Pediatric Surgery International (2022) 38:1235–1240
https://doi.org/10.1007/s00383-022-05178-z

ORIGINAL ARTICLE

How should we treat representative neonatal surgical diseases with congenital heart disease?

Mitsuru Muto[1] · Koshiro Sugita[1] · Tomoyuki Matsuba[2] · Chihiro Kedoin[1] · Mayu Matsui[1] · Shinichiro Ikoma[3] · Masakazu Murakami[1] · Keisuke Yano[1] · Shun Onishi[1] · Toshio Harumatsu[1] · Koji Yamada[1] · Waka Yamada[1] · Makoto Matsukubo[1] · Takafumi Kawano[3] · Seiro Machigashira[3] · Motofumi Torikai[3] · Tatsuru Kaji[4] · Satoshi Ibara[5] · Yutaka Imoto[2] · Yoshiharu Soga[2] · Satoshi Ieiri[1]

Accepted: 6 July 2022 / Published online: 15 July 2022
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

Abstract

Purpose Representative neonatal surgical diseases are often complicated by congenital heart disease (CHD). We reviewed our decade of experience from the perspective of the prognosis and report on the management of infants with CHD.

Methods Cases with and without CHD between 2011 and 2020 were retrospectively compared. Qualitative data were analyzed using a chi-square test with Yates' correction, and quantitative data were compared using Student's *t*-test.

Results Of the 275 neonatal surgical cases, 36 had CHD (13.1%). Ventricular septal defect was the most common cardiac anomaly, followed by atrial septal defect. Esophageal atresia showed the highest complication rate of CHD (43.8%, 14/32) followed by duodenal atresia (38.5%, 10/26). The mortality rates of patients with and without CHD (22.2% [8/36] vs. 1.3% [3/239]) were significantly different ($\chi^2 = 30.6$, $p < 0.0001$). Of the eight deaths with CHD, six patients had cyanotic complex CHD. Notably, four of these patients died from progression of inappropriate hemodynamics in the remote period after definitive non-cardiac surgery.

Conclusion Considering its high-mortality, the presence of CHD, especially cyanotic heart disease, is an important issue to consider in the treatment of neonatal surgical diseases. Pediatric surgeons should be alert for changes in hemodynamics after surgery, as these may affect mortality.

Keywords Neonatal surgical disease · Congenital heart disease · Mortality · Cyanotic heart disease · Hemodynamics

Introduction

Congenital heart disease (CHD) is seen in approximately 1% of the pediatric population [1]. The prevalence of CHD reportedly varies geographically and Asia has the highest prevalence, with 9.3 cases reported for every 1000 live births [2]. About 40% of children who require cardiac surgery by 1 year old are said to undergo non-cardiac surgery by 5 years old [3, 4]. The frequency of pediatric gastrointestinal disorders combined with CHD has been reported to be 16.5–28.5% [5–7] in the relevant literature.

It has been 10 years since the Department of Pediatric Cardiovascular Surgery was established at our institution, allowing us to consolidate CHD cases requiring surgical intervention. With the establishment of this department, cases that previously required maternal or neonatal transport to distant facilities can now be treated entirely within our local area. We therefore reviewed our decade experience

Mitsuru Muto and Koshiro Sugita are contributed equally to this work.

✉ Mitsuru Muto
mitsuru@m3.kufm.kagoshima-u.ac.jp

1 Department of Pediatric Surgery, Research Field in Medicine and Health Sciences, Medical and Dental Sciences Area, Research and Education Assembly, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890 -8520, Japan

2 Department of Cardiovascular Surgery, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

3 Department of Pediatric Surgery, Kagoshima City Hospital, Kagoshima, Japan

4 Department of Pediatric Surgery, Kurume University School of Medicine, Kurume, Japan

5 Department of Neonatology, Perinatal Medical Center, Kagoshima City Hospital, Kagoshima, Japan

from the perspective of the prognosis and report how we pediatric surgeons should manage infants with CHD who require surgery for representative neonatal surgical diseases.

Materials and methods

Study design and data collection

A retrospective chart review was performed on congenital neonatal surgical cases with and without CHD treated from January 1, 2011 to December 31, 2020. Low-birth-weight infants (LBWIs), very-low-birth-weight infants (VLBWIs), and extremely low-birth-weight infants (ELBWIs) with congenital neonatal surgical disease complicated with patent ductus arteriosus (PDA) alone were excluded from this study. In addition, LBWIs, VLBWIs, and ELBWIs with necrotizing enterocolitis, focal intestinal perforation, and meconium related ileus, which are also associated with some acquired factors, were excluded from this study. We focused on the relationship between congenital neonatal surgical disease and CHD and the associated mortality rate in this study.

Statistical analyses

The qualitative data were analyzed using a chi-square test with Yates' correction, and the quantitative data were compared using Student's *t*-test. Statistical analyses were performed using the IBM SPSS Statistics software program, version 27 (IBM, Tokyo, Japan), for Windows. *P* values of <0.05 were considered to indicate statistical significance.

Ethical approval

This study was performed in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects by the Ministry of Health, Labor and Welfare of Japan in 2014 and in compliance with the 1964 Declaration of Helsinki (revised in 2013). Patient data were collected with blinding of personal information and registered using consecutive patient numbers. This study was also approved by the local ethics committee of our institution (27–119).

Results

Differences in patient background characteristics by the presence of CHD

There were 416 neonatal surgical cases during the 10-year period, 68 cases with neonatal asphyxia who required extracorporeal membrane oxygenation catheter insertion for cerebral hypothermia, and 73 cases who met the aforementioned criteria were excluded. Remaining 275 cases were included in the present study. Thirty-six patients (13.1%) had CHD. Differences in patient background characteristics by the presence of CHD are shown in Table 1. There were no marked differences in the proportion of gender and gestational age between the groups with and without CHD. Infants with CHD tended to be lighter in weight (2355.5 g vs. 2716 g; $p<0.001$) and had a higher delivery rate with Caesarean Sect. (63.9% vs. 42.3%; $p=0.024$). The total number of deaths was 11. While the mortality rate in patients without CHD was 1.3% (3/239), that of patients with CHD was 22.2% (8/36), as shown in Table 1. The mortality rate was significantly higher in patients with CHD than in those without it ($\chi^2=30.6$, $p=3.23$ E–8). The relative risk for death along with CHD was estimated to be 17.1

Frequency of CHD in congenital neonatal surgical disease

The frequency of CHD in congenital neonatal surgical disease is summarized in Table 2. Esophageal atresia (EA) showed the highest complication rate with CHD (43.8%), followed by duodenal atresia (DA; 38.5%), intermediate-high anorectal malformation (ARM; 18.8%), low ARM (15.4%), omphalocele (15.4%), and congenital diaphragmatic hernia (CDH; 8.0%). The most common CHD was ventricular septal defect (VSD), followed by atrial septal defect (ASD), tetralogy of Fallot (TOF), total anomalous pulmonary venous return (TAPVR), double-outlet right ventricle (DORV), coarctation of aorta (CoA), pulmonary atresia (PA), and single ventricle (SV), as shown in Table 2.

Table 1 Differences in patient background characteristics according to the presence or absence of CHD

	CHD present ($n=36$)	CHD absent ($n=239$)	*P* value
Sex (male: female)	18:18	143:96	0.3498
Mean gestational weeks (range)	36.7 weeks (29–41)	37.5 weeks (31–42)	0.0712
Mean birth weight (range)	2355.5 g (1108–3466)	2716.3 g (1148–4050)	0.0004
Caesarean section rate	63.9% (23/36)	42.3% (101/239)	0.0243
Mortality rate	22.2% (8/36)	1.3% (3/239)	<0.0001

CHD congenital heart disease

Table 2 Frequency of CHD (including duplicate cases)

Neonatal surgical disease with CHD	Percentage of CHD	VSD	ASD	TOF	TAPVR	DORV	PA	CoA	SV	miscellaneous
Esophageal atresia ($n=14$)	43.8% (14/32)	7	4	1	1[a]	1[a]	1			
Duodenal atresia ($n=10$)	38.5% (10/26)	7	4	2	1	1[a]	1[a]	1	1[a]	1[a]
Intermediate•High anorectal malformation ($n=6$)	18.8% (6/32)	3	1	1	1	2[a]	2[a]		1[a]	1[a]
Low anorectal malformation ($n=2$)	15.4% (2/13)	2	1					1		
Omphalocele ($n=2$)	15.4% (2/13)	2	1							1
Congenital diaphragmatic hernia ($n=2$)	8.0% (2/25)			1[a]						1
Miscellaneous ($n=11$)	–	2	1	1	1					2
Total		23	12	6	4	4	4	2	2	6

CHD congenital heart disease, *VSD* ventricular septal defect, *ASD* atrial septal defect, *TOF* tetralogy of Fallot, *TAPVR* total anomalous pulmonary venous return, *DORV* double-outlet right ventricle, *PA* pulmonary atresia, *COA* coarctation of aorta, *SV* single ventricle

[a]denotes CHD considered an anomaly associated with patient's death

Details of fatal cases

Among the eight fatal cases with CHD, four (case 1–4) died when their general condition was stable after surgery for congenital non-cardiac surgical disease. Notably, all had cyanotic complex heart disease, such as TAPVR, DORV, and TOF, which brought sudden hemodynamic changes in patients and which was associated with death. Two (case 1, 2) of the four patients had undergone cardiac surgical intervention by cardiovascular surgeons. Before cardiac arrest, there was a marked drop in the percutaneous oxygen saturation (SpO_2) in all cases. In the remaining four, the respiratory failure was thought to be the direct cause of death. Three (case 5, 6, 7) of these four cases had a background of congenital airway anomalies. One patient died of sudden unexplained ventilator failure during esophageal reconstruction for EA. A summary of eight cases concerning mortality with CHD is shown in Table 3.

There were three deaths among the cases without CHD: a patient with bilateral kidney anomalies (right anaplastic kidney + left atrophic multi cystic kidney) and ARM without fistula, who died of renal failure with difficulty in continuing peritoneal dialysis; a patient with bilateral diaphragmatic hernia, who died due to septic shock; and a patient with septic shock after surgery for strangulated ileus due to the mesodiverticular band in Meckel's diverticulum.

Discussion

The present study revealed the following findings: (1) the mortality rate of 36 children with congenital neonatal surgical disease complicated by CHD was considerably higher than that of 239 children without CHD (8/36, 22.2% vs. 3/239, 1.3%, $p<0.0001$); (2) the birth weight of neonates with congenital surgical disease complicated with CHD was significantly lower than that of uncomplicated neonates; (3) patients with cyanotic complex CHD, such as TAPVR, DORV, and TOF, showed rapid hemodynamic changes, which were associated with patient mortality.

The prognosis for CHD is reported to be about 85% based on a 5-year survival assessment, ranging from 14% with complex CHD, such as hypoplastic left heart, to 96% with simple CHD, such as VSD [8]. In general, the mortality rate for pediatric cardiovascular surgery are approximately 3–4% [9, 10]. However, when CHD is associated with congenital neonatal surgical disease, the mortality rate is reported to increase nearly three to fourfold [10–13]. The mortality rate of our 36 infants, 22.2%, was slightly higher in comparison to these former reports, and was 17 times higher than that of infants without CHD. Given the high mortality rate, the presence of CHD is an important issue to be considered in the treatment of neonatal surgical diseases.

In general, the survival of infants with CHD is known to be influenced by gestational age at birth (especially < 32 weeks) and birth weight (especially smaller than − 2 standard deviations [SD] for gestational age) [14]. We found no difference in gestational age between patients with and without CHD in our study ($p=0.0712$), but birth weight was smaller in patients with CHD than in those without it ($p=0.0004$). On comparing surviving and deceased cases with CHD, the mean gestational age was younger in fatal cases (37.0 weeks vs. 35.8 weeks, $p=0.1954$), and the mean birth weight was significantly lower in fatal cases (2468.3 g vs. 1960.5 g, $p=0.0121$). Of the eight deaths in our study, two (Table 3, case 5 and 6) were born before 32 weeks of gestation, and two (Table 3, case 3 and 8) were born with weights smaller than − 2 SD for their gestational age. These seem to be important factors to keep in mind.

On reviewing the causes of death, the association of CHD was implicated in four cases (Table 3, case 1–4). All four patients had cyanotic complex cardiac anomalies and died once their condition had stabilized after surgery for congenital neonatal surgical diseases. Two patients died

Table 3 Details concerning mortality with CHD

Case	Neonatal surgical disease	Complicated CHD	Sex	GA	Delivery	Birth weight (SD)	Initial surgical treatment	Intervention for CHD	Course
1	EA (type C)	TAPVR (typeII a + Ia) + ASD	F	40w5d	NVD	2884 g (− 0.6SD)	Radical surgery for EA with right thoracotomy (day 1)	Cut back TAPVR repair (day 6), pulmonary vein plasty (day 47)	Pulmonary congestion and pulmonary hypertension continued to progress, and poor oxygenation led to cardiac arrest (day 88)
2	DA ARM	DORV + PA + MVO + SV + PPVRA	M	39w3d	CS	2832 g (− 0.6SD)	Radical surgery for DA + colostomy (day 1)	Central shunt formation + ASD enlargement + PDA ligation (day 72)	Sudden bradycardia following desaturation required PCPS, but withdrawal of PCPS was determined due to no improvement of cardiac output (day 77)
3	Left CDH (total defect, L/T ratio = 0.12) + 13 trisomy	TOF	F	36w6d	CS	1740 g (− 2.5SD)	Patch repairing of the diaphragm (day 2), had difficulty in extubation	Echocardiography suggested presence of PH under mechanical ventilation (day 40)	Desaturation and bradycardia began to occur without incentive, even on mechanical ventilation, along with sudden bradycardia while exchanging the tracheal tube progressing to cardiac arrest (day 42)
4	EA (type C) ARM rt MCDK	DORV	M	37w2d	CS	2018 g (− 2.0SD)	Radical surgery for EA with right thoracotomy + colostomy (day 1)	Echocardiography suggested no signs of PH (day 0)	Sudden bradycardia and metabolic acidosis became apparent under mechanical ventilation, and deterioration of cardiac contraction led to cardiac arrest (day 4)
5	TA GP	TAPVR + TOF	F	30w3d	NVD	1108 g (− 1.6SD)	Gastric wall repairing (day 2)	Sequential echocardiography	Died of ventilation failure (day 6)
6	TS DA ARM	TOF + PA	M	31w2d	CS	1266 g (− 1.6SD)	Radical surgery for DA + colostomy (day 12)	Sequential echocardiography	Died of ventilation failure (day 115)
7	TA EA ARM	VSD	M	37w3d	NVD	2634 g (− 0.2SD)	VA-ECMO catheterization (day 0)	Sequential echocardiography	Died of ventilation failure (day1)

Table 3 (continued)

Case	Neonatal surgical disease	Complicated CHD	Sex	GA	Delivery	Birth weight (SD)	Initial surgical treatment	Intervention for CHD	Course
8	EA (type C) GP 18 trisomy	VSD + ASD + PDA	M	37w3d	CS	1202 g (− 4.5SD)	Gastric wall repairing + esphageal banding + gastrostomy (day 3)	Sequential echocardiography	Died of ventilation failure during esophageal repairing (day 180) (sudden ventilation failure resulted in the disturbance of hemodynamics, but its cause was not clear)

EA esophageal atresia, *DA* duodenal atresia, *ARM* anorectal malformation (without fistula), *CDH* congenital diaphragmatic hernia, *L/T* ratio lung-to-thorax ratio, *rtMCDK* right multicystic dysplastic kidney, *TAPVR* total anomalous pulmonary venous return, *ASD* atrial septal defect, *DORV* double-outlet right ventricle, *PA* pulmonary atresia, *MVO* mitral valve obstruction, *SV* single ventricle, *PPVRA* partial pulmonary venous return anomaly, *TOF* tetralogy of Fallot, *PDA* patent ductus arteriosus, *PCPS* percutaneous cardiopulmonary support, *PH* pulmonary hypertension, *GA* gestational age, *NVD* normal vaginal delivery, *CS* Caesarean section, *TA*, tracheal agenesis (esophageal bronchus), *GP* gastric perforation, *TS* tracheal stenosis, *VSD* ventricular septal defect, *VA-ECMO* veno-arterial extracorporeal membrane oxygenation

despite intervention by pediatric cardiovascular surgeons to improve their circulation dynamics. The adverse events are considered to be possible complications after cardiovascular surgery for CHD. There was no time to perform rescue intervention for the sudden changes in hemodynamics in the remaining two cases. It was difficult to determine retrospectively whether or not the deaths in these two cases were avoidable.

Patients with cyanotic CHD are known to be capable of maintaining an adequate cardiac output and oxygen delivery even in situations where pulmonary blood flow is restricted, unless the arterial oxygen saturation is not too low and adequate hemoglobin levels are maintained [15]. However, when metabolic acidosis or lactic acidosis are observed, the oxygen delivery may already be recognized to be inadequate [16], and it is easily assumed that intervention may be difficult because the patient's general condition deteriorates rapidly. According to a report that examined the relationship between desaturation and adverse events during invasive procedures in children with CHD, when a decrease in saturation of more than 30% with pulse oximetry is shown, it is 4.03 times more likely to cause adverse hemodynamic events in patients with cyanotic heart disease [17]. Maintaining an adequate oxygen saturation may help to avoid such adverse changes in hemodynamics in patients with cyanotic heart disease. Pediatric surgeons should take care to observe the oxygen saturation over time and maintain adequate hemoglobin levels, and by sharing this information promptly with pediatric cardiologists and pediatric cardiovascular surgeons, patient mortality may decrease and become closer to that of patients with CHD alone.

The limitation of this study is the restricted number of cases. The proportion of cases with cyanotic complex CHD was 50.0% (18/36) in our study. This fact may explain the higher mortality of patients with CHD compared to that of the relevant literature [10–13]. Although it has been 10 years since the Department of Pediatric Cardiovascular Surgery was established at our institution, there is still room for improvement in the perioperative management of patients represent neonatal surgical diseases with CHD.

Conclusions

Considering its high mortality, the presence of CHD is an important issue to be considered in the treatment of congenital neonatal surgical diseases. Particularly in the treatment of patients with cyanotic complex CHD, changes in the circulatory dynamics, not only in the perioperative period, but also in a remote period after the initial operation for congenital diseases, have to be kept in mind. Pediatric surgeons should be aware of the importance of a decrease in oxygen saturation which may result in adverse hemodynamic events in

children with CHD. At the same time, prompt sharing of the information with pediatric cardiologists, cardiovascular surgeons, intensivists, and neonatologists should be emphasized in a daily management.

Acknowledgements We thank Mr. Brian Quinn for his comments and help with the manuscript.

Author contributions M.M. wrote the main manuscript text and K.S. collected data for table 1-3. Y.I. commented on the clinical evaluation of the subject cases underwent cardiac surgeries with congenital heart disease. All authors reviewed the manuscript.

Declarations

Competing interests The authors declare no competing interests.

Conflict of interest The authors have no conflicts of interest to declare with regard to this article.

References

1. Hoffman JL, Kaplan S (2002) The incidence of congenital heart disease. J Am Coll Cardiol 39:1890–1900. https://doi.org/10.1016/s0735-1097(02)01886-7
2. Hoffman JI, Kaplan S, Liberthson RR (2004) Prevalence of congenital heart disease. Am Heart J 147:425–439. https://doi.org/10.1016/j.ahj.2003.05.003
3. Faraoni D, Zurakowski D, Vo D, Goobie SM, Yuki K, Brown ML, DiNardo JA (2016) Post-operative outcomes in children with and without congenital heart disease undergoing noncardiac surgery. J Am Coll Cardiol 67:793–801. https://doi.org/10.1016/j.jacc.2015.11.057
4. Baum VC, Barton DM, Gutgesell HP (2000) Influence of congenital heart disease on mortality after noncardiac surgery in hospitalized children. Pediatrics 105:332–335. https://doi.org/10.1542/peds.105.2.332
5. Thompson AJ, Mulholland HC (2000) The incidence of cardiac lesions in infants born with major gastrointestinal malformations in northern Ireland. Ulster Med J 69:23–26
6. Wojtalik M, Mrowczynski W, Henschke J, Wronecki K, Siwinska A, Piaszczynski M, Wojtalik MP, Mrozinski B, Bruska M, Blaszczynski M, Surmacz R (2005) Congenital heart defect with associated malformations in children. J Pediatr Surg 40:1675–1680. https://doi.org/10.1016/j.jpedsurg.2005.06.004
7. Olgun H, Karacan M, Caner I, Oral A, Ceviz N (2009) Congenital cardiac malformations in neonates with apparently isolated gastrointestinal malformations. Pediatr Int 51:260–262. https://doi.org/10.1111/j.1442-200X.2008.02711.x
8. Best KE, Rankin J (2016) Long-term survival of individuals born with congenital heart disease: a systematic review and meta-analysis. J Am Heart Assoc 5:e002846. https://doi.org/10.1161/jaha.115.002846
9. Hirata Y, Hirahara N, Murakami A, Motomura N, Miyata H, Takamoto S (2021) Status of cardiovascular surgery in Japan: a report based on the japan cardiovascular surgery database 2017–2018. 1. congenital heart surgery. Asian Cardiovasc Thorac Ann 29:289–293. https://doi.org/10.1177/0218492320981501
10. Oster ME, Strickland MJ, Mahle WT (2011) Impact of prior hospital mortality versus surgical volume on mortality following surgery for congenital heart disease. J Thorac Cardiovasc Surg 142:882–886. https://doi.org/10.1016/j.jtcvs.2011.04.011
11. Mery CM, De León LE, Rodriguez JR, Nieto RM, Zhang W, Adachi I, Heinle JS, Kane LC, McKenzie ED, Fraser CD Jr (2017) Effect of gastrointestinal malformations on the outcomes of patients with congenital heart disease. Ann Thorac Surg 104:1590–1596. https://doi.org/10.1016/j.athoracsur.2017.04.042
12. Cohen LL, Przybylski R, Marshall AC, Emans JB, Hedequist DJ (2021) Surgical correction of scoliosis in children with severe congenital heart disease and palliated single ventricle physiology. Spine 46:E791-796. https://doi.org/10.1097/BRS.0000000000003905
13. Pilkington M, Egan JC (2019) Noncardiac surgery in the congenital heart patient. Semin Pediatr Surg 28:11–17. https://doi.org/10.1053/j.sempedsurg.2019.01.003
14. Best KE, Tennant PWG, Rankin J (2017) Survival, by birth weight and gestational age, in individuals with congenital heart disease: a population-based study. J Am Heart Assoc 6:e005213. https://doi.org/10.1161/JAHA.116.005213
15. Singh Y, Lakshminrusimha S (2021) Perinatal cardiovascular physiology and recognition of critical congenital heart defects. Clin Perinatol 48:573–594. https://doi.org/10.1016/j.clp.2021.05.008
16. Hines MH (2013) Neonatal cardiovascular physiology. Semin Pediatr Surg 22:174–178. https://doi.org/10.1053/j.sempedsurg.2013.10.004
17. Mokhateb-Rafii T, Bakar A, Gangadharan S, Gradidge EA, Tellez D, Ruppe M, Tallent S, Bird G, Lavin N, Lee A, Napolitano N, Nadkarni V, Shults J, Nishisaki A (2019) Hemodynamic impact of oxygen desaturation during tracheal intubation among critically ill children with cyanotic and noncyanotic heart disease. Pediatr Crit Care Med 20:19–26. https://doi.org/10.1097/PCC.0000000000001766

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.