

## ORIGINAL PAPER

**CIGARETTE SMOKING INTENSIFIES TENDINOPATHY OF THE LHBT.  
A MICROSCOPIC STUDY AFTER ARTHROSCOPIC TREATMENT**JAN ZABRZYŃSKI<sup>1</sup>, JACENTY SZUKALSKI<sup>2</sup>, ŁUKASZ PACZESNY<sup>3</sup>, DAWID SZWEDOWSKI<sup>4</sup>, DARIUSZ GRZANKA<sup>5</sup><sup>1</sup>Department of Orthopedic Surgery, Multidisciplinary Hospital, Inowrocław, Poland<sup>2</sup>Department of Pathology, Multidisciplinary Hospital, Inowrocław, Poland<sup>3</sup>Department of Orthopedic Surgery, Orvit Clinic, Toruń, Poland<sup>4</sup>Department of Orthopedic and Trauma, District Hospital, Toruń, Poland<sup>5</sup>Department of Clinical Pathomorphology, Ludwik Rydygier's Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Bydgoszcz, Poland

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Smoking has a damaging effect on the musculoskeletal system, which was presented by authors in the rotator cuff and Achilles tendons studies; however, there are a lack of data about the effect of smoking on disorders of the long head of the biceps tendon (LHBT), particularly at the microscopic level.

The purpose of this study was to investigate the effect of the tobacco smoking on the histopathologic alterations of the LHBT.

Thirty-six patients with preoperatively diagnosed tendinopathy of the LHBT were referred to the Orthopaedics Department. All patients underwent arthroscopic treatment with further macroscopic and microscopic evaluation of biceps tendon samples.

The active and former smokers were characterised by more advanced degenerative process of the tendinous tissue; moreover, it was intensified in the group of former smokers. Subjects who smoke more than 20 cigarettes per day also had more advanced microscopic alterations. The most severe microscopic alterations occurred in the former smokers who used tobacco for more than 20 years. However, the non-smokers group revealed moderate degeneration in all LHBT samples.

Tobacco smoking is an important risk factor of the LHBT disease, which essentially intensifies the degeneration of the tendinous tissue.

**Key words:** smoking, tendinopathy, LHBT, tendon, biceps tendon.

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**Introduction**

Tobacco smoking is a significant cause of illness and premature death in the world [1]. The latest reports in Poland revealed that almost 29% of the adult population of this country are active smokers, which is about 9 million of people, and it is becoming a 21<sup>st</sup>-century burden and a real civilisation threat [2]. About 66,000 people in Poland died from smoking-related diseases in 2016, which accounts for 17% of the total death causes in this country [2].

Tobacco smoke, which is exhaled from cigarettes, constitutes an aerosol of more than 4000 chemicals, e.g. nicotine, aromatic hydrocarbons, carbon monoxide, N-nitrosamines, hydrogen cyanide, and aldehydes [3]. All of these substances have a huge and negative impact on human cells and their metabolism. Tobacco smoking leads to the development of neoplasms, pulmonary, cardiovascular, and endocrinology diseases.

Preoperative smoking, in the field of surgery, is commonly associated with a significantly increased

risk of: wound complications, infections, and bleeding [1]. The complications are frequent in almost all areas of orthopaedic surgery: spine surgery, arthroplasty, and trauma surgery, as well as in tendon and ligament surgery [1]. Smoking is a tremendous risk factor for the development of the rotator cuff (RC) tendinopathy, which is strongly associated with the occurrence of pathology of the long head of the biceps tendon (LHBT) [4].

Tendinopathy is a common disorder of tendons with multi-factorial aetiology, involving intrinsic and extrinsic factors, particularly tobacco smoking [5]. The most recent theory assumes that microtrauma to the tendon structure with associated neurovascular ingrowth leads to degeneration of the tendinous tissue [6]. In such cases, there is a chaotic production of extra-cellular matrix by tenocytes and chaotic expansion of newly formed capillary vessels, and this results in decreased mechanical durability of the tendon and the clinical manifestation of its disorder. Smoking has a significant effect on the musculoskeletal system, which was presented by authors in the RCT and Achilles tendon studies; however, there are a lack of data about the effect of smoking on LHBT disorders, particularly at the microscopic level [7].

The purpose of this study was to investigate the effect of tobacco smoking on the histopathological alterations of the LHBT. We assumed that smoking is associated with more advanced degeneration of the pathological biceps tissue.

## Material and methods

The study was approved by local Bioethics Committee (approval no. KB 598/2016). All patients were volunteers and gave informed consent. The study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

This study included 36 consecutive patients treated arthroscopically due to LHBT tendinopathy and concomitant shoulder disorders, recruited from the Department of Orthopaedic Surgery. The inclusion criteria for taking part in the study was a diagnosed tendinopathy of the LHBT, based on clinical examination (special clinical tests for LHBT tendinopathy: tenderness over the bicipital groove, Speed test, Yergason test), sonographic examination, or non-contrast magnetic resonance scans. Patients were a non-athlete population, with no history of inflammatory or rheumatic diseases, and no previous surgical treatment or corticosteroid injections in the past 12 months. The mean age of the subjects was 53 years (28-75; SD – 10.3), and the cohort included 18 males and 18 females.

Data about the smoking habits and the history of smoking among all included subjects was collected,

including current cigarette smoking, time period of cigarette smoking (smoking age), and the number of cigarettes smoked per day.

All patients underwent shoulder arthroscopy under general anaesthesia and in a beach chair position, assisted by biceps tenodesis or tenotomy and concomitant surgical procedures. The intra-articular part of the LHBT, which is a remnant after surgery, was harvested for further investigation. A portion of about 1-2 cm × 0.5 cm of the intra-articular part of the LHBT was removed by arthroscopic scissors near its origin point – at the supraglenoid tubercle.

Next, all obtained tissue fragments were immediately prepared in 10% buffered formalin and sent to the Department in a transport container. Samples were dehydrated in increasing concentrations of ethanol, cleared in xylene, embedded in paraffin, cut into sections of 4 µm thickness by microtome, and floated onto glass slides. Haematoxylin and eosin (HE) staining was used for the routine histopathologic examination, and Alcian Blue, Masson, and Mallory methods were used for detection of the non-collagen extracellular matrix (ECM) rich in glycosaminoglycans and mucopolysaccharides. All slides of the tendon portions, with different staining techniques, were analysed independently by three authors, using a light optical microscope (Olympus, model BX46, Tokyo, Japan) at magnifications of 20x, 100x, 200x, and 400x, with non-random selection of all areas of the slides. The assessment of the degeneration of the tendinous tissue was supported by the dedicated Bonar scale [8]. This semiquantitative system evaluates four main variables: tenocyte morphology, changes in the ground substance and its accumulation, and neovascularity and collagen bundles architecture; 0 points are given for normal tendons, while 12 points corresponds to maximal damage. The microscope examiners were blinded to smoking data.

Data were then used for statistical analysis using Statistica 12 software; normality of data distribution was evaluated using Shapiro-Wilk test, and correlation analysis was performed using Spearman's test.

## Results

The data about the groups of smokers, non-smokers, and former smokers are presented and summarised in Table I and Table II. The study population consisted of active smokers (31%; 11/36), former smokers (42%; 15/36), and non-smokers (27%; 10/36). The mean number of cigarettes smoked per day in the active smokers group was 12, and all subjects from the group used tobacco for more than 10 years. The mean duration of smoking in the active smokers group was 22 years and in former smokers group it was 16 years.

Arthroscopic investigation revealed additional pathologies of the affected shoulders, such as RCTs in 25 subjects. Nine patients underwent a tenotomy procedure, and 27 patients underwent a tenodesis procedure. There were no different anatomic variants of LHBT origin found in the study.

The macroscopic evaluation of the harvested LHBT portions in the Pathology Department revealed heterogeneous morphology, with signs of degeneration

**Table I.** Comparison of the smoking, non-smoking, and former smoking groups

	ACTIVE SMOKERS	FORMER SMOKERS	NON-SMOKERS
Mean age (years)	56	53	50
Mean Bonar score	8	9.1	7

**Table II.** Summary of the tobacco usage-dependent Bonar scoring

	TOBACCO USE DATA	MEAN BONAR SCORE	NO. OF SUBJECTS
Former smokers	Smoking age > 20 years	10	7
	Smoking age < 20 years	9	8
Active smokers	Cigarettes per day < 20	7	3
	Cigarettes per day > 20	8.4	8

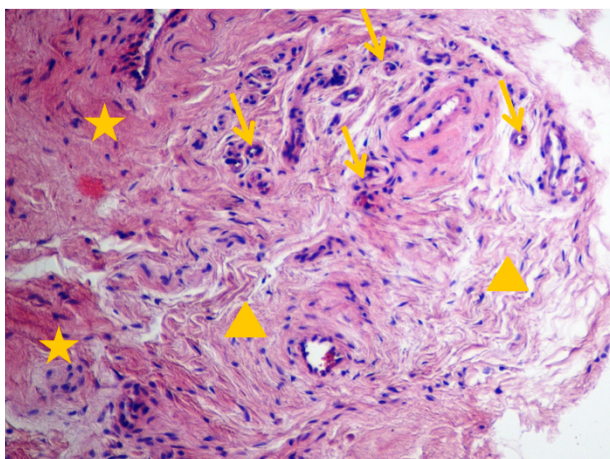
among all specimens: visible tears, fraying, widening, and flattening. Microscopic investigation demonstrated different pathological, structural changes with advanced degeneration of the tendinous tissue. In the examined cohort the mean Bonar score was 8.25 (range 4-11 and SD – 1.97).

Statistical analysis demonstrated that there was a weak correlation between the Bonar score and number of cigarettes smoked per day in the active smokers group (Spearman’s coefficient = 0.271;  $p = 0.4198$ ). The statistical correlation between Bonar score and the smoking age in years in the former smokers group was moderate (Spearman’s coefficient = 0.445;  $p = 0.0964$ ).

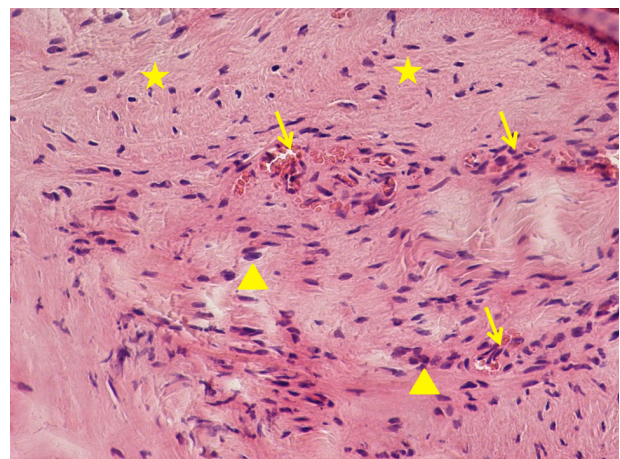
Comparing these three main groups of subjects, it was found that the active and former smokers groups were characterised by more advanced degenerative process of the tendinous tissue (Figs. 1, 2); moreover, it was intensified in the former smokers group. Subjects who smoked more than 20 cigarettes per day had also more advanced microscopic alterations. However, the non-smokers group also revealed moderate degeneration in all LHBT samples (Fig. 3).

## Discussion

The aerosol of tobacco smoke contains a group of substances harmful to the human body [4]. Nicotine is a vasoconstrictor, which effects exposed tissues by limiting the oxygen supply; furthermore, it is a toxic and anti-proliferative substance [7]. Moreover, nicotine is also responsible for decreased collagen synthesis. Authors showed that the tobacco smokers had significant alterations in collagen synthesis and wound



**Fig. 1.** Microscopic evaluation of LHBT sample in a former smoker: advanced degeneration of the tissue with vascular expansion (arrows), accumulation of the ground substance (asterisk) between completely disorganised collagen fibres (arrowheads), and proliferation of the pathologically transformed tenocytes. (Stain: HE; magnification 100×)



**Fig. 2.** Microscopic evaluation of LHBT sample in an active smoker: Advanced degeneration of the tendinous tissue with prominent accumulation of round-shaped pathological tenocyte (arrowheads), disturbed architecture of the collagen fibres (asterisk) and neovascularisation (arrows). (Stain: HE; magnification 200×)

healing [9]. Other substances, such as carbon monoxide, decrease cellular oxygen tension levels necessary for cellular metabolism [4]. Tobacco smoke substances lead to delayed healing and impaired regeneration processes with serious microvascular disorders. However, the toxic dose of smoke and its dose-dependent effects on tendinous tissue are still unknown.

This study compared the data about the tobacco smoking with light microscopic analysis of the intra-articular parts of pathologically transformed biceps tendons. All included patients suffered from chronic tendinopathy of the LHBT, and the tendinous tissue samples were characterised by moderate to severe degenerative alterations. As was hypothesised, the smoking group of patients had more serious histopathological alterations of the LHBT samples. However, an interesting fact was that more advanced degenerative alterations occurred in samples obtained from the former smokers. This might be caused by undisclosed smoking and not completely quitting from this harmful habit.

The development of the tendon pathology remains mysterious; however, there are an increasing number of reports about the harmful influence of tobacco smoking. Tendinopathy of the LHBT is one of the most common causes of chronic anterior shoulder pain, and almost 90% of cases of its tendinopathy are associated with massive RCTs. Numerous authors have reported about the negative influence of tobacco smoking on the quality of RC tissue, difficulties with recovery, and poor clinical outcomes in smokers receiving rotator cuff surgery [3, 4]. Smokers more often require surgical revision, as presented by Cancieene *et al.* after LHBT tenodesis and labrum reconstruction [10]. We can conclude that RCT and LHBT are both victims of tobacco smoke also at the microscopic level [11, 12]. All active or former smokers in our study had severe degenerative alterations, progressing with the intensity of their smoking habit. However, there are limited data in the literature about the biceps tendon pathology (especially its proximal part) and its connection with smoking. In studies of the distal biceps tendon, the authors proved that tobacco smoking is associated with a greater risk of distal biceps tendon rupture compared to non-smokers [13, 14]. Studies of the RCT and smoking are more numerous. Mallon *et al.* found that cigarette smoking had an adverse effect on the postsurgical outcomes of rotator cuff repairs [15].

These reports, compared to our LHBT study, are very similar because active smoking increased the degeneration level of the tissue and exacerbated the tendinopathy process, leading to more serious injuries, with increased size and impaired regenerative process. Additionally, smoking patients with the LHBT tendinopathy are even more exposed to other shoulder lesions, e.g. RCT, subacromial impingement.

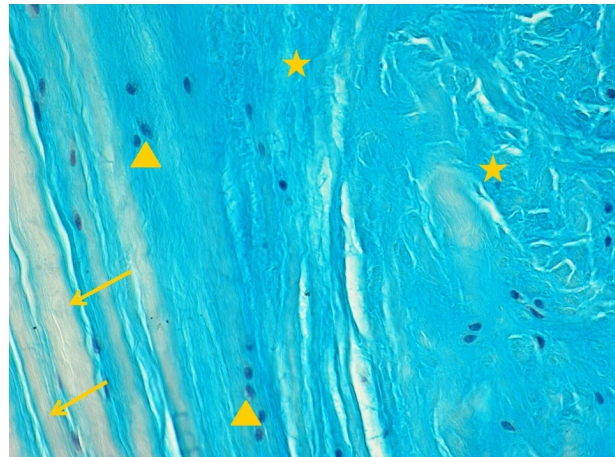


Fig. 3. Microscopic evaluation of LHBT sample in a non-smoker: moderate degeneration of the tendinous tissue with accumulation of the ground substance (asterisk), modest number of round-shaped pathological tenocyte (arrowheads), with partially preserved collagen fibres architecture (arrows). (Stain: Alcian Blue, magnification 200 $\times$ )

The main limitation of our study was the investigation of patients without isolated LHBT tendinopathy. Another weakness comes from the fact that the group of patients included in this study was relatively small, non-homogenous, and elderly. However, isolated LHBT tendinopathy occurs in young athletes involved in throwing sports such as the javelin. The association with RCT is undeniable, common, and unfortunately is increasing with age. Additionally, since we did not harvest all of the tendon adjacent to its insertion and the extra-articular part, we were unable to investigate all of the proximal part of the LHB tendon, which could potentially be characterised by different pathological changes. During the arthroscopic procedure we were unable to obtain a complete proximal tendon of the biceps; however, we attempted to obtain a part that was most exposed to friction and compression forces in the shoulder joint. The medical discussion and data about smoking could be biased, but this limitation concerns all authors. Moreover, we could not obtain reliable information about the nicotine concentration that the subjects consumed.

Discussing smoking and histopathological alterations, it is obligatory to mention vascular disorders. The aetiopathology of tendinopathy assumes a theory about the hypovascular or avascular areas, which are essentially prone to subsequent hypoxia; however, tendons are characterised by a low vascular perfusion and low oxygen consumption. Tobacco smoking additionally impairs the microvascular circulation, limiting the oxygen supply, which, in the LHBT hypovascular area, 1-3 cm from its origin, can lead to irreversible degeneration [16].

## Conclusions

Tobacco smoking is a serious risk factor of LHBT disease and essentially exacerbates the degeneration of tendinous tissue. Impairing the microvascular perfusion and collagen synthesis, it plays a negative role in tendon healing and regeneration, leading to a vicious cycle of tendinopathy.

*The authors declare no conflict of interest.*

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