Predictors of Intensive Care Unit Morbidity and Midterm Follow-up after Primary Repair of Tetralogy of Fallot

Alexander C. Egbe, M.D., Khanh Nguyen, M.D., Alexander J. C. Mittnacht, M.D., Umesh Joashi, M.D.

**Background:** Our objectives were to review our institutional early and midterm experience with primary tetralogy of Fallot (TOF) repair, and identify predictors of intensive care unit (ICU) morbidity. **Methods:** We analyzed perioperative and midterm follow-up data for all cases of primary TOF repair from 2001 to 2012. The primary endpoint was early mortality and morbidity, and the secondary endpoint was survival and functional status at follow-up. **Results:** Ninety-seven patients underwent primary repair. The median age was 4.9 months (range, 1 to 9 months), and the median weight was 5.3 kg (range, 3.1 to 9.8 kg). There was no early surgical mortality. The incidence of junctional ectopic tachycardia and persistent complete heart block was 2% and 1%, respectively. The median length of ICU stay was 6 days (range, 2 to 21 days), and the median duration of mechanical ventilation was 19 hours (range, 0 to 136 hours). By multiple regression analysis, age and weight were independent predictors of the length of ICU stay, while the surgical era was an independent predictor of the duration of mechanical ventilation. At the 8-year follow-up, freedom from death and reintervention was 97% and 90%, respectively. **Conclusion:** Primary TOF repair is a safe procedure with low mortality and morbidity in a medium-sized program with outcomes comparable to national standards. Age and weight at the time of surgery remain significant predictors of morbidity.

**INTRODUCTION**

Tetralogy of Fallot (TOF) is the most common congenital cyanotic heart disease with an incidence of 3 per 10,000 live births, and accounts for about 5% to 7% of all congenital heart disease [1]. From the time of the first surgical palliation of TOF by Blalock and Taussig in 1945, surgical management has evolved to primary corrective repair that can safely be performed in all age groups [2]. The safety of early primary repair is well documented in the literature with several studies showing that it is a safe procedure even in neonates [3]. As a result, primary repair of TOF is now a routine procedure with a low surgical mortality rate of 0% to 2% [3-7]. Advocates of early primary repair believe that early relief of right ventricular outflow tract (RVOT) obstruction will prevent right ventricular hypertrophy and dysfunction, as well as establish unobstructed pulmonary blood flow, which will encourage alveologenesis [8-10]. However, the data also clearly...
suggest an increased incidence of junctional ectopic tachycardia (JET), longer intensive care unit (ICU) and hospital stays, more complicated recovery, and increased need for valve-sacrificing transannular patch (TAP) repairs in patients who undergo primary repair in the neonatal period [4-6,11,12]. Some centers including ours perform neonatal repair when clinically indicated for severe RVOT obstruction, cyanosis, and hypercyanotic spells.

In spite of low surgical mortality, ICU morbidity is relatively common after primary TOF repair [13]. There is a strong correlation between ICU morbidity and intraoperative factors such as cardiopulmonary bypass (CPB) time, cross clamp, and surgical techniques [3,11,13]. However, our ability to identify patients at risk for significant ICU morbidity based on their preoperative characteristics is limited because of conflicting evidence in the literature [4,5,11,13]. We have hypothesized that certain preoperative demographic and morphologic characteristics increase the risk of ICU morbidity after primary TOF repair.

METHODS

1) Patient population

All patients with the diagnosis of TOF with pulmonic stenosis who underwent primary repair between January 2001 and December 2012 at Mount Sinai Hospital, New York, were identified from the hospital database. Our surgical database reported that 126 patients underwent TOF repair within the study period. We excluded patients who had a prior Blalock-Taussig shunt, patients who were older than 12 months of age at the time of repair, and patients with associated anatomic defects such as absent pulmonary valve syndrome, atrioventricular septal defect, or pulmonary atresia. Based on our inclusion criteria, we identified 99 patients within this study period who underwent primary TOF repair in infancy. We divided the study period into the early surgical era (January 2001–December 2006) and the late surgical era (January 2007–December 2012) to evaluate the impact of evolving changes in surgical/anesthesia technique and perioperative management in the observed time period. Our study was approved by the hospital’s institutional review board.

The primary objective of this study was to determine overall survival and incidence of complications. Our secondary objectives were to identify predictors of ICU morbidity as well as survival and functional status at midterm follow-up. We defined ICU morbidity as prolonged ICU stay (length of ICU stay ≥ 7 days) and/or prolonged mechanical ventilation (duration of mechanical ventilation ≥ 48 hours). For midterm follow-up, we analyzed survival, freedom from re-intervention, and freedom from a severe residual lesion at 1 year, 3 years, 5 years, and 8 years postoperatively.

2) Data collection

(1) Preoperative data: Demographic information evaluated included age at the time of surgery, gestational age, gender, weight, history of hypercyanotic spells, baseline systemic saturation, history of associated genetic disorders inclusive of Down’s syndrome, and presence of other extracardiac comorbidities.

(2) Echocardiographic data: The pulmonary valve annulus z-score and main pulmonary artery z-score were evaluated as measures of RVOT obstruction.

(3) Operative data: The following were collected and analyzed: CPB time, aortic cross-clamp time, and presence of a hemodynamically significant residual lesion on intraoperative transesophageal echocardiogram (TEE). We defined the residual hemodynamic lesion as greater than trivial residual ventricular septal defect (VSD) or greater than trivial residual pulmonic stenosis (maximum instantaneous gradient of 20 mmHg).

(4) Postoperative intensive care unit data: After the operation, the following were recorded: length of ICU stay, duration of mechanical ventilation, duration of inotropic support, postoperative arrhythmia such as junction ectopic tachycardia (JET), need for extracorporeal membrane oxygenation (ECMO) support, readmission within 30 days of surgery, and death within 30 days of surgery. Hemodynamic data and lab values collected and reviewed include heart rate, central venous pressure, systemic arterial pressure (systolic, diastolic, and mean), serum lactate, blood gases, chemistry, and complete blood count.

(5) Midterm follow-up data: We collected and analyzed data on survival, freedom from re-intervention, and freedom from a significant residual lesion at 1 year, 3 years, 5 years,
Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Demographic and preoperative data</th>
<th>No. of patients (%)</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at surgery (mo)</td>
<td></td>
<td>4.9</td>
<td>1–9</td>
</tr>
<tr>
<td>Weight at surgery (kg)</td>
<td></td>
<td>5.3</td>
<td>3.1–9.8</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>51 (54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prematurity</td>
<td>26 (26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonates</td>
<td>9 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>11 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22q11 deletion</td>
<td>5 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercyanotic spell</td>
<td>19 (19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary valve annular hypoplasia (z-score &lt; -2)</td>
<td>73 (73)</td>
<td>83</td>
<td>71–94</td>
</tr>
<tr>
<td>Preop oxygen saturation(a) median (%)</td>
<td>4.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal coronary anatomy(b)</td>
<td>2 (2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(a\)Oxygen saturation during pre-surgical evaluation usually about 1 week prior to surgery.

\(b\)Large conal branch or left anterior descending artery crossing the right ventricular outflow tract.

and 8 years postoperatively. A significant residual lesion was defined as moderate/severe pulmonary regurgitation or tricuspid regurgitation, moderate/severe right ventricular dilation, or systolic dysfunction.

3) Statistical analysis

Standard descriptive statistical methods were used. Data were described as frequencies and median with ranges as appropriate. To assess the differences between groups, the Mann–Whitney test or Student t-test for continuous data and the chi-square test or Fisher’s exact test for categorical data were used. Multiple logistic regression analysis was performed to determine the independent risk factors of prolonged length of ICU stay and prolonged duration of mechanical ventilation. A p-value of <0.05 was considered statistically significant. All analyses were performed using the SAS ver. 7.0 statistical software (SAS Institute Inc., Cary, NC, USA) with default settings except where indicated.

RESULTS

Over the 12-year study period, 99 patients with TOF underwent primary repair in infancy in Mount Sinai Hospital. Two patients had incomplete hemodynamic data and were excluded from the study. Table 1 shows the demographic and preoperative data of the study population. The median age at the time of surgery was 4.9 months (range, 1 to 9 months), and the median weight was 5.3 kg (range, 3.1 to 9.8 kg). There were 51 males and 46 females making up 53% and 47% of the study population, respectively. Twenty-six patients (26%) were premature (delivery prior to 37 completed weeks of gestation). Nine patients (9%) underwent TOF repair within the first month of life. The indication for neonatal surgery was severe hypoxia due to severe RVOT obstruction in all 9 patients. It is Mount Sinai Hospital’s policy to avoid palliative shunts and to perform primary repair irrespective of age whenever possible. Eleven patients (11%) had Down’s syndrome, five patients (5%) had 22q11 deletion, and 19 patients (19%) had at least one episode of hypercyanotic spells prior to TOF repair. The median pulmonary valve z-score for our population was -3.6 (range, -5.1 to -0.3), and 73 patients (75%) had pulmonary valve annular hypoplasia (pulmonary valve z-score < -2). The median CPB time was 114 minutes (range, 61 to 205 minutes), and the median aortic cross-clamp time was 61 minutes (range, 30 to 104 minutes). Twenty-one patients underwent TAP repair, and 38 patients underwent additional pulmonary arterioplasty as part of surgical relief for RVOT obstruction. The decision to perform TAP repair versus a valve-sparing procedure was based on the pulmonary valve z-score (greater or less than -2) or the decision of the surgeon. The decision to perform pulmonary arterioplasty was based entirely on the surgeon’s intraoperative assessment of size on branch pulmonary arteries (Table 2). Intraoperative TEE showed residual hemodynami-
Table 2. Intraoperative and postoperative data

<table>
<thead>
<tr>
<th>Intraoperative &amp; postoperative data</th>
<th>No. of patients (%)</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>115</td>
<td></td>
<td>61–205</td>
</tr>
<tr>
<td>Aortic cross-clamping time (min)</td>
<td>61</td>
<td></td>
<td>30–104</td>
</tr>
<tr>
<td>Pulmonary artery arterioplasty</td>
<td>38 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transannular patch repair</td>
<td>21 (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transatrial VSD closure</td>
<td>68 (70)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transventricular VSD closure</td>
<td>29 (30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual defect by Transesophageal echo</td>
<td>8 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early surgical era</td>
<td>52 (54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of intensive care unit stay (day)</td>
<td>6</td>
<td>2–21</td>
<td></td>
</tr>
<tr>
<td>Duration of hospital stay (day)</td>
<td>8</td>
<td>2–38</td>
<td></td>
</tr>
<tr>
<td>Patients extubated in the operating room</td>
<td>26 (27)</td>
<td>21</td>
<td>0–136</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (hr)</td>
<td>33</td>
<td>16–104</td>
<td></td>
</tr>
<tr>
<td>Duration of inotropic support (hr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation support</td>
<td>4 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junctional ectopic tachycardia</td>
<td>2 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinterventions</td>
<td>5 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early surgical mortality (within 30 days)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VSD, ventricular septal defect.

cally insignificant lesions in eight patients (8%). These residual lesions were a trivial/small residual VSD patch leak in 5 patients, mild residual RVOT obstruction in 2 patients, and small VSD patch leak plus mild RVOT obstruction in 1 patient, none of which required a repeat bypass run. Five patients (5%) underwent reintervention before hospital discharge. Four of these reinterventions were re-exploration for bleeding. One patient underwent placement of a permanent epicardial pacemaker for persistent complete heart block. The median length of ICU stay was 6 days (range, 2 to 21 days), and the median duration of mechanical ventilation was 19 hours (range, 0 to 136 hours). Four patients (4%) required ECMO support for hemodynamic instability. The clinical courses of these 4 patients were as follows: patient #1 (age, 3 months; weight, 5.8 kg) and #2 (age, 2 months; weight, 4.1 kg) were placed on veinarterial extracorporeal-ECMO support on the first postoperative night because of hemodynamic instability due to intractable JET. In both cases, JET resolved with amiodarone (patient #1) and amiodarone with procaimidine (patient #2). Both patients were successfully decannulated on postoperative day 2 (patient #1) and postoperative day 3 (patient #2). Patient #3 underwent neonatal TOF repair (age, 4 days; weight, 3.9 kg). The patient also underwent TAP repair with extensive pulmonary artery plasty and was placed on ECMO in the operating room (OR) because of inability to wean the patient from CPB. Intraoperative TEE did not show any significant anatomic residual lesion, and the patient has normal coronary artery anatomy. The patient was decannulated on postoperative day 2. Patient #4 (weight, 9.4 kg) was an 11-month-old infant with severe RVOT obstruction and restrictive RV physiology who had marginal cardiac output coming off bypass and had cardiac arrest within 6 hours of arrival in the ICU. The patient was immediately “crashed” onto ECMO support. Atrial communication was created percutaneously in the catheterization lab on postoperative day 3 because of persistent right ventricular diastolic dysfunction. The patient was successfully decannulated on postoperative day 6. All of the patients survived to hospital discharge, and there was no early surgical mortality (Table 2).

Comparing surgical eras, we found that there was a statistically significant decrease in the duration of mechanical ventilation from the early surgical era (2001–2006) to the late surgical era (2007–2012) (p-value=0.01). The median duration of ventilation in the patients who were not extubated in the OR decreased from 36 hours (range, 0 to 112 hours) in the
Table 3. Data by surgical era

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>52 (54)</td>
<td>45 (46)</td>
<td></td>
</tr>
<tr>
<td>Age (mo)</td>
<td>5.1 (1–9)</td>
<td>4.8 (1–8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>5.4 (3.1–9.4)</td>
<td>5.1 (3.2–9.8)</td>
<td>0.6</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>121 (61–205)</td>
<td>113 (65–196)</td>
<td>0.4</td>
</tr>
<tr>
<td>Cross-clamping time (min)</td>
<td>58 (35–104)</td>
<td>63 (30–101)</td>
<td>0.3</td>
</tr>
<tr>
<td>Transannular patch repair</td>
<td>12 (23)</td>
<td>9 (20)</td>
<td>0.7</td>
</tr>
<tr>
<td>Residual lesions</td>
<td>5 (10)</td>
<td>3 (7)</td>
<td>0.6</td>
</tr>
<tr>
<td>Duration of intensive care unit stay (day)</td>
<td>7 (4–20)</td>
<td>6 (2–21)</td>
<td>0.2</td>
</tr>
<tr>
<td>Duration of hospital stay (day)</td>
<td>7 (4–28)</td>
<td>8 (2–38)</td>
<td>0.3</td>
</tr>
<tr>
<td>Patients extubated in the operating room</td>
<td>9 (17)</td>
<td>17 (38)</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (hr)</td>
<td>36 (0–112)</td>
<td>15 (0–136)</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of inotropic support (hr)</td>
<td>32 (16–91)</td>
<td>36 (18–104)</td>
<td>0.8</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation support</td>
<td>2 (4)</td>
<td>2 (4)</td>
<td>0.9</td>
</tr>
<tr>
<td>Junctional ectopic tachycardia</td>
<td>2 (4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Reintervention</td>
<td>3 (4)</td>
<td>2 (13)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or median (range).

<sup>a</sup>Statistical significance in multivariate analysis.

early surgical era to 13 hours (range, 0 to 136 hours) in the late era. Apart from the change in the duration of mechanical ventilation, there was no significant difference in the length of ICU stay, patient demographics, surgical technique, intraoperative factors (CPB time and aortic cross-clamping time), and postoperative complications between the two surgical eras (Table 3).

Based on our definition of prolonged ICU stay (length of ICU stay ≥7 days), 22 patients (23%) had prolonged ICU stay. These patients with prolonged ICU stay underwent surgical repair at a younger age (median, 3.8 months; range, 1 to 7 months) as compared to patients with ICU stay <7 days (median, 5.1 months; range, 1 to 9 months) (p-value=0.001). Also, there was a significant difference in the weight of patients with prolonged ICU stay (median, 4.8 kg; range, 3.1 to 7.5 kg) as compared to patients with the length of ICU stay <7 days (median, 6.2 kg; range, 3.2 to 9.8 kg) (p-value=0.001). A majority of the patients (73%) with prolonged ICU stay underwent TOF repair in the early surgical era as compared to 48% of the patients with an ICU stay duration of <7 days, p-value=0.02. Additionally, there was higher incidence of pulmonary valve annular hypoplasia in the patients with prolonged ICU stay than in those with normal ICU stay duration (100% vs. 68%, p-value=0.002). However, on multivariate analysis, only age and weight at the time of surgery emerged as statistically significant predictors of prolonged ICU stay as shown in Table 4.

Table 5 compares the preoperative and intraoperative characteristics of patients with prolonged duration of mechanical ventilation (≥48 hours) to patients with a normal duration of mechanical ventilation (<48 hours). Patients with a prolonged duration of mechanical ventilation underwent surgical repair at a younger age (median, 3.6 months; range, 1 to 8 months) as compared to patients with a duration of mechanical ventilation of <48 hours (median, 5.4 months; range, 1 to 9 months) (p-value=0.001). Also, there was a significant difference in the weight of patients with a prolonged duration of mechanical ventilation (median, 5.5 kg; range, 3.5 to 7.2 kg) as compared to patients with a duration of mechanical ventilation of <48 hours (median, 6.4 kg; range, 3.2 to 9.8 kg) (p-value=0.001). Eighty-five percent of the patients (n=17) with a prolonged duration of mechanical ventilation underwent TOF repair in the early surgical era as compared to 45% (n=35) of the patients with a duration of mechanical ventilation of <48 hours (p-value=0.002). Additionally, there was a higher incidence of pulmonary valve annular hypoplasia in the patients with a prolonged duration of mechanical ventilation than in those with a duration of mechanical ven-
Table 4. Length of intensive care unit stay

<table>
<thead>
<tr>
<th>Variable</th>
<th>A (&lt;7 days)</th>
<th>B (≥7 days)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>75 (77)</td>
<td>22 (23)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (mo)</td>
<td>5.1 (1-9)</td>
<td>3.8 (1-7)</td>
<td>0.4</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>41 (54)</td>
<td>10 (45)</td>
<td>0.6</td>
</tr>
<tr>
<td>Prematurity</td>
<td>21 (28)</td>
<td>5 (22)</td>
<td>0.01</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>6.2 (3.2-9.8)</td>
<td>4.8 (3.1-7.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypercyanotic spell</td>
<td>10 (13)</td>
<td>9 (40)</td>
<td>0.07</td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>7 (9)</td>
<td>4 (18)</td>
<td>0.3</td>
</tr>
<tr>
<td>22q11 deletion</td>
<td>3 (4)</td>
<td>1 (5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Pulmonary valve annular hypoplasia (z-score &lt; -2)</td>
<td>51 (68)</td>
<td>22 (100)</td>
<td>0.07</td>
</tr>
<tr>
<td>Nakata index ($mm^2/m^2$)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>284 (251-326)</td>
<td>262 (207-314)</td>
<td>0.1</td>
</tr>
<tr>
<td>Transannular patch repair</td>
<td>16 (21)</td>
<td>5 (23)</td>
<td>0.2</td>
</tr>
<tr>
<td>Preoperative oxygen saturation (%)</td>
<td>85 (71-94)</td>
<td>82 (74-91)</td>
<td>0.4</td>
</tr>
<tr>
<td>Patients extubated in the operating room</td>
<td>21 (28)</td>
<td>5 (23)</td>
<td>0.6</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>118 (75-205)</td>
<td>114 (61-175)</td>
<td>0.6</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>58 (34-98)</td>
<td>60 (30-104)</td>
<td>0.8</td>
</tr>
<tr>
<td>Residual lesions</td>
<td>5 (6)</td>
<td>3 (13)</td>
<td>0.3</td>
</tr>
<tr>
<td>Early surgical era</td>
<td>36 (48)</td>
<td>16 (73)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or median (range).

<sup>a</sup> Statistical significance in multivariate analysis.

<sup>b</sup> Nakata index data were only available in 76 patients (78% of our cohort).

Table 5. Duration of mechanical ventilation

<table>
<thead>
<tr>
<th>Variable</th>
<th>A (&lt;48 hours)</th>
<th>B (≥48 hours)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>77 (80)</td>
<td>20 (20)</td>
<td>0.07</td>
</tr>
<tr>
<td>Age (mo)</td>
<td>5.4 (1-9)</td>
<td>3.6 (1-8)</td>
<td>0.5</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>42 (54)</td>
<td>9 (46)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prematurity</td>
<td>24 (31)</td>
<td>2 (10)</td>
<td>0.07</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>6.4 (3.2-9.8)</td>
<td>5.5 (3.5-7.2)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hypercyanotic spell</td>
<td>9 (12)</td>
<td>10 (50)</td>
<td>0.07</td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>7 (9)</td>
<td>4 (18)</td>
<td>0.2</td>
</tr>
<tr>
<td>22q11 deletion</td>
<td>3 (4)</td>
<td>1 (5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Pulmonary valve annular hypoplasia (z-score &lt; -2)</td>
<td>53 (68)</td>
<td>20 (100)</td>
<td>0.08</td>
</tr>
<tr>
<td>Nakata index ($mm^2/m^2$)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>271 (244-326)</td>
<td>266 (207-318)</td>
<td>0.6</td>
</tr>
<tr>
<td>Transannular patch repair</td>
<td>15 (29)</td>
<td>6 (30)</td>
<td>0.3</td>
</tr>
<tr>
<td>Preoperative oxygen saturation (%)</td>
<td>81 (76-92)</td>
<td>84 (71-94)</td>
<td>0.2</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>126 (75-205)</td>
<td>108 (61-196)</td>
<td>0.9</td>
</tr>
<tr>
<td>Cross-clamping time (min)</td>
<td>58 (34-98)</td>
<td>60 (30-104)</td>
<td>0.8</td>
</tr>
<tr>
<td>Residual lesions</td>
<td>5 (6)</td>
<td>3 (13)</td>
<td>0.2</td>
</tr>
<tr>
<td>Early surgical era</td>
<td>35 (45)</td>
<td>17 (85)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or median (range).

<sup>a</sup> Statistical significance in multivariate analysis.

<sup>b</sup> Nakata index data were only available in 76 patients (78% of our cohort).

However, on the multivariate analysis, only the surgical era reached statistical significance as a predictor of duration of mechanical ventilation. Fig. 1 shows the median duration of mechanical ventilation by year of surgery.

Table 6 shows short and midterm follow-up data for our
During the 8-year follow-up period, only one patient died at 28 months postoperatively, and the cause of death was pneumonia/acute respiratory distress syndrome. Three patients had re-intervention in our cohort. These re-interventions were balloon dilation with stent placement in the branch pulmonary arteries in 2 patients at 18 months and 41 months postoperatively; and surgical pulmonary valve replacement in one patient at 5 years postoperatively. At the 8-year follow-up, 18 patients (54%) had at least one significant residual hemodynamic lesion. The most common lesion was moderate/severe pulmonary regurgitation in 13 patients. Nine of these 15 patients had TAP repair.

**DISCUSSION**

From the first surgical palliation of TOF by Blalock and Taussig in 1945 and the first intracardiac repair of TOF using controlled cross-circulation by Lillehei, surgical management of TOF has evolved significantly over the years. The initial approach was surgical palliation with systemic-to-pulmonary shunt and subsequent intracardiac repair later in life. This approach resulted in a myriad of complications such as distortion of pulmonary arteries, suboptimal development of pulmonary vasculature, shunt thrombosis, risk of pulmonary vascular diseases, end-organ dysfunction due to the prolonged period of cyanosis, right ventricular hypertrophy, and diastolic dysfunction, which leads to arrhythmia and sudden death later in life [3,8,10,14]. To avoid these complications, this initial two-stage approach evolved into primary repair in infancy. Primary repair of TOF is now the standard of care and has been safely applied to all age groups including neonates with low surgical mortality [4]. In spite of low early surgical mortality after primary TOF repair, some patients still experience significant ICU morbidity. In order to assess the preoperative risk factors for ICU morbidity, we reviewed our 12-year single center experience with primary TOF repair in infancy.

Our series reported zero surgical mortality, which compares favorably to that published in the literature. Knott-Craig et al. [15] reported a decrease in surgical mortality after primary repair of TOF in all ages from 11% before 1990 to 2.1% after 1990. Two additional series by Reddy et al. [6] and Touati et al. [7] reported a similar low mortality rate of 1% to 3% after primary repair with the tendency for slightly higher mortality rates in neonates. Nine of our patients (9%) underwent primary repair in the neonatal period without any early mortality. Unfortunately, this number is too small to draw any reasonable inference from it. Unlike our study population that consisted of TOF with pulmonic stenosis only, Reddy et al. [6] and Touati et al. [7] included other extreme forms of TOF such as TOF with pulmonary atresia and TOF with absent pulmonary valve syndrome. The anatomic complexity of their patient population must have contributed significantly to the slightly higher mortality in their study as compared to ours.

With respect to other postoperative morbidities in our series, one patient required placement of a permanent epicardial pacemaker for complete heart block that persisted beyond 7 days postoperatively, and two patients had JET yielding an incidence rate of 1% and 2% for complete heart block and JET, respectively. Our JET incidence rate appears lower than

### Table 6. Outcomes at midterm follow-up

<table>
<thead>
<tr>
<th>Follow-up (yr)</th>
<th>Cohort no.</th>
<th>Freedom from death</th>
<th>Freedom from re-intervention</th>
<th>Freedom from a significant residual lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82</td>
<td>82 (100)</td>
<td>82 (100)</td>
<td>79 (96)</td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>63 (98)</td>
<td>62 (96)</td>
<td>57 (89)</td>
</tr>
<tr>
<td>5</td>
<td>47</td>
<td>46 (97)</td>
<td>44 (94)</td>
<td>32 (68)</td>
</tr>
<tr>
<td>8</td>
<td>33</td>
<td>32 (97)</td>
<td>29 (90)</td>
<td>15 (46)</td>
</tr>
</tbody>
</table>

Values are presented as number (%).
the incidence rate of 3% to 10% reported in the literature [16-18]. Andreasen et al. [17] and Batra et al. [18] reported the incidence rate for JET after congenital heart surgery to be 8% and 10%, respectively [16]. These studies included lesions such as transposition of great arteries with VSD and Truncus arteriosus, which involve intracardiac repair in the neonatal period. Both studies also identified younger age (<1 month of age), longer CPB time, and inotropic score as risk factors for JET.

The median length of ICU stay in our institution was 6 days (range, 2 to 21 days), and this is consistent with data from other studies [5,12,19]. Hirsh et al. [12] reported the mean length of ICU stay of 9 days +/- 8 days, Kolcz and Pizarro [5] reported the mean duration of ICU stay of 7 days, and Tamesberger et al. [19] reported the median length of ICU stay of 6 days (range, 1 to 77 days) after the primary repair of TOF. We identified age and weight as independent predictors of the length of ICU stay. Our finding is in agreement with the findings of van Dongen et al. [13] and van Arsdel et al. [20] who also identified younger age at time of TOF repair as an independent predictor of prolonged ICU stay, prolonged duration of mechanical ventilation, and prolonged inotropic support.

The median duration of mechanical ventilation in our cohort during the entire study period was 19 hours (range, 0 to 136 hours). There was a significant decrease in the median duration of mechanical ventilation from 33 hours in the first half of the study period (early surgical era), to 13 hours in the second half of the study period (late surgical era). Modifications in perioperative care, such as surgical and anesthetic techniques, as well as postoperative sedation strategies contributed significantly to help decrease the overall duration of mechanical ventilation. Despite the decrease in the duration of mechanical ventilation seen in the later time period, there was no significant change in the length of ICU stay in this specific patient cohort.

Our study had some limitations. First, the retrospective nature of the study and the lack of randomization made it susceptible to bias. Secondly, the low incidence of complications and the small number of patients with significant ICU morbidity (prolonged length of ICU stay and prolonged duration of mechanical ventilation) could have affected the accuracy of statistical analysis for potential predictors of morbidity. Additionally, there are a multitude of other variables associated with evolving perioperative management, variables associated with physician care givers and surgical expertise (despite the same surgeon throughout the course of this study) that can have an impact on outcomes, particularly the length of ICU stay.

In conclusion, Mount Sinai Hospital’s experience with the primary repair of TOF in infancy demonstrates excellent outcomes with zero mortality and low morbidity, which compares favorably with published data. The length of ICU stay was independent of the associated chromosomal and extracardiac anomalies, gender, prematurity, morphologic surrogates of severity of TOF, cyanosis, and clinical symptoms. The surgical era had a direct impact on the duration of mechanical ventilation, while age and low weight at surgery were independent risk factors for prolonged ICU stay.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES


