Abstract

OBJECTIVES: Clinical outcomes for neonatal cardiac surgery have improved dramatically over the last decade in Japan; however, few nationwide surveys have been reported in this field. The aim of this study was to investigate the current trends and outcomes of neonatal cardiac surgery in Japan over a period of 15 years.

METHODS: All data were derived from the official annual reports by the Japanese Association for Thoracic Surgery (JATS) between 1996 and 2010. Data collected included patient age (neonates, 0–30 days), cardiac diagnosis, operative procedure with or without cardiopulmonary bypass (CPB or non-CPB) and hospital death.

RESULTS: The number of neonatal cardiac surgeries annually in children during the study period significantly increased from 791 cases (9.4%) in 1996 to 1585 cases (16.6%) in 2010. The major diagnoses were simple transposition of the great arteries (TGA) (20.0%) and total anomalous pulmonary venous return (19.2%) in the CPB group, and patent ductus arteriosus (35.5%) in the non-CPB group. The annual number of cardiac surgeries for hypoplastic left heart syndrome gradually increased during the study period, and it has been increasingly performed in neonates with preponderance, since 2007, of non-CPB procedures over the Norwood procedure with CPB since 2007. The hospital mortality of neonatal cardiac surgery has dramatically decreased from 21.2% to 6.9% (P < 0.0001), and especially in neonates with hypoplastic left heart syndrome from 75.4% in 1996 to 17.6% in 2010.

CONCLUSIONS: Current neonatal cardiac surgery trends during the past decade were clearly identified, and hospital mortality in Japan was comparable with that of recent reports from other national databases.

Keywords: Neonate • Congenital heart disease • Cardiac surgery • Japan

INTRODUCTION

The recent advances of perinatal medicine have significantly improved postoperative outcomes of cardiac surgery in neonates with congenital heart disease (CHD). Neonatal hospital mortality from the European Association for Cardio-Thoracic Surgery (EACTS) Congenital Database [1] was 10.7% in 1999–2008. The Society of Thoracic Surgeons (STS) Congenital Heart Surgery database [2] reported the mortality rate of 10.1% in 2010–2013. The Japanese Association for Thoracic Surgery (JATS) has conducted annual surveys of thoracic surgery throughout Japan since 1986, and has been collecting and analysing nationwide patient data with regard to the number of procedures by operative category. These data have been published in English since 1996, and the JATS gave us a valuable opportunity to work with the national thoracic surgical database. Using the official data reported by JATS, current trends and outcomes of neonatal cardiac surgery in Japan over a period of 15 years were investigated in the present study.

MATERIALS AND METHODS

This study was approved by the JATS Committee for Scientific Affairs on November 2013. All data were derived from the annual reports by JATS, ‘Thoracic and Cardiovascular Surgery in Japan’ between 1996 and 2010 [3–17]. These data, including patient age, cardiac diagnosis, operative procedure with or without cardiopulmonary bypass (CPB or non-CPB), and hospital death, were based on survey questionnaires that were sent out annually to their board-certified member institutions and affiliated institutions. Definitions for diagnostic and procedural terms are uniform in the JATS annual surveys. During the study period, the annual number of institutions that responded to the survey of
Cardiovascular surgery ranged from 413 to 593, and the median response rate was 95.2% (range, 85.2%–99.0%). In these institutions, the annual number of institutions that performed paediatric cardiac surgery ranged from 316 to 419 (Table 1).

For the purpose of analysis, the year of cardiac surgery in neonates (age, 0–30 days) with CHD was considered separately, both as a continuous variable as well as in three subgroups of the 5-year period as: early period (1996–2000), middle period (2001–2005), and late period (2006–2010). Hospital mortality was defined as death within any time interval after an operation and before the patient was discharged from the hospital. Hospital-to-hospital transfer was not considered discharge; transfer to a nursing home or a rehabilitation unit was considered hospital discharge unless the patient subsequently dies of surgical complications [18].

Statistical analysis

Continuous data are presented as median and interquartile range unless otherwise specified. Statistical analyses were conducted using GraphPad Prism software 5.0 (GraphPad Software Inc., San Diego, CA, USA). A chi-square test was used to compare annual numbers and hospital mortality of neonatal cardiac surgery each year, whereas a chi-square test for trend was used to analyse trends of annual numbers and hospital mortality of neonatal cardiac surgery throughout the study period. Differences were considered statistically significant at \( P < 0.05 \).

RESULTS

In total, 138 675 cardiac surgeries for CHD were identified during this 15-year period; of these, 18 304 (13.2%) were performed in neonates. The number of neonatal cardiac surgeries and subsequent hospital mortality by cardiac diagnosis or operative procedure for CHD are summarized in Supplementary materials 1 and 2. The annual numbers and hospital mortality of the cardiac surgery for CHD by age are shown in Figs 1A and 2A. The total number of cardiac surgeries reported for CHD has remained essentially stable, between 9000 and 9600 cases per year since 1998, and the annual number of cardiac surgeries for CHD in neonates has steadily increased during the past 15 years. The percentage of neonates to all patients increased from 9.4% (791 cases) in 1996 to 16.6% (1585 cases) in 2010, with a significant increasing trend in the annual number of neonatal cardiac surgeries throughout this period \(( P < 0.0001)\). In 1996, there were 168 hospital deaths (hospital mortality, 21.2%) among the 791 neonates operated on for CHD, which was considerably higher than those in infants (7.0%) and children older than 1 year (2.3%). However, hospital mortality in neonates has dramatically decreased to less than 10% in 2006, and fell to 6.9% in 2010. A significant decreasing trend in hospital mortality of neonatal cardiac surgery was observed through the past 15 years \(( P < 0.0001)\).

Cardiac surgery with CPB or non-CPB

Among the 18 304 neonatal cardiac surgeries performed during the study period, 42.5% (7783 cases) were CPB and 57.5% (10 521 cases) were non-CPB procedures. The annual numbers of cardiac surgeries for CHD and hospital mortality by age in the CPB or non-CPB setting are shown in Figs 1B, C and 2B. During the past 15 years, annual numbers of both CPB and non-CPB procedures have increased significantly \(( P < 0.0001 \text{ for both})\). The percentage of CPB neonates among all CPB patients increased gradually from 5.6% (374 cases) in 1996 to 8.0% (575 cases) in 2010, whereas the percentage of non-CPB neonates in all non-CPB patients increased remarkably from 23.2% (417 cases) in 1996 to 42.8% (1010 cases) in 2010. Comparison between CPB and non-CPB procedures showed that the proportion of non-CPB procedures to all neonatal cardiac surgical procedures has significantly increased from 52.7% in 1996 to 63.7% in 2010 \(( P < 0.0001)\). The hospital mortality of the CPB procedures has markedly improved from 34.5% in 1996 to 11.5% in 2010, and that of the non-CPB procedures has steadily decreased from 9.4% in 1996 to 4.3% in 2010. Both procedures showed significant decreasing trends throughout the study period \(( P < 0.0001 \text{ for both})\).

Cardiac diagnosis

The major cardiac diagnoses of neonatal cardiac surgery using CPB or non-CPB procedures during the study period are shown in Fig. 3A. In the CPB group, simple transposition of the great arteries (TGA) was the most frequent diagnosis necessitating neonatal cardiac surgery (20.0%), followed by total anomalous pulmonary venous return (TAPVR; 19.2%), hypoplastic left heart syndrome (HLHS; 11.9%), TGA with ventricular septal defect (TGA/VSD; 5.6%) and interrupted aortic arch with VSD (IAA/VSD; 5.4%). In the non-CPB group, patent ductus arteriosus (PDA) was the most frequent diagnosis (35.5%), followed by single ventricle (SV; 7.2%), coarctation of the aorta with VSD (CoA/VSD; 6.6%), HLHS (4.7%) and pulmonary atresia with intact ventricular septum (PA/IVS; 4.3%). The number of cardiac surgeries and hospital mortality of neonates with these major CHDs by 5-year period in the CPB or non-CPB setting are shown in Figs 3B and C. The annual number of neonatal cardiac surgeries with CPB has remarkably increased from 424 cases in the early period to 566 cases in the late period for TAPVR, which was the most frequent diagnosis in the later period.

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<th>Table 1: Response to annual survey of cardiac surgery from 1996 to 2010</th>
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<td>Returned institutions: Total (CHD)</td>
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Total: annual number of institutions that responded to the survey of cardiovascular surgery; CHD: number of institutions that performed paediatric cardiac procedures in all of the institutions.
Compared with the early period, neonatal cardiac surgery with CPB for simple TGA, TGA/VSD and IAA/VSD also had an increasing tendency annually in the later period. However, the annual number of surgeries with CPB for HLHS decreased by 8.4% in the late period following an increase of 19.8% in the middle period. In the non-CPB procedures, the greatest increases of annual numbers from the early to late period have occurred in surgery for HLHS (20-fold) and PDA (2.5-fold). The hospital mortality of cardiac surgery with CPB in neonates with major CHD has significantly improved from the early to the later period ($P < 0.0001$ for simple TGA, TAPVR, HLHS and TGA/VSD and $P = 0.0472$ for IAA/VSD). In contrast, the number of HLHS surgeries with non-CPB has considerably increased since 2002, and reached 79 cases per year in 2010. Since 2007, neonatal cardiac surgery for HLHS has been performed with more non-CPB than CPB procedures. The hospital mortality of cardiac surgery in neonates with HLHS has markedly improved from 75.4% in 1996 to 17.6% in 2010, with a significant decreasing trend throughout the study period ($P < 0.0001$).

**Hypoplastic left heart syndrome**

With a focus on neonates with HLHS, the annual numbers and hospital mortality of the cardiac surgery for HLHS are shown in Fig. 4. The total number of HLHS surgery per year has gradually increased during the past 15 years. The annual number of surgeries with CPB initially increased and reached a peak in 2002 (87 cases per year), and then reduced to approximately 50 cases per year. In contrast, the number of HLHS surgeries with non-CPB has considerably increased since 2002, and reached 79 cases per year in 2010. Since 2007, neonatal cardiac surgery for HLHS has been performed with more non-CPB than CPB procedures. The hospital mortality of cardiac surgery in neonates with HLHS has markedly improved from 75.4% in 1996 to 17.6% in 2010, with a significant decreasing trend throughout the study period ($P < 0.0001$).

**Main procedures**

Among the main procedures of neonatal cardiac surgery between 2004 and 2010, pulmonary artery banding (PA banding; 1892 cases) was the most frequent procedure, followed by systemic-to-pulmonary artery shunt (SP shunt; 1201 cases), arterial switch procedure (1060 cases), and Norwood procedure (397 cases). The annual numbers of those main procedures by age are shown in Fig. 5A. During the study period, the annual number of PA banding in neonates increased significantly ($P = 0.0006$), and the percentage compared to all patients with PA banding has gradually increased from 45.9% (198 cases) in 2004 to 54.4% (341 cases) in 2010. The annual number of Norwood procedure in neonates has declined since 2006, and its percentage compared
with all patients undergoing Norwood procedures has significantly decreased from 63.7% (65 cases) in 2004 to 38.1% (45 cases) in 2010 ($P < 0.0001$). Approximately 80% of arterial switch procedures were performed in neonates during the study period, and its percentage to all patients with arterial switch procedures has significantly increased from 73.7% (160 cases) in 2004 to 83.5% (157 cases) in 2010 ($P = 0.0050$). The hospital mortality of those main procedures during the study period is shown in Fig. 5B. The hospital mortality of the arterial switch procedure significantly decreased from 11.3% in 2004 to 7.0% in 2010 ($P = 0.0046$). Although the hospital mortality of Norwood procedure has significantly improved from 40.0% in 2004 to 15.6% in 2010 ($P = 0.0055$), it was still significantly higher than that of the other main procedures (15.6% vs 5.2% in 2010, $P = 0.0041$).

DISCUSSION

Congenital heart disease is the most common birth defect, with an estimated prevalence of 10.6 per 1000 of all live births in Japan [19]. According to the Vital Statistics of the Ministry of Health, Labour and Welfare of Japan [20], the annual number of live births in 2010 was 1.07 million per year, which translates to an annual incidence of CHD that is estimated to approximately 11 340 live births in Japan. Because the annual incidence of neonatal cardiac surgery was 1585 cases in 2010, the annual incidence of neonatal cardiac surgery in all neonates with CHD in 2010 was calculated to be 14.0%. Based on the JATS annual survey in 2010, 316 cardiovascular institutions in Japan performed 9558 cardiac surgeries on pediatric patients [5]. The Japan Cardiovascular Surgery Database Organization established the Japan Congenital Cardiovascular Surgery Database in 2008, and reported the annual number of pediatric cardiac surgeries was 7051 at the 93 registered cardiovascular institutions in 2010 [21]. These results indicated that 73.8% of all pediatric cardiac surgeries in 2010 were performed at the 93 registered institutions. The actual number of cardiovascular institutions at which the cardiac surgery was performed on neonatal patients in Japan could not be provided by this study; however, most neonatal cardiac surgeries were performed at the registered institutions.

Although the number of births has decreased each year during the past 40 years in Japan, the present study demonstrated that the annual number of cardiac surgeries for CHD in neonates has steadily increased during the last 15 years. The annual number of
Figure 4: Neonatal cardiac surgeries performed for hypoplastic left heart syndrome (HLHS). (A) Number and hospital mortality of operations by year. Y-axis on the left represents the number of operative cases (bar graph), whereas Y-axis on the right represents hospital mortality (line graph). (B) Distribution of cardiopulmonary bypass (CPB+), operation with CPB procedure; CPB(–), operation with non-CPB procedure.

Institutions that responded to the survey of cardiovascular surgery increased during this study period. However, since 2000 the annual number of responded institutions that performed paediatric cardiac procedures was roughly 400 with a high response rate of 96.1 ± 2.5%, and the total number of cardiac surgeries reported for CHD has remained essentially stable with 9393 ± 151 cases per year. Therefore, the increase in the number of neonatal surgery cases despite the declining birth rate would not be simply associated with the increased number of the responded institutions. The present study showed that the percentage of neonates to all paediatric patients for CHD increased from 9.4% in 1996 to 16.6% in 2010. This higher proportion of patients undergoing initial cardiac surgery in the first 30 days of life rather than later could possibly be influenced by the following potential explanations for the increase in the number of neonatal surgery cases.

One of the main reasons for this increase is technical advancement of diagnostic capabilities in the field of CHD and perinatal intensive care management. The efficacy of routine prenatal screening for CHD by echocardiography has been a worldwide concern since the 1990s, and prenatal mortality in patients diagnosed on foetal echocardiography has significantly decreased from 41.2% to 13.2% during the last 15 years in Japan [22]. Although the estimated prevalence of congenital cardiac anomalies among live births has been regarded as a constant in Japan [19], foetal diagnosis is beneficial in counselling prospective parents as well as in the immediate management of the newborn with CHD, with resultant prevention of postnatal shock from hypoxia or pulmonary overcirculation in neonates with ductal-dependent systemic or pulmonary circulation. Continual advances in neonatal intensive care are associated with improved clinical outcomes of very-low-birth-weight (VLBW) infants who have a mortality rate of 8.7% in Japan [23]. The number of VLBW infants has increased annually, resulting in a significantly increased incidence of symptomatic PDA. PDA was diagnosed in 37.2% of VLBW infants, and surgical closure of the PDA was performed in 6.1% of these patients in 2008 [23]. The present study revealed 2.5-fold increases in surgery for PDA from the early to late period. The crude mortality rates of the PDA surgery decreased significantly from 6.2% to 2.2%.

Technical advances in surgical procedures with CPB may contribute to the increased number of neonatal cardiac surgeries. Miniaturization of the bypass circuits resulted in minimized prime volume, decreased hemodilution on CPB, fewer blood product transfusions, and a lesser degree of activation of the inflammatory pathway [24]. Modified ultrafiltration after CPB brought about immediate improvement in hemodynamics and pulmonary function [25]. These advances now allow surgeons to perform safe cardiac surgery with CPB even in neonates with low birth weight. During the last 15 years, from 1996 to 2010, there was a 1.5-fold increase in neonatal cardiac surgery with CPB in Japan. TAPVR and simple TGA, two leading diagnoses necessitating neonatal cardiac surgery with CPB, have increased with average annual incidences of 113 and 107 cases in the late period, respectively.

The most important trend over the 15-year study period is the significant decrease in the mortality rate of cardiac surgery in neonates. Although neonatal hospital mortality in Japan was more than 15% in the 1990s, it has dramatically decreased to 6.9% in 2010. Modified neonatal hospital mortality, except in patients undergoing surgical closure of the PDA in Japan was 8.4% in 2010, which was lower than those in the congenital databases of EACTS (10.7% in 1999–2008) and STS (10.1% in 2010–2013) [1, 2]. The modified neonatal hospital mortalities of the CPB and non-CPB procedures in Japan were 11.5% and 5.4% in 2010, respectively, and were also lower than those in the EACTS congenital database (15.9% in the CPB procedure and 5.9% in the non-CPB procedure) [1]. The establishment of a standardized medical approach to the diagnosis and surgical treatment for neonates with complex CHD has a potentially positive impact on improved postoperative outcomes. HLHS is one of the most challenging forms of CHD to treat. Despite recent innovative improvements in surgical techniques and perioperative management, mortality in neonates with HLHS undergoing stage 1 palliation remains high. National data extracted from the STS Congenital Heart Surgery database showed that the overall hospital mortality of the stage 1 palliation for HLHS was 17.5% in 2010–2012: 29.7% for hybrid palliation (pulmonary arterial banding with ductal stenting) and 15.7% for Norwood palliation [26]. In Japan, the hospital mortality following cardiac surgery in neonates with HLHS has dramatically improved from 75.4% in 1996 to 17.6% in 2010, and the hospital mortality following the Norwood procedure was 15.6% in 2010, which was comparable or superior to those in the STS and EACTS congenital databases [1, 2]. In the past decade, the right ventricle–pulmonary artery conduit [27, 28] represented one of most important advances in the surgical technique of the Norwood procedure. Proved benefits include higher diastolic blood pressure, prevention of retrograde diastolic flow in the aorta, and higher coronary perfusion pressure when compared with the classical Norwood procedure. In addition, bilateral PA banding with or without stenting of the ductus arteriosus for the management of HLHS has been more recently developed as an alternative strategy for the initial treatment of high-risk neonates.
with HLHS [29]. Although the JATS annual survey did not show whether the trend seen in the increased numbers of PA banding included bilateral branch PA banding, or was limited to the traditional banding of the main pulmonary trunk, encouraging results from this development for the management of HLHS could contribute to the increase in annual numbers of PA banding and the recent decrease in the annual number of Norwood procedures in neonates. Now, we are interested to know whether the adoption of bilateral PA banding as an initial palliative stage for patients with HLHS has led to an overall reduction in mortality for HLHS or a push-back after the first 30 days of life. A full study of outcomes in neonatal cardiac surgery using the Japan Congenital Cardiovascular Surgery Database is expected to be conducted in the near future.

The limitations of this study are primarily related to the nature of the annual reports by JATS [3–17]. Because the survey of cases was voluntary with no validation of the data, it might account for few cases more. However, the median response rate of institutional registry to the survey was 95.2% (range, 85.2–99.0%, Table 1).

The data mainly comprise patient age, diagnosis, operative procedure, number of cases, and hospital mortality, but do not capture every possible perioperative variable. Two important limitations were observed while comparing the outcomes of neonatal cardiac surgery with those reported in the STS Congenital Heart Surgery Databases and the EACTS Congenital Databases. First, these comparisons did not take into account case mix such as a different condition of neonates undergoing surgery. Second, the congenital databases of STS and EACTS do not include patients weighing less than or equal to 2500 g undergoing PDA ligation as their primary procedure for the mortality calculations [30].

In summary, current trends and clinical outcomes in neonatal cardiac surgery for CHD in Japan were identified by the annual reports of the JATS between 1996 and 2010. The neonatal population and rate of patients undergoing cardiac surgery for CHD in Japan increased gradually in this period, and the surgical outcomes of CHD in neonates have improved markedly with a reduction of the hospital mortality, which was comparable with that of recent reports from other national databases.
SUPPLEMENTARY MATERIAL

Supplementary material is available at EJCTS online.

Conflict of interest: none declared.

REFERENCES


