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REVIEW

A retrospective review of the perioperative management of patients with congenital oesophageal atresia and tracheo-oesophageal fistula at a South African third level hospital

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Background: The perioperative management of neonates with oesophageal atresia and tracheo-oesophageal fistula (OA/TOF) is challenging. There is currently very little South African data available about the perioperative management of this condition. Current management is therefore informed by institutional experience and international studies. This study aims to describe the patient population with OA/TOF presenting for surgery, to evaluate the preoperative factors affecting early mortality, and to report on intraoperative ventilation and haemodynamic complications.

Methods: A single-centre retrospective review was conducted of electronic medical records of patients less than 28 days old undergoing initial surgical intervention between January 2007 and December 2017 at a third level hospital.

Results: A total of 107 patients were included in this study. A delay in transfer to our institution was found in 63% of the patients. Roughly half of the patients (52%) required preoperative mechanical ventilation. The incidence of major cardiac and other congenital abnormalities was 29% and 33%, respectively. Survival rates within the lowest and the highest risk groups (Okamoto class 1 and 4) were 90% and 45%, respectively. Airway and ventilation difficulties were described in 8.4% of patients and these patients required intervention in the form of reintubation, gastrostomy or abandoning surgery. Haemodynamic instability occurred in 27% of the patients, more commonly in those with preoperative pneumonia and major cardiac comorbidities.

Conclusion: The lack of antenatal diagnosis, together with delays in transferring patients to an appropriate referral centre, resulted in a high incidence of pneumonia requiring ventilatory support and delays in first surgical intervention. The incidence of major cardiac and other abnormalities was similar to other international data, with the exception of VACTERL associated anomalies, which was lower in this cohort. Survival outcome, however, was worse in this cohort than international studies. This study gives local context to risk stratification systems and highlights the challenges of managing these patients in a developing country.

Keywords: oesophageal atresia, oesophageal fistula, infant, newborn, South Africa, anaesthesia, retrospective studies

Introduction

Congenital tracheo-oesophageal fistula (TOF) is the anomalous connection between the mucosal surface of the oesophagus and that of the trachea, and is one of the most common errors of development encountered in children with an estimated incidence of 1:3 000–4 500 live births.[1] In 1929, Vogt described an anatomical classification which was adapted by Ladd in 1944 and then by Gross in 1953. The Gross classification is referenced to most commonly in the modern literature. Types A through E are described, with the Type C being the most encountered variant in international data (Figure 1).[2] Types B, C and D often require urgent surgery – within the first two days of life – to avoid aspiration and respiratory compromise.[1] Factors affecting morbidity and mortality in these patients are: low birth weight, prematurity, intercurrent chest infections, and congenital abnormalities such as VACTERL association, CHARGE syndrome, Trisomy 13, 18 or 21 and Chromosome 22q11.2 deletion syndrome.[3] Congenital cardiac pathology has been shown to be an independent predictor of mortality and intraoperative critical

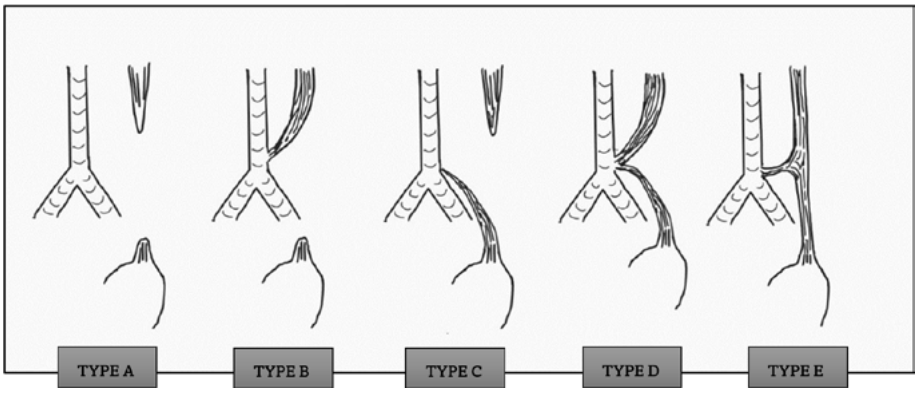

Figure 1: Anatomical classification of oesophageal atresia and tracheo-oesophageal fistula

Table I: Risk classification

Okamoto classification	Class	Birth weight	Cardiac comorbidity	Survival rate %
	I	> 2 kg	NIL	100
	II	< 2 kg	NIL	81
	III	> 2 kg	Major cardiac abnormalities	72
	IV	< 2 kg	Major cardiac anomalies	27

Source: Modified from Okamoto et al.[4]

events in infants with OA/TOF.[1] In considering the preoperative factors contributing to early mortality in this patient group, review texts often refer to the prognostic classifications by Waterston, Spitz and, more recently, Okamoto (Table I).[4]

Difficulties in the provision of anaesthesia arise from airway management, ventilation and the occurrence of haemodynamic instability.[5] The perioperative management of these neonates is not standardised and little to no data exists on local population characteristics or outcomes.

Aim

The purpose of this study is to describe the characteristics and perioperative management of infants presenting to a third level hospital between 1 January 2007 and 31 December 2017 for surgical correction of congenital tracheo-oesophageal fistulae (TOF) and oesophageal atresia (OA) and to evaluate the pre-operative patient factors affecting mortality. The secondary objective was to determine the nature and frequency of intraoperative complications related to airway management and haemodynamic instability in this group.

Methods

Following ethical (BE 526/18) and hospital approval, a retrospective clinical audit of neonates undergoing initial surgical treatment for oesophageal atresia with tracheo-oesophageal fistula (OA/TOF) at Inkosi Albert Luthuli Central Hospital (IALCH), Durban, South Africa, was conducted. Patients undergoing surgery between January 2007 and December 2017 were identified from the hospital's electronic medical record (EMR) system. The variables were extracted and placed in a Microsoft® Excel spreadsheet by the principal investigator and then deidentified.

The variables collected included demographic data; preoperative data – including the timing of the diagnosis, delays in transfer, associated congenital anomalies (cardiac and non-cardiac), the presence of pneumonia and the need for preoperative ventilation; intraoperative data and complications; and post-operative and outcomes data.

Statistical methods

Categorical data were analysed in Microsoft® Excel (2016), using simple descriptive statistics and were presented as number (*n*) and percentage (%).

Results

A total of 129 patients were identified. Patients with incorrect diagnoses, patients with pure OA without a fistula and patients not receiving surgical intervention were excluded. The final number of patients recruited was 107 (Figure 2). This cohort's characteristics are shown in Table II.

In this cohort, the majority of the patients (95%) were diagnosed with OA/TOF postnatally.

When categorised according to the World Health Organization's (WHO) subcategories of preterm birth, 49% of the cohort were born prematurely, the majority of those (73%) being moderate to late preterm (33–37 weeks), and one participant born at less than 28 weeks gestation. The average birth weight was 2 400 g.

The average age at transfer to the referral hospital was three days. Six patients were only referred after ten days postbirth. From arrival at the hospital until surgery, a further two days elapsed on average, which resulted in most patients receiving the first surgical intervention between day four and five of life (Figure 3).

Roughly half of the patients (52%) were ventilated preoperatively, with the diagnosis of aspiration pneumonia being the most common indication (70%).

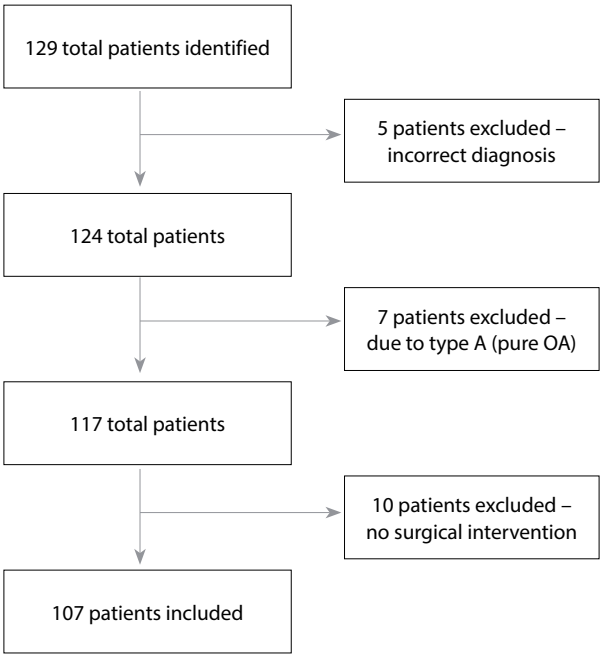

Figure 2: Patient recruitment analysis

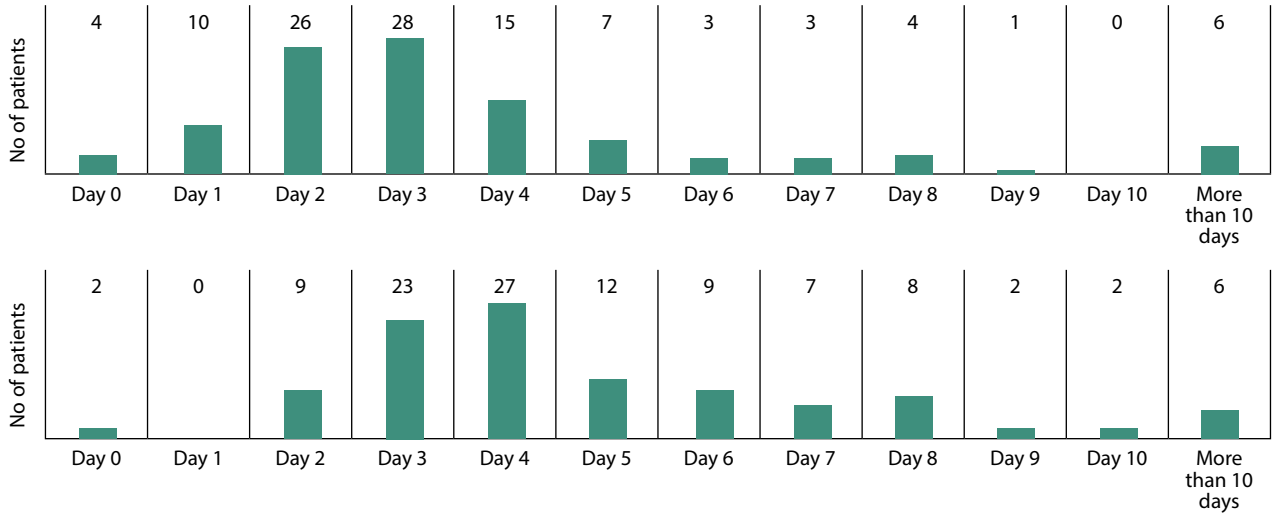

Figure 3: Days from birth until transfer to the referral hospital (upper graph); days from birth until surgery (lower graph)

Table II: Cohort characteristics

Category	Number (*n* = 107)	%
Gender		
Male	62	58%
Female	45	42%
Gestational age at birth		
Average	36 weeks (27–40 weeks)	
Preterm	53	49.5%
Moderate to late preterm (33–37 weeks)	39	73% of preterm
Very preterm (28–32 weeks)	13	24% of preterm
Extremely preterm (< 28 weeks)	1	2% of preterm
Birth weight		
Average	2 400 g (1 000 g–4 500 g)	
> 2 000 g	79	74%
< 2 000 g	28	26%
Timing of diagnosis		
Antenatal	5	5%
Postnatal	102	95%
Preoperative ventilation requirement and indication		
Ventilated	56	52%
Indication for ventilation		
Pneumonia	40	37%
RDS	13	12%
Other	3	2%
Not ventilated	51	48%

RDS – respiratory distress syndrome

All the patients who were taken for surgery received a pre-operative echocardiogram which demonstrated major structural cardiac abnormalities in 29% and minor defects in a further 48% of patients (Table III). The aortic arch was shown to be right-sided in 7% of the patients during preoperative assessment. One patient had a different finding at surgery than what was reported preoperatively.

Table III: Cardiac and congenital anomalies

Cardiac anomaly	*n* = 107	Percentage (%)
Minor	51	48%
Major	32	29%
Aortic arch side	***n* = 107**	
Left	99	92.5%
Right	8	7.5%
Congenital anomalies	***n* = 107**	**Percentage (%)**
VACTERL association	6	5%
Other	30	28%
Minor cardiac anomalies	**Major cardiac anomalies**	
Patent ductus arteriosus	ASD	
Patent foramen ovale	VSD	
	Tetralogy of Fallot	
	Tricuspid regurgitation	
	Pulmonary stenosis	
	Pulmonary hypertension	
	Transposition of the great arteries	
	Aortic stenosis and tubular hypoplasia of aortic arch	
	Common atrium	
	Double outlet right ventricle	

VACTERL – vertebral, ano-rectal, cardiac, tracheo-oesophageal, renal, limb, ASD – atrial septal defect, VSD – ventriculo-septal defect

All patients were investigated preoperatively using plain x-ray as well as abdominal and cranial ultrasound. Of all patients, 28% were found to have associated congenital abnormalities with 5% meeting the criteria for VACTERL association (three or more defects). Congenital abnormalities are listed by organ system in Table IV.

Intraoperatively, the majority of patients (89%) received an inhalational induction with sevoflurane as the agent of choice (Table V). Bronchoscopy was performed on most patients (96%) prior to surgical incision, 87% via rigid and 9% via flexible bronchoscope.

Table IV: Breakdown of non-cardiac congenital abnormalities by organ system

System	Congenital abnormalities	*n* = 36 (%)
Skeletal		
Bilateral club feet		1 (2.7%)
Syndactyly		1 (2.7%)
Radial hypoplasia		1 (2.7%)
Clavicular agenesis		1 (2.7%)
Extra digit		1 (2.7%)
Missing digit		1 (2.7%)
Vertebral: hemivertebra/sacral anomaly/scoliosis		3 (8.3%)
Gastrointestinal tract		
Duodenal atresia		5 (13.8%)
Ano-rectal malformation		4 (11.1%)
Imperforate anus		4 (11.1%)
Gastroschisis		1 (2.7%)
Omphalocoele		1 (2.7%)
Umbilical hernia		1 (2.7%)
Renal		
Agenesis		1 (2.7%)
Hydronephrosis		2 (5.5%)
Ectopic kidney		1 (2.7%)
Chromosomal		
Trisomy 18		4 (11.1%)
CHARGE syndrome		2 (5.5%)
Other		
Situs inversus		1 (2.7%)
Cataract		1 (2.7%)

CHARGE – coloboma, heart defects, atresia choanae, growth retardation or genital abnormalities, ear abnormalities

The fistula was located at the carina in 43% of cases. In 45% of the patients, the fistula was between 0.5 and 1 cm from the carina, and in a further 12% of the patients, it was more than 1 cm away from the carina. The size of the fistula was not consistently described across cases and could, therefore, not be included in this analysis. Following bronchoscopy, the patients were all intubated and anaesthesia was maintained with sevoflurane in oxygen and air.

Almost all cases (96%) were ventilated using a control mode while 4% were reported to be breathing spontaneously throughout the procedure. A neuromuscular blocking agent was used in 35 patients (32.7%), either cisatracurium (60%) or atracurium (25%). Analgesia was managed in all cases with fentanyl and ketamine, while nine patients (8.4%) also had epidural analgesia. Ventilatory difficulty and desaturation were documented in nine patients (8.4%). Haemodynamic instability was indicated in up to 26 patients (24%) by need for fluid boluses with or without the use of inotropes. The mean duration of anaesthesia was 164 minutes (range: 75–330 minutes).

The surgical technique in 90% of the cases was a right-sided thoracotomy. Thoracoscopic access was used in the other 10% of the cases, one of which required conversion to open surgery. Characteristics of the OA/TOF found at surgery are shown in Table V. The most common type was Type C (91%), while 7% was Type B and 2% was Type E. Five of the 107 patients were described as having a 'long gap atresia'.

Table V: Perioperative management

Induction	*n* = 107	Percentage (%)
Inhalational	95	89%
Intravenous	12	11%
Muscle relaxant		
Used	35	33%
Not used	72	66%
Maintenance		
Inhalational	107	100%
Intravenous	0	0
Analgesia		
Intravenous	98	92%
Regional and IV	9	8%
Mode of ventilation		
Controlled	103	96%
Spontaneous	4	4%
Ventilation difficulties	9	8,4%
Tube displaced	3	2.8%
Large fistula leak	2	1.8%
Emergency gastrostomy required to decompress	1	0.9%
Desaturation due to cardiac cause	2	1.8%
Unspecified	1	0.9%
Haemodynamic instability	26	24.3%
Inotrope requiring	8	7.5%
Other§	18	16.8%
ICU transfer		
Ventilated	107	100%
Extubated	0	0
Days to extubation in ICU		
Mode	5	
Min	0	
Duration of case		
Average	164 minutes	
Maximum	330 minutes	
Mode	180 minutes	
Surgical approach		
Thoracotomy	96	90%
Thoracoscopy	11	10%
Findings Gross type	**Number**	**Percentage**
Type B	8	7%
Type C	97	91%
Type E	2	2%
Types A, D	0	0%

IV – intravenous, ICU – intensive care unit, § – transfusions, fluid boluses, cardiac arrest

All neonates were transferred intubated and ventilated to neonatal ICU, where they were ventilated for an average of seven days postoperatively. The 60-day in-hospital survival rate in this cohort was 79%. Mortalities were stratified by gestational age,

Table VI: Mortalities and survival rates by Okamoto class

Factors contributing to mortality		Number of mortalities *n* = 22 (%)		
Birthweight				
< 2 000 g		13 (59%)		
> 2 000 g		9 (41%)		
Cardiac comorbidity				
Major		13 (59%)		
Minor		6 (27%		
None		3 (14%)		
Preoperative ventilation				
Yes		18 (82%)		
No		4 (18%)		
Okamoto class	***n* (%)**	**Survived**	**Died**	**Survival rate by class**
I	60 (56%)	54	6	90%
II	15 (14.2%)	12	3	80%
III	21 (19.6%)	14	7	66%
IV	11 (10.2%)	5	6	45%
	Overall survival rate	79.4%		

birth weight, cardiac comorbidity and preoperative ventilation (Table VI).

Discussion

The most recent large, prospective, observational cross-sectional study of 146 patients with congenital OA/TOF was undertaken across 52 units in Italy via survey in 2011.[7] In their study, the majority of the patients were examined by antenatal ultrasound and the diagnosis of OA was suspected in 29.6% of the cases. Polyhydramnios was the most frequent finding in 55% of the patients examined antenatally.[6] This is in direct contrast to our patient population, where the majority were diagnosed postnatally. This led to delays in transfer to the appropriate referral centre which could provide both paediatric surgical expertise and neonatal intensive care service. Only four patients in our cohort were transferred to the centre on the day of birth. Surgical intervention for OA/TOF is recommended on the first or second day of life.[1] However, our population experienced delays in transfer of 3–4 days on average. A 2011 audit carried out by Knottenbelt et al.[7] on patients with OA/TOF in Australia and New Zealand, reported first surgical intervention on average at 1.3 days post-birth. Although the Italian and Australian research did not comment on the incidence of preoperative pneumonia, these studies do report the need for preoperative mechanical ventilation for respiratory distress in 26.7% and 18.8% of the patients, respectively.[6,7] Similarly, in a United Kingdom-based study, Burge et al.[8] reported that 36.4% of their 151-patient cohort required preoperative mechanical ventilation, although the indication was often prematurity and respiratory distress. In a multi-institutional retrospective cohort study of 356 patients conducted from 2009 to 2014 in the USA, the incidence of preoperative mechanical ventilation was 20.9% and the indication cited was prematurity and congenital heart disease.[9]

In this review, the incidence of preoperative pneumonia was shown to be 39%, with 52% of patients requiring mechanical ventilation. Of the 67 patients who were transferred after day two of life, 46% required ventilation for pneumonia as opposed to 27% of the patients who were transferred in by day two of life. It is, therefore, demonstrated that OA/TOF patients in the South African context have a higher incidence of pneumonia and requirement of preoperative ventilation than patients from developed countries. This could be linked to the delay in diagnosis and transfer to a specialist centre.

The incidence of major congenital cardiac comorbidity in this cohort (25%) was similar to that of other studies (30%).[1,5] In four of the patients with cardiac anomalies, Edward's syndrome (Trisomy 18) was diagnosed via chromosomal analysis postoperatively. In these patients, OA and cardiac defects were accompanied by microcephaly, omphalocele, gastroschisis and choanal atresia, either separately or in combination. Of the patients, 54% had a patent foramen ovale (PFO) or patent ductus arteriosus (PDA) at the preoperative echocardiogram but these were described as non-contributory to the haemodynamic status of the neonates at rest.

The VACTERL association of structural abnormalities (vertebral, ano-rectal, cardiac, tracheo-oesophageal, renal and limb) is commonly associated in patients with OA/TOF. The incidence of at least three of these lesions reported in other studies was variable from 12–30%.[1,6,7] In this study, the incidence of VACTERL association was 5%. Skeletal defects were the most common abnormality, followed by ano-rectal malformations.

In the 1960s, Waterston's initial risk stratification system included the factors of low birth weight, preoperative pneumonia and associated congenital abnormalities.[10] By the 1990s, Spitz et al.[11] found preoperative pneumonia to be so rarely encountered as to propose a new risk classification which considered only the birth weight and presence or absence of congenital cardiac comorbidity in its prediction of survival rate. Okamoto et al.[4] modified the Spitz classification in 2009. The two predictive factors were still birth weight and presence of cardiac comorbidities but included four categories from low risk to high risk.

The survival rates in this study deviated from those in Okamoto's particularly in the Class 1 and Class 4 risk profiles with a lower survival rate of 90% in Class 1 and a higher survival rate of 45% in Class 4. The differences can be explained by our higher rate of preoperative pneumonia, which is rare in other cohorts, as well as by slight differences in inclusion and exclusion criteria between the study groups. In our study, the factors leading to an increased mortality rate included low birth weight, major cardiac comorbidity and preoperative ventilation.

Difficulties in placing the endotracheal tube (ETT) and ventilating the OA/TOF patients are often encountered at induction and other key points in the surgery, such as turning to left lateral position and lung retraction.[1,12] A large fistula in a Type C configuration can result in gastric distention and acute

ventilatory compromise. Placement of the ETT tip can be guided by flexible bronchoscopy and occlusion of a large fistula by a Fogarty catheter has been described in other texts.[5,12] In this cohort, ETT dislodgement was the most common (2.8%) documented complication intraoperatively requiring repositioning of the tube. Additionally, gastric distention necessitated an emergency gastrostomy in one of the cases. Maintaining spontaneous breathing prior to ligation of the fistula is beneficial as the negative pressure allows preferential ventilation of the lungs instead of the digestive tract.[5] In a patient with compromised lungs, this can result in inadequate minute ventilation and hypercapnia. In our cohort, 98% of patients were maintained with positive pressure ventilation (PPV). Knottenbelt et al.[7] reported the use of neuromuscular blockers in 64% of patients for intubation and 98% of patients during maintenance and thoracotomy. The incidence of ventilation difficulties found in that cohort was 6.9%.

Intraoperative haemodynamic instability is usually only anticipated in patients with sepsis or patients with cardiac abnormalities.[5] The incidence of haemodynamic instability was not reported in other studies. In our study, intraoperative haemodynamic support was needed in patients requiring preoperative ventilation and patients with major cardiac abnormalities.

All of our patients were ventilated for at least 24 hours in the neonatal ICU and for 3–5 days in 44.8% of the cases. Factors affecting the timing of extubation in our cohort included the patient's gestational age, weight, presence of cardiac comorbidity or pneumonia as well as surgical factors such as the tension on the anastomosis, ease of the operation or complications encountered. Additionally, the adequacy of analgesia contributes to the predicted success of liberation from the ventilator. In our study, patients were usually extubated by day five postoperatively following further radiographic study (contrast swallow). A prospective audit by Burge et al.[8] of 151 patients with OA/TOF in the United Kingdom and Ireland described a postoperative ventilation period on average of three days. This compares with the Australian/New Zealand cohort, which had 35% extubated by 48 hours postoperatively and 12.9% extubated on the table. Reasons for differences in this parameter can be attributed to specific institutional policies which would request routine elective mechanical ventilation postoperatively.

Strengths and limitations

As a retrospective study, the researchers were able to collate information from over ten years which has allowed analysis of a large cohort for what is a relatively infrequently encountered pathology.

The source for data collection, however, was not purposefully designed and there were many variations in the manner in which information was recorded on the anaesthetic charts, surgical operative record, and in-patient charts. Much of the required detail regarding difficulties encountered with intubation and ventilation was not available as there was no dedicated space to record this by the anaesthesia provider. A prospective audit would better provide more specific information. This study also only reports on those patients accessing public sector healthcare in a single institution.

Conclusion

Although the survival rate of OA/TOF is improving globally, there are still many challenges to overcome in our setting. In this cohort, the lack of antenatal diagnosis, delay in transfer and delay in surgery was linked to a high incidence of preoperative pneumonia requiring ventilatory support. There is a high incidence of associated congenital anomalies in these patients. Inhalational induction of anaesthesia and PPV was not associated with an increased rate of intraoperative complications. Haemodynamic instability is more likely to be encountered in those patients with preoperative pneumonia and major cardiac comorbidities. Improvements in antenatal care policies focusing on prenatal diagnosis and early postnatal diagnosis would assist in timeous referral of these patients to the appropriate facility. Risk stratification for postoperative mortality should consider the requirement for preoperative ventilation, the presence of major cardiac comorbidities and low birth weight in our setting. A prospective observational study of OA/TOF involving multiple institutions in South Africa would be valuable to further delineate the risk factors for poor outcomes and improve risk stratification in these patients.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

Ethical approval was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE526/18) and hospital approval was obtained at Inkosi Albert Luthuli Central Hospital (IALCH), Durban, South Africa.

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