

Neonatal Cardiac Surgery in the New Era: Lessons Learned from 1000 Consecutive Cases

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ABSTRACT: **Background:** Neonatal cardiac surgery has evolved over the last 50 years with a large percentage of the patients achieving complete physiological repair in the neonatal period. The remaining patients achieve staged palliation with an increasing amount of success.

Objectives: To report our experience with 1000 neonatal cardiac surgical procedures performed in the last 10 years.

Methods: We conducted a retrospective analysis of surgical outcome in all neonatal patients who underwent cardiac surgery between January 2007 and July 2016 at Schneider Children's Medical Center of Israel.

Results: A total of 1003 neonates aged < 30 days underwent surgery for congenital heart defects at our center. Neonatal surgery accounted for 22.5% of all cardiac surgeries. Neonatal operative mortality was 7.3%. Operative mortality for individual lesions were: simple aortic coarctation (CoA) (198 patients, 2.5%), CoA with hypoplastic arch (24, 4%), CoA with ventricular septal defect (VSD) (84, 2.3%), transposition of the great arteries (TGA, simple and complex, 185, 6.3%), TGA with VSD (37, 0%), truncus arteriosus (26, 3.8%), interrupted aortic arch (25, 4%), Norwood Sano (71, 19.7%), neonatal tetralogy of Fallot (41, 0%), and shunt (131 patients, 12%).

Conclusions: Neonatal surgical capabilities have improved substantially over the last decades. Excellent results can be expected for lesions that can be repaired to create biventricular circulation. Improved results can be attributed in part to the evolution of surgical strategies and assistive technologies, but essential is the collaborative effort of surgeons, cardiologists, anesthesiologists, and intensive care specialists acting as a cohesive team whose performance far exceeds the sum of its individual members' contributions.

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KEY WORDS: neonate, cardiac surgery, mortality, cardiac team

Neonates undergoing cardiac surgery are the most vulnerable surgical patients due to the fragility of their immature body systems and the complex reconstructions needed to overcome their congenital malformations and achieve hemodynamic repair. Cardiac surgery has evolved dramatically over the last 50 years: a large percentage of the patients achieve complete repair in the neonatal period, and the remaining ones achieve staged palliation with an increasing amount of success.

Many factors are responsible for the improved results: improvement in diagnostic abilities and surgical techniques, innovation in cardiopulmonary bypass, and the creation of specialized intensive care units. Over the past 10 years, we have been committed to the improved care of neonatal patients with congenital cardiac malformations, striving to achieve the best possible results. We report our experience with 1003 consecutive neonatal cardiac surgical procedures performed in the last 10 years.

PATIENTS AND METHODS

We conducted a retrospective analysis of all neonatal patients who underwent cardiac surgical procedures at Schneider Children's Medical center of Israel between January 2007 and July 2016. Patients were enrolled if age at operation was less than 30 days. Operative mortality was defined as occurring prior to discharge from the hospital. Preoperative and operative diagnosis was determined by the cardiology team and operating surgeon.

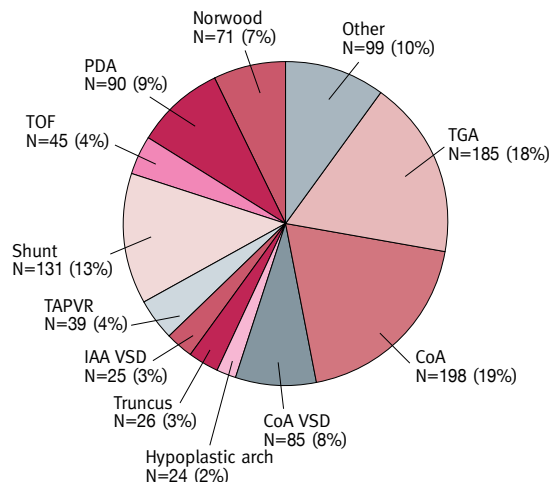
RESULTS

Between January 2007 and June 2016, 1003 neonates under 30 days of age underwent surgery for congenital heart defects at Schneider. During the same period, 4450 pediatric patients underwent surgery for congenital heart defects. Overall operative mortality for the whole cohort of patients was 2.96%. Neonatal surgery accounted for 22.5% of all cases performed at our center. The most prevalent operation performed was the repair of aortic coarctation (CoA, 198 patients) and transposition of the great arteries (TGA, 185 patients). Figure 1 depicts the distribution of operative diagnosis of all patients who underwent surgery. Neonatal out-of-hospital postoperative mortality was 7.3%. Table 1 presents the operative mortality for each of the main neonatal diagnoses and operations, compared with results obtained from international databases and leading centers worldwide.

DISCUSSION

The care for patients with congenital heart disease has evolved over the last decades and has changed significantly. Neonatal cardiac surgery is the most demanding field among surgeries

Figure 1. Patient diagnosis of all neonates operated 2007–2016



TGA = transposition of great arteries, VSD = ventricular septal defect, IAA = interrupted aortic arch, TAPVR = total anomalous venous repair, TOF = tetralogy of Fallot, CoA = coarctation, PDA = patent ductus arteriosus, N = number of operations

Table 1. Neonatal surgical mortality

Diagnosis	Sub-diagnosis	No. of patients	Mortality	
			Schneider (No. %)	STS / EACTS / selected references
TGA	Total	185	12, 6.4%	6% [1]
	TGA VSD	37	0	11% [1]
	TGA CoA	4	0	
	TGA VSD CoA	11	1, 9%	
	Taussig Bing	15	3, 20%	
CoA	Total	338	5, 2.5%	2.8% [2] / 4.6% [3]
	Simple	198	2, 2.3%	5.3% [4] / 4% [5]
	CoA VSD	85	1, 6%	
	TGA CoA	15	1, 4%	
	Hypoplastic arch	24	2	
	Single ventricle	7	1	
	CoA AVSD	4		
Shunt	Total	131	16, 12%	12% [2] / 12.1% [3]
	PA IVS	40	5, 12.5%	15.6% [6]
	TOF	4	0	
TOF	Complete repair	41	0	6% [7] / 1.6% [8] / 0% [9]
	Shunt	4	0	6% [7]
Truncus		26	1, 3.8%	15.4% [2]
IAA VSD		25	1, 4%	14.5% [2] / 19.2% [3]
TAPVR	Total	39	2, 5.1%	10.7% [2] / 16.5% [3] / 14% [10]
	Infra-cardiac obstructed	10	2, 20%	
	Other	29	0	
Norwood		71	14, 19.7%	24% [2] / 36.2% [3] / 17% [11]

Neonatal surgical mortality by diagnosis for patients operated.

TGA = transposition of great arteries, VSD = ventricular septal defect, IAA = interrupted aortic arch, TAPVR = total anomalous venous repair, TOF = tetralogy of Fallot, CoA = coarctation, PA IVS = pulmonary atresia intact septum

for congenital heart disease due to the high surgical complexity and the fragility of the immature systems [12]. The exposure to surgical trauma and to the effects of heart and lung machines provokes an intense inflammatory response accompanied by hemodilution and hypothermia [13].

Since the first pioneering neonatal surgeries performed on patients with transposition of the great arteries in the 1970s [14], surgical techniques evolved and were gradually standardized, allowing complex repairs and palliation for lesions such as hypoplastic left heart syndrome that were previously considered inoperable [15]. With time, even symptomatic neonates with tetralogy of Fallot were repaired in the neonatal period rather than being subject to palliative shunts [16,17]. Recent advances in the treatment of these patients, e.g., the introduction of the RV-to-PA shunt (the Sano shunt) for patients with hypoplastic heart syndrome, further improved results [18].

OVERALL PEDIATRIC CARDIAC SURGERY RESULTS

During the past decade, 4450 pediatric patients underwent cardiac surgery at our institution, of whom 1003 (22.5%) were neonates. We sought to assess our results and compare them with the results of leading centers in the world.

Surgical results can be evaluated using formulated complexity scores, the most recent being the Aristotle Complexity Score (ACS), which is based on the primary procedure of a given operation. Huge databases have been created. In 2005, the American Society of Thoracic Surgeons (STS) database accounted for 18,928 patients, and the European database (EACTS) added 21,916 patients [19]. For the whole patient cohort, operative mortality at our institution was 2.96%. This is substantially lower than the mortality reported in the American STS database (4.5%) and in the European EACTS database (5.4%). Moreover, our complexity scores (measured annually), 7.2–7.4, were higher than the STS mean complexity score (7.1) and the European score (6.5).

Nevertheless, comparing results is a difficult task. There is a complex relationship between cardiac surgical case volumes and mortality rates [11]. Overall mortality in centers performing more than 350 cases annually was 3.2%, while in centers performing 250–350 cases annually the mortality was 3.7%, and in smaller centers 4.1%. This difference is more pronounced in high complexity cases, where mortality was found to be 7.2%, 8.4%, and 13% respectively [11]. Comparisons aside, this sends a clear message, namely, that in this field one must create a few, very high volume centers of excellence rather than focus on patient convenience and geographic distribution.

NEONATAL CARDIAC SURGERY RESULTS

Neonatal cardiac surgical mortality was also evaluated using these large databases. The STS reported neonatal operative mortality of 12.2%, and the EACTS reported 13.3% [19]. More recently, the EACTS reported their results in 14,843 neonates operated on between 1999 and 2009 [3]. For this cohort of patients, out-of-hospital postoperative mortality was 10.7%. Out-of-hospital mortality at our institution for neonates was only 7.2%, which compares favorably with the international results.

RESULTS FOR SPECIFIC LESIONS IN THE NEONATAL GROUP

In order to further scrutinize our results, we sought to compare surgery for specific important lesions with published results of leading international cardiovascular centers. Transposition of the great arteries (TGA) is a congenital cardiac malformation in which both great vessels emerge from the “wrong” ventricle; consequently, the systemic circulation and the myocardium receive deoxygenated blood while the lungs recirculate oxygenated blood. Survival of the neonate is only possible due to mixing of oxygenated and deoxygenated blood via communication between the two circulations. Operative repair is achieved by “switching” back the great arteries and the coronary arteries, the arterial switch operation (ASO). There is a wide spectrum of anatomic variants that make the operation much more complex, as reflected in the operative results of the different subgroups [20]. Complex transpositions include associated ventricular septal defects (VSD), coronary anomalies, malposition of the great vessels and aortic coarctation (CoA). In 2010, the group from Ann Harbor Michigan published results for their complete cohort of ASOs. Their demographics are similar to ours, and their operative mortality was 6%, similar to our result of 6.2% [20]. Taking a closer look at the various subgroups of the complex transpositions, we had no mortality in the complex group of TGA VSD (37 patients), and only one patient died in the TGA VSD CoA group (11 patients). Taussing-Bing anomaly is one of the most complex anomalies within the transposition spectrum. In this anomaly, both great vessels arise from the right ventricle alongside each other, making the operative reconstruction extremely difficult. In this challenging subgroup of patients we lost 3 of the 15 patients.

EARLY COMPLETE REPAIR VS. MULTI-STATE STRATEGIES

Single-stage repair and complete and early physiological correction are the hallmarks of modern neonatal cardiac surgery. As neonatal cardiac surgery evolved, however, it became apparent that early surgical correction is also beneficial to palliation; benefits include promotion of normal growth and development of organs, and the elimination of hypoxemia. These benefits had to outweigh the surgical risks at an early age. Improved surgical results have been made possible by meticulous surgical techniques and improved cardiopulmonary bypass protocols and hardware.

Surgical treatment of tetralogy of Fallot (TOF) has changed dramatically since the first palliation was performed by Alfred Blalock in 1945; palliative procedures have been replaced with complete repair in infancy, but treatment of symptomatic neonatal patients is still controversial. Advocates of neonatal palliation claim that it reduces the need for future trans-annular patching and decreases the risk of early mortality, while advocates of neonatal complete repair claim that mortality is lower and the avoidance of cyanosis and chronic right ventricular overload beneficial to the patient in the long run. A multicenter

analysis published just recently reports that of 845 patients with ductal-dependent TOF, 41% underwent complete repair, while 59% underwent initial palliation [7]. Operative mortality was found to be similar for the first operation (7.8% vs. 6%), though the staged palliative approach was associated with higher morbidity [7]. Our approach has been towards early complete repair; although it is more technically challenging, in our opinion it yields better results. Of 45 patients presenting with clinically symptomatic neonatal TOF who required surgery, 4 patients (10%) were palliated while complete neonatal repair was performed in 41 patients. There was no operative mortality, which is comparable with contemporary leading cardiosurgical centers (1.6% [8], 0% [9]). Such low mortality in the complete repair of neonatal TOF is a clear reflection of the sum ability of all teams caring for the neonate with complex congenital heart disease.

Another lesion that demonstrates the advantage of complete early correction is coarctation of aorta in conjunction with a hemodynamically significant VSD (CoA VSD). The optimal surgical strategy has been controversial [21]. There are three surgical options: the first and most conservative is the two-stage repair, in which the coarctation is repaired through a left thoracotomy and a band is placed around the pulmonary artery through the same incision; the VSD is closed when the child is older and bigger. The second option is a single-stage repair with two incisions, whereby the coarctation is repaired through a left thoracotomy incision, followed by a VSD closure through a sternotomy. The third strategy is concomitant repair of the arch and the VSD through sternotomy using regional cerebral perfusion. The latter is our preferred strategy.

NEUROLOGICAL IMPLICATIONS

With the significant advances achieved in the repair of complex congenital heart defects and the consistent reduction in mortality, focus was directed towards preservation of the neurological status. One of the most important technical modifications was the use of selective cerebral perfusion when performing arch reconstruction [22]. Historically, repair of complex congenital heart defects was associated with a high incidence of clinical and subclinical seizures (28% and 67% respectively in patients with TGA VSD) [23]. In our neonates the rate of postoperative seizure is well under 2% over the last 5 years. Clearly, further evaluation and follow-up are required to assess the issue of neurological outcome of neonatal cardiac surgery, which is beyond the scope of this paper.

Cardiopulmonary bypass is initiated by cannulating the innominate artery and lowering the core temperature to 28°C. Once the target temperature has been reached, total body circulatory arrest is initiated and the brain is selectively perfused through the innominate artery. The aortic arch is then repaired, usually taking 20–30 minutes. Total body perfusion is then re-instituted, and the VSD is subsequently closed. Among 85 patients with CoA VSD who were operated upon using this

technique, there were 2 deaths (2.3%), similar to the results published by Sandhu et al. (5.3%) [4] and Gaynor et al. (4%) [5].

Using selective cerebral perfusion, we have performed 206 arch reconstructions without noticing clinically significant neurological events. Furthermore, we have performed 71 Norwood Sano operations with 19% mortality, which favorably compares with the results reported by the STS (24%), EACTS (36.2%), and with results reported from high volume leading North American institutions (17%) [11].

OUR SERVICE

Neonatal cardiac surgery has evolved and changed over the last two decades, many insights were acquired, and as experience and confidence were built the surgical procedures were stretched even further and closer to the limit. With time, our specialized neonatal service has evolved as well, and 1000 cases have taught us many lessons. Strategically, the quest to achieve complete and early physiologic repair, although technically more complex and demanding, is for the benefit of the patient. The evolution of new surgical routines and the use of selective cerebral perfusion further allowed us to improve our results and decrease morbidity and mortality.

Achieving surgical results that are on par with the highest international standards has been made possible through years of cumulative experience and the incorporation of improvements and innovations into our service. The success of a cardiovascular service is not only dependent on flawless, non-compromising surgical results but also on a sound and solid supporting infrastructure providing accurate diagnosis and making the correct preoperative decisions. Prenatal diagnosis allows better planning of birth place and immediate postnatal assessment and treatment. Intraoperative cardiology support is imperative for confirming the diagnosis and for providing perioperative online quality control. Smooth and experienced anesthesia decreases the morbidity associated with the treatment of the smaller babies. Postoperative proactive intensive care unit (ICU) treatment with tight cooperation between the surgeons, the intensivists and the cardiologists provide continuity of care, where the sick child is at all times treated by a senior physician well acquainted with his or her disease.

Finally, beyond technological advances and the availability of the various disciplines, we strongly believe that two additional elements are absolutely necessary (but not sufficient) for achieving the results like the ones we have attained: (i) concentration of the activity in order to gain expertise through experience, even at the expense of patient convenience, and (ii) a truly cohesive team that works together, putting the optimal outcome of the patient as its only goal and achieving a total that far exceeds its components.

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References

1. Qamar ZA, Goldberg CS, Devaney EJ, Bove EL, Ohye RG. Current risk factors and outcomes for the arterial switch operation. *Ann Thorac Surg* 2007; 84: 871-8; discussion 78-9.
2. O'Brien SM, Jacobs JP, Clarke DR, et al. Accuracy of the Aristotle basic complexity score for classifying the mortality and morbidity potential of congenital heart surgery operations. *Ann Thorac Surg* 2007; 84: 2027-37; discussion 27-37.
3. Kansy A, Tobota Z, Maruszewski P, Maruszewski B. Analysis of 14,843 neonatal congenital heart surgical procedures in the European Association for Cardiothoracic Surgery Congenital Database. *Ann Thorac Surg* 2010; 89: 1255-9.
4. Sandhu SK, Beekman RH, Mosca RS, Bove EL. Single-stage repair of aortic arch obstruction and associated intracardiac defects in the neonate. *Am J Cardiol* 1995; 75: 370-3.
5. Gaynor JW, Wernovsky G, Rychik J, Rome JJ, DeCampi WM, Spray TL. Outcome following single-stage repair of coarctation with ventricular septal defect. *Eur J Cardiothorac Surg* 2000; 18: 62-7.
6. Petrucci O, O'Brien SM, Jacobs ML, Jacobs JP, Manning PB, Eghtesady P. Risk factors for mortality and morbidity after the neonatal Blalock-Taussig shunt procedure. *Ann Thorac Surg* 2011; 92: 642-51; discussion 51-2.
7. Steiner MB, Tang X, Gossett JM, et al. Alternative repair strategies for ductal-dependent tetralogy of Fallot and short-term postoperative outcomes, a multicenter analysis. *Pediatr Cardiol* 2015; 36: 177-89.
8. Hirsch JC, Mosca RS, Bove EL. Complete repair of tetralogy of Fallot in the neonate: results in the modern era. *Ann Surg* 2000; 232: 508-14.
9. Kanter KR, Kogon BE, Kirshbom PM, Carlock PR. Symptomatic neonatal tetralogy of Fallot: repair or shunt? *Ann Thorac Surg* 2010; 89: 858-63.
10. Kirshbom PM, Myung RJ, Gaynor JW, et al. Preoperative pulmonary venous obstruction affects long-term outcome for survivors of total anomalous pulmonary venous connection repair. *Ann Thorac Surg* 2002; 74: 1616-20.
11. Welke KF, O'Brien SM, Peterson ED, Ungerleider RM, Jacobs ML, Jacobs JP. The complex relationship between pediatric cardiac surgical case volumes and mortality rates in a national clinical database. *J Thorac Cardiovasc Surg* 2009; 137: 1133-40.
12. Hines MH. Neonatal cardiovascular physiology. *Semin Pediatr Surg* 2013; 22: 174-8.
13. Kozik DJ, Tweddell JS. Characterizing the inflammatory response to cardiopulmonary bypass in children. *Ann Thorac Surg* 2006; 81: S2347-54.
14. Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg* 1976; 72: 364-70.
15. Norwood WI, Lang P, Hansen DD. Physiologic repair of aortic atresia-hypoplastic left heart syndrome. *N Engl J Med* 1983; 308: 23-6.
16. Reddy VM, Liddicoat JR, McElhinney DB, Brook MM, Stanger P, Hanley FL. Routine primary repair of tetralogy of Fallot in neonates and infants less than three months of age. *Ann Thorac Surg* 1995; 60: S592-6.
17. Di Donato RM, Jonas RA, Lang P, Rome JJ, Mayer JE Jr, Castaneda AR. Neonatal repair of tetralogy of Fallot with and without pulmonary atresia. *J Thorac Cardiovasc Surg* 1991; 101: 126-37.
18. Tweddell JS. Advances in neonatal cardiac surgery: recent advances, the low-hanging fruit, what is on the horizon and the next moonshot. *Curr Opin Cardiol* 2016; 31: 109-16.
19. Jacobs JP, Jacobs ML, Maruszewski B, et al. Current status of the European Association for Cardio-Thoracic Surgery and the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Ann Thorac Surg* 2005; 80: 2278-83; discussion 83-4.
20. Bove EL, Behrendt DM. Open-heart surgery in the first week of life. *Ann Thorac Surg* 1980; 29: 130-4.
21. Kanter KR. Management of infants with coarctation and ventricular septal defect. *Semin Thorac Cardiovasc Surg* 2007; 19: 264-8.
22. Amir G, Ramamoorthy C, Riemer RK, Reddy VM, Hanley FL. Neonatal brain protection and deep hypothermic circulatory arrest: pathophysiology of ischemic neuronal injury and protective strategies. *Ann Thorac Surg* 2005; 80: 1955-64.
23. Bellingier DC, Jonas RA, Rappaport LA, et al. Developmental and neurologic status of children after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. *N Engl J Med* 1995; 332: 549-55.