The XXXVII[th] Annual International Occupational Ergonomics and Safety Conference
Orlando, Florida
July 24-25, 2025

Graded Compression Sleeves Reduce the Expression of Micro RNA 192-5p in Mechanically Loaded Tendons of the Forearm

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Abstract: This exploratory case study investigated the effects of graded compression sleeves on the acute expression of miRNA 192-5p derived from mechanically loaded tendons in the upper extremities. miRNA 192-5p (miR-192-5p) plays a crucial role in tendon healing by regulating collagen III (COL3) and tumor necrosis factor-α (TNF-α), both of which are associated with fibrosis and inflammation. When tendons sustain damage, miR-192-5p is upregulated to initiate the tendon healing process. While compression sleeves are commonly used as preventive and therapeutic aids for injured tendons, their effects on circulating miRNAs remain largely unexplored. Two healthy males (aged 20 and 24 years) were recruited – one sedentary and one competitive volleyball player representing different levels of habitual mechanical tendon loading. The volleyball player's inclusion was particularly relevant as this sport involves repetitive mechanical loading of the upper extremity tendons, potentially providing insight into adaptive miRNA responses. Following anthropometric measurements and maximal grip strength (MGS) assessment of the dominant hand, participants completed a standardized hand-gripping task (2-second grip, 3-second rest for two minutes at 60% of their MGS) under two conditions: with and without wearing graded compression sleeves on both upper limbs. Venous blood samples were taken before and after completing the task to assess circulating miR-192-5p expression. Total circulating miRNAs were extracted and reverse transcribed, with the expression of miR-192-5p analyzed relative to the small nuclear RNA (snRNA) U6, which was assessed using the $2^{-\Delta\Delta Ct}$ method. This approach allowed for the precise quantification of changes in miRNA expression resulting from the experimental conditions. Results indicated that performing the gripping task without compression sleeves increased expression of miR-192-5p in both participants, with greater elevation observed in the volleyball player. Notably, wearing

ISBN: 9781938496639

DOI: https://doi.org/10.47461/ISOES.2025.Conde2

compression sleeves attenuated the expression of miR-192-5p in both participants, suggesting potential inhibition of the tendon fibrosis process, particularly in individuals who routinely load their upper limbs. These preliminary findings suggest that graded compression sleeves appear to modulate molecular responses to mechanical loading in uninjured tendons. Future research will include a larger sample size and additional analysis of COL3 and TNF-α to evaluate miR-192-5p as a potential biomarker of mechanical tendon load in uninjured tendons.

Keywords: miR-192-5p, compression sleeves, tendon mechanical load, inflammation.

1. Introduction

Mechanical tendon loading is a significant factor contributing to the development or worsening of work-related musculoskeletal disorders (WMSDs), especially in occupations involving repetitive or forceful tasks. Sustained or excessive loading of the tendons can lead to microtears and inflammation. If these injuries are not allowed to heal, they can progress to chronic tendinopathies (Cook & Purdam, 2009). WMSDs impose a significant economic burden, costing billions of dollars annually in health care costs and productivity losses. In the United States, employers spend over $20 billion every year on direct costs associated with WMSDs, with indirect costs estimated to be double (OSHA 2024). These conditions are the leading cause of days away from work, particularly among labor-intensive occupations, including manufacturing, construction, and health care (BLS, 2024). To reduce the risks, interventions such as the use of compression sleeves have been explored.

Compression garments may enhance proprioception, reduce muscle oscillation, and potentially support tendon health by modulating local circulation and inflammation (Ali et al., 2007). Although further research is needed, these ergonomic interventions may help reduce the incidence and severity of musculoskeletal disorders in high-risk occupational environments.

MicroRNAs (miRNAs) are small, non-coding RNA molecules of approximately 18-24 nucleotides that regulate post-transcriptional gene expression. miRNAs bind to target messenger RNA (mRNA), leading to mRNA degradation or translational repression (Bartel, 2004). In tendon biology, miRNAs are important mediators of mechanotransduction, the process through which mechanical stimuli are converted into cellular responses (Nakamichi & Asahara, 2024). Mechanical tendon loading has been shown to influence miRNA expression, which can alter key molecular processes such as inflammation, extracellular matrix (ECM) turnover, and cell proliferation (Dubin et al., 2018). These load-induced changes in miRNA expression suggest that miRNAs may serve as potential biomarkers and therapeutic targets in tendon injury and repair.

Among the miRNAs associated with musculoskeletal tissue remodeling, mir-192-5p has emerged as a regulator of inflammatory and fibrotic signaling pathways. miR-192-5p has been implicated in the regulation of transforming growth factor-β (TGF-β) signaling and extracellular matrix (ECM) remodeling, processes that are critical for tissue adaptation and repair (Chung et al., 2010; Kato et al., 2009). Dysregulation of miR-192-5p has been reported in several fibrotic and inflammatory conditions, where it influences the expression of genes involved in collagen synthesis, matrix turnover, and cellular stress responses (Krupa et al., 2010; Putta et al., 2012). Because tendon loading can alter molecular pathways involved in ECM homeostasis and inflammation, changes in circulating miR-192-5p levels may reflect physiological responses to mechanical tendon stress (Dubin et al., 2018).

Based on the relationship between mechanical tendon loading and tendon pathology, as well as the regulatory role of miR-192-5p in inflammation and ECM remodeling, understanding how ergonomic interventions influence this molecular response may provide insight into strategies for preventing tendon injury. One potential intervention is the use of graded compression sleeves, which may influence local mechanical and physiological responses during tendon loading tasks (Ali et al., 2007). Therefore, the purpose of this study was to investigate the effects of wearing graded compression sleeves on the expression of circulating miR-192-5p following a tendon loading task.

2. Methods

2.1 Participants

Two apparently healthy, 20-year-old and 24-year-old males from the University of Texas at El Paso agreed to participate in the study. Only male participants were included to minimize the possible effects of estradiol and progesterone

on miRNA expression (Schisterman et al., 2014). Both participants had no history of tendon injuries: one was a sedentary individual and the other a competitive volleyball player, representing different levels of habitual upper-extremity tendon loading. Participants were asked to continue their normal routine if they engaged in regular physical activity.

2.2 Anthropometric Measurements

Body weight (kg) and height (m) were measured using a Detecto™ scale with a stadiometer. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters (BMI = weight (kg) / height (m^2). Resting blood pressure (mmHg) and heart rate (BPM) were measured using an Omron™ digital blood pressure monitor after participants rested for at least 10 minutes upon arrival in the laboratory.

2.3 Surface Electromyography and Maximal Grip Strength

During each visit, before the start of the hand-gripping task, the research assistant attached dual surface electromyography (sEMG) electrodes in the extensor digitorum longus and the flexor digitorum superficialis muscles of the participant's dominant hand. After the electrodes were attached, the participants were asked to hold a wireless hand dynamometer in their dominant hand, grip it as hard as possible, and maintain a 90° elbow angle (Figure 1a, 1b, and 1c). The maximum force (N) was recorded during the grip strength assessment and used to calculate 60% of the participant's maximal grip force for the hand-gripping task.

Figure 1. Participant showing a sEMG electrode placed on the extensor digitorum muscle (a). Participant showing a sEMG electrode placed on the flexor digitorum superficialis muscle (b). Participant showing gripping the hand dynamometer while maintaining a 90° angle at the elbow (c).

2.4 Blood Sampling and Lactate Measurements

After measuring the maximal grip strength, a registered nurse (RN) used a Vacutainer Safety-Lok Blood Collection Set to procure a sample from the mid-cubital vein of the dominant and non-dominant arms. The needle was secured with Tegaderm to prevent movement during the procedure (Figure 2). A blood sample of approximately 20 cc was obtained from the dominant arm (localized) and the non-dominant arm (systemic) before and after the hand-gripping task. Once the 20-cc sample was obtained, a small drop was used to measure circulating blood lactate using the Nova Biomedical lactate meter. The remaining sample was immediately centrifuged to separate the plasma from red and white blood cells. A small plasma sample of about 100 µL was used for miRNA extraction, and the rest was stored at -80°C.

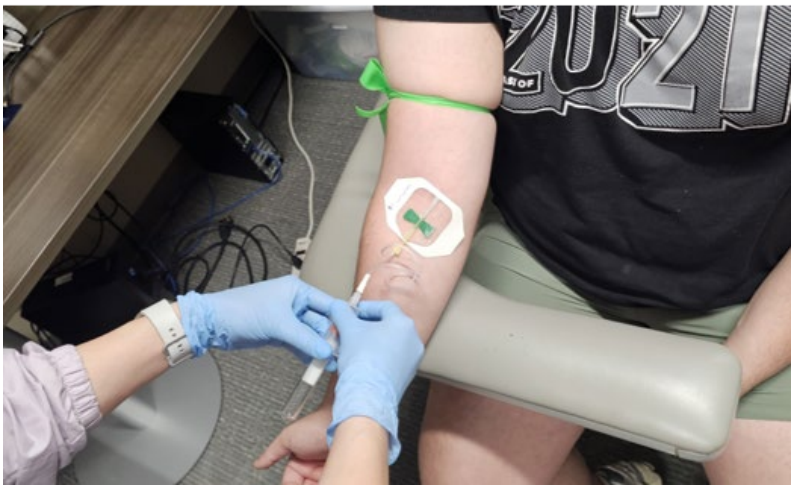

Figure 2. A Vacutainer Safety-Lok Blood Collection Set was inserted into the mid-cubital veins of both arms to procure a blood sample before and after the hand-gripping task.

2.5 Hand Gripping Task

The participants were asked to grip the hand dynamometer to produce and maintain a force equal to 60% of maximal grip for two seconds, then rest for three seconds. The participants followed this pace using a metronome. The cycle was repeated for two minutes. The participants completed the same task under two randomly assigned conditions: without sleeves (NS) and with sleeves (S) (Figures 3a and 3b).

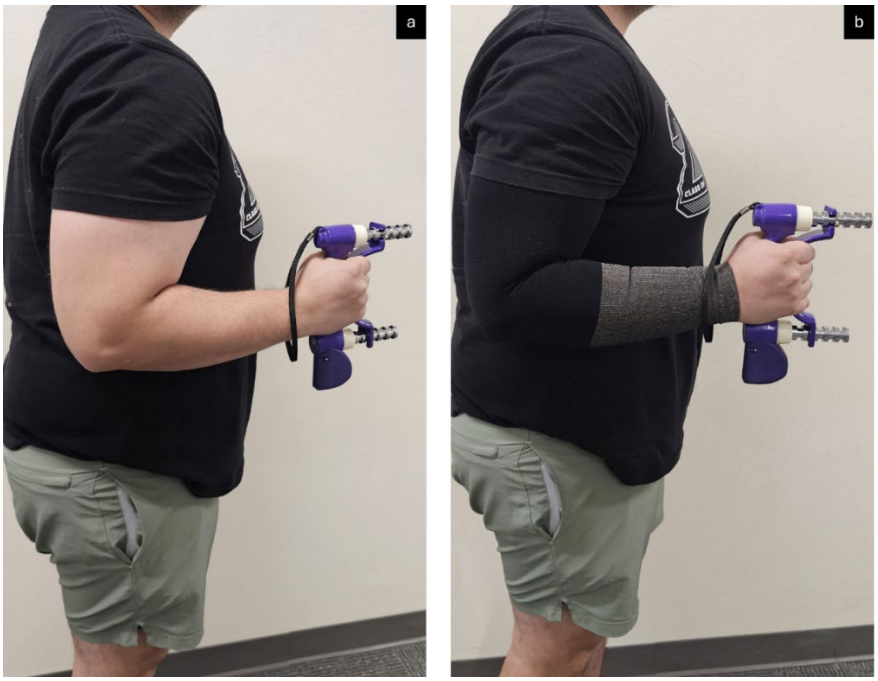

Figure 3. Participant showing the different hand-gripping task conditions. a) no sleeves. b) sleeves

2.5 miR-192-5p Expression

Total circulating miRNA was extracted using the Qiagen miRNeasy kit, following the manufacturer's instructions, and stored at -80°C until all samples were extracted and ready for analysis. Once all the miRNAs were extracted from the

samples, they were reverse transcribed into complementary DNA (cDNA) using the Taqman Advanced miRNA cDNA synthesis kit. The target miR192-5p was amplified using the Taqman Fast Advanced Master Mix, and its expression was assessed using the StepOne PCR system. The relative expression of miRNA was determined using the $2^{-\Delta\Delta Ct}$ method, with small nuclear RNA U6 (snU6) serving as the internal loading control for normalization. All results are presented as fold changes relative to snU6.

3. Results

The analysis of miR-192-5p showed a lower expression when the participants completed the manual task using graded compression sleeves, compared with completing the task without using graded compression sleeves. For subject 1, the expression on the dominant hand (right side) was about 3-fold lower when compression sleeves were used, and the expression in the non-dominant hand (left side) was similar. For subject 2, expression was lower in both the dominant and non-dominant hands when graded compression sleeves were used (Figure 4).

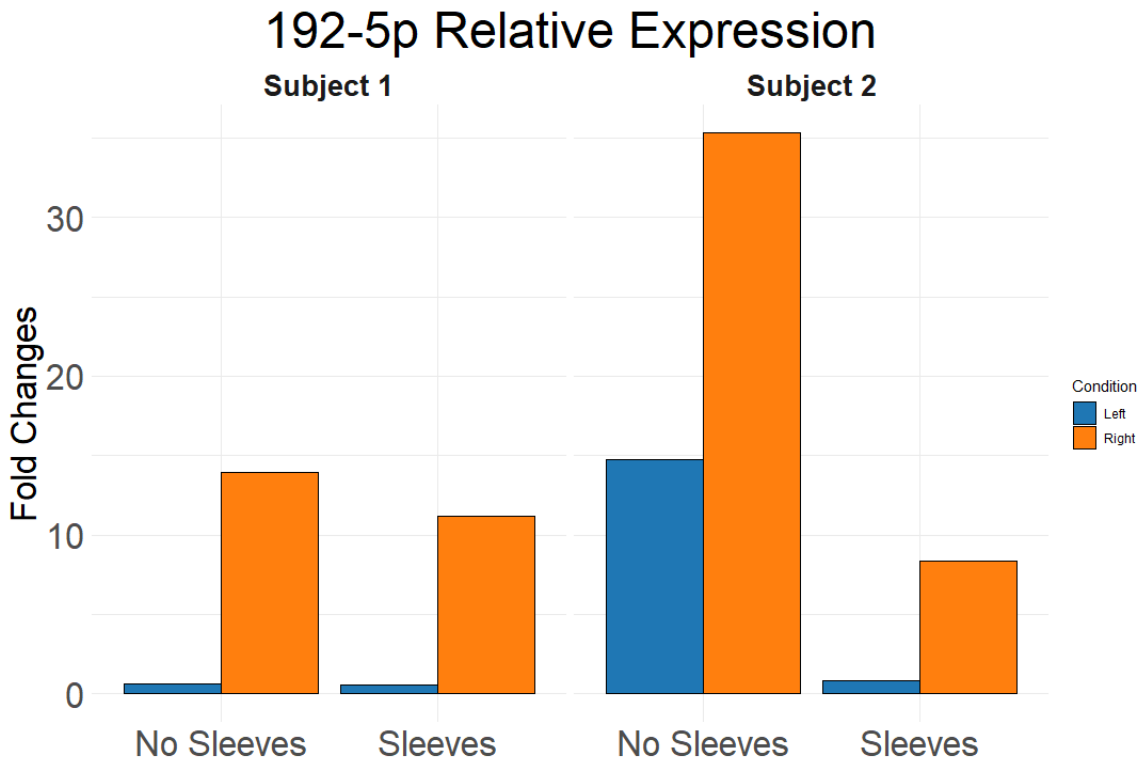

Figure 4. Relative expression of miR-192-5p was lower in the right arm of subject 1 and in the dominant and non-dominant arms of subject 2.

4. Concluding Remarks and Future Directions

The findings of this research suggest that mechanical tendon loading is associated with changes in circulating miR-192-5p expression, and the use of graded compression sleeves may influence this molecular response. In both subjects, the highest expression of miR192-5p happened when no compression sleeve was being used. In contrast, when graded compression sleeves were used, there was a substantial reduction in miR-192-5p expression. This pattern is particularly evident in subject 2, where the relative expression was dramatically reduced with the use of sleeves. These results suggest that compression sleeves may attenuate the molecular response to mechanical tendon loading, potentially by modifying local mechanical or physiological conditions in the tendons. Previous work shows that mechanical loading can modify the

expression of microRNAs associated with tendon mechanotransduction and tissue remodeling (Dubin et al., 2018; Nakamichi & Asahara, 2024).

The lower expression of miR192-5p when graded compression sleeves were used may reflect alterations in the inflammatory signaling or in the ECM remodeling pathway activated during tendon loading. miR-192-5p has been shown to regulate fibrotic and inflammatory signaling through pathways including the TGF-β, which plays a central role in ECM turnover and tissue remodeling (Chung et al., 2010; Kato et al., 2009). Changes in the expression of miR-192-5p have also been associated with the regulation of collagen synthesis and fibrosis-related signaling in several tissues (Putta et al., 2012). Even though these mechanisms are unclear, graded compression sleeves may influence factors such as tissue oscillation, local circulation, or proprioceptive feedback, which in turn, may alter the molecular response to mechanical load (Ali et al., 2007). While these results are preliminary, they support the possibility that ergonomic interventions may influence the expression of circulating makers associated with tendon load and its adaptation to it.

In conclusion, these preliminary results suggest that graded compression sleeves can reduce miR-192-5p expression, particularly in individuals with chronic overuse of the upper limbs. A larger-sample study that includes analysis of other circulating molecules associated with ECM remodeling and tendon fibrosis is needed to determine the role of miR-192-5p in these pathways. Future research will assess the interaction of miRNAs associated with tendon load and molecules associated with tendon remodeling.

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