

A potential factor in the pathophysiology of lateral epicondylitis: The long sarcomere length of the extensor carpi radialis brevis muscle and implications for physiotherapy

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ABSTRACT

Lateral epicondylitis is a chronic angiofibroblastic degeneration of the origins of the wrist extensor muscles and is characterized by diffuse elbow pain. Although it is the most common syndrome of the elbow joint, the most affected structure is the tendon of the extensor carpi radialis brevis (ECRB) muscle. Several theories have been proposed to explain the pathophysiology of lateral epicondylitis, however, there is no evidence to show that the sarcomere length and microanatomical features of the ECRB muscle can be affected by the elongated position of the muscle. We hypothesized that the tensile response may be the responsible mechanism in the pathophysiology of lateral epicondylitis due to the microanatomy of the ECRB muscle and its functioning in the elongated position. Elongated position leads to elongation of the sarcomere length by forming a functional traction angle in the ECRB muscle. The elongated sarcomere length negatively affects muscular microcirculation. Poor microcirculation triggers ischemia in the muscle and tendon and leads to an increase in immature Type III collagen synthesis. Disruption of the collagen continuity and the loss of load-bearing capacity initiate the neovascularization process. This situation accelerates the degeneration process in the tendon and prevents healing. Furthermore, based on our hypothesis, we recommend new physiotherapy approaches that may contribute to reducing the increased incidence of tendinopathy and to the healing process.

Introduction

Lateral epicondylitis (LE), or tennis elbow, is defined as the chronic symptomatic degeneration of the origins of the wrist extensor muscles attached to the lateral epicondyle of the humerus [1]. The condition is usually encountered in the 45–57 age range, with no apparent difference of prevalence between genders. While the incidence of traumatic LE is 1–3%, the incidences due to idiopathic causes is about 1.3% [2,3]. Lateral epicondylitis affects around 10,000 people in the US every year and causes a significant increase in healthcare costs each year [4]. Although the etiology of LE is not exactly known, excessive use, microtraumas, age, smoking and obesity have been defined as risk factors [1,5–7].

The first remark on the pathophysiology of LE has been made by Nirschl and Petrone, and in their histopathological studies, the researchers described the condition as an angiofibroblastic degeneration characterized by fibroblastic and vascular responses known as tendinosis, rather than an inflammatory condition [8].

Cook and Purdam, on the other hand, have recently suggested a

clinical model for the histopathological changes. According to this model, the histopathological changes that occurred were reactive tendinopathy, tendon disrepair and degenerative tendinopathy. Reactive tendinopathy is defined as non-inflammatory proliferative cellular and matrix response due to overloads. Excessive use and overloading, along with repeated microtraumas, cause partial or full rupture of the tendon and thus tendon disrepair. Angiofibroblastic hyperplasia develops with the increase of collagen accumulation and the development of neovascularization in the degenerative phase [9].

Extensor carpi radialis brevis muscle (ECRB) is the most affected muscle [10]. Repeated microtraumas in the extensor tendon attachment sites cause severe pain at the attachment sites of the extensor tendons on the lateral of the elbow joint and disruption of collagen organization is observed in the origin of the ECRB [11]. Studies have shown that the length and architectural features of the muscle sarcomere may be responsible for the pathophysiology of tendinopathy [12,13].

Several microscopic changes at the cellular level were also indicated to explain the pathophysiology of LE. However, heterogeneity of the cases, differences in the initiation mechanisms of traumatic or non-

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traumatic LE and inconsistency of the responses to treatment suggest that other factors may as well cause LE and alter the response to treatment.

In this case, microanatomic and physiological features of the muscles may be an important risk factor in the development of LE. We believe the sarcomere lengths of the ECRB and other extensor muscles may have an impact on the development of LE.

The Hypothesis. We suggest that a long sarcomere of the ECRB muscle may be a responsible mechanism in the pathophysiology of LE.

Evidence for this hypothesis will be based on consideration

The sarcomere length of the ECRB muscle is higher than the normal physiological sarcomere length

The sarcomere, the smallest functional unit of a muscle, is activated by actin and myosin proteins. Even if the results from different regions of the muscle are different, the sarcomere length is almost constant along a muscle [14–17]. In a study by Gordon et al., it was shown that the sarcomere length was affected by passive muscle tension and the optimum sarcomere length was 2.13 μm . In a later study, Friden and Lieber's indicated that the optimum sarcomere length was 2.6 μm and that an increase or decrease in this length caused changes in the power generation of the skeletal muscle. Increased passive muscle tension increases the length of the sarcomere by pulling the actin filaments. Thus, due to the reduced overlap between actin and myosin, the power generating capacity of the muscle is reduced. Again, in Gordon's study, there was no overlap between the actin and myosin proteins when the length of the sarcomere reached 3.65 μm [18–22].

In Lieber et al.'s study on healthy subjects evaluating the sarcomere length of ECRB, the sarcomere lengths at full extension and full flexion of the wrist were evaluated using intraoperative laser and it was shown that the sarcomere length increased from 2.60 μm during extension to 3.40 μm during flexion. In Loren et al.'s study, the shortest sarcomere length was 2.00 μm and the longest sarcomere length was 3.10 μm . In another study on LE patients, it was reported that the ECRB sarcomere length varied based on joint rotation. As a result of the wrist movement from full extension to full flexion, the sarcomere length of 2.80 μm increased to 4.26 μm [22,23]. In conclusion, the sarcomere length of ECRB while the wrist is in flexion is much longer compared to the optimal sarcomere length.

The number of studies reporting about how to increase or decrease the sarcomere length are limited. Animal studies have shown that there is a phase which initiates after birth and decelerates when the growth is complete and during which the number of sarcomere increases. Previous studies have suggested that muscle elongation is associated with the increased length of each sarcomere; however, in Day et al.'s study, the researchers showed that with the growth of the extremities the number of sarcomeres increased. On the other hand, a weekly immobilization of the muscle in a shortened position provides a significant reduction in the length of the sarcomere, while long-term immobilization in an elongated position has been reported to optimize the sarcomere length [24–27].

The sarcomere length of the ECRB muscle increases in different functional positions of the wrist and elbow

In a study examining the change of the ECRB sarcomere length with wrist and elbow movements, sarcomere length in different positions was evaluated using intraoperative laser and it was determined that the ulnar deviation of the wrist was an effective parameter on sarcomere length [28]. In a study examining the effect of the elbow position on the ECRB sarcomere length, an unexpected biphasic response was detected in the ECRB sarcomere length during the movement of the elbow from full extension to full flexion. The initial sarcomere length of 3.49 μm

during the extended position of the elbow changed gradually to 3.68 μm , 3.34 μm , 3.81 μm and 3.45 μm with the flexing elbow. Based on the mechanical properties of the skeletal muscle, this response of the ECRB with the progressing degrees of flexion was expressed as "biphasic elongation" [14]. In a study where the sarcomere length at 45° of flexion and 45° of extension was measured via microendoscopy, it was observed that the sarcomere length was 2.93 μm at 45° of extension and 3.58 μm at 45° of flexion [15].

The ECRB muscle is activated more with daily functional movements. In EMG studies, the activation of the ECRB muscle was shown to occur more often than other wrist extensor muscles [29]. In addition, in the biomechanical studies on the ECRB muscle, the ECRB muscle has been reported to be used actively in an elongated position for long periods of time with the extension of the elbow and pronation of the forearm, along with the ulnar deviation and flexion position of the wrist [30–32]. In this position, the sarcomere of the ECRB muscle is much longer than its normal physiological length. Accordingly, sarcomere length of the ECRB muscle appear to increase with certain functional positions of both the wrist and the elbow.

Increased sarcomere length is associated with decreased microcirculation and ischemia

The sarcomere length has an important place in the physiology of muscle circulation. The capillary lumen diameter is narrowed by the increased sarcomere length with the passive tension of the muscle. Especially in cases where the sarcomere length is longer than 2.9 μm , the capillary lumen diameter is significantly reduced. This may cause a decrease in circulation in the muscle and the tendon [33–35]. The neurovascular features of the tendon are found in the endotenon and epitenon. Vascular support to the tendon is provided through the musculotendinous junction and the teno-osseous junction [36–38]. Most tendons have zones characterized by hypovascularity caused by the poor overlap between the muscle and bone microcirculation sources.

Since the sarcomere length of the ECRB muscle is greater than 2.9 μm , the capillary lumen diameter of the muscle and tendon decreases and causes ischemia. At the same time, the continuance of the tension of the ECRB muscle against gravity causes deterioration of the ischemic muscle and tendon structure. The musculotendinous junction becomes more fragile and sensitive especially as the hypovascularized musculotendinous junction is more affected with this condition and the immature Type III collagen synthesis accelerates.

Evaluation of the hypothesis

We believe that microanatomy and the architectural features of the ECRB muscle may be a new factor in the pathophysiology of LE. The ECRB muscle starts over the anterior aspect of the lateral epicondyle of the humerus and attaches to the posterior base of the third metacarpal. ECRB works against gravity. In studies on healthy individuals, the ECRB muscle had a sarcomere length of about 3.81 μm . However, when the length of elongated sarcomere is more than 2.9 μm , microcirculation has been shown to decrease in the muscle [33–35]. In addition, the ECRB sarcomere length was also shown to have increased with the flexed wrist and elbow during daily living activities [14,28].

Our hypothesis in the pathophysiology of LE is the effect of the activity of the elongated ECRB muscle for long periods of time on the muscle origin. With the effect of gravity, the wrist and elbow are pulled downwards with a chronic traction direction. With the effect of gravity and depending on the position of the wrist and the elbow, the sarcomere length of ECRB gets longer than its usual length. As a result of the elongated sarcomere length, microcirculation in ECRB decreases due to capillary insufficiency. In addition, ECRB has to function more due to the elongated sarcomere length. Increased activity due to fatigue and decreased circulation causes ischemia in the ECRB muscle and tendon.

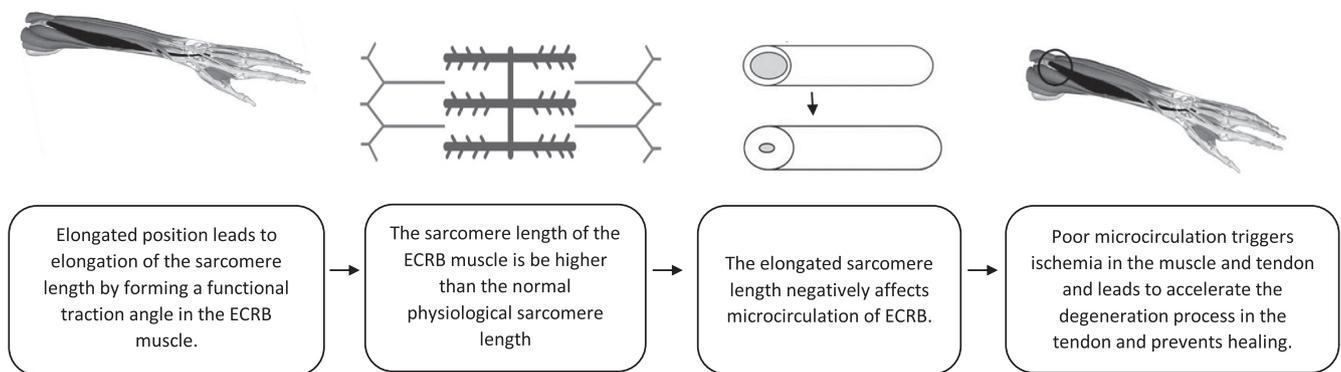


Fig. 1. Possible mechanism of idiopathic lateral epicondylitis.

This causes repeated inflammation of the muscle and tendon. For example, it can be considered that flexion and ulnar deviation of the wrist and flexion of the elbow while walking are positions where the sarcomere becomes longer and that the ECRB muscle is activated against gravity. We believe that the ECRB muscle and tendon exposed to both reduced blood circulation and gravity effect may return fibroangiogenic responses (Fig. 1).

Physiotherapy & rehabilitation: clinical implications

Physiotherapy and rehabilitation is important component to treatment of lateral epicondylitis and includes activity modification, stretching and strengthening exercises, counterforce braces, shockwave therapy, low-level laser therapy, manual therapy, non-steroidal anti-inflammatory drugs, corticosteroid injections, autologous blood injections, platelet-rich plasma injections [4–6].

We can use this new pathophysiological factor to indicate the physiotherapeutic and rehabilitative approach in LE. Based on our hypothesis, the wrist can be immobilized at 45° of extension and 15° of radial deviation and the elbow at 90° of flexion in order to reduce the sarcomere length of ECRB and increase the muscle–tendon microcirculation. An immobilization period of 5–7 days may be preferred in accordance with the inflammation phases. Unfortunately, the literature holds no studies performed on humans, investigating the effect of immobilization on the sarcomere length. We believe that the relationship between immobilization and the sarcomere length in humans is worthy of research.

In our hypothetical physiotherapy protocol, joint range of motion exercises should be started to prevent muscle contracture and stiffness after a week of immobilization. However, the exercise for the ECRB muscle should be continued with the wrist at 45° of extension and 15° of radial deviation and the elbow at 90° of flexion. Allowing muscle tension in the early phase of our protocol can be harmful. The movement should be started when the wrist is extended 45° and continued to 70°–90° of extension and the ECRB muscle should be protected from the gravitational effect when the wrist falls below 45°. This movement can be called “short arc motion pattern for the elbow and wrist”. Pain should be the main point of consideration in the progression of the protocol. As soon as the painless range of motion is reached, strengthening exercises can be started with the eccentric loading model. Eccentric exercises are known to optimize the sarcomere length and provide a significant increase in strength. Eccentric exercises can be started in the extension position with the help of appropriate weights or resistance bands and can be performed within the range of 45°–70°/90°. In advanced stages, the wrist and elbow position can be adjusted at appropriate angles to continue with eccentric exercises. ECRB stretching exercises should be carried out in conjunction with strengthening trainings to the extent possible against pain. Stretching will be probably of importance in our hypothesis protocol since we can increase the number of sarcomere even after the proliferation phase is

over. Also, previous animal studies have shown that the number of sarcomeres can be increased by distraction. Our aim is to increase the number of sarcomeres and to keep the length of the sarcomeres at an optimal level [39–42]. In this context, we propose that further studies should investigate the variance in the length of the sarcomere by age. We believe that these data will support our hypothesis and be confirmed by the clinical studies on physiotherapy and rehabilitation for LE patients.

Conclusion

We believe that the ECRB muscle may affect the pathophysiology of the elongated sarcomere length, along with the effect of gravity, in individuals with LE. An elongated sarcomere is associated with decreased blood circulation. Poor circulation causes ischemia in the muscle and the tendon in addition to fibroblastic and vascular responses in the ECRB muscle due to inflammation.

The advantages of this new pathophysiological factor may be to establish loading models in the optimal physiological sarcomere range and to be able to create new approaches for treatments. When the inflammatory process begins at the level of the lateral epicondyle, the ECRB sarcomere length can be reduced and vascular support for the muscle may be provided if the elbow is positioned at 90° of flexion, the wrist at 45° of extension and the distal radioulnar joint at 15° of radial deviation. With exercises aimed at increasing the number of sarcomeres, the inflammation in the ECRB muscle and tendon can be reduced and the pathologies of LE may be encountered less frequently.

Declaration of Competing Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

- [1] Waseem M, Nuhmani S, Ram C, Sachin Y. Lateral epicondylitis: a review of the literature. *J Back Musculoskelet Rehabil* 2012;25(2):131–42.
- [2] Nirschl R, Ashman E. Tennis elbow tendinosis (epicondylitis). *Instr Course Lect* 2004;53:587–98.
- [3] Cicotti MG, Charlton WP. Epicondylitis in the athlete. *Clin Sports Med* 2001;20(1):77–93.

- [4] Degen RM, Conti MS, Camp CL, Altchek DW, Dines JS, Werner BC. Epidemiology and disease burden of lateral epicondylitis in the USA: analysis of 85,318 Patients. *HSS J* 2018;14(1):9–14.
- [5] Herquelot E, Bodin J, Roquelaure Y, Ha C, Leclerc A, Goldberg M, et al. Work-related risk factors for lateral epicondylitis and other cause of elbow pain in the working population. *Am J Ind Med* 2013;56(4):400–9.
- [6] Taylor SA, Hannafin JA. Evaluation and management of elbow tendinopathy. *Sports Health* 2012;4(5):384–93.
- [7] Bugajska J, Żolnierczyk-Zreda D, Jędryka-Góral A, Gasik R, Hildt-Ciupińska K, Malińska M, et al. Psychological factors at work and musculoskeletal disorders: a one year prospective study. *Rheumatol Int* 2013;33(12):2975–83.
- [8] Nirschl RP, Petrone F. Tennis elbow. The surgical treatment of lateral epicondylitis. *J Bone Joint Surg Am* 1979;61(6A):832–9.
- [9] Cook J, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. *Br J Sports Med* 2009;43(6):409–16.
- [10] Vaquero-Picado A, Barco R, Antuña SA. Lateral epicondylitis of the elbow. *EFORT Open Rev* 2016;1(11):391–7.
- [11] Hume PA, Reid D, Edwards T. Epicondylar injury in sport. *Sports Med* 2006;36(2):151–70.
- [12] Frat T, Türker T. Is the long sarcomere length responsible for non-traumatic supraspinatus tendinopathy? Potential novel pathophysiology and implications for physiotherapy. *Pathophysiology* 2012;19(3):179–83.
- [13] Lieber RL, Ljung B-O, Fridén J. Sarcomere length in wrist extensor muscles changes may provide insights into the etiology of chronic lateral epicondylitis. *Acta Orthop Scand* 1997;68(3):249–54.
- [14] Lieber RL, Fridén J. Functional and clinical significance of skeletal muscle architecture. *Mus Ner Off J Am Associat Electrodiagnos Med* 2000;23(11):1647–66.
- [15] Cromie MJ, Sanchez GN, Schnitzer MJ, Delp SL. Sarcomere lengths in human extensor carpi radialis brevis measured by microendoscopy. *Muscle Nerve* 2013;48(2):286–92.
- [16] Lieber RL, Fridén J. The 2002 Nicolas andry award: implications of muscle design on surgical reconstruction of upper extremities. *Clin Orthop Relat Res* 2004;419:267–79.
- [17] Ward SR, Hentzen ER, Smallwood LH, Eastlack RK, Burns KA, Fithian DC, et al. Rotator cuff muscle architecture: implications for glenohumeral stability. *Clin Orthop Relat Res* 2006;448:157–63.
- [18] Gordon A, Huxley AF, Julian F. The variation in isometric tension with sarcomere length in vertebrate muscle fibres. *J Physiol* 1966;184(1):170–92.
- [19] Infantolino BW, Ellis MJ, Challis JH. Individual sarcomere lengths in whole muscle fibers and optimal fiber length computation. *Anat Rec* 2010;293(11):1913–9.
- [20] Kawakami Y, Fukunaga T. New insights into in vivo human skeletal muscle function. *Exerc Sport Sci Rev* 2006;34(1):16–21.
- [21] Tomioka T, Minagawa H, Kijima H, Yamamoto N, Abe H, Maesani M, et al. Sarcomere length of torn rotator cuff muscle. *J Shoulder Elbow Surg* 2009;18(6):955–9.
- [22] Lieber RL, Loren GJ, Fridén J. In vivo measurement of human wrist extensor muscle sarcomere length changes. *J Neurophysiol* 1994;71(3):874–81.
- [23] Loren GJ, Shoemaker SD, Burkholder TJ, Jacobson MD, Fridén J, Lieber RL. Influences of human wrist motor design on joint torque. *J Biomech* 1996;29:331–42.
- [24] Day CS, Moreland MS, Floyd SS, Huard J. Limb lengthening promotes muscle growth. *J Orthop Res* 1997;15(2):227–34.
- [25] Okita M, Yoshimura T, Nakano J, Motomura M, Eguchi K. Effects of reduced joint mobility on sarcomere length, collagen fibril arrangement in the endomysium, and hyaluronan in rat soleus muscle. *J Muscle Res Cell Motil* 2004;25(2):159–66.
- [26] Simpson A, Williams P, Kyberd P, Goldspink G, Kenwright J. The response of muscle to leg lengthening. *Bone Joint J* 1995;77(4):630–6.
- [27] Williams PE, Goldspink G. Changes in sarcomere length and physiological properties in immobilized muscle. *J Anat* 1978;127(Pt 3):459.
- [28] Ljung B-O, Fridén J, Lieber RL. Sarcomere length varies with wrist ulnar deviation but not forearm pronation in the extensor carpi radialis brevis muscle. *J Biomech* 1999;32(2):199–202.
- [29] Riek S, Carson RG, Wright A. A new technique for the selective recording of extensor carpi radialis longus and brevis EMG. *J Electromyogr Kinesiol* 2000;10(4):249–53.
- [30] Green HJ, Ranney D, Kyle N, Lounsbury D, Smith IC, Stewart R, et al. Neuromuscular manifestations of work-related myalgia in women specific to extensor carpi radialis brevis. *Can J Physiol Pharmacol* 2016;95(4):404–19.
- [31] Briggs CA, Elliott BG. Lateral epicondylitis. A review of structures associated with tennis elbow. *Anat clin* 1985;7(3):149–53.
- [32] Shetty A, Randolph MA. Biomechanical analysis of injury, prevention, and rehabilitation exercises for lateral epicondylitis: A Review. In ISBS-Conference. *Proced Arch* 2000;1(1).
- [33] Kagaya A, Muraoka Y. Muscle architecture and its relationship to muscle circulation. *Int J Sport Stud Hlth* 2005;3(Special_Issue_2005):171–80.
- [34] Nakao M, Segal SS. Muscle length alters geometry of arterioles and venules in hamster retractor. *Am J Physiol Heart Circ Physiol* 1995;268(1):H336–44.
- [35] Poole DC, Musch TI, Kindig CA. In vivo microvascular structural and functional consequences of muscle length changes. *Am J Physiol Heart Circ Physiol* 1997;272(5):H2107–14.
- [36] Aström M, Westlin N. Blood flow in chronic Achilles tendinopathy. *Clin Orthop Relat Res* 1994;308:166–72.
- [37] Langberg H, Bulow J, Kjar M. Blood flow in the peritendinous space of the human Achilles tendon during exercise. *Acta Physiol Scand* 1998;163(2):149–54.
- [38] Carr A, Norris S. The blood supply of the calcaneal tendon. *Bone Joint J* 1989;71(1):100–1.
- [39] Boakes JL, Foran J, Ward SR, Lieber RL. Case report: muscle adaptation by serial sarcomere addition 1 year after femoral lengthening. *Clin Orthop Relat Res* 2007;456:250–3.
- [40] Caiozzo VJ, Utkan A, Chou R, Khalafi A, Chandra H, Baker M, et al. Effects of distraction on muscle length: mechanisms involved in sarcomerogenesis. *Clin Orthop Relat Res* 2002;403:S133–45.
- [41] Fridén J, Ponten E, Lieber RL. Effect of muscle tension during tendon transfer on sarcomerogenesis in a rabbit model. *J Hand Surg* 2000;25(1):138–43.
- [42] Williams P. Use of intermittent stretch in the prevention of serial sarcomere loss in immobilised muscle. *Ann Rheum Dis* 1990;49(5):316.