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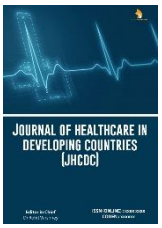

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RESEARCH ARTICLE

CONNECTIVE TISSUE HEART DYSPLASIA IN CHILDREN (LITERATURE REVIEW)

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ABSTRACT

This article highlights the main domestic and foreign publications on the problem of connective tissue dysplasia of the heart in children. An interpretation of minor heart anomalies is given. Currently, the collection of additional high-quality data on the course and treatment of children is important to identify the most effective algorithms for patient management. Proper monitoring, early detection of complications of the disease, and the possibility of timely treatment are essential.

KEYWORDS

children, connective tissue dysplasias of the heart, minor anomalies of the heart, clinic, treatment.

1. INTRODUCTION

Cardiovascular pathology in children is now an increasingly serious health problem (Gnusaev, 2006). The share of cardiovascular pathology in the structure of child disability is quite high (Gnusaev, 1997; Moroshkin, 1999). An even greater deterioration of the medical and demographic situation is predicted in the future, if the emerging threatening trends in the growth and prevalence of diseases of the circulatory system cannot be overcome. In newborns, the pathology of the cardiovascular system is one of the urgent problems of perinatology, its frequency does not tend to decrease and is, according to different authors, from 17 to 36% (Alekseev, 2005).

Conditions associated with minor heart anomalies are of great importance. These anomalies are the morphological basis of functional changes in cardiac activity, and with organic lesions of the heart, they can aggravate their prognosis (Trisvetova, 2002).

The structure of many anomalies in the development of the heart is dysplasia of the connective tissue of the heart. According to L.I. Menshikova. Dysplasia of the connective tissue of the heart in children from 0 months. up to 14 years old occurs with a frequency of about 33%. A feature of the morphogenesis of connective tissue is its participation in the formation of the heart at almost all stages of ontogenesis (Storozhakov, 2001). Exposure to a damaging factor at any stage of pregnancy can lead to various disorders, including minor anomalies in the development of the heart. The importance of genetic factors in the development of this pathology is also great (Zemtsovsky, 2007). The increase in the number of cases of connective tissue dysplasia, which has been observed recently, is associated with pathogenic influences that took place in ontogenesis, due to the deterioration of the ecological situation, poor nutrition and stress.

2. CURRENT ISSUES

Until now, the attitude towards small heart anomalies remains ambiguous. Given the significant prevalence of minor heart anomalies in the adult population and, in most cases, the favorable course and prognosis, many clinicians generally do not consider minor heart anomalies as a pathological condition. However, the accumulated long-term experience of practical work shows that such a view cannot be extended to all patients with this heart pathology. The evidence is the increased risk of a number of complications in these individuals (Viktorova, 2004). About 30% of primary infective endocarditis develops against the background of mitral valve prolapse. In the presence of severe mitral regurgitation, the risk of sudden death in patients with mitral valve prolapse increases 50-100 times. Dysplastic heart underlies many cases of sudden cardiac death in young people, the causes are fatal rhythm and conduction disturbances, ruptures and aneurysms of the aorta, coronary and cerebral arteries (Zemtsovsky, 2000). According to I.A. Viktorova. in half of young people who died suddenly, signs of connective tissue dysplasia are found (Pigarevsky and Mitrofanova, 2004). Mitral valve prolapse is considered one of the leading causes of stroke in people under 40. The prevalence of minor heart anomalies has been studied mainly in the entire population, but the data on the prevalence of this pathology are contradictory. Thus, the frequency of detection of abnormally located chords ranges from 2.5 to 95%, and the population frequency of mitral valve prolapse ranges from 1.8 to 58% (Yagoda, 2005). In the presence of the syndrome of small heart anomalies in this group of young people, the risk of developing organic heart disease increases. For example, mitral regurgitation with mitral valve prolapse can occur suddenly due to rupture of tendon chords or develop gradually. In this case, possible complications of mitral insufficiency are heart failure, sudden death, infective endocarditis, cardiac arrhythmias, thromboembolism. According to L.B. Mitrofanova, E.V. Shlyakhto, the presence of myxomatous degeneration of the valve leaflets may precede the development of atherosclerosis and valve calcification, and in the case of a bicuspid aortic valve, it can lead to aortic stenosis (Gnusaev and Belozerov, 1997). Attention is drawn to the frequent combination of coronary artery anomalies with mitral valve prolapse and external stigmas of dysembryogenesis, probably due to their common mesenchymal origin. B.C. Zhdanov (1998), studying coronary blood flow in young people with mitral valve prolapse, found that in a number of cases there is fibromuscular dysplasia of small coronary arteries, topographic anomalies of the left circumflex artery and its branches, muscle bridges, ectasias, muscular-elastic hyperplasia of the intima. In recent years, there has been a distinct increase in the incidence of acute myocardial infarction in young people. Among them, a group of patients with the absence of "classical" risk factors for coronary heart disease and signs of coronary cardiosclerosis can be distinguished. There are reasonable assumptions about the trigger role of coronary artery anomalies in the development of stenosing atherosclerosis of the coronary

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vessels. At the same time, despite the significant prevalence, undifferentiated connective tissue dysplasia often falls out of the sphere of attention of practitioners, although the need for an individual approach to these young patients, due to the possibility of suspecting congenital features of the anatomical structure of the coronary vessels by external dysmorphogenetic signs, is beyond doubt (Evsevieva, 2006).

The first attempt to systematize small heart anomalies belongs to S.F. Gnusaev and Yu.M. Belozerov (Hereditary, 2009), who proposed a working classification of small heart anomalies, based on the principle of anatomical localization of the identified abnormalities. On a large material (echocardiography - examination of 1061 children aged 2 to 12 years), the authors analyzed minor heart anomalies occurring in children, and included in the classification all possible anomalies that differ not only in localization, but also in their clinical significance. This work gave impetus to a whole direction in the study of the structural features of the heart and served as the basis for considering minor anomalies of the heart as a particular manifestation of a systemic defect (dysplasia) of connective tissue. Note that the not entirely successful term "connective tissue dysplasia" in the Russian medical literature has become synonymous with the concept of "inherited connective tissue disorders". In 2009, by the Committee of Experts of the All-Russian Scientific Society of Cardiology, the concept of connective tissue dysplasia was narrowed down to several syndromes and phenotypes of polygenic-multifactorial nature, as opposed to monogenic "mendelian" inherited disorders of connective tissue (Trisvetova, 2006). Among such syndromes and phenotypes, the following are named: mitral valve prolapse, marfan-like phenotype, marfanoid appearance, eler-like and mixed phenotypes, as well as joint hypermobility syndrome and an unclassified phenotype. At the same time, the term dysplasia of connective tissue over the past quarter of a century has firmly entered the medical lexicon in the post-Soviet space, which gives reason today to consider its use as permissible in both broad and narrow senses of the word.

2.1 Classification of small heart anomalies according to S.F.Gnusaev, 2001 (as amended)

1) Localization and shape: - atria and interatrial septum: prolapsing valve of the inferior vena cava, enlarged Eustachian valve more than 1 cm, open oval window, small atrial septal aneurysm, prolapsing comb muscles in the right atrium; - tricuspid valve: displacement of the septal leaflet into the cavity of the right ventricle within 10 mm, dilatation of the right atrioventricular opening, prolapse of the tricuspid valve;

– Pulmonary artery: dilatation of the pulmonary artery trunk, leaflet prolapse;

– aorta: borderline narrow and wide aortic root, dilatation of the Valsalva sinus, bicuspid aortic valve, asymmetry and prolapse of the aortic valve cusps;

– left ventricle: trabeculae (transverse, longitudinal, diagonal), a small aneurysm of the interventricular septum; mitral valve: mitral valve prolapse, ectopic attachment of chords, impaired distribution of chords of the anterior and (or) posterior cusp, fluttering chords, additional and abnormally located papillary muscles.

2) Complications and concomitant changes: infectious carditis, calcification, myxomatosis, fibrosis of the valve leaflets, chordal ruptures, cardiac arrhythmias.

3) Characteristics of hemodynamics: regurgitation, its degree, the presence of circulatory failure, pulmonary hypertension.

The working classification proposed by the authors was created on the basis of the analysis of the echocardiography of children. This suggests that age-related heart remodeling can affect the prevalence and dynamics of the severity of minor heart anomalies and suggests that some of the minor heart anomalies included in the classification should be attributed to the anatomical and physiological characteristics of childhood (Zemtsovsky, 2012). According to a research, for the diagnosis of such small heart anomalies as borderline wide aorta, borderline narrow aorta without indicating the range of age dynamics of their sizes and without normalizing the measurement results to the size of the body surface, conditions arise for overdiagnosis of small heart anomalies (Mattioli, 2001; Medical Bulletin, 2018).

2.2 From the standpoint of a clinician-cardiologist, E. V. Zemtsovsky et al. [16], all minor heart anomalies included in the working classification of S.F. Gnusaeva, 2001 (as amended), divided into four groups.

1) Defects and syndromes that should be excluded from the classification:

- mitral valve prolapse;

- bicuspid aortic valve;

- expansion of the sinuses of the Valsalva and / or the ascending aorta.

The group of minor cardiac anomalies should include mitral valve prolapse in the case of borderline prolapse (less than 3 mm) without thickening of the mitral valve leaflets (i.e. leaflets less than 5 mm) and significant mitral regurgitation (no more than 1 degree). If a family or myxomatous prolapse is detected, it should be an independent nosological form. In such cases, it should be clarified whether mitral valve prolapse is classical or non-classical, myxomatous or without signs of myxomatosis. The bicuspid aortic valve should be considered as a congenital heart disease, which, as a rule, does not manifest clinically in childhood and adolescence, however, in dynamics it can result in the formation of calcifying aortic stenosis. Thus, according to these authors (Mattioli, 2001), familial or myxomatous mitral valve prolapse or bisupid aortic valve should be excluded from the list of minor anomalies. When measuring the absolute sizes of the Valsalva sinuses and the sinotubular zone of the aorta, it is necessary to use a nomogram, which allows normalizing the obtained value to the size of the body surface and taking into account the patient's age. If there is an expansion of the aortic root that exceeds the permissible limits, then it should be considered as an independent clinically significant disorder that requires constant monitoring and special preventive measures aimed at reducing afterload and slowing the heart rate.

2) A group of small heart anomalies that have independent clinical significance, but are differently associated with a systemic defect in connective tissue. This group should include:

• open oval window;

• atrial septal aneurysm; false chords and abnormal trabeculae of the left ventricle.

An open oval window is a very common anomaly (up to 20% of cases according to autopsy data), which in most cases does not manifest itself clinically, but can cause the development of paradoxical embolism. Atrial septal aneurysm occurs in 1% of cases during screening studies (Medical Bulletin, 2018). As a rule, an atrial septal aneurysm proceeds favorably, without hemodynamic changes and clinical manifestation. However, with a significant size of the aneurysm and its excessive amplitude characteristics, prerequisites for thromboembolic complications are created (Mattioli, 2001**)**. An atrial septal aneurysm can act as an isolated minor anomaly of the heart, but is more often combined with other signs of connective tissue dysplasia, indicating a "systemic involvement" of connective tissue. False chords of the left ventricle are connective tissue cords running from the papillary muscles to the walls of the heart, abnormal trabeculae of the left ventricle are connective tissue cords that go from one wall of the heart to another. In conditions of difficult visualization during echocardiography in persons of older age groups, it is quite acceptable to combine these two variants of minor heart anomalies. Transverse, diagonal and longitudinal false chords of the basal and median localization, as well as multiple false chords of the left ventricle and abnormal trabeculae of the left ventricle have independent clinical significance, often acting as an independent cause of ventricular extrasystole.

3) A group of small heart anomalies, definitely associated with a systemic defect in connective tissue, but with different independent clinical significance. This group should include:

- hemodynamically insignificant prolapse of the cusps of the mitral and tricuspid valves, aortic crescents and the pulmonary valve without signs of myxomatosis and a minimal degree of regurgitation on the corresponding valves;

- Borderline dilatation of the pulmonary artery and asymmetry of the tricuspid aortic valve. Primary myxomatous and familial mitral valve prolapse, as well as aortic aneurysm, are considered by the authors as independent syndromes requiring preventive measures and appropriate management tactics.

4) A group of minor heart anomalies related to normal variants or anatomical and physiological characteristics of childhood.

The open oval window is the atrial communication - a form of atrial communication, anatomically representing the "probe" opening located in

the central part of the interatrial septum - in the fossa oval region. In fact, this is a rudiment of normal fetal blood circulation, which is not a congenital heart defect and belongs to minor heart anomalies. According to echocardiography, the incidence of an open oval window in the general population ranges from 15 to 25%. As a rule, such patients do not present complaints, therefore, this small heart anomaly is clinically detected extremely rarely. It is possible to assume the presence of a valve-defective (functioning) open oval window with a persistent predisposition to frequent colds and inflammatory diseases of the bronchopulmonary system; the occurrence of unexplained loss of consciousness, fainting, symptoms of passing cerebrovascular accident, especially in young people and patients with varicose veins and / or thrombophlebitis of the lower extremities and / or pelvis. Most often, paradoxical venous embolism and migraine with aura are associated with an open oval window. In case of paradoxical venous embolism, a thrombus migrates from the venous system to the left atrium through the open foramen ovale, followed by embolism into the systemic circulation. Clinically paradoxical venous embolism can manifest as ischemic stroke or transient ischemic attack. Typically, strokes associated with an open oval window are defined as cryptogenic strokes. In the presence of a cryptogenic stroke, an open oval window is diagnosed very often - from 24 to 66% of cases. It is believed that the open foramen ovale itself may be a potential source of paradoxical embolism. In this case, thrombi are formed either inside the open oval window, or near it, combined with an atrial septal aneurysm (Gnusaev, 1997). Persons with an open oval window working at depth (divers, divers) or in high altitude conditions are at risk of developing decompression sickness (decompression sickness) with clinical manifestations in the form of pulmonary edema and / or transient global amnesia. These clinical manifestations are caused by secondary air embolism during right-to-left shunting through the open foramen ovale. Diagnostics of LLC is aimed at its identification and assessment of the hemodynamic significance of the shunt using transthoracic echocardiography. Transthoracic echocardiography is usually sufficient for the initial diagnosis of a functioning open foramen ovale. The main diagnostic criterion for the presence of a hole is the identification of a discharge through it of blood and the diameter of the hole, which is set along the width of the blood stream. The most informative method for diagnosing an open oval window is transesophageal echocardiography.

An atrial septal aneurysm is the primary anomaly in the development of the interatrial septum. An atrial septal aneurysm is a pronounced protrusion of the interatrial septum due to the presence of excess tissue in the projection of the oval fossa. In accordance with the recommendations for echocardiographic diagnosis of 2015, an atrial septal aneurysm is diagnosed when the maximum excursion of part or all of the interatrial septum towards the left atrium or right atrium is> 10 mm or> 15 mm in total. In cases of lesser excursion, the term "mobile interatrial septum" is used. Atrial septal aneurysm most often proceeds favorably, without hemodynamic changes and clinical manifestation. As with the foramen ovale, an atrial septal aneurysm can be classified as a low risk factor for stroke. A mobile interatrial septum has no clinical significance.

Mitral valve prolapse. In clinical practice, it is required to differentiate the primary prolapse of the mitral valve leaflets as an independent disease - “mitral valve prolapse syndrome”, and mitral valve leaflet prolapse as a structural anomaly of the heart. Secondary mitral valve prolapse can be due to a variety of causes. The most common causes of secondary prolapse of the mitral valve leaflets are ischemic heart disease (ischemic dysfunction of the papillary muscles), acute rheumatic fever, diseases and conditions accompanied by a decrease in the size of the left ventricle and mitral valve ring (hypertrophic cardiomyopathy, pulmonary hypertension, atrial septal defect, degeneration straight back and funnel chest deformity) (Zemtsovsky and Malev, 2012; Silvestry F.E., 2015). There is currently no uniform terminology and classification of mitral valve prolapse. It is generally accepted to divide it into primary and secondary. Primary mitral valve prolapse is subdivided into familial (myxomatous) and nonfamilial (sporadic) (Nechaeva, 2017; Kadurina and Gorbunova, 2009). The echocardiographic approach involves the identification of two variants of mitral valve prolapse based on thickening of the leaflets in diastole: classical (myxomatous) mitral valve prolapse - with a MC leaflet thickness> 5 mm; nonclassical (nonmyxomatous) mitral valve prolapse - with a thickness of <5 mm (Nechaeva et al., 2015; Trisvetova, 2015; Styazhkina, 2017).

3. Diagnostic Approaches

The examination of children with small heart anomalies should be comprehensive and carried out according to the algorithm (Bova, 2001):

1. Complaints, mainly as a manifestation of dysfunction of the autonomic nervous system.

2. Determination of external "small" developmental anomalies (asthenic type, dolichostenomelia, kyphoscoliosis, excavation of the sternum, etc.).

3. Auscultatory signs ("click", murmur over the region of the heart, arrhythmias).

4. Monitoring of electrography.

5. Echocardiography.

6. Dosed physical activity, non-invasive electrophysiological examination of the heart.

7. Examination of organs and systems to identify internal "small" anomalies (X-ray, ultrasound, determination of psychological status, etc.).

4. Therapy Principles

The principles of therapy for children with minor heart anomalies have not been fully formulated. N.A. Korovina et al., Proposed the following tactics for the management of children with small heart anomalies:

• Comprehensive assessment of health status, including various types of research of children.

• The choice of therapy depending on the clinical, electrophysiological and echocardiographic changes.

• The use of drugs aimed at normalizing the metabolism of connective tissue.

• Determination of adequate physical activity depending on the functional state of the myocardium. It is generally accepted to use non-drug methods of treatment, including:

• age-appropriate organization of work and rest;

• compliance with the daily routine;

• rational, balanced nutrition;

• psychotherapy and auto-training;

• water and balneotherapy;

• massage (manual, underwater, etc.);

• physiotherapy, electrosleep, etc.);

• classes in medical physical culture.

The issue of admission to sports is decided individually. In the presence of mitral valve prolapse, it is necessary to take into account the family history (cases of sudden death in relatives), the presence of complaints of palpitations, cardialgia; syncope; changes in electrocardiography (heart rhythm disturbances, shortened and prolonged QT syndrome) are the basis for deciding on contraindications for sports training. This concerns the presence of abnormally located chords with the syndrome of early excitation of the ventricles, which, being arrhythmogenic small heart anomalies, can provoke heart rhythm disturbances in athletes under conditions of physical and psycho-emotional stress.

Drug treatment includes the use of:

• magnesium preparations;

• cardiotrophic therapy (in violation of repolarization processes in the myocardium);

• antibacterial therapy for exacerbation of foci of infection, surgical interventions (prevention of infective endocarditis);

• antiarrhythmic drugs (according to indications, with pure group extrasystole with impaired repolarization processes).

At present, therapy with magnesium preparations for small heart anomalies is approaching pathogenetic. This is due to the fact that magnesium is part of the main substance of connective tissue and is necessary for the proper formation of collagen fibers. Under conditions of magnesium deficiency, the ability of fibroblasts to produce collagen is impaired. In addition, magnesium has a membrane stabilizing effect, retains potassium inside the cell, and prevents sympathicotonic influences, which makes it possible to use it for the treatment of cardiac arrhythmias. The appointment of the following drugs may be considered

expedient: - Magnerot containing magnesium salt and orotic acid.

The latter not only enhances the reabsorption of magnesium in the intestine, but also has an independent metabolic effect. Children are prescribed 500 mg of Magnerot (32.8 mg of magnesium 3 times a day for 1 week, then 250 mg 3 times a day for the next 5 weeks. The drug is taken 1 hour before meals). - Magne B6. Available in tablets (48 mg magnesium or in solution for oral administration (100 mg magnesium). Children weighing more than 10 kg (over 1 year) - 5-10 mg / kg / day in 2-3 doses. Children over 12 years old - 3-4 tablets per day, in 2-3 doses The duration of the course is 6-8 weeks - Potassium orotat For children, the drug is prescribed at the rate of 10-20 mg / kg / day in 2-3 doses 1 hour before meals or 4 hours after a meal The duration of the course of treatment is 1 month It should be repeated courses of therapy with these drugs (3-4 times a year).

To improve the cellular energy of the myocardium, drugs are used that have a complex effect on metabolic processes in the body, as well as are active antioxidants and membrane stabilizers:

• L-carnitine (elkar - 20% solution of carnitine hydrochloride) Doses: 1-6 years, 0.1 g per day (14 drops) 3 times a day; 6-12 years - 0.2-0,3 g per day (1/4 tsp) 3 times a day Course - 1-1.5 months

• Coenzyme Q10 (ubiquinone) is prescribed for children over 12 years old, 1 capsule (500 mg) 1-2 times per day Ki. Kudesan belongs to preparations containing ubiquinone: 1 drop per year of life (up to 12 years), then 12 drops 1 time per day. The duration of the course should be at least 1 month.

• Cytochrome C (cyto-mac). Available in ampoules (4 ml = 15 mg). Assign intramuscularly, 4 ml, No. 10.

There are 2-4 courses per year. In addition to these drugs, to improve metabolic processes in the connective tissue, myocardium and in the body as a whole, the following is shown to be used:

• nicotinamide (vitamin PP) - 20 mg per day for 1.5–2 months;

• riboflavin (vitamin B2) - 10-15 mg per day for 1.5-2 months;

• thiamine (vitamin B1) - 10 mg per day and lipoic acid 100–500 mg per day for 1.5 months;

• lemontara (complex of citric and succinic acid) 5 mg / kg per day for 3-4 days, weekly for 2 months;

• biotin - 2-5 mg / day - 1.5-2 months.

Repeated courses of treatment are shown (up to 3 times a year).

5. Conclusions

The ambiguous interpretation of the clinical significance, the difficulties of early diagnosis and the absence of diagnostic criteria indicate the need to study minor heart anomalies in children.

References

Alekseev, AA. 2005. Integrative (systemic, family) connective tissue medicine. - M., T. 4. 592 s

Bova, A.A. 2001. Minor heart anomalies (clinical significance, diagnosis, complications). Instructions for use / A.A. Bova. - UO "BSMU" - 17 s.

Evsevieva M.E; 2006. Small heart anomalies as a particular manifestation of connective tissue dysplasia. Tutorial. Stavropol.

Gnusaev S.F., Belozerov Yu.M. 1997; Working classification of minor heart anomalies. Ultrasound diagnostics. 3: 21-27.

Gnusaev, S. F. 2006. Clinical significance of small anomalies of heart development Text. / S.F. Gnusaev, Yu.M. Belozerov, A.F. Vinogradov, Ros. vestn. perinatology and pediatrics. No. 4, P. 20-25., 75

Gnusaev, SF. 1997. Echocardiographic criteria for diagnosis and classification of minor heart anomalies in children Text. / S. F. Gnusaev, Yu. M. Belozerov, Ultrasound diagnostics. No. 3, P. 23-27.

Hereditary connective tissue disorders. 2009. Russian recommendations. Cardiovascular Therapy and Prevention; 6 (appendix 5): 1–24

Kadurina T.I., Gorbunova V.N. 2009. Connective tissue dysplasia: a guide for physicians. - SPb.: Elbi-SPb, 704 p.

Mattioli, A.V. et al., 2001. Atrial septal aneurism as a cardioembolic source in adult patients with stroke and normal carotid arteries, European Heart Journal. No. 22. P. 261–268.

Medical Bulletin of the North Caucasus. 2018. Supranational (international) recommendations for structural anomalies of the heart. T. 13, No. 1-2. S. 272-324.

Moroshkin VS. 1999. Late ventricular potentials in patients with dilated cardiomyopathy and their relationship with ventricular arrhythmias. Cardiology. No. 3, P. 41-44.

Nechaeva GI, Drokina OV, Martynov AI, et al. 2015. Fundamentals of supervision of patients with connective tissue dysplasia in primary health care, Therapy. No. 1. S. 29-36.

Nechaeva. G. I. 2017. Connective tissue dysplasia: cardiovascular changes, modern approaches to diagnosis and treatment / G.I. Nechaeva, A.I. Martynov. - M.: Medical Information Agency, 399 p.

Pigarevsky P.V. et al. Mitrofanova, L.B. 2004. The role of mesenchymal dysplasia in aortic valve calcification. Cardiovascular therapy and prevention. No. 4 (appendix 2). p. 329.2004

Silvestry F.E. et al. 2015. Guidelines for the Echocardiographic Assessment of Atrial Septal Defect and Patient Foramen Ovale: From the American Society of Echocardiography and Society for Cardiac Angiography and Interventions, Journal of the American Society of Echocardiography. 28. P. 910-58.

Storozhakov, G.I. 2001. Risk stratification and choice of clinical tactics in patients with mitral valve prolapse / G.I. Storozhakov et al., Heart failure. No.6, P. 287-290

Styazhkina S.N. 2017. Connective tissue dysplasia in surgical patients / S.N. Styazhkina, T.E. Chernyshova, M. Yu. Smetanin, Health and education in the XXI century. T. 19, No. 12. S. 281-284.

Trisvetova E.L. 2015. Strategy and tactics of treatment of patients with hereditary connective tissue disorders, International reviews: clinical practice and health. No. 2. S. 80-92.

Trisvetova, E. JI. 2002. Modern approach to the diagnosis of primary mitral valve prolapse. Materials of the Second All-Russian Conference "Preventive Cardiology". Saratov, S. 354-355

Trisvetova, E.L, 2006. Anatomy of small heart anomalies, E.L. Trisvetova, O.A. Yudin. - Minsk: Belprint LLC.

Viktorova, I.A, 2004. Methodology of supervision of patients with connective tissue dysplasia by a family doctor in the aspect of prevention of early and sudden death: author. dis. ... Dr. med. sciences / I.A. Viktorov. Omsk, 41 p.

Yagoda, A.V. 2005. Small heart anomalies / A.V. Yagoda, N.N. Gladkikh, Stavropol. 246 p.

Zemtsovsky E.V., Malev E.G. 2012. Minor heart anomalies and dysplastic phenotypes. - SPb: IVESEP, 160 p.

Zemtsovsky, E.V. 2000. Connective tissue dysplasias of the heart / E.V. Zemtsovsky. SPb., 115 p.

Zemtsovsky, E.V. 2007. Dysplastic phenotypes. Dysplastic heart. Analytical review / E.V. Zemtsovsky. SPb., 80 p.

Zemtsovsky, E.V. 2012. Small heart anomalies. Russian journal of cardiology. No. 1 (93). S. 77-81.