

Residual anatomic, hemodynamic and functional abnormalities after Tetralogy of Fallot repair: a systematic literature review

Anormalidades residuais anatômicas, hemodinâmicas e funcionais após a correção da Tetralogia de Fallot: uma revisão sistemática da literatura

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ABSTRACT

Objective: Most patients are left with residual abnormalities after post-surgical repair of Tetralogy of Fallot. The aim of this study is to assess anatomic, hemodynamic and functional outcomes after surgical repair of this congenital heart disease, long-term follow-up and factors that influence these results. **Methods:** It was performed a systematic literature review through “Preferred Reporting Items for Systematic review and Meta-Analysis Protocols” (PRISMA-P) checklist. The following databases were included: PubMed, Virtual Health Library, Cochrane Library, and Scientific Electronic Library Online of studies published from 2018 to 2022. **Results:** The transannular patch and homograft/conduit implant techniques expose patients to chronic pulmonary regurgitation, while valve-sparing procedures may cause residual pulmonary stenosis. After surgical repair, most patients remain with residual lesions, such as right ventricular dilatation from chronic pulmonary regurgitation, pulmonary artery stenosis, right ventricular outflow tract aneurysm, tricuspid regurgitation, ventricular septal defects and dilation of aorta. Dysfunction of the right ventricle may appear and, subsequently, the left, arrhythmias, right ventricular strain, pulmonary edema, heart failure, and sudden death. Anatomical and functional cardiac alterations may arise, like obstruction of the right ventricular outflow tract, pulmonary artery branch stenosis, and pulmonary valve regurgitation. **Conclusion:** Residual lesions after repair lead to significant morbidity in adult patient's lives. The knowledge of outcomes provides opportunities to assess treatment decisions and guide surgical strategies. It is essential to evaluate the adverse clinical events to improve the quality of life of these patients and reduce morbidity and mortality.

Keywords: Tetralogy of Fallot; heart defects, congenital; cardiovascular surgical procedures; treatment outcome.

RESUMO

Objetivo: após o reparo cirúrgico da Tetralogia de Fallot, a maioria dos pacientes apresenta anormalidades residuais. O objetivo deste estudo é avaliar os resultados anatômicos, hemodinâmicos e funcionais após o tratamento dessa cardiopatia congênita, o seguimento a longo prazo e os fatores influenciadores. **Métodos:** revisão sistemática da literatura por meio do *checklist* “Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols” (PRISMA-P). Foram incluídas as bases de dados PubMed, Biblioteca Virtual em Saúde, Cochrane Library e Scientific Electronic Library Online de estudos publicados de 2018 a 2022. **Resultados:** as técnicas de retalho transanular e implante de homoenxerto/conduto expõem os pacientes à regurgitação pulmonar crônica, enquanto os procedimentos poupadores de válvula podem causar estenose pulmonar residual. Após o reparo, a maioria dos pacientes permanece com lesões residuais, como a dilatação do ventrículo direito por regurgitação pulmonar crônica, estenose da artéria pulmonar, aneurisma da via de saída do ventrículo direito, regurgitação tricúspide, defeitos do septo ventricular e dilatação da aorta. Pode aparecer disfunção do ventrículo direito e, posteriormente, do esquerdo, arritmias, distensão ventricular direita, edema pulmonar, insuficiência cardíaca e morte súbita. Podem surgir alterações cardíacas anatômicas e funcionais, como obstrução da via de saída do ventrículo direito, estenose do ramo da artéria pulmonar e regurgitação da valva pulmonar. **Conclusão:** lesões residuais após o reparo levam à morbidade significativa na vida adulta. O conhecimento dos resultados fornece oportunidades para melhor decidir o tratamento e orientar estratégias cirúrgicas. É fundamental avaliar os eventos clínicos adversos para melhorar a qualidade de vida e reduzir a morbimortalidade.

Palavras-chave: Tetralogia de Fallot; cardiopatias congênitas; procedimentos cirúrgicos cardiovasculares; resultado do tratamento.

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INTRODUCTION

Tetralogy of Fallot (ToF) is one of the most common congenital cardiac disorders, accounting for roughly 10% of all congenital heart malformations and representing the most prevalent form of cyanotic congenital cardiac disease.¹⁻³ Its main features include a typical ventricular septal defect (VSD) associated with an anterior displacement of the infundibular septum, leading to different degrees of overriding aorta, hypertrophy of the right ventricle (RV), and obstruction of the right ventricular outflow tract (RVOT) at several levels. Nevertheless, ToF includes a broad anatomical and clinical spectrum, mainly determined by the morphology of the RVOT, the size of the pulmonary valve (PV), and the pulmonary artery branches (PAs).^{2,3} These anatomopathological changes result in cyanosis and other symptoms, which are determined by the degree of RVOT obstruction and PAs anatomy and can range from asymptomatic patients to severe hypoxemia.⁴

An increased number of patients reach adulthood after repaired ToF due to advances in interventional techniques and the improvement of specialized medical care.⁵⁻⁷ Performing surgical treatment in the first year of life improves the patient's survival rate and reduces the risk of sudden death⁴.

Total correction of TOF has low perioperative mortality and good long-term survival, but the need for reinterventions is high.⁵ Generally, these patients require constant surgical reoperations to minimize the long-term effects of volume and pressure overloads in cardiac chambers.⁶ Post-surgical repair, most patients remain with residual anatomic, hemodynamic, and functional abnormalities, which reduces their survival.⁷ It is important to know the residual lesions after surgical repair because they may influence the trajectory of care.

The objective of this study is to analyze the outcomes after surgical repair of ToF, long-term follow-up and factors that influence these results. So that it allows for assessing the residual anatomic, hemodynamic, and functional abnormalities of a ToF repair.

MATERIAL AND METHODS

A systematic literature review of the studies that analyzed the main outcomes of surgical repair of ToF was performed. This is a quantitative and retrospective study of the literature. This study has been included in the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols

(PRISMA-P) checklist. The following databases were PubMed, Virtual Health Library (VHL) from Latin American and Caribbean Center on Health Sciences Information (BIREME), Cochrane Library, and Scientific Electronic Library Online (SciELO) of studies published from 2018 to 2022. A systematic search was made for published articles with filters for free access to full text, research in humans, and the best match articles.

The descriptors used for the search followed the description of the Health Sciences Descriptors (DeCS) terms of the Virtual Health Library developed from the Medical Subject Headings (MeSH) of the United States National Library of Medicine. The keywords were combined using the Boolean operators OR and AND, without linguistic restriction using the following words: "Tetralogy of Fallot", "repair", "outcomes" e "follow-up". All the articles obtained in the databases through the research suffered the application of inclusion and exclusion criteria.

Primarily, the review consisted of analyzing the titles and abstracts of the articles related to the topic, which were identified and evaluated, to select those that met the eligibility criteria, such as being published between 2018 - 2022, having in their title and/or in their abstract some of the descriptors used in the searches to the databases.

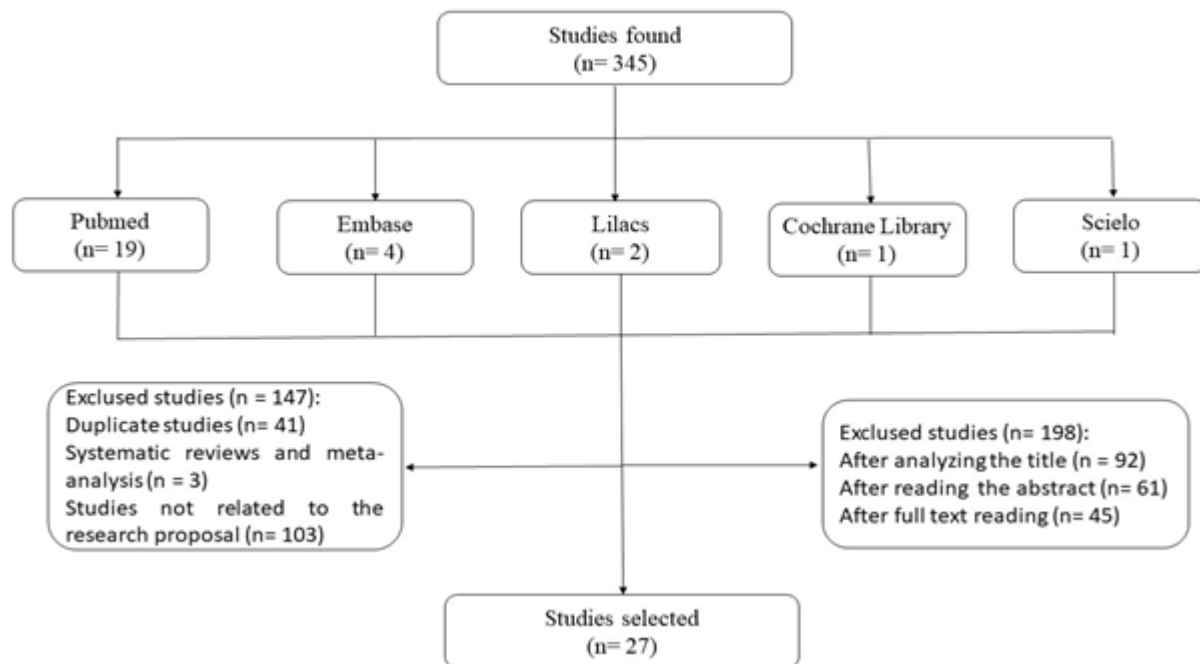
Articles that presented repeated information, animal studies, letters to the editor, comments, errata, and duplicates or that the topic addressed was unrelated to the research proposal were excluded.

The studies that were selected as relevant and generated doubts were retained for further analysis of the text. Secondly, the review consisted of extracting data from the studies selected previously. All eligible records were read, and data available in the text were extracted. Despite appearing in the search results, all studies without the subject adequately with the variables of interest in this study were not included.

Other exclusion criteria were nonoriginal articles, systematic reviews, case reports, meta-analyses, non-published work, or studies not describing any of the outcomes of ToF repair. Additionally, references and related citations were manually searched to identify any further relevant articles, so that studies not found in the database search were included. The presentation of the articles found, both included and excluded, and their applied distribution is shown in the PRISMA flow (Figure 1).



Figure 1. The search flowchart shows the study selection process for this literature review.



RESULTS

By searching the databases cited, the search found 345 studies in the period, but 318 were rejected, as they did not meet the inclusion criteria. Thus, a total of 27 publications were selected on the subject based on the inclusion and exclusion criteria, covering the main outcomes of surgical repair of ToF in the period highlighted in this study, which were accessed and read for

subsequent selection of the characteristics that incorporated the research. The data were extracted and processed using a tool designed by the authors with the following fields: authors, year of publication, periodical, description of the methodology, type of surgical intervention, and main results. The characteristics of each study are presented in Table 1.

Table 1. The main aspects of residual anatomic, hemodynamic, and functional alterations after Tetralogy of Fallot repair, in chronological order, found in the literature review.

| Author(s) (year) | Periodical | Methodology | Surgical intervention | Results |
|---|---|--|---|---|
| DiLorenzo <i>et al.</i> ²⁶ (2018) | Journal of the American Society of Echocardiography | Retrospective cohort study of 47 patients | TAP repair and homograft/conduit approach | Measurement of RV strain in the immediate postoperative period, using echocardiography, showed worse strain compared to the preoperative measurement. |
| Hickey <i>et al.</i> ¹⁷ (2018) | The Annals of Thoracic Surgery | Retrospective cohort study of 434 patients | TAP repair and pulmonary valve-sparing | Risk factors for RV dilation included TAP approach, worse degree of postoperative PR, larger RV end-diastolic diameter at the time of diagnosis, and higher preoperative infant weight. |
| Kwak <i>et al.</i> ²¹ (2018) | Korean Circulation Journal | Retrospective cohort study of 50 patients | Extensive commissurotomy with annulus saving and RV infundibular area | Preserving the pulmonary valve and RV infundibular area may minimize long-term ventricular dysfunction. |
| Smith <i>et al.</i> ¹⁵ (2018) | JAMA Cardiology | Retrospective cohort study of 3,283 patients | Staged repair with initial palliative shunt and primary repair with non-valve-sparing | Increased risk of early mortality is associated with staged and non-valve-sparing approaches. |

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| Author(s) (year) | Periodical | Methodology | Surgical intervention | Results |
|--|--|---|--|---|
| Ramdjan <i>et al.</i> ²⁰ (2018) | Journal of cardiovascular electrophysiology | Retrospective longitudinal study of 29 patients | Primary total correction and initial palliative shunt | Atrial fibrillation can develop at a younger age and can worsen ventricular dysfunction, in addition to presenting rapid progression. |
| Andrade <i>et al.</i> ²⁹ (2019) | American Heart Association | Prospective cross-sectional study of 103 patients with a control group of 63 patients | TAP repair and initial palliative shunt | Patients had lower LV ejection fraction, lower LV mass index, lower LV mass/volume ratio and impaired left atrial function. |
| Castilhos <i>et al.</i> ⁶ (2019) | Pediatric Cardiology | Retrospective cohort study of 206 patients | Transventricular approach via right ventricle and transatrial-transpulmonary route and initial palliative shunt | Age at surgery, QRS duration, and tricuspid regurgitation moderate were independent risk predictors for atrial flutter/fibrillation. |
| Dłużniewska <i>et al.</i> ⁷ (2019) | Cardiovascular Ultrasound | Retrospective cohort study of 83 patients | TAP repair and initial palliative shunt | Patients showed a severe decrease in oxygen consumption, a lower peak oxygen pulse and a lower heart rate during peak exercise. |
| Mouws <i>et al.</i> ¹⁶ (2019) | Seminars in Thoracic and Cardiovascular Surgery | Retrospective cohort study of 177 patients | Transatrial-transpulmonary approach with TAP or valve-sparing and initial palliative shunt | Pulmonary valve sparing had better survival and lower occurrence of PR. |
| Simon <i>et al.</i> ¹¹ (2019) | Seminars in Thoracic and Cardiovascular Surgery | Retrospective cohort study of 42 patients | Extensive right ventriculotomy and limited right ventriculotomy with transatrial ventricular septal defect closure | Extensive ventriculotomy was associated with the development of arrhythmia, ventricle dysfunction, reoperation and death. |
| Ducas <i>et al.</i> ⁹ (2020) | Canadian Journal of Cardiology | Retrospective cohort study of 230 patients | TAP repair and pulmonary valve-sparing | Reintervention of any type was significantly more common in the TAP repair group during both childhood and adulthood. |
| Lee <i>et al.</i> ²³ (2020) | European Journal of Cardio-Thoracic Surgery | Retrospective cohort study of 190 patients | TAP repair and pulmonary valve-sparing | Pulmonary valve replacement before the onset of advanced symptoms, tachyarrhythmias and ventricular dysfunction may further improve long-term survival. |
| Hoelscher <i>et al.</i> ²⁵ (2020) | Annals of Pediatric Cardiology | Retrospective cohort study of 85 patients | TAP repair, infundibular patch, commissurotomy, homograft approach | Not only RV hypertrophy and dysfunction but also LV dysfunction was a strong predictor for adverse outcome. |
| Padalino <i>et al.</i> ¹⁰ (2020) | European Journal of Cardio-Thoracic Surgery | Retrospective cohort study of 720 patients | TAP repair, pulmonary valve-sparing and homograft/conduit approach | Pulmonary valve-sparing associated with fewer reoperations, postoperative complications and late adverse events. |
| Ali <i>et al.</i> ²⁴ (2021) | European Review for Medical and Pharmacological Sciences | Retrospective cohort study of 219 patients | TAP repair and initial palliative shunt | An increase of ventricular dimensions and worsening of right and left ejection fractions were found over an average period of 5 years of follow-up. |

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| Author(s) (year) | Periodical | Methodology | Surgical intervention | Results |
|--|---|--|---|---|
| Blais <i>et al.</i> ⁸ (2021) | JAMA Network Open | Retrospective cohort study of 683 patients | TAP repair and pulmonary valve-sparing | Valve-sparing procedures had increased 30-year survival, fewer cardiovascular reinterventions and pulmonary valve replacements. |
| Blais <i>et al.</i> ¹³ (2021) | Canadian Journal of Cardiology | Retrospective cohort study of 960 patients | TAP repair and pulmonary valve-sparing | ToF patients with pulmonary atresia or those with a concomitant genetic condition were associated with increased mortality, interventions and adverse cardiac events. |
| de Alba <i>et al.</i> ³⁰ (2021) | International Journal of Cardiology | Retrospective observational study of 48 patients with a control group of 20 patients | TAP repair, pulmonary valve-sparing and homograft/conduit approach | LV strain abnormalities and fibrosis are correlated with changes in ventricular volumes and function. |
| Dluzniwska <i>et al.</i> ²⁷ (2021) | Indian Heart Journal | Retrospective cohort study of 52 patients with a control group of 33 patients | TAP repair, pulmonary valve-sparing and initial palliative shunt | The decreased exercise capacity is correlated with impaired RV and LV ventricle function. |
| Leonardi <i>et al.</i> ¹⁹ (2021) | International Journal of Environmental Research and Public Health | Retrospective cohort study of 342 patients | Transventricular approach via right ventricle and transatrial- transpulmonary route and initial palliative shunt | Transventricular and ventricular septal defect closure and previous palliation significantly affected LV function and RV size, respectively. |
| Kwak <i>et al.</i> ¹⁴ (2021) | Korean Circulation Journal | Retrospective cohort study of 180 patients | TAP repair and initial palliative shunt | TAP repair is associated with the need for valve replacement reoperations, arrhythmia and RV dilatation. |
| Ravaglioli <i>et al.</i> ³ (2021) | Cardiovascular Ultrasound | Retrospective cohort study of 239 patients | TAP repair, infundibular patch and commissurotomy | Pulmonary valve hypoplasia and size change of pulmonary arteries affects surgical strategy and follow- up. |
| Agarwal <i>et al.</i> ⁵ (2022) | Heart Views | Retrospective cohort study of 230 patients | TAP repair, pulmonary valve-sparing and homograft/conduit approach | Worse survival and adverse outcomes in cases of pulmonary atresia and in homograft/conduit approach. |
| Latus <i>et al.</i> ²⁹ (2022) | Journal of the American Heart Association | Prospective cohort study of 296 patients | Staged repair with initial palliative shunt and primary repair with TAP or pulmonary valve-sparing | RVOT stenosis after repair has been linked with RV remodeling, ventricular tachycardia and cardiac death. |
| Kleinöder <i>et al.</i> ² (2022) | Pediatric and Congenital Cardiology | Retrospective cohort study of 306 patients | TAP repair, pulmonary valve-sparing and homograft/conduit approach | TAP repair, primary palliation and aortopulmonary collateral arteries increase the risk of pulmonary valve replacement. |

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| Author(s) (year) | Periodical | Methodology | Surgical intervention | Results |
|---|---|--|--|--|
| Kobayashi <i>et al.</i> ¹⁸ (2022) | The Annals of Thoracic Surgery | Retrospective cohort study of 330 patients | Staged repair with initial palliative shunt and primary repair with TAP or pulmonary valve-sparing | Initial palliative shunt can avoid primary TAP repair, facilitate pulmonary valve annulus growth and result in less surgical reinterventions. |
| Mira <i>et al.</i> ³⁰ (2022) | Journal of Cardiovascular Magnetic Resonance | Retrospective cohort study of 192 patients | TAP repair, pulmonary valve-sparing and homograft/conduit approach | Pathological remodeling patterns after ToF repair, such as more circular left ventricle (decreased eccentricity), dilated (increased sphericity) LV base, increased RV apical sphericity, and decreased RV basal sphericity. |

RV: right ventricle; LV: left ventricle; TAP: transannular patch; PR: pulmonary regurgitation.

DISCUSSION

The satisfactory repair of ToF results in a complete closure of VSD, a functioning PV, and no residual RVOT obstruction.⁸

The choice of surgical technique may influence long-term outcomes, as it may result in residual damage to the patient. The first intracardiac repair included a VSD closure and RV infundibular resection.⁹

As intracardiac repair became increasingly used, the surgical techniques evolved over time. The first surgical approach was right ventriculotomy/transventricular, however, the transatrial-transpulmonary form was introduced to minimize structural damage to the RV and preserve its function, consequently, avoiding major long-term complications such as arrhythmia, ventricle dysfunction, reoperation and death.¹⁰⁻¹² These types of repair can be with or without pulmonary valve preservation/transannular patch (TAP) and also can be treated primarily with conduits from the RV to the PAs.^{4,9,10} However, this technique had the unintended consequence of causing severe pulmonary regurgitation (PR) and also progressive RV dilatation.

Long-standing PR initiates a downward spiral of chronic RV volume overload and RV dysfunction, associated with an increased risk of exercise intolerance, heart failure, sustained ventricular arrhythmia, sudden death, and a need for repeated cardiac interventions.¹²⁻¹⁵

These findings led to further modifications in surgical techniques during the 1980s-1990s to favor preservation of the pulmonary annulus with the hopes of reducing the severity of PR and allowing some degree of residual stenosis to improve outcomes.⁹ Therefore, the techniques of TAP and homograft/conduit implant expose patients to chronic PR, while valve-sparing procedures may incompletely relieve pulmonary obstruction, causing residual pulmonary stenosis.¹⁵⁻¹⁷ Furthermore, another surgical strategy includes a palliative approach through a staged repair using the Blalock-Taussig shunt. It facilitates the growth of the pulmonary valve annulus so that repair can be performed later with preservation of the valve to avoid primary TAP repair and adverse events from PR.^{15,18}

However, patients undergoing initial shunt palliation may also have residual deleterious effects, such as pulmonary artery distortion, excessive pulmonary blood flow, left heart overload and increased RV dilatation, and pulmonary vascular resistance.^{14,15,19,20,21}

After surgical repair, most patients are left with residual lesions that will need reoperation, such as RV dilatation from chronic PR, PAs stenosis, RVOT aneurysm, tricuspid regurgitation, residual VSD, and dilation of aorta.^{1,8,22,23,24}

With the progression of PR, dysfunction of the RV appears and subsequently the left, arrhythmias, and sudden death.^{4,7,11} There is left ventricular (LV) dilation along with progressive RV dilation, which suggests an unfavorable interventricular interaction, leading to hypertrophy and dysfunction of both cardiac chambers.^{21,24}

Hoelscher *et al.*²⁵ showed that some patients with ToF repaired presented a progression of RV dilatation over time, while others had an early progressive RV dilatation due to postoperative remodeling and subsequently stabilized during a follow-up of three years. DiLorenzo *et al.*²⁶ revealed that in the early post-operative period following initial TOF repair, RV dysfunction is associated with a longer need for intensive care as well as a longer need for inotropic support. There is a RV global longitudinal strain worsens in the early post-operative period following surgical repair for TOF but is overall diminished by two years following surgical repair. As the patient ages, these abnormalities become harmful, causing exercise intolerance, dysrhythmias, endocarditis, heart failure symptoms, and even death.^{21,27,28}

Dłużniewska *et al.*²⁷ mentioned that exercise intolerance in adults with repaired ToF is markedly depressed and correlates with impaired RV function and LV dysfunction, suggesting right-left ventricular interaction. The RV dilation can lead to RV strain and subsequently affect the LV, causing an abnormality of repolarization that is an indicator of cardiac dysfunction. So, these conditions reflect different long-term adverse adaptations to abnormal hemodynamics and have prognostic implications.



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The residual pulmonary stenosis over time can trigger a reperfusion injury of the lungs, which manifests as potentially fatal pulmonary edema.¹ Postoperatively, neonates may have decreased sensitivity to beta-adrenergic receptor stimulation and develop adrenal insufficiency, which may lead to a state of low cardiac output at follow-up.¹⁴ Other postoperative complications include conduit rupture, pericardial or pleural effusion, endocarditis, venous thrombosis, PAs perforation, coronary artery compression, sepsis, valve thrombosis, junctional ectopic tachycardia, chylothorax, bleeding requiring reoperation, superficial wound infection, central nervous system paresthesia and respiratory distress.¹⁶

Patients with repaired ToF have lower LV ejection fraction due to impaired systolic and diastolic function, adverse remodeling with extracellular matrix expansion, reduced cardiomyocyte mass causing LV atrophy, and impaired left atrial function.^{29,30}

The RVOT stenosis and RV dilation represent postoperative remodeling and, over time, a gradual enlargement occurs with a decline in RV systolic function, which is associated with increased PR.^{25,30} Unfavorable remodeling mechanisms result in a cycle of metabolic and structural changes.

The anatomical alterations resulting from remodeling include more circular LV with decreased eccentricity, dilated LV base with increased sphericity, increased RV apical sphericity, and decreased RV basal sphericity.³⁰

Mira *et al.*³⁰ determined these alterations as “maladaptive remodeling”, which refers to shape and size changes occurring due to an adverse cycle of metabolic and structural changes resulting in heart failure. Although the hemodynamic burden from chronic RV volume load may be tolerated without symptoms during childhood, evidence suggests that the incidence of arrhythmia, heart failure, and death increases substantially in adult life. Thus, initiating a surgical intervention to treat pulmonary or cardiac failure can help to delay the progression of cardiomyopathic changes and improve the long-term prognosis.

It is not only PR that is involved with RV dilation. Other factors are also involved, such as the age of the patient when the repair was performed, the type of repair, the presence of a systemic-pulmonary shunt for previous palliation, RVOT residual obstruction, and PAs stenosis.²⁴ As ventricular dilation develops and the patient ages, adverse cardiac events arise, such as atrial arrhythmias, failure heart symptoms, junctional ectopic tachycardia, persistent complete heart block, supra-ventricular tachyarrhythmias, symptomatic sustained ventricular tachycardia, and asymptomatic no sustained ventricular arrhythmias.^{6,21,24}

Chronic volume overload and persistent pressure contribute to the persistence of electrical and structural remodeling of the heart. This favors the development of arrhythmias together with the presence of hypertrophy and extensive fibrotic regions in the atria, allowing multiple reentrant circuits to occur.³⁰

Thus, the rate of survival in repaired ToF is associated with the concomitant presence of comorbidities, such as arrhythmia, cardiac arrest, congestive heart failure, myocardial ischemia, endocarditis, stroke, and other congenital and genetic abnormalities.^{13,15,21}

These conditions are associated with adverse cardiovascular events that require hospitalization, such as endocarditis, arrhythmia, and heart failure.⁸

Smith *et al.*¹⁵ showed that in the 25-year follow-up period, most deaths were associated with the underlying diagnosis of ToF and mediated by arrhythmias and congestive heart failure. In addition, the outcomes can be influenced by the severity of the ToF, which is described by the pre-operative size of the pulmonary valve and PAs, RV and pulmonary artery pressure gradient, and oxygen saturation.¹⁷ Also, prematurity and small body size—associated lesions were associated with increased mortality from residual lesions.¹⁵ Therefore, these data indicate that residual morbidity remains a major factor affecting the survival of these patients and predisposes to a greater need for surgical reinterventions.

It is essential to point out the limitations found in carrying out this systematic review of the literature. Among the limitations, the publication period's delimitation stands out, excluding relevant studies previously published. Another limitation is the general heterogeneity between the results obtained, since ToF is a complex congenital disease with anatomical variables, rarely analyzed separately, which can interfere with long-term results.

One important limitation is that the late sequelae of TOF repair typically take decades to manifest, so it is impossible to draw firm conclusions about the surgical repair's long-term outcomes and other consequences. Most studies are retrospective cohort studies, which have a limited follow-up of the analyzed group without taking into account individual patient data.

The retrospective nature of the cohort studies collected may increase the possibility of information bias and misclassification of study groups. Despite all this data collected, there is still a lack of more multicenter cohort studies with a larger patient population sample. So, it is still essential that more studies of this type, as well as prospective cohort and randomized trials, be performed to analyze the results of the surgical repair of the ToF, its residual lesions, and its consequences for the patient.

The findings of this study may encourage further studies and help healthcare professionals understand the variety of adverse events that can occur after surgical repair of the ToF. Therefore, it is relevant to elaborate and publish new studies to provide more information about the clinical outcomes after ToF repair.

CONCLUSION

Results were good from the earliest era of total correction, with most of the patients reaching adulthood. Despite medical advances, ToF remains a life-long disease with high morbidity in adult life due to residual post-surgical structural lesions.

Surgical repair of ToF can be performed with low perioperative mortality and good long-term survival, but as more and more patients continue to survive into adulthood, many will require subsequent interventions and reoperations in follow-up. Most patients are left with residual anatomic, hemodynamic, and functional abnormalities post-repair.

The knowledge of these ToF outcomes provides opportu-



nities to assess treatment decisions and guide surgical strategies for patients with repaired ToF. So, it is essential to promptly identify and evaluate the full range of residual lesions in order to intervene in these alterations to improve patients' quality of life and reduce morbidity and mortality.

Conflicts of interest

The authors declare that there is no conflict of interest in carrying out this work.

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