Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 63, No. 5, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.08.1645

Earlier Arterial Switch Operation Improves Outcomes and Reduces Costs for Neonates With Transposition of the Great Arteries

Brett R. Anderson, MD, MBA,* Adam J. Ciarleglio, PHD,† Denise A. Hayes, MD,* Jan M. Quaegebeur, MD, PHD,‡ Julie A. Vincent, MD,* Emile A. Bacha, MD‡

New York, New York

Objectives This study sought to examine the impact of surgical timing on major morbidity and hospital reimbursement for late preterm and term infants with dextrotransposition of the great arteries (d-TGA).

Background Neonatal arterial switch operation is the standard of care for d-TGA. Little is known about the effects of age at operation on clinical outcomes or costs for these neonates.

Methods We conducted a retrospective cohort study of infants at ≥36 weeks' gestation, with d-TGA, with or without ventricular septal defects, admitted to our institution at 5 days of age or younger, between January 1, 2003 and October 1, 2012. Children with other cardiac abnormalities or other major comorbid conditions were excluded. Univariable and multivariable analyses were performed to determine the effects of age at operation on major morbidity and hospital reimbursement.

Results A total of 140 infants met inclusion criteria. Reimbursement data were available for them through January 1, 2012 (n = 128). The mortality rate was 1.4% (n = 2). Twenty percent (n = 28) experienced a major morbidity. The median costs were $60,000, in 2012 dollars (range: $25,000 to $549,000). The median age at operation was 5 days (range: 1 to 12 days). For every day later that surgery was performed, beyond day of life 3, the odds of major morbidity increased by 47% (range: 23% to 66%, $p < 0.001$) and costs increased by 8% (range: 5% to 11%, $p < 0.001$), after considering the effects of sex, birth weight, gestational age, year at which surgery was performed, transfer, weekend admission, insurance, surgeon, septostomy, bypass and cross-clamp times, and the presence of ventricular septal defects or abnormal coronary anatomy.

Conclusions Delay of neonatal arterial switch operation beyond 3 days is significantly associated with increased morbidity and healthcare costs. (J Am Coll Cardiol 2014;63:481–7)

Neonatal arterial switch operation (ASO) is the treatment of choice for infants with dextrotransposition of the great arteries (d-TGA) (1). According to the Society of Thoracic Surgeons Congenital Heart Surgery Database, operative mortality for infants undergoing ASO between 2005 and 2009 was <5% (2). Patient factors, such as ventricular septal defects (VSDs) (3,4), left ventricular outflow tract or arch obstruction (3,4), coronary anomalies (5), low birth weight (6), and early gestational age (7) have generally been associated with increased morbidity or mortality. The median costs for the neonatal management of these infants have been estimated to be $55,000, in 2001 dollars (8).

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The ASO is now typically performed shortly after birth, before the left ventricle has time to decondition. With the widespread availability of prostaglandin and atrial balloon septostomy (BAS), however, the exact timing of surgery has become largely discretionary. Although 1 report showed an association between earlier arterial switch and reduced post-operative periventricular leukomalacia (9), we were unable to find any published studies that evaluated the effects of the timing of ASO during the first month of life on overall morbidity or mortality or on the costs of

From the *Division of Pediatric Cardiology, NewYork-Presbyterian/Morgan Stanley Children's Hospital Columbia University Medical Center, New York, New York; †Department of Biostatistics, Columbia University, New York, New York; and the ‡Division of Cardiothoracic Surgery, Columbia University College of Physicians and Surgeons, New York, New York. Dr. Ciarleglio is currently at the Division of Biostatistics, Department of Child and Adolescent Psychiatry, New York University, New York, New York. Dr. Hayes is currently at the Division of Pediatric Cardiology, Hofstra North Shore-LIJ School of Medicine, New York, New York. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received July 31, 2013; accepted August 6, 2013.

Abbreviations and Acronyms

ASO = arterial switch operation

BAS = balloon atrial septostomy

BP = bypass

d-TGA = dextrotransposition of the great arteries

MRI = magnetic resonance imaging

VSD = ventricular septal defect

XC = cross-clamp

management for infants with d-TGA. The purpose of our study was to determine the association between the timing of ASO and major morbidity and total in-patient hospital costs for late preterm and term infants with d-TGA. We hypothesized that delayed ASO would be associated with increased morbidity and costs.

Methods

Patients. A retrospective cohort study was performed using clinical and financial data for all infants at ≥36 weeks' gestation with d-TGA, admitted to NewYork–Presbyterian/Morgan Stanley Children's Hospital of Columbia University at 5 days of age or younger, between January 1, 2003, and October 1, 2012. Children were excluded if they had cardiac anomalies other than VSDs, atrial septal defects, and/or patent ductus arteriosi, as demonstrated on a pre-operative echocardiogram. In particular, infants with double-outlet right and left ventricular outflow tract or arch obstruction were excluded. Children were also excluded if they had other major comorbid conditions (as defined by Feudtner et al. [10]). Children were further excluded if they underwent a primary surgical repair other than ASO (such as a Rastelli procedure), if they were discharged from the hospital alive before undergoing ASO, or if cardiac surgery was deliberately postponed due to patient-related factors (including intracranial hemorrhage on routine magnetic resonance imaging [MRI] or positive blood culture) within the first 72 h of life. This study was approved by the Columbia University Medical Center Institutional Review Board, with waiver of informed consent.

Predictor variables. The primary predictor of interest was age at operation (in days). Other variables considered included sex, birth weight (in kilograms), year of surgery (to reflect surgical era), transfer from an outside hospital, insurance type (Medicaid or other), day of admission, surgeon, BAS, bypass (BP) and cross-clamp (XC) times, and the presence of VSDs or abnormal coronary artery anatomy. Day of admission was considered in 2 ways. First, it was included in the analysis as a set of 6 indicator variables, with Sunday serving as the reference. Then, it was dichotomized to indicate weekday or weekend (Friday through Sunday) admission, after examining trends in the association with admission day and major morbidity.

Although most patient anatomy was characterized pre-operatively by echocardiography, for purposes of this study, the presence of a VSD and coronary anatomy were defined by the surgeon at the time of repair. Normal coronary anatomy was defined as a left anterior descending artery and a circumflex artery from sinus 1 and a right coronary artery from sinus 2, with only 2 ostia and no intramural course. Abnormal coronary anatomy was defined as all other patterns. In secondary analyses, the presence of a single or intramural coronary was also assessed as predictors of clinical outcomes and costs, as was the presence of left ventricular outflow tract or arch obstruction.

Surgical technique and perioperative management. All patients were admitted pre-operatively and managed post-operatively in the cardiac neonatal intensive care unit. All infants underwent pre-operative echocardiogram. The majority received prostaglandin E1 at a dose of 0.01 to 0.05 μg/kg/min; dose was determined by the clinical judgment and style of the individual in-patient cardiologist. Patients also underwent BAS on the basis of the clinical judgment of the in-patient cardiologist; BAS was performed secondary to either hypoxia or a subjective concern for restrictive atrial septa. After 2008, all infants who underwent BAS at our institution also underwent brain MRI. Cardiac surgery for infants with significant intracranial hemorrhage was electively postponed; these infants were excluded from the analysis. Infants were not routinely intubated pre-operatively.

All operations were performed by 1 of 4 surgeons at NewYork–Presbyterian/Morgan Stanley Children's Hospital. In the operating room, all patients underwent median sternotomy. Cardiopulmonary BP and aortic XC, with moderate hypothermia, were used on all patients. A brief period of circulatory arrest was common (>85%), mainly due to closure of atrial septal defects. The sternum was routinely closed and was considered a complication if left open (>90% closed, see the Results section).

Primary outcomes. The primary outcomes were major morbidity and costs. Major morbidity was defined as cardiac arrest, extracorporeal membrane oxygenation, delayed sternal closure, systemic infection (including sepsis, fungemia, endocarditis, and meningitis), necrotizing enterocolitis, seizure, stroke on MRI with clinical sequelae, diaphragmatic paralysis/paresis, reoperation before discharge, or readmission at ≤30 days. All patients who died experienced a morbidity before death and, therefore, were included in the analyses of major morbidity. Mortality is reported in descriptive statistics only, as the expected (and observed) incidence was too low to anticipate meaningful associations with predictor variables. Costs were defined as total in-patient hospital reimbursement, so as to most accurately reflect societal costs. All costs were adjusted to 2012 dollars using the Medical Consumer Price Index (http://www.bls.gov/cpi/#tables). Costs did not include outpatient expenses or physician reimbursement. Length of stay was assessed both as a predictor variable and as a secondary outcome.

Statistical analysis. All statistical analyses were conducted using SPSS Statistics versions 19.0 or 20.0 (IBM Corporation, Armonk, New York). Clinical and demographic variables were described with standard summary statistics, using mean ± SD or median (range) for continuous variables and using frequencies and proportions for categorical variables. To assess the marginal associations between predictor variables and major morbidity, the chi-square or Fisher exact test was used for categorical variables, and the Student *t* or Wilcoxon rank sum test was used for continuous variables. To assess the marginal associations between the predictor variables and adjusted costs, the Wilcoxon rank sum or Kruskal-Wallis test was used for categorical variables, and Spearman correlation was used for continuous variables (costs are right skewed). Variables with p values ≤0.10 in univariable analyses were evaluated together in multivariable analyses. We hypothesized that the relationship between major morbidity and age at ASO might not be linear. To investigate this relationship, a nonparametric logistic regression, based on locally weighted scatterplot smoothing (lowess), was used. A logit link was used to model the relationship between the predictors of interest and the outcome of major morbidity. To estimate the parameters of the logit model, we used generalized estimating equations with an exchangeable working correlation structure to account for possible correlation between infants operated on by the same surgeon. To account for the right-skewed nature of costs, costs were log-transformed and linear mixed-effects models were used to assess the association between the predictors of interest and the log of the total adjusted in-patient hospital costs, where a random intercept, corresponding to surgeon, was included in the model. A p value <0.05 was considered statistically significant in the multivariable analyses. Final multivariable models were determined via a forward stepwise procedure, where age at operation was automatically included in the models jointly as age at ASO and the positive part of age minus 3 (11). Other variables were left in the final models if their p values met the significance criterion or if their inclusion changed the magnitude of the coefficients for age at operation by ≥10%.

Results

A total of 140 infants met inclusion criteria. Reimbursement data were available for all infants through January 1, 2012 (n = 128). There was a slight male predominance (64% boys). The birth weight was 3.30 ± 0.52 kg. Fifty-one percent of infants were transferred from an outside hospital (n = 72). Transfer was highly associated with year of surgery ($t = 5.62$; $p < 0.001$), with 85% of infants in 2003 and only 9% of infants in 2012 transferred from outside hospitals, likely associated with both an increase in the number of surgeons in our region (and nationwide) who are capable of performing the ASO and an increase in prenatal diagnosis and, therefore, prenatal referrals. The median age at admission was 0 days (range: 0 to 4 days), with all infants born at our institution recorded as admitted on day of life 0. The median age at admission if transferred was 1 day (range: 0 to 4 days). More than 90% of infants were admitted on weekdays, and 95% were born on weekdays. Surgical volume was relatively constant over time. Twenty percent of infants (n = 28) were covered by Medicaid insurance. Fifty-six percent of operations (n = 78) were performed by a single surgeon. Only this surgeon was at our institution for the entire duration of the study. The other 44% of surgeries were distributed among the 3 other surgeons, with those employed at our institution longer performing more surgeries. Seventy-one percent of infants (n = 100) underwent BAS at a median age of 0 days (range: 0 to 6 days).

The median age at operation was 5 days (range: 1 to 12 days; 97% at ≤10 days). Twenty-five percent were operated on at or before day of life 3. Median BP and aortic XC times were 127 min (range: 66 to 288 min) and 77 min (range: 23 to 154 min), respectively. Thirty-five infants (25%) underwent VSD closure. The majority of infants had a left coronary off sinus 1 and a right coronary off sinus 2 (total,

Table 1 Patient Characteristics

Male	89 (63.6%)
Birth weight, kg	3.30 ± 0.52
Gestational age <38 weeks	26 (18.6%)
Transfer from an outside hospital	72 (51.4%)
Age at admission, days	0.0 (0–4)
Age at admission, days, if transferred	1.0 (0–4)
Friday to Sunday admission	38 (27.1%)
Insurance type, Medicaid	28 (20.0%)
Balloon atrial septostomy performed	100 (80.0%)
Age at balloon atrial septostomy, days	0.0 (0–6)
Age at ASO, days	5.0 (1–12)
Bypass time during ASO, min	127 (66–288)
Cross-clamp time during ASO, min	77 (23–154)
Ventricular septal defect repair	35 (25.0%)
Coronary anatomy	
1LCx-2R	84 (60.0%)
1L-2RCx	24 (17.1%)
1LCx-2RCx	2 (1.4%)
1L-2R, Cx not defined	3 (2.1%)
Inverted	8 (5.7%)
Intramural	7 (5.0%)
Single ostium	7 (5.0%)
≥3 ostia	5 (3.6%)
Mortality	2 (1.4%)
Major post-operative morbidity	28 (20.0%)
Arrest	5 (3.6%)
Extracorporeal membrane oxygenation	1 (0.7%)
Delayed sternal closure	10 (7.1%)
Heart block necessitating pacemaker placement	3 (2.1%)
Other reoperation prior to discharge	3 (2.1%)
Diaphragmatic paralysis/paresis	3 (2.1%)
Major infection	7 (5.0%)
Sepsis	6 (4.3%)
Fungemia	1 (0.7%)
Endocarditis	1 (0.7%)
Meningitis	0 (0.0%)
Necrotizing enterocolitis	2 (1.4%)
Seizure	4 (2.9%)
Stroke by MRI with associated clinical findings	2 (1.4%)
Readmission at ≤30 day	1 (0.7%)

Values are n (%), mean ± SD, median (range).
ASO = arterial switch operation; Cx = circumflex artery; L = left coronary artery; MRI = magnetic resonance imaging. R = right coronary artery; 1 = sinus 1; 2 = sinus 2.

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81%; left coronary off sinus 1 and a right coronary off sinus 2, 60%). For anatomic details, see Table 1.

Major morbidity. In-hospital and 30-day mortality was 1.4% (n = 2). Twenty percent (n = 28) experienced a major morbidity (including the 2 infants who subsequently died). The most frequent morbidities were delayed sternal closure (n = 10), major systemic infection (n = 7), and reoperation before discharge (n = 6), including 3 for complete heart block, 1 for pulmonary arterioplasty, 1 for coronary artery reanastomosis, and 1 for reopening of the chest for signs and symptoms of tamponade (Table 1).

In univariable analyses, age at operation, birth weight, weekend admission, surgeon, and BP and XC times were all significantly associated with major morbidity. Although other studies have shown an association between morbidity or mortality and earlier gestational age, we found no such association when considering late preterm infants (36 to <38 weeks) versus term infants (≥38 weeks) (Table 2). As expected, given the low mortality (n = 2), we were unable to detect any significant associations between predictor variables and mortality alone.

The logistic lowess model suggested a nonlinear relationship between age at operation and major morbidity. More specifically, we found that the odds of major morbidity decreased over the range of 1 to 3 days, but increased for ages older than 3 days.

Costs. Median hospital costs were $60,000 in 2012 dollars (range: $25,000 to $549,000), with a median length of stay of 13 days (range: 5 to 122 days). Median hospital costs per day were $4,900 in 2012 dollars (range: $1,500 to $8,600). The median length of stay post-operatively was 7 days (range: 0 to 116 days) (Table 3).

Table 2 Predictors of Morbidity and Costs in Univariable Analyses

	Morbidity, p Value	Adjusted Costs, p Value
Male	0.429	0.789
Birth weight, kg	0.044*	0.016*
Gestational age <38 weeks	0.664	0.220
Transferred from outside hospital	0.499	0.001*
Year of surgery	0.602	<0.001*
Friday to Sunday admission	0.010*	0.478
Insurance type (Medicaid)	0.833	0.554
Surgeon	0.007*	0.029*
Balloon atrial septostomy performed	1.000	0.243
Age at balloon atrial septostomy, days	0.965	0.605
Age at ASO, days	0.047*	<0.001*
Bypass time during ASO, min	0.001*	<0.001*
Cross-clamp time during ASO, min	0.022*	0.004*
Ventricular septal defect repair	0.384	0.018*
Coronary anatomy (1LCx-2R vs. other)	0.101	0.287
Intramural coronary	0.143	0.987
Single coronary	0.627	0.718
Length of stay	<0.001*	<0.001*
Length of stay after operation	<0.001*	<0.001*
Major morbidity	—	<0.001*

*Variables with p values <0.05.
Abbreviations as in Table 1.

Table 3 Adjusted Costs, Costs per Day, Length of Stay, and Post-Operative Length of Stay

	Adjusted Costs, $	Adjusted Costs per Day, $	Length of Stay, days	Post-Operative Length of Stay, days
Median	60,500	4,900	13	7
Minimum	24,600	1,500	5	0
Maximum	549,000	8,600	122	116

In univariable analyses, age at operation, birth weight, transfer from an outside hospital, year of surgery, surgeon, BP and XC times, and VSD repair were significantly associated with costs. As mentioned above, transfer from an outside hospital was highly correlated with both year of surgery and age at admission. Total length of stay, post-operative length of stay, and major morbidity were also significantly associated with costs (Table 2).

Age at operation. To assess the association between age at operation and both major morbidity and total in-patient hospital costs, multivariable regressions were performed, using the results of the bivariate analyses described above. On the basis of our findings in the logistic lowess model, age at operation was included in the multivariable logistic regression model in a way that allowed for different linear relationships between age at operation and the log odds of major morbidity before and after 3 days of age. Between ages 1 and 3 days, for every day later that surgery was performed, the odds of a major morbidity decreased by 46% (range: 3% to 70%). For ages older than 3 days, for every day later that surgery was performed, the odds of a major morbidity increased by 47% (range: 23% to 66%). The p value for the association between age at operation and major morbidity was <0.001. For every day later that surgery was performed, costs increased by 8% across all ages (range: 5% to 11%; p < 0.001) (Tables 4 and 5).

In the generalized estimating equation model, aside from age at operation, the other variables that remained significantly associated with major morbidity were BP (p = 0.003) and XC times (p = 0.005), birth weight (p < 0.001), and weekend admission (p = 0.016). In the linear mixed-effects model, aside from age at operation, the other variables that remained significantly associated with the log of adjusted total costs were transfer from an outside hospital (p = 0.012) and the presence of a VSD (p = 0.022). None of these

Table 4 Effects of Age at Operation on Major Morbidity

Parameter	Odds Ratio	95% Confidence Interval	p Value
Age at operation at ≤3 days	0.539	0.299–0.971	
Age at operation at >3 days	2.730	1.423–5.236	
Age at operation			<0.001*
Bypass time, min	1.039	1.017–1.062	0.001*
Birth weight, kg	0.472	0.335–0.664	<0.001*
Weekend admission	4.482	1.321–15.206	0.016*
Cross-clamp time, min	0.965	0.932–1.000	0.050*

*Variables with p values <0.05.

Table 5 Effects of Age at Operation on the Log of Adjusted Costs

Parameter	Coefficient	95% Confidence Interval	p Value
Age at operation	0.080	0.052 to 0.110	<0.001*
Transfer	−0.171	−0.303 to −0.038	0.012*
Ventricular septal defect	0.172	0.025 to 0.318	0.022*
Year of operation	0.024	−0.004 to 0.052	0.089
Birth weight, kg	−0.091	−0.213 to 0.031	0.143

*Variables with p values <0.05.

variables was independently associated with age at operation. The effects of age at operation on outcomes, and the impact by age of BP time, the presence of VSDs, transfer status, and birth weight, are depicted in Figures 1 and 2.

To investigate the broader applicability of our study, we ran secondary analyses, this time including patients with left ventricular outflow tract or arch obstruction. Over the study period, there were 12 additional patients identified, representing 7.3% of the new total population. The results of these analyses confirmed the associations between age at operation and both morbidity and costs. In this less homogeneous population, the inflection point for the effects of age at operation on morbidity remained at day of life 3, and the association between age at operation and the log of adjusted costs remained linear across all ages. Between ages 1 and 3 days, for every day later that surgery was performed, the odds of a major morbidity decreased by 41% (range: 0.4% to 65%).

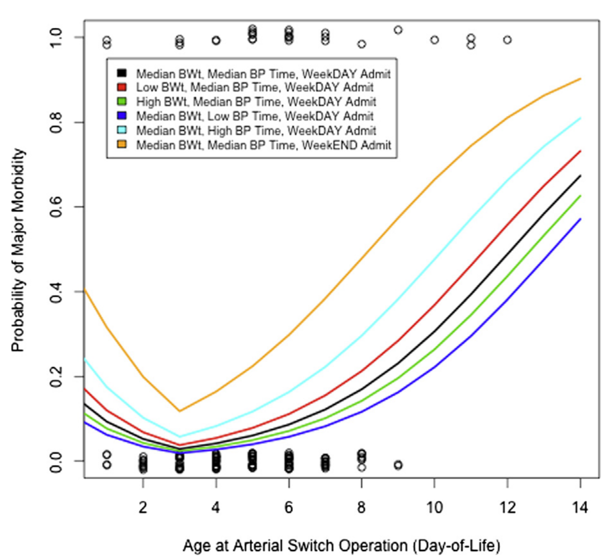

Figure 1 Effects of Age at Arterial Switch Operation on Major Morbidity

Scatterplot depicting the probability of major morbidity as a function of age at operation. Representative curves are drawn to depict expected probabilities of major morbidity, given long (75th percentile), median, or short (25th percentile) bypass (BP) times, high (75th percentile), median, or low (25th percentile) birth weight (BWt), and weekend or weekday admission, accounting for the effects of surgeon, given a median cross-clamp time.

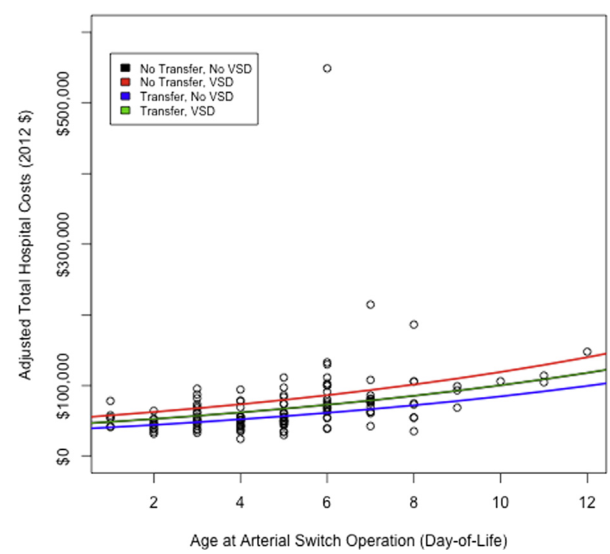

Figure 2 Effects of Age at Arterial Switch Operation on Adjusted Total Hospital Costs

Scatterplot depicting the adjusted total hospital costs as a function of age at operation. Representative curves are drawn to depict expected costs for patients, given transfer status and the presence or absence of a ventricular septal defect (VSD), accounting for the effects of surgeon, given a median operative year and birth weight.

For ages older than 3 days, for every day later that surgery was performed, the odds of a major morbidity increased by 29% (range: 4% to 60%). Considered jointly, the p value for the association between age at operation and major morbidity in this more inclusive population was 0.024. For every day later that surgery was performed across all ages, costs increased by 9% (range: 6% to 11%; $p < 0.001$) (Tables 4 and 5). In multivariable modeling, left ventricular outflow tract or arch obstruction was a significant predictor of morbidity (associated with a 4.2 times increase in the odds of major morbidity; range: 2.5 to 7.0, $p \leq 0.001$), but was not a significant predictor of costs. There was minimal change in the other predictor variables that remained significant in these models, and left ventricular outflow tract or arch obstruction was not independently associated with age at operation ($p = 0.072$).

Discussion

In this retrospective cohort study, we found that older age at operation was significantly associated with increased morbidity, as well as with increased costs, for late preterm and term infants with d-TGA undergoing ASO during the first month of life. These associations persisted, even after considering the effects of sex, birth weight, year of surgery, transfer from an outside hospital, insurance type, weekend admission, surgeon, BAS, BP and XC times, and the presence of VSDs or abnormal coronary artery anatomy.

Although other studies have looked at the associations between clinical outcomes and patient-related factors (3–7) and although studies have established the safety of neonatal repair (12), to the best of our knowledge, no published studies have looked at the timing of surgery in this population and its association with either major morbidity or costs. One study from the Children's Hospital of Philadelphia has shown that lower mean pre-operative partial pressure of oxygen (PaO_2) and longer time to surgery may be additive risk factors for the development of periventricular leukomalacia (9). One study from the University of Michigan, published in abstract form only, considered the effects of age at operation on mortality and length of intensive care unit stay in infants with d-TGA, hypoplastic left heart syndrome, and obstructed pulmonary blood flow (13). These investigators were unable to detect significant associations. Their study, however, included only 77 d-TGA patients and did not exclude those with more complex anatomy, such as those with a double-outlet right ventricle. Assuming a mortality rate similar to our own, we would only have expected 1 child in their study to have died, and this would clearly not have allowed for the identification of significant differences.

In interpreting our data for clinical application, we were interested in identifying an ideal day for operation. We hypothesized that there might be an age below which maternal factors and/or persistent fetal physiology might lead to an increase in the associated morbidity. To investigate this hypothesis and to determine an ideal day for operating, we first investigated the marginal association between age at operation and morbidity using scatterplot smoothing methods. Our models suggested that the association between morbidity and age was negative at or before day of life 3 and positive after day of life 3. The association between age at operation and the log of adjusted costs appeared linear and positive across all ages. We examined age at operation using logistic and linear regressions, accounting for possible correlations between subjects operated on by the same surgeons. Between days 1 and 3, for every day later that surgery was performed, the odds of a major morbidity decreased by 46% and for ages older than 3 days, for every day later that surgery was performed, the odds of a major morbidity increased by 47% (joint $p \leq 0.001$), after adjusting for BP and XC times, birth weight, and weekend admission. Across all ages, for every day later that surgery was performed, costs increased by 8% ($p < 0.001$), after adjusting for transfer from an outside hospital, the presence of VSDs, year of surgery, and birth weight. An infant, therefore, without a VSD, with a median birth weight and median BP and XC times, born at our institution on a weekday, and operated on at day of life 3, would have an expected probability of morbidity of 3% and projected total hospital costs of $57,000. In comparison, similar infants operated on at days of life 7 and 10 would have expected probabilities of morbidity of 13% and 31% and projected total hospital costs of $79,000 and $100,000, respectively.

In addition to identifying a strong association between outcomes and age at operation, our study also confirmed the associations that have previously been described between major morbidity and both birth weight and BP time. We failed to show associations between morbidity and the presence of coronary anomalies or VSDs. As other authors with similar results have suggested, this lack of associations might be attributable to improvements in the management of d-TGA patients since the early 2000s (7). In our study, the lack of association between morbidity and VSDs might also be due to our exclusion of patients with more complex anatomies that are often associated with VSDs (such as a double-outlet right ventricle).

Interestingly, the only variables other than age at operation that were significantly associated with costs in our study were transfer from an outside hospital and the presence of VSDs. The negative association between costs and transfer status is likely secondary to the fact that our analyses did not include costs incurred at outside hospitals. The positive association between costs and VSDs is likely secondary to an increase in the post-operative length of stay in these patients (median: 7.0 vs. 9.0; $p = 0.016$). It is unlikely the result of differences in morbidity, as no significant association was found between the presence of VSDs and morbidity. We find it relevant to note that, in our study, neither late preterm status (between 36 and 38 weeks) nor insurance type was associated with either clinical outcomes ($p = 0.664$ and 0.833, respectively) or costs ($p = 0.220$ and 0.554, respectively).

Study limitations. The key to interpreting our results lies in the hypotheses around causation. One must ask whether major morbidity and costs were higher in infants operated on later because the operation was delayed or because there were confounders that led both to delays in operation and to increased morbidity and costs. Although we hypothesized that delayed operation causes increased morbidity and costs (as the result of prolonged exposure to medical interventions such as central lines, or as the result of increased total length of hospital stay), and although we eliminated patients electively delayed within the first 72 h for patient-related factors, expressly to address the question of cause and effect, our study is retrospective. This limits our ability to imply causality.

Our study has a few other notable limitations. First, this study represented a single institutional experience and-did not consider regional differences in either care or reimbursement. Our infants were managed both pre- and post-operatively in our cardiac neonatal intensive care unit and were all operated on by 1 of 4 surgeons, with an uneven distribution of cases (50% operated on by a single surgeon). Second, although we were able to identify statistically significant results with regard to the effects of age at operation on morbidity and costs, as a single-center study, our sample size was small. It is, therefore, possible that we were unable to detect meaningful associations that exist between other predictors and outcomes in our multivariable models. Third, our follow-up only extended through hospital discharge and did not consider potential differences in long-term outcomes or outpatient costs. Fourth, physician costs were not included; this was thought to be acceptable and is done routinely in cost analyses, as physician reimbursement typically constitutes <5% to 10% of total in-patient reimbursement. Finally, as mentioned, costs were defined by hospital reimbursement. Although reimbursement costs are typically considered the gold standard because they reflect most accurately societal costs, they do not necessarily correlate with actual resource use.

Conclusions

In this retrospective cohort study of late preterm and term infants with d-TGA with or without VSDs undergoing ASO, we found delay in operation during the first month of life to be significantly associated with increases in both morbidity and total in-patient hospital reimbursement. Assuming a causal association, these findings would have several significant implications. First, we would conclude that the ASO ought to be performed in late preterm and term infants no later than the first week of life and that even earlier operation might be preferable; in our study, day of life 3 appears to be the optimal day. Second, for infants undergoing timed deliveries, our findings would suggest that delivery dates ought to be coordinated with surgeons' schedules to minimize wait times. Third, for infants born at institutions that do not perform ASOs, our findings suggest that the coordination of transfer, or at least of surgical scheduling, should not be delayed, and, instead, should begin as soon as diagnoses are made. Larger, prospective studies are needed to confirm the ideal day of operation and the causal relationship of this association.

Acknowledgments
The authors thank the care providers who contributed to the clinical care of these patients, especially Jonathan Chen and Ralph Mosca.

Reprint requests and correspondence: Dr. Emile A. Bacha, NewYork–Presbyterian/Morgan Stanley Children's Hospital; Columbia University Medical Center, 3959 Broadway, 2 North, New York, New York 10032-3784. E-mail: eb2709@columbia.edu.

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Key Words: arterial switch operation ▪ costs ▪ outcomes ▪ surgical timing ▪ transposition of the great arteries.