Timing of complete repair of non-ductal-dependent tetralogy of Fallot and short-term postoperative outcomes, a multicenter analysis

Matthew B. Steiner, MD,^a Xinyu Tang, PhD,^b Jeffrey M. Gossett, MS,^b Sadia Malik, MD,^a and Parthak Prodhan, MBBS^{a,c}

Objective: There is cross-center variability with regard to timing repair of non-ductal-dependent tetralogy of Fallot (TOF). We hypothesized that earlier repair in the neonatal period is associated with increased mortality and morbidity.

Methods: This was a retrospective analysis of the Pediatric Health Information System of tetralogy of Fallot patients undergoing complete repair from 2004 through 2010 between the ages of 1 day to younger than 19 years. Patients with pulmonary valve atresia, those who received prostaglandin during hospital admission, and those who underwent prior shunt palliation were excluded.

Results: A total of 4698 patients met our inclusion criteria, of whom 202 were younger than 30 days old (group A), 861 were 31 to 90 days old (group B), 1796 were 91 to 180 days old (group C), and 1839 were older than 180 days (group D). In-hospital mortality, intensive care unit length of stay, and total hospital length of stay were significantly higher in group A. Patients in group A had a significantly increased postoperative requirement for mechanical ventilation, intravenous blood pressure support, medical diuresis, extracorporeal membrane oxygenation, gastrostomy tube insertion, heart catheterization, and surgical revision. Significant institutional variability was noted for timing of TOF complete repair, with one third of the centers performing 75% of the repairs at younger than 30 days old. The institutional approach to timing TOF complete repair showed no relation to surgical volume.

Conclusions: Across all centers analyzed, primary neonatal elective TOF repair (<30 days of age) is associated with significantly higher postoperative in-hospital morbidity and mortality, although a few centers have shown an ability to use this strategy with excellent survivability. (J Thorac Cardiovasc Surg 2014;147:1299-305)

Tetralogy of Fallot (TOF) represents 5% to 7% of all congenital cardiac lesions¹ and is the most common form of cyanotic congenital heart disease, with a prevalence of approximately 3.9 per 10,000 live births.² As the first intracardiac lesion to be addressed surgically, with the creation of a systemic to pulmonary artery shunt by Alfred Blalock³ in 1945, the surgical strategy has evolved considerably over the years, and mirrors the evolution of the field of cardiothoracic surgery as a whole. In the 1950s and 1960s high mortality precluded complete neonatal primary repair and the accepted approach was a 2-stage repair, with initial systemic to pulmonary artery shunt palliation followed by

complete repair at a later age. With the innovation of hypothermic circulatory arrest in the 1970s, the approach began to shift from initial shunt palliation toward primary repair.^{4,5}

Over subsequent decades, advancements in surgical techniques and postoperative intensive care unit (ICU) care allowed for primary complete repair on younger and smaller infants.⁶ The trend in management has been shifting over time toward complete repair performed at an earlier age,⁷ and some centers have adopted a strategy of elective primary repair for asymptomatic patients in the neonatal period.^{8,9} The physiologic rationale underlying early primary repair strategies include the prevention of cyanotic end organ damage, removing the stimulus for right ventricular hypertrophy and fibrosis, promoting pulmonary artery growth, and improved vascular and alveolar lung development.¹⁰⁻¹²

With some centers progressing toward repair for asymptomatic TOF in the early neonatal period, there has been concern for increased potential postoperative morbidity associated with subjecting a fragile newborn to an elective cardiac surgery. Considerable controversy exists as to the optimal timing of repair,¹³ and a recent multicenter analysis has shown that significant cross-center variability exists concerning timing strategy.¹⁴

From the Division of Cardiology,^a Biostatistics Program,^b and Division of Critical Care,^c Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, Little Rock, Ark.

Disclosures: Authors have nothing to disclose with regard to commercial support. X.T., S.M., and P.P. were co-senior authors who made equal contributions to the manuscript.

Received for publication Dec 20, 2012; revisions received April 30, 2013; accepted for publication June 14, 2013; available ahead of print July 22, 2013.

Address for reprints: Matthew B. Steiner, MD, University of Arkansas for Medical Sciences, Pediatric Cardiology, Arkansas Children's Hospital, One Children's Way, Little Rock, AR 72202 (E-mail: mbsteiner@uams.edu).

0022-5223/\$36.00

Copyright © 2014 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2013.06.019>

Abbreviations and Acronyms

ECMO	= extracorporeal membrane oxygenation
ED	= emergency department
ICD-9	= International Classification of Diseases, 9th revision
ICU	= intensive care unit
LOS	= length of stay
PGE1	= prostaglandin E1
PHIS	= Pediatric Health Information System
TOF	= tetralogy of Fallot

To our knowledge, there have been no multi-institutional studies relating immediate postoperative hospital-based outcomes to timing of elective repair of TOF. We hypothesized that earlier repair of asymptomatic infants in the neonatal period was associated with increased mortality and morbidity. A large multicenter database of pediatric hospital admissions was queried to determine the prevalence of alternative strategies with regard to timing of elective complete repair. The objective of the study was to identify an association of postoperative morbidity and mortality to age of complete repair.

METHODS

The University of Arkansas for Medical Sciences Institutional Review Board for the Protection of Human Subjects reviewed the study protocol and determined that querying de-identified patient data does not fall under the jurisdiction of the Institutional Review Board review process.

Data Source

Patient demographic data and data relating to postoperative outcomes were abstracted from the Pediatric Health Information System (PHIS), an administrative database that contains inpatient data from 43 free-standing, tertiary care children's hospitals in North America.¹⁵ Institutions are affiliated with the Child Health Corporation of America (Shawnee Mission, Kan), a business alliance of children's hospitals, and account for 20% of all tertiary care children's hospitals. Institutions are labeled within the database but cannot be identified in public reporting. For the purposes of external benchmarking, participating hospitals provide discharge data including demographic information as well as diagnoses and procedures coded with International Classification of Diseases, 9th Revision (ICD-9) codes.¹⁶ Billing data also are available detailing medications, imaging studies, laboratory tests, and supplies charged to each patient, and are coded under the Clinical Transaction Classification (CTC) System (Truven Health Analytics, Ann Arbor, Mich).¹⁷ Data quality and reliability are ensured through a joint effort between the Child Health Corporation of America and participating hospitals. The data warehouse function for the PHIS database is managed by Thomson Healthcare (Durham, NC). Individual patient medical record numbers, billing numbers, and zip codes are encrypted. Data are de-identified at the time of submission and are subjected to a number of reliability and validity checks before being processed into data quality reports. Data are accepted into the database once classified errors occur less frequently than a criterion threshold, and the database is updated quarterly by the Child Health Corporation of America. If a hospital's quarterly data are unacceptable according to these limits, all of their quarterly data are rejected; however, these data can be resubmitted and re-evaluated before inclusion in the database.¹⁸

PHIS data updates through the fourth quarter of 2011 are reflected in our data set.

Identification of the Study Population

The study group was defined as all patients between the ages of 1 day to younger than 19 years who were discharged from a PHIS-participating hospital between January 1, 2004, and December 31, 2010, with a diagnosis of TOF (ICD-9 code, 745.2) who underwent surgical complete repair (ICD-9 code, 35.81) during their admission.

Exclusion Criteria

Patients with a co-existing diagnosis of pulmonary valve atresia (ICD-9 code, 746.01), patients who were administered prostaglandin E1 (PGE1) (CTC code, 191315) at any time during the admission, and patients with a history of having undergone a prior systemic to pulmonary artery shunt surgery (ICD-9 code, 39.0) were excluded from the analysis. Patients with an Emergency Department (ED) charge during the admission also were excluded. The rationale for exclusion of these groups was an effort to eliminate symptomatic patients requiring urgent surgical attention, thus analyzing only the electively repaired patients around which the controversy of optimal timing of complete repair is centered. Because early and/or emergent surgical intervention generally is required in cases of pulmonary atresia and ductal-dependent pulmonary circulation, these groups were excluded from the analysis. Likewise, if a patient presented to the ED and subsequently was admitted and underwent a TOF repair during the admission, it is reasonable to assume that surgery was performed on a nonelective basis. A total of 422 patients were excluded based on receiving prostaglandin, 274 patients were excluded because an ED charge was associated with the admission, and 562 patients were excluded on the basis of having undergone a prior shunt palliation. Patients who were admitted and underwent surgical repair in 2003 but were discharged in 2004 also were excluded from the analysis. Figure 1 shows the inclusion and exclusion criteria underlying the make-up of our cohort.

Variables Queried

Patient abstract data queried included the following: age, sex, presence of a chromosomal abnormality, dates of admission and discharge, history of prior shunt palliation, total hospital length of stay (LOS), ICU LOS, postoperative days requiring mechanical ventilation, whether an ED encounter was associated with the admission, and hospital code performing the surgery.

To identify patients with a history of shunt palliation before complete surgical repair, all cases of hospital admissions with a diagnosis of TOF excluding pulmonary atresia within the date range were screened for systemic to pulmonary artery shunt (ICD-9 code, 39.0). Identification numbers for these patients were noted and cross-checked against the patients in the cohort meeting all the inclusion criteria and who underwent a complete repair. If the shunt surgery occurred before the complete surgical repair it was counted as a prior palliation. This enabled us to determine which patients had a history of prior shunt palliation occurring on a previous admission to complete repair, so as to exclude these patients from the analysis.

Various interventions associated with postsurgical morbidity were analyzed for their relative frequency of occurrence. These interventions included extracorporeal membrane oxygenation (ECMO) (ICD-9 code, 39.65), ventricular assist device (ICD-9 code, 37.6x), pacemaker implantation (ICD-9 code, 37.81-83), hemodialysis (ICD-9 code, 39.95), peritoneal dialysis (ICD-9 code, 54.98), pericardiocentesis (ICD-9 code, 37.0), pericardiotomy (ICD-9 code, 37.12), thoracentesis (ICD-9 code, 34.91), chest tube insertion (ICD-9 code, 34.04), plerodesis (ICD-9 code, 34.92), gastrostomy tube insertion (ICD-9 code, 43.0, 43.11-43.19), cardiac catheterization (ICD-9 code, 37.21-37.23), and blood product transfusion (ICD-9 code, 99.00-99.06). Requirement for surgical revision

FIGURE 1. Study population. TOF, Tetralogy of Fallot; ED, emergency department.

was queried as either revision of surgical procedure on the heart (ICD-9 code, 35.95) or subsequent instances of surgical complete repair of TOF (ICD-9 code, 35.81). Only interventions occurring during the same hospital admission as the complete repair of TOF were included.

Abstracted pharmacy data included names of medications administered, route of administration, and number of postoperative days required. In the case of prostaglandin, any administration during the admission was considered. Inotropes/pressors administered included epinephrine (CTC code, 131321), milrinone (CTC code, 131111), norepinephrine (CTC code, 131351), dopamine (CTC code, 131311), dobutamine (CTC code, 131305), and fenoldopam (CTC code, 134111). Diuretics included furosemide (CTC code, 191135), bumetanide (CTC code, 191131), chlorothiazide (CTC code, 191111), and hydrochlorothiazide (CTC code, 191113).

The total hospital charges associated with each surgical admission were abstracted from the database. Charges were converted to 2010 dollars by multiplying the 2010 consumer price index adjustment factors and dividing by the consumer price index factor for the year in which the charges were incurred (discharge year). The consumer price index adjustment factors were downloaded online (<ftp://ftp.bls.gov/pub/special.requests/cpi/cpiat.txt>).

Definitions

For the purposes of this study, a neonate was defined as younger than 30 days old. Elective complete TOF repair was defined as complete TOF repair performed on a patient who had not been administered PGE1 during the hospital admission, had not undergone a prior shunt palliation, and had not had an ED encounter associated with the admission. Hospital mortality was defined as death before discharge. Days for

LOS variables were defined as any portion of a calendar day before discharge. Postoperative days requiring pressors/inotropes (epinephrine, milrinone, norepinephrine, dopamine, dobutamine, or fenoldopam) was defined as a summation of the total number of postoperative calendar days for which each medication was administered. Postoperative days requiring medical diuresis was defined as a summation of the total number of postoperative calendar days in which any of the following were administered: furosemide, bumetanide, chlorothiazide, or hydrochlorothiazide.

Statistical Analysis

All the data were analyzed using R v2.15.0 (R Development Core Team, Vienna, Austria). Descriptive statistics were expressed as medians and interquartile ranges for continuous variables, and percentages and frequencies for categorical variables. We compared the demographic and clinical data among the 4 age groups using the Kruskal-Wallis 1-way analysis of variance for continuous variables, and the chi-square test for categorical variables. Kaplan-Meier curves were plotted for hospital LOS, ICU LOS, and the duration of mechanical ventilation for each age group. Log-rank tests were performed to evaluate whether there was a significant difference in the survival distribution among the 4 age groups with respect to hospital LOS, ICU LOS, and duration of mechanical ventilation. Deaths before discharge were considered to be censored when we assessed the difference in in-hospital morbidity among age groups. The percentages of children having complete repair in different age groups were calculated for each center, and the chi-square test was performed to evaluate the center variability in the age distribution for complete repair. *P* values less than .05 indicated statistical significance.

RESULTS

Cohort Description

The summaries and testing results are shown in Table 1. Of the 4698 subjects who met our inclusion criteria, the median age at complete repair was 153 days (interquartile range, 96-239 days) and the mean age at complete repair was 332 days (standard deviation, 760 days). A total of 42.4% of the cohort was female and 6.3% had a co-existing chromosomal abnormality.

To determine the distribution of morbidity and mortality, the cohort was stratified by age at complete repair into the following groups. Group A: 0 to 30 days (n = 202; 4.3%); group B: 31 to 90 days (n = 861; 18.3%); group C: 91 to 180 days (n = 1796; 38.2%); and group D: 181 days to 18 years (n = 1839; 39.1%).

Postsurgical In-Hospital Mortality

Increased hospital mortality was found to be associated significantly with younger age at repair. Across all age ranges there were 63 deaths before discharge (1.3%). Death before discharge occurred in 6.4% of the neonatal group (group A), and in 1.9%, 0.7%, and 1.1% of groups B, C, and D, respectively ($P < .001$).

Postsurgical In-Hospital Morbidity

Duration of total hospital LOS, ICU LOS, and postoperative mechanical ventilation were found to have an inverse relationship with age at repair. The median group A ICU LOS was 9 days, which was significantly higher compared with group B (median, 5 days), group C (median, 4 days), and group D (median, 3 days). Similarly,

TABLE 1. Summaries of demographic and clinical data by age at complete repair

	N	Group A: 0-30 days (N = 202)	Group B: 31-90 days (N = 861)	Group C: 91-180 days (N = 1796)	Group D: 181 days to 18 years (N = 1839)	P*
Demographic data						
Age at surgery (d)	4698	16 (9-23)	67 (51-80)	133 (111-155)	277 (214-472)	
Female	4698	40% (81)	41% (350)	40% (721)	46% (841)	.003
Year surgery	4698	2008 (2006-2010)	2008 (2006-2010)	2008 (2006-2009)	2007 (2005-2009)	<.001
Chromosomal abnormality	4698	3% (7)	5% (45)	7% (124)	7% (120)	.127
Outcome data						
Death before discharge	4698	6.4% (13)	1.9% (16)	0.7% (14)	1.1% (20)	<.001
Hospital LOS (d)	4698	18 (12-32)	8 (6-15)	7 (5-10)	7 (5-10)	<.001
ICU LOS (d)	4698	9 (5-17)	5 (3-8)	4 (2-6)	3 (2-6)	<.001
Length of mechanical ventilation (d)	4698	3 (0-7)	1 (0-3)	0 (0-2)	0 (0-2)	<.001
Time on pressers/inotropes (d)	4698	4 (2-6)	3 (2-4)	2 (1-4)	2 (1-4)	<.001
Time on diuretics (d)	4698	11 (7-19)	7 (5-11)	6 (5-9)	6 (5-9)	<.001
Dysrhythmias	4698	9% (19)	12% (103)	8% (145)	6% (111)	<.001
Interventions						
Transfusion blood	4698	42% (84)	47% (408)	45% (809)	45% (828)	.433
Chest tube insertion	4698	11% (22)	8% (67)	7% (120)	8% (140)	.156
Heart Catheterization	4698	7% (14)	4% (31)	2% (40)	3% (58)	.002
ECMO	4698	4% (8)	1% (12)	1% (18)	1% (26)	.008
Gastrostomy	4698	7% (14)	3% (23)	1% (14)	0% (8)	<.001
Pacemaker	4698	2% (5)	1% (8)	2% (27)	1% (14)	.048
Peritoneal dialysis	4698	1% (2)	1% (8)	1% (15)	1% (17)	.989
Surgical revision	4698	4% (9)	1% (7)	1% (13)	0% (7)	<.001
Thoracentesis	4698	2% (4)	1% (6)	1% (14)	1% (18)	.323
Pericardiotomy	4698	0% (0)	0% (3)	0% (4)	1% (10)	.335
Pericardiocentesis	4698	0% (1)	0% (2)	0% (5)	0% (6)	.927
Hemodialysis	4698	0% (1)	0% (2)	0% (1)	0% (6)	.264
VAD	4698	0% (1)	0% (3)	0% (1)	0% (0)	.019
Pluerosdesis	4698	0% (1)	0% (1)	0% (0)	0% (0)	.006
Hospital charges						
Adjusted billed charges, 2010 dollars†	4698	244,192 (141,370-395,570)	136,436 (99,551-232,943)	112,122 (84,379-156,560)	106,230 (79,997-158,666)	<.0001
Raw billed charges	4698	239,747 (137,081-379,070)	133,146 (95,137-221,126)	107,424 (79,996-152,857)	101,510 (75,444-150,809)	<.001

Data are expressed as median (interquartile range), or percentage (number). VAD, Ventricular assist device; LOS, length of stay; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation. *P values were obtained using the Kruskal-Wallis 1-way analysis of variance for continuous variables, and the chi-square test for categorical variables.

†Adjusted billed charges were converted to 2010 dollars using annual average adjustment factors (available from: <http://ftp.bls.gov/pub/special.requests/cpi/cpiat.txt>).

total hospital LOS was significantly higher in group A (median, 18 days), compared with group B (median, 8 days), and groups C and D (median, 7 days). Group A patients had a greater requirement for mechanical ventilation, with a median of 3 postoperative days intubated in comparison with 1 day for group B, and 0 days for groups C and D. Figure 2 shows Kaplan-Meier curves for hospital LOS, ICU LOS, and the duration of mechanical ventilation by age groups.

The following interventions were associated with increased postoperative morbidity and were found to have a significant correlation with younger age at complete repair: need for surgical revision, ECMO, gastrostomy tube insertion, heart catheterization, and pacemaker implantation. Requirement for surgical revision before discharge occurred with more than 5-fold increased frequency in group A patients.

Time to be weaned off all pressors/inotropes was significantly longer for group A (median, 4 days) in comparison with group B (median, 3 days), and groups C and D (median, 2 days). The duration of the postoperative diuretic requirement was significantly longer for group A (median, 11 days) in comparison with group B (median, 7 days), and groups C and D (median, 6 days).

Hospital Charges

The median total billed hospital charges, adjusted to 2010 dollars, were found to be significantly higher in group A (\$244,192) in comparison with group B (\$136,436), group C (\$112,122), and group D (\$106,230).

Center Variability

Figure 3 shows a bar plot of the percentage of surgical distribution of group A repairs by center, with marks overlaid representing total surgical volume that met inclusion criteria. It is notable that center preference with regards to propensity to perform group A repairs showed no linear correlation to volume of repairs performed; some high-volume centers showed group A representing a relatively small proportion of their distribution, whereas some low-volume centers showed group A representing a relatively large proportion of their distribution.

Within the entire cohort of 4698 subjects, group A repairs were performed with a mean frequency of 4%, represented as a horizontal line in Figure 3. The 13 centers with group A surgical distribution greater than 4% cumulatively performed 153 of the total group A repairs, meaning that one third of the centers (13 of 39) performed more than 75% of the total group A repairs (153 of 202). Four institutions in the cohort were particularly inclined to perform group A repairs, performing them at a rate greater than 3 times that seen in the cohort as a whole, and with greater than 10% of their surgical distribution categorized as group A.

FIGURE 2. A, Kaplan-Meier curves for total hospital LOS by age group. B, Kaplan-Meier curve for ICU LOS by age group. C, Kaplan-Meier curve for duration of mechanical ventilation by age group. ICU, Intensive care unit.

FIGURE 3. Percentage of surgical distribution of neonatal (group A) repairs for each hospital (vertical bars correspond to the left-side of the y-axis). Each hospital's total number of surgeries performed across all age groups meeting inclusion criteria also is shown (diamonds correspond to the right-side of the y-axis). A horizontal line is drawn at 4%, the mean percentage distribution of group A surgeries performed across the entire cohort of 4698 subjects at all 39 hospitals.

Mortality by Center

A subanalysis of the distribution of mortality stratified by age at repair within each center was performed. It was notable that among the 4 centers noted earlier to show a particular propensity for performing neonatal repairs, 3 experienced no mortality within group A.

Among the 13 centers performing group A repairs with relative frequency ($>4\%$ of their caseload), there were 4 group A deaths of 153 group A patients, representing a 2.6% mortality rate for group A. Although considerably better than the overall group A mortality rate (6.4%), it is still twice the mortality rate seen across all age groups (1.3%).

Among the remaining hospitals with a relative disinclination to perform group A repairs ($<4\%$ of their caseload), there were 9 group A deaths of 49 group A patients. This represents a group A mortality rate of 18.4%, which is nearly triple the overall group A mortality of 6.4%.

DISCUSSION

Our data confirm our hypothesis, suggesting that, across all centers, complete primary repair of acyanotic TOF in neonates (<30 days old) is associated with increased mortality and morbidity. We found a significantly higher overall in-hospital postoperative mortality rate (6.4%) for elective neonatal complete repairs. In addition, total billed hospital charges, the total hospital LOS, ICU LOS, time until extubation, postoperative requirement for revision, medications, and secondary procedures all were increased significantly for elective neonatal complete repairs. There is no consensus regarding the optimal timing of complete repair of acyanotic TOF, and to our knowledge this is the first large-scale multi-institutional analysis of postsurgical morbidity stratified by age at complete repair.

With advancement in intraoperative technology and postoperative ICU care there is an increasing trend to move toward primary complete surgical repair,¹⁹ reserving initial palliation only for extreme cases with limiting anatomic features such as anomalous coronary arteries or pulmonary artery discontinuity.¹² Because forgoing the step of initial shunt palliation and performing early primary neonatal repair has become an accepted strategy for these cyanotic infants⁷ with pulmonary atresia or severe right ventricular outflow tract obstruction, some centers have extended this strategy to include asymptomatic infants. There was a single-center experience to show that the strategy can be performed safely,^{8,9} but the escalated need for ICU care has led other centers to advocate delaying repair in asymptomatic neonates until after 3 months of age.²⁰ Thus, optimal timing for complete primary repair of asymptomatic TOF has remained controversial. These data would suggest that, when possible, delaying complete repair of asymptomatic infants until a later age could have an increased survival benefit, as well as decreased postoperative morbidity.

Relative differences in functional maturity across all organ systems might provide a mechanistic understanding of our findings. In particular, alveolarization in the lungs and nephron maturation in the kidneys continue postnatally. Allowing time for further maturation of these organ systems may allow older infants to better handle the stress of surgery and enhance postoperative recovery. Recovery from pediatric cardiac surgery can be tenuous in the best of circumstances, and our data suggest that the fragility of the newborn period complicates and prolongs the postoperative course.

By excluding infants with pulmonary atresia, those who were administered prostaglandin, those who underwent prior shunt palliation, and those who presented to an emergency room and went on to require surgery, we have attempted to eliminate symptomatic emergent repairs and analyze cases of elective primary complete repair of asymptomatic infants. The extreme variation of age distribution found between centers, with a substantial number of centers performing few or no neonatal repairs whereas others performed neonatal repairs as a significant percentage of their caseload, suggests that the age range variation found in our cohort was a function of differences of strategic preference with regards to timing, and not dictated by symptomatology or anatomy. The subgroup analysis showed that centers favoring the strategy of early repair did in fact achieve lower mortality than what was found for early repairs overall, with the bulk of the deaths occurring at institutions performing early repairs as a smaller percentage of their surgical distribution. It was notable that 3 of the 4 centers showing a particular propensity to perform neonatal repairs did not experience any group A mortality whatsoever, indicating that it is possible to achieve excellent survivability when a center has committed to this strategy.⁸ The by-center analysis for

morbidity, however, still mirrored that seen across the entire cohort, with total hospital LOS, ICU LOS, time on mechanical ventilation, medication requirement, and postoperative procedural complication rates all increased with earlier repairs, even at centers achieving low mortality after neonatal repair.

Study Limitations

The study data provide limited specific details of cardiac anatomy (degree of subpulmonary stenosis, pulmonary valve annulus size, and coronary and pulmonary artery morphology), and limited specific details of surgical variables (transannular patch placement vs valve-sparing techniques, surgical approach via a right ventriculotomy vs via the right atrium or pulmonary artery,¹⁸ length of infundibulectomy,¹⁴ duration of cardiopulmonary bypass time, and aortic cross-clamp time). Specific details of the clinical course (threshold for starting PGE, extended follow-up evaluation throughout subsequent hospitalizations and outpatient visits) also were limited. Patients who might have undergone shunt placement before the date range or at a different hospital from the one where they underwent complete repair were not counted as having undergone an initial first stage; thus, some patients with a history of a prior shunt may not have been identified for exclusion. Also, it should be noted that a recent study raised concern for differences in case ascertainment when comparing the number of cases of pediatric cardiac surgery abstracted from the PHIS database with the number of cases abstracted from the clinical Society of Thoracic Surgeon's database.²¹

Finally, the study was subject to the limitations of any observational investigation, including selection bias and the potential impact of confounders. Despite the limitations inherent in an administrative database such as the PHIS, we believe that there is a strong ability to address immediate postoperative outcome measures correlated to timing strategy, and that the limitations of the database are outweighed by the magnitude of the sample size.

CONCLUSIONS

Primary neonatal elective TOF repair is associated with significantly higher postoperative in-hospital mortality, although selected centers have shown an ability to use this strategy with excellent survivability. It is associated with increased morbidity (ICU LOS, total hospital LOS, duration of mechanical ventilation, requirement for intravenous blood pressors/inotropes, duration of medical diuresis, postoperative requirement for ECMO, surgical revision, cardiac catheterization, and gastrostomy tube placement) and increased resource use as reflected by the total cost of hospital admission. Future directions of this research might include merging our data with large surgical databases to seek differences associated with variable postoperative outcomes within each age group based on detailed preoperative

and peri-operative surgical risk factors. A prospective study following up patients with early versus late repair of asymptomatic TOF to determine mid- and late-term outcomes would provide additional information to aid cardiologists and surgeons in deciding on the optimal time for repair of this challenging group of infants.

References

1. Talner CN. Report of the New England Regional Infant Cardiac Program. *Pediatrics*. 1980;65(Suppl):375-461.
2. Improved national prevalence estimates for 18 selected major birth defects – United States 1999–2001. *MMWR Morb Mortal Wkly Rep*. 2006;54:1301-5.
3. Blalock A. Physiopathology and surgical treatment of congenital cardiovascular defects. *Harvey Lect*. 1955;41:90-116.
4. Barratt-Boyes BG, Neutze JM. Primary repair of tetralogy of Fallot in infancy using profound hypothermia with circulatory arrest and limited cardiopulmonary bypass: a comparison with conventional two stage management. *Ann Surg*. 1973; 178:406-11.
5. Castaneda AR, Lamberti J, Sade RM, Williams RG, Nadas AS. Open-heart surgery during the first three months of life. *J Thorac Cardiovasc Surg*. 1974; 68:719-31.
6. Pigula FA, Khalil PN, Mayer JE, del Nido PJ, Jonas RA. Repair of tetralogy of Fallot in neonates and young infants. *Circulation*. 1999;100(Suppl):III157-61.
7. Mulder TJ, Pyles LA, Stolfi A, Pickoff AS, Moller JH. A multicenter analysis of the choice of initial surgical procedure in tetralogy of Fallot. *Pediatr Cardiol*. 2002;23:580-6.
8. Parry AJ, McElhinney DB, Kung GC, Reddy VM, Brook MM, Hanley FL. Elective primary repair of acyanotic tetralogy of Fallot in early infancy: overall outcome and impact on the pulmonary valve. *J Am Coll Cardiol*. 2000;36:2279-83.
9. Reddy VM, Liddicoat JR, McElhinney DB, Brook MM, Stanger P, Hanley FL. Routine primary repair of tetralogy of Fallot in neonates and infants less than three months of age. *Ann Thorac Surg*. 1995;60:S592-6.
10. Fermanis GG, Ekangaki AK, Salmon AP, Keeton BR, Shore DF, Lamb RK, et al. Twelve year experience with the modified Blalock-Taussig shunt in neonates. *Eur J Cardiothorac Surg*. 1992;6:586-9.
11. Gladman G, McCrindle BW, Williams WG, Freedom RM, Benson LN. The modified Blalock-Taussig shunt: clinical impact and morbidity in Fallot's tetralogy in the current era. *J Thorac Cardiovasc Surg*. 1997;114:25-30.
12. Sousa Uva M, Chardigny MC, Galetti L, Lacour Gayet F, Roussin R, Serraf A, et al. Surgery for tetralogy of Fallot at less than six months of age. Is palliation "old-fashioned"? *Eur J Cardiothorac Surg*. 1995;9:453-9; discussion 459-60.
13. Van Arsdell GS, Maharaj GS, Tom J, Rao VK, Coles JG, Freedom RM, et al. What is the optimal age for repair of tetralogy of Fallot? *Circulation*. 2000; 102(Suppl 3):III123-9.
14. Al Habib HF, Jacobs JP, Mavroudis C, Tchervenkov CI, O'Brien SM, Mohammadi S, et al. Contemporary patterns of management of tetralogy of Fallot: data from the Society of Thoracic Surgeons Database. *Ann Thorac Surg*. 2010;90:813-9; discussion 819-20.
15. Owner Hospitals. *Child Health Corporation of America*. Available from: http://www.chca.com/index_flash.html. Accessed December 3, 2012.
16. Centers for Disease Control and Prevention, National Center for Health Statistics. *International Classification of Diseases, Ninth Revision, Clinical Modification*. Available from: <http://www.cdc.gov/nchs/icd/icd9cm.htm>. Accessed December 7, 2012.
17. CTC Resources. *Child Health Corporation of America*. Available from: http://www.chca.com/index_flash.html. Accessed: Dec 03, 2012.
18. Karl TR, Sano S, Pornviliwan S, Mee RB. Tetralogy of Fallot: favorable outcome of neonatal transatrial, transpulmonary repair. *Ann Thorac Surg*. 1995;109: 332-44.
19. Vobecky SJ, Williams WG, Trusler GA, Coles JG, Rebeyka IM, Smallhorn J, et al. Survival analysis of infants under 18 months presenting with tetralogy of Fallot. *Ann Thorac Surg*. 1993;56:944-50.
20. Ooi A, Moorjani N, Baliulis G, Keeton BR, Salmon AP, Monro JL, et al. Medium term outcome for infant repair in tetralogy of Fallot: indicators for timing of surgery. *Eur J Cardiothorac Surg*. 2006;30:917-22.
21. Pasquali S, Peterson E, Jacobs J, He X, Li J, Jacobs M, et al. Differential case ascertainment in clinical registry versus administrative data and impact on outcomes assessment for pediatric cardiac operations. *Ann Thorac Surg*. 2013;95: 197-203.