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**Apoptoza w przewlekłej tendinopatii ścięgna głowy długiej mięśnia dwugłowego  
ramienia i jej związek ze zmianami degeneracyjnymi ścięgna oraz wynikami  
klinicznymi**

**Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu**

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## Summary

Tendinopathy is a chronic pathology of the tendon caused mainly by a disturbance in the balance between the processes of regeneration and degeneration of tendon tissue. This is one of the most common causes of chronic anterior shoulder pain. The etiopathology of tendinopathy remains unknown and is believed to be multifactorial. Microscopically, tendinopathy is characterized by defects in collagen architecture, accumulation of proteoglycans, changes in tenocyte morphology and population, and capillary expansion. Apoptosis, also called programmed cell death, plays a key role in regulating cell proliferation and is responsible for maintaining homeostasis in many tissues. In the context of tendons, apoptosis has been observed both in the natural healing process of tendon tissue and in degenerative changes, therefore its role in the process of tendinopathy is still not entirely clear.

The study included patients who underwent arthroscopic tenodesis or tenotomy of the long head of the biceps tendon due to symptomatic tendinopathy with or without concomitant rotator cuff damage. Intra-articular fragments of biceps tendons prepared based on hematoxylin and eosin and Alcian blue staining. Then, they were examined histopathologically, based on the BOnar scale and its modifications, and measuring the expression level of apoptotic cell markers, such as BCL2, caspase 3 and p53 protein. Pre- and postoperative clinical outcomes were analyzed based on the American Shoulder and Elbow Surgeons (ASES) scales and the visual analogue scale (VAS).

Microscopic assessment of tendons based on the Bonar scale and its modifications showed advanced degenerative changes in tendons, the average score was 8.65 (range 5-11), and based on the modified Bonar scale: 7.61 (range 4-11). Tendon tissue degeneration assessed using the modified Bonar scale correlated with patient age ( $p=0.0022$ ). Moreover, a correlation was observed between age and disturbances of collagen architecture in the tendon and accumulation of non-collagen extracellular substance ( $p=0.0036$  and  $p=0.0166$ , respectively). The expression of p53 protein also

correlated positively with increasing patient age ( $p=0.0441$ ). In the group of smokers, the mean pack-year index was 13.12 (SD = 9.94), the mean number of cigarettes smoked per day was 14.77 (SD = 4.64) and the mean smoking duration was 16.38 (SD = 10.1) years. . Among smoking indicators, the number of cigarettes smoked per day showed a positive correlation with the Snyder classification of rotator cuff tendon pathology ( $p=0.0459$ ,  $\rho=0.3682$ ). The caspase 3 expression index showed a negative correlation with the severity of degenerative changes in the rotator cuff in the total population ( $p=0.0193$ ,  $\rho=-0.4651$ ).

People with chronic LHBT tendinopathy who smoke cigarettes do not show an increased severity of the apoptosis process, despite poorer pre- and postoperative clinical results and the accompanying severe rotator cuff pathology. A relationship was found between the severity of rotator cuff tendon pathology and the level of caspase 3 expression in the biceps tendon. Additionally, being an active smoker is associated with worse clinical outcomes, especially pain after biceps tendon tenodesis or tenotomy. In advanced biceps tendinopathy, the expression of apoptotic proteins does not directly correlate with the degree of tendon tissue degeneration. Changes in the architecture of collagen and extracellular ground substance were correlated with age, as well as the degree of tendon tissue degeneration, quantified according to the modified Bonar scale. Given the significant role of apoptosis in regulating the local fibroblast population in tendons and its contribution to tendinopathy, it may be necessary to reconsider the inclusion of the apoptosis index as a fifth variable in modified tendon pathology scoring systems.