A uniform strategy of primary repair of tetralogy of Fallot - Transventricular approach results in low reoperation rate in the first decade

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A uniform strategy of primary repair of tetralogy of Fallot - Transventricular approach results in low reoperation rate in the first decade

N=244 (2004-2019)
All patients underwent transventricular repair
Age: 71 days, Prematurity: 23%, Low birth weight: 23%, Genetic syndrome: 16%

Operative mortality: 1.2% Survival at 10 years: 94.6 ± 1.8%

Freedom from reintervention

All cause

For RVOTO

For RV dilatation

A uniform strategy of primary repair of TOF through a transventricular approach resulted in low reoperation rate in the first decade.

RVOTO: right ventricular outflow tract obstruction  RV: right ventricular, CI confidence interval
Title: A uniform strategy of primary repair of tetralogy of Fallot - Transventricular approach results in low reoperation rate in the first decade

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Informed Consent Statement: Informed consent was obtained from each patient to include their information in this publication.
Glossary of Abbreviations:

AUC-ROC; area under the curve-receiver operator characteristic

HR; hazard ratio

IQR; inter-quartile range

PA; pulmonary artery

RV; right ventricular

RVOT; right ventricular outflow tract

RVOTO; right ventricular outflow tract obstruction

TOF; tetralogy of Fallot

VSD: ventricular septal defect

Central Message:

A uniform strategy of primary repair of tetralogy of Fallot through a transventricular approach results in low reoperation rate in the first decade.
Perspective Statement:

Transventricular repair of tetralogy of Fallot as a technique used in a uniform strategy of early repair resulted in a minimal rate of reintervention over the first post-operative decade. Preservation of the musculature of the pulmonary infundibulum may be crucial.

Central picture. Kaplan-Meier curve for freedom from all reinterventions after transventricular full repair (95% CI).
Abstract

Objectives: To review outcomes after a uniform strategy of transventricular repair of tetralogy of Fallot (TOF).

Methods: A total of 244 consecutive patients underwent transventricular primary repair of TOF from 2004 to 2019. Median age at operation was 71 days; 57 (23%) patients were premature; 57 (23%) patients had low birth weight (<2.5kg) and 40 (16%) genetic syndromes. The diameter of pulmonary valve annulus, right pulmonary artery (PA) and left PA were 6.0±1.8 mm (Z score: -1.7±1.3), 4.3±1.4 mm (Z score: -0.9±1.2) and 4.1±1.5 mm (Z score: -0.5±1.3).

Results: Three (1.2%) operative deaths were recorded. Ninety patients (37%) underwent transannular patching. Postoperative echocardiographic peak right ventricular outflow tract (RVOT) gradient decreased from 72±27 mmHg to 21±16 mmHg. Median ICU and hospital stay were 3 and 7 days. The survival rate at 10 years was 94.6±1.8%. Reintervention was required 86 times (55 catheter interventions) in 56 patients following TOF repair. The freedom from all cause reintervention rate at 10 years was 71.1±3.6%. Cyanotic spells (HR:2.14, 95%CI:1.22-3.90, p<.01) and smaller pulmonary valve annulus Z-score (HR:1.26, 95%CI:1.01-1.59, p=.04) were associated
with increasing risk of all reinterventions. Freedom from redo surgery for RVOT obstruction and right ventricular dilatation at 10 years were respectively 85.0±3.1% and 98.7±0.9%. Freedom from valve implantation was 96.7±1.5% at 10 years.

**Conclusions:** A uniform strategy of primary repair of TOF through a transventricular approach resulted in low reoperation rate in the first decade. The need of pulmonary valve implantation was limited to less than 4% at 10 years.

**Keywords:** tetralogy of Fallot, transventricular approach, Primary full repair
Introduction:

During the recent decades, surgical repair of tetralogy of Fallot (TOF) has evolved (1,2) and outcomes have improved consistently, with excellent short- and long-term survival (3). The optimal age and surgical approach of repair of TOF are still being debated (4). The advocates of the right atrial approach, first described by Hudspeth et al. (5) and Edmunds et al. (6), claim that performing a smaller right ventriculotomy allows preservation of early and late right ventricular function and may protect against the occurrence of late arrhythmias. Although many articles have compared the transatrial and transventricular approach in TOF repair (7-13), these articles were retrospective, observational, and have some confounding bias based on sample size, patient's characteristics, and the surgical techniques. To the best of our knowledge, there were no studies that have compared transatrial and transventricular approach in a prospective randomized fashion to assess long-term outcomes.

Over a 15-year period, our institution maintained a uniform policy of early transventricular primary repair of patients with TOF. We retrospectively reviewed early and mid-term surgical outcomes of this uniform strategy in patients with TOF.
**Patients and Methods:**

**Patient population and definition**

This study was approved by the institutional Review Board at Children’s National Hospital on February 13, 2020 (#13608), with patients consent waived.

We retrospectively reviewed consecutive patients with TOF who underwent primary full repair through a transventricular approach from September 2004 to December 2019 at the Children’s National Heart Institute, Children’s National Hospital, Washington, DC. Over the same time period, only 31 patients received a transatrial repair and none a palliation by shunting. This choice was made following surgical preference and they seemed to have a more favorable anatomy (Supplementary table 1). Patients with prior palliation in other hospital, pulmonary atresia, absent pulmonary valve, or atrioventricular septal defects were excluded. A total of 244 patients were analyzed.

Prematurity was defined as babies born alive before 37 weeks of pregnancy are completed. Major extracardiac anomalies were defined as abnormalities of the tracheo–bronchial tree, lungs, gastrointestinal tract, and central nervous system. Operative mortality was defined as all deaths, regardless of cause, occurring during the same
hospitalization in which the operation was performed, and within 30 days postoperatively.

Follow-up data were obtained by clinical visit, e-mail, or written correspondence. The closing date of follow-up for this study was December 31, 2022.

Operative techniques

Repair of TOF was carried out on continuous cardiopulmonary bypass with bicaval cannulation. Under moderate hypothermia, a limited ventriculotomy was performed. The length of the incision was dependent on the length of the conal septum. If hypoplastic or absent the incision could be limited to no more than 5mm. In all cases the incision finished several millimeters cephalad to the connection of the moderator band to the free wall of the right ventricle. The ventricular incision was intentionally kept small in order to prevent the impact on the long-term right ventricular function. By keeping this in mind the incision can almost always be limited to solely be able to visualize the lower margin of the conoventricular ventricular septal defect (VSD) that is in the vertical plane in relation the right ventricular anterior surface. Initial sutures can be placed with the help of a forceps at 6 o’clock position and each suture enable the placement of the next one by gentle traction at the ventricular incision or the previous
suture at times. Only limited incision of 2 to 3 muscle bundles in the outflow tract were
performed. No major resection of the musculature of the right ventricular outflow tract
(RVOT) were performed so that the enlargement of the right ventricular outflow tract
relied primarily on the patching of the narrow outflow tract. Hegar dilator was passed
thorough pulmonary valve and the incision was extended across the pulmonary annulus
(transannular incision) when the Z score of pulmonary anulus was smaller than 2 to 3
standard deviations below normal, following surgeon preference. Ventricular septal
defect was closed through the RVOT with Dacron or autologous pericardial patch using
interrupted braided pledgeted sutures. A pear shaped autologous pericardial patch
soaked in 0.6% glutaraldehyde for 20 min was ideal for use as a RVOT patch. Patching
was limited to an enlargement of the pulmonary annulus no greater than the 0 Z-score
value of the pulmonary annulus. Weaning from bypass should be uncomplicated. If the
child does not wean easily there is almost certainly a residual anatomical problem.

Statistical analysis

There was no missing data. Age and follow-up period was expressed as median and
inter-quartile range (IQR). Other continuous variables were expressed as mean ±
standard deviation. Categorical variables are expressed as number (%) of patients. Data
were analyzed by the Chi-square test for categorical variables. Assumption of normality of continuous data was tested with visual diagnostics. If the assumption of normality was met, continuous variables were compared using the analysis of variance. The overall survival and freedom from reintervention were calculated using the Kaplan-Meier methods with the rate ± standard error.

The overall survival was calculated from the date of the surgery to the date of a death or to the date of data censoring. Freedom from reintervention was calculated from the date of the surgery to the date of a primary reintervention or to the date censoring (death or alive without reintervention). The multivariable Cox-proportional hazards model yielding hazard ratio (HR) and 95% confidence was used to determine variables that are independently associated with overall reintervention or redo surgery during mid-term period, reintervention within 1 year after primary repair and developing moderate to severe RV dilatation during follow-up period. Variables selection was based on preoperative and intraoperative factors, which including prematurity, low birth weight, genetic syndrome, cyanotic spell, age at surgery, Z score of pulmonary valve annulus and trans annular patch. These predictors were entered into univariable analysis, and any variable with p values <.10 was entered into the multivariable mode. The area under
the curve-receiver operator characteristic (AUC-ROC) curve was generated for prediction of the reintervention within 1 year after primary repair. To determine the best predictive threshold value of the AUC-ROC curve, the analysis was performed at every threshold value and every decline from the baseline value. All data analyses were performed with the JMP 11.0 software (SAS Institute, Cary, NC, USA).

Results:

Preoperative patient characteristics

Preoperative patient characteristics are listed in Table 1. Of the 244 newborns, 57 (24%) patients were born premature, and 55 (23%) patients had a low birth weight (<2.5kg). Median age at surgery was 71 (42-106) days. The age at surgery for elective patients varied over the study period. Over the years, following our study of the optimal age for repair, elective surgery was planned after the 55th day of life (14).

Intra operative data

Intraoperative characteristics shown in Table 2. The mean aortic cross clamp time was 54±16 minutes, and the mean cardiopulmonary bypass time was 98±31 minutes. A total
of 4 patients (2%) required a second run of cardiopulmonary bypass for re-releasing of RVOTO (n=1) or closure of residual VSD (n=3). Ninety patients (37%) had a transannular patch (Supplementary table 2, 3). Diameter of pulmonary valve and right and left pulmonary artery were 6.0±1.8 mm (Z score: -1.7±1.3), 4.3±1.4 mm (Z score: -0.9±1.2) and 4.1±1.5 mm (Z score: -0.5±1.3). RVOT peak gradient was 72±27 mmHg.

**Early outcomes**

Three (1.2%) operative mortality were recorded. All these 3 patients were born with prematurity, genetic syndrome and weighing less than 2000gs. Of 3 patients, 1 patient (0.4%) died within 30 days after full repair. The cause of death included acute myocardial infarction (n=1), renal failure (n=1) or sepsis (n=1). (Supplementary table 4). Median (IQR) length of staying at intensive care unit and hospital were 3 (2-7) and 7 (5-12) days. Mean postoperative RVOT peak gradient was 21±16 mmHg and 32 patients (13%) had severe pulmonary regurgitation at discharge.

**Mid-term outcomes**

**Survivals**
Median (IQR) follow-up period was 6.3 (1.8-10.7) years after primary full repair of TOF. The 5- and 10-year overall Kaplan-Meier survival estimate was 97.1±1.2% and 94.6±1.8%, respectively. Besides the 3 in-hospital deaths, 8 patients died during follow-up period. The cause of death included sepsis (n=3), cardiac failure due to severe tricuspid valve stenosis (n=1), respiratory failure (n=1), hepatoblastoma (n=1), sudden death (n=1) and unknown (n=1). In the 233 survivors, 4 patients (1.7%) were in NYHA functional class III or IV at the point of the latest follow-up.

**Reinterventions**

Freedom from all cause reintervention at 1-, 5- and 10-year were 85.7 ± 2.5%, 75.0±3.2% and 70.5±3.6%, respectively (Figure 1A). A total of 56 patients required 86 reinterventions (re-operation: 32 times, transcatheter interventions: 54 times). Nineteen patients required multiple reinterventions. Of 56 patients, 30 patients required reinterventions within 1 year after primary repair. Median (IQR) duration from primary full repair to reintervention was 0.9 (0.4-3.3) years. The main cause of primary reintervention was right ventricular outflow tract obstruction (RVOTO) (n=29), right ventricular (RV) dilatation (n=6) and pulmonary artery (PA) stenosis (n=21). Freedom from reintervention for RVOTO, RV dilatation or PA stenosis at 5- and 10-year by
Kaplan-Meier estimate were 85.5±2.7% and 83.3±3.0%, 98.5±1.1% and 97.2±1.6% or 89.1±2.3 and 87.0±2.7%, respectively (Figure 1B-D). By multivariable Cox-hazard regression analysis, independent risk factors for all reintervention were preoperative cyanotic spells (HR: 2.00, 95% CI: 1.12-3.71, p=.018) and smaller Z score of the PV annulus (HR: 1.26, 95% CI: 1.01-1.58, p=.04) (Table 3). Older age at surgery (HR: 0.99, 95% CI: 0.97-1.00, p=0.002) was identified as independent protective factor for re-intervention within 1 year after primary repair (Supplementary table 5). AUC-ROC curve analysis was performed, which showed that below 49 days of age at surgery was the cut-off value of a trend towards a higher necessity of reintervention within 1 year after primary repair (Area under the curve: 0.72).

Cardiac reoperations were recorded in 32 patients in follow-up period, with 13 patients following a failed trans-catheter reintervention. All patients who required redo open cardiac surgery were discharged alive after procedure. Median (IQR) duration from primary full repair to redo open cardiac surgery was 2.5 (0.9-7.3) years. Freedom from all cause reoperative cardiac surgery at 5- and 10-year was 88.7±2.3 % and 83.0±3.1 % (Figure 2A). Of 32 patients who were underwent redo open cardiac
surgeries, 24 were required for RVOTO, 6 for RV dilatation and 2 for PA stenosis. The level of RVOT was mostly at the infundibular level. Seven out of the 24 requiring a reoperation had undergone a previous failed attempt of balloon dilatation. Freedom from reoperative cardiac surgery for RVOTO, RV dilatation or PA stenosis at 5- and 10-year by Kaplan Meier estimate were 90.9±2.1% and 85.0±3.1%, 98.7±0.9% and 98.7±0.9% or 98.9±0.8% and 98.9±0.8% (Figure 2B-D). Freedom from valve implantation at 10 years was 96.7±1.5%.

Multivariable Cox-hazard regression analysis demonstrated that cyanotic spells was an independent risk factor for redo open surgery (HR: 2.40, 95% CI: 1.07-5.89, p=0.03) (Table 3).

Follow-up echocardiography

Median (IQR) duration from primary full repair to latest follow-up echocardiography was 5.5 (0.3-9.7) years. At recent postoperative follow-up echocardiography, no or mild pulmonary regurgitation was found in 139 patients (57.0%), moderate in 66 patients (27.0%) and severe in 39 patients (16.0%). Moderate and severe RV dilatation was recorded respectively in 32 (13.1%) and 10 patients (4.1%). Out of the 10 patients with severe RV dilatation, 8 patients received transannular patching technique and 5 patients
required valve replacement 11.5 (IQR: 7.3-12.7) years after primary repair. By multivariable Cox-hazard regression analysis, an independent protective factor for developing moderate and severe RV dilatation was low birth weight (HR: 0.18, 95% CI: 0.05-0.52, p<0.001) and an independent risk factors were smaller PV z-score (HR: 1.46, 95% CI: 1.07-2.02, p=0.015) and transannular patching (HR: 2.01, 95% CI: 1.02-4.04, p=0.04) (Supplementary Table 6). Mean RVOT peak gradient at last follow-up was 20.4±14.6 mmHg.

**Discussion:**

We believed that this is one of the largest series of transventricular approach in uniform strategy of TOF repair in a single center cohort. In this series comprising a high proportion of premature babies with small birth weight, we revealed that this strategy resulted in excellent early- and 10-year survival but also low reoperation rate in the first decade. Only 3.3% of our patients required pulmonary valve implantation within the first 10 years following primary repair.

Despite a considerable amount of debate, there has been so far only limited comparative studies of transatrial and transventricular approaches. Most of the
comparison concerned the right ventricular function. Miura et al. (9) reported in 62 patients that transatrial approach provided better postoperative RV function than transventricular approach. Dietl et al. (10) reported in 107 patients that the transatrial approach was associated with a lower prevalence of RV dysfunction and moderate-severe PR at mean follow-up 8.9 years. The patient population in these studies were older (Miura; mean age: 5.5 years old, Dietl; mean age: 7.2 years old). On the other hand, Alexiou et al. found that both approaches were associated with low incidence of arrhythmia and good ventricular function in a large series of 160 infants at a mean follow-up of 10.8 years (7). In the present study, severe right ventricular dilatation developed in only 2.5% of survived patients after 10 years. There had been only 1 sudden death (0.4%) and 98.3% of patients still maintained an excellent functional status at a median follow-up of 6 years.

Several factors need to be considered to elaborate our outcomes in this series. Wald RM et al. demonstrated that larger ventriculotomy correlated with worse RV function and arrhythmias (15) and Bojorquez-Ramos et al. found that morbidity and mortality was higher in patients with classical ventriculotomy compared those who with the small infundibulotomy (16). Talwar et al. concluded their prospective randomized study that
limited ventriculotomy neither leads to deleterious effects on early RV function and the
incidence of arrhythmia (17). Avoiding extended right ventriculotomy in our patients
might have prevented from adverse outcomes. Additionally, the resection of the right
ventricular outflow tract musculature was limited in our patients. Mainly because our
population was young with a high proportion of small babies, we have adopted a
technique that only division of parietal and septal muscular bundles without resection.
No patient had extensive coring out of the infundibular musculature and that fact may
explain why the right ventricular size of our patients seemed preserved in the medium
term. The fact that the majority of reintervention were for residual RVOTO also points
to the limited resection of the outflow tract and the preservation of the pulmonary
infundibulum musculature.

Review of data pertaining to more than 3000 surgical cases of TOF with pulmonary
stenosis in the Society of Thoracic Surgeon’s Congenital Heart Surgery (STS Database)
suggested that primary repair in the first year of life is the most prevalent strategy (18).
We believe that there are some advantages of early primary repair in young infants. The
organs which undergo the most sensitive development in the first year of life is the
brain. Getting out of hypoxia as early as possible would be important for neurological
Development (19). Development of heart is also abnormal in patients with unrepaired TOF. Persistent of systemic high pressure in the right ventricle results in abnormal right ventricular hypertrophy with subsequent fibrosis and decreased complications.

Unrepaired condition may lead to increasing the incidence of malignant ventricular arrhythmias (20, 21). There is also evidence that the left ventricular function is less good when repair of TOF delayed (22). In addition to development of organs, there are economic advantage of early primary repair (23).

As previously demonstrated, patients with preoperative cyanotic spells and smaller PV annulus are at the worst end of the spectrum of this condition and have a higher risk of reintervention. In the latest echo follow-up, 42 patients developed moderate or severe RV dilatation, and it is possible that a few of those will require reintervention in future years.

Limitations

It is possible that our rate of valve implantation has been low because we tried to defer this surgery to an older age. Even in this perspective, we believe that our rate of valve implantation remains remarkably low.
Conclusion:

A uniform strategy of primary repair of TOF through a transventricular approach resulted in low reoperation rate in the first decade. The need of valve implantation was limited to less than 4% at 10 years.

Acknowledgement

A very large part of this work was contributed by the procedures performed and the pioneering work of Dr Richard Jonas. He mentored several of the authors in this technique.
**Table 1.** Preoperative characteristics of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients N=244</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks (IQR)</td>
<td>39 (37-40)</td>
</tr>
<tr>
<td>Prematurity, n (%)</td>
<td>57 (23)</td>
</tr>
<tr>
<td>&lt;32 weeks, n (%)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Age at surgery, days (IQR)</td>
<td>71 (42-106)</td>
</tr>
<tr>
<td>Body weight at surgery, kg</td>
<td>4.9 ± 1.7</td>
</tr>
<tr>
<td>Neonate, n (%)</td>
<td>38 (16)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>151 (62)</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>&lt;2.5 kg, n (%)</td>
<td>57 (23)</td>
</tr>
<tr>
<td>Genetic syndrome, n (%)</td>
<td>40 (16)</td>
</tr>
<tr>
<td>Major extracardiac anomaly</td>
<td>30 (12)</td>
</tr>
<tr>
<td>Cyanotic spells, n (%)</td>
<td>128 (52)</td>
</tr>
<tr>
<td>PGE1 infusion, n (%)</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>10 (4)</td>
</tr>
</tbody>
</table>

*IQR: interquartile range, PGE1: prostaglandin E1*
### Table 2. Intraoperative data

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients N=244</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent or emergent surgery</td>
<td>38 (16)</td>
</tr>
<tr>
<td>Aortic cross clamp time, minutes</td>
<td>54±16</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time, minutes</td>
<td>98±31</td>
</tr>
<tr>
<td>Second run of cardiopulmonary bypass, n (%)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>For closure of residual VSD, n (%)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>For re-releasing of RVOTO, n (%)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Combination of transatrial approach</td>
<td>54 (22)</td>
</tr>
<tr>
<td>Transannular patch, n (%)</td>
<td>90 (37)</td>
</tr>
<tr>
<td>Valve sparing, n (%)</td>
<td>154 (63)</td>
</tr>
<tr>
<td>Valvotomy (Hegar dilatation), n (%)</td>
<td>81 (33)</td>
</tr>
<tr>
<td>Pulmonary artery patch plasty, n (%)</td>
<td>18 (7)</td>
</tr>
<tr>
<td>Diameter of pulmonary valve annulus, mm (Z score)</td>
<td>6.0±1.8 (-1.7±1.3)</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>113 (46)</td>
</tr>
<tr>
<td>Diameter of right pulmonary artery, mm (Z score)</td>
<td>4.3±1.4 (-0.9±1.2)</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>34 (14)</td>
</tr>
<tr>
<td>Diameter of left pulmonary artery, mm (Z score)</td>
<td>4.1±1.5 (-0.5±1.3)</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>19 (8)</td>
</tr>
<tr>
<td>RVOT peak gradient, mmHg</td>
<td>72±27</td>
</tr>
</tbody>
</table>

VSD; ventricular septal defect, RVOTO; right ventricular outflow tract obstruction, RVOT; right ventricular outflow tract
Table 3. Risk analysis for multivariable Cox-regression analysis of reintervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Cyanotic spells</td>
<td>2.34 (1.34-4.24)</td>
<td>&lt;.001</td>
<td>2.14 (1.22-3.90)</td>
<td>.007</td>
</tr>
<tr>
<td>Z score of Pulmonary valve annulus (-1)</td>
<td>1.32 (1.06-1.66)</td>
<td>.012</td>
<td>1.26 (1.01-1.59)</td>
<td>.04</td>
</tr>
<tr>
<td>Prematurity</td>
<td>0.65 (0.30-1.27)</td>
<td>.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic syndrome</td>
<td>0.70 (0.29-1.45)</td>
<td>.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transannular patching</td>
<td>1.19 (0.69-2.02)</td>
<td>.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low birth weight</td>
<td>0.83 (0.41-1.55)</td>
<td>.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at surgery (+1 day)</td>
<td>1.00 (0.99-1.00)</td>
<td>.58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HR; hazard ratio, CI; confidence interval
**Table 4.** Risk analysis for multivariable Cox-regression analysis of redo cardiac surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Cyanotic spells</td>
<td>2.95</td>
<td>.005</td>
</tr>
<tr>
<td></td>
<td>(1.37-7.04)</td>
<td></td>
</tr>
<tr>
<td>Z score of Pulmonary valve annulus (-1)</td>
<td>1.28</td>
<td>.048</td>
</tr>
<tr>
<td></td>
<td>(0.97-1.71)</td>
<td></td>
</tr>
<tr>
<td>Prematurity</td>
<td>0.48</td>
<td>.13</td>
</tr>
<tr>
<td></td>
<td>(0.14-1.22)</td>
<td></td>
</tr>
<tr>
<td>Genetic syndrome</td>
<td>0.49</td>
<td>.20</td>
</tr>
<tr>
<td></td>
<td>(0.12-1.39)</td>
<td></td>
</tr>
<tr>
<td>Age at surgery (+1 day)</td>
<td>1.00</td>
<td>.57</td>
</tr>
<tr>
<td></td>
<td>(0.99-1.00)</td>
<td></td>
</tr>
<tr>
<td>Transannular patching</td>
<td>1.09</td>
<td>.81</td>
</tr>
<tr>
<td></td>
<td>(0.52-2.21)</td>
<td></td>
</tr>
<tr>
<td>Low birth weight</td>
<td>0.95</td>
<td>.91</td>
</tr>
<tr>
<td></td>
<td>(0.38-2.11)</td>
<td></td>
</tr>
</tbody>
</table>

*HR: hazard ratio, CI: confidence interval*
**Supplementary Table 1.** Characteristics of patients received transatrial approach (N=31)

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks (IQR)</td>
<td>39 (36-40)</td>
</tr>
<tr>
<td>Prematurity, n (%)</td>
<td>7 (22)</td>
</tr>
<tr>
<td>&lt;32 weeks, n (%)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Age at surgery, days (IQR)</td>
<td>86 (65-121)</td>
</tr>
<tr>
<td>Body weight at surgery, kg</td>
<td>4.8 ± 2.1</td>
</tr>
<tr>
<td>Neonate, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>20 (65)</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>&lt;2.5 kg, n (%)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Genetic syndrome, n (%)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Major extracardiac anomaly, n (%)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Cyanotic spells, n (%)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>PGE1 infusion, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mechanical ventilation, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diameter of pulmonary valve annulus, mm (Z score)</td>
<td>8.8 ± 2.4</td>
</tr>
<tr>
<td>Diameter of right pulmonary artery, mm (Z score)</td>
<td>5.1 ± 1.4</td>
</tr>
<tr>
<td>Diameter of left pulmonary artery, mm (Z score)</td>
<td>4.7 ± 1.9</td>
</tr>
<tr>
<td>RVOT peak gradient, mmHg</td>
<td>55 ± 28</td>
</tr>
<tr>
<td>Operative mortality, n (%)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*BW: body weight, IQR: interquartile range, PGE1: prostaglandin E1*
**Supplementary Table 2.** Preoperative characteristics of patients: transannular patching versus valve sparing

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients N=244</th>
<th>Transannular patching N=90</th>
<th>Valve sparing N=154</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks (IQR)</td>
<td>39 (37-40)</td>
<td>39 (37-40)</td>
<td>39 (36-40)</td>
<td>.38</td>
</tr>
<tr>
<td>Prematurity, n (%)</td>
<td>57 (23)</td>
<td>19 (21)</td>
<td>38 (25)</td>
<td>.52</td>
</tr>
<tr>
<td>&lt;32 weeks, n (%)</td>
<td>9 (4)</td>
<td>2 (2)</td>
<td>7 (5)</td>
<td>.34</td>
</tr>
<tr>
<td>Age at surgery, days (IQR)</td>
<td>71 (42-106)</td>
<td>57 (30-106)</td>
<td>78 (47-108)</td>
<td>.96</td>
</tr>
<tr>
<td>Body weight at surgery, kg</td>
<td>4.9±1.7</td>
<td>4.8±1.4</td>
<td>5.0±1.9</td>
<td>.40</td>
</tr>
<tr>
<td>Neonate, n (%)</td>
<td>38 (16)</td>
<td>22 (24)</td>
<td>16 (10)</td>
<td>.004</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>151 (62)</td>
<td>56 (62)</td>
<td>95 (62)</td>
<td>.93</td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>2.9±0.7</td>
<td>2.9±0.6</td>
<td>2.8±0.7</td>
<td>.56</td>
</tr>
<tr>
<td>&lt;2.5 kg, n (%)</td>
<td>57 (23)</td>
<td>18 (20)</td>
<td>37 (24)</td>
<td>.52</td>
</tr>
<tr>
<td>Genetic syndrome, n (%)</td>
<td>40 (16)</td>
<td>16 (18)</td>
<td>24 (16)</td>
<td>.66</td>
</tr>
<tr>
<td>Major extracardiac anomaly</td>
<td>30 (12)</td>
<td>8 (9)</td>
<td>22 (14)</td>
<td>.19</td>
</tr>
<tr>
<td>Cyanotic spells, n (%)</td>
<td>128 (52)</td>
<td>57 (63)</td>
<td>71 (46)</td>
<td>.01</td>
</tr>
<tr>
<td>PGE1 infusion, n (%)</td>
<td>13 (5)</td>
<td>10 (11)</td>
<td>3 (2)</td>
<td>.09</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>10 (4)</td>
<td>4 (4)</td>
<td>6 (4)</td>
<td>.84</td>
</tr>
</tbody>
</table>

*IQR; interquartile range, PGE1: prostaglandin E1*
### Supplementary Table 3. Intraoperative data: transannular patching versus valve sparing

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients N=244</th>
<th>Transannular patching N=90</th>
<th>Valve sparing N=154</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent or emergent surgery</td>
<td>38 (16)</td>
<td>17 (19)</td>
<td>22 (14)</td>
<td>.35</td>
</tr>
<tr>
<td>Aortic cross clamp time, minutes</td>
<td>54±16</td>
<td>55±15</td>
<td>53±16</td>
<td>.33</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time, minutes</td>
<td>98±31</td>
<td>101±34</td>
<td>96±29</td>
<td>.24</td>
</tr>
<tr>
<td>Pulmonary artery patch plasty, n (%)</td>
<td>18 (7)</td>
<td>3 (3)</td>
<td>15 (10)</td>
<td>.05</td>
</tr>
<tr>
<td>Diameter of pulmonary valve annulus, mm (Z score)</td>
<td>6.0±1.8 (-1.7±1.3)</td>
<td>4.9±1.3 (-2.5±0.9)</td>
<td>6.7±1.8 (-1.2±1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>113 (46)</td>
<td>68 (76)</td>
<td>45 (29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diameter of right pulmonary artery, mm (Z score)</td>
<td>4.3±1.4 (-0.9±1.2)</td>
<td>4.2±1.7 (-1.0±1.5)</td>
<td>4.3±1.1 (-0.9±1.0)</td>
<td>.63</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>34 (14)</td>
<td>17 (19)</td>
<td>17 (11)</td>
<td>.09</td>
</tr>
<tr>
<td>Diameter of left pulmonary artery, mm (Z score)</td>
<td>4.1±1.5 (-0.5±1.3)</td>
<td>4.0±1.8 (-0.8±1.4)</td>
<td>4.2±1.4 (-0.4±1.2)</td>
<td>.27</td>
</tr>
<tr>
<td>Z score &lt; -2.0, n (%)</td>
<td>19 (8)</td>
<td>14 (16)</td>
<td>5 (3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>RVOT peak gradient, mmHg</td>
<td>72±27</td>
<td>73±30</td>
<td>72±25</td>
<td>.63</td>
</tr>
</tbody>
</table>

*RVOT: right ventricular outflow tract*
**Supplementary Table 4.** Characteristic of in-hospital dead patients.

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Birth weight (kg)</th>
<th>Genetic syndrome</th>
<th>Age at surgery (days)</th>
<th>Preoperative specific condition</th>
<th>Cross clamp time (minutes)</th>
<th>CPB time (minutes)</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>1.5</td>
<td>Yes</td>
<td>20</td>
<td>No</td>
<td>44</td>
<td>94</td>
<td>Renal failure</td>
</tr>
<tr>
<td>31</td>
<td>1.7</td>
<td>Yes</td>
<td>11</td>
<td>Mechanical ventilation, PGE1</td>
<td>60</td>
<td>113</td>
<td>Sepsis</td>
</tr>
<tr>
<td>33</td>
<td>1.6</td>
<td>Yes</td>
<td>19</td>
<td>Mechanical ventilation, PGE1</td>
<td>69</td>
<td>123</td>
<td>Myocardial infarction</td>
</tr>
</tbody>
</table>

*CPB; Cardiopulmonary bypass, PGE1; Prostaglandin E1*
**Supplementary Table 5.** Risk analysis for multivariable Cox-regression analysis of reintervention within 1 year after primary repair

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Age at surgery (+1 day)</td>
<td>0.98</td>
<td>&lt;.001</td>
<td>0.99</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>(0.97-0.99)</td>
<td></td>
<td>(0.97-1.00)</td>
<td></td>
</tr>
<tr>
<td>Z score of Pulmonary valve annulus (-1)</td>
<td>1.39</td>
<td>.031</td>
<td>1.29</td>
<td>.13</td>
</tr>
<tr>
<td></td>
<td>(1.03-1.93)</td>
<td></td>
<td>(0.93-1.81)</td>
<td></td>
</tr>
<tr>
<td>Cyanotic spells</td>
<td>2.63</td>
<td>.013</td>
<td>1.50</td>
<td>.37</td>
</tr>
<tr>
<td></td>
<td>(1.22-6.30)</td>
<td></td>
<td>(0.63-3.87)</td>
<td></td>
</tr>
<tr>
<td>Prematurity</td>
<td>0.79</td>
<td>.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.29-1.81)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic syndrome</td>
<td>0.79</td>
<td>.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.23-2.02)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transannular patching</td>
<td>1.05</td>
<td>.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.48-2.18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low birth weight</td>
<td>0.96</td>
<td>.93</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.38-2.13)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*HR; hazard ratio, CI; confidence interval*
**Supplementary Table 6.** Risk analysis for multivariable Cox-regression analysis of developing moderate and severe right ventricular dilatation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>0.34 (0.10-0.86)</td>
<td>.019</td>
</tr>
<tr>
<td>Z score of Pulmonary valve annulus (-1)</td>
<td>1.39 (1.08-1.80)</td>
<td>.009</td>
</tr>
<tr>
<td>Transannular patching</td>
<td>2.89 (1.56-5.53)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cyanotic spells</td>
<td>1.78 (0.94-3.50)</td>
<td>.07</td>
</tr>
<tr>
<td>Age at surgery (+1 day)</td>
<td>0.99 (0.98-1.00)</td>
<td>.003</td>
</tr>
<tr>
<td>Prematurity</td>
<td>0.68 (0.28-1.45)</td>
<td>.34</td>
</tr>
<tr>
<td>Genetic syndrome</td>
<td>0.91 (0.37-1.93)</td>
<td>.81</td>
</tr>
</tbody>
</table>

*HR; hazard ratio, CI; confidence interval*
References


Wald RM, Haber I, Wald R, Valente AM, Powell AJ, Geva T. Effects of regional dysfunction and late gadolinium enhancement on global right ventricular
function and exercise capacity in patients with repaired tetralogy of Fallot.


Figure legend:

Figure 1. Kaplan-Meier curves for freedom from reintervention for (A) all cause, (B) right ventricular outflow tract obstruction, (C) right ventricular dilatation and (D) pulmonary artery stenosis after primary full repair of tetralogy of Fallot. Shaded areas indicate 95% confidence interval.

Figure 2. Kaplan-Meier curves for freedom from redo open cardiac surgery for (A) all cause, (B) right ventricular outflow tract obstruction, (C) right ventricular dilatation and (D) pulmonary artery stenosis after primary full repair of tetralogy of Fallot. Shaded areas indicate 95% confidence interval.

Figure 3 (Graphical abstract). A uniform strategy of primary repair of tetralogy of Fallot through a transventricular approach results in low reoperation rate in the first decade.
A. All cause

B. Right ventricular outflow tract obstruction

C. Right ventricular dilatation

D. Pulmonary artery stenosis
A uniform strategy of primary repair of tetralogy of Fallot - Transventricular approach results in low reoperation rate in the first decade

N=244 (2004-2019)
All patients underwent transventricular repair
Age: 71 days, Prematurity: 23%, Low birth weight: 23%, Genetic syndrome: 16%

Operative mortality: 1.2%  Survival at 10 years: 94.6 ± 1.8%
Freedom from reintervention

- All cause: 71.1 ± 3.6% at 10 years
- For RVOTO: 83.3 ± 3.0% at 10 years
- For RV dilatation: 97.2 ± 1.6% at 10 years

95% CI are shown in shading bar

A uniform strategy of primary repair of TOF through a transventricular approach resulted in low reoperation rate in the first decade.

RVOTO: right ventricular outflow tract obstruction  RV: right ventricular, CI confidence interval

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