Left ventricular efficiency after ligation of patent ductus arteriosus for premature infants

Hazumu Nagata, MD,[a] Kenji Ihara, MD, PhD,[a] Kenichiro Yamamura, MD,[a] Yoshihisa Tanoue, MD, PhD,[b] Yuichi Shiokawa, MD, PhD,[b] Ryuji Tominaga, MD, PhD,[b] and Toshiro Hara, MD, PhD[a]

Objective: The purpose of this study was to evaluate the hemodynamic changes in left ventricular function before and after patent ductus arteriosus ligation in premature infants with regard to the energetic efficiency of left ventricular pumping.

Methods: Thirty-five premature infants who underwent patent ductus arteriosus ligation were enrolled in this study. Left ventricular efficiency was evaluated at 4 points: within 24 hours before patent ductus arteriosus ligation, within 24 hours after patent ductus arteriosus ligation, between postoperative days 2 and 4, and on postoperative day 7. The indices of contractility (end-systolic elastance) and afterload (effective arterial elastance) were approximated on the basis of the systemic blood pressure and systolic or diastolic left ventricular volume. The ratio of stroke work and pressure-volume area, representing the ventricular efficiency, was estimated using the following theoretic formula: the ratio of stroke work and pressure-volume area = 1/(1 + 0.5 ventriculoarterial coupling).

Results: Left ventricular efficiency was transiently deteriorated within 24 hours after patent ductus arteriosus ligation because of the marked increase of the afterload and the slight increase of contraction, and then recovered to preoperation levels by 2 to 4 days after patent ductus arteriosus ligation.

Conclusions: Analysis of indices representing the afterload, contractility, and energetic efficiency of the left ventricle may provide practical information for the management of premature infants during the postoperative period after patent ductus arteriosus ligation. (J Thorac Cardiovasc Surg 2013;146:1353-8)

Patent ductus arteriosus (PDA) is one of the most critical problems of the respiratory and circulatory system that can occur during the first few weeks after birth in premature infants.[1] The occurrence of PDA in premature infants increases with a lower gestational age and lower birth weight. In the EPICure cohort, the occurrence of PDA was approximately 65% for infants who were born at less than 28 weeks of gestational age and approximately 80% for infants with a birth weight less than 800 g.[2,3] The first-line treatment or prophylaxis for PDA is administration of indomethacin, and the second-line treatment is surgical ligation. The surgical procedure has been safely carried out by pediatric cardiothoracic surgeons; nevertheless, the postoperative intensive management is sometimes complicated because the pulmonary vascular compliance, contraction power of the cardiac muscle, and renal function are physiologically changing during the few weeks after birth.[4]

For the evaluation of the hemodynamic change before and after PDA ligation, previous reports investigated the left ventricular (LV) function by echocardiogram using the indices of ejection fraction (EF), shortening fraction, mean velocity of circumferential fiber shortening, end-systolic wall stress, or systemic vascular resistance,[5-8] or those by tissue Doppler imaging.[9] These reports demonstrated that the increase of afterload after PDA ligation influenced LV function.[5-7] However, these reports investigated only hemodynamic changes within 24 hours of PDA ligation, and dynamic changes in the LV efficiency after PDA ligation have not been sufficiently studied. The other study using an animal model showed that PDA ligation for premature baboon neonates increased the afterload and decreased LV function as evaluated by the index of shortening fraction.[10] As a new evaluation method of hemodynamics, the concept of energy efficiency has been recently applied for patients who have undergone cardiac surgery. The indices of end-systolic elastance (Ees), effective arterial elastance (Ea), and ventriculoarterial coupling (Ea/Ees) were simply calculated from blood pressure and measurements by echocardiogram, and provided a useful framework for investigating ventricular performance.[11] With the use of these indices, previous reports studied the ventricular efficiency before and after aortic valve replacement[12] and mitral valve surgery,[13] or for congenital heart disease.[14-16] The current study evaluated the hemodynamic changes in LV function before and after

From the Departments of Pediatrics[a] and Cardiovascular Surgery,[b] Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Nov 6, 2012; revisions received Jan 22, 2013; accepted for publication Feb 12, 2013; available ahead of print March 8, 2013.

Address for reprints: Hazumu Nagata, MD, Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan (E-mail: dadan@pediatr.med.kyushu-u.ac.jp).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.02.019

Abbreviations and Acronyms

Ea = effective arterial elastance
Ees = end-systolic elastance
Ea/Ees = ventriculoarterial coupling
EF = ejection fraction
LV = left ventricular
LVEDV = left ventricular end-diastolic volume
LVEDVI = left ventricular end-diastolic volume index
LVESV = left ventricular end-systolic volume
LVESVI = left ventricular end-systolic volume index
PDA = patent ductus arteriosus
POD = postoperative day
SD = standard deviation
SW/PVA = ratio of stroke work and pressure-volume area

PDA ligation in premature infants with regard to the energetic efficiency of LV pumping.

MATERIALS AND METHODS

Patient Information

A total of 847 premature infants (gestational age <36 weeks) were admitted to Kyushu University Hospital from January 2003 to December 2010. The cases accompanied with congenital heart diseases and chromosomal disorders, or in poor clinical condition, such as those with severe respiratory syndrome, bacterial sepsis, or necrotic enterocolitis, were excluded from this study. All of the premature infants born at less than 25 weeks of gestational age without an apparently severe critical condition were routinely administered prophylactic indomethacin 3 times after birth: 0.1 mg/kg/6 hours at 12 to 15 hours after birth, 0.1 mg/kg/6 h 24 hours after the first administration, and 0.1 mg/kg/6 hours 24 hours after the second administration. The infants born at 25 weeks and more than 25 weeks of gestational age were treated with indomethacin only when clinical symptoms were observed, such as tachypnea, tachycardia, and a reduction of urine output due to PDA. The dose of indomethacin was 0.1 mg/kg/6 hours; if the PDA did not close, the same dose was administered a second and third time 24 hours after the first and second treatments, respectively. If the indomethacin treatment did not effectively close the PDA and symptomatic heart failure persisted because of the presence of PDA, surgical PDA ligation was performed. Informed consent for the surgery was obtained from the parents of all patients. All retrospective data used in this study were obtained by means of charts and electronic database reviews.

Surgical Technique

PDA ligation was performed using standard methods. Anesthesia was conducted in intubated infants by a standard technique, with intravenous infusions of fentanyl and the muscle relaxant pancuronium. The patients were placed in a right lateral position, and a standard left posterolateral thoracotomy was performed through the third intercostal space. A single ligation of the PDA was performed with a silk suture.

Analysis of Cardiovascular Function by Echocardiogram

The LV efficiency before and after PDA ligation was evaluated by transthoracic echocardiogram at 4 points: within 24 hours before PDA ligation, within 24 hours after PDA ligation, between postoperative days (PODs) 2 and 4, and on POD 7. The LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were calculated by the Teichholz M-mode method based on the data about the LV end-diastolic dimension and the end-systolic dimension obtained from the echocardiogram.[17] The LV end-diastolic volume index (LVEDVI), LV end-systolic volume index (LVESVI), and EF were calculated as follows: LVEDVI (mL/m^2) = LVEDV/body surface area, LVESVI (mL/m^2) = LVESV/body surface area, EF (%) = (1-LVESV/LVEDV) × 100. The arterial blood pressure was measured by the Korotkoff technique using the manchette method. The indices of contractility (Ees) and afterload (Ea) were calculated on the basis of the systemic blood pressure and cardiac volume data using the approximation method, as described previously.[18] The approximation of the Ees and Ea was performed as follows: Ees = mean blood pressure /minimal LV volume; Ea = maximal LV pressure/(maximal LV volume − minimal LV volume). The mean blood pressure was calculated as follows: mean blood pressure = (systolic blood pressure + diastolic blood pressure×2)/3. The maximal LV pressure was approximated by the systolic blood pressure. The maximal LV volume was defined as being equal to the LVEDV, and the minimal LV volume was defined as being equal to the LVESV. The Ea/Ees indicates the ventriculoarterial coupling between the left ventricle and the arterial system.[11] The ratio of stroke work and pressure-volume area (SW/PVA) represents the LV efficiency, which was estimated using the theoretic formula SW/PVA = 1/(1 + 0.5 Ea/Ees).[19]

Statistical Analysis

The values are presented as the mean values ± standard deviation (SD). An analysis of variance with repeated measures on 1 factor was used for the variables measured at the 4 points (within 24 hours before PDA ligation, within 24 hours after PDA ligation, between PODs 2 and 4, and on POD 7). The Student Newman–Keuls test was used as a post hoc test.

RESULTS

Clinical Manifestations

Among the 847 premature infants, 98 were treated with indomethacin for the closure of or prophylaxis for PDA, and 63 of these PDA cases were closed by 5.8 ± 4.1 days of age. There were 35 patients with persistent PDA even after indomethacin treatment, and surgical PDA ligation was performed in all of these infants. The mean ± SD gestational age of these infants was 27.2 ± 4.4 weeks, and their birth weight was 934 ± 499 g. The narrowest PDA diameter was 2.43 ± 1.08 mm. The blood-flow speed in the PDA was 2.16 ± 0.80 m/sec. Surgical PDA ligation was performed at 23.5 ± 11.6 days of age. The body weight of the infants at PDA ligation was 978 ± 504 g. The length of the operation was 37.2 ± 9.3 minutes. No critical complications developed in any of the patients during the operation (Table 1). Eighteen of 35 patients were treated with dopamine or dobutamine before surgery to assist cardiac function. After surgery, all patients, including these 18, were given a dopamine or dobutamine infusion at a dose of 3 to 5 μg/kg/min for at least 24 hours, but vasodilating agents (eg, phosphodiesterase 3 inhibitors) were not used. Eighteen patients were managed under mechanical ventilation before the surgery, and all of the patients were controlled under mechanical ventilation for at least 3 days after the surgery. Detailed data on circulatory and respiratory supports for the patients