ANNOTATION

Dissertation by Azhar Muslyumkanovna Kabdullina on the topic: "Combination of Radiological Imaging Methods in Assessing Functional Efficiency and Predicting Outcomes of Surgical Correction of Tetralogy of Fallot", submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D10102 – "Medicine".

Relevance.

etralogy of Fallot (TOF) is the most common cyanotic congenital heart defect, characterized by four main features: ventricular septal defect (VSD), right ventricular outflow tract obstruction (RVOTO), right ventricular (RV) myocardial hypertrophy, and overriding aorta.

In Kazakhstan, approximately 3,000 children are born annually with congenital heart defects, and 80% of them require surgical correction. Currently, congenital heart diseases (CHD) account for more than 30% of all congenital malformations (Balmagambetova G.N., et al., 2019).

In the mid-20th century, only 20% of children with CHD survived to adulthood. Today, due to advances in pediatric cardiac surgery, mortality has significantly decreased, and most TOF patients live up to 60 years (Hsu D.T., et al., 2005). Unfortunately, many patients who undergo complete surgical repair in childhood face late complications such as heart failure, pulmonary artery stenosis, infectious endocarditis, growth and developmental delays, the need for reinterventions, and arrhythmias.

The surgical correction of TOF aims to relieve RVOTO and close the VSD. In cases of significant pulmonary valve annulus hypoplasia, extensive infundibulectomy and transannular patching are required, which often result in severe pulmonary regurgitation (PR). PR leads to chronic RV volume overload, resulting in progressive RV dilation and dysfunction, with further consequences including atrial and ventricular arrhythmias and sudden cardiac death (Alipour Symakani R.S., et al., 2023).

Timely pulmonary valve replacement (PVR) using a bioprosthesis or conduit is an effective treatment for PR after TOF repair, promoting remodeling and functional recovery of the RV. Established indications for PVR include arrhythmias, reduced exercise tolerance, worsening NYHA functional class, severe pulmonary artery stenosis, and progressive tricuspid regurgitation in combination with moderate to severe PR. However, the optimal timing for PVR in asymptomatic patients remains uncertain and debatable (Del K., 2016). Currently, the only widely accepted predictor for intervention in asymptomatic patients is an indexed RV end-diastolic volume (RVEDV) of 150–170 ml/m².

According to modern literature, there are still unresolved issues in determining the optimal timing for PVR in asymptomatic post-TOF repair patients. Furthermore, no studies have evaluated the contractile and relaxation function (strain) of both ventricles in children following TOF repair using MRI as a predictive tool for the need for PVR. Considering these factors, this study aims to use multislice computed tomography (MSCT) to detect complications in pediatric patients after complete TOF correction and assess the role of myocardial strain parameters in guiding the decision for PVR.

The purpose of the study: To evaluate the functional effectiveness and predict the outcomes of surgical correction of Tetralogy of Fallot (TOF) using CT and MRI methods.

Research Objectives:

1. To determine the frequency of various postoperative complications following radical correction of TOF using MSCT.
2. To assess the impact of clinical characteristics and associated factors on the likelihood of developing common postoperative complications in children, identified through MSCT.
3. To study gender-specific functional characteristics and the contractile and relaxation capacity of both ventricles in children after radical correction of TOF using the "Strain" MRI program.
4. To identify threshold values of additional parameters from the "Strain" MRI program that serve as indications for performing planned pulmonary valve replacement (PPVR).

Object of Study:

At the Department of Radiology of the "National Scientific Cardiac Surgery Center" JSC, the medical records of 613 patients (children aged 7 days to 18 years) diagnosed with Tetralogy of Fallot were analyzed from October 2011 to December 2020.

The study analyzed patients with complications after radical TOF correction and according to imaging modality used:

– MSCT data were analyzed for 116 patients (mean age 2.2±3.54 years), including 69 (80%) boys and 47 (20%) girls;

– MRI data were analyzed for 69 patients (mean age 11±4.69 years), including 45 (65%) boys and 24 (35%) girls.

Based on MRI results, right ventricular end-diastolic volume (RV EDV) ≥ 150 ml/m² was considered an indication for PPVR. The cohort was divided into two groups:

– Group 1: RV EDV < 150 ml/m²;

– Group 2: RV EDV ≥ 150 ml/m².

Research Methods:

– Echocardiography;

– Cardiac MSCT;

– Cardiac MRI (with "Strain" software);

– Statistical methods;

– NTproBNP (N-terminal pro-B-type natriuretic peptide) level assessment.

Scientific Novelty:

1. For the first time in the Republic of Kazakhstan, comparative data on the features of frequently occurring complications after radical correction of TOF were studied using MSCT (Certificate of authorship "The Role of Computed Tomography in Diagnosing Complications Following Radical Correction of Tetralogy of Fallot," No. 47707 dated 20.06.2024, NIIS RK, Appendix A).
2. A novel study was conducted using the "MRI Strain" program to assess both ventricles in children after radical correction of TOF, with comparative data obtained on gender-specific functional differences in the contractile and relaxation

capacity of the myocardium.

3. A correlation was identified between deformation of both ventricles and key indicators (RV ejection fraction, RV end-systolic volume, NTproBNP, and pressure gradient between the RV and pulmonary artery) and the RV end-diastolic volume (EDV) (Certificate of authorship No. 47818 dated 24.06.2024, NIIS RK, Appendix A).

4. The study revealed high diagnostic efficiency of the MRI "Strain" program in assessing the contractile and relaxation function of both ventricles as an additional predictor for performing planned pulmonary valve replacement (PPVR) (Certificate of authorship No. 47756 dated 21.06.2024, NIIS RK, Appendix A).

Practical Significance:

1. The results of the study and the developed diagnostic algorithm for patients after radical correction of Tetralogy of Fallot have been implemented into clinical practice (implementation act, "National Scientific Cardiac Surgery Center" JSC, Astana, 2019, Appendix B, C).

2. MSCT enabled the assessment of the risk of pulmonary artery stenosis after radical TOF correction: the relative risk (odds ratio) of developing right pulmonary artery stenosis in patients with left pulmonary artery stenosis was 6.5 times (550%) higher compared to patients without LPA stenosis ($p<0.001$).

Main Provisions to be Defended:

1. The most common complications in pediatric patients after radical TOF correction, as identified by MSCT, were stenosis of the pulmonary artery and its branches.

2. The presence of right pulmonary artery stenosis significantly increases the likelihood of developing left pulmonary artery stenosis.

3. Significant gender differences were found in the deformation characteristics of the left ventricle in children: circumferential strain in the basal inferior segment ($p<0.001$) and longitudinal strain in the mid anterolateral segment ($p<0.001$) were more pronounced in girls.

4. Circumferential strain in the basal anteroseptal and basal inferior segments of the left ventricle showed statistically significant differences between groups, indicating correlation with RV EDV and potential use as a predictor for surgery. In addition, RV end-systolic volume (ESV) was found to be directly proportional to RV EDV.

Approbation of the Work:

The dissertation was reviewed and approved at the extended meeting of the Research Institute of Radiology named after Academician Zh.Kh. Khamzabayev and the Department of Surgical Diseases (Protocol No. 11 dated 21.06.2024).

The main results and thesis findings were presented at the following events:

- XIX Asian Oceanian Congress of Radiology, July 1–4, 2021, Kuala Lumpur, Malaysia.
- VII International Congress and School for Physicians, Cardiothoracic Radiology, April 10–11, 2020, Moscow, Russia.
- International Scientific-Practical Conference "New Technologies in Radiation Diagnostics and Therapy," May 5–6, 2022, Samarkand, Uzbekistan.

A total of 8 scientific papers have been published on the dissertation topic, including:

– 1 article in a Scopus-indexed journal ("Digital Diagnostics," 30th percentile, Q3);

– 3 review articles in peer-reviewed Kazakhstani journals recommended by the Committee for Quality Assurance in the Sphere of Education and Science, MES RK;

– 4 conference papers in proceedings of international scientific-practical conferences (Kazakhstan, Uzbekistan, Russia, Korea).

Three certificates of authorship and one act of implementation into clinical practice (JSC "National Scientific Cardiac Surgery Center") were obtained.

Conclusions:

1. Cardiac CT angiography revealed that the most common complications in pediatric patients after radical correction of TOF were stenosis of the pulmonary artery and its branches (79.3%).
2. There were no statistically significant differences between groups with various types of pulmonary artery stenosis in terms of age, anthropometric parameters (height, weight, body surface area), or gender composition. No correlations were found with TOF type, presence of shunt thrombosis, history of palliative surgery, or features of surgical intervention ($p > 0.05$).
3. The presence of right pulmonary artery stenosis increases the risk of developing left pulmonary artery stenosis by 6.5 times (OR=6.5, $p<0.001$).
4. Gender-based differences were observed: end-diastolic volumes of both right and left ventricles were significantly higher in boys than in girls ($p=0.001$, $p=0.036$).
5. MRI "Strain" analysis revealed gender differences in contractile and relaxation properties of the myocardium: in the basal inferior segment, circumferential strain was more pronounced in girls ($p<0.001$); differences were also noted in the mid anterolateral segment ($p=0.006$), where longitudinal strain was significantly higher in girls ($p<0.001$); statistically significant differences in peak global circumferential strain of the right ventricle were observed between genders ($p=0.039$).
6. Circumferential strain in the basal anteroseptal and basal inferior segments of the left ventricle, measured by MRI "Strain," showed statistically significant differences between groups and correlated with RV end-diastolic volume, making it a potential predictor for surgical intervention ($p<0.003$ and $p<0.014$).
7. A statistically significant relationship was established between RV end-systolic and end-diastolic volumes ($p<0.001$), confirming the high diagnostic value of MRI "Strain" in assessing biventricular myocardial function and its role as an additional predictor for pulmonary valve replacement.

Practical Recommendations:

1. The implementation of the study results will have significant practical value in outpatient screening for preclinical right ventricular dysfunction, facilitating comprehensive surgical planning.
2. The introduction of MRI "Strain" analysis into broad clinical practice will enhance diagnostic accessibility and improve the range of available investigations in Kazakhstan, ensuring timely and effective treatment for patients after radical correction

of Tetralogy of Fallot.

3. The developed diagnostic algorithm provides a systematic approach to the examination and treatment of patient's post-radical correction of TOF, taking into account possible complications and individual hemodynamic characteristics.

4. The identified threshold values of additional parameters from the MRI "Strain" program can serve as indications for pulmonary valve replacement.

Volume and Structure of the Dissertation: The dissertation comprises 82 typed pages, illustrated with 22 figures, 12 tables, and 4 appendices (A, B, C, D). The list of references includes 152 sources. The dissertation consists of the following parts: introduction, literature review, description of materials and methods, three sections presenting the research findings, conclusion, key findings, practical recommendations, and bibliography.