Hospital Outcomes of Surgical Closure of Patent Ductus Arteriosus: 19 Years Experience at Shahid Gangalal National Heart Center

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ABSTRACT

Background

Ductus arteriosus is a vascular structure which connects the roof of main pulmonary artery near the origin of the left branch pulmonary artery to the proximal descending aorta. Patent ductus arteriosus (PDA) closure is indicated for any patient who is symptomatic from left to right shunting.

Objective

To investigate the hospital outcomes of surgical closure of patent ductus arteriosus over last 19 years starting from the very first case of our center.

Method

This is a retrospective analysis of all patent ductus arteriosus treated surgically from August 2001 to July 2019. Patients who underwent isolated surgical closure of patent ductus arteriosus were included. Data have been presented in three different eras (Era 1: 2001-2007, Era 2: 2008-2013, and Era 3: 2014-2019) to see the trend of evolution of this surgery.

Result

A total of 901 patients aged 8.67±8.76 years under went patent ductus arteriosus surgical closure over last 19 years. Patients in the initial era 2001-2007 were significantly older compared with other 2 eras (p=0.000). Males accounted for 35.5% of all cases. Twenty percent had severe pulmonary artery hypertension.Duration of mechanical ventilation was 3.57±9.64 hours with ICU stay of 1.55±1.53 days, and hospital stay of 3.9±2.3 days. Overall in hospital mortality was 0.8%; for isolated patent ductus arteriosus diagnosis, mortality was 0.2%. Chylothorax was noted in 0.4%.

Conclusion

This is the first report to analyze surgical outcomes of patent ductus arteriosus ligation in our center. We have discussed the evolution of patent ductus arteriosus surgery in our center, and have shown favorable outcomes in terms of morbidity and mortality.

KEY WORDS

Catheter occlusion, Division, Ligation, Patent ductus arteriosus

INTRODUCTION

Ductus arteriosus is a vascular structure which connects the roof of main pulmonary artery near the origin of the left branch pulmonary artery to the proximal descending aorta.[1] This is an essential structure during intrauterine life which should close spontaneously after birth; thereby the persistence of ductal patency after first few weeks of life is abnormal.[1] The reported incidence of patent ductus arteriosus (PDA) varies with the age at the time of study and the gestational age of the patients. Preterm infants have an increased incidence of PDA. A review of 62 different studies published after 1955 revealed that PDA is reported in almost 1 in 1000 live births.[2] When preterm babies are excluded, its incidence has been reported to be 1 in 2000 live birth term infants.[3,4] Left to right shunting through the ductus arteriosus leads to pulmonary overcirculation and left ventricular volume overload resulting into left heart failure.[1] In preterm infants the initial treatment plan is medical with indomethacin or ibuprofen, which induces the ductus to close.[5] Ductus closure is indicated for any child or adult who is symptomatic from left to right shunting.[1] First surgery performed in our center after its establishment was PDA ligation in a seven-year-old girl on Aug 23, 2001 (2058/5/7 BS). After that landmark surgery, we have performed hundreds of PDA ligation; recently device closure being more common. Here, we share our experience with surgical closure of PDA over last 19 years.

METHODS

This is a retrospective analysis of all PDAs treated surgically at Shahid Gangalal National Heart Center, Bansbari, Kathmandu from August 2001 to July 2019. Patients who underwent isolated PDA ligation or PDA division were included. Operation theatre (OT) record files, anesthesia record files, intensive care unit (ICU) record files, and discharge files were reviewed for relevant information. In case of missing data, the analysis was performed considering the number of available data alone. Ethical approval was obtained from Institutional Review Board of Shahid Gangalal National Heart Center (approval ID: SGNHC/IRB no: 13-2020). Statistical analysis was done using SPSS version 26 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). Data were expressed using mean ± SD, range, and percentage wherever appropriate. Analysis of variance (ANOVA), and chi-square tests were utilized depending on the variables. To see the evolution of this surgery at different timeframes, data have been presented arbitrarily in three different eras of roughly 6 years (Era 1: 2001 - 2007, Era 2: 2008 - 2013, and Era 3: 2014 - 2019). A p value of < 0.05 was considered as significant.

RESULTS

Baseline characteristics

Baseline characteristics of patients in all three eras were similar except for age (table 1). Mean age of the patients was 8.67 ± 8.76 years (range: 16 days - 46 years). Patients in the initial era 2001-2007 were significantly older compared with other 2 eras (p=0.000). Males accounted for 35.5% of all cases. Mean weight of the patients was 19.42 ± 14.76 kg (range: 2 - 70 kg). Left ventricular ejection fraction was 63.3 ± 6.28% (range: 20 - 75%). Left ventricular end diastolic dimension was 4.42 ± 1.2 cm (range: 1.7 - 8.1 cm). Mean pulmonary artery systolic pressure (PASP) was 53.14 ± 17.98 mmHg (range: 14 - 107 mmHg). Twenty percent of the patients had severe pulmonary artery hypertension, while 45% had normal pulmonary artery pressure. Mean PDA size was 5.3 ± 2.33 mm (range: 2 - 15 mm). Peak pressure gradient across the PDA was 64.95 ± 24.26 mmHg (range: 15 - 118 mmHg). Ten percent (n=95) had additional diagnosis besides PDA, with mitral regurgitation (MR) of at least moderate degree being most common (3%; n=28), followed by ventricular septal defect (VSD) (1.9%), atrial septal defect (ASD) (1.8%). Other concomitant diagnoses have been presented in table 1. In the most recent era, 3 patients (0.3%) were operated after initial device closure was unsuccessful. One patient (0.1%) had to be emergently operated to for device dislodgement where the dislodged device was removed and PDA was ligated. Two patients (0.2%) were with Down's syndrome and one patient (0.1%) had congenital rubella syndrome.

Intraoperative and postoperative characteristics

Intraoperative and postoperative characteristics were similar in all three groups except for ICU stay (p=0.011), use of inotropes (p=0.001), and incidence of postoperative chylothorax (p=0.026) (table 2). Almost 99% of patients (n=891) underwent PDA ligation, and remaining 1% (n=10) underwent PDA division. Posterolateral thoracotomy approach was utilized in all except in 3 patients, who underwent PDA ligation via median sternotomy approach. Cardiopulmonary bypass was utilized in 2 patients. Additional procedures included balloon aortic valvotomy via femoral route, division of aberrant right subclavian artery, epicardial pacing lead implantation, repair of aortic arch tear, and PDA device removal, each accounting for 1 patient (0.1%).

Duration of mechanical ventilation was 3.57 ± 9.64 hours (range: 0 - 240 hours). Mean ICU stay was 1.55 ± 1.53 days (range: 0 - 31 days). For patients who were discharged home, hospital stay duration was 3.9 ± 2.3 days (range: 2 - 27 days). Three patients (0.3%) required reexploration, 6 patients (0.7%) required reintubation in ICU. Nitroglycerine (GTN) was the most commonly used vasodilator in ICU (71.6%), followed by combination of GTN and sodium nitroprusside (5.4%). Dopamine combined with other inotropes (4.5%), and dopamine alone (2.6%) were the most common inotropes. Sixteen percent of the patients did not require any kind of vasodilator or inotropic support. Trend of use of inotropes in three different eras was significantly

Table 1. Baseline characteristics

Variables	Overall (n=901)	2001-2007 (n=268)	2008-2013 (n=444)	2014-2019 (n=189)	P value
Age, years; (mean±SD)	8.67±8.76	10.65±9.68	7.97±8.5	7.46±7.48	0.000
Sex, male; n(%)	320 (35.5)	98 (36.6)	155 (34.9)	67 (35.4)	0.904
Weight (N=586), kg; (mean±SD)	19.42±14.76	20.54±15.61	19.2±14.55	19.49±14.96	0.818
LVDd (N=318), cm; (mean±SD)	4.42±1.2	NA	4.4±1.26	4.44±1.15	0.752
EF (N=332), (%);(mean±SD)	63.3±6.28	NA	62.25±7.48	64.11±5.02	
PASP (N=85), mmHg; (mean±SD)	53.14±17.98	NA	50.1±16.23	55.6±19.1	
PAH (N=267)					
Normal PAP; n (%)	121 (45.3)	NA	48 (45.2)	73 (48.3)	
Mild; n (%)	46 (17.2)	NA	22 (20.7)	24 (15.9)	
Moderate; n (%)	47 (17.6)	2 (20)	22 (20.7)	23 (15.2)	
Severe; n (%)	53 (19.9)	8 (80)	14 (13.2)	31 (20.5)	
PDA size (N=315), mm; (mean±SD)	5.3±2.33	NA	5.43±2.35	5.19±2.32	
Peak gradient across PDA (N=109), mmHg; (mean±SD)	64.95±24.26	NA	64.55±22.79	65.21±25.35	
Concomittant diagnosis, n (%)					0.127
MR	28 (3.1)	5 (1.9)	12 (2.7)	11 (5.8)	
VSD	17 (1.9)	3 (1.1)	10 (2.3)	4 (2.1)	
ASD/PFO	16 (1.8)	3 (1.1)	6 (1.4)	7 (3.7)	
Aortic valve pathology (AS, AR, ASR, BCAV)	8 (0.9)	6 (2.2)	1 (0.2)	1 (0.5)	
CoA	6 (0.7)	2 (0.8)	1 (0.2)	3 (1.6)	
Infective endocarditis	6 (0.7)	1 (0.4)	3 (0.7)	2 (1.1)	
LVOTO/subaortic membrane	4 (0.4)	1 (0.4)	1 (0.2)	2 (1.1)	
Device failure	3 (0.3)	0 (0)	0 (0)	3 (1.6)	
Aberrant RSCA, dysphagia lusoria	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
Aortic root, ascending aorta, and arch aneurysm	1 (0.1)	0 (0)	0 (0)	1 (0.5)	
CHB	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
PS	1 (0.1)	1 (0.4)	0 (0)	0 (0)	
TR	1 (0.1)	1 (0.4)	0 (0)	0 (0)	
Device dislodgement	1 (0.1)	0 (0)	0 (0)	1 (0.5)	
RV dysfunction	1 (0.1)	0 (0)	1 (0.2)	0 (0)	

N=number of data available for that particular variable, NA= not available, LVDd= left ventricular end diastolic dimension, EF= ejection fraction, PASP= pulmonary artery systolic pressure, PAH= pulmonary artery hypertension, PDA= patent ductus arteriosus, MR= mitral regurgitation, VSD= ventricular septal defect, ASD/PFO= atrial septal defect/patent foramen ovale, AS= aortic stenosis, AR= aortic regurgitation, ASR= aortic stenosis and regurgitation, BCAV= bicuspid aortic valve, CoA= coarctation of aorta, RSCA= right subclavian artery, CHB= complete heart block, PS= pulmonary stenosis, TR= tricuspid regurgitation, RV= right ventricle, SD= standard deviation.

different, however, this difference might be due to small number of data available in the era 2001 - 2007. A total of 7 patients (0.8%) died, 5 patients (0.6%) required ICU readmission for various reasons, 2 patients (0.2%) required tracheostomy, and 4 patients (0.4%) developed chylothorax of which 2 patients required thoracic duct mass ligation, and remaining 2 patients were managed conservatively with chest tube insertion and octreotide. Two patients (0.2%) required tracheostomy for prolonged ventilation, and both of them survived.

DISCUSSION

Since the first successful ligation of ductus by Dr Robert E Gross on a seven-and-half-year-old girl on August 26, 1938, this surgery has been described as a relatively safe procedure.[6] It is of a nice coincidence that our first case was also performed on the month of August and on a seven-year-old girl. For many more years following the first successful ligation, left posterolateral thoracotomy approach has been the standard approach for PDA ligation and/or division. With time and technological advancement, catheter occlusion has slowly replaced surgical ligation. As the pioneer center of the country in the field of cardiovascular surgery, we have prepared this comprehensive report of our results over last two decades.

We performed our first case on Aug. 23, 2001 (2058/5/7 BS). Within the first month, we performed 3 cases of PDA ligation (second and third cases being 10 days, and 18 days later, respectively). Our landmark for 100th case was achieved three-and-half years later (Feb. 15, 2005). We achieved landmark for 500th case after nine years (Nov. 30,

Table 2. Intraoperative and postoperative characteristics

Variables	Overall (n=901)	2001-2007 (n=268)	2008-2013 (n=444)	2014-2019 (n=189)	P value
Operative procedure					0.339
PDA ligation; n (%)	891 (98.9)	263 (98.1)	441 (99.3)	187 (98.9)	
PDA division; n(%)	10 (1.1)	5 (1.9)	3 (0.7)	2 (1.1)	
Thoracotomy approach; n (%)	898 (99.7)	267 (99.6)	443 (99.8)	188 (99.5)	0.824
Additional procedures					0.387
BAV; n (%)	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
Division of aberrant RSCA; n (%)	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
Epicardial PPI; n (%)	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
Repair of aortic arch tear; n (%)	1 (0.1)	0 (0)	0 (0)	1 (0.5)	
PDA device removal; n (%)	1 (0.1)	0 (0)	0 (0)	1 (0.5)	
Use of CPB, yes; n(%)	2 (0.2)	1 (0.4)	0 (0)	1 (0.5)	0.355
Duration of mechanical ventilation (N=758), hours; (mean±SD)	3.57±9.64	2.32±4.47	4.01±12.72	4.11±3.64	0.091
ICU stay (N=839), days; (mean±SD)	1.55±1.53	1.31±0.91	1.67±1.38	1.61±2.34	0.011
Hospital stay (N=314), days; (mean±SD)	3.9±2.3	NA	3.85±2.05	3.94±2.5	
Reexploration, yes; n(%)	3 (0.3)	0 (0)	3 (0.7)	0 (0)	0.212
Reintubation, yes; n(%)	6 (0.7)	2 (0.7)	3 (0.7)	1 (0.5)	0.961
Inotropes/vasodilators (N=465)					0.001
GTN; n (%)	333 (71.6)	34 (91.9)	173 (67.6)	126 (73.3)	
Dopamine; n (%)	12 (2.6)	1 (2.7)	8 (3.1)	3 (1.7)	
GTN plus SNP; n (%)	25 (5.4)	2 (5.4)	15 (5.9)	8 (4.7)	
Dopamine, adrenaline, milrinone, noradrenaline, amrinone in varying combinations; n (%)	21 (4.5)	0 (0)	6 (2.3)	15 (8.7)	
None; n (%)	74 (15.9)	0 (0)	54 (21.1)	20 (11.6)	
Mortality, yes; n (%)	7 (0.8)	1 (0.4)	4 (0.9)	2 (1.1)	0.654
ICU readmission, yes; n (%)	5 (0.6)	1 (0.4)	2 (0.5)	2 (1.1)	0.572
Chylothorax, yes; n (%)	4 (0.4)	0 (0)	1 (0.2)	3 (1.6)	0.026
Tracheostomy, yes; n (%)	2 (0.2)	0 (0)	2 (0.5)	0 (0)	0.356

PDA= patent ductus arteriosus, BAV= balloon atrial valvotomy, RSCA= right subclavian artery, PPI= permanent pacemaker implantation, CPB= cardiopulmonary bypass, ICU= intensive care unit, N= number of data available for that particular variable, GTN= nitroglycerine, SNP= sodium nitroprusside, SD= standard deviation.

2010) of the initial surgery. Our patients aged from 16 days of birth to 46 years. In the initial era, the patients tended to be older compared to the following 2 eras. We have operated on patients with weight as low as 2 kg, and EF as low as 20%. Majority of our patients (45.3%) had normal PA pressure, while 20% of the patient population had severe pulmonary artery hypertension. Almost all of the patients with concomitant diagnosis (table 1) were judged to benefit from PDA ligation alone, leaving the concomitant diagnosis as it is except for aberrant right subclavian artery causing dysphagia lusoria, where aberrant RSCA was divided; complete heart block, where epicardial pacemaker was implanted; and PDA occlusion device dislodgement, where the dislodged device was removed.

Our routine approach is to doubly ligate the PDA with number 2 silk and transfix it with 5-0 prolene. Almost all of the patients underwent this procedure except very few who underwent PDA division. We approach PDA via left posterolateral thoracotomy incision. Majority (99.7%, n=898) of the patients underwent PDA closure via this

approach. In the remaining 3 patients median sternotomy approach was utilized (case 1: epicardial PPI had to be implanted; case 2: initial diagnosis was aortopulmonary window; case 3: device was dislodged during device closure). In 2 cases (aortopulmonary window and PDA device dislodgement), cardiopulmonary bypass was utilizedwith mean CPB time of 29 ± 4.2 min (range: 26-32 min). In the patient with preoperative diagnosis of aortopulmonary window, the intraoperative diagnosis was PDA, and PDA was ligated on pump.

Mean duration of mechanical ventilation in our series was 3.57 ± 9.64 hours. Although statistically not significant, the initial era had shorter duration of mechanical ventilation. In that era, a significant number of patients used to be extubated in operating room itself, thereby reducing the duration of mechanical ventilation. Also, duration of ICU stay was significantly less for the initial era as compared to other recent 2 eras. It is due to the fact that we had less ICU beds in the initial era, and had to transfer patients faster to the general ward so as to accommodate ICU beds

for other cases. As we have increased the capacity of our ICU beds, we were more liberal to keep patients longer in ICU. Our reexploration rate was 0.3% (n=3). In one of the patients, the reexploration was undertaken to remove an inadvertently sutured chest tube, during sternal closure for anteriorly approached PDA. One case was reexplored because of suture impingement on the descending aorta causing significant visceral malperfusion. This patient later died in ICU. Of the five cases requiring ICU readmission, 1 was for unstable hemodynamics, 1 for chest tube insertion, 1 for fever due to UTI, and 2 were for mass ligation for chylothorax.

Seven patients died after surgery. Five out of these 7 patients (71%) had concomitant diagnosis besides PDA. A seven-month-old boy weighing 6 kg who had concomitant ASD and persistent left superior vena cava (PLSVC) died on 1st postoperative day (POD 1). A nine-year-old boy weighing 20 kg who had concomitant VSD with severe PAH and had undergone pulmonary artery (PA) banding 1 year earlier, died on POD 1. This patient required reexploration on POD 0. A six-month-old boy with concomitant diagnosis of ASD and severe PAH died on POD 12. A one-year-old girl with concomitant diagnosis of ASD with normal PA pressure died on POD 31. When she was taken to OT for surgical procedure, we noticed that she had difficult intubation; so the planned operation was abandoned and she was taken back to ICU with laryngeal mask airway. The same evening, she was taken back to the OT and retrograde intubation was done; and the procedure was carried out. She died because of sepsis and multiple organ failure. An eleven-month-old boy with concomitant diagnosis of VSD, PLSVC and severe PAH died on POD 6 due to acute pulmonary edema. He was treated for neonatal sepsis and acute kidney injury prior to surgery. Of the remaining two patients who had diagnosis of PDA alone, one patient (12-year-old boy with severe PAH and bidirectional shunt) died in OT; and next patient (4-month-old boy weighing 2 kg) died on POD 9. This brings us to the results that with isolated PDA alone, the mortality rate remains pretty low (2 out of 901, which is 0.2%.

Thoracic duct is liable to injury due to its close proximity to great vessels in the mediastinum.[7] Chylothorax after PDA ligation has been reported as early as in 1960s.[8] Post cardiac surgery chylothorax itself is not so common, and post PDA surgery chylothorax is even rare and has been described mostly in terms of case reports.[7,9] In our experience of over 900 patients over 2 decades, we witnessed only 0.4% of chylothorax, of which half responded to conservative management and half required thoracic duct mass ligation.

Nitroglycerine (GTN), either alone or in combination with sodium nitroprusside has been the major vasodilator we have been using postoperatively. Post PDA ligation syndrome has recently been defined as the need for escalating hemodynamic support in the first 24 hours following surgical or device closure of PDA, which is common in premature infants.[10] Extensive work has been done to treat patent ductus arteriosus in preterm infants. Although debatable, the general consensus is that a PDA in a preterm infant should be closed to control problems associated with the persistence of the shunt such as heart failure and prolonged dependency on mechanical ventilation.[11] We do not receive much of premature neonates because our center does not provide obstetric service, and those populations might have been encountered more in the University Hospital which provides both obstetric and neonatal care.

Increase of diastolic pressure post ligation has been reported graphically in the very first case of successful human ligation of PDA by Gross and Hubbard in their landmark article back in 1939. The seven-and-half year old girl had her diastolic blood pressure of 38 mmHg preoperatively and 80 mmHg postoperatively.[6] We always witness some increase of diastolic blood pressure after ligation of PDA. Almost every time, we do test occlusion with forceps to make sure that it is the ductus we are about to ligate. We have mistakenly ligated descending thoracic aorta for PDA in one patient. After that incident, to prevent the inadvertent ligation of descending aorta, we now put the saturation probe on great toe, and insert arterial line in femoral artery or dorsalis pedis artery whenever possible. PDA ligation in itself looks relatively easy procedure, however, catastrophic complication like tear of the ductus can be challenging even in experienced hands; and most of the times it is life threatening. Because there is usually no control of the circulation as usually the case in cardiac surgery using cardiopulmonary bypass, the patient can easily exsanguinate and die on operating table should this complication not be anticipated and tackled immediately. The ductus tissue is usually fragile and can easily tear during ligation. In one patient, we have witnessed tear of aortic wall near the insertion of PDA, which was successfully repaired. Proper judgment is required for the use of force while tying the knots, so as not to tear the ductus and at the same time, not to leave residual leak by loose ligatures.

Infective endocarditis (IE) prophylaxis has been routinely recommended for patients with PDA. Of the 901 cases we treated, only 0.7% had previous IE, and only 1 patient had vegetations present in the ductus. After analysis of over an aggregate 1196 years at risk, a group of Swedish researchers suggest that routine closure of a patent ductus arteriosus, for the sole purpose of eliminating the risk of infective endocarditis, is unnecessary with the exception of patients with PDA who have already incurred infective endocarditis.[12] Vocal cord paralysis has been a widely known complication following PDA ligation. A recent meta-analysis reported an overall pooled incidence of vocal cord paralysis to be 6.9%, incidence being higher in premature infants (11.7%).[13] Although we have recalled few cases of symptomatic vocal cord palsy, we do not have precise numerical data.

Recently, device closure has been established as the first

line of treatment should pharmacological treatment fail. In our center, catheter based procedures are slowly replacing surgical closure of PDA; which is demonstrated by the less number of surgeries in recent era 2014 - 2019. There used to be a time when we used to surgically ligate four PDAs in a single operative day; and recently we ligate one PDA in almost 3 - 4 months. Only those patients who are not device suitable get referred to us for surgical closure. Our surgical team has swiftly handled some complications after catheter occlusion, like we removed the device in a 13-year-old girl after device was dislodged during catheter occlusion.

Because of the retrospective design of the study, it carries inherent flaws related to retrospective nature. Because we could not obtain all variables dated back to 19 years prior, not every variable has the n of 901. We have mentioned only the available numbers as N after each variable in the two tables presented.

CONCLUSION

This is the first report of its kind to analyze surgical outcomes of PDA ligation in our center. We have discussed the history and evolution of PDA surgery in our center, and have shown favorable outcomes in terms of morbidity and mortality. We have also highlighted the trend going slowly towards catheter-based closure as opposed to surgical closure in our center. Surgical closure always remains as the gold standard should any complications arise during catheter based closure.

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