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The Role Of Biochemical And Morphological Changes In The Development Of Pectus Carinatum In Children

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ABSTRACT

Background: Pectus carinatum is a congenital deformity of the anterior chest wall characterized by abnormal protrusion of the sternum and costal cartilages. Despite extensive research, the etiology and pathogenesis of the deformity remain insufficiently understood.Objective: To summarize and systematize current literature data on the biochemical and morphological mechanisms involved in the development of pectus carinatum in children.Methods: A comprehensive review of published studies focusing on structural, biochemical, and genetic alterations of costal cartilage in patients with pectus carinatum was conducted.Results: Literature data suggest that changes in collagen composition, abnormalities of glycosaminoglycans, impaired water-binding capacity, altered biomechanical properties, and disturbances in connective tissue metabolism contribute to reduced cartilage strength. Evidence also indicates that genetic factors, connective tissue dysplasia, and abnormalities in collagen cross-linking play a significant role in the formation of the deformity. Morphological studies reveal ultrastructural alterations of chondrocytes, extracellular matrix disruption, and premature aging characteristics of costal cartilage.Conclusion: The development of pectus carinatum is associated with complex biochemical and morphological alterations of costal cartilage, combined with genetic predisposition and connective tissue abnormalities. Modern high-resolution analytical methods are required to further clarify the underlying mechanisms and to improve diagnostic and therapeutic approaches.

KEYWORDS: pectus carinatum, keeled chest, heredity, children.

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INTRODUCTION

Chest wall deformities represent a heterogeneous group of congenital abnormalities that affect the structural integrity, biomechanics, and functional capacity of the thoracic cage. Among these deformities, pectus carinatum (PC) is the second most common, surpassed only by pectus excavatum, and accounts for 6% to 22% of all anterior chest wall anomalies in children. Clinically, the condition is characterized by an anterior protrusion of the sternum and costal cartilages, which may present symmetrically or asymmetrically and often becomes more pronounced during periods of rapid growth. While the deformity is frequently perceived as a cosmetic issue, it can significantly influence emotional well-being, self-esteem, and social adaptation in affected children. In addition, PC has been associated with functional impairments in the cardiovascular and respiratory systems, further underscoring its clinical relevance.

Despite decades of investigation, the etiology and pathogenesis of pectus carinatum remain subjects of debate. Numerous hypotheses have been proposed, yet no single theory adequately explains the wide variability in clinical presentation. Suggested mechanisms range from metabolic bone disturbances such as rickets and respiratory obstruction during early childhood to increased intrauterine pressure and imbalances between diaphragmatic traction and thoracic rigidity during fetal development. However, none of these theories fully accounts for the structural abnormalities consistently observed in costal cartilage.

An increasing body of evidence indicates that altered biochemical and morphological properties of costal cartilage play a fundamental role in the development of PC. Studies suggest disturbances in collagen composition, abnormal levels and sulfation patterns of glycosaminoglycans, reduced water-binding capacity, and impaired extracellular matrix organization. These biochemical abnormalities contribute to decreased biomechanical strength and elasticity of the chest wall, potentially predisposing costal cartilage to abnormal growth patterns. Furthermore, some authors attribute PC to chondrodysplasia, leading to premature or excessive growth of the rib cartilages, although the exact mechanisms remain uncertain and sometimes contradictory.

The potential contribution of hereditary and connective tissue disorders has also gained considerable attention. A significant proportion of patients exhibit features of connective tissue dysplasia or have a family history of chest deformities, suggesting a genetic predisposition. Conditions such as Marfan syndrome demonstrate a notably high incidence of anterior chest wall abnormalities, highlighting the relevance of mutations affecting collagen synthesis and extracellular matrix stability.

Despite the considerable interest in this condition, many foundational studies on costal cartilage morphology and biochemistry were conducted several decades ago, using methodologies that lack the precision of contemporary molecular and imaging technologies. Consequently, there is a pressing need to reevaluate the structural and biochemical characteristics of costal cartilage using updated scientific approaches to better understand the underlying mechanisms of PC.

This article aims to synthesize and systematize current knowledge on the biochemical and morphological alterations associated with pectus carinatum in children. By integrating data from modern and classical research, we seek to clarify existing discrepancies, outline prevailing scientific perspectives, and highlight key directions for future investigation into the etiology and pathogenesis of this deformity.

Pectus carinatum (PC) is a congenital malformation of the sternum and ribs, which may have a genetic origin and manifests as a symmetrical or asymmetrical increase in the anteroposterior diameter of the chest. Among all chest wall deformities, PC ranks second after pectus excavatum and accounts for 6% to 22% of cases [3, 11, 12, 25]. In addition to the cosmetic defect, which often causes feelings of inferiority and psychosocial difficulties, the deformity leads to pathological changes in the cardiovascular and respiratory systems [27].

The etiology and pathogenesis of PC remain unclear. Despite numerous hypotheses and theories, no unified opinion exists regarding the cause of this deformity. Several assumptions have been proposed, including the development of PC as a consequence of rickets [30], airway obstruction [22, 30], increased intrauterine pressure during fetal development [40], and an imbalance between diaphragmatic traction and the strength of the chest wall [17, 18].

It has been suggested that the basis of PC development is a decrease in the strength of costal cartilage due to changes in the quantitative and qualitative composition of collagen [5, 7], glycosaminoglycans, and water [13]. Many researchers believe that the cause of PC formation is chondrodysplasia of the costal cartilage, leading to accelerated rib growth [6, 8–10, 41]. The theory of excessive growth of costal cartilage is still considered by many authors to be the most likely mechanism in the development of PC. The exact cause of this excessive growth remains unknown, and study results are contradictory. T. Nakaoka and colleagues found that the costal cartilages in children with PC are not longer than those in healthy children [36].

Some researchers regard PC as one of the phenotypic manifestations of connective tissue dysplasia (CTD) [1, 2]. The term “dysplasia” refers to abnormal growth or development of tissue or an organ. CTD is diagnosed based on a careful analysis of symptoms and clinical findings. However, in practice, this diagnosis rarely includes specific histological confirmation. Therefore, dysplasia identified clinically may correspond to numerous structural changes within the tissue [11].

Connective tissue dysplasia is a genetically determined process caused by mutations in genes responsible for collagen fiber synthesis. A significant role of abnormal costal cartilage structure in the pathogenesis of PC is supported by the high incidence of anterior chest wall deformities in patients with connective tissue disorders such as Marfan syndrome and scoliosis [31, 32, 38, 40]. A positive family history of chest wall deformities is observed in 37% of probands with PC [38], indirectly confirming the genetic nature of the pathological process. As a result of mutations, the original triple-helical conformation of collagen macromolecules becomes distorted, decreasing their stability. Fibrils and fibers are formed with defects, and the fibrous structures cannot withstand normal mechanical loads.

Interestingly, in a comparative study by J. Feng and colleagues on the biomechanical, morphological, and histochemical characteristics of costal cartilage in PC, reduced stiffness (Young’s modulus, compression, and shear) and decreased tensile, compressive, and shear strength were reported [23].

Let us examine in more detail the studies devoted to biochemical and morphological investigations of costal cartilage in PC.

CHANGES IN CHEMICAL COMPOSITION AND MORPHOLOGY IN PC.

Costal cartilage belongs to the hyaline type. The key components of the extracellular matrix of hyaline cartilage are type II collagen and glycosaminoglycans (GAGs). Rod-shaped type II collagen macromolecules form fibrils that are stabilized by intermolecular cross-links, which increase with age [14]. A fine fibrillar network forms the structural framework of the hyaline cartilage matrix. GAGs consist of polymeric chains of sulfated amino sugars and carboxylated sugars (uronic acids). The degree and stereometry of sulfation and carboxylation determine the GAG profile. The polysaccharide chains of GAGs attach to a core protein to form proteoglycans, which aggregate with hyaluronic acid into massive complexes (up to 10^8 Da). These aggregates stabilize the fibrillar network and mechanically immobilize the fibrils, providing resistance to shear stress. Additionally, the high concentration of anionic groups in GAGs creates high osmotic pressure, which helps retain water during compressive loads [34]. Data on the chemical composition of costal cartilage and its changes in PC are scarce. According to T.A. Tsvetkova and colleagues, collagen content in dehydrated samples is 56.2±1.6%, which does not differ statistically from cartilage samples in isolated (55.7±0.5%) and syndromic PC (55.6±1.1%). In hydrated samples, collagen content was higher in PC than in controls (by ≈45–60% depending on the form). The authors suggested that this difference is due to reduced water-binding capacity of the cartilage matrix in PC. The level of uronic acids, however, remained similar in control samples (3.3±0.5%) and isolated PC (3.5±0.7%) and syndromic PC (3.6±0.1%). They hypothesized that the GAG profile changes in PC [13].

Data from J. Feng and colleagues showed no differences in GAG staining (safranin O and PAS) between PC and controls [23]. However, this does not rule out changes in GAG composition.

A 2011 study by V.L. David and colleagues provided indirect support for this hypothesis. Using combined safranin O and alcian blue staining, they found that PC samples bound more strongly to alcian blue, whereas controls showed safraninophilia. Since a shift from alcianophilia to safraninophilia indicates increased GAG sulfation, the authors concluded that PC is associated with decreased GAG sulfation. This may reduce water-binding capacity and impair mechanical properties of costal cartilage [20].

Regarding collagen composition, immunohistochemical analysis shows that type II collagen is the main component in both PC and controls [23]. Both groups also exhibit significant amounts of type V collagen [5]. However, PC differs from controls in the following ways: heterogeneous distribution of type II collagen in deeper zones, with areas of increased concentration and areas of decreased staining, up to complete disappearance [23]; presence of type III and type IV procollagens [5]; increased levels of type V collagen and fibronectin [5].

Furthermore, the proportion of soluble collagen is significantly reduced in PC. Soluble collagen (extractable by salt solution, acetic acid, or pepsin) is decreased, suggesting increased inter- and intramolecular cross-linking (premature aging). Indeed, N.V. Borisova and colleagues found increased levels of hydroxylysylpyridinoline cross-links characteristic of type II collagen [16], as well as lysylpyridinoline cross-links typical of type I collagen, indicating impaired post-translational modification of the collagen matrix. Reduced urinary excretion of hydroxyproline-containing peptides also supports this. Elemental analysis shows elevated magnesium and calcium and decreased zinc levels in PC cartilage compared to controls [40]. Zinc is part of the active center of matrix metalloproteinases (MMPs), the only enzymes capable of degrading the collagen triple helix. Reduced MMP activity may impair collagen remodeling, contributing to connective tissue imbalance.

CHANGES IN CELLULAR STRUCTURE AND EXTRACELLULAR MATRIX IN PC.

Another body of research examines chondrocyte structure and extracellular matrix changes in PC. Some authors believe PC is caused by hyperplasia of costal cartilage [24, 37], while others find no significant differences in chondrocytes between PC and controls [4, 20, 23, 28].

According to K. Mullard, reduced biomechanical properties of costal cartilage are secondary to impaired chondrogenesis and osteogenesis [35].

H. Rupprecht and N. Freiberger reported that PC costal cartilage contains blood vessels throughout all sections, with similar vessel density in deformed and intact areas. They also noted an age-related increase in chondrocyte number within a single chondrone compared to controls [37]. J. Feng and colleagues did not confirm these findings; they found intact chondrocytes and nuclei and no signs of hypo- or hyperplasia under electron microscopy. The number of blood vessels and chondrocytes did not differ between PC and healthy children [23].

E.A. Bardakhchyan and colleagues suggested that morphological changes in PC involve ultrastructural abnormalities of chondrocytes, extracellular matrix, and fibrous components [4]. The most characteristic changes include dystrophic processes—lipid and carbohydrate dystrophy, atypical asbestoid fibrils in the pericellular zone, and significant loss of functioning organelles. V.M. Kuritsyn and colleagues noted that both normal and PC cartilage contain acellular regions, map-like areas, desquamated chondrin fibers, and "cerebral" cavities [5]. However, these features appear 6–7 years earlier and nearly three times more frequently in PC than in normally developed chest walls.

Thus, despite many studies on the structure and properties of costal cartilage in normal and pathological conditions, the etiology and pathogenesis of pectus carinatum and related deformities remain unknown. Most studies were conducted decades ago. Modern high-resolution analytical techniques may provide more precise data on cartilage structure, composition, and properties and help identify the true cause of chest wall deformities.

CONCLUSION

The analysis of the available literature demonstrates that pectus carinatum in children is a complex congenital chest wall deformity with multifactorial origins involving biochemical, morphological, and genetic components. Despite decades of research, the precise etiology and pathogenesis of the deformity remain unresolved. However, accumulated evidence indicates that abnormalities in the structure and function of costal cartilage play a central role in its development.

Biochemical studies reveal significant alterations in the composition of costal cartilage, including changes in collagen types, degrees of sulfation of glycosaminoglycans, water-binding capacity, and cross-link density. These modifications lead to impaired biomechanical properties—reduced stiffness, tensile strength, and elasticity—which weaken the structural stability of the anterior chest wall. The presence of atypical collagen cross-links and decreased levels of soluble collagen suggest premature aging and disrupted post-translational modification of the extracellular matrix.

Morphological investigations further support these findings by demonstrating ultrastructural abnormalities of chondrocytes and the surrounding matrix. Dystrophic cellular transformations, atypical fibrillar structures, and premature development of degenerative changes indicate chronic impairment of cartilage homeostasis. Although some studies debate the degree of hyperplasia or structural variation within chondrones, the majority concur that costal cartilage in children with pectus carinatum exhibits early-onset degenerative and dysplastic characteristics not present in healthy children.

Genetic factors appear to have considerable influence, as evidenced by the high incidence of pectus deformities among patients

with hereditary connective tissue disorders such as Marfan syndrome, as well as the presence of familial clustering. Mutations affecting collagen synthesis and connective tissue metabolism likely contribute to the reduced structural resilience and aberrant growth patterns of cartilage. These hereditary influences highlight the importance of viewing pectus carinatum not merely as an isolated chest wall abnormality but as a potential manifestation of systemic connective tissue pathology.

Taken together, the findings suggest that pectus carinatum arises from a complex interplay between impaired biochemical integrity of the extracellular matrix, altered biomechanical properties of costal cartilage, morphological degeneration of chondrocytes, and genetic predispositions. This multifactorial nature explains why a single unifying theory of pathogenesis has not been established and why clinical presentations vary widely among patients.

Given that most foundational studies were conducted several decades ago, there is an urgent need for modern research employing advanced molecular, biomechanical, and imaging technologies. High-resolution analyses of collagen architecture, GAG composition, gene expression patterns, and biomechanical modeling may provide deeper insights into the fundamental mechanisms underlying cartilage deformities. Such research could significantly improve diagnostic accuracy, enable early identification of at-risk children, and guide the development of more effective, individualized treatment strategies.

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