

Neonatal Patent Ductus Arteriosus Ligation Operations Performed by Adult Cardiac Surgeons

Yoon Sang Chung, M.D., Ph.D.¹, Dai Yun Cho, M.D., Ph.D.¹, Hyun Kang, M.D., Ph.D.², Na Mi Lee, M.D., Ph.D.³, Joonhwa Hong, M.D., Ph.D.¹

Departments of ¹Thoracic and Cardiovascular Surgery, ²Anesthesiology and Pain Medicine, and ³Pediatrics, Chung-Ang University Hospital

Background: Patent ductus arteriosus (PDA) ligation is usually performed by congenital cardiac surgeons. However, due to the uneven distribution of congenital cardiac surgeons in South Korea, many institutions depend solely on adult cardiac surgeons for congenital cardiac diseases. We report the outcomes of PDA ligations performed by adult cardiac surgeons at our institution. **Methods:** The electronic medical records of 852 neonates at Chung-Ang University Hospital, Seoul, South Korea from November 2010 to May 2014 were reviewed to identify patients with PDA. **Results:** Of the 111 neonates with a diagnosis of PDA, 26 (23%) underwent PDA ligation. PDAs were ligated within 28 days of birth (mean, 14.5±7.8 days), and the mean gestational age of these patients was 30.3±4.6 weeks (range, 26 to 40 weeks) with a mean birth weight of 1,292.5±703.5 g (range, 480 to 3,020 g). No residual shunts through the PDA were found on postoperative echocardiography. There was 1 case of 30-day mortality (3.8%) due to pneumonia, and 6 cases of in-hospital mortality (23.1%) after 30 days, which is comparable to results from other centers with congenital cardiac surgery programs. **Conclusion:** Although our outcomes may not be generalizable to all hospital settings without a congenital cardiac surgery program, in select centers, PDA ligations can be performed safely by adult cardiac surgeons if no congenital cardiac surgery program is available.

Key words: 1. Cardiac surgical procedures
2. Congenital heart defects
3. Ligation
4. Patent ductus arteriosus

Introduction

Institutions with neonatal intensive care units (NICUs) encounter premature newborns with congenital anomalies that require surgical procedures. The most common congenital heart defect is patent ductus arteriosus (PDA), with an incidence of 15% among preterm newborns [1,2]. Approximately 70% of preterm infants delivered at less than 28 weeks of

gestation require medical or surgical closure of PDA because of the reduced likelihood of spontaneous PDA closure [3]. Although conflicting and inconclusive results have been reported regarding the optimal treatment strategies for preterm PDA, many reports have supported PDA ligation for symptomatic PDA refractory to pharmacologic treatment [4,5].

In South Korea, several reports have shown that the number of newborns has decreased over the last

Received: December 1, 2016, Revised: April 13, 2017, Accepted: April 19, 2017, Published online: August 5, 2017

Corresponding author: Joonhwa Hong, Department of Thoracic and Cardiovascular Surgery, Chung-Ang University Hospital, 102 Heukseok-ro, Dongjak-gu, Seoul 06973, Korea
(Tel) 82-2-6299-1638 (Fax) 82-2-827-0160 (E-mail) jhong@cau.ac.kr, Joonhwa.hong@gmail.com

© The Korean Society for Thoracic and Cardiovascular Surgery. 2017. All right reserved.

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

20 years, but the percentage of newborns with congenital heart disease, including PDA, has remained the same [6,7]. Not all institutions with a NICU have a congenital cardiac surgery program, and pediatric surgical subspecialists show a geographically uneven distribution in South Korea [8]. Our institution is a training hospital with a NICU, a neonatology department, and a pediatric cardiologist. However, no congenital cardiac surgery program is available at our site, although we have an adult cardiac surgery program. Patients who need PDA ligation are treated by 2 adult cardiac surgeons in our center. We report the outcomes of PDA surgery performed urgently by surgeons from an adult cardiac surgery program at our institution.

Methods

The electronic medical records of 852 neonates at Chung-Ang University Hospital, Seoul, South Korea from November 2010 to May 2014 were reviewed to identify neonates with PDA. Patients with other congenital cardiac anomalies or chromosomal abnormalities were excluded from this study. The baseline characteristics evaluated were sex, mean gestational age, birth weight, body weight at operation, preoperative ventilator application, changes in blood pressure before and after the operation, surgery timing, and size of the PDA, and all variables were compared between cases of survival and cases of mortality. Surgical, 30-day, and in-hospital mortality and morbidity of the PDA ligation operations were evaluated.

The decision to perform a PDA ligation operation was made after an average of 2 cycles of ibuprofen treatment or immediately after diagnosis in neonates with contraindications against ibuprofen. All patients underwent double ligation of the PDA with a left muscle-sparing posterolateral thoracotomy through the fourth intercostal space in the operating theater.

This study received ethics approval from the institutional review board (IRB) of Chung-Ang University Hospital (C2015263 [1720]). The IRB waived the requirement of informed consent since the data had already been collected.

Continuous data were analyzed using the Mann-Whitney U-test and categorical data were analyzed using the Fisher exact test. Data were expressed as the mean±standard deviation or absolute number

(%) and analyzed using IBM SPSS ver. 20.0 (IBM Corp., Armonk, NY, USA). All p-values < 0.05 were considered to indicate statistical significance.

Results

A total of 111 neonates (13.0% of 852) with a diagnosis of PDA made by echocardiography were identified. Among them, 26 (23%) underwent urgent PDA ligation because of hemodynamically significant PDA contributing to heart failure symptoms such as respiratory compromise with prolonged hypoxemia and impaired systemic perfusion, resulting in hypotension and pulmonary hemorrhage. The baseline characteristics of these patients are summarized in Table 1. The mean gestational age of these patients was 30.3±4.6 weeks (range, 26 to 40 weeks) with a mean birth weight of 1,292.5±703.5 g (range, 480 to 3,020 g). There were 2 patients with a birth weight of 2,500 g or greater. Five were low-birth-weight (LBW: 1,500 g ≤ birth weight < 2,500 g) patients, 6 were very-low-birth-weight (VLBW: 1,000 g ≤ birth weight < 1,500 g) patients, 8 were extremely-low-birth-weight (ELBW: 750 g ≤ birth weight < 1,000 g) patients, and 5 were incredibly-low-birth-weight (ILBW: birth weight < 750 g) patients. The mean body weight at the time of the PDA ligation operation was 1,273.3±700.0 g (range, 430 to 3,110 g). Seventeen patients (65.4%) needed mechanical ventilator treatment preoperatively. The mean PDA size at the time of surgery was 3.5±1.3 mm, as determined by echocardiography. PDAs were ligated within 28 days of birth (mean, 14.5±7.8 days) depending on their clinical significance (5.5±4.9 days for patients with a birth weight ≥ 2,500 g, 12.4±5.3 days for LBW infants, 20.8±2.1 days for VLBW infants, 15.5±7.5 days for ELBW infants, and 7.8±7.0 days for ILBW infants).

There were no instances of operative mortality. No residual shunt flow through the PDA was seen in the postoperative echocardiographic evaluation in any case. With the exception of 1 case of bleeding that required prolonged chest tube drainage and transfusion, there was no morbidity related to PDA ligation. There were 7 cases of mortality: 1 case of 30-day mortality (3.8%) due to pneumonia; and 6 cases of in-hospital mortality (23.1%) due to necrotizing enterocolitis with bowel perforation (n=3), sepsis with disseminated intravascular coagulation (n=2),

Table 1. Baseline characteristics

Characteristic	Total (n=26)	Survival group (n=19)	Mortality group (n=7)	p-value	Chi-square or p for trend
Male	14 (53.8)	10 (52.6)	4 (57.1)	1.000	
Mean gestational age (wk)	30.3±4.6	31.5±4.8	27.0±1.2	0.013	
Birth weight (g)	1,292.5±703.5	1,443.7±764.4	882.1±201.3	0.083	0.240 ^a , 0.045 ^b
Normal birth weight (≥2,500)	2	2 (100.0)	0		
LBW (<2,500)	5	5 (100.0)	0		
Very LBW (<1,500)	6	5 (83.3)	1 (16.7)		
Extremely LBW (<1,000)	8	4 (50.0)	4 (50.0)		
Incredibly LBW (<750)	5	3 (60.0)	2 (40.0)		
Body weight at operation (g)	1,273.3±700.0	1,418.2±762.8	880.0±221.9	0.094	
Preoperative ventilator application	17 (65.4)	11 (57.9)	6 (85.7)	0.186	
Changes in blood pressure (mm Hg)					
Systolic	7.0±10.6	7.0±10.6	13.4±11.1	0.187	
Diastolic	6.8±8.5	6.3±9.1	8.1±6.9	0.626	
Time of surgery (days of life)	14.5±7.8	13.6±7.6	16.7±8.5	0.572	
Patent ductus arteriosus size (mm)	3.5±1.3	3.7±1.3	3.1±1.2	0.427	

Values are presented as absolute number (%) or mean±standard deviation.

LBW, low birth weight.

^a)Chi-square (p-value). ^b)p for trend.

and intussusception with bowel perforation (n=1). The other 19 patients (73.1%) were discharged from the hospital on postoperative day 70±42.

The gestational age of the cases of mortality was lower than that of the patients who survived (p=0.013). Although there was no statistically significant difference in birth weight between the survival and mortality groups, a significant trend towards mortality was seen as the birth weight became lower (p for trend=0.045). Between the survival and mortality groups, there were no statistically significant differences in gender, body weight at the time of surgery, preoperative ventilator application, surgery timing after birth, or blood pressure elevation after surgery.

Discussion

Most university hospitals in Korea have a NICU. However, congenital cardiac surgery programs are limited to a small number of larger centers in each geographic region. According to the Korean Society for Thoracic and Cardiovascular Surgery, there are approximately 70 teaching hospitals with a thoracic and cardiovascular surgery department in South Korea, and 65 of them have a cardiac surgery program. Only about 10 of those hospitals have a con-

genital cardiac surgery program.

Based on recent studies conducted in South Korea, unlike in the past, a high percentage of patients requiring heart surgery underwent surgery in Seoul. For simple congenital heart surgery, among patients living in Seoul, 93.9% underwent procedures or surgery in Seoul. In comparison, even in other metropolitan cities, the percentages of patients who underwent the operation in the region of their residence were as low as 14.8% in some cities [8]. For complex congenital heart surgery, the percentage of patients who underwent the operation in the region of their residence was as low as 1.5% in some cities in Korea. These results suggest that candidates for congenital heart surgery tend to seek treatment in large medical centers in Seoul with a congenital cardiac surgery program. Moreover, although the mortality rate of prenatally detected congenital heart disease has continued to decrease in South Korea, the pregnancy termination rate remains high [9]. This factor has contributed to a reduced need for congenital cardiac specialists, even in training hospitals, and a decreased preference among young surgeons to be trained as a congenital cardiac surgeon. Therefore, the Korean government employed a strategy to designate and run a single regional center in each area to achieve the goal of alleviating the overconcent-

tration of patients in only a few cities. However, this has caused unnecessary competition among comparable university hospitals, resulting in the absence of mutual beneficial cooperation among such centers [8].

Our institution is a training hospital without a congenital cardiac surgery program. Nonetheless, newborns with common congenital heart defects such as PDA, ventricular septal defect, and atrial septal defect are occasionally born, and 2 adult cardiac surgeons are responsible for dealing with any urgent situations requiring congenital cardiac surgery. One surgeon completed his residency at a university hospital in South Korea, and his adult cardiac surgery fellowship training was done at a large-volume center in the United States. Another surgeon did his residency in a training hospital with a congenital cardiac surgery program in Seoul.

The outcomes of PDA ligation, including the mortality rate, in our center are comparable to the outcomes in other large centers with a congenital cardiac surgery program in South Korea [10-12]. In the current study, there were 7 cases of in-hospital mortality (26.9%), and younger gestational age was the most important risk factor for in-hospital mortality ($p=0.013$). All cases of mortality were born at a gestational age of 26 to 29 weeks. Birth weight and body weight at the time of surgery were also lower in the mortality group than in the survival group, but these differences were not statistically significant. However, a significant trend towards mortality was seen as the birth weight became lower (p for trend = 0.045). As most instances of mortality occurred more than 30 days after the PDA ligation operation, we assume that the cases of in-hospital mortality in our study were related to the preoperative clinical condition associated with the underlying prematurity, rather than with the PDA ligation operation itself.

There is some debate over the timing of PDA ligation in premature neonates. Some studies have shown early surgical ligation of PDA to be beneficial for infants with a very low birth weight [10,13], but others have suggested that PDA ligation surgery should be considered when ibuprofen fails to close the PDA and that the timing may not affect the outcome of PDA ligation [12]. In our institution, we prefer early surgical ligation before the patient's hemodynamics become compromised. As a result, most of

our patients underwent early surgical ligation (at a mean of 14.5 ± 7.8 days of life), and only 4 patients underwent surgical closure after 3 weeks of life. In our study, the timing of surgery did not have a significant impact on patient survival.

Some studies have suggested that performing PDA ligation in a NICU is safer, and in particular that doing so reduces the risks encountered while transferring infants to the operating theater, such as unstable hemodynamics, hypothermia, or dislodgement of the endotracheal tube [12,14]. We performed all PDA closures in the operating theater because of limitations of resources in the NICU and the possibility of surgical infection. We have not seen any undesired complications associated with transferring the patient, and we believe that performing PDA ligation in the operating theater is safe when adequate care is taken.

The presence of a congenital cardiac surgeon is preferred in all institutions with a NICU, but because of a lack of these subspecialists, many centers are dependent on adult cardiac surgeons or general surgeons for PDA ligation [15]. The surgical outcomes of PDA ligation procedures performed by these surgeons were not found to be inferior to those performed by pediatric cardiac surgeons. As transferring hemodynamically unstable premature neonates with PDA to other institutions could be very difficult and would likely put them at an increased risk of unwanted complications, we believe that non-complex conditions, such as PDA, in premature infants can be considered for surgical correction by adult cardiac surgeons with sufficient experience and competence. Although a fundamental nationwide plan is needed to solve the problem of uneven distribution and the shortage of congenital cardiac surgery programs throughout South Korea, we think that training adult cardiac surgeons to be ready for urgent surgical situations involving congenital cardiac disease is critically important. We would like to suggest a short-term congenital cardiac surgery training program for adult cardiac surgeons; another proposal would be that sharing programs across institutions may help when dealing with urgent surgical situations involving congenital cardiac disease.

This study has several limitations. First, the number of patients was small. Second, our study was non-randomized and retrospective. Last, our out-

comes were those of 2 surgeons who were relatively well exposed to congenital cardiac surgery during their training. Our outcomes may not be generalizable to all hospital settings without a congenital cardiac surgery program.

In conclusion, our findings provide information regarding PDA ligation outcomes at a site without a congenital cardiac surgery program. We believe that PDA ligation can be safely performed by adult cardiac surgeons in select centers.

Conflict of interest

No potential conflicts of interest relevant to this article are reported.

Acknowledgments

This study was supported by a Grant of the Samsung Vein Clinic Network (Daejeon, Anyang, Cheongju, Cheonan; Fund no. KTCS04-079).

References

1. Kitterman JA, Edmunds LH Jr, Gregory GA, Heymann MA, Tooley WH, Rudolph AM. *Patent ducts arteriosus in premature infants: incidence, relation to pulmonary disease and management.* N Engl J Med 1972;287:473-7.
2. Hoffman JI, Kaplan S. *The incidence of congenital heart disease.* J Am Coll Cardiol 2002;39:1890-900.
3. Clyman RI. *Ibuprofen and patent ductus arteriosus.* N Engl J Med 2000;343:728-30.
4. Lee JA, Kim MJ, Oh S, Choi BM. *Current status of therapeutic strategies for patent ductus arteriosus in very-low-birth-weight infants in Korea.* J Korean Med Sci 2015; 30 Suppl 1:559-66.
5. Alan S, Karadeniz C, Okulu E, et al. *Management of patent ductus arteriosus in preterm infants: clinical judgment might be a fair option.* J Matern Fetal Neonatal Med 2013; 26:1850-4.
6. Jang SH, Kim JH, Yeom JS, et al. *Incidence of congenital heart disease in the western part of Gyeongnam Province in Korea.* Korean J Pediatr 2008;51:848-55.
7. Lee JH, Shim GH, Shin KS, et al. *Congenital heart disease in Jeju: postnatal incidence and clinical features.* Korean J Pediatr 2004;47:294-303.
8. Lee KS, Kim CS, Park JH, et al. *The longitudinal trend of cardiac surgery in Korea from 2003 to 2013.* Korean J Thorac Cardiovasc Surg 2016;49(Suppl 1):S1-S13.
9. Lee JE, Jung KL, Kim SE, et al. *Prenatal diagnosis of congenital heart disease: trends in pregnancy termination rate, and perinatal and 1-year infant mortalities in Korea between 1994 and 2005.* J Obstet Gynaecol Res 2010;36: 474-8.
10. Lee LC, Tillett A, Tulloh R, Yates R, Kelsall W. *Outcome following patent ductus arteriosus ligation in premature infants: a retrospective cohort analysis.* BMC Pediatr 2006;6:15.
11. Raval MV, Laughon MM, Bose CL, Phillips JD. *Patent ductus arteriosus ligation in premature infants: who really benefits, and at what cost?* J Pediatr Surg 2007;42:69-75.
12. Lee GY, Sohn YB, Kim MJ, et al. *Outcome following surgical closure of patent ductus arteriosus in very low birth weight infants in neonatal intensive care unit.* Yonsei Med J 2008;49:265-71.
13. Jaillard S, Larrue B, Rakza T, Magnenant E, Warembourg H, Storme L. *Consequences of delayed surgical closure of patent ductus arteriosus in very premature infants.* Ann Thorac Surg 2006;81:231-4.
14. Gould DS, Montenegro LM, Gaynor JW, et al. *A comparison of on-site and off-site patent ductus arteriosus ligation in premature infants.* Pediatrics 2003;112(6 Pt 1):1298-301.
15. Markush D, Briden KE, Chung M, et al. *Effect of surgical subspecialty training on patent ductus arteriosus ligation outcomes.* Pediatr Surg Int 2014;30:503-9.