Transannular Patch Repair of Tetralogy of Fallot With or Without Monocusp Valve Reconstruction: A Meta-analysis

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Abstract

Background: Tetralogy of Fallot (TOF) is one of the most common cyanotic congenital heart diseases. Pulmonary regurgitation is the most common and severe comorbidity after transannular patch (TAP) repair of TOF patients. It has not been confirmed whether a TAP repair with monocusp valve reconstruction would benefit TOF patients in perioperative period compared to those without monocusp valve reconstruction. The purpose of the study is to review and analyze all clinical studies that have compared perioperative outcomes of TOF patients undergoing TAP repair with or without monocusp valve reconstruction and conduct a preferable surgery.

Methods: Eligible studies were identified by searching the electronic databases. The primary outcome was perioperative mortality. Secondary outcomes included cardiopulmonary bypass time, aortic cross-clamp time, ventilation duration, ICU length of stay, hospital length of stay, and perioperative right ventricular outflow tract (RVOT) pressure gradient. The meta-analysis and forest plots were drawn using Review Manager 5.3. Statistically significant was considered when $p\text{-value} \leq 0.05$.

Results: Eight studies were included which consisted of 7 retrospective cohort study and 1 randomized controlled trial. The 8 studies formed a pool of 526 TOF patients in total, in which are 300 undergoing TAP repair with monocusp valve reconstruction (monocusp group) compared to 226 undergoing TAP repair without monocusp valve reconstruction (non-monocusp group). It demonstrated significant differences between two groups in perioperative cardiopulmonary bypass time (21.86, 95% CI 16.51-27.21), perioperative aortic cross-clamp time (11.20, 95% CI 1.06 - 21.34), mean length of ICU stay (-1.55, 95% CI -3.90 - -0.81), and the degree of perioperative PR (OR=0.02, 95% CI 0.00 - 0.15).

Conclusion: Transannular patch repair with monocusp valve reconstruction seems to have significant advantages on some perioperative outcomes of TOF patients. Large, multicenter, randomized, prospective studies focusing on differences between TAP repair with and without monocusp valve reconstruction are needed.

1 Background

Tetralogy of Fallot (TOF) represents the most common form of a cyanotic congenital heart defect. It is associated with the morbidity of approximately 1/3500 in the newborns and accounts for 7–10% of all congenital cardiac malformations.¹ In TOF, there are four types of defects, including the overriding of the aorta, pulmonary stenosis or right ventricular outflow tract (RVOT) obstruction, ventricular septal defect (VSD), and right ventricular hypertrophy (RVH). A complete surgical repair to all these defects are commonly required, which consists of two main operations, namely enlarging the narrowed RVOT and closing the VSD.²

Transannular patch (TAP) repair is one of the most effective approaches to enlarge the ROVT when the narrowed pulmonary annulus is insufficient to warrant a total correction.³ This procedure includes an incision to the annulus of a malformed valve, and enlargement of the infundibulum and main pulmonary

artery with a TAP,⁴ which is commonly performed when the RVOT is severely narrowed. The most obvious advantage of a TAP is that it can resolve right ventricular hypertension immediately.⁴ However, it may also cause significant pulmonary regurgitation (PR),⁵ leading to marked pulmonary incompetence and chronic delayed right ventricular dysfunction. Although a reoperation for ROVT obstruction is uncommon, late pulmonary valve insertion is rather frequent.⁶ To prevent postoperative PR, a monocusp valve has been used in some practices.^{4,7-9} However, to date, monocusp valve reconstruction is not routinely practiced in TOF patients undergoing TAP repair for severe ROVT stenosis, given that the benefits of this approach comparing with non-monocusp valve reconstruction remains unclear. Our study aimed to systematically review and analyze all clinical studies that have compared perioperative outcomes of TOF patients undergoing TAP repair with or without monocusp valve reconstruction. The findings of this study would inform the best evidence-based practice in the field.

2 Methods

2.1 Perioperative outcomes

This systematic review was conducted to identify clinical studies that compared differences in the perioperative outcomes in TOF patients undergoing TAP repair with or without monocusp valve reconstruction. In our searching process, no relevant review article or meta-analysis protocol was found. In our study, perioperative mortality was determined as the primary outcome. For secondary outcomes, continuous variables including cardiopulmonary bypass time, aortic cross-clamp time, ventilation duration, ICU length of stay, hospital length of stay, and perioperative RVOT pressure gradient were assessed. Dichotomous variables included moderate or severe pulmonary regurgitation in the perioperative period, besides perioperative mortality.

2.2 Search Strategy

Eligible studies were identified by searching the electronic databases including PubMed, Science Direct, Web of Science, EMBASE, and Ovid. The following search terms were used to identify potentially eligible studies: “tetralogy of Fallot (MeSH)” as well as its free terms, (“transannular patch” AND “monocusp valve”) OR “transannular monocusp”. The year of publication of studies was not specifically restricted. The inclusion criteria included original clinical studies, articles published in English, TOF patients without endocardial pad defect or other complications, comparison between TOF patients undergoing TAP repair with or without monocusp valve reconstruction, and at least one of the perioperative outcomes stated above was investigated. Studies were excluded for the following criteria: (1) articles published in a language other than English, (2) not an original clinical study, (3) in vitro studies or animal studies, (4) not TOF patients but patients with other diseases undergoing TAP repair, (5) non-comparative study reporting outcomes of patients undergoing TAP repair with or without monocusp valve reconstruction only, (6) conference abstract without a full-text, (7) lack of reported target perioperative outcomes as set out by this study. The sample size was not taken into consideration when screening for eligible studies.

2.3 Data Extraction

Data on patient baseline characteristics and perioperative outcomes were extracted from the included studies by two authors independently and repeated twice to ensure the veracity of data. The following data were extracted: study characteristics (including first author, publication year, study design, and sample size), patient baseline characteristics (including gender, age, weight), and all reported target perioperative outcomes stated above.

2.4 Bias Analysis and quality assessment

The risk of bias was assessed for all the included studies, in which a retrospective cohort study was assessed using the Tool to Assess Risk of Bias in Cohort Studies, and a randomized controlled trial was assessed using the Review Manager 5.3. The quality of outcomes was assessed using the GRADEpro. Publication bias was evaluated by funnel plots.

2.5 Data Analysis

Dichotomous variables were described as frequencies with absolute numbers, and continuous variables were presented as means with standard deviations or medians with ranges. The meta-analysis, forest plots, and funnel plots were drawn using Review Manager 5.3. The Mantel–Haenszel model was used to analyze dichotomous variables, and the inverse variance model was used to analyze continuous variables. Results of dichotomous variables were presented as odds ratios (OR) with 95% confidence intervals (CI), whereas results of continuous variables were presented as the mean difference with 95% CI. Chi^2 , degree of freedom, and I^2 were used for heterogeneity test between studies. A fixed-effects model was used if no significant heterogeneity, while a random-effects model was used if either the p -value of Chi^2 was significant or the I^2 was $> 50\%$. A p -value of ≤ 0.05 was considered statistically significant.

3 Results

3.1 Study Selection

The initial literature search yielded 437 articles after removing duplication. Upon reviewing titles and abstracts, 54 studies remained and full-text articles were obtained. Of these, 3 studies were excluded as these were conference summary and without full-text articles, whereas 43 studies did not fulfill our study criteria, given that studied patients were either not of TOF only, or no comparison was made between the outcomes of patients undergoing TAP repair with or without monocusp valve reconstruction. Finally, 8 articles were included in our analysis (Fig. 1),^{10–17} which consisted of only 1 randomized controlled trial (RCT)¹² while the others were retrospective cohort study.^{10,11,13–17}

3.2 Study Characteristics

Baseline characteristics were variably reported in these 8 studies. Only 5 studies^{10,12,13,15,16} reported gender ratio in both the study group and the control group, other studies only reported the number of patients in each group. The mean age at operation was reported in 7 studies,^{10,12–17} and the mean body weight was reported in 5 studies^{10,12,13,15,17}. The 8 included studies formed a pool of 526 TOF patients in

total. Of these, 300 patients underwent TAP repair with monocusp valve reconstruction (monocusp group) and 226 patients underwent TAP repair without monocusp valve reconstruction (non-monocusp group). The gender ratio of male to female was 1.2: 1 (119 males, 97 females) in the monocusp group compared to 1:1 (87males, 90females) in the non-monocusp group. The specific gender of 133 patients was not reported. The mean age and mean weight at operation were 42.91 ± 39.13 months and 9.00 ± 4.43 kg respectively in the monocusp group, compared with 33.84 ± 29.32 months and 8.32 ± 3.32 kg respectively in the non-monocusp group (Table 1). There was no significant difference between the two groups in patient baseline characteristics according to forest plots.

3.3 Bias analysis and outcomes assessment

The assessment of 7 cohort studies by the Tool to Assess Risk of Bias in Cohort Studies revealed a low level of bias. Similarly, the 1 RCT included in our study showed a low level of bias determined by the Review Manager (Table 2). According to the funnel plots, publication bias of all outcomes was at a low level. Furthermore, findings from GRADEpro showed that the primary outcome (perioperative mortality) had a moderate quality of evidence; one of the secondary outcomes (moderate or severe pulmonary regurgitation in the perioperative period) had a high quality of evidence; other secondary outcomes were however very low in the quality of evidence.

3.4 Outcomes analysis

3.4.1 Perioperative Mortality

There was 1% (3/300) perioperative death in the monocusp group compared with 1.7% (4/226) in the non-monocusp group, which was not significantly different between the two groups (OR = 0.57, 95% CI 0.14–2.32, $p = 0.43$). Heterogeneity assessment showed an I^2 value of 0%, indicating no significant heterogeneity in this analysis and thus, a fixed-effects model was used (Fig. 2).

3.4.2 Cardiopulmonary Bypass Time

There was a significant difference in the perioperative cardiopulmonary bypass time between the two groups, with the standard mean difference of 21.86 (95% CI 16.51–27.21, $p < 0.0001$). A total of 6 studies^{10,12,13,15–17} reported this outcome, with 226 patients in the monocusp group and 187 patients in the non-monocusp group for the analysis. For this analysis, the I^2 value was 42%, indicating no significant heterogeneity in this analysis and thus, a fixed-effects model was used (Fig. 3).

3.4.3 Aortic cross-clamp Time

A significant difference in the perioperative aortic cross-clamp time between the two groups was demonstrated with the standard mean difference of 11.20 (95% CI 1.06–21.34, $p = 0.03$). Data were extracted from 6 studies,^{10,12,13,15–17} with 226 patients in the monocusp group and 187 in the non-monocusp group for the analysis. An I^2 value of 71% indicated significant heterogeneity in this analysis, thus, a random-effects model was used (Fig. 3).

3.4.4 Ventilation Duration

There was no significant difference in the perioperative ventilation duration between the two groups with the standard mean difference of -14.06 (95% CI -39.76–11.64, $p = 0.03$). Data were obtained from 4 studies^{12–15} and comprised of 207 patients in the monocusp group and 156 in the non-monocusp group for the analysis. An I^2 value of 93% indicated significant heterogeneity in this analysis. Thus, a random-effects model was used (Fig. 3).

3.4.5 Length of Stay in the Intensive Care Unit

There was a significant difference in the length of stay in the Intensive Care Unit (ICU) between the two groups with the standard mean difference of -1.65 (95% CI -3.09 - -0.22, $p = 0.02$). Data were obtained from 5 studies^{12–14, 16, 17} and comprised of 218 patients in the monocusp group and 130 patients in the non-monocusp for the analysis. An I^2 value of 64% indicated significant heterogeneity in this analysis, and thus, a random-effects model was used (Fig. 3).

3.4.6 Length of Stay in the Hospital

No significant difference was demonstrated in the length of stay in the hospital between the two groups with the standard mean difference of -1.55 (95% CI -3.90 - -0.81, $p = 0.20$). Data were extracted from only 3 studies^{15–17} including 97 patients in the monocusp group and 125 patients in the non-monocusp group for the analysis. An I^2 value of 45% indicated no significant heterogeneity in this analysis, and thus, a fixed-effects model was used (Fig. 3).

3.4.7 Perioperative Right Ventricular Outflow Tract Pressure Gradient

There was no significant difference in the perioperative ROVT pressure gradient between the two groups with the standard mean difference of -1.04 (95% CI -4.56–2.47, $p = 0.56$). Data were obtained from 4 studies^{12–15} including 207 patients in the monocusp group and 156 patients in the non-monocusp group for the analysis. An I^2 value of 86% indicated significant heterogeneity in this analysis, and thus, a random-effects model was used (Fig. 3).

3.4.8 Moderate or Severe Pulmonary Regurgitation in the Perioperative Period

A total of 6% (15/232) of patients in the monocusp group developed moderate or severe perioperative PR compared with 73.6% (123/167) in the non-monocusp group, which was significantly different between the two groups (OR = 0.02, 95% CI 0.00–0.15, $p = 0.0001$). Data were obtained from 5 studies^{10, 12–15} comprised of 232 patients in the monocusp group and 167 patients in the non-monocusp for the analysis. An I^2 value of 81% indicated significant heterogeneity in this analysis, thus, a random-effects model was used (Fig. 2).

4 Discussion

Our analyses have demonstrated several differences in the perioperative outcomes comparing TOF patients undergoing TAP repair with and without monocusp valve reconstruction. TAP repair with monocusp valve reconstruction was associated with significant benefits to the perioperative cardiopulmonary bypass time, perioperative aortic cross-clamp time, mean length of ICU stay, and the degree of perioperative PR. In particular, several studies^{4,9,12-15} have reported a prominent effect of monocusp valve reconstruction in reducing the degree of perioperative PR, which may then confer to improvements of respiratory symptoms and quality of life. Although the cost of hospitalization has not been investigated by any studies, the evidence of the shorter length of stay in the ICU may potentially reduce the healthcare cost in patients undergoing TAP repair with monocusp valve reconstruction.

Analyses of other clinical outcomes including perioperative mortality, ventilation duration, length of hospital stay, and perioperative right ventricular outflow tract pressure gradient demonstrated some minor superiority in the monocusp group when compared with those without monocusp valve reconstruction, the differences however was not statistically significant.

To reduce the risk of perioperative PR, TAP repair should be avoided to preserve the pulmonary valve.⁹ This may be feasible in the repair of early TOF.¹⁸ However, TOF patients with a severe deformity of pulmonary artery annulus leading to severe RVOT obstruction would necessitate a TAP repair. Our analyses have shown the advantages of TAP repair with monocusp valve reconstruction in the perioperative in-hospital period. We have excluded investigating long-term postoperative outcomes, given that very few studies to date have compared the long-term outcomes of TAP repair with or without monocusp valve reconstruction in patients with TOF, and the limited data available would not be sufficient for a meta-analysis. Besides, some studies have shown a low mortality rate at two or three years after surgery for TOF^{4,19,20} which may result in a higher rate of loss to follow-up, leading to lower quality of long-term outcome data.

In our analysis, no differentiation was imposed on the types of materials of the monocusp valve being used in the studies, which include autologous pericardium and polytetrafluoroethylene (PTFE). This allows a larger sample size in the analyses to improve the impacts of the results of our analysis. Besides, we have noted that 1 of the included studies has compared outcomes between the autologous pericardium and PTFE monocusp valve, which showed no significant difference in the outcomes at 3 years.¹⁴

Our meta-analysis represents the first to combine clinical studies to address a currently controversial practice concerning monocusp valve reconstruction during TAP repair in patients with TOF. However, our study was limited by the lack of data and large-scale high-quality studies, which therefore, warrants a large, multicenter, randomized, prospective study to validate our findings.

5 Conclusion

Transannular patch repair with monocusp valve reconstruction seems to have significant advantages on some perioperative outcomes of TOF patients, but demonstrate no significant benefit on perioperative mortality. Further well-designed, multicenter, randomized, prospective studies focusing on differences between TAP repair with and without monocusp valve reconstruction with large samples are needed.

Abbreviations

TOF Tetralogy of Fallot

TAP Transannular Patch

RVOT Right Ventricular Outflow Tract

VSD Ventricular Septal Defect

RVH Right Ventricular Hypertrophy

ICU Intensive Care Unit

GRADE Grading of Recommendations Assessment, Development and Evaluation

PRISMA Preferred Reporting Items in Systematic Reviews and Meta-Analysis

RCT Randomized Controlled Trial

OR Odds Ratio

CI Confidence Interval

Declarations

Ethics approval and consent to participate

Not applicable. This systematic review and meta-analysis did not involve research on any human subjects requiring informed consent.

Consent for publication

Not applicable.

Availability of data and materials

All relevant data has been provided in figures, tables and text.

Competing interests

There are no financial disclosures or conflicts of interest for any of the authors.

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Authors' contributions

Study concept: Tiange Li and Yunfei Ling. Study design: Tiange Li, Yunfei Ling and Xiaodong Wei. Data acquisition: Tiange Li and Xiaodong Wei. Quality control of data and algorithms: Tiange Li and Zheng Chai. Data analysis: Tiange Li and Zhongze Cao. Manuscript preparation: Tiange Li, Xiaodong Wei and Kerun Chen. Manuscript editing: Yongjun Qian, Tiange Li and Yunfei Ling. Manuscript review: Xiaodong Wei and Yunfei Ling. All the authors have read and approved the final version of the manuscript.

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Tables

Due to technical limitations, table 1 & 2 png are only available as a download in the Supplemental Files section.

Figures

Figure 1

Figure of search results and study selection

Figure 2

Forest plot demonstrating results of dichotomous variables

Figure 3

Forest plot demonstrating results of continuous variables

Supplementary Files

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