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ORIGINAL ARTICLE

# Early Surgical Closure of Atrial Septal Defect Improves Clinical Status of Symptomatic Young Children with Underlying Pulmonary Abnormalities

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**Abstract**
Elective closure of atrial septal defect (ASD) is usually recommended during preschool ages. However, ASD may contribute to deteriorating health in the presence of significant comorbidity and, thus, may need earlier closure. There is a lack of clarity regarding the indications for and outcomes after ASD closure in infancy and early childhood. We investigated the benefits and safety of surgical ASD closure in symptomatic patients under 2 years of age. Retrospective chart review was conducted in patients who underwent surgical ASD closure within the first 2 years of life. Of 31 symptomatic ASD patients, 22 had persistent respiratory symptoms, 24 failure to thrive, and 9 pulmonary hypertension. Overall, 26 patients (84.0%) showed clinical improvement after ASD closure, including improved respiratory status (17/22; 77.3%), resumption of normal growth (15/24; 62.5%), and resolution of pulmonary hypertension (7/7; 100%, 2 patients unable to assess postoperatively). Two medically complicated patients died a few months after surgery unrelated to surgical complications. Four out of 8 ventilator-dependent patients were weaned from mechanical ventilation within 1 month after ASD closure. Closure of ASD did not improve those patients with highly advanced lung disease and/or medically complex conditions including underlying genetic abnormalities. Surgical complications were uncommon. Postoperative hospital stay was 4 to 298 days (median 8 days). The majority of our patients demonstrated significant clinical improvement after ASD closure. Early ASD closure is safe and beneficial for symptomatic infants and young children with associated underlying pulmonary abnormalities, especially bronchopulmonary dysplasia.

**Keywords** Atrial septal defect (ASD) · Bronchopulmonary dysplasia (BPD) · Failure to thrive (FTT) · Respiratory distress · Congestive heart failure · Pulmonary hypertension

## Introduction

Atrial septal defect (ASD) is the second-most common congenital heart disease presenting during childhood and is defined as an anatomical deficiency of the atrial septum. Clinical manifestations of ASD are primarily attributed to persistently increased pulmonary blood flow and dilated right atrium (RA) and right ventricle (RV) due to volume overload [1]. Despite markedly increased pulmonary blood flow, patients with ASD rarely become symptomatic or develop pulmonary vascular obstructive disease until mid-adulthood [2]. Traditionally, patients have been referred for ASD closure during childhood, before school-age, to prevent later complications [2, 3].

Early closure of ASD during infancy has been historically more controversial. Occasionally, an isolated ASD may be associated with congestive heart failure in infancy, and the early closure appears to be beneficial [4–6]. In addition, patients with underlying pulmonary abnormalities including lung disease related to prematurity, bronchopulmonary dysplasia (BPD), or chronic aspiration may be adversely affected by increased pulmonary blood flow, and some have advocated early ASD closure to improve outcome in these patients [7]. However, the potential for spontaneous closure has led others to recommend conservative medical

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management even for symptomatic ASD in young children [8–10]. The historical concern with high surgical morbidity and mortality among infants with ASD and complex comorbidities [5] may no longer be applicable [7]. There is a lack of clarity regarding the indications for and outcomes after ASD closure in infancy and early childhood.

Percutaneous ASD device closure has become a standard option for asymptomatic older children and adults with secundum ASD [11]. However, its indication in infants and small children may be limited because of underlying ASD anatomy (defect too large, sinus venosus type or primum type ASD, deficient rim, multiple defects, and aneurysmal septum), small left atrium, and small size of an access vessel [12–14]. Surgical ASD closure is frequently indicated for those who are not amenable to the device closure and those who are clinically deteriorating despite maximum medical support, especially in infants and young children with known comorbidity.

The purpose of this study is to assess the benefits and safety of surgical ASD closure in symptomatic young children with significant clinical symptoms. We reviewed our institutional experience with symptomatic ASD patients who underwent surgical closure within the first 2 years of life. We retrospectively examined the clinical course and outcome after early surgical ASD closure and discuss the rationale of early surgical ASD closure in symptomatic young children.

## Methods

### Patients

A retrospective chart review was conducted in symptomatic patients with isolated ASD who underwent surgical ASD closure before 2 years of age at Nemours Cardiac Center, Nemours/Alfred I. duPont Hospital for Children, between January 1998 and December 2018. The study was approved by the Institutional Review Board of the hospital. Patients with ASD and either a small patent ductus arteriosus (PDA), partially anomalous pulmonary venous connection (in the setting of a sinus venosus ASD), or bicuspid aortic valve without significant hemodynamic abnormalities were included, whereas patients with other major concomitant congenital cardiac anomalies were excluded. Anatomical diagnosis was made primarily by echocardiogram. Inclusion criteria of "symptomatic" patients were based on the following definitions. The respiratory symptoms included: (a) the presence of baseline respiratory distress (tachypnea, retraction, hypoxia, apnea, increased work of breathing, or feeding difficulty); (b) persistent dependency on respiratory support including supplemental oxygen, continuous positive airway pressure (CPAP), or positive pressure ventilation; or (c) recurrent respiratory illness requiring hospitalization at least twice a year. The respiratory symptoms were divided into two groups: (1) "severe" (ventilator-dependent) and (2) "mild to moderate" (spontaneous breathing). Failure to thrive was defined as either (a) persistent low weight below 3 standard deviations (SD) from the mean value for age without improvement or (b) suboptimal weight gain falling below a standard growth curve (growth charts by Centers for Disease Control and Prevention, 0 to 36 months: www.cdc.gov/growthcharts/). Pulmonary hypertension was defined as either (a) estimated RV pressure by tricuspid regurgitation (TR) jet measurement by echocardiogram exceeding 2/3 of simultaneous systemic pressure, or cardiac catheterization findings of (b) mean pulmonary arterial pressure (MPAP) > 25 mmHg, (c) pulmonary vascular resistance (Rp) ≥ 3.5 U·m$^2$, or (d) pulmonary vascular resistance/systemic vascular resistance (Rp/Rs) ratio ≥ 0.3.

All patients were evaluated by our interventional cardiologist for possible percutaneous device closure before surgery, including patient size (weight) and transthoracic or transesophageal echocardiography to assess anatomy with particular attention to the size of the atrial septal rims in relation to the anticipated size of the ASD closure device. Those patients who underwent percutaneous ASD device closure were not included in this study.

### Surgical Technique

Closure of ASD was performed via full or partial median sternotomy using cardiopulmonary bypass at mild hypothermia. Closure was performed using a patch of polytetrafluoroethylene (PTFE), Dacron, or autologous pericardium or by primary suture at discretion of the surgeon.

### Outcomes

Clinical improvement in respiratory symptoms was defined as (a) resolution of respiratory symptoms, (b) withdrawal from positive pressure ventilation or supplemental oxygen within 1 month, or (c) freedom from recurrent respiratory illnesses requiring hospital admission. Improvement in growth was defined as a more than 1.0 $z$ score increase in standard growth chart (weight-for-age percentiles: birth to 36 months in each sex) within one year after ASD closure. Improvement in pulmonary hypertension was defined as a reduction of estimated pressure gradient of TR jet by continuous wave Doppler becoming less than half systemic blood pressure within 6 months after the ASD closure.

### Statistical Analysis

The data are shown as mean ± SD unless indicated otherwise. The comparison of the two groups was performed by

two-tailed Student's *t* test, and *p* value of less than 0.05 was considered statistically significant.

## Results

### Clinical Profile of the Recruited Patients

Table 1 summarizes the clinical profile of 31 patients who underwent surgical ASD closure in the first 2 years of life for one or more of the followings: respiratory symptoms ($n=22$), failure to thrive (FTT) ($n=24$), or pulmonary hypertension ($n=9$). The majority of patients had secundum type ASD (26/31; 83.9%) with female predominance (19/31; 61.3%). Commonly associated clinical conditions were prematurity/BPD (11/31; 35.5%) and trisomy 21 (6/31; 19.4%). Ten patients underwent preoperative hemodynamic assessment by cardiac catheterization (Table 2). The ratio of total pulmonary blood flow to total systemic blood flow (Qp/Qs) was less than 2 in 6 patients and higher than 2 in 4 patients. Six patients were diagnosed as having pulmonary hypertension by cardiac catheterization (MPAP > 25 mmHg, $R_p \geq 3.5$ U $m^2$, or $R_p/R_s \geq 0.3$). None had a right to left shunt. Pulmonary vasodilators were tested in 6 patients. Four patients responded to increased inspired oxygen and nitric oxide with either increased $Q_p/Q_s$ or decreased $R_p/R_s$, whereas 2 patients showed minimum response (Pts 10 and 14). Of note, Pt 14 was found to have associated functional left pulmonary vein stenosis by cardiac catheterization.

**Table 1** Patients who underwent ASD closure before 2 years of age ($n=31$)

| | Patients ($n=31$) |
|---|---|
| Age of surgery | 49–409 days (231 ± 154) |
| M:F | 12:19 |
| Anatomy | |
| Secundum | 26 |
| Sinus venosus | 3 |
| Secundum and sinus venosus | 1 |
| Primum | 1 |
| Other cardiac/hemodynamic anomalies | |
| PDA (small) | 7 (4 previously closed) |
| PAPVR | 1 |
| Aortic arch hypoplasia (mild) | 2 |
| Pulmonary hypertension | 9 |
| Underlying conditions | |
| Prematurity/BPD | 11 |
| Trisomy 21 | 6 |
| Pierre–Robin sequence | 2 |
| Chromosome 3/4 translocation | 1 |
| 1p36 deletion | 1 |
| Kabuki syndrome | 1 |
| CODAS syndrome | 1 |
| Congenital CMV infection | 1 |
| Unknown multiple congenital anomalies | 2 |

*PDA* patent ductus arteriosus, *PAPVR* partial anomalous of pulmonary venous return, *BPD* bronchopulmonary dysplasia, *CODAS syndrome* cerebral, ocular, dental, auricular, skeletal syndrome (MIM 600,373), *CMV* cytomegalovirus

### Surgical Approach and Complications

Surgical procedures and postoperative complications are listed in Table 3. Complications were relatively limited. A total of 4 patients had a patch with fenestration. Total hospital stay after the surgery was 4 to 298 days (median 8 days). The incidence of significant pericardial effusion that required medical treatment (steroids or ibuprofen) and/or pericardiocentesis was 2/31 (6.5%). Postoperative mortality was 2/31 (6.5%), although both deaths occurred late after surgery (108 and 145 days) and were unrelated to the surgical procedure or postoperative complications (Pts 15 and 21). One additional patient (Pt 16) died 6 years after surgery with unimproved respiratory status (Table 4).

### Clinical Improvement after ASD Repair

Clinical improvement in any of 3 categories was noted in 26/31 (83.9%) in our cohort.

#### Respiratory Symptoms

Twenty-two patients (71.0%) had variable degrees of respiratory symptoms (Table 5). Eight patients were classified as "severe" because of their ventilator-dependent chronic respiratory failure with multiple underlying medical problems; 5 patients were ventilated via endotracheal tube, and the other 3 were via tracheostomy. Two patients, Pts 16 and 21, underwent tracheostomy 9 and 3 months after ASD closure, respectively. Five patients had BPD, and 5 patients had underlying genetic abnormalities including trisomy 21 (2 patients) and Pierre–Robin sequence (2 patients). Four of 8 patients were successfully weaned from positive pressure ventilation within 1 month after ASD closure. Among these 4 patients with improvement, 2 were the patients with tracheostomy; one was transitioned to tracheostomy-collar within 1 month after ASD closure (Pt 3), and the other was off positive pressure ventilation on postoperative day 4 and the tracheostomy was taken down on postoperative day 82 (Pt 24). Fourteen patients were grouped as "mild to moderate," consisting of clinical symptoms of congestive heart failure including tachypnea, retractions, and/or feeding difficulties ($n=8$); mild supplemental oxygen dependence ($n=5$); and recurrent respiratory infections ($n=1$). After ASD closure, 92.9% (13/14) of mild-to-moderate respiratory symptoms resolved. Among 15

**Table 2** Hemodynamic data: baseline and provocative studies

| Pt | Age (mo) | $Q_p/Q_s$ | pPA (mmHg) | $R_p$ (U $m^2$) | $R_p/R_s$ | Others | PH | $FiO_2$ | Provocative condition | $Q_p/Q_s$ | $R_p$ ($Um^2$) | $R_p/R_s$ | Response | ASD patch fenestration |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 5 | 1.5 | 51/14 (**28**) | 4 | **0.31** | BPD | Y[a] | 0.5 | | | | | | |
| 3 | 9 | 1.5 | 24/13 (18) | 1.6 | 0.1 | BPD | N | RA | | | | | | Y |
| 4 | 8 | 2.7 | 74/28 (**42**) | 5.7 | **0.3** | Trisomy 21 | Y[b] | 0.5 | $FiO_2$ 0.5, NO 40 ppm | 4.6 | 3.7 | – | Y | Y |
| 7 | 3 | 2.3 | 40/13 (24) | 2.1 | 0.1 | BPD, Pierre–Robin | N | 0.4 | | | | | | |
| 10 | 7 | 1.8 | 47/17 (**32**) | **3.5** | 0.26 | BPD | Y[a] | RA | FiO2 1.0 | 1.5 | 3.3 | 0.3 | N | |
| 14 | 3 | 1.9 | 57/20 (**37**) | 8.4 | **0.4** | Trisomy 21 | Y[a] | RA | $FiO_2$ 1.0, NO 40 ppm | 1.9 | 6.45 | 0.4 | N | |
| 15 | 1 | 2.5 | 38/11 (24) | 3.4 | 0.17 | Trisomy 21 | Y[a,c] | 0.24 | $FiO_2$ 1.0 | 3.4 | 1.93 | 0.08 | Y | Y |
| 19 | 1 | 1.8 | 44/7 (22) | **3.7** | 0.24 | 1p38 deletion | Y[a] | RA | $FiO_2$ 1.0 | 4 | 1.16 | 0.11 | Y | |
| 30 | 19 | 1.5 | 43/19 (**31**) | 3.1 | **0.34** | BPD | Y[a] | RA | $FiO_2$ 1.0, NO 20 ppm | 2.5 | 2.2 | 0.16 | Y | Y |
| 31 | 5 | 3 | 31/13 (22) | 1.1 | 0.1 | BPD | N | RA | | | | | | |

Bold numbers indicate the presence of PH

*Age (mo)* age (months) at cardiac catheterization, *BPD* bronchopulmonary dysplasia, *pPA* pulmonary arterial pressure, ( ) indicates mean pressure, *PH* pulmonary hypertension, *Rp* pulmonary vascular resistance, *Rs*: systemic vascular resistance, *RA* room air, *Y* yes, *N* no

[a]Showed amelioration of PH after ASD closure

[b]Lost follow up

[c]Diagnosed as PH based upon echo criterion

**Table 3** Surgical procedures and postoperative complications

| | Symptomatic ASD ($n=31$) | % |
|---|---|---|
| Materials | | |
| PTFE | 19 (3 with fenestration) | 61.3 |
| Suture | 6 | 19.4 |
| Dacron | 2 | 6.5 |
| PTFE and suture | 1 | 3.2 |
| Autologous pericardium | 4 (1 with fenestration) | 12.9 |
| Complications | | |
| Pericardial effusion[a] | 2 | 6.5 |
| Hypertension (transient) | 2 | 6.5 |
| Pleural effusion | 3 | 10 |
| Atrial flutter | 1 | 3.2 |
| SVC-RA obstruction (mild) | 1 | 3.2 |
| Seizure | 1 | 3.2 |
| Hospital days after surgery | 4–298 days (median 8) | |

*PTFE* polytetrafluoroethylene, *SVC* superior vena cava, *RA* right atrium

[a]Clinically significant pericardial effusion that required specific treatment including medications (corticosteroid, ibuprofen), pericardiocentesis, or creation of pericardial window

patients with improved respiratory symptoms without tracheostomy (2 severe and 13 mild to moderate), liberation of mechanical ventilation after the cardiac surgery occurred a median of 1 day postoperatively (ranging from 3 h to 15 days).

Three of 4 patients without clinical improvement in respiratory status after surgical ASD closure died of severe respiratory disease despite maximum supportive therapy (Table 4). Pt 15 was an infant with trisomy 21 with severe BPD, cystolic fibrosis, and recurrent aspiration who was ventilation-dependent before ASD closure. The support was withdrawn 145 days after ASD closure, as the family declined tracheostomy and further escalation of treatment. Pt 16 was a premature, low-birth-weight infant with Pierre–Robin sequence and cleft palate who underwent tracheostomy 9 months after ASD closure for chronic respiratory failure and who never recovered from the baseline pulmonary disability and died at 6 years of age at a chronic care facility. Pt 21 was a premature infant with trisomy 21, BPD, and chronic aspiration who underwent tracheostomy 3 months after ASD closure and who died of intractable lung disease 108 days after surgery. These deaths were not directly related to postoperative complications from surgical ASD closure.

With "severe" respiratory symptoms ($n=8$), 4 patients had FTT, and 5 patients had pulmonary hypertension (Pt 3 did not have follow up evaluation as the patient was transferred back to the referring hospital after surgery). Only 2 patients in this group showed improvement in growth (50%), whereas pulmonary hypertension was improved in all 4 patients (100%). In the "mild-to-moderate" group ($n=14$), 13 patients had FTT, and 3 patients had pulmonary hypertension. In this group, growth failure improved in 10/13 (76.9%), and pulmonary hypertension showed significant improvement in all 3 patients after ASD closure.

### Growth Failure

Failure to thrive improved in 15/24 (62.5%) patients (Fig. 1a). While 11/16 patients (68.8%) with growth failure associated with respiratory symptoms improved (Table 5), 4/8 (50%) of those without respiratory symptoms showed improvement. Among those 9 patients with FTT who did not exhibit improvement, 7 had either chromosomal or genetic abnormalities, including trisomy 21 ($n=3$), Pierre–Robin

**Table 4** Mortality cases

| Pt | Clinical information | Total hosp stay | Age of death | Cause of death |
|---|---|---|---|---|
| 15 | Trisomy 21, FT, severe tracheobronchomalacia, BPD, CF, PH, chronic aspiration, seizure,<br>Chronic respiratory failure, FTT<br>Sinus venosus (IVC) type ASD, PDA (small) | 115 days | 5 months | Persistent respiratory failure |
| 16 | Pierre–Robin sequence, multiple congenital anomalies, cleft palate, prematurity, PH<br>Static encephalopathy, agenesis of corpus callosum, GER<br>Tracheostomy 9 months after ASD repair for worsening respiratory status, chronic respiratory failure, recurrent respiratory illness, FTT<br>Secundum type ASD, mild AS (bicuspid aortic valve) | 23 days | 6 years | Cardiopulmonary arrest |
| 21 | Trisomy 21, ex-32 wk prematurity, BPD, chronic aspiration, PH, Hirschsprung disease<br>Tracheostomy after ASD repair for worsening respiratory status<br>Secundum type ASD | 192 days | 7 months | Persistent respiratory failure |

*FT* full term, *IVC* inferior vena cava, *BPD* bronchopulmonary dysplasia, *CF* cystic fibrosis, *PH* pulmonary hypertension, *Pt* patient, *FTT* failure to thrive, *IVC* inferior vena cava, *GER* gastroesophageal reflux

**Table 5** Clinical responses to surgical ASD closure in 22 patients with variable respiratory symptoms

| Pt | Diagnosis | Improvement in | | | |
|---|---|---|---|---|---|
| | | DOS | Respiratory Symptoms | FTT | PH |
| [1] Severe: Ventilator-dependent chronic respiratory failure ($n=8$) | | | | | |
| 1 | Ex-27w, BPD, laryngomalacia, GER. PH | 162 | Y: Extubated (3 days[d]), off suppl. oxygen (7 days[d]) | – | Y |
| 3 | Ex-24w, BPD, tracheobronchomalacia, subglottic stenosis, **Trach** | 290 | Y: Off vent 1 month after surgery | – | [b] |
| 7 | Ex-32w, BPD, Pierre–Robin sequence, cleft palate, **Trach** | 104 | N | Y | – |
| 12 | Chr 3/4 translocation, spastic quadriplegia, seizure, multiple congenital anomalies | 379 | Y: Extubated (15 days[d]) | Y | – |
| 15 | Trisomy 21, BPD, PH, severe laryngomalacia, seizures, CF, FTT | 63 | N[a] | N | Y[c] |
| 16 | Multiple congenital anomalies, Pierre–Robin sequence, prematurity, PH, apnea | 54 | N[a] | N | Y[c] |
| 21 | Ex-32w, BPD, trisomy 21, **Trach**, aspiration, Hirschsprung disease | 81 | N[a] | – | Y[c] |
| 24 | CODAS syndrome, **Trach**, imperforate anus, congenital skeletal anomalies | 409 | Y: Off vent (4 days[d]) | – | – |
| [2] Mild to moderate ($n=14$) | | | | | |
| (1) CHF symptoms (tachypnea, poor feeding, and retraction) ($n=8$) | | | | | |
| 8 | Mild arch hypoplasia, CHF, FTT | 339 | Y | Y | – |
| 9 | Ex-27w, BPD, mild arch hypoplasia, CHF, FTT | 193 | Y | Y | – |
| 11 | Ex-31w, BPD, twin, CHF, FTT | 251 | Y | Y | – |
| 13 | Trisomy 21, CHF, FTT, PH | 162 | Y | N | – |
| 18 | Mild PS, tachypnea, CHF, FTT | 121 | Y | Y | – |
| 19 | Ex-37w, IUGR (BW 1.76 kg), 1p36 del, CHF, PH | 60 | Y | – | Y |
| 22 | PAPVR with sinus venosus type ASD, congenital CMV, CHF, FTT | 105 | Y | Y | – |
| 23 | Ex-34w, BPD, tachypnea, CHF, FTT | 123 | Y | Y | – |
| (2) Supplemental oxygen ($n=5$) | | | | | |
| 10 | Ex-29w BPD, CHF, PH, GER, aspiration, oxygen-dependent | 232 | Y: Off suppl. oxygen | Y | Y |
| 14 | Trisomy 21, small transverse arch, FTT, CHF, PH | 114 | N | N | Y |
| 20 | Ex-26w, BPD, CHF, FTT | 158 | Y: Off suppl. oxygen | Y | – |
| 26 | Ex-30w, BPD, FTT | 385 | Y: Off suppl. oxygen | Y | – |
| 28 | Trisomy 21, CLD, history of PPHN, FTT | 237 | Y: Off suppl. oxygen | Y | – |
| (3) Recurrent infections ($n=1$) | | | | | |
| 17 | Ex-35w, BPD, Kabuki syndrome, GER, recurrent respiratory infections, FTT | 33 | Y: No recurrence of infection | N | – |
| | | | **17/22** | **12/16** | **7/7** |

Bold words are for emphasis of trache (tracheostomy)

*DOS* days (post-natal) of surgery, *BPD* bronchopulmonary dysplasia, *GER* gastroesophageal reflux, *suppl.* supplemental, *Chr* chromosome, *Trach* tracheostomy, *PH* pulmonary hypertension, *FTT* failure to thrive, *CHF* congestive heart failure, *CMV* cytomegalovirus, *PS* pulmonary stenosis, *PAPVR* partial anomalous of pulmonary venous return, *CLD* chronic lung disease (without premature lung), *Y* yes, *N* no

[a]Deceased (see Table 5), [b]had pulmonary hypertension but was lost to follow up after surgery, [c]diagnosed by echocardiogram only, [d]after surgical ASD closure

sequence ($n=1$), Kabuki syndrome ($n=1$), or unknown syndromic disorder ($n=2$), but 2 did not have any clinical features suggestive of underlying genetic abnormalities.

### Pulmonary Hypertension

Pulmonary hypertension was diagnosed by cardiac catheterization ($n=6$, see Table 2) or echocardiogram ($n=3$; Pts 15, 16, and 21, see Table 5). Predicted systolic pulmonary arterial pressure estimated by TR jet velocity decreased to less than half systolic in 7 out of 7 (100%, Fig. 1b) patients with pulmonary hypertension following ASD closure. One patient (Pt 4, Table 2) was lost to follow up, and the other (Pt 30) did not have sufficient tricuspid valve regurgitation in postoperative echocardiogram. In 2 patients with preoperative catheterization demonstrating elevated and relatively unchanged pulmonary vascular resistance (Pts 10 and 14 in Table 2), there was a significant reduction in RV

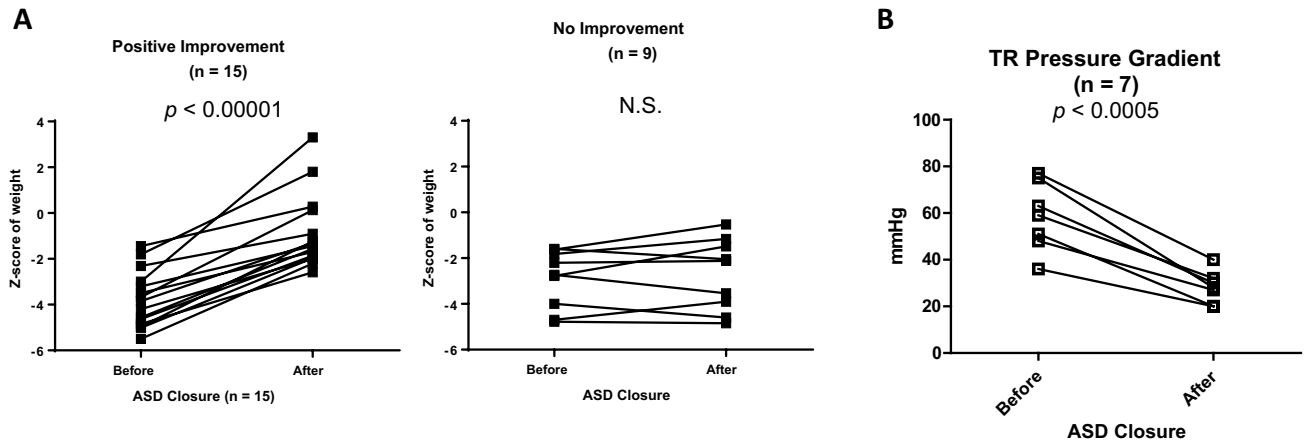


**Fig. 1** **a** Resumption of normal physical growth after ASD closure. *Y* axis represents *z* score of body weight at standard growth chart (CDC 0 to 36 months, male or female). Positive trend was noted in 15 patients (left; *z* score from $-3.8 \pm 1.2$ to $-0.9 \pm 1.6$: $p < 0.00005$), whereas there was no improvement in 7 patients (right; *z* score from $-2.9 \pm 1.3$ to $-2.7 \pm 1.6$). One patient in the nonresponsive group was not included because the patient died 3 months after ASD closure (Pt 15). **b** Improvement of pulmonary hypertension (PH) after ASD closure. *Y* axis represents pressure gradient (mmHg) of tricuspid regurgitation (TR) jet assessed by continuous pulse Doppler method before and after ASD closure. Postoperative echocardiogram was performed within 6 months after surgery. All 7 patients showed significant decrease in TR pressure gradient ($62.8 \pm 14.8$ to $29 \pm 7.0$ mmHg; $p < 0.005$)

pressure after ASD closure. Both patients received inhaled nitric oxide immediately after surgery and were discharged home with oral sildenafil, whereas only Pt 14 with trisomy 21 and elevated Rp (8.4 units·m$^2$) underwent ASD patch closure with fenestration. Even in the 3 patients who died after surgery because of progressive lung disease (Table 4), preoperatively noted elevated pulmonary arterial pressure was significantly reduced after ASD closure without specific pulmonary vasodilator treatment.

## Discussion

This study demonstrates that early surgical ASD closure can be beneficial for symptomatic patients with underlying pulmonary abnormalities, especially those with BPD. In fact, among the patients with ventilator-dependent chronic respiratory failure, half of them improved sufficiently to achieve liberation from ventilator support. It should be noted that the beneficial effects of eliminating the excessive pulmonary blood flow did outweigh the open heart surgery-related morbidity and mortality even among patients with the most severe forms of pulmonary disease. Similarly, growth retardation was improved in most of the patients without underlying genetic abnormalities. Finally, ASD closure resulted in reduction of estimated RV pressure by echocardiogram in all cases with pulmonary hypertension.

### ASD Closure Resulted in Significant Clinical Improvement in Symptomatic Patients Younger Than 2 Years of Age

Patients with isolated ASD usually remain asymptomatic throughout childhood and early adulthood despite increased pulmonary blood flow and RV volume overload. However, the patients with ASD may become symptomatic in combination with decreased left ventricular compliance, marginal left heart structure, or left ventricular dysfunction [15]. Increased pulmonary blood flow as a result of ASD may lead to deleterious effects on those patients with lung diseases related to prematurity, BPD, and recurrent aspiration and may be responsible for significant morbidity and mortality [16]. In our study, 80.6% of patients with respiratory symptoms had resolution after ASD closure (50% in severe cases and 92.9% in mild-to-moderate cases). Four of 5 patients who did not respond to ASD closure were those with advanced pulmonary disease with ongoing complex medical problems (Pts 7, 15, 16, and 21 in Table 5). Three of these 4 patients died (Table 4). Earlier surgery might have been beneficial for those patients with ASD and worsening respiratory status. For clinically complicated patients, the defect is best closed sooner to prevent the development of further pulmonary vascular damage and perhaps may improve their clinical condition [6, 17].

### Post-surgical Clinical Improvement is Determined by Underlying Pulmonary Status

Our data suggest that reducing pulmonary blood flow by ASD closure effectively improved pulmonary mechanics in the majority of symptomatic patients with underlying lung disease, especially with BPD, as is commonly seen in closing PDA in these patients [18]. Reduction in pulmonary blood flow by closing ASD may facilitate natural improvement of BPD over time [18]. Resumption of normal growth was noted more frequently in the patients with respiratory symptoms. This finding is, in part, in agreement with the previous observation that non-cardiac reasons were frequently responsible for FTT in infants with ASD not associated with significant respiratory symptoms [19, 20].

Pulmonary hypertension was significantly reduced after surgical ASD closure in nearly all patients, as was previously reported [7, 21–23]. The patients with increased risk of postoperative pulmonary hypertension were managed with inhaled nitric oxide and/or sildenafil with favorable outcome. Fenestrated patch was applied in two cases with pulmonary hypertension (Pts 2 and 30) to prevent potential pulmonary hypertensive crisis. We did not encounter any cases with severe pulmonary vascular obstructive disease, as reported by others [17, 20]. According to the current American and European guidelines, ASD can be safely closed if $R_p/R_s < 1/3$ or $Q_p/Q_s > 1.5$ [24, 25], but the surgical indications may be further liberated as there are more pulmonary vasodilators available in recent years [26]. Careful preoperative hemodynamic evaluation with or without preoperative medical treatment is warranted for all patients with severe pulmonary hypertension beyond these indications.

### Surgical ASD Closure Can be Performed Safely in Symptomatic Young Children

Surgical closure of ASD in the contemporary era can be safely accomplished in younger children with similar or lower incidence of complications as reported in older children [3, 27, 28]. Pericardial effusion after surgical ASD closure is reported to be less frequent in infants or younger children than in older children [28–30]. The incidence of postoperative complications in symptomatic patients in our study (Table 3) is comparable to what has been reported in older asymptomatic patients [28–30]. Indeed, some sick infants with progressively worsening respiratory status (Pts 1 and 3 in Table 5) showed compelling clinical improvement after surgical ASD closure without postoperative complications. Due to significant improvement of intensive care management after open heart surgery in sick infants, the benefit of preventing chronic pulmonary complications by surgical ASD closure in young patients with underlying pulmonary abnormalities may prevail over the risk of potential short-term surgical complications when the patients are not clinically improving despite maximum medical treatment and when percutaneous ASD device closure is not indicated.

During the same period of time, we have performed transcatheter device closure in 22 symptomatic ASD patients younger than 2 years ($356 \pm 200$ days; 10 males and 12 females) who also had postoperative assessment at least for a year (unpublished data). Ten patients were former premature infants, 2 were trisomy 21, and one had multiple congenital anomalies. Clinical indications for ASD closure include respiratory symptoms ($n = 15$), FTT ($n = 10$), pulmonary hypertension ($n = 9$), and multiple cerebral infarcts ($n = 1$). With ASD device closure, improvement of respiratory status, growth, and estimated pulmonary arterial pressure was noted in 60% (9/15), 40% (4/10), and 100% (9/9), respectively, which are essentially similar to the results after surgical ASD closure in this study. Collectively, our current data indicate that the elimination of excessive pulmonary blood flow by closing ASD in symptomatic infants and young children helps improve homodynamic status and ameliorate clinical symptoms regardless of the therapeutic modalities.

## Limitations

There are several limitations in this study. First, this is a retrospective study in a single institution with a relatively small number of the patients with heterogenous backgrounds. Secondly, all symptomatic infants and young children with ASD underwent ASD closure in our hospital. Thus, there were no control symptomatic patients who were solely managed non-surgically without ASD closure. Instead, we compared the 3 clinical parameters before and after ASD closure and assessed the outcomes in an objective manner. Thirdly, pulmonary hypertension was not strictly defined in this study, and not all patients underwent diagnostic catheterization. Only 6 patients were diagnosed with pulmonary hypertension by cardiac catheterization, and 3 patients were diagnosed by echocardiogram only. Improvement of pulmonary hypertension was assessed only by decrease in echocardiographic measurement of estimated RV pressure, not by decrease in pulmonary vascular resistance. Lastly, there were 3 symptomatic ASD patients with small unclosed PDA. Although these PDAs were small, we cannot underestimate a significant contribution of PDA ligation to the observed improvement.

## Conclusion

We have demonstrated that early ASD closure in infants and young children with underlying chronic lung disease may improve respiratory symptoms and overall clinical outcomes. Surgical ASD closure can be performed safely in symptomatic infants and young children with no significant incidence in perioperative morbidity and mortality. We suggest early closure of ASD, either by device or by surgery, in all symptomatic infants and young toddlers with underlying chronic lung disease to mitigate ongoing parenchymal and vascular injury to the lung while enhancing improvement of lung function.

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### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict ofinterest.

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