International Journal of Medical Sciences And Clinical Research
(ISSN – 2771-2265)
VOLUME 04 ISSUE 06 PAGES: 24-31
OCLC – 1121105677
Crossref doi Google Scholar WorldCat MENDELEY
Publisher: Oscar Publishing Services

Journal Website: https://theusajournals.com/index.php/ijmscr



Research Article

# FUNCTIONAL COMPONENT OF THE CARDIOVASCULAR SYSTEM IN INDIVIDUALS WITH CONNECTIVE TISSUE DYSPLASIA

**Submission Date:** June 05, 2024, **Accepted Date:** June 10, 2024,
**Published Date:** June 15, 2024
**Crossref doi:** https://doi.org/10.37547/ijmscr/Volume04Issue06-05

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## ABSTRACT

The article discusses connective tissue dysplasia (CTD) and its genetic basis, classification issues in the International Classification of Diseases (ICD), research on CTD in Uzbekistan, and the association of CTD with cardiovascular complications, particularly arrhythmias. Various studies and classifications related to CTD are mentioned, emphasizing the genetic mutations underlying the disease and the prevalence of arrhythmias in syndromic forms such as Marfan syndrome and Ehlers-Danlos syndrome. The text underscores the importance of close monitoring, early detection, and appropriate management of arrhythmias in patients with CTD to optimize outcomes and reduce complications.

Based on the foregoing, the purpose of this work is to establish in posttal ontogenesis the laws of the formation and involution of bronchial vascular and lymphatic systems in a person, epithelial connective tissue relationships in the air and respiratory parts of the lung (1.4).

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KEYWORDS

Connective tissue (CT), Connective tissue dysplasia (CTD), Classification, heart rhythm disorders, functional component of the cardiovascular system.

## INTRODUCTION

Connective tissue is an integral structure, as a result of which damage to one or another of its components is accompanied by the development of inevitable pathological changes in neighboring ones, which results in a decrease in its functional capabilities [3, 4, 5, 6]. It is assumed that the substrate of the nature of the alterative component in the pathogenesis of CT dysplasia is not known for certain, because, as stated above, to one degree or another, both fibers and the ground substance of a given tissue are involved, often to an equal extent [4, 7].

At the current stage of studying CTD, the leading role of genetics in pathogenesis has been revealed. The basis for the changes is mutations of genes that store hereditary information on the processes of synthesis of the constituent parts of connective tissue, a violation of which potentiates the disintegration of the components of the extracellular matrix, which is in the genesis of the violation of the organ framework and significantly affects the clinic of associated nosologies [4, 7, 8, 9, 10, 11, 12].

A study of the genetic load of CTD per population cell, i.e. a certain family or genus using genealogy, determining the distinctive properties of the morphological disorder showed that as we approach the studied proband and his sibs, dysmorphism is characterized by the presence of a progressive increase in persistent and specific signs of CTD, which can indirectly demonstrate the dominance of mutations characteristic of this pathology. This category of patients, receiving the CTD pool of genetic information from their ancestors, is characterized by a rapid increase in a specific symptom complex already in the early extrauterine period of development, which perturbs in the key periods of childhood and puberty with the preservation of the desired disorders until the end of life [7].

### Classification issues

The International Classification of Diseases WHO (ICD-10) does not cover CTD as a separate nosological unit; on the contrary, there is a need to classify many pathologies similar to code M35.9 - Systemic lesions of connective tissue, unspecified, which may in some situations create inconvenience for their descriptions, both in the international literature and in the practical activities of a doctor. Some of the nosologies that

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collectively constitute the vanguard of the connective tissue dysplasia clinic have separate classification codes I34.1 - Mitral valve prolapse, H52.1. – Myopia, Q87.4 – Marfan syndrome, Q79.6 – Ehlers-Danlos syndrome, etc.

In ICD-11, despite the introduction of significant changes compared to the previous version, and as WHO experts emphasize - more significant clinical content, DST is not assigned a separate code and it can refer to LD28.Y - Other specific syndromes with connective tissue damage as the main symptom or LD28.Z - Syndromes with connective tissue damage as the main symptom, unspecified, which once again indicates the need to conduct research on this problem from the point of view of different areas of medicine because the issue of DST is interdisciplinary.

The most common clinical classification of DST is the division into 2 groups according to differentiation, i.e. into differentiated and undifferentiated types. Differentiated dysplasias relative to undifferentiated ones are quite rare, they are distinguished by the presence of a clear clinical symptom complex, represented by gene abnormalities, and are characterized by established Mendeleevian inheritance: Schwarz-Yampel Meester-Loeys, Knobloch, Marfan, Ehlers-Danlos, Alport syndromes, spondyloepimetaphyseal dysplasia, osteogenesis imperfecta, congenital muscular dystrophy Ulrich, etc.); whereas nonspecific symptoms, widespread prevalence in the population and an uncertain form of inheritance characterize undifferentiated forms.

**Research in Uzbekistan on this topic**

Connective tissue dysplasia and associated diseases of various organ systems are attracting the attention of an increasing number of researchers due to the relatively high prevalence of this group of pathologies. In our country, scientific research was carried out, which was fragmentary, until the study by G.Z. Shodikulova was initiated. Then, under her leadership, several works were carried out to study connective tissue dysplasia, the features of the course, diagnosis and treatment of pathology of the upper gastrointestinal tract in patients with connective tissue dysplasia were studied (Samatov D.K., 2023), the prevalence and features of the course were characterized undifferentiated connective tissue dysplasia using the example of Samarkand and Jizzakh regions (Mirzaev O.V., 2022), the significance of phenotypic, genetic markers on the development, course and early diagnosis of undifferentiated connective tissue dysplasia was determined (Babamuradova Z.B., 2020). Despite the significant progress in understanding CTD, there are several issues affecting the state of the cardiovascular system in patients with connective tissue dysplasia, in particular with heart rhythm disturbances, which require more in-depth research to prevent cardiac complications and reduce the burden of their mortality on the population.

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Modern literature is replete with data on a whole group of monogenic DSTs associated with mutations in genes responsible for the synthesis of extracellular matrix proteins (various types of collagens, tenaskin, fibrillin), genes for growth factor receptors and matrix metalloproteinases [13].

Data from Lamandé SR, Bateman JF (2020) based on an analysis of the literature indicate that the set of genes responsible for the synthesis of vital components of the extracellular matrix, i.e. The human matrisome (1,027 genes) is represented by 274 central genes that make up its "core" and 753 genes "associated" with it. The most important genes included in the matrisome core store genetic information for the biosynthesis of ECM glycoproteins - 195 genes, proteoglycans - 35 and collagens - 44. Genes interconnected with this set form groups of genes responsible for the secretion of factors - 344, synthesis of regulators - 238, and those closely associated with the ECM - 171 (the number of genes studied is indicated after the dash). The authors also note that of the 195 genes responsible for the genetic information of ECM glycoproteins, 67 correlate with genetic diseases or predisposition to them; 27 out of 44 collagen and 11 out of 35 proteoglycan genes are associated with a number of this type of pathology [14].

The literature varies on the prevalence of CTD, which may be due to the genetic heterogeneity of different populations, the lack of a clear classification and criteria for stigmatization [7, 15, 16, 17] and a number of other factors. Methodological approaches and their heterogeneity in the study of this group of pathologies deserve special attention:

Martynov A.I. et al. (1998) stated that the presence of 3 signs is sufficient to confirm dysplasia; Klemenov A.B. (2005) – 4 for women, 5 for men; N.P. Shabalov, V.A. Tabolin (1984), E.V. Zemtsovsky (2000) – 6 signs; Gorbunova V.N., Kadurina T.I. (2007) – from 6 to 8 signs;

The above aspects of research complicate the process of collecting and collating research results. Also, it is worth noting a different opinion of a number of researchers on the diagnosis of DST, testing the likelihood of an erroneous medical conclusion about the presence of this disease in the subjects - overdiagnosis due to the introduction of a quantitative approach, and therefore, the determination of qualitative dysmorphogenesis and associated manifestations may be important [7, 16, 18]. However, even here, scientists' views on the degree of quality of certain characteristics began to differ [7, 19, 20, 21, 22]. The introduction of the latest achievements of biostatistics into scientific medical use has made it possible to determine the statistical indicators of diagnostic measures for the detection of study participants with and without DST, derived from errors of the first and second types, i.e. sensitivity and

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specificity, on the basis of which it became possible to determine the predictive diagnostic value. This approach made it possible to systematize the diagnostic significance of individual DST parameters and, as a result, develop special DST tables aimed at monitoring the clinic of children and adults [7, 18]. The practical and clinical significance of the above method is difficult to deny.

Some studies [7, 17, 19, 21, 23] show wide variation in the phenotypic burden of CTD, ranging from 1–80%. In Uzbekistan, the incidence of this pathology, according to the analysis (Shodikulova G.Z., Mirzaev O.V., 2022) among respondents in Samarkand and Jizzakh regions was without a significant difference by region, and the average value of the required indicators in both regions was about 9%, in particular in Samarkand - 9.9%, and in Jizzakh - 8.8%, which indicates that almost every 10th resident has a predisposition to CTD or suffers from it, which, given the age composition of the study participants, confirms clinical and scientific significance of the study of this problem.

Connective tissue dysplasia, especially syndromic forms such as Marfan syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome, is associated with an increased risk of cardiovascular complications, including arrhythmias. Although exact prevalence data may vary depending on the specific syndrome and population studied, research suggests that arrhythmias are relatively common in patients with connective tissue dysplasia.

For example, studies have shown a higher prevalence of atrial fibrillation/flutter, ventricular arrhythmias, and conduction abnormalities in patients with Marfan syndrome [4, 5, 16, 17] compared with the general population. Similarly, people with Ehlers-Danlos syndrome [8, 9, 10] may experience a variety of arrhythmias, especially those associated with structural cardiac abnormalities such as mitral valve prolapse and aortic root dilatation.

The occurrence of arrhythmias in patients with connective tissue dysplasia is influenced by many factors, including the genetic mutation underlying the disease, the severity of damage to the cardiovascular system, and the presence of comorbidities such as hypertension and valvular abnormalities of the heart. In addition, age, gender, and lifestyle may also contribute to the development of arrhythmias in these patients.

Given the increased risk of arrhythmias in patients with connective tissue dysplasia, close monitoring, early detection, and appropriate management strategies are necessary to optimize outcomes and reduce the risk of complications.

## CONCLUSION

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Thus, the morphological and physiological properties of the cardiovascular system, mediating the occurrence of rhythm disturbances in CDT, have a significant impact on the likelihood of developing cardiac complications and can negatively affect the quality of life of patients and the prognosis of existing cardiac pathologies; CTD accelerates pathological changes that occur in the heart, which requires a separate approach to early diagnosis.

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