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ORIGINAL RESEARCH

Trend and Outcomes for Surgical Versus Transcatheter Patent Ductus Arteriosus Closure in Neonates and Infants at US Children's Hospitals

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BACKGROUND: Pharmacologic therapy for patent ductus arteriosus closure is not consistently successful. Surgical ligation (SL) or transcatheter closure (TC) may be needed. Large multicenter analyses comparing outcomes and resource use between SL and TC are lacking. We hypothesized that patients undergoing TC have improved outcomes compared with SL, including mortality, hospital and intensive care unit length of stay, and mechanical ventilation.

METHODS AND RESULTS: Using the 2016 to 2020 Pediatric Health Information System database, characteristics, outcomes, and charges of patients aged <1 year who underwent TC or SL were analyzed. A total of 678 inpatients undergoing TC (n=503) or SL (n=175) were identified. Surgical patients were younger (0.1 versus 0.53 years; *P*<0.001) and more premature (60% versus 20.3%; *P*<0.001). Surgical patients had higher mortality (1.7% versus 0%; *P*=0.02). Using inverse probability of treatment weighting by the propensity score, multivariable-adjusted analyses demonstrated favorable outcomes in TC: intensive care unit admission rates (adjusted odds ratio [OR], 0.2; 95% CI, 0.11–0.32; *P*<0.001); mechanical ventilation rates (adjusted OR, 0.3; 95% CI, 0.19–0.56; *P*<0.001); and shorter hospital (adjusted coefficient, 2 days shorter; 95% CI, 1.3–2.7; *P*<0.001) and postoperative (adjusted coefficient, 1.2 days shorter; 95% CI, 0.1–2.3; *P*=0.039) stays. Overall charges and readmission rates were similar. Among premature neonates and infants, hospital (adjusted difference in medians, 4 days; 95% CI, 1.7–6.3 days; *P*<0.001) and postoperative stays (adjusted difference in medians, 3 days; 95% CI, 1.1–4.9 days; *P*=0.002) were longer for SL.

CONCLUSIONS: TC is associated with lower mortality and reduced length of stay compared with SL. Rates of TC continue to increase compared with SL.

Key Words: cardiac catheterization ■ cardiovascular surgical procedure ■ cost ■ outcomes ■ patent ductus arteriosus

Patency of the ductus arteriosus beyond 3 days of age is common in preterm neonates, with an incidence close to 50% in infants born younger than 32 weeks of gestational age, and >80% in those aged <24 weeks.[1–3] In term newborns, functional closure typically occurs within 24 to 48 hours after delivery, with anatomic closure following over the subsequent 2 to 3 weeks.[4] Although spontaneous closure often occurs in preterm infants, it may not occur until 6 weeks of age.[5] Furthermore, extremely low-birth-weight infants aged <24 weeks gestational age show a low rate of spontaneous closure (<15%).[3] A hemodynamically significant patent ductus arteriosus (PDA) may exacerbate common complications of prematurity, including bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, and intraventricular hemorrhage (IVH); other complications, including heart failure and pulmonary hypertension, can also occur.[3,6–9]

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CLINICAL PERSPECTIVE

What Is New?

- Using a large database, we have demonstrated increasing rates of transcatheter patent ductus arteriosus closure being performed relative to surgical ligation among neonates and infants between 2016 and 2020.
- Patients undergoing surgical ligation tended to have more comorbid conditions, whereas patients undergoing transcatheter closure had lower mortality, and decreased postoperative length of stay.

What Are the Clinical Implications?

- Transcatheter patent ductus arteriosus closure should be considered over surgical ligation when feasible.

Nonstandard Abbreviations and Acronyms

IPTW	inverse probability of treatment weighting
IVH	intraventricular hemorrhage
PHIS	Pediatric Health Information System
SL	surgical ligation
TC	transcatheter closure

Failure of PDA closure by day 3 of age has also been associated with mortality in preterm infants.[6,8]

Appropriate treatment remains a topic of debate.[7,10] Pharmacologic therapy is not consistently successful[5] and has been associated with renal and gastrointestinal complications.[3] Surgical ligation (SL) or transcatheter closure (TC) can be performed subsequent to or in place of pharmacologic therapy, although both methods involve procedural and anesthetic risks. Such risks include those of thoracic dissection, vocal cord paralysis, or diaphragm paresis during SL, and device embolization/migration, vascular injury, aortic arch obstruction, or left pulmonary artery obstruction during TC.[11–13] In addition, the abrupt change in loading conditions of the left ventricle secondary to PDA closure can lead to a significant cardiopulmonary compromise known as postligation cardiac syndrome. Although postligation cardiac syndrome has been described with both treatment modalities, its incidence seems to be lower after TC.[14] Newer technologies have allowed TC to be safely performed even in extremely low-birth-weight premature infants as small as 700 g.[15,16] The proportion of PDA closures performed by TC relative to SL is increasing.[11,17] Recent work has shown improved outcomes with TC, including decreased IVH,[18] decreased inotrope use,[18] and shorter duration of mechanical ventilation.[19,20] Small studies have shown higher procedural charges for TC compared with SL; however, the benefits in terms of reducing procedure duration are less clear.[11,21,22] Large-scale multicenter analyses comparing outcomes and resource use between SL and TC are lacking. This study aims to compare the trend of surgical and transcatheter PDA closure techniques, outcomes, and cost in neonates, infants, and premature patients at US children's hospitals using a large administrative database.

METHODS

This protocol was submitted to the Institutional Review Board at Boston Children's Hospital and determined to meet the requirements for Institutional Review Board exemption. No written informed consent was required from study subjects. This protocol adheres to the applicable Consolidated Standards of Reporting Trials guidelines. The corresponding author (V.N.) and the coauthor (S.S.) had full access to all data and take responsibility for data integrity and analysis.

The data that support the findings of this study are available from the corresponding author on request and following approval by the Pediatric Health Information System (PHIS) database.

Data Source

The PHIS is an administrative database that contains discharge/encounter data from 52 freestanding children's hospitals in the United States that are part of the Children's Hospital Association. The PHIS contains *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) and *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) diagnostic and procedure codes, date-stamped billing data, and other administrative data.[23]

Study Population

This study was performed using data from the 2016 to 2020 PHIS database. Patients aged <18 years with a diagnosis of PDA undergoing transcatheter ductus closure or open surgical procedures for ductal ligation based on *ICD-10-CM* procedure codes and Current Procedural Terminology codes were initially included (Data S1); the study cohort was subsequently limited to neonates (aged <1 month) and infants (aged 1 month to <1 year). Patients with an additional congenital heart disease diagnosis other than PDA were excluded. Outpatient procedures were excluded. Patients with missing data on patient type (inpatient versus outpatient) were excluded.

Exposure and Baseline Variables

Among inpatients with PDA, the primary exposure variable was procedure type: TC or SL. Full data analysis was performed for neonates and infants, stratified by procedure type. Baseline factors analyzed were age group, prematurity, sex, and comorbid conditions (bronchopulmonary dysplasia, necrotizing enterocolitis, pulmonary hypertension, IVH, sepsis, endocarditis, renal insufficiency, and heart failure). Comorbid conditions were identified on the basis of *ICD-10* diagnosis codes.

Study Outcomes

The study outcomes included cost of living adjusted charges (billed [overall] charges, clinical charges [including physician fees and procedure charges], imaging charges, laboratory charges, pharmacy charges, supply charges, and other charges, which include time spent as inpatient or in the intensive care unit [ICU]), in-hospital mortality, ICU and neonatal ICU (NICU) admission at any time during the admission to the hospital, postoperative ICU or NICU admission, duration of postoperative ICU or NICU admission, mechanical ventilation, postoperative mechanical ventilation, duration of postoperative mechanical ventilation, hospital length of stay (LOS), postoperative LOS, and hospital readmission (within 7, 30, and 90 days). The adjusted charges are based on the charges of the patient in the medical record and adjusted based on the Centers for Medicare and Medicaid Services wage/price index for the hospital's location.

Statistical Analysis

All described baseline factors and outcomes are stratified by procedure type: TC or SL. Analyses were performed in the full cohort of neonates and infants, the neonate and infant subgroups separately, and more specifically the subgroup of neonates and infants born premature. TC and SL numbers were calculated per institution. Continuous variables are presented as medians and interquartile ranges (IQRs), and categorical variables are presented as frequencies and percentages. Comparisons of baseline factors and unadjusted analyses of outcomes were performed using the Wilcoxon rank sum test and the Fisher exact test. Changes in rates over time were analyzed using the Cochran-Armitage test for trend. Unadjusted analyses of charges were performed using the Kruskal-Wallis test. A 2-tailed $P<0.05$ was used for determining statistical significance.

Multivariable-adjusted analyses were performed using inverse probability of treatment weighting (IPTW) by the propensity score to compare surgical and transcatheter encounters after controlling for baseline confounders. Propensity scores were calculated using multivariable logistic regression based on baseline demographics and comorbidities, with significant differences between surgical and transcatheter cases. In the main analyses, the following variables were included in the propensity score logistic regression model: age, prematurity, sex, bronchopulmonary dysplasia, necrotizing enterocolitis, IVH, sepsis, and renal insufficiency. In the full data set, the inverse of the propensity scores was used as weights in median regression modeling to estimate adjusted differences in median charges between surgical and transcatheter cases. IPTW by the propensity score was implemented rather than propensity score matching because matching in these data leads to a substantially reduced sample size in the matched cohort attributable to substantial inherent baseline variable differences without overlap between transcatheter and surgical patients. Results from median regression analyses are presented as adjusted differences in medians with corresponding 95% CIs and P values. A 2-tailed $P<0.01$ was used for determining statistical significance to account for testing of multiple outcomes.

Statistical analyses were performed using Stata version 16.0 (StataCorp LLC, College Station, TX).

RESULTS

Of 1605 inpatient encounters involving TC or SL of a PDA in patients aged <18 years, 678 involved neonates or infants (Figure 1). Demographics and comorbidities of all 1605 patients are presented in Table S1.

Demographics and patient comorbidities for the final cohort of neonates and infants are presented in Table 1. Transcatheter patients were older (0.53 years [IQR, 0.27–0.75 years] versus 0.1 years [IQR, 0.05–0.23 years]; $P<0.001$), and surgical patients were more likely to have been premature (60% versus 20.3%; $P<0.001$). The following comorbid conditions were more prevalent in the surgical group of neonates and infants: bronchopulmonary dysplasia (28.6% versus 16.3%; $P<0.001$), necrotizing enterocolitis (9.7% versus 0.4%; $P<0.001$), IVH (21.7% versus 2.4%; $P<0.001$), sepsis (11.4% versus 0.6%; $P<0.001$), and renal insufficiency (7.4% versus 0.8%; $P<0.001$).

The number of inpatient cases over time and stratified by age category is presented in Figure 2 and Table S2, showing significantly increased proportions of transcatheter cases over time. Prematurity rates increased over time for TC ($P<0.001$) and decreased over time for SL ($P=0.008$) (Table 2). The median number of TC (26; IQR, 14–44) and SL (26; IQR, 15–44) ($P=0.82$) procedures performed was similar at each institution.

Outcomes are displayed in Table 3; significant differences were observed for all outcome variables except

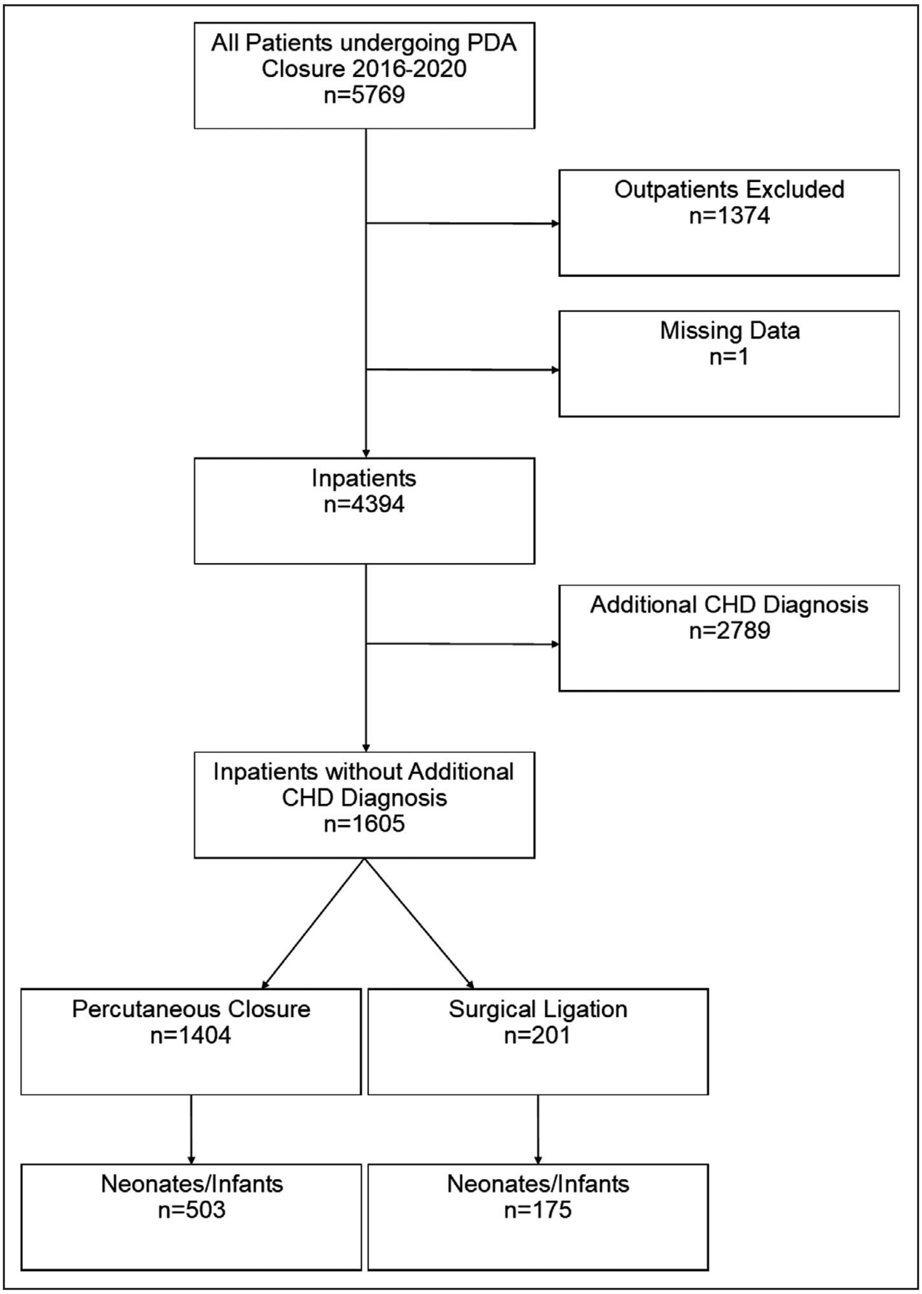

Figure 1. Patient cohort flowchart.
CHD indicates congenital heart disease; and PDA, patent ductus arteriosus.

hospital readmission and ICU/NICU admission beginning on or after procedure day, with TC showing lower incidence of in-hospital mortality (0% versus 1.7%; *P*=0.02), ICU admission during the admission (15.7% versus 31.4%; *P*<0.001), NICU admission during the admission (18.3% versus 62.9%; *P*<0.001), duration of postoperative ICU/NICU admission (median, 2 versus 4 days; *P*=0.004), mechanical ventilation during admission (19.3% versus 74.3%; *P*<0.001), duration of postoperative mechanical ventilation (median, 2 versus 3 days; *P*=0.002), and hospital (median, 1 versus 6 days; *P*<0.001) and postoperative (median, 1 versus 4 days; *P*<0.001) LOS. Mechanical ventilation started on or after the day of the procedure for more patients in the TC group (76.6% versus 52%; *P*<0.001). Rates of hospital readmission were similar between groups.

The univariate analysis of adjusted charges is presented in Table 4. Clinical and supply charges were significantly higher for TC, whereas billed (overall), laboratory, pharmacy, and other charges were significantly higher for SL. There was no difference between case types for imaging charges. A comparison of baseline

Table 1. Demographics and Patient Comorbidities of Neonates and Infants Undergoing Transcatheter PDA Closure or Surgical PDA Ligation

Variable	Transcatheter closure (n=503)	Surgical ligation (n=175)	*P* value
Age, y	0.53 (0.27–0.75)	0.1 (0.05–0.23)	<0.001*
Prematurity diagnosis	102 (20.3)	105 (60)	<0.001*
Sex			
Men	191 (38)	86 (49.1)	0.01*
Women	312 (62)	89 (50.9)	
Comorbid conditions			
Bronchopulmonary dysplasia	82 (16.3)	50 (28.6)	<0.001*
Necrotizing enterocolitis	2 (0.4)	17 (9.7)	<0.001*
Pulmonary hypertension	23 (4.6)	11 (6.3)	0.37
Intraventricular hemorrhage	12 (2.4)	38 (21.7)	<0.001*
Sepsis	3 (0.6)	20 (11.4)	<0.001*
Endocarditis	0 (0)	0 (0)	0.99
Renal insufficiency	4 (0.8)	13 (7.4)	<0.001*
Heart failure	41 (8.2)	22 (12.6)	0.08

Continuous data are presented as median (interquartile range), and categorical data are presented as number (percentage). *P* values were obtained using the Wilcoxon rank sum test, the χ^2 test, or the Fisher exact test, as appropriate. PDA indicates patent ductus arteriosus.

*Statistically significant.

characteristics between groups after implementing IPTW by the propensity is shown in Table S3. Following multivariable adjustment using IPTW by the propensity score to control for baseline demographics and comorbidities, the following charges were significantly higher for SL: laboratory charges (adjusted difference in medians, $3100; 95% CI, $100–$6100; *P*=0.04) and other charges (adjusted difference in medians, $33 900; 95% CI, $25 500–$42 200; *P*<0.001). Clinical charges (adjusted difference in medians, −$7800; 95% CI, −$11 900 to −$3700; *P*<0.001) and supply charges (adjusted difference in medians, −$8100; 95% CI, −$10 000 to −$6400; *P*<0.001) were significantly higher for TC (Figure 3 and Table S4). There was no significant difference in overall charges for neonates and infants after using IPTW by propensity score.

After adjusting using IPTW by the propensity score, hospital LOS (adjusted difference in medians, 2 days; 95% CI, 1.3–2.7 days; *P*<0.001) and postoperative LOS (adjusted difference in medians, 1.2 days; 95% CI, 0.06–2.31 days; *P*=0.039) were significantly longer for SL compared with TC (Table 5). Using IPTW by the propensity score, multivariable-adjusted analyses demonstrated more favorable outcomes in the TC group with regard to ICU admission rates (adjusted odds ratio [OR], 0.2; 95% CI, 0.11–0.32; *P*<0.001) and mechanical ventilation at any time during admission (adjusted OR, 0.3; 95% CI, 0.19–0.56; *P*<0.001).

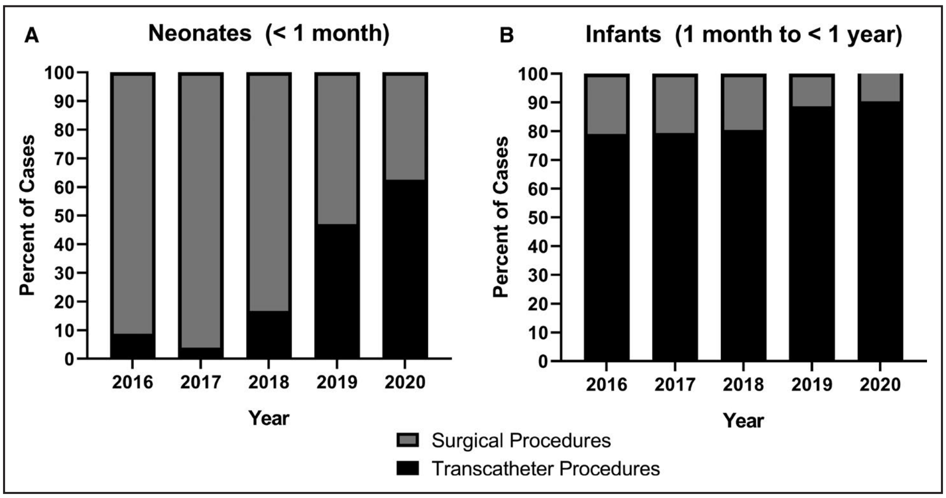

Figure 2. Trends of surgical and transcatheter procedures from 2016 to 2020 in neonates (A) and infants (B).

Table 2. Prematurity Rates Over Time in Neonates and Infants

Year	Total	Transcatheter closure cases	Surgical ligation cases
2016	53/172 (30.8)	15/112 (13.4)	38/60 (63.3)
2017	51/152 (33.6)	15/101 (14.9)	36/51 (70.6)
2018	30/109 (27.5)	13/80 (16.3)	17/29 (58.6)
2019	37/123 (30.1)	26/102 (25.5)	11/21 (52.4)
2020	36/122 (29.5)	33/108 (30.6)	3/14 (21.4)
P value	0.62	<0.001*	0.008*

Data are presented as prematurity rates in each year (number/total [percentage]). *P* values were calculated using the Cochran-Armitage test for trend.

*Statistically significant.

Outcomes for the neonate only and infant only subanalyses are shown in Tables S5 and S6. It is important to note the smaller number of neonates in the TC group. Demographics and patient comorbidities for the subgroup of premature patients (n=102 TC and n=105 SL) are displayed in Table S7. The univariate analysis of charges is presented in Table S8, and the multivariable regression analysis of charges is shown in Table S9. Outcomes among premature patients are summarized in Table 6. In this subgroup, TC showed significant differences compared with SL with regard to ICU at any time during admission (23.5% versus 7.6%; *P*=0.002), NICU at any time during admission (58.8% versus 89.5%; *P*<0.001), duration of postoperative ICU/NICU admission (median, 3 versus 7 days; *P*=0.002), mechanical ventilation at any time during admission (61.8% versus 87.6%; *P*<0.001), duration of postoperative mechanical ventilation (median, 2 versus 3.5 days; *P*=0.007), and duration of hospital (median, 4 versus 12 days; *P*<0.001) and postoperative (median, 3 versus 8 days; *P*<0.001) LOS. After performing IPTW by the propensity score in the subgroup of premature patients, hospital LOS (adjusted difference in medians, 4 days; 95% CI, 1.7–6.3 days; *P*<0.001) and postoperative LOS (adjusted difference in medians, 3 days; 95% CI, 1.1–4.9 days; *P*=0.002) values were significantly longer for SL compared with TC.

DISCUSSION

Over the course of the study period (2016–2020), TC represented a progressively increasing proportion of PDA closures performed. Among neonates and infants, SL was associated with higher resource use, including higher rates of ICU admission, longer duration of postoperative ICU or NICU admission, higher rates of mechanical ventilation, longer duration of postoperative mechanical ventilation, longer LOS, and higher in-hospital mortality. There was no difference in overall charges after IPTW. Premature neonates and infants undergoing SL showed longer duration of postoperative ICU or NICU admission, higher rates of mechanical ventilation at any time during admission, longer duration of postoperative mechanical ventilation, and longer LOS.

The increasing rate of TC compared with SL in this study is consistent with previous findings. Multiple centers now report performing the vast majority of PDA closures in preterm infants using a transcatheter

Table 3. Outcomes in Neonates and Infants Following Transcatheter PDA Closure or Surgical PDA Ligation

Outcome variable	Transcatheter closure (n=503)	Surgical ligation (n=175)	*P* value
In-hospital mortality	0 (0)	3 (1.7)	0.02*
ICU admission	79 (15.7)	55 (31.4)	<0.001*
NICU admission	92 (18.3)	110 (62.9)	<0.001*
ICU/NICU admission began on or after procedure day†	71/151 (47)	69/158 (43.7)	0.554
Duration of postoperative ICU/NICU admission, d	2 (1–6)	4 (1–42)	0.004*
Mechanical ventilation	97 (19.3)	130 (74.3)	<0.001*
Mechanical ventilation started on or after procedure day†	72/94 (76.6)	65/125 (52)	<0.001*
Duration of postoperative mechanical ventilation, d	2 (2–4)	3 (2–16)	0.002*
Hospital length of stay, d	1 (1–2)	6 (3–73)	<0.001*
Postoperative length of stay, d	1 (1–2)	4 (2–42)	<0.001*
Readmission			
Within 7 d	3 (0.6)	3 (1.7)	0.17
Within 30 d	11 (2.2)	6 (3.4)	0.37
Within 90 d	24 (4.8)	15 (8.6)	0.06

Continuous data (unweighted) are presented as median (interquartile range), and categorical data are presented as number (percentage). *P* values were obtained using the Wilcoxon rank sum test, the χ^2 test, or the Fisher exact test, as appropriate. ICU indicates intensive care unit; NICU, neonatal ICU; and PDA, patent ductus arteriosus.

*Statistically significant.

†Data missing for date of ICU admission and mechanical ventilation.

Table 4. Univariate Analysis of Cost of Living Adjusted Charges in Neonates and Infants Undergoing Transcatheter PDA Closure or Surgical PDA Ligation

Adjusted charge	Transcatheter closure (n=503)	Surgical ligation (n=175)	*P* value
Billed charges (overall charges), $	63 300 (44 900–91 900)	105 800 (48 800–750 600)	<0.001*
Clinical charges, $	14 000 (1300–28 500)	9200 (2600–80 200)	0.04*
Imaging charges, $	5900 (2600–22 300)	6800 (2700–23 900)	0.27
Laboratory charges, $	2300 (1200–4600)	9700 (3700–29 000)	<0.001*
Pharmacy charges, $	1800 (900–3100)	5000 (2000–35 700)	<0.001*
Supply charges, $	9700 (6200–17 300)	1300 (400–3600)	<0.001*
Other charges, $	15 000 (9000–31 000)	64 000 (30 600–465 100)	<0.001*

Unweighted data are shown as median (interquartile range), rounded to the nearest hundreds. The Wilcoxon rank sum test was implemented to calculated *P* values. PDA indicates patent ductus arteriosus.
*Statistically significant.

technique.[24,25] An analysis of the PHIS database between 2007 and 2017 demonstrated decreasing rates of PDA closure overall, with an increasing proportion of closures being performed by transcatheter methods. There was, however, considerable practice variation in the use of TC between institutions.[17]

Patients undergoing SL in both the overall and premature cohorts were younger, consistent with what others have demonstrated.[11,17] There has, however, been a trend among neonates and infants toward performing more TC over time. In addition, the rate of prematurity has been increasing for TC while simultaneously decreasing for SL. The approval of the Amplatzer Piccolo Occluder (Abbott, Santa Clara, CA) for infants as small as 700 g in January 2019 has presumably played a substantial role in the trend toward more TC in neonates, as well as the increasing rate of prematurity for transcatheter patients.[16,24,25]

The rates of comorbid conditions are higher in surgical patients in our study; premature patients also showed higher rates of comorbid conditions among surgical patients, with the exception of the higher rate of heart failure among premature patients undergoing TC. Higher rates of IVH, preprocedural blood transfusion, inotrope use, and mechanical ventilation have been demonstrated for surgical patients compared with those undergoing TC.[11,18] This trend is not universal as recent data demonstrated a higher rate of gastrointestinal and respiratory comorbidities among patients undergoing TC.[17,20] Interestingly, the rate of initiating mechanical ventilation on or after the procedure day was higher in patients undergoing TC for both the overall and premature cohort. This may be because patients undergoing SL were more often intubated before the day of the procedure.

Several studies have shown no difference between mortality after either procedure.[11,22,26–29] These reports, however, contain smaller cohorts and are possibly underpowered to detect mortality. Regan et al, analyzing the outcomes of 147 neonates, found no difference in mortality between SL and TC.[20] Ahmadi et

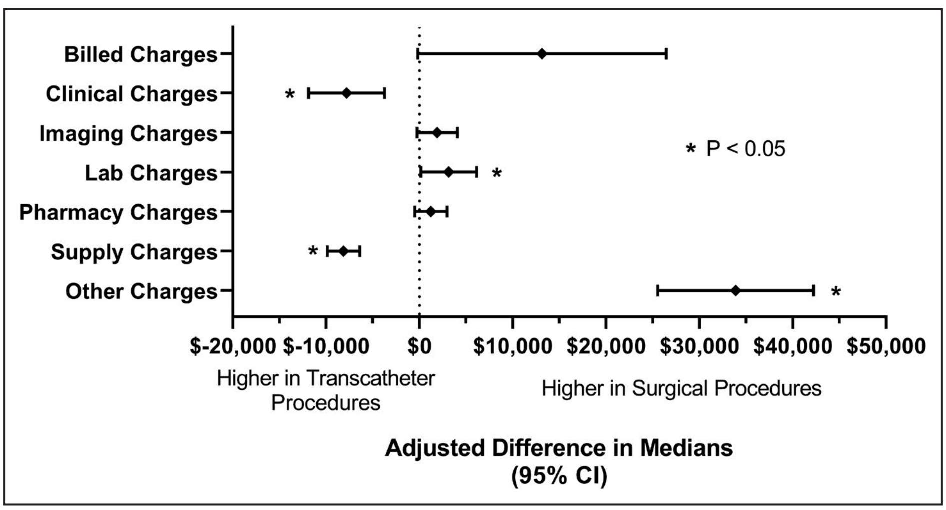

Figure 3. Multivariable median regression analysis of cost of living adjusted charges in neonates and infants.
Lab indicates laboratory.

Table 5. Multivariable Median Regression Analysis of Hospital and Postoperative LOS Using IPTW by the Propensity Score in Neonates and Infants Undergoing Transcatheter PDA Closure Versus Surgical PDA Ligation

Outcome	Adjusted difference in medians (surgical ligation– transcatheter closure)	95% CI	*P* value
Hospital LOS, d	2	1.3–2.7	<0.001*
Postoperative LOS, d	1.2	0.06–2.31	0.039

The propensity scores were calculated on the basis of baseline demographics and comorbidities, with significant differences between surgical and transcatheter cases. IPTW by the propensity score was implemented in median regression analysis. Values are adjusted on the basis of IPTW. IPTW indicates inverse probability of treatment weighting; LOS, length of stay; and PDA, patent ductus arteriosus.

*Statistically significant.

al, in their cohort of 201 patients, reported 2 in-hospital deaths after SL and none after TC.[30] Sathanandam et al, comparing a group of 80 extremely low-birth-weight infants undergoing TC with 40 infants undergoing SL by propensity score matching,[19] reported 4 deaths in the SL group and 1 death in the TC group. Similarly, Ogando et al found a higher mortality up to 36 weeks postconceptual age for patients undergoing SL; the mortality difference was no longer present by hospital discharge.[18] Our study involving 678 patients confirms these findings and demonstrates a statistically significant difference in mortality between neonates and infants undergoing SL (n=3) versus TC (n=0). This difference is not entirely surprising given the higher rate of comorbid conditions in surgical patients.

Our study demonstrated substantially higher ICU (admission and duration) and mechanical ventilation use and longer LOS with surgery. Although premature neonates and infants undergoing SL had a lower rate of ICU admission, this may be attributable to the high rate of NICU (rather than ICU) admission. Nonetheless, the duration of postoperative ICU or NICU admission was still longer after SL among premature patients. Longer length of stay after surgical closure has also been shown in other studies.[22,26–28,31] However, as some patients are referred to tertiary care centers specifically to undergo TC and return shortly thereafter to their original facility, it is difficult to draw conclusions about the lower median LOS for patients undergoing TC. Duration of mechanical ventilation and time until return to preprocedural respiratory status has been shown to improve with TC,[18–20,29,32] although this benefit has not been consistently demonstrated.[11] In a cohort of neonates weighing <3 kg, Hubbard et al found that 40% of patients intubated for the purpose of the procedure required ongoing mechanical ventilation after TC.[33] We demonstrated a lower rate of mechanical ventilation among patients undergoing TC overall (19.3%).

The overall charges associated with SL versus TC were not statistically different after adjusting using IPTW by the propensity score. However, clinical and supply charges were higher with TC, whereas laboratory and other charges were higher with SL. No charge

Table 6. Outcomes in Premature Neonates and Infants Following Transcatheter PDA Closure or Surgical PDA Ligation

Outcome variable	Transcatheter closure (n=102)	Surgical ligation (n=105)	*P* value
In-hospital mortality	0 (0)	3 (2.9)	0.247
ICU admission	24 (23.5)	8 (7.6)	0.002*
NICU admission	60 (58.8)	94 (89.5)	<0.001*
ICU/NICU admission began on or after procedure day†	20/74 (27)	28/96 (29.2)	0.759
Duration of postoperative ICU/NICU admission, d	3 (2–7)	7 (2–100)	0.002*
Mechanical ventilation	63 (61.8)	92 (87.6)	<0.001*
Mechanical ventilation started on or after procedure day†	40/61 (65.6)	34/89 (38.2)	0.001*
Duration of postoperative mechanical ventilation, d	2 (2–4)	3.5 (2–30)	0.007*
Hospital length of stay, d	4 (1–9)	12 (3–115)	<0.001*
Postoperative length of stay, d	3 (1–7)	8 (2–89)	<0.001*
Readmission			
Within 7 d	1 (1)	3 (2.9)	0.621
Within 30 d	4 (3.9)	5 (4.8)	0.999
Within 90 d	7 (6.9)	9 (8.6)	0.796

Continuous data (unweighted) are presented as median (interquartile range), and categorical data are presented as number (percentage). *P* values were obtained using the Wilcoxon rank sum test, the χ^2 test, or the Fisher exact test, as appropriate. ICU indicates intensive care unit; NICU, neonatal ICU; and PDA, patent ductus arteriosus.

*Statistically significant.

†Data missing for date of ICU admission and mechanical ventilation.

categories showed a significant difference between SL and TC in the premature group. Several prior studies have shown higher costs for patients undergoing TC compared with SL,[21,28,34] even when considering the cost for hospital stay.[22] In our study, supply charges include cardiovascular devices and supplies, and hence are expected to be higher in the transcatheter group. One study comparing procedural charges showed that although the device cost itself can contribute significantly to higher costs, removing the cost of the PDA device still resulted in higher charges for TC.[11] In fact, our study shows that clinical charges are also higher in the transcatheter group. Clinical charges in the PHIS database include cardiac catheterization and cardiovascular services. However, others have shown higher total cost in surgical patients.[26,35] Prieto et al specifically noted that hospital stay and professional costs accounted for the increased cost associated with SL.[35] In our study, laboratory and other charges were higher in surgical patients. Laboratory charges might be related to the increased ICU use and higher rate of comorbid conditions, which may lead to more frequent laboratory use. Other charges in the PHIS database include the time spent as inpatient or in the ICU. Hence, this is a reflection of the longer LOS in surgical patients.

We separately analyzed the neonate and infant subgroups; however, because there were only 19 neonates who underwent TC, we did not think conclusions from this analysis were highly meaningful. Because prematurity is an important risk factor for PDA, we chose instead to include the analysis of neonates and infants with a prematurity diagnosis.

Our study was limited in that it is a retrospective database review. The PHIS database is an administrative database, and miscoding may occur.[36] In addition, some patients in the cohort may have been transferred to a different hospital solely for the purpose of having a PDA closure, only to be returned to their original hospital shortly thereafter. This may lead to underdetection of postprocedural details, including hospital LOS, in-hospital mortality, and readmission. Furthermore, cause of death cannot be determined through the PHIS database, so whether the mortality difference was attributable to procedural factors cannot be determined. Because of the retrospective nature of the study, the type of intervention performed was not controlled, and despite the adjusted analyses performed, we cannot guarantee that the 2 populations present different risks at baseline. In addition, data about postprocedural residual lesions are not available from PHIS, and we are unable to contextualize our results relative to procedural success. Although TC is increasingly performed in neonates, the decision to choose one technique over the other is based on the patient's size and weight, the size and anatomical features of the duct, the comorbidities and level of mechanical ventilatory support, as well as institutional guidelines. Overall, TC appears to be a safe and cost-effective alternative to SL and offers the benefit of being less invasive.

In summary, our study confirms that TC rates continue to increase compared with SL of PDA. Patients undergoing TC have shorter postoperative LOS and lower mortality. Prospective clinical trials are necessary to evaluate clinically relevant differences, such as low cardiac output syndrome following TC versus SL.

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Disclosures

None.

Supplemental Material

Data S1
Tables S1–S9

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Supplemental Material

Data S1.

International Classification of Disease (ICD)-10 codes and Current Procedural Terminology (CPT) Codes for Patent Ductus Arteriosus Procedure.

ICD 10 codes

1. 02LR0ZT
2. 02LR0CT
3. 02LR0DT
1. 02LR3ZT
2. 02LR3CT
3. 02LR3DT
4. 02LR4ZT
5. 02LR4CT
6. 02LR4DT

CPT Codes

33820
33822
33824
93582

Table S1. Demographics and Patient Comorbidities of all patients undergoing Transcatheter PDA Closure or Surgical PDA Ligation.

Variable	Transcatheter (n=1404)	Surgical (n=201)	P value
Age (years)	1.49 (0.71, 3.89)	0.15 (0.06, 0.41)	**<0.001***
Age Group			
Neonates (< 1 month)	19 (1.4%)	78 (38.8%)	
Infants (1 month to < 1 year)	484 (34.5%)	97 (48.3%)	**<0.001***
1 to < 18 years	901 (64.2)	26 (12.9%)	
Prematurity Diagnosis	119 (8.5%)	107 (53.2%)	**<0.001***
Sex			
Male	488 (34.8%)	93 (46.3%)	**0.001***
Female	916 (65.2%)	108 (53.7%)	
Comorbid Conditions			
Bronchopulmonary Dysplasia	101 (7.2%)	50 (24.9%)	**<0.001***
Necrotizing Enterocolitis	2 (0.1%)	17 (8.5%)	**<0.001***
Pulmonary Hypertension	48 (3.4%)	13 (6.5%)	**0.03***
Intraventricular Hemorrhage	12 (0.9%)	38 (18.9%)	**<0.001***
Sepsis	3 (0.2%)	20 (10%)	**<0.001***
Endocarditis	0 (0%)	0 (0%)	0.99
Renal Insufficiency	5 (0.4%)	13 (6.5%)	**<0.001***
Heart Failure	56 (4%)	24 (11.9%)	**<0.001***

Continuous data are presented as median (IQR) and categorical data are presented as n (%).

P values were obtained using the Wilcoxon rank sum test, the Chi-square test, or Fisher's exact test, as appropriate.

*Statistically significant.

Table S2. Number of surgical and transcatheter procedures from 2016 to 2020 in neonates and infants

Neonates (< 1 month)			
Year	**Transcatheter**	**Surgical**	**P value**
2016	3 (8.8%)	31 (91.2%)	
2017	1 (3.9%)	25 (96.2%)	
2018	2 (16.7%)	10 (83.3%)	**<0.001***
2019	8 (47.1%)	9 (52.9%)	
2020	5 (62.5%)	3 (37.5%)	
Infants (1 months to < 1 year)			
Year	**Transcatheter**	**Surgical**	**P value**
2016	109 (79%)	29 (21%)	
2017	100 (79.4%)	26 (20.6%)	
2018	78 (80.4%)	19 (19.6%)	**0.003***
2019	94 (88.7%)	12 (11.3%)	
2020	103 (90.4%)	11 (9.7%)	

Data are presented as n (row %).
P values were calculated using the Cochran-Armitage test for trend.
*Statistically significant.

Table S3. Demographics and Patient Comorbidities in Neonates and Infants with and without IPTW by the Propensity Score.

Variable	Without IPTW		With IPTW	
	Transcatheter Closure (n=503)	**Surgical Ligation (n=175)**	**Transcatheter Closure (n=503)**	**Surgical Ligation (n=175)**
Age (years)	0.53 (0.27, 0.75)	0.1 (0.05, 0.23)	0.83 (0.67, 0.92)	0.50 (0.18, 0.89)
Prematurity Diagnosis	102 (20.3%)	105 (60%)	8.6%	24%
Sex				
Male	191 (38%)	86 (49.1%)	31.2%	40.4%
Female	312 (62%)	89 (50.9%)	68.8%	59.6%
Comorbid Conditions				
Bronchopulmonary	82 (16.3%)	50 (28.6%)	12.6%	13.2%
Dysplasia				
Nectrotizing Enterocolitis	2 (0.4%)	17 (9.7%)	0.03%	2.5%
Pulmonary Hypertension	23 (4.6%)	11 (6.3%)	3.2%	5.2%
Intraventricular Hemorrhage	12 (2.4%)	38 (21.7%)	0.3%	6.4%
Sepsis	3 (0.6%)	20 (11.4%)	0.1%	2.9%
Endocarditis	0 (0%)	0 (0%)	0.0%	0.0%
Renal Insufficiency	4 (0.8%)	13 (7.4%)	0.2%	2.1%
Heart Failure	41 (8.2%)	22 (12.6%)	5.2%	9.6%

Unweighted and weighted continuous data are presented as median (IQR) and categorical data are presented as n (%).

IPTW, inverse probability of treatment weight by the propensity score.

Table S4. Multivariable Median Regression Analysis of Cost of Living Adjusted Charges using IPTW by the Propensity Score in Neonates and Infants.

Adjusted Charge	Adjusted Difference in Medians (Surgical - Transcatheter)	95% CI	P value
Billed Charges (overall charges)	13,100	(-200, 26,400)	0.06
Clinical Charges	-7,800	(-11,900, -3,700)	**<0.001***
Imaging Charges	1,900	(-300, 4,000)	0.08
Lab Charges	3,100	(100, 6,100)	**0.04***
Pharmacy Charges	1,200	(-500, 3,000)	0.17
Supply Charges	-8,100	(-10,000, -6,400)	**<0.001***
Other Charges	33,900	(25,500, 42,200)	**<0.001***

The propensity scores were calculated based on baseline demographics and comorbidities with significant differences between surgical and transcatheter cases.

Inverse probability of treatment weighting by the propensity score was implemented in median regression analysis.

*Statistically significant.

Table S5. Outcomes in Neonates Following Transcatheter PDA Closure or Surgical PDA Ligation.

Outcome Variable	Transcatheter (n=19)	Surgical (n=78)	P value
In-hospital mortality	0 (0%)	3 (3.9%)	0.999
ICU admission	1 (5.3%)	6 (6.4%)	0.999
NICU admission	18 (94.7%)	71 (91%)	0.999
ICU/NICU admission began on or after procedure day	7/16 (43.8%)	20/73 (27.4%)	0.235
Duration of postoperative ICU/NICU admission (days)	6 (2, 25)	29 (3, 109)	0.075
Mechanical ventilation	18 (94.7%)	73 (93.6%)	0.999
Mechanical ventilation started on or after procedure day only	9/17 (47.1%)	23/71 (32.4%)	0.16
Duration of postoperative mechanical ventilation (days)	3 (2, 5)	4 (2, 45)	0.301
Hospital Length of Stay (days)	8 (2, 98)	58 (5, 123)	0.156
Postoperative Length of Stay (days)	6 (2, 76)	27 (3, 112)	0.237
Readmission			
within 7 days	0 (0%)	3 (3.9%)	0.999
within 30 days	2 (10.5%)	5 (6.4%)	0.62
within 90 days	5 (26.3%)	9 (11.5%)	0.141

Continuous data are presented as median (IQR) and categorical data are presented as n (%).
P values were obtained using the Wilcoxon rank sum test, the Chi-square test, or Fisher's exact test, as appropriate.

Table S6. Outcomes in Infants Following Transcatheter PDA Closure or Surgical PDA ligation.

Outcome Variable	Transcatheter (n=484)	Surgical (n=97)	P value
In-hospital mortality	0 (0%)	0 (0%)	0.999
ICU admission	78 (16.1%)	50 (51.6%)	**<0.001***
NICU admission	74 (15.3%)	39 (40.2%)	**<0.001***
ICU/NICU admission began on or after procedure day	64/135 (47.4%)	49/85 (57.7%)	0.139
Duration of postoperative ICU/NICU admission (days)	2 (1, 4)	2 (1, 4)	0.528
Mechanical ventilation	79 (16.3%)	57 (58.8%)	**<0.001***
Mechanical ventilation started on or after procedure day only	63/78 (80.8%)	42/54 (77.8%)	0.675
Duration of postoperative mechanical ventilation (days)	2 (1, 3)	3 (1.5, 4.5)	0.100
Hospital Length of Stay (days)	1 (1, 2)	4 (2, 7)	**<0.001***
Postoperative Length of Stay (days)	1 (1, 2)	3 (2, 6)	**<0.001***
Readmission			
within 7 days	3 (0.6%)	0 (0%)	0.999
within 30 days	9 (1.9%)	1 (1%)	0.999
within 90 days	19 (3.9%)	6 (6.2%)	0.284

Continuous data are presented as median (IQR) and categorical data are presented as n (%).
P values were obtained using the Wilcoxon rank sum test, the Chi-square test, or Fisher's exact test, as appropriate.
*Statistically significant.

Table S7. Demographics and Comorbidities among Premature Patients.

Variable	Transcatheter Closure (n=102)	Surgical Ligation (n=105)	P value
Age (years)	0.23 (0.12, 0.37)	0.06 (0.02, 0.10)	**<0.001***
Sex			
Male	46 (45.1%)	56 (53.3%)	0.236
Female	56 (54.9%)	49 (46.7%)	
Comorbid Conditions			
Bronchopulmonary Dysplasia	47 (46.1%)	43 (41%)	0.457
Necrotizing Enterocolitis	2 (2%)	17 (16.2%)	**<0.001***
Pulmonary Hypertension	5 (4.9%)	6 (5.7%)	0.999
Intraventricular Hemorrhage	10 (9.8%)	34 (32.4%)	**<0.001***
Sepsis	2 (2%)	20 (19.1%)	**<0.001***
Endocarditis	0 (0%)	0 (0%)	0.999
Renal Insufficiency	1 (1%)	13 (12.4%)	**0.001***
Heart Failure	8 (7.8%)	1 (1%)	**0.018***

Continuous data are presented as median (IQR) and categorical data are presented as n (%).
P values were obtained using the Wilcoxon rank sum test, the Chi-square test, or Fisher's exact test, as appropriate.
*Statistically significant.

Table S8. Univariate Analysis of Cost of Living Adjusted Charges among Premature Patients.

Adjusted Charge	Transcatheter Closure (n=102)	Surgical Ligation (n=105)	P value
Billed Charges (overall charges)	113,100 (64,500 - 175,800)	208,800 (61,300 - 1,280,700)	**0.014***
Clinical Charges	26,700 (1,800 - 44,600)	25,300 (5,700 - 153,700)	**0.015***
Imaging Charges	13,200 (7,200 - 27,500)	10,700 (2,800 - 39,400)	0.324
Lab Charges	4,600 (2,200 - 7,600)	13,600 (5,600 - 54,300)	**<0.001***
Pharmacy Charges	2,400 (1,200 - 4,500)	9,300 (2,100 - 80,500)	**<0.001***
Supply Charges	11,000 (7,000 - 29,100)	1,300 (400 - 3,500)	**<0.001***
Other Charges	36,200 (19,100 - 79,200)	131,400 (35,000 - 875,000)	**<0.001***

Data are shown as median (IQR) rounded to the nearest hundreds.

The Wilcoxon rank sum test was implemented to calculated P values.

*Statistically significant.

Table S9. Multivariable Median Regression Analysis of Adjusted Charges using IPTW by the Propensity Score among Premature Patients.

Adjusted Charge	Adjusted Difference in Medians (Surgical - Transcatheter)	95% CI	P value
Billed Charges (overall charges)	-3,214	(-45,400, 39,000)	0.881
Clinical Charges	2,800	(-23,800, 29,500)	0.835
Imaging Charges	-700	(-3,200, 1,800)	0.598
Lab Charges	3,500	(-900, 8,000)	0.116
Pharmacy Charges	900	(-800, 2,500)	0.308
Supply Charges	-10,300	(-21,700, 1,100)	0.076
Other Charges	17,700	(-14,300, 49,700)	0.278

The propensity scores were calculated based on baseline demographics and comorbidities with significant differences between surgical and transcatheter cases.

Inverse probability of treatment weighting by the propensity score was implemented in median regression analysis.

*Statistically significant.