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Cardiovascular Adaptation And Functional Responses To Physical Stress In Children And Adolescents With Undifferentiated Connective Tissue Dysplasia

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Abstract
Undifferentiated connective tissue dysplasia (UCTD) is a genetically determined condition characterized by systemic manifestations affecting multiple organs, including the cardiovascular system. Children and adolescents with UCTD demonstrate impaired structural, functional, and autonomic regulation of cardiac activity, which reduces their tolerance to physical stress. **Aim.** To analyze current scientific evidence on cardiovascular adaptation to physical loads in children and adolescents with UCTD, focusing on myocardial function, autonomic regulation, and exercise-induced physiological responses. **Methods.** A narrative literature review was conducted using peer-reviewed publications from PubMed, Scopus, Web of Science, and Google Scholar (2010–2024). Studies on myocardial morphology, heart rate variability (HRV), autonomic dysfunction, exercise tolerance, and rehabilitation outcomes in children with UCTD were included. **Results.** Children with UCTD exhibit structural myocardial features such as mitral valve prolapse (MVP), increased trabecularity, reduced myocardial mass, and decreased contractile function. Cardiac functional assessment shows reduced ejection fraction (55–58%), mild diastolic dysfunction, and 10–15% reduction in stroke volume. HRV analysis demonstrates sympathetic predominance and reduced parasympathetic tone, indicating limited adaptive reserve. These abnormalities prolong recovery time after physical activity, reduce exercise tolerance, and increase the risk of orthostatic reactions. Individualized rehabilitation programs improve autonomic balance and enhance cardiovascular stability. **Conclusion.** Cardiovascular adaptation to physical loads is significantly impaired in pediatric UCTD. Early recognition of autonomic and myocardial dysfunction, combined with personalized physical training strategies, may prevent complications and improve long-term cardiovascular outcomes.
Keywords. connective tissue dysplasia; UCTD; cardiovascular adaptation; physical exercise; autonomic imbalance; HRV; mitral valve prolapse; pediatric cardiology; exercise tolerance.

Introduction.

Undifferentiated connective tissue dysplasia (UCTD) is a genetically mediated condition characterized by structural and functional abnormalities of the extracellular matrix, affecting multiple organ systems, including the cardiovascular apparatus. According to recent studies, the prevalence of connective tissue dysplasia in children ranges from 20% to 30%, with up to 50–70% of affected patients demonstrating cardiovascular manifestations such as mitral valve prolapse (MVP), conduction disturbances, autonomic dysfunction, and decreased exercise tolerance (Ivanov et al., 2020; Deuster et al., 2022).

Children and adolescents with UCTD exhibit increased elasticity and reduced tensile strength of connective tissue fibers, which directly influence myocardial structure, valvular competence, and vascular tone. Morphological studies indicate that these patients often have thinner myocardial walls, decreased cardiomyocyte density, and increased trabecular patterning, contributing to reduced contractile capacity and early fatigue during physical efforts (Smirnova et al., 2019; O'Byrne et al., 2018).

Exercise-induced cardiovascular responses in UCTD are significantly altered due to impaired autonomic regulation. Heart rate variability (HRV) analysis consistently demonstrates sympathetic dominance and reduced parasympathetic modulation, leading to diminished adaptive capacity during physical load (Briceno et al., 2021; Malik et al., 2015). Autonomic imbalance results in inadequate chronotropic response, orthostatic instability, delayed recovery, and a tendency toward hypotensive reactions after physical exertion (Radzikowska et al., 2020).

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Functional echocardiographic assessments in children with UCTD reveal lowered ejection fraction (55–58%), reduced stroke volume, mild diastolic dysfunction, and increased frequency of minor structural anomalies such as MVP, tricuspid valve prolapse, and aortic root dilation (Lombardi et al., 2021; Aypar et al., 2017). These alterations contribute to decreased exercise capacity, early exhaustion, and reduced tolerance to routine physical activity.

Given the chronic nature of UCTD, early identification of cardiovascular abnormalities is essential. Numerous studies confirm that timely introduction of individualized rehabilitation programs, autonomic training, controlled aerobic activity, and postural regulation exercises significantly enhance adaptation to physical loads and reduce the severity of clinical symptoms (Sartori et al., 2023; Wasilewski et al., 2022).

Therefore, understanding the mechanisms of cardiovascular adaptation in pediatric UCTD is of great clinical importance. Comprehensive evaluation of myocardial structure, functional capacity, and autonomic regulation enables the development of targeted therapeutic and rehabilitation strategies aimed at improving exercise tolerance, preventing complications, and ensuring better long-term outcomes for affected children.

Aim of the Study. The aim of this study is to analyze and systematize current scientific data on the cardiovascular adaptation to physical stress in children and adolescents with undifferentiated connective tissue dysplasia (UCTD). The study seeks to identify key structural, functional, and autonomic abnormalities of the cardiovascular system in this population, evaluate their impact on exercise tolerance, and determine the role of individualized rehabilitation and physical training programs in improving adaptive cardiovascular responses and preventing potential complications.

Materials and methods. This review was conducted using a structured narrative approach aimed at summarizing contemporary scientific evidence related to cardiovascular adaptation to physical stress in children and adolescents with undifferentiated connective tissue dysplasia (UCTD). A comprehensive search of the literature was performed across international scientific databases, including PubMed, Scopus, Web of Science, Google Scholar, and the Cochrane Library, covering the period from 2010 to 2024. The search strategy included combinations of relevant keywords such as "undifferentiated connective tissue dysplasia," "UCTD in children," "cardiovascular adaptation," "physical load," "heart rate variability," "autonomic dysfunction," "mitral valve prolapse," and "exercise tolerance." Boolean operators (AND, OR) were applied to refine the search and improve retrieval sensitivity.

Publications were selected based on predefined inclusion criteria that required studies to involve children and adolescents aged 5 to 18 years with a confirmed diagnosis of UCTD and to provide information about structural or functional cardiovascular characteristics, autonomic regulation, or responses to physical exercise. Only peer-reviewed journal articles in English or Russian were included. Studies focusing exclusively on adult populations, isolated case reports, non-reviewed materials, and publications unrelated to cardiovascular function were excluded. Research involving other hereditary connective tissue disorders such as Marfan syndrome or Ehlers–Danlos syndrome was also excluded to avoid diagnostic overlap.

Eligible studies were carefully examined, and relevant data were extracted systematically. Key parameters included echocardiographic findings—such as ejection fraction, stroke volume, and diastolic function—along with indicators of autonomic activity obtained from heart rate variability (HRV) analysis, including LF, HF, and LF/HF ratios. Additionally, information regarding exercise tolerance was gathered from standardized physical load tests, including treadmill protocols, bicycle ergometry, 6-minute walk tests, and Ruffier indices. Data describing rehabilitation approaches, autonomic training, and individualized physical training programs were also considered.

To ensure the quality of the reviewed material, the methodological soundness of each selected study was assessed using STROBE criteria for observational research and PRISMA principles for review transparency. Only studies meeting moderate to high methodological standards were included in the final synthesis. Extracted data were then organized into central thematic categories, including myocardial structural features, cardiac functional performance, autonomic regulation, and exercise-induced physiological responses. This systematic process enabled a comprehensive and reliable synthesis of current scientific knowledge regarding cardiovascular adaptation in pediatric patients with UCTD.

Results. The analysis of selected scientific studies revealed that children and adolescents with undifferentiated connective tissue dysplasia (UCTD) demonstrate a complex spectrum of cardiovascular alterations that significantly limit their adaptation to physical stress. Echocardiographic findings across multiple studies

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consistently show the presence of structural myocardial changes, including a high prevalence of mitral valve prolapse (MVP), which is detected in 35–60% of patients and is often accompanied by tricuspid valve prolapse and mild dilation of the aortic root. These structural deviations reflect the inherent weakness of connective tissue fibers, resulting in reduced stability of the valvular apparatus and lower mechanical efficiency of the myocardium. In addition, several authors report decreased myocardial mass and increased trabecularity, indicating insufficient myocardial remodeling and compromised contractile potential.

Functional cardiac assessments further support the presence of significant impairments. Many children with UCTD exhibit a reduction in left-ventricular ejection fraction, typically ranging between 55–58%, compared to higher values observed in healthy controls. Stroke volume and overall cardiac output are also reduced by an estimated 10–15%, which mirrors the diminished ability of the myocardium to respond to increased metabolic demands during physical exercise. Diastolic abnormalities, particularly impaired relaxation and slowed ventricular filling, are frequently documented, and these changes contribute to early fatigability and prolonged recovery. Additionally, peripheral vascular tone is often decreased in this population, leading to clinical manifestations of hypotonic syndrome, including low blood pressure, reduced systemic resistance, and fragile hemodynamic stability during exercise.

Autonomic regulation plays a crucial role in cardiovascular adaptation, and the evaluated studies reveal a distinct pattern of dysautonomia in children with UCTD. Heart rate variability (HRV) parameters consistently demonstrate increased sympathetic dominance, characterized by elevations in low-frequency (LF) components and suppression of high-frequency (HF) components, indicating reduced parasympathetic activity. The LF/HF ratio is markedly elevated, which corresponds to autonomic imbalance and diminished adaptive reserve. Children with such autonomic disturbances show delayed heart rate recovery after exercise, inadequate chronotropic response, proneness to orthostatic reactions—including dizziness, tachycardia, and transient hypotension—and earlier onset of fatigue even with moderate workloads.

Exercise testing across reviewed studies highlights additional limitations. Children with UCTD perform significantly worse on standardized exercise assessments such as the Ruffier index, 6-minute walk test, treadmill protocols, and bicycle ergometer trials. They exhibit shortened endurance time, lower maximal workload achievement, and prolonged recovery periods, sometimes lasting two to three times longer than observed in unaffected children. Physiologically, these responses reflect a combination of inadequate myocardial contractile reserve, autonomic instability, and reduced vascular elasticity. Many studies also note that affected children develop marked cardiorespiratory discomfort during physical exertion, which includes palpitations, shortness of breath, chest discomfort, and excessive fatigue.

Overall, the compiled results strongly indicate that cardiovascular adaptation to physical stress in children and adolescents with UCTD is significantly compromised at several regulatory levels—structural, functional, autonomic, and exercise-induced. These findings underscore the necessity of early screening, routine monitoring, and the integration of targeted rehabilitation programs to support cardiovascular stability and improve adaptive responses in this vulnerable patient group.

Discussion. The findings of this review highlight that children and adolescents with undifferentiated connective tissue dysplasia (UCTD) experience multilevel disturbances in cardiovascular adaptation to physical stress, reflecting a complex interaction between structural myocardial anomalies, functional impairments, and autonomic dysregulation. The presence of connective tissue weakness fundamentally shapes the pathophysiology observed in these patients, as abnormalities of collagen synthesis and extracellular matrix organization affect both the mechanical stability of cardiac structures and the regulatory mechanisms responsible for maintaining homeostasis during physical exertion.

The high prevalence of mitral valve prolapse (MVP) and other minor structural cardiac anomalies observed in UCTD can be explained by the decreased firmness and elasticity of valvular tissue, which compromises valvular coaptation and leads to mild regurgitation under stress conditions. Although often considered benign in the general pediatric population, MVP in the context of UCTD gains clinical significance as it contributes to reduced stroke volume and increased hemodynamic vulnerability during exercise. These structural variations often correlate with reduced myocardial mass and decreased contractile reserve, limiting the heart's ability to augment cardiac output in response to increased metabolic demands, as also indicated by lower ejection fraction values in several studies.

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Functional cardiovascular limitations seen in this group, such as mild diastolic dysfunction and diminished systolic reserve, further impair the efficiency of blood circulation during physical activity. The inability of the myocardium to relax properly during diastole prolongs ventricular filling time and restricts preload reserve, which is essential for enhancing cardiac output during exertion. These dysfunctions are particularly significant for adolescents and pre-teens who are undergoing rapid physiological maturation and thus require robust cardiovascular adaptability.

A central and recurring theme in the literature is the dominance of autonomic dysfunction in shaping the exercise responses of children with UCTD. The sympathetic overactivation and parasympathetic suppression identified through HRV analysis suggest a chronic autonomic imbalance that limits the ability to mount coordinated cardiovascular reactions to stress. This autonomic rigidity results in insufficient chronotropic response during exercise and delays post-exercise recovery, which may lead to exaggerated fatigue, orthostatic intolerance, and exercise avoidance. Such patterns can negatively influence long-term physical development, psychological well-being, and overall functional capacity.

Alterations in vascular tone—particularly the tendency toward hypotonic syndrome—exacerbate cardiovascular instability during physical load. Reduced peripheral resistance and decreased venous return during exercise limit the augmentation of cardiac output, making even moderate physical activity challenging. These hemodynamic vulnerabilities may explain why many children with UCTD complain of fatigue, dizziness, palpitations, or near-syncope during exertion.

The evidence also supports the concept that decreased cardiovascular adaptability in UCTD patients should not be viewed solely as a series of isolated abnormalities but rather as manifestations of a unified pathophysiological syndrome rooted in connective tissue dysregulation. This systemic perspective emphasizes the need for multidisciplinary management, including cardiology, rehabilitation medicine, pediatrics, and, when necessary, genetics.

Importantly, research indicates that targeted, individualized rehabilitation strategies have a substantial positive impact on cardiovascular outcomes. Aerobic training tailored to the child's tolerance, combined with postural and breathing exercises, has been shown to improve HRV, increase parasympathetic tone, and stabilize autonomic function. Strengthening the muscular corset enhances venous return and reduces the hemodynamic consequences of hypotonia. The efficacy of these programs emphasizes the importance of early detection and timely intervention to prevent further deterioration of cardiovascular adaptability.

Overall, the discussion supports the view that cardiovascular impairments in children with UCTD are complex but modifiable. While the underlying connective tissue disorder is congenital and lifelong, its functional consequences—such as autonomic imbalance, reduced endurance, and prolonged recovery—can be mitigated significantly with targeted interventions. Therefore, structured rehabilitation, regular monitoring, and personalized physical education plans represent essential components of long-term management aimed at improving exercise tolerance, preventing deconditioning, and enhancing quality of life in this vulnerable population.

Conclusion. The findings of this review demonstrate that cardiovascular adaptation to physical stress in children and adolescents with undifferentiated connective tissue dysplasia (UCTD) is significantly compromised due to a combination of structural, functional, and autonomic abnormalities. Morphological cardiac features such as mitral valve prolapse, reduced myocardial mass, and minor structural anomalies weaken the mechanical efficiency of the heart. Functional impairments—including decreased ejection fraction, reduced cardiac output, and mild diastolic dysfunction—further limit the capacity of the cardiovascular system to respond adequately to increased physical demands. Autonomic dysregulation, reflected by sympathetic predominance and diminished parasympathetic activity, results in inadequate chronotropic response, orthostatic intolerance, delayed recovery, and reduced exercise tolerance.

These multidimensional disturbances highlight UCTD as a clinical condition requiring early and careful cardiovascular assessment. Evidence strongly supports the role of individualized rehabilitation programs, including controlled aerobic exercise, autonomic training, postural correction, and breathing techniques, in improving autonomic balance and enhancing cardiovascular resilience. Timely implementation of such interventions can significantly improve exercise capacity, reduce symptomatic burden, and prevent long-term complications. Therefore, a comprehensive, multidisciplinary, and personalized approach is essential for optimizing cardiovascular health and physical adaptation in pediatric patients with UCTD.

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