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Conflict of interest

The authors declare that they have no conflicts of interest

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TETRALOGY OF FALLOT: MODERN DATA. REVIEW OF LITERATURE

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Abstract

Tetralogy of Fallot (ToF) is a congenital heart disease that includes ventricular septal defect (VSD), right ventricular outflow tract obstruction, aortic root dextraposition, and right ventricular hypertrophy. ToF occurs in 3 out of 10,000 live births and accounts for 7–10% of all congenital heart defects.

The etiology of ToF is multifactorial and may include untreated maternal diabetes, phenylketonuria, and retinoic acid intake. Associated chromosomal abnormalities include trisomies 21, 18, and 13, but recent studies indicate a much higher association with microdeletion of chromosome 22. The familial risk of ToF is 3%.

The article presents the results of scientific publications about ToF. In particular, modern and topical issues of genetic predisposition, morphology, diagnosis, indications for surgical treatment, including radical and staged, are considered.

Фалло тетрадасы: ағымдағы деректер. Әдебиет шолуы

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Аңдатпа

Фалло тетрадасы (ФТ) – жүректің туа біткен ақауы, оған қарыншааралық ақау (ҚАА), оң жақ қарыншаның ағу жолдарының бітелуі, қолқа түбірінің декстропозициясы және оң жақ қарыншаның гипертрофиясы жатады. ФТ 10 000 тірі туылғандардың 3-інде кездеседі және барлық туа біткен жүрек ақауларының 7-10% құрайды.

ФТ-ның этиологиясы көп факторлы және емделмеген анасының қант диабеті, фенилкетонурия және ретиноин қышқылын қабылдауды қамтуы мүмкін. Ассоциацияланған хромосомалық аномалияларға 21, 18 және 13 трисомиялар жатады, хромосоманың 22-ші хромосоманың микроделециясымен анағұрлым жиі байланысуы бойынша мәліметтер бар. ФТ-ның отбасылық қауіп 3% құрайды.

Мақалада ФТ-на қатысты ғылыми жарияланымдардың нәтижелері берілген. Атап айтқанда, генетикалық бейімділіктің, морфологияның, диагностиканың, хирургиялық емдеуге көрсеткіштердің, оның ішінде радикалды және кезеңділігінің заманауи және өзекті мәселелері қарастырылады.

Тетрада Фалло: современные данные. Обзор литературы

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Аннотация

Тетрада Фалло (ТФ) – это врожденный порок сердца, который включает в себя дефект межжелудочковой перегородки (ДМЖП), обструкцию выводного тракта правого желудочка, декстропозицию корня аорты и гипертрофию правого желудочка. ТФ встречается у 3 из 10 000 живорождений и составляет 7-10% от числа всех врожденных пороков сердца.

Этиология ТФ многофакторная, и может включать нелеченый диабет матери ребенка, фенилкетонурию и прием ретиноевой кислоты. Ассоциированные хромосомные аномалии включают трисомии 21, 18 и 13, но последние исследования указывают на гораздо более частую ассоциацию с микроделецией хромосомы 22. Семейный риск возникновения ТФ составляет 3%.

В статье представлены результаты научных публикаций относительно ТФ. В частности, рассмотрены современные и актуальные вопросы генетической предрасположенности, морфологии, диагностики, показаний к хирургическому лечению, в том числе радикальному и поэтапному.

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Фалло тетрадасы, морфология, диагностика, түзету, нәтижелер

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Конфликт интересов

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Introduction

The frequency of tetralogy of Fallot (ToF) reaches 6-7% among all congenital heart diseases (CHD) or 0,21-0,26 per 1000 newborns. 30% of children with ToF die within the first year of life [1-7]. Among the cyanotic forms of CHD in children older than one year, its frequency reaches 50-75%. Among the defects requiring surgical treatment in early childhood, ToF ranks third after patent ductus arteriosus and VSD, accounting for 14,9%. ToF includes four anomalies: VSD, obstruction of blood outflow from the right ventricle, location of the aorta over a ventricular septal defect (dextraposition), right ventricular hypertrophy [1-7].

ToF is the most common cyanotic congenital heart disease. From a genetic point of view, the etiology of ToF is multifactorial, with a familial risk of 3%. Magnetic resonance imaging of the heart is the «gold standard» in the diagnosis of ToF, based on good visualization of RVOT, pulmonary arteries, aorta, aortopulmonary collateral arteries, etc. Atrial reciprocal tachycardia develops in more than 30% of patients, and ventricular arrhythmias are observed in approximately 10% in ToF patients. The frequency of sudden cardiac death is 0.2% per year [54].

New in the diagnosis and clinical manifestations of ToF

Anomalies of the coronary arteries occur in 2-23% of cases in patients with ToF. Examination of the coronary arteries anatomy before corrective surgery is very important in order to avoid damage to the vessels crossing the right ventricular outflow tract.

According to some meta-analyses, the prevalence of anomalies of the coronary arteries in ToF is 4–6%, of which in 72% of cases the abnormal coronary artery crosses the right ventricular outflow tract (RVOT). The combined risk of encountering an anomalous coronary artery or large conus artery crossing the RVOT is 10,3% [8, 9].

It is desirable that the features of the anatomy of the coronary arteries in ToF be determined before surgery, and the surgical tactics adapted accordingly.

In cardiac surgery practice, there are anomalies of the coronary arteries, which can be essential in the choice of treatment tactics. According to some authors, the coronary artery traverses the RVOT in almost one-twentieth of cases. Most commonly, the LAD either originated directly from the right coronary artery or originated from its own ostium in the right coronary sinus. Abnormal coronary arteries in patients with ToF are at risk of being cut during radical correction, especially when they are mistaken for a large right marginal or conical branch.

To date, among cardiac surgeons there is no consensus on what tactics should be chosen in such cases. Numerous methods have been reported, including placement of the right ventricle in a pulmonary arterial conduit, custom patched right ventriculotomy proximal or distal to the coronary artery, and transatrial-transpulmonary access with or without pulmonary valve commissurotomy. In our archive the operated hearts have historically been repaired without conduit by cutting the anomalous branch of the coronary artery and inserting 1 or 2 funnel-shaped patches under the

vessel to widen the right ventricular outflow tract. Until recently, the embryological development of the coronary circulation has been the subject of serious debate. Recent evidence suggests that truncus arteriosus grows out of the adjacent sinuses of the aortic root rather than out of the arteries growing in. This well explains the detection of a high origin of the coronary artery from the aortic root, which can be considered a variant of the norm, and not a congenital anomaly. We found that nearly a fifth of the coronary arteries in our cohort originated at or above the sinotubular junction. However, such variations may have implications late after surgery if reoperation is required due to aortic root dilatation, which is commonly seen in adulthood [52].

Three out of ten patients with ToF showed signs suggestive of possible liver fibrosis. Two of them underwent a liver biopsy, which revealed stage 1 and 2 fibrosis, respectively. In the same three patients, elevated central venous pressure was assessed on previous echocardiograms. In conclusion, the authors point out that some patients with ToF had moderate hepatic fibrosis, which may be associated with increased central venous pressure.

Modern views on the tactics of surgical treatment of patients with ToF

As some authors show, transannular RVOT repair with unicuspid valve reconstruction has significant advantages in reducing the length of stay in the intensive care unit and reducing the degree of regurgitation on the pulmonary valve in patients with ToF [10].

The optimal timing for percutaneous pulmonary valve implantation (PPVI) in patients with RVOT dysfunction remains challenging. This is well stated in recent review articles: the American Heart Association/ American College of Cardiology, the Canadian Society of Cardiovascular Diseases, the European Society of Cardiology have guidelines for dealing with this problem, each with slight variations. Pulmonary valve replacement is generally recommended for all patients with RVOT dysfunction (> mild pulmonary regurgitation and/or RV systolic pressure >2/3 of systemic pressure) and symptoms associated with this dysfunction. Different thresholds have been proposed for EDVI and ESVI of the right ventricle, as well as other parameters of right ventricular and left ventricular function, to determine when to intervene in asymptomatic patients. These indications are less clear and are evolving with PPVI experience and knowledge about the fate of the right ventricle after PPVI. There is a need to balance too late PPVI, when RV dysfunction is too severe and RV will not recover, versus too early intervention with the risk of unintended consequences such as heart failure or arrhythmias. We consider PPVI if any of these criteria are met: $RVVEVI > 150 \text{ ml/m}^2$, $RVESVI > 82 \text{ ml/m}^2$, severe right ventricular dysfunction (right ventricular ejection fraction < 45%), progressive tricuspid regurgitation with right ventricular dilatation or sustained arrhythmias with right ventricular dilatation.

Right ventricular dysfunction in patients with ToF after surgery manifests itself as regurgitation, stenosis, or a combination of both. Most patients had a non-conduit (transannular) type of repair, but for patients with a conduit or bioprosthetic valve approved in the US,

transcatheter options included the Melody and SAPIEN XT valves. These valves have shown very good results for 7 years after Melody implantation and 3 years after SAPIEN implantation. However, these valves require careful monitoring in patients underwent implantation for potential complications such as endocarditis, etc [11].

Results of surgical treatment of patients with tetralogy of Fallot

The analysis showed that premature children have an increased risk of postoperative mortality. At 16 years of follow-up, mortality in full-term infants was 0,7%, while mortality in preterm infants was 9,5% (N=4, P<0,003) [12-24].

In this cohort study of 3283 patients with ToF, survival after radical correction was 98,6%, 97,8%, 97,1%, 95,5% and 94,5% at 1 year, 5 years, 10 years, 20 years, and 25 years respectively [25]. Multivariate analysis demonstrated an increased risk of early mortality with staged repair (RR 2,68; 95% CI 1,59–4,49) and surgery without valve preservation (RR 3,76; 95% CI 1,53–9,19). The presence of established genetic factors was associated with increased mortality risks both in the early (RR 3,64; 95% CI 2,05–6,47) and late postoperative periods (RR 4,41; 95% CI 2,62–7,44) [25].

Forecast

Chronic hypoxemia with pathophysiological changes significantly reduces the quality of life of pediatric patients with ToF, including their psychological and neurological development, as well as school performance. The natural course of the defect is unfavorable and ranges from the first to the fourth decade of life, while the mortality of patients may be associated with manifestations of heart failure, arrhythmia, recurrent respiratory infection and thromboembolic complications.

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