mechanische ondersteuning van de bloedcirculatie met LVAD wordt meer en meer toegepast tijdens de behandeling van hartfalen bij kinderen als overbrugging naar een uiteindelijke harttransplantatie. Totnogtoe was er geen informatie beschikbaar over de rol van intra-operatieve TEE en het hemodynamisch stabiliseren tijdens LVAD implantatie bij kinderen.

De ingewikkelde interactie van de rechter- en linker hartkamer functie en de correcte positie van de LVAD canules wordt inzichtelijker door de simultane visualisatie van de hartfunctie en de positie van de canules met intra-operatieve multiplane TEE.

Hoofdstuk 5 behandelt de **allereerste** klinische introductie van drie-dimensionele echocardiografie tijdens pediatrische hartchirurgie en -anesthesie. De beschikbaarheid van drie-dimensionele (3D) echocardiografie laat ons toe om zeer gedetailleerd de morfologie te beoordelen. Wij evalueerden de haalbaarheid van 3D echografie tijdens het beoordelen van de morfologische details van aorta coarctatie (CoA) en zijn herstel. Intra-operatieve 3D echografie is een praktische, makkelijk uitvoerbare, niet invasieve methode voor de intra-operatieve beoordeling van CoA en zijn herstel, en kan vroege of late heringrepen helpen voorkomen.

In **hoofdstuk 6** beschrijven we dat het meten van het eind-expiratoire long volume (EELV) ons waardevolle informatie verschaft om de mechanische beademing bij kinderen te optimaliseren. EELV is de Functioneel Residuele Capaciteit (FRC) van de beademde patiënt.

We evalueerden de precisie en haalbaarheid van een intensive care unit (ICU) beademingstoestel met een ingebouwde stikstof was-uit/was-in techniek bij beademde pediatrische patiënten. We besluiten dat dit ICU beademingstoestel gebruiksvriendelijk is en nauwkeurig het EELV bij kinderen kan meten zonder losgekoppeld te worden van de patiënt

Hoofdstuk 7 bestudeert het optimaliseren van het EELV door "een manoeuvre om de kleine longblaasjes (alveolen) te rekruteren" samen met het gebruik van positieve eind-expiratoire druk (PEEP) om de long open te houden, hetwelk kunstmatig beademing gerelateerde longschade helpt te voorkomen.

Bij kinderen leidt kunstmatige beademing tot een daling van de longdoorbloeding en dus van het hartdebiet. De daling van het hartdebiet neemt toe bij stijgende PEEP, en de daling wordt significant vanaf PEEP > 6 cm H_2O. Dit zou verklaard kunnen worden door een te hard oprekken van de beademde longgebieden en de aanwezigheid van samengevallen longgebieden, hetwelk resulteert in een toegenomen longvaatweerstand en/of in een vermindering van de veneuze bloed terugstroom naar het hart. Om te voorkomen dat sommige longgebieden samenvallen werd, een long beschermende kunstmatige beademingsvorm voorgesteld.

Dit wordt bekomen door tijdens een korte periode van hoge beademingsdruk de long volledig te openen (rekruteren), gevolgd door het toepassen van een relatief hoge PEEP om de longblaasjes open te houden. Dit samen met kleine teugvolumes vermindert de kans om longgebieden te hard op te rekken. Wetende dat PEEP zijn voordeligste effect heeft op de hemodynamiek als de dynamische compliantie van het ademhalingstelsel (Crs) maximaal is, vertrekken we van de hypothese dat het gebruik van 8 cm H_2O PEEP + rekruteren van de long resulteert in een verbetering van de Crs en het EELV, dit in vergelijking met 8 cm H_2O PEEP zonder long rekruterings manoeuvre en in vergelijking met 0 cm H_2O PEEP tijdens hart operaties bij kinderen met aangeboren hartafwijkingen.

We besluiten onze studie met het feit dat, een long rekruterings manoeuvre samen met relatief hoge PEEP (8 cm H_2O) de Crs, de oxygenatie, het P_aCO_2 – $P_{ET}CO2$ verschil, en het EELV significant verbetert tijdens hart operaties bij kinderen met aangeboren hartafwijkingen.

In **hoofdstuk 8** evalueren we het effect van ons anesthesie beleid ten opzichte van de bloedsuikerspiegels tijdens de operatie. Gezien de optimale intraoperatieve bloedsuikerspiegel nog niet gekend is voor hart operaties bij kinderen met aangeboren hartafwijkingen, lijkt het dat een conventioneel (zonder insuline, zonder suiker) anesthesie beleid afdoende is in het overgrote deel van de patiënten (95%). Speciale aandacht is nodig voor kleine pasgeborenen die ingewikkelde hartoperaties moeten ondergaan, want zij hebben een verhoogd risico op te hoge bloedsuikerspiegels. Bij deze kinderen kan een striktere controle van bloedsuikerspiegels ((90-140 mg/dl; 5-7.7 mmol/l) of zelfs (110-126 mg/dl; 6.1-7 mmol/l)) doormiddel van een insuline infuus en continue bloedsuikerspiegel controle nuttig zijn.

We concluderen dat het intraoperatief toedienen van hoge dosissen opioïden (sufentanil 10mcg/kg) en het niet toedienen van suikers ons toelaat om veilig en gemodereerd de bloedsuikerspiegel te controleren (< 180 mg/dl; < 10 mmol/l) tijdens hartoperaties bij kinderen met aangeboren hartafwijkingen.

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CURRICULUM VITAE

Thierry Scohy is op 12 maart 1969 geboren te Lier (België). Na het behalen van zijn Bekwaamheidsdiploma dat toegang verleent tot het Hoger onderwijs, studeerde hij geneeskunde aan de Universitaire Instelling Antwerpen (UIA). In 1996 behaalde hij de academische graad van Arts, waarna hij startte met de opleiding Anesthesie van 01-08-96 tot 30-09-01 in het A.Z.Middelheim te Antwerpen en het Universitair Ziekenhuis Antwerpen te Edegem, met als stagemeester: Prof. Dr. H. Adriaensen, U.I.A.

In januari 2002 ging hij in Nederland werken als staflid Pediatrische Anesthesie in het Sophia Kinderziekenhuis, Erasmus MC, Rotterdam. Vanaf juni 2003 tot heden is hij werkzaam als staflid Thoracale Anesthesie en Pediatrische Cardio Anesthesie in het Thoraxcentrum, Erasmus MC, Rotterdam.

Thierry is gelukkig getrouwd met Carmen Ruiz Ferrer en ze hebben vier geweldige kinderen: Sarah (13), Sofía (9), Luca (7) en Alexander (2).

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J Card Surg. 2007 Jan-Feb;22(1):74-5. PubMed PMID: 17239222.

PHD PORTFOLIO SUMMARY

Summary of PhD training and teaching activities

Name PhD student: Scohy Thierry	PhD period: 2007-2011
Erasmus MC Department: Anesthesia	Promotor(s): Pr. A. Bogers / Pr. J. Klein
Research School: COEUR	Supervisor: Dr. D. Gommers / Dr. J. Hofland

1. PhD training

	Year	Workload (Hours/ECTS)
General courses		
- Echocardiography in Congenital and Pediatric Heart Disease	2009	22
- Philips 3D teaching site	2008	14
- Cursus Praktische Echocardiografie	2007	24
- 1st European Course on 3D Echocardiography	2006	12
- Course Echocardiography in Congenital Heart Disease	2006	22
Research skills		
Biostatistics for Clinicians (Nihes)	2009	20
BROK Masterclass	2010	4
Presentations		
Scohy TV Intraoperative MicroTEE in pediatric surgery. Latest advances in 2D echocardiography. Nederlandse Vereniging voor Anesthesiologie (NVA), Ledenvergadering Sektie KinderAnesthesiologie (SKA). Jan 11, 2010, Amsterdam, The Netherlands.	2010	3
Scohy TV. Alveolar Recruitment Strategy and PEEP Improves Oxygenation, Dynamic Compliance of the Respiratory System and End Expiratory Lung Volume in Mechanically Ventilated Pediatric Patients. Nederlandse Vereniging voor Anesthesiologie (NVA), Ledenvergadering Sektie KinderAnesthesiologie (SKA). Jan 11, 2010, Amsterdam, The Netherlands	2010	3
Scohy TV. Benefits of intraoperative MicroTEE in pediatric surgery. Latest advances in 2D and 3D echocardiography. Satellite Symposium organised by Philips Healthcare. EUROECHO 2009. Dec 9-12, 2009, Madrid, Spain.	2009	3

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Scohy TV, Gommers D. Maat A., de Jong PL, Bogers AJ, Hofland J. Intraoperative transesophageal echocardiography is beneficial for haemodynamic stabilisation during LVAD implantation in children. ErasmusMC Rotterdam, The Netherlands. 016 European Conference on Pediatric Anaesthesia. Sept 25-27, 2008, Athens. Greece.	2008	3

International conferences

- Euroanesthesia 2010 Meeting	2010	18
- World Anesthesia Congress	2011	30
- Inspiration at work	2009	2
- Euroecho	2009	19
- European Conference Paediatric Anaesthesia	2008	4
- European Congenital Heart Surgeons Association	2008	18
- European Conference Paediatric Anaesthesia	2007	13
- EACTA annual meeting	2007	18
- Euroanaesthesia	2006	18

Reviewer for:

- European Journal Cardio-thoracic Surgery (EJCTS)
- Journal of the American Society of Echocardiography (JASE)
- European Journal of Echocardiography (EUJE)
- Journal of Cardiac Surgery (JCS)
- Annals of Cardiac Anesthesia (ACA)

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