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Research Paper Review

Biological Factors in the Pathogenesis of Rotator Cuff Tears

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ABSTRACT

Rotator cuff tears are common, and lead to shoulder pain and functional impairment. Despite their frequency and related disability, etiology and pathogenesis are still debated. Multiple factors contribute to tears of the rotator cuff. Extrinsic factors are anatomic variables, such as acromial morphologic characteristics, os acromiale, and acromial spurs that compress the rotator cuff by bony impingement or direct pressure from the surrounding soft tissue. Intrinsic factors arise from the tendon itself, because of tensile overload, aging, microvascular supply, traumatisms, or degeneration. Little information is available from a cellular and molecular point of view. We reviewed the biological factors involved in the pathogenesis of rotator cuff tears. Understanding the mechanism of rotator cuff pathology would facilitate the rationale for therapeutic interventions, by guiding the design, selection, and implementation of treatment strategies such as biologic modulation and preventive measures.

ANALYSIS

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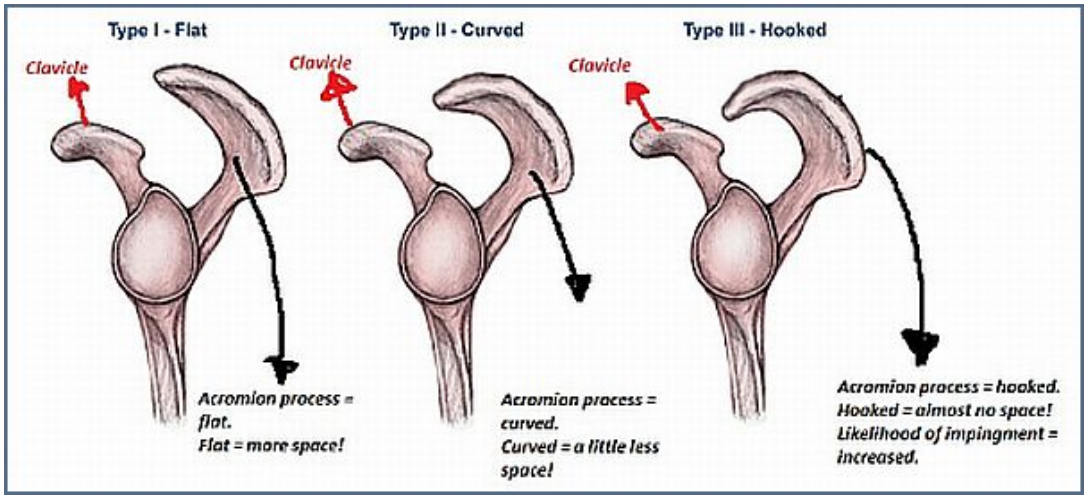
Introduction

Rotator cuff tears are a common injury seen in musculoskeletal practices. It is generally accepted that these injuries are multifactorial. In this paper, Nicola Maffulli (a renowned expert on tendon pathology) and colleagues examined various factors that contribute toward rotator cuff tears, including intrinsic, extrinsic and biological factors. The focus was directed at biological factors such as apoptosis, cytokines, metalloproteinase, genetics, lipids and glucose.

EXTRINSIC FACTORS

Extrinsic factors have been proposed to be a cause of rotator cuff disease because of tendon compression through bony impingement and surrounding soft tissue problems (1). Neer found that tendinopathy and rupture occur mainly in the supraspinatus tendon, in an area that abutted against the coracoacromial ligament, the anterior acromion, and sometimes the acromioclavicular joint during forward elevation (2). As you probably know, acromial shape has long been correlated with rotator cuff tears. To review, acromial shape has been classified in three types: flat (Type I), curved (Type II) and hooked (Type III). Flat acromions are typically not associated with rotator cuff tendon tears (3)



Rotator cuff tears may also be degenerative in nature, as it has been suggested that superior migration of the humeral head, after failure of the rotator cuff, could be responsible for acromial degeneration (4). Observation of joint side rotator cuff pathology, internal impingement, or superior and posterosuperior impingement has been proposed, but evidence is still incomplete. In these instances, the superior aspect of the glenoid fossa and the greater tuberosity of the humerus would be responsible for rotator cuff compression (5). In addition, enthesopathy, likely resulting from strain in the coracoacromial ligament, has been postulated to create acromial spurs which are a secondary phenomenon induced by primary bursal-side cuff tears (6).

Further, environmental factors (such as mechanical overuse) are another contributing factor to rotator cuff tears which is explained by the microtrauma theory (7). Repetitive stress is responsible for a vicious circle which can predispose a tendon to rupture. Tobacco use may also influence rotator cuff tears through vasoconstrictive properties of nicotine, which decrease the delivery of oxygen to tissues (8). Finally, systemic diseases such as diabetes mellitus can negatively impact tendon healing and raise the risk of significant pathology (9).

INTRINSIC FACTORS

Intrinsic factors act within the tendon itself. Overall, a greater percentage of rotator cuff tears occur on the articular side, which is supported by histological and biomechanical studies showing a smaller cross-sectional area and a greater vulnerability of articular side fibers (10). Chronic microtrauma (involving

insufficient time between repetitive stresses allowing small injuries that worsen), in addition to histological age-related characteristics (thinning and disorientation of the collagen fibers, myxoid degeneration, hyaline degeneration, chondroid metaplasia, calcification vascular proliferation, and fatty infiltration) play a large intrinsic role in partial tendon tears that then develop into full rotator cuff tears (7, 11).

Another potential intrinsic factor includes microvascular supply. Many authors have referred to a 'critical zone', a vulnerable, hypovascular area proximal to the insertion of the supraspinatus tendon. This 'critical zone' has been implicated in tears due to reduced perfusion (12), yet controversy remains in the literature because some studies actually demonstrate hyper-perfusion in the area of a tear. Finally, muscle degeneration and fatty infiltration can occur. These factors exert an important role in the pathogenesis of rotator cuff tears, and have marked clinical implications (13).

OTHER BIOLOGICAL FACTORS

Apoptosis is a process of programmed cell death involved in the development of multi-cellular organisms. This process may also have a role in tendinopathy, as excessive numbers of apoptotic cells have been found in the torn edges of rotator cuff tendons. As apoptotic mediators are modulated by exercise-induced oxidative stress, it is possible that repetitive stress causes the tendon cells to undergo apoptosis, with subsequent weakening of collagenous matrix.

Cytokines may also play a role in tendinopathies, as they are regulators of host responses to infection, immune responses, inflammation, and trauma. They act as molecular messengers and are involved in matrix turnover in tendinopathy, tenocyte activity, and expression of tendon matrix genes. Cytokines are involved in the pathogenesis of tendinopathies as evidenced by the up-regulation of pro-inflammatory cytokines seen in rotator cuff tendinopathy.

The pathogenesis of tendinopathy may also include decreased collagen synthesis by tendon cells and increased degradation of synthesised collagen in tendon matrix. Metalloproteinase (MMP-1 or collagenase I) is responsible for the natural turnover of collagen. The concentration of MMP-1 is very low in normal tendon, but it increases in damaged tendon. Oxidative stress induces JNK (a protein kinase) phosphorylation that activates the apoptotic pathway and up-regulates MMP-1, leading to tendon matrix degradation.

Studies have also suggested the contribution of genetic factors in the pathogenesis of rotator cuff tears. Results from clinical studies on patients with full-thickness tears, siblings, compared to matched controls, have shown double the risk of developing rotator cuff tears and 5 times the chance to experience symptoms. Therefore, it is possible that only those individuals with a genetic predisposition may evolve age-related degeneration.

There is conflicting evidence on the possible relationship between elevated serum lipid profiles and tendon ruptures. More information is needed to clarify this topic. There is also a hypothesis that there is a link between hyperglycemia and collagen structure alterations arises from the fact that tendons may be directly affected by nonenzymatic glycosylation processes, which change collagen cross-links. However, additional studies are required to confirm this association and to understand its causative role in the pathogenesis of rotator cuff tears.

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