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CONGENITAL HEART DEFECTS AND THEIR ASSOCIATION WITH CONNECTIVE TISSUE DYSPLASIA IN CHILDREN (REVIEW)

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Summary.

Congenital heart disease (CHD) remains a leading cause of paediatric morbidity and mortality, necessitating early diagnosis and timely surgical intervention. The reported incidence is 6-10 per 1 000 live births. Comorbid connective tissue dysplasia (CTD) significantly influences the clinical course of CHD, contributing to structural weakness of cardiac and vascular tissues, elevated risk of postoperative complications, and poorer long-term outcomes.

Objective. *To synthesise current evidence regarding the clinical features, complications, and management of congenital heart disease in children with concomitant connective tissue dysplasia; to identify key pathophysiological mechanisms and highlight promising diagnostic and therapeutic strategies.*

Materials and methods. *This review analyses global trends in the association between CHD and CTD in the paediatric population. Scientific literature indexed in PubMed, ScienceDirect, and Google Scholar from 2017 to 2024 was systematically evaluated.*

Results. *Current research indicates that molecular alterations in connective tissue components – particularly fibrillin, collagen, and transforming growth factor-β (TGF-β) receptors – impair myocardial and vascular remodelling, thereby increasing susceptibility of valves and arterial walls to haemodynamic stress. Children with CTD frequently exhibit valve prolapse with regurgitation, aortic dilatation, aneurysm formation, vascular dissection, and heightened risk of perioperative haemorrhage and infection. These patients are more likely to require repeat surgical procedures and demonstrate delayed wound healing. Well-characterised syndromes – including Marfan, Loeys–Dietz, and Ehlers–Danlos – demonstrate unequivocal cardiovascular involvement. Optimal management mandates a multidisciplinary strategy encompassing early recognition of phenotypic features, comprehensive imaging (echocardiography, cardiac magnetic resonance imaging, angiography), and targeted genetic testing. Regular surveillance of aortic dimensions and valvular function, judicious timing of interventions, and appropriate pharmacological prophylaxis are critical to mitigating severe complications.*

Conclusions. *Connective tissue dysplasia constitutes a significant comorbidity that exacerbates the natural history of congenital heart disease, increases surgical risk, and necessitates individualised therapeutic planning. Phenotypic signs of CTD must be actively sought and integrated into preoperative assessment and surgical decision-making. A coordinated, multidisciplinary approach – supported by advanced imaging, genetic counselling, and longitudinal follow-up – is essential for risk reduction and improved long-term prognosis. Further research into the molecular genetics and pathogenesis of CTD holds promise for early risk stratification and personalised management in children with CHD.*

Keywords: *Congenital Heart Disease; Connective Tissue Dysplasia; Child; Communication.*

The study of congenital heart disease (CHD) in children remains a central focus of contemporary paediatric cardiology and cardiac surgery, owing to its high prevalence, the substantial proportion of prognostically unfavourable forms, and the frequent requirement for surgical intervention during early infancy – when morphological and functional organ systems remain immature. According to international registries, the incidence of CHD averages 6-10 per 1 000 births, with approximately one-quarter of affected children requiring surgical correction within the first year of life [1-4].

Advances in cardiac surgery, anaesthesiology, and paediatric intensive care have reduced postoperative mortality in high-volume specialised centres to less than 2% [4-6]. Nevertheless, long-term outcomes are substantially influenced by the presence of associated comorbidities and dysfunction of non-cardiac organ systems. Extracardiac anomalies or disorders in children with CHD complicate clinical management, expand the scope of diagnostic and therapeutic interventions, and elevate the risk of postoperative complications, long-term disability, and mortality. Current evidence indicates that approximately 30% of CHD cases are associated with malformations of the central nervous, musculoskeletal, gastrointestinal, or genitourinary systems, or with immunodeficiency syndromes. The aetiology of CHD remains multifactorial and incompletely elucidated, with current models implicating complex interactions among genetic, epigenetic, and environmental determinants [9-11].

The apparent rise in reported CHD incidence may reflect both increased exposure to adverse environmental and genotoxic agents and the expanding recognition of intrauterine infections that disrupt cardiac morphogenesis during critical embryonic windows. A notable trend is the increasing proportion of CHD cases involving valvular anomalies, with clinically significant sequelae – including acute cardiovascular events – frequently presenting in adulthood [3,12-14].

For instance, cytomegalovirus infection has been identified as a significant contributor to CHD and other congenital malformations, with reported incidence rates of 4-50 per 1 000 births and 4-10 per 1 000 live births, and a detection rate of approximately 40% within the first year of life [15,16].

Conversely, the stroma of all human organs and tissues is composed of connective tissue, which provides not only mechanical but also regulatory support to cellular architecture. The functional versatility and structural ubiquity of connective tissue underlie the high propensity for its developmental and functional abnormalities, including their contribution to congenital heart disease (CHD) [17-19].

According to the definition adopted by the Congress of Cardiologists of Ukraine (2009), connective tissue dysplasia (CTD) is a multifactorial hereditary disorder of connective tissue, classified into syndromes and phenotypic variants based on shared external and/or visceral manifestations – ranging from benign, subclinical forms to severe multisystem involvement [17,18].

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Hereditary connective tissue disorders (HCTDs) encompass a spectrum of genetically determined defects in extracellular matrix components, including collagen, elastin, fibrillin, and other structural proteins. Given the dependence of cardiac and vascular integrity on connective tissue scaffolding, these conditions are frequently associated with cardiovascular anomalies – such as CHD, valvular malformations, arterial dilatation, aneurysm formation, and aortic dissection [19-21].

Connective tissue constitutes the structural framework of cardiac valves, vascular walls, and septal partitions, and participates in their dynamic remodelling via signalling pathways, notably the transforming growth factor-β (*TGF*-β) cascade. Pathogenic variants in genes encoding fibrillin-1 (*FBN1*), collagens, *TGF*-β receptors, and related matrix proteins result in structural instability, clinically manifesting as CHD, valvular dysfunction, and aortopathies [20,22,23].

In paediatric cohorts with clinical signs of CTD, echocardiography frequently reveals minor cardiac anomalies – including accessory chordae tendineae and valvular prolapse; abdominal ultrasonography demonstrates gallbladder deformation and renal structural anomalies; Doppler ultrasonography of the head and neck vessels reveals asymmetry of internal carotid artery flow and tortuosity of vertebral arteries; and radiographic assessment shows a high prevalence of spinal deformities (e.g., scoliosis), atlantoaxial subluxation, C_1 hypoplasia, and odontoid anomalies. These findings collectively support the classification of CTD as a multisystem disorder [17-19].

Other investigators note that, beyond the core phenotypic features of CTD, individual children may exhibit manifestations across multiple organ systems. On average, approximately nine stigmata per child are documented. These may be functional (e.g., electrocardiographic alterations, haemodynamic asymmetry on Doppler ultrasonography, gallbladder deformity) or structural in nature (e.g., cervical vertebral hypoplasia and subluxation, minor cardiac anomalies, renal dysmorphology) [20-22].

Hereditary connective tissue diseases constitute a heterogeneous group of over 200 monogenic disorders, characterised by deficiency or dysfunction of key connective tissue constituents. Prototypical examples include Marfan syndrome, Ehlers–Danlos syndromes, and osteogenesis imperfecta. These conditions necessitate a multidisciplinary diagnostic and management approach, as well as lifelong surveillance [17-22].

In recent years, the frequency of surgical interventions for congenital heart disease (CHD) in children with comorbid conditions or significant premorbid burden has increased While this does not constitute an absolute contraindication to surgery, such patients are at elevated risk of postoperative complications, necessitating meticulous preoperative planning and a multidisciplinary diagnostic and therapeutic approach [7,13,23,24]. Despite substantial advances, the scientific literature contains relatively few systematic studies addressing comorbidity profiling and integrated management strategies in paediatric cardiac surgery, underscoring the continued relevance of research in this domain.

The aim of the study was to identify and identify and synthesise current evidence regarding the clinical and pathophysiological interrelationship between CHD and connective tissue dysplasia (CTD) in children, and to review contemporary trends in diagnostic refinement and therapeutic optimisation.

Materials and methods. This review analyses global trends in the association and natural history of CHD in the context of CTD in the paediatric population. A systematic search of the international scientometric databases PubMed, ScienceDirect, and Google Scholar was performed using predefined keywords. Peer-reviewed studies published between 2017 and 2024 were included.

Results and discussion. Contemporary research confirms the predominantly genetic aetiology of CHD and delineates the pivotal roles of specific genes and signalling pathways in cardiogenesis. Valve morphogenesis occurs during the embryonic period, between gestational weeks 2 and 8. As described by Papoutsi et al. (2018), valve development requires precise spatiotemporal activation: myocardial expression of bone morphogenetic protein 2 (*BMP2*) initiates the process, followed by induction of the transcription factor *TBX2*. Outside the valve-forming region, alternative cardiogenic programmes prevail: *TBX20* activates *HEY1* and *HEY2*, which subsequently suppress *TBX2* and restrict *BMP2* activity. In the endocardium, *NOTCH1* further attenuates *BMP2* signalling via *HEY1*/*HEY2*-mediated repression. Concurrently, *HEYL* marks endothelial cells of the atrioventricular canal that possess morphogenetic competence for valvulogenesis [25-27].

Analysis of the literature regarding the potential role of nuclear factor of activated T cells (*NFATC*) gene polymorphisms in valvular heart disease reveals that *NFATC1-4* expression in cardiovascular pathologies – both in CHD and systemic hypertension – is adaptive and stress-responsive, induced by elevated haemodynamic load. Given the central involvement of *NFATC* proteins in cardiac development and their contribution to pathological myocardial and vascular hypertrophy, these factors represent promising biomarkers for early risk stratification in patients with valvular forms of congenital heart disease and concomitant hypertension [22,28,29].

In recent years, numerous studies have established that endocardial endothelial development is governed by the integrated interplay between transforming growth factor-β (*TGF*-β) and the *Notch* signalling pathway [26-29]. Additionally, nuclear factor of activated T cells 1 (*NFATC1*) is upregulated by vascular endothelial growth factor (*VEGF*), where it regulates endothelial-to-mesenchymal transition, sustains endocardial cell proliferation, and promotes elongation of valve leaflets. Collectively, these findings indicate that the genetic regulation of cardiac valve morphogenesis constitutes an evolutionarily conserved, yet highly coordinated and intricately integrated process. Desynchronisation or functional disruption within this signalling cascade during embryogenesis results in valvular malformations in individuals with congenital heart disease (CHD) [30-32].

Concurrently, investigations into the pathogenetic role of connective tissue in CHD have primarily identified molecular defects in *FBN1* (fibrillin-1), collagen genes,

and *TGF*-β receptors, leading to dysregulated matrix organisation, diminished vascular wall integrity, and aberrant cardiac remodelling during embryogenesis. Impaired *TGF*-β signalling underlies pathological vascular and valvular remodelling; structural weakness of valve complexes manifests clinically as prolapse, regurgitation, or contributes to septal defect formation [33,34]. Matrix instability secondary to fibrillin or collagen deficiencies predisposes to aortic root dilatation, valvular prolapse, and heightened susceptibility to rupture or dissection.

The principal hereditary connective tissue dysplasia (CTD) syndromes with cardiovascular involvement include Marfan syndrome (MFS), Loeys–Dietz syndrome (LDS), Ehlers–Danlos syndrome (EDS), and related disorders [35].

Marfan syndrome, caused by pathogenic variants in *FBN1*, exhibits mutations distributed across the gene; however, genotype–phenotype correlations remain limited [36-43]. *FBN1* mutations result in deficient or dysfunctional fibrillin-1, disrupting connective tissue architecture and homeostasis. The cardinal cardiovascular features include aortic root dilatation, aneurysm formation, dissection, and mitral valve prolapse. Isolated congenital septal defects (e.g., atrial or ventricular septal defects) are less common but, when present, are frequently associated with concomitant valvular and aortic wall abnormalities – conditions that may culminate in critical events during childhood.

Loeys–Dietz syndrome is an autosomal dominant connective tissue disorder with multisystem involvement, first described in 2005 [44-47]. It is caused by pathogenic variants in *TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, or *TGFB3*, leading to dysregulated *TGF*-β signalling. Clinical hallmarks include aggressive, early-onset, and multifocal aortic and arterial aneurysms/dilatations, arterial tortuosity, valvular anomalies, and a markedly elevated risk of vascular rupture – even at modest degrees of dilatation. The most frequently reported craniofacial features include high-arched palate, bifid uvula, and hypertelorism. A reported 4% incidence of aortic dissection has been documented in the perinatal period. This pronounced genetic heterogeneity underlies extensive phenotypic variability – particularly in age of onset, penetrance, severity of life-threatening vascular complications, and extent of multiorgan involvement – highlighting the necessity of establishing robust genotype–phenotype correlations to enable personalised management and genetic counselling.

Vascular Ehlers–Danlos syndrome (vEDS) constitutes a genetically heterogeneous disorder within the spectrum of hereditary connective tissue diseases, characterised by generalised joint hypermobility, skin hyperextensibility, and tissue fragility [48-50]. In vEDS, pathogenic variants in *COL3A1* (less commonly *COL5A1* or *COL5A2*) result in defective type III collagen, compromising the structural integrity of hollow organs and vasculature. Clinical hallmarks include spontaneous arterial rupture, vascular wall insufficiency, and, less frequently, classical congenital septal defects. Although the direct association with isolated septal defects is weak, cardiovascular manifestations – such as aneurysm formation and valvular dysfunction – can be life-threatening. Joint hypermobility (JH) in EDS arises from genetic alterations in structural proteins that confer tensile strength and elasticity to joints, ligaments, and tendons, predominantly fibrillar collagens. Membrane proteins – integral components of the cell membrane – mediate critical functions including signal transduction, molecular transport, and cell–cell adhesion. While recent research has emphasised abnormalities in collagen and extracellular matrix composition, a more comprehensive elucidation of membrane protein dysfunction is essential for a complete understanding of the complex pathogenesis of these disorders [48-50].

Additional hereditary conditions with cardiovascular involvement include familial thoracic aortic aneurysm and dissection (TAAD). Pathogenic variants in *ACTA2* and *MYH11* are associated with aortic wall pathology and, in some cases, concomitant valvular anomalies – most notably bicuspid aortic valve [51]. In the absence of a positive family history or diagnostic clinical criteria, the proportion of sporadic thoracic and abdominal aortic aneurysms and dissections attributable to monogenic predisposition remains undefined. The aforementioned syndromes account for the majority of aortopathies in paediatric and young adult populations. The discovery of novel causative genes and their phenotypic correlations will not only advance our understanding of aortic aneurysm pathophysiology but also inform the development of refined clinical surveillance protocols and surgical strategies.

Congenital contractural arachnodactyly (Beals syndrome) is an autosomal dominant disorder caused by pathogenic variants in the *FBN2* gene (*5q23*), encoding fibrillin-2. Cardiovascular involvement typically includes mitral valve prolapse; severe congenital heart defects are uncommon [52]. Clinical features encompass multiple congenital flexion contractures, arachnodactyly, progressive kyphoscoliosis, crumpled ear helices, and muscular hypoplasia. Significant phenotypic overlap with Marfan syndrome is observed. Spontaneous improvement of joint contractures often occurs with age, whereas spinal deformities typically progress. The severe neonatal form is usually attributable to de novo mutations. Prenatal molecular diagnosis is feasible.

Additional syndromes exhibiting partial mechanistic overlap include Turner syndrome (notably associated with aortic coarctation), Noonan syndrome (frequently associated with septal defects), and Desbuquois dysplasia [53-55]. Classical diagnosis relies on recognition of characteristic phenotypic features, such as distinctive facies, webbed neck, and peripheral lymphoedema. More recently, the clinical spectrum of Turner syndrome has been expanded to encompass, individually or in combination: short stature, primary ovarian insufficiency, early-onset sensorineural hearing loss, congenital cardiovascular, skeletal, and renal anomalies, specific neurocognitive profiles, and an increased prevalence of autoimmune conditions – including autoimmune thyroiditis and coeliac disease. Both congenital and acquired cardiovascular disease are highly prevalent in Turner syndrome and constitute the leading cause of premature mortality in adulthood. Congenital heart defects occur in approximately 50% of affected individuals and may include bicuspid aortic valve, aortic coarctation, hypoplastic left heart

syndrome, and aortic arteriopathy. Lifelong surveillance is warranted, as nearly 25% of individuals develop aortic dilatation or aneurysm over time [53].

Zhdan and Katerenchuk (2018) provided a comprehensive review of cardiac anomalies in Noonan syndrome, which arise from germline pathogenic variants in genes encoding components of the RAS/MAPK signalling pathway, resulting in dysregulated intracellular signal transduction. The phenotype is characterised by multisystem congenital anomalies and an elevated predisposition to malignancy [54]. Cardiovascular disease is the principal determinant of life expectancy. Pulmonary valve stenosis is the most prevalent lesion, affecting more than 50% of patients; hypertrophic cardiomyopathy occurs in approximately one-third, and mitral valve disease in a smaller proportion. Additional features may include characteristic facial morphology, intellectual disability, learning difficulties, short stature, renal structural anomalies, lymphatic dysplasia, and haemostatic abnormalities [54].

Desbuquois dysplasia (DD) is a rare a rare autosomal recessive disorder defined by severe prenatal and postnatal growth deficiency, distinctive skeletal dysplasia (including advanced carpal ossification, joint laxity, and spinal deformities), and multisystem involvement. Cardiac manifestations – including aortic root dilatation and mitral valve prolapse – have been documented, likely attributable to defective proteoglycan biosynthesis. Aortic root and ascending aortic dilatation, along with mitral valve prolapse, are relatively common; septal defects and bicuspid aortic valve are less frequently observed. Aortopathy tends to manifest early and may progress to critical stages. Early identification of cardiovascular involvement and prompt initiation of pharmacological therapy significantly improve long-term prognosis [56].

Aortopathy encompasses a broad spectrum of pathological conditions predisposing to aortic dilatation, aneurysm formation, dissection, or rupture, as well as analogous processes in other arterial territories. In paediatric populations, aortopathy is typically diagnosed from birth through adolescence, predominantly involving the thoracic aorta, with variable peripheral vascular involvement. Pathogenetic mechanisms include heritable connective tissue disorders, smooth muscle dysfunction, and congenital heart disease – particularly bicuspid aortic valve. Although the American Heart Association has issued guidelines for the management of thoracic aortic disease in adults, these are not directly applicable to children. Paediatric management strategies remain heterogeneous, likely reflecting the pathogenetic diversity of aortopathy (encompassing both genetic and acquired aetiologies) and the current paucity of high-quality evidence to guide therapeutic decision-making in this age group [57].

Connective tissue dysplasia (CTD) represents a significant risk factor for cardiovascular disease, with a phenotypic spectrum extending from isolated vascular pathologies (e.g., aneurysms, dissections) to valvular anomalies, and, to a lesser extent, congenital septal defects. All patients with suspected Marfan syndrome, Loeys–Dietz syndrome, or vascular Ehlers–Danlos syndrome warrant comprehensive cardiovascular assessment, confirmatory genetic testing, and individualised long-term surveillance.

The pathophysiological complexity of CTD necessitates continued investigation across multiple domains – from elucidation of molecular mechanisms and refinement of diagnostic criteria to development of targeted therapeutic strategies and evaluation of comorbidity interactions. Ongoing research holds substantial promise for advancing both understanding and management of congenital heart disease (CHD) in the context of CTD.

The association between CTD and adverse outcomes in CHD is well established, manifesting as increased frequency of specific complications and a more severe postoperative course. A detailed analysis reveals that CTD exerts profound effects on cardiac anatomy and physiology in CHD. Primarily, structural weakness of the cardiac fibrous skeleton – encompassing valves, septa, and vessel walls – predisposes to valvular prolapse, accelerated progression of regurgitation following surgical correction, and heightened risk of recurrent defects after valvuloplasty. Diminished arterial elasticity contributes to aortic and arterial dilatation, aneurysm formation, and dissection, even under normotensive conditions. A systematic review of the literature enabled the compilation of the most frequently reported clinical complications in the course and management of CHD among children with CTD (Table 1) [23, 32, 51, 58, 59].

Table 1

Most common clinical complications of congenital heart disease in children with connective tissue dysplasia

Complication	Mechanism in CTD	Examples
Progressive aortic dilatation	Fibrillin and collagen deficiency → impaired structural integrity of the aortic media	Ventricular septal defect (VSD), aortic coarctation in Marfan or Loeys–Dietz syndrome
Valvular regurgitation	Weakening of valvular leaflets and chordae tendineae → prolapse and insufficiency	Atrial septal defect (ASD) or VSD with mitral or tricuspid regurgitation
Aneurysm or pseudoaneurysm formation postoperatively	Inadequate tissue tensile strength → poor suture retention	Following aortic repair or right ventricular outflow tract (RVOT) reconstruction
Vascular rupture or dissection	Fragmentation of elastic fibres→ thin, fragile arterial wall	In patients with CTD + aortic coarctation
Impaired endocardial healing	Dysregulated collagen synthesis → delayed wound repair	Risk of endocarditis after surgical interventions
Restenosis / dilatation after balloon angioplasty	Reduced strength and increased elasticity of the vessel wall	Coarctation following balloon dilatation

In addition to the aforementioned anatomical and functional consequences, connective tissue dysplasias (CTDs) significantly influence the postoperative trajectory in CHD. Children with CTD more frequently require reoperation due to progressive dilatation of reconstructed segments or recurrent valvular insufficiency. Tissue and vascular fragility elevate the risk of perioperative haemorrhage, while collagen abnormalities impair wound healing and reduce suture retention following cardiac surgery. Long-term follow-up reveals an increased incidence of aortopathy following CHD correction – particularly in cases such as ventricular septal defect (VSD) closure in the setting of pre-existing aortic root dilatation associated with CTD [23,32,51,58,59].

In summary, the principal mechanisms underlying the elevated risk of complications in CHD with CTD are as follows:

– Pathogenic variants in connective tissue genes (*FBN1, COL3A1, TGFBR2*, etc.) result in diminished structural integrity of cardiac and vascular tissues;

- Dysregulated transforming growth factor-β (*TGF*-β) signalling drives chronic pathological remodelling of valves and vessels, persisting even after surgical correction;
- The systemic nature of CTD entails multisystem involvement, extending beyond the heart to the entire vascular system;
- Microstructural abnormalities confer vulnerability even in anatomical regions not directly affected by the primary cardiac defect.

Therefore, optimal management of CHD in children with suspected or confirmed CTD necessitates a structured, multidisciplinary diagnostic and therapeutic algorithm, initiated at the time of initial evaluation and incorporating both general and specialised assessment modalities. This approach mandates coordinated input from paediatric cardiology, clinical genetics, cardiac surgery, vascular surgery, orthopaedics, and ophthalmology.

The diagnostic pathway comprises three sequential stages:

Stage 1: Comprehensive clinical assessment, including systematic evaluation for dysmorphic features suggestive of CTD – such as generalised joint hypermobility, skin hyperextensibility, arachnodactyly, characteristic facies, and other minor anomalies. Given the autosomal dominant inheritance of many CTD syndromes, a detailed family history is essential for cascade screening.

Stage 2: Advanced instrumental evaluation, including: echocardiography and/or cardiac magnetic resonance imaging (MRI) to assess aortic root dimensions, valvular morphology and function, and the presence of septal defects; computed tomographic angiography (CTA) or conventional angiography for detailed vascular mapping, particularly when Loeys–Dietz or vascular Ehlers–Danlos syndromes are suspected; additional targeted investigations as indicated by specialist consultation.

Stage 3: Molecular genetic testing, guided by phenotypic and imaging findings. Targeted gene panel analysis is recommended, including *FBN1, TGFBR1, TGFBR2, SMAD3, COL3A1, ACTA2,* and *MYH11,* among others.

The findings of a comprehensive evaluation enable an integrated, lifelong management strategy – spanning conservative therapy, preoperative optimisation, intraoperative planning, and long-term postoperative surveillance – aimed at preventing complications across all stages of care, including adulthood, thereby reducing the risk of disability and premature mortality. For instance, pharmacological intervention with beta-blockers and renin–angiotensin system inhibitors has been shown to attenuate the rate of aortic root dilatation in Marfan syndrome [5, 49].

These data are critical for surgical decision-making, including the timing of prophylactic interventions – such as aortic root replacement at smaller diameter thresholds than in non-CTD patients – as well as valve repair/replacement and aneurysm correction [47]. Longitudinal follow-up in individuals with CTD mandates periodic assessment of aortic dimensions, valvular function, and vascular stability, with heightened vigilance in Loeys–Dietz and vascular Ehlers–Danlos syndromes. Certain rare CTD phenotypes may exhibit attenuated or incomplete cardiovascular involvement, necessitating individualised risk stratification and management [46]. Psychosocial support is an indispensable component of care, facilitating adherence to surveillance and empowering patients to recognise and report early warning signs of life-threatening complications – such as acute chest pain or dyspnoea suggestive of aortic dissection or rupture [35, 36, 43, 48, 55].

The pathophysiological complexity of CTD underscores the need for sustained research across multiple domains – including molecular pathogenesis, diagnostic refinement, development of targeted therapeutics, and elucidation of comorbidity interactions. Such efforts hold considerable potential to enhance both prognostic accuracy and therapeutic efficacy in CHD associated with CTD.

Conclusions

1. CTD constitutes a significant risk factor for cardiovascular disease, including CHD, adversely influencing natural history, surgical complexity, and postoperative outcomes.

2. Clinicians must remain vigilant for phenotypic markers of CTD during the evaluation of children with CHD, as early recognition is pivotal for complication prevention. Molecular mediators of cardiac and vascular morphogenesis – particularly components of the *TGF*-β and *RAS/MAPK* signalling pathways – represent promising candidates for biomarker development and risk prediction.

3. Optimal management of CHD in children with CTD unequivocally requires a multidisciplinary framework: a standardised diagnostic algorithm for syndromic identification and comorbidity profiling, coupled with coordinated therapeutic planning across all phases of care, involving cardiology, genetics, cardiac and vascular surgery, orthopaedics, and allied specialties.

Evidence-based recommendations for CHD–CTD comorbidity include: serial echocardiographic and/or cardiac MRI surveillance of the aortic root and ascending aorta – at least biannually, even after complete CHD correction; consideration of prophylactic aortic root replacement at lower diameter thresholds compared with isolated CHD; Provision of genetic counselling to inform familial risk assessment and enable cascade screening.

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References:

1. Jacobs ML, Backer CL. World Journal for Pediatric and Congenital Heart Surgery-The Official Journal of the Congenital Heart Surgeons' Society. World J Pediatr Congenit Heart Surg. 2023 Sep;14(5):572-574. doi: 10.1177/21501351231174815. PMID: 37737600.

2. Liu Y, Chen S, Zühlke L, Black GC, Choy MK, Li N, Keavney BD. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol. 2019 Apr 1;48(2):455-463. doi: 10.1093/ije/dyz009. PMID: 30783674.

3. Mamasoula C, Addor MC, Carbonell CC, Dias CM, Echevarría-González-de-Garibay LJ, Gatt M, Khoshnood B, Klungsoyr K, Randall K, Stoianova S, Haeusler M, Nelen V, Neville AJ, Perthus I, Pierini A, Bertaut-Nativel B, Rissmann A, Rouget F, Schaub B, Tucker D, Wellesley D, Zymak-Zakutnia N, Barisic I, de Walle HEK, Lanzoni M, Mullaney C, Pennington L, Rankin J. Prevalence of congenital heart defects in Europe, 2008-2015: A registry-based study. Birth Defects Res. 2022 Dec 1;114(20):1404-1416. doi: 10.1002/bdr2.2117. Epub 2022 Nov 8. PMID: 36345679.

4. Allen P, Zafar F, Mi J, Crook S, Woo J, Jayaram N, Bryant R 3rd, Karamlou T, Tweddell J, Dragan K, Cook S, Hannan EL, Newburger JW, Bacha EA, Vincent R, Nguyen K, Walsh-Spoonhower K, Mosca R, Devejian N, Kamenir SA, Alfieris GM, Swartz MF, Meyer D, Paul EA, Billings J, Anderson BR; New York State CHS-COLOUR. Risk Stratification for Congenital Heart Surgery for ICD-10 Administrative Data (RACHS-2). J Am Coll Cardiol. 2022 Feb 8;79(5):465-478. doi: 10.1016/j.jacc.2021.11.036. PMID: 35115103.

5. Morris SA, Flyer JN, Yetman AT, Quezada E, Cappella ES, Dietz HC, Milewicz DM, Ouzounian M, Rigelsky CM, Tierney S, Lacro RV; American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young (Young Hearts); Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; and Council on Cardiovascular Surgery and Anesthesia. Cardiovascular Management of Aortopathy in Children: A Scientific Statement From the American Heart Association. Circulation. 2024 Sep 10;150(11): e228-e254. doi: 10.1161/CIR.0000000000001265. PMID: 39129620.

6. Pierpont ME, Brueckner M, Chung WK, Garg V, Lacro RV, McGuire AL, Mital S, Priest JR, Pu WT, Roberts A, Ware SM, Gelb BD, Russell MW; American Heart Association Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; and Council on Genomic and Precision Medicine. Genetic Basis for Congenital Heart Disease: Revisited: A Scientific Statement From the American Heart Association. Circulation. 2018 Nov 20;138(21): e653-e711. doi: 10.1161/CIR.0000000000000606. Erratum in: Circulation. 2018 Nov 20;138(21): e713. doi: 10.1161/CIR.0000000000000631. PMID: 30571578.

7. STS Congenital Heart Surgery Database. Society of Thoracic Surgeons [Internet]. Available from: https://publicreporting.sts.org/chsd-about

8. Dewangan M. Association of congenital heart diseases with extracardiac anomalies. International Journal of Contemporary Pediatrics. 2017;4(5):1807-1810. https://doi.org/10.18203/2349-3291.ijcp20173790

9. Huang X, Gao Y, Chen W, Sheng W and Huang G. Noncardiac anomalies in children with congenital heart disease. Front. Cardiovasc. Med. 2023; 10:1293210. doi: 10.3389/fcvm.2023.1293210

10. Lim TB, Foo SYR, Chen CK. The Role of Epigenetics in Congenital Heart Disease. Genes (Basel). 2021;12(3):390. doi: 10.3390/genes12030390. PMID: 33803261.

11. Balasubramanian R, Vuppalapati S, Avanthika C, Jhaveri S, Peddi NC, Ahmed S, Reddy A, Kaur J. Epidemiology, Genetics and Epigenetics of Congenital Heart Diseases in Twins. Cureus. 2021;13(8): e17253. doi: 10.7759/cureus.17253. PMID: 34540478.

12. Sood E, Newburger JW, Anixt JS, Cassidy AR, Jackson JL, Jonas RA, Lisanti AJ, Lopez KN, Peyvandi S, & Marino BS. Ne urodevelopmental Outcomes for Individuals With Congenital Heart Disease: Updates in Neuroprotection, Risk-Stratification, Evaluation, and Management: A Scientific Statement From the American Heart Association. Circulation, 2024;149(13): E997: E1022. https://doi.org/10.1161/CIR.0000000000001211

13. Nurkeyev B.; Marassulov S.; Aldabergenov Y.; Adilbekova A.; Murzabayeva S.; Kuandykova E.; Akhmoldaeva A. A Clinical Case of Successful Surgical Correction of Tetralogy of Fallot by Using the Right Atrial Appendage as a Neopulmonary Valve. J Clin Med Kaz 2024, 21(4), 71-73. DOI: https://doi.org/10.1161/10.23950/jcmk/14968

14. Singhi A. K.; Mukherji A.; De A. Perimembranous ventricular septal defect closure in infants with KONARMF occluder. Prog Pediatr Cardiol 2022, 65, 101489. DOI: https://doi.org/10.1161/10.1016/j.ppedcard.2022.101489

15. Michelena HI, Prakash SK, Della Corte A, Bissell MM, Anavekar N, Mathieu P, Bossé Y, Limongelli G, Bossone E, Benson DW, Lancellotti P, Isselbacher EM, Enriquez-Sarano M, Sundt TM 3rd, Pibarot P, Evangelista A, Milewicz DM, Body SC; BAVCon Investigators. Bicuspid aortic valve: identifying knowledge gaps and rising to the challenge from the International Bicuspid Aortic Valve Consortium (BAVCon). Circulation. 2014;129(25):2691-704. doi: 10.1161/CIRCULATIONAHA.113.007851. PMID: 24958752.

16. Britt WJ, Prichard MN. New therapies for human cytomegalovirus infections. Antiviral Res. 2018; 159:153-174. doi: 10.1016/j.antiviral.2018.09.003. PMID: 30227153.

17. Muller C, Alain S, Gourin C, Baumert TF, Ligat G, Hantz S. New Insights into Human Cytomegalovirus pUL52 Structure. Viruses. 2021;13(8):1638. doi: 10.3390/v13081638. PMID: 34452502.

18. Biesiedina AA, & Demenko MM. Spadkovi khvoroby: navchal′nyi posibnyk [Hereditary Diseases: A Textbook. Sumy: Sumy State University]. 2024. 144 p. https://essuir.sumdu.edu.ua/bitstream- download/123456789/94986/3/Biesiedina_spadkovi_khvoroby.pdf (In Ukrainian)

19. Crawford MH. CURRENT Diagnosis and Treatment: Cardiology [Internet]. 5th. McGraw-Hill Education; 2017[cited 2025 Jun 2]. 640 p. Chapter 35. Roldan CA. Connective Tissue Diseases and the Heart. Available from: https://accessmedicine.mhmedical.com/content.aspx?bookid=2040&sectionid=152997983

20. Richards AA, Garg V. Genetics of congenital heart disease. Curr Cardiol Rev. 2010 May;6(2):91-7. doi: 10.2174/157340310791162703. PMID: 21532774; PMCID: PMC2892081.

21. Zaidi S, Brueckner M. Genetics and Genomics of Congenital Heart Disease. Circ Res. 2017;120(6):923-940. doi: 10.1161/CIRCRESAHA.116.309140. PMID: 28302740.

22. Bentsa TM. Dysplaziia spoluchnoi tkanyny ta arterial′na hipertenziia: suchasnyi pohliad na problemu: (ohliad literatury). [Connective Tissue Dysplasia and Arterial Hypertension: A Modern View on the Problem (Literature Review)]. Zdobutky klinichnoi i eksperimentalnoi medytsyny. 2020; 2:7-12. https://doi.org/10.11603/1811-2471.2020.v.i2.11293 (In Ukrainian)

23. Bolunduț AC, Lazea C, Mihu CM. Genetic Alterations of Transcription Factors and Signaling Molecules Involved in the Development of Congenital Heart Defects-A Narrative Review. Children (Basel). 2023;10(5):812. doi: 10.3390/children10050812. PMID: 37238360.

24. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, Lung B, Kluin J, Lang IM, Meijboom F, Moons P, Mulder BJM, Oechslin E, Roos-Hesselink JW, Schwerzmann M, Sondergaard L, Zeppenfeld K; ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. Eur Heart J. 2021;42(6):563-645. doi: 10.1093/eurheartj/ehaa554. PMID: 32860028.

25. Gunaydin S, Simsek E, Engelman D. Enhanced recovery after cardiac surgery and developments in perioperative care: A comprehensive review. Turk Gogus Kalp Damar Cerrahisi Derg. 2024;33(1):121-131. doi: 10.5606/tgkdc.dergisi.2024.26770. PMID: 40135093.

26. Papoutsi T, Luna-Zurita L, Prados B, Zaffran S, de la Pompa JL. Bmp2 and Notch cooperate to pattern the embryonic endocardium. Development. 2018;145(13): dev163378. doi: 10.1242/dev.163378. PMID: 29853617.

27. Luxán G, D'Amato G, MacGrogan D, de la Pompa JL. Endocardial Notch Signaling in Cardiac Development and Disease. Circ Res. 2016;118(1): e1-e18. doi: 10.1161/CIRCRESAHA.115.305350. PMID: 26635389.

28. Stefanovic S, Etchevers HC, Zaffran S. Outflow Tract Formation-Embryonic Origins of Conotruncal Congenital Heart Disease. J Cardiovasc Dev Dis. 2021;8(4):42. doi: 10.3390/jcdd8040042. PMID: 33918884.

29. Gunawan F, Gentile A, Gauvrit S, Stainier DYR, Bensimon-Brito A. Nfatc1 Promotes Interstitial Cell Formation During Cardiac Valve Development in Zebrafish. Circ Res. 2020;126(8):968-984. doi: 10.1161/CIRCRESAHA.119.315992. PMID: 32070236.

30. Li B, Li T, Pu T, Liu C, Chen S, Sun K, Xu R. Genetic and functional analyses detect one pathological NFATC1 mutation in a Chinese tricuspid atresia family. Mol Genet Genomic Med. 2021;9(9): e1771. doi: 10.1002/mgg3.1771. PMID: 34363434.

31. de la Pompa JL, Epstein JA. Coordinating tissue interactions: Notch signaling in cardiac development and disease. Dev Cell. 2012;22(2):244-254. doi: 10.1016/j.devcel.2012.01.014

32. Duan S, Li G, Qiu F, Zhao L, Zhao M, Wang L, Feng Z, Ma X. [Case-control study on the association between four single nucleotide polymorphisms in folate metabolism way and the risk of congenital heart disease]. Wei Sheng Yan Jiu. 2018;47(4):536-542. Chinese. PMID: 30081977.

33. Obi CA, Mostertz WC, Griffin JM, Judge DP. ATTR Epidemiology, Genetics, and Prognostic Factors. Methodist Debakey Cardiovasc J. 2022;18(2):17-26. doi: 10.14797/mdcvj.1066. PMID: 35414855.

34. Wang F, Wang H, Wang L, Zhou S, Chang M, Zhou J, Dou Y, Wang Y, Shi X. Association Between Single Nucleotide Polymorphisms in NFATC1 Signaling Pathway Genes and Susceptibility to Congenital Heart Disease in the Chinese Population. Pediatr Cardiol. 2016;37(8):1548-1561. doi: 10.1007/s00246-016-1469-5. PMID: 27567908.

35. Kamenshchyk AV. Ekspresiia hena NFATC1 u ditei z dvostulkovym aortal′nym klapanom sertsia v zalezhnosti vid naiavnosti klapannoho fibrozy [Expression of the NFATC1 Gene in Children with Bicuspid Aortic Valve Depending on the Presence of Valvular Fibrosis. Zdobutky klinichnoi i eksperimentalnoi medytsyny]. 2019; 3:73-78. DOI 10.11603/1811-2471.2019.v.i3.10401 (In Ukrainian)

36. Asta L, D'Angelo GA, Marinelli D, Benedetto U. Genetic Basis, New Diagnostic Approaches, and Updated Therapeutic Strategies of the Syndromic Aortic Diseases: Marfan, Loeys-Dietz, and Vascular Ehlers-Danlos Syndrome. Int J Environ Res Public Health. 2023;20(16):6615. doi: 10.3390/ijerph20166615. PMID: 37623198.

37. Salik I, Rawla P. Marfan Syndrome. 2023 Jan 23. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 30726024.

38. Pees Christiane Marfan syndrome meta-analysis: individual patient data analysis reduces heterogeneity. The Lancet. 2022;400(10355):790-791. https://doi.org/10.1016/S0140-6736(22)01642-7

39. Parlapiano G, Di Lorenzo F, Salehi LB, Ruvolo G, Novelli G, Sangiuolo F. Neurovascular manifestations in connective tissue diseases: The case of Marfan Syndrome. Mech Ageing Dev. 2020; 191:111346. doi: 10.1016/j.mad.2020.111346. PMID: 32920077.

40. van Andel MM, Groenink M, van den Berg MP, Timmermans J, Scholte AJHA, Mulder BJM, Zwinderman AH, de Waard V. Genome-wide methylation patterns in Marfan syndrome. Clin Epigenetics. 2021;13(1):217. https://doi.org/10.1186/s13148-021-01204-4. PMID: 34895303.

41. Coelho SG, Almeida AG. Marfan syndrome revisited: From genetics to the clinic. Rev Port Cardiol (Engl Ed). 2020;39(4):215-226. English, Portuguese. doi: 10.1016/j.repc.2019.09.008. PMID: 32439107.

42. von Kodolitsch Y, Demolder A, Girdauskas E, Kaemmerer H, Kornhuber K, Muino Mosquera L, Morris S, Neptune E, Pyeritz R, Rand-Hendriksen S, Rahman A, Riise N, Robert L, Staufenbiel I, Szöcs K, Vanem TT, Linke SJ, Vogler M, Yetman A, De Backer J. Features of Marfan syndrome not listed in the Ghent nosology – the dark side of the disease. Expert Rev Cardiovasc Ther. 2019;17(12):883-915. doi: 10.1080/14779072.2019.1704625. PMID: 31829751.

43. Chen ZX, Jia WN, Jiang YX. Genotype-phenotype correlations of marfan syndrome and related fibrillinopathies: Phenomenon and molecular relevance. Front Genet. 2022; 13:943083. doi: 10.3389/fgene.2022.943083. PMID: 36176293.

44. Thacoor A. Mitral valve prolapse and Marfan syndrome. Congeni Heart Dis. 2017;12(4):430-434. https://doi.org/10.1111/chd.12467

45. Camerota L, Ritelli M, Wischmeijer A, Majore S, Cinquina V, Fortugno P, Monetta R, Gigante L, Marfan Syndrome Study Group Tor Vergata University Hospital, Sangiuolo FC, Novelli G, Colombi M, Brancati F. Genotypic Categorization of Loeys-Dietz Syndrome Based on 24 Novel Families and Literature Data. Genes (Basel). 2019;10(10):764. doi: 10.3390/genes10100764. PMID: 31569402.

46. Gouda P, Kay R, Habib M, Aziz A, Aziza E, Welsh R. Clinical features and complications of Loeys-Dietz syndrome: A systematic review. Int J Cardiol. 2022; 362:158-167. doi: 10.1016/j.ijcard.2022.05.065. PMID: 35662564.

47. MacCarrick G, Black JH 3rd, Bowdin S, El-Hamamsy I, Frischmeyer-Guerrerio PA, Guerrerio AL, Sponseller PD, Loeys B, Dietz HC 3rd. Loeys-Dietz syndrome: a primer for diagnosis and management. Genet Med. 2014;16(8):576-87. doi: 10.1038/gim.2014.11. PMID: 24577266.

48. Patel ND, Crawford T, Magruder JT, Alejo DE, Hibino N, Black J, Dietz HC, Vricella LA, Cameron DE. Cardiovascular operations for Loeys-Dietz syndrome: Intermediate-term results. J Thorac Cardiovasc Surg. 2017;153(2):406-412. doi: 10.1016/j.jtcvs.2016.10.088. Erratum in: J Thorac Cardiovasc Surg. 2017;153(5):1219. https://doi.org/10.1016/j.jtcvs.2017.03.001. PMID: 27955909.

49. Demirdas S, van den Bersselaar LM, Lechner R, Bos J, Alsters SIM, Baars MJH, Baas AF, Baysal Ö, van der Crabben SN, Dulfer E, Giesbertz NAA, Helderman-van den Enden ATJM, Hilhorst-Hofstee Y, Kempers MJE, Komdeur FL, Loeys B, Majoor-Krakauer D, Ockeloen CW, Overwater E, van Tintelen PJ, Voorendt M, de Waard V, Maugeri A, Brüggenwirth HT, van de Laar IMBH, Houweling AC. Vascular Ehlers-Danlos Syndrome: A Comprehensive Natural History Study in a Dutch National Cohort of 142 Patients. Circ Genom Precis Med. 2024;17(3): e003978. doi: 10.1161/CIRCGEN.122.003978. PMID: 38623759.

50. Knight DRT, Bruno KA, Singh A, Munipalli B, Gajarawala S, Solomon M, Kocsis SC, Darakjian AA, Jain A, Whelan ER, Kotha A, Gorelov DJ, Phillips SD, Fairweather D. Cardiac defects of hypermobile Ehlers-Danlos syndrome and hypermobility spectrum disorders: a retrospective cohort study. Front Cardiovasc Med. 2024; 11:1332508. doi: 10.3389/fcvm.2024.1332508. PMID: 38562189.

51. Miklovic T, Sieg VC. Ehlers-Danlos Syndrome. 2023 May 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 31747221.

52. Yagyu T, Noguchi T. Diagnosis and treatment of cardiovascular disease in patients with heritable connective tissue disorders or heritable thoracic aortic diseases. Cardiovasc Interv Ther. 2024;39(2):126-136. doi: 10.1007/s12928-023-00977-0. PMID: 38182694.

53. Meena JP, Gupta A, Mishra D, Juneja M. Beals-Hecht syndrome (congenital contractural arachnodactyly) with additional craniospinal abnormality: a case report. J Pediatr Orthop B. 2015;24(3):226-9. doi: 10.1097/BPB.0000000000000121. PMID: 25493702.

54. Sharma L, Shankar Kikkeri N. Turner Syndrome. 2025 Jun 22. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 32119508.

55. Zhdan VM, & Katerenchuk OI. Vady sertsia pry syndromi Nunan: literaturnyi ohliad ta vypadok z praktyky. [Heart Defects in Noonan Syndrome: Literature Review and a Case from Practice]. Aktual′ni problemy suchasnoi medytsyny: Visnyk ukrains′koi medychnoi stomatolohichnoi akademii.2018;18(3):345-348. http://nbuv.gov.ua/UJRN/apsm_2018_18_3_73 (In Ukrainian)

56. Galante N, Bedeschi MF, Beltrami B, Bailo P, Silva Palomino LA, Piccinini A. Reviewing hereditary connective tissue disorders: Proposals of harmonic medicolegal assessments. Int J Legal Med. 2024;138(6):2507-2522. https://doi.org/10.1007/s00414-024-03290-4. PMID: 39008115.

57. Öztürk M, Türk MT, Demir GÜ, Ütine GE, Ertuğrul İ, Aypar E, Karagöz T, Alehan D, Kiper PÖŞ, Aykan HH. Desbuquois dysplasia and cardiovascular complications: a retrospective cohort study. Eur J Pediatr. 2025;184(7):388. https://doi.org/10.1007/s00431-025-06231-4. PMID: 40461715.

58. Cury M, Zeidan F, Lobato AC. Aortic disease in the young: genetic aneurysm syndromes, connective tissue disorders, and familial aortic aneurysms and dissections. Int J Vasc Med. 2013; 2013:267215. doi: 10.1155/2013/267215. PMID: 23401778.

59. Distler O, Ofner C, Huscher D, Jordan S, Ulrich S, Stähler G, Grünig E, Held M, Ghofrani HA, Claussen M, Lange TJ, Klose H, Rosenkranz S, Vonk-Noordegraaf A, Vizza CD, Delcroix M, Opitz C, Pausch C, Scelsi L, Neurohr C, Olsson KM, Coghlan JG, Halank M, Skowasch D, Behr J, Milger K, Remppis BA, Skride A, Jureviciene E, Gumbiene L, Miliauskas S, Löffler-Ragg J, Wilkens H, Pittrow D, Hoeper MM, Ewert R. Treatment strategies and survival of patients with connective tissue disease and pulmonary arterial hypertension: a COMPERA analysis. Rheumatology (Oxford). 2024;63(4):1139-1146. doi: 10.1093/rheumatology/kead360. PMID: 37462520.

60. O'Connor M, Well A, Hoyos ME, Stauber CE, Fraser CD, Martinez H. Surgical Intervention in Pediatric Marfan Syndrome: A Multiinstitutional Study. World J Pediatr Congenit Heart Surg. 2025 May 15:21501351251335474. doi: 10.1177/21501351251335474. PMID: 40370284.

ВРОДЖЕНІ ВАДИ СЕРЦЯ ТА ЇХ ЗВ'ЯЗОК ІЗ ДИСПЛАЗІЄЮ СПОЛУЧНОЇ ТКАНИНИ У ДІТЕЙ (ОГЛЯД)

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Резюме.

Вроджені вади серця (ВВС) у дітей залишаються однією з провідних причин дитячої захворюваності та смертності, що потребує ранньої діагностики та хірургічної корекції. Частота ВВС становить 6-10 випадків на 1000 новонароджених. Значний вплив на перебіг ВВС мають супутні патології, зокрема дисплазія сполучної тканини (ДСТ), яка зумовлює слабкість структур серця й судин, підвищує ризик післяопераційних ускладнень і погіршує довгостроковий прогноз.

Мета. Узагальнити сучасні літературні дані щодо особливостей перебігу та ускладнень ВВС у дітей з ДСТ, визначити ключові механізми ризику та перспективні підходи до діагностики й лікування.

Матеріали та методи. У статті розглянуто та проаналізовано світові тенденції щодо особливостей зв'язку та перебігу ВВС із ДСТ у дітей. Проводився аналіз наукових публікацій розміщених у міжнародних електронних наукометричних базах даних PubMed, ScienceDirect та Google Scholar за дослідженнями 2017-2024 років.

Результати. Аналіз сучасних досліджень свідчить, що молекулярні дефекти білків сполучної тканини (фібрилін, колаген, рецептори TGF-β) призводять до порушення ремоделювання серця й судин та підвищують вразливість клапанів і артерій. Для дітей з ДСТ характерні пролапси та регургітації клапанів, аортальні дилатації, аневризми, дисекції судин і підвищений ризик кровотеч та інфекцій після операцій. У таких пацієнтів частіше виникає потреба у повторних втручаннях, а загоєння ран відбувається повільніше. Найбільш відомі синдроми – Марфана, Лойса-Дітца, Елерса–Данлоса – мають чіткий зв'язок із серцево-судинними ураженнями. Ефективне ведення цих пацієнтів потребує мультидисциплінарного підходу: раннього виявлення фенотипових ознак, інструментальної діагностики (ЕХО, МРТ, ангіографії) та генетичного тестування. Регулярний моніторинг аорти й клапанів, своєчасне планування операцій та адекватна медикаментозна профілактика дозволяють знизити ризики тяжких ускладнень.

Висновки. ДСТ є важливим фактором ризику, що ускладнює перебіг ВВС, збільшує ймовірність післяопераційних ускладнень і потребує індивідуалізованої тактики лікування. Фенотипові прояви ДСТ мають враховуватися під час діагностики та планування хірургічних втручань у дітей із ВВС. Мультидисциплінарний підхід та використання сучасних інструментів діагностики й генетичного консультування є ключовими для зниження ризиків і покращення віддаленого прогнозу. Подальші дослідження у сфері молекулярної генетики та патогенезу ДСТ здатні забезпечити нові можливості для раннього прогнозування й персоналізованого лікування дітей з ВВС.

Ключові слова: вроджені вади серця; дисплазія сполучної тканини; діти; зв'язок.

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