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# An Evaluation of Predictive Factors for Pulmonary Valve Replacement after Total Correction in Children with tetralogy of Fallot

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## *Abstract*

***Background:*** Congenital heart defects, with a prevalence of 4-8 cases per 1000 births, are one of the most common congenital defects. Tetralogy of Fallot (ToF) is the most common congenital cyanotic disease. There are several techniques for correcting this anomaly and ToF total correction is a routine option. Approximately 40% of patients undergoing ToF, need Pulmonary Valve Replacement (PVR) in the years after primary surgery. In this study, we investigated the predictive factors of PVR in patients with ToF.

***Method:*** The participants included 204 ToF patients who had undergone ToFTC surgery during 2004-2020. Many factors inducing age, sex, weight, pre-ToFTC echocardiographic findings, pre-ToFTC angiographic findings, pre-ToFTC palliative care, type of ToFTC surgery, and echocardiographic features of PVR were extracted and studied.

***Results:*** The mean age at ToFTC was 27.8 months in the PVR group and 58.8 months in ToFTC + PVR group ($P < 0.001$). Among echocardiographic findings before ToFTC surgery, RV function ($P = 0.003$), RPA ($P = 0.015$) and MPA ($P = 0.036$) were significantly different between the two groups. Valvotomy + VSD Closure surgery were significantly more prevalent among ToFTC patients ($P = 0.001$); however, Transannular Patch and Monocusp Implantation were done at higher rates among PVR patients. More palliative care before surgery was reported among PVR patients ($P = 0.001$), but ASD repair was more prevalent in the other group ($P < 0.001$) which was probably due to two more prevalence of ASD among patients of ToFTC group.

***Conclusion:*** Need for PVR surgery is affected by several factors, including demographic characteristics of patients and characteristics of surgical interventions, along with the anatomical and functional features of the heart.

***Key Words:*** Pulmonary stenosis, Pulmonary valve insufficiency, Pulmonary valve replacement, Tetralogy of Fallot.

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## 1- INTRODUCTION

For every 100 to 150 live births, there is one case with heart abnormalities, the prevalence of which is slightly higher in males. Among them, tetralogy of Fallot (ToF), described and named in 1888 by a French physician named Fallot Arthur Louis Etienne (1), is the most common cyanotic congenital heart disease (2–4), and the most common congenital heart disorder in patients older than one year; it accounts for about 10% of all congenital heart diseases (5). On average, 3 to 5% of infants are born with CHD each year (6).

The therapeutic goal in patients with tetralogy of Fallot is to repair the obstruction of the ventricular outflow tract (RVOTO) and ventricular septal defect (VSD) (7). ToF surgical repair was first proposed in 1955 by Lillehei et al. (8). In this procedure, RVOTO was corrected with a ventriculostomy in the anterior wall of the right ventricle and a transannular patch (TAP), if necessary. According to preliminary results showing that residual RVOTO after tetralogy of Fallot total correction (ToFTC) is associated with an increased risk of premature death, invasive correction of RVOTO leading to a relatively good and long-term survival of patients (9,10) was highly recommended (11). However, residual abnormalities after repair are still common, and one of them is Pulmonary Regurgitation (PR).

To effectively repair the right ventricular outflow tract (RVOT), the surgeon often disrupts the integrity of the pulmonary valve, leading to PR. Five to ten years after ToFTC, 40 to 85% of patients develop moderate to severe PR (12–16). PR was initially thought to be a benign hemodynamic residual lesion, but it was later found to be associated with decreased physical performance and progressive RV dilation. RV dilatation, in turn, may be associated with ventricular arrhythmias and ventricular dysfunction (17–19). In addition, the patients are at greater risk for sudden death (20–25). PR is more common in patients who receive TAP (26).

PVR is an effective therapeutic approach for patients with chronic PR and has been shown in various studies to improve the symptoms of the disease and reverse the ventricular deformity, although it highly depends on the time of intervention (27–29). PVR is increasingly being performed as more ToF patients survive into adulthood (30).

There are several factors involved in the need for PVR after ToFTC in children with ToF, some of which are adjustable and some are not (31, 32). By better understanding these adjustable factors, we can reduce the incidence of PR after ToFTC surgery, thus less PVR will be necessary which leads to better prognosis and quality of life in ToF patients. The goal of this study was to investigate the predictive factors of PVR after ToFTC surgery in children with ToF.

## 2- Materials and Methods

### 2-1. Participants

In this cross sectional study, 244 children with a diagnosis of ToF who had undergone ToFTC surgery at Shahid Madani hospital of Tabriz, Iran, from 2004 to 2021 were included. 40 patients were excluded from the study due to postoperative death or follow up failure of the patient. Factors consisting of age and weight at the time of ToFTC and PVR, echocardiographic and angiographic findings before ToFTC, preoperative palliative care, type of ToFTC surgery, and echocardiographic findings at the time of PVR were evaluated in all patients; then, they were studied in patients who had PVR surgery. Also, the relation between these features and risk of PVR was calculated.

### 2-2. Inclusion and exclusion criteria

Inclusion criteria encompassed all patients with tetralogy of Fallot who underwent complete correction. Exclusion criteria included children who had diseases other than tetralogy of Fallot (including Pulmonary atresia, absent pulmonary valve, Truncus Arteriosus, single ventricle, and Complete AV canal), patients whose extracted files from the archives of Shahid Madani Hospital in Tabriz were incomplete, those who were expired after surgery, and those who had undergone simultaneous ToFTC and PVR surgeries, were excluded from the study.

### 2-3. Data Analysis

All data were analyzed using SPSS software version 26 (IBM SPSS Inc., New York, NY, USA). Kolmogorov–Smirnov test was used to evaluate the normality of quantitative data. Qualitative data were presented as Frequency, and quantitative data were presented as mean and standard deviation.

Chi-squared or Fisher's exact test was used to compare qualitative data between the two groups. Independent T-test and Mann-Whitney U test were used to compare quantitative data with normal and abnormal distributions between the two groups, respectively. Binary logistic regression test was used to predict the relationship between variables. P-value<0.05 was considered significant.

## 3- RESULTS

### 3-1. Demographic features of patients at the time of ToFTC and PVR

Among all examined patients with ToF, 112 were male (54.9%) and 92 were female (45.1%). Of these, 35 cases underwent PVR, among whom 16 were males (45.7%) and 19 were females (54.3%). So, the gender of the patients did not affect the need for PVR. The average age of the patients at the time of ToFTC was 32.7 months. The average age of patients who underwent PVR after ToFTC was 58.82 months. Thus, the age of patients had an effect on the need for PVR, so that the need for PVR increased with increasing age during ToFTC. The average age of patients at the time of PVR was 144 months. The average time interval between two surgeries was 90 months. The average weight of patients during ToFTC was 12 kg among all ToF patients and 16.47 kg among patients who underwent PVR after ToFTC, and this difference in weight was statistically significant, so that the increase in weight of patients during ToFTC led to an increase in patients' need for PVR. The average weight of patients during PVR was 34.8 kg.

### 3-2. Echocardiographic findings of patients at the time of ToFTC

Echocardiographic findings of patients at the time of ToFTC are shown in **Table 2**. The only echocardiographic factor RV function (P = 0.003) significantly affected the need for PVR [MPA (P = 0.036)]. Most of the patients in both groups had normal RV functions. 22 cases (13.3%) had mild systolic dysfunction, all of whom were in the Only ToFTC group. There were only three cases of moderate systolic dysfunction in both groups. The only case of severe systolic dysfunction was in the ToFTC + PVR group. Most of the cases had normal RPA anatomy (157 cases), but its frequency was higher among the patients in the Only ToFTC group. Both of the patients with small size RPA were in the ToFTC + PVR group. RPA origin stenosis was more frequent among ToFTC + PVR patients (11.4% vs. 7.1%).

**Table-1:** Demographic characteristics of patients at the time of ToFTC and PVR

| Characteristics | Only ToFTC | ToFTC + PVR | Total (n = 204) | P-Value |
|---|---|---|---|---|

| | | (n = 169) | (n = 35) | | |
|---|---|---|---|---|---|
| Sex | Male | 96 (56.8%) | 16 (45.7%) | 112 (54.9%) | 0.230 |
| | Female | 73 (43.2%) | 19 (54.3%) | 92 (45.1%) | |
| Age at TOFTC | | 27.8 (21.8) | 58.82 (44.02) | 32.7 (28.8) | < 0.001 |
| Age at PVR | | - | 144 (76) | - | - |
| Time interval | | - | 90 (51.14) | - | - |
| Weight at TOFTC | | 11.5 (4.03) | 16.47 (10.85) | 12 (9.58) | < 0.001 |
| Weight at PVR | | - | 34.8 (18.4) | - | - |

* Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).

** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.

*** P-Value < 0.05 is considered as significant.

**Table-2:** Echocardiographic findings of patients at the time of ToFTC

| Findings | | | Only ToFTC (n = 169) | ToFTC + PVR (n = 35) | Total | P-Value |
|---|---|---|---|---|---|---|
| LVEF | | | 59% (4%) | 59% (5%) | 59% (4%) | 0.346 |
| RV function | Normal | | 143 (84.6%) | 30 (88.2%) | 173 (85.2%) | 0.003 |
| | Mild Systolic Dysfunction | | 23 (13.6%) | 0 (0%) | 23 (11.3%) | |
| | Moderate Systolic Dysfunction | | 3 (1.8%) | 3 (8.8%) | 6 (3%) | |
| | Severe Systolic Dysfunction | | 0 (0%) | 1 (2.9%) | 1 (0.5%) | |
| PS Severity | Mild | | 3 (1.8%) | 0 (0%) | 3 (1.5%) | 0.755 |
| | Moderate | | 2 (1.2%) | 0 (0%) | 2 (1%) | |
| | Severe | | 164 (97%) | 34 (100%) | 198 (97.5%) | |
| CA anatomy | Normal | | 153 (90.5%) | 35 (100%) | 188 (92.2%) | 0.440 |
| | Single Ostium Coronary Arteries | | 12 (7.1%) | 0 (0%) | 12 (5.9%) | |
| | Dilated Coronary Sinus | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | Dilated Valsalva Sinus | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | Abnormal RCA or/and LCA | | 2 (1.2%) | 0 (0%) | 2 (1%) | |
| PA branches anatomy | RPA | Normal size RPA | 157 (92.9%) | 29 (82.9%) | 186 (91.2%) | 0.015 |
| | | Small size RPA | 0 (0%) | 2 (5.7%) | 2 (1%) | |
| | | RPA origin stenosis | 12 (7.1%) | 4 (11.4%) | 16 (7.8%) | |
| | LPA | Normal size LPA | 151 (89.3%) | 29 (82.9%) | 180 (88.2%) | 0.421 |

| Findings | | | Only ToFTC (n = 169) | ToFTC + PVR (n = 35) | Total | P-Value |
|---|---|---|---|---|---|---|
| | | Small size LPA | 1 (0.6%) | 1 (2.9%) | 2 (1%) | |
| | | LPA origin stenosis | 14 (8.3%) | 5 (14.3%) | 19 (9.3%) | |
| | | Tortuous LPA | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | | Absence of LPA | 2(1.2%) | 0 (0%) | 2(1%) | |
| | MPA | Normal MPA | 2 (1.2%) | 0 (0%) | 2 (1%) | 0.036 |
| | | Small size MPA | 167 (98.8%) | 32 (91.4%) | 199 (97.5%) | |
| | | Dilated MPA | 0 (0%) | 1 (2.9%) | 1 (0.5%) | |
| | | Aneurysm of MPA | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | | Stenosis of MPA | 0 (0%) | 1 (2.9%) | 1 (0.5%) | |

* Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).

** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.

*** P-Value < 0.05 is considered as significant.

Four specific types of MPA anatomy abnormality were seen among our patients, including small size MPA, dilated MPA, aneurysm of MPA, and stenosis of MPA, the most frequent of which was stenosis of MPA. However, there was only one patient with this abnormality within each group. And there was only one patient in each of the other disorders. Patients with small size MPA and aneurysm of MPA were in Only ToFTC group and the patient with dilated MPA was in ToFTC + PVR group.

### 3-3. Angiographic findings of patients at the time of ToFTC

The angiographic findings of patients at the time of ToFTC are shown in **Table 3**. Like echocardiographic findings at the time of ToFTC, angiographic findings also confirmed a significant difference in the frequency of RPA and MPA abnormalities between the two groups ($P < 0.05$). The other angiographic finding which was significantly different between the two groups was ASD, and it was more common in the Only ToFTC group (45% vs. 11.4%, respectively).

**Table-3:** Angiographic findings of patients at the time of ToFTC

| Findings | Only ToFTC (n = 169) | ToFTC + PVR (n = 35) | Total | P-Value |
|---|---|---|---|---|
| PV gradient | 73 (20) | 76 (18) | 73 (20) | 0.392 |
| RV pressure | 95 (15) | 103 (23) | 97 (17) | 0.065 |

| Findings | | | Only ToFTC (n = 169) | ToFTC + PVR (n = 35) | Total | P-Value |
|---|---|---|---|---|---|---|
| CA anatomy | Normal | | 154 (91.1%) | 35 (100%) | 189 (92.6%) | 0.479 |
| | Single Ostium Coronary Arteries | | 11 (6.5%) | 0 (0%) | 11 (5.4%) | |
| | Dilated Coronary Sinus | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | Dilated Valsalva Sinus | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | Abnormal RCA or/and LCA | | 2 (1.2%) | 0 (0%) | 2 (1%) | |
| PA Branches Anatomy | RPA | Normal size RPA | 153 (90.5%) | 29 (82.9%) | 182 (89.2%) | 0.030 |
| | | Small size RPA | 0 (0%) | 2 (5.7%) | 2 (1%) | |
| | | Dilated RPA | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | | RPA origin stenosis | 15 (8.9%) | 4 (11.4%) | 19 (9.3%) | |
| | LPA | Normal size LPA | 150 (88.8%) | 29 (82.9%) | 179 (87.7%) | 0.456 |
| | | Small size LPA | 1 (0.6) | 1 (2.9%) | 2 (1%) | |
| | | Tortuous LPA | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | | LPA origin stenosis | 17 (10.1%) | 5 (14.3%) | 22 (10.8%) | |
| | MPA | Normal MPA | 167 (98.8%) | 32 (91.4%) | 199 (97.5%) | 0.036 |
| | | Small size MPA | 0 (0%) | 1 (2.9%) | 1 (0.5%) | |
| | | Dilated MPA | 1 (0.6%) | 0 (0%) | 1 (0.5%) | |
| | | Aneurysm of MPA | 0 (0.0%) | 1 (2.9%) | 1 (0.5%) | |
| | | Stenosis of MPA | 1 (0.6%) | 1 (2.9%) | 2 (1%) | |
| Other findings | Sub Aortic VSD | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | 1.000 |
| | Sub Aortic Web | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | 1.000 |
| | right aortic arch | | 2 (1.2%) | 0 (0%) | 2 (1%) | 1.000 |
| | Left aortic arch | | 1 (0.6%) | 0 (0%) | 1 (0.5%) | 1.000 |
| | PFO | | 35 (20.7%) | 6 (17.1%) | 41 (20.1%) | 0.632 |
| | PDA | | 56 (33.1%) | 7 (20%) | 63 (30.9%) | 0.126 |
| | ASD | | 76 (45%) | 4 (11.4%) | 80 (39.2%) | < 0.001 |
| | LSVC | | 2 (1.2%) | 0 (0%) | 2 (1%) | 1.000 |
| | MAPCA | | 1 (0.5%) | 0 (0%) | 1 (0.5%) | 1.000 |

* Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).
** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.
*** P-Value < 0.05 is considered as significant.

### 3-4. ToFTC surgery methods and preoperative care

The frequency of different ToFTC surgery methods and consumption of preoperative care among patients are shown in **Table 4**. Three main surgical methods were used among our patients, including Valvotomy + VSD Closure, Transannular Patch, and Monocusp Implantation. Valvotomy + VSD Closure was the most common method, and it was used in 163 cases (79.9%). The following common surgical method was Transannular Patch, used in 53 patients (26%). Valvotomy + VSD Closure was significantly more common among Only ToFTC patients (P = 0.001). However, the two other methods were significantly more common among ToFTC + PVR patients (P = 0.001 and 0.009, respectively). Preoperative palliative care

was more commonly used among ToFTC + PVR patients (P = 0.001).

**Table-4:** ToFTC surgery methods in each patient group

| Surgery Method | Only ToFTC (n = 169) | ToFTC + PVR (n = 35) | Total | P-Value |
|---|---|---|---|---|
| Valvotomy + VSD Closure | 131 (77.5%) | 17(48.5%) | 148 (72.5%) | 0.001 |
| Transannular Patch | 36 (21.3%) | 17(48.6%) | 53(26%) | 0.001 |
| Monocusp Implantation | 2 (1.1%) | 1(2.8%) | 3 (1.4%) | 0.009 |
| Palliative Care before ToFTC | 16 (9.4%) | 11(32.4%) | 27(13.3%) | 0.001 |

* Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).
** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.
*** P-Value < 0.05 is considered as significant.

### 3-5. Echocardiographic findings of patients at the time of PVR

The echocardiographic findings of patients at the time of PVR are shown in **Table 5**. While 29.4% of patients did not have pulmonary stenosis (PS), the most common form of PS was the severe form (38.2%).

**Table-5:** Echocardiographic findings of patients at the time of PVR

| Findings | | N/Mean | Findings | | | N/Mean |
|---|---|---|---|---|---|---|
| PS Severity | No PS | 10(29.4%) | PA Branches Anatomy | RPA | Normal size RPA | 32 (91.4%) |
| | Mild | 8(23.5%) | | | Small size RPA | 1 (2.9%) |
| | Moderate | 3(8.8%) | | | RPA origin stenosis | 2 (5.7%) |
| | Severe | 13(38.2%) | | LPA | Normal size LPA | 30 (85.8%) |
| PI Severity | No PI | 3(9.4%) | | | Small size LPA | 1 (2.9%) |
| | Mild | 2(6.3%) | | | LPA origin stenosis | 4 (11.4%) |
| | Moderate | 4(12.5%) | | MPA | Normal size MPA | 32 (91.4%) |
| | Severe | 23(71.9%) | | | Small size MPA | 1 (2.9%) |
| Residual VSD | Normal | 20(58.8%) | | | Dilated MPA | 2 (5.7%) |
| | Small | 10(29.4%) | * Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).<br>** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.<br>*** P-Value < 0.05 is considered as significant. | | | |
| | Moderate | 1(2.9%) | | | | |
| | Large | 3(8.8%) | | | | |
| RV Function | Normal | 1(2.9%) | | | | |
| | Mild Systolic Dysfunction | 12(35.3%) | | | | |
| | Moderate Systolic Dysfunction | 8(23.5%) | | | | |
| | Severe Systolic Dysfunction | 13(38.2%) | | | | |

The severe form of PI was more common than severe PS among the patients (71.9% vs. 38.2%). 9.4% of the patients did not have PI. Residual VSD was not so common among our patients, and only 41.2% of them had a residual VSD. Only 2.9% of the patients had normal right ventricle function. The median of left

ventricular ejection fraction (LVEF) among the patients was 52%. The other factor evaluated among patients who had PVR surgery was the PA branch's anatomy. The normal form of all components of PA was the most common among the patients. The most frequent abnormalities of PA branches included LPA and RPA origin stenosis (11.4% and 5.7%, respectively).

### 3-6. Correlation between studied factors and risk of PVR need

Correlation between studied factors and risk of PVR need were evaluated using binary logistic regression and the results are presented in **Table 6**.

The only statistically significant findings were age and weight of patients at the time of ToFTC and use of transannular patch ($p < 0.001$, $p = 0.045$, and $p = 0.002$, respectively).

**Table-6:** Correlation between studied factors and risk of PVR need based on binary logistic regression

| Variable | | | | Odds Ratio | CL 95% | P-Value |
|---|---|---|---|---|---|---|
| Age at ToFTC | | | | 1.086 | 1.013-1.037 | < 0.001 |
| Weight at ToFTC | | | | 0.820 | 0.675-0.996 | 0.045 |
| RV Function | | | Normal | Reference | | |
| | | | Mild Systolic Dysfunction | 0 | 0 | 0.997 |
| | | | Moderate Systolic Dysfunction | 3.176 | 0.176-57.2 | 0.433 |
| | | | Severe Systolic Dysfunction | 10+7E | - | 1.000 |
| Surgery Method | | | Valvotomy + VSD Closure | 2.106 | 0.376-11.8 | 0.397 |
| | | | Transannular Patch | 12 | 2.458-59.1 | 0.002 |
| | | | Monocusp Implantation | 18.7 | 0.720-487 | 0.078 |
| PA Branches Anatomy | Echocardiography | RPA | Normal size RPA | Reference | | |
| | | | Small size RPA | 10+E3.3 | - | 1.000 |
| | | | RPA origin stenosis | - | - | 0.999 |
| | | MPA | Normal size LPA | Reference | | |
| | | | Small size LPA | 15+E2.24 | - | 0.999 |
| | | | Dilated PAB | 0 | - | 1.000 |
| | | | Aneurysm of MPA | 0.12 | - | 1.000 |
| | | | Stenosis of MPA | 2.129 | 0.38-120 | 0.714 |
| | Angiography | RPA | Normal size RPA | Reference | | |
| | | | Small size RPA | 10+E1 | - | 1.000 |
| | | | Dilated RPA | 0 | - | 1.000 |
| | | | RPA origin stenosis | 1.890 | 0.565-6.322 | 0.301 |
| | | MPA | Normal size LPA | Reference | | |
| | | | Small size LPA | 1.000 | - | 1.000 |
| | | | Dilated PAB | 6.797 | 0.407-113 | 0.182 |

| Variable | | | | Odds Ratio | CL 95% | P-Value |
|---|---|---|---|---|---|---|
| | | | Aneurysm of MPA | 0 | - | 1.000 |
| | | | Stenosis of MPA | 10+E3.36 | - | 1.000 |

* Quantitative data are shown as mean ± standard deviation and qualitative data are shown as frequency (percent).

** P-Values are calculated using Mann Whitney and Chi-Squared tests for quantitative and qualitative data, respectfully.

*** P-Value < 0.05 is considered as significant.

## 4- DISCUSSION

Our findings suggest that several factors may be involved in increased risk for PVR surgery in infants with ToF who underwent ToFTC surgery. Factors such as age and weight of infants at the time of ToFTC were higher in infants who later required PVR surgery. However, right ventricular dysfunction was significantly lower among these patients. Among the angiographic and echocardiographic anatomical abnormalities of the PA branches, which were significantly more frequent in the ToFTC + PVR group of patients, the disorders of the RPA and MPA branches can be mentioned. In addition, ASD, as another angiographic finding, was less common among patients who underwent PVR surgery.

In addition to the above, factors such as surgery methods including Valvotomy + VSD Closure, Transannular Patch, Monocusp Implantation were significantly different between the two groups, so that the first method was more common among patients in the Only ToFTC group, while the other two methods were more commonly used among the ToFTC + PVR patients.

Finally, the relationship between the studied factors that were significantly different between the two groups and the risk of PVR was assessed by the use of a binary logistic regression model that was only significant for age and weight at the time of ToFTC surgery and transannular patch surgery.

Mitropoulos et al., in a study on patients with ToF who underwent ToFTC surgery, described the characteristics of these patients during PVR surgery (33). 99 patients including 71 men and 28 women with a mean age of 38 years at the time of study were enrolled. Similar to our study in which the mean age of patients with ToFTC was higher in patients undergoing PVR surgery than in the Only ToFTC patients, the study by Mitropoulos et al. showed that the likelihood of need for PVR surgery with delayed ToFTC surgery is increased. Besides, they showed that timely PVR is necessary to prevent RV changes and, thus, improves the prognosis of patients. The prognosis of patients who underwent PVR was not, however, examined in our study.

In another study, van der Hulst et al. (31) showed that the risk of PVR surgery in ToF patients with mild PS is lower than that in patients with normal pulmonary valve. However, in the present study, no significant difference in terms of PS severity at the time of ToFTC surgery was found between the two groups. In their study, out of 171 patients who underwent ToFTC, 71 (41.5%) needed PVR surgery. However, in our study only 8.5% of our patients underwent PVR surgery. Factors such as age, sex, surgical methods including transventricular and transabdominal or transpulmonary, pulmonary valve shape and its correction method were studied in that study. Only the pulmonary valve correction method and the ToFTC method were significantly

different between the two groups. The RVOT modification and PA patch methods were significantly more commonly used in the ToFTC + PVR group.

Also, the transventricular method was used in 81% of TOFTC + PVR cases, while this method was used in only 18% of ToFTC cases (31). As in Van der Hulst's study, the use of the PA patch method was more common among our patients in the ToFTC + PVR group.

Similar to our study, Ylitalo et al. assessed the factors related to the increased risk of reoperation in patients with ToF who underwent ToFTC surgery before the age of 15 years old. The results of this study were exactly similar to the results of our study in terms of palliative measures and TAP surgery method in relation to the risk of PVR need. This study showed that patients who received palliative measures before primary surgery or were operated by TAP method had greater risks for PVR surgery. These patients also had a poorer prognosis (32).

### 4-1. Limitations of the study

Being cross sectional is one of the limitations of our study; those patients who had ToFTC surgery in the recent years did not have a chance to undergo PVR surgery and so was in the ToFTC + PVR group. Moreover, the average age of patients at the time of PVR surgery was 144 months, which is equivalent to more than 12 years. Lastly, as previously mentioned, in this study the prognosis of patients undergoing PVR surgery was not examined, which can be considered in future studies.

## 5- CONCLUSION

In summary, it can be concluded that the risk of need for PVR surgery in infants with ToF is influenced by several factors, including demographic characteristics and cardiovascular status of the patients as well as the characteristics of surgical interventions. Therefore, by considering these factors at the time of ToFTC surgery, the risk of need for PVR surgery can be reduced, resulting in improved prognosis and life quality of the patient. This study is one of the few studies investigating the factors affecting the need for PVR in infants with ToF.

## 6- ETHICAL CONSIDERATIONS

This study was approved by the regional ethic committee of research with No.: 45765. All patients completed the consent form before entering the study.

## 7- ACKNOWLEDGMENT

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## 8- AUTHORS CONTRIBUTION

AM, AJK and SG designed the study and carried out the sample recruitments. MG was the pediatric resident and aided in procedures. MM analyzed the data. MG and SS took the lead in writing the manuscript. All authors read and approved the final manuscript, provided critical feedback, discussed the results, and commented on the manuscript.

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