

EFFECT OF INSTRUMENT-ASSISTED SOFT TISSUE MOBILIZATION ON EXERCISE-INDUCED MUSCLE DAMAGE AND FIBROTIC FACTOR: A RANDOMIZED CONTROLLED TRIAL

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Submitted: September 10, 2019. Accepted: October 3, 2019. Published: 26 November 2019.

ABSTRACT

Background and Objective

The instrument-assisted soft tissue mobilization (IASTM) is a form of mechanical stimulation. This treatment is known to provide an effective way to improve muscle function and attenuate muscle pain. However, limited study showed the effect of the IASTM on acute condition such as exercise-induced muscle damage. This study aimed to examine the effects of IASTM on exercise-induced muscle damage and fibrotic factor.

Material and Methods

Sixteen healthy male college students were randomly assigned to IASTM (n=8) and control (n=8). After performing two sets of 25 eccentric contractions of elbow flexors, IASTM was applied for 8 min immediately and 48 h after exercise. Maximal isometric strength (MIS), muscle soreness, and creatine kinase (CK) activity were measured as indicators of muscle damage. Transforming growth factor- β 1 (TGF- β 1) levels were assessed as a fibrotic factor.

Results

The recovery of MIS was faster (control vs. IASTM: 96 h: 60.7% \pm 7.9% vs. 89.1% \pm 10.4%, $P < 0.001$), and TGF- β 1 level was lower (control vs. IASTM: 48 h: 5.5 \pm 1.9 vs. 2.4 \pm 0.6, $P < 0.01$; 72 h: 5.6 \pm 1.7 vs. 2.6 \pm 0.5, 96 h: 5.2 \pm 1.6 vs. 1.9 \pm 0.5 ng/mL, $P < 0.001$) in the IASTM group than in the control group. However, no significant differences in muscle soreness or CK activity were found between groups ($P > 0.05$).

Conclusion

IASTM may be an effective method for reducing scar tissue and restoring muscle function quickly after exercise-induced muscle damage.

Key Words: *eccentric exercise, fibrosis, instrument-assisted soft tissue mobilization, muscle damage, transforming growth factor- β 1*

INTRODUCTION

Repeated high-force eccentric exercise can elicit muscle damage.¹ Muscle damage is characterized by declining muscle function, such as maximal isometric strength (MIS), delayed-onset muscle soreness (DOMS), and increased plasma creatine kinase (CK) activity.² In addition, Matrix Metalloproteinase-induced tissue degradation decreases force transmission, and there is recruitment of inflammatory cells to the site of muscle damage.^{1,3,4} Transforming growth factor- β 1 (TGF- β 1) is one of the several cytokines released from immune cells into the damaged muscles.⁵ It is capable of regulating the balance between muscle fibrosis and regeneration.⁶ However, TGF- β 1 also triggers fibrosis when overexpressed and hence scar tissue formation, which in turn interferes with the muscle recovery process and eventually reduces muscle function.⁷⁻⁹ Several interventions including drugs, hyperbaric oxygen therapy, low-level laser therapy, mechanical stimulation, nutrition supplements, and ultrasound have been used to reduce fibrosis in damaged muscles and to promote recovery.¹⁰⁻¹⁶

Mechanical stimulation, in particular, is known to be a simple and effective way to promote recovery in damaged muscles.^{12,17,18} Mechanically stimulated cells modify their micromechanical environment through cytoskeletal rearrangement, initiating a molecular response that subsequently induces extracellular matrix synthesis. Thus, the altered mechanical properties of cells can help in regaining normal muscle function.¹⁸ Huang et al.¹⁹ asserted that mechanical stimulation is required in reversing scar tissue formation. Cezar et al.¹² also reported that mechanical stimulation effectively

reduced inflammation and fibrosis in damaged muscles and boosted muscle regeneration, leading to an increase in maximum contractile force. Several other studies have also reported that mechanical stimulation delivered through massages or physical manipulation exerts positive effects on the functions of damaged muscles.^{9,11,20-22}

Recently, instrument-assisted soft tissue mobilization (IASTM) has gained increasing attention, as it provides a form of mechanical stimulation. IASTM is designed to both treatment of soft tissue injuries and promotion of recovery, and is increasingly used in sport rehabilitation and athletic training settings.²³⁻²⁵ Davidson et al.²⁶ reported that IASTM was particularly useful in the early recovery of limb function by increasing fibroblast recruitment and activation in Achilles tendon injuries. Loghmani and Warden²⁷ also reported faster recovery from an injured knee medial collateral ligament following IASTM application and noted poor alignment of collagen along with substantial scar tissue formation around the injured ligament in the absence of IASTM intervention. In addition, IASTM was reportedly found to be effective in improving grip strength in patients with elbow tendinopathy and the lower extremity functional scale in patients with Achilles tendinopathy.²⁸⁻³⁰ In summary, IASTM can be an effective method for improving functional recovery after soft tissue injury.

Although most available studies on IASTM have addressed chronic ligament and tendon injuries,²⁶⁻²⁹ only few studies have investigated acute functional changes in skeletal muscle injury

following IASTM application. In a recent study by Kivlan et al.,²⁴ muscle strength significantly improved immediately after IASTM intervention in patients with lower extremity musculoskeletal injuries. However, the authors did not use an acute injury protocol.

IASTM is able to deliver mechanical force deeper into the site of muscle injury compared with conventional massages,^{31,32} and practitioners can perform IASTM without fatigue as its application only requires a short amount of time.^{33,34} Therefore, the purpose of the study was to examine the effects of IASTM on eccentric exercise-induced muscle damage and TGF- β 1. It was hypothesized that applying IASTM subsequent to eccentric exercise would reduce muscle soreness and CK and TGF- β 1, and improve MIS.

METHODS

Subjects

In total, 16 healthy male college students participated in this study. Subjects were nonsmokers, did not participate in strength training in the past 6 months, had no musculoskeletal diseases, and did not take any medications or dietary supplements. One week prior to the experiment, each subject completed a health screening questionnaire that reviews the eligibility for the study. All subjects provided written informed consent approved by the University Institutional Review Board (KMU-201705-HR-147). The subjects were randomly assigned to either IASTM group (n=8) or control group (n=8). The characteristics of the subjects in each group are summarized in Table 1.

Exercise-induced muscle damage protocol

The exercise protocol used in this study was a single bout of eccentric contractions of the elbow flexor muscle on a modified preacher curl machine as described by Clarkson et al.'s study.³⁵ This exercise model has been previously used in muscle damage studies.^{35,36} Before starting the eccentric

TABLE 1 Subject Characteristics and Baseline Measurements (Mean \pm SD)

	Control (n=8)	IASTM (n=8)
Age (years)	22.6 \pm 3.2	23.5 \pm 2.0
Height (cm)	175.1 \pm 5.5	178.1 \pm 3.3
Weight (kg)	66.3 \pm 18.7	76.8 \pm 5.1
CK (U/L)	198 \pm 177.8	288 \pm 229.7
TGF- β 1 (ng/mL)	2.05 \pm 0.7	1.68 \pm 0.4

IASTM, instrument-assisted soft tissue mobilization; CK, creatine kinase; TGF- β 1, transforming growth factor- β 1.

exercise, the subject's nondominant arm was placed on the pad of a modified preacher curl machine (ECC-MC, Kookmin University, Seoul, Korea) and the elbow joint was set at 90°. The eccentric contraction was induced by each subject pulling the pad toward them, while the researcher lowered the lever attached to the curl machine until the subject's arm was fully extended. The exercise was conducted for 3 s followed by 12 s of rest. A total of two sets consisting of 25 repetitions were performed; rest time between the sets was 5 min.

Instrument-assisted soft tissue mobilization

IASTM was applied immediately and 48 h after the exercise by a certified practitioner sufficiently trained with IASTM. For the IASTM group, while each subject sat down on a chair, emollient was applied to the subject's elbow flexor area to prevent skin irritation and to help facilitate movement of the instrument over the skin. Then, a single concave-shaped stainless-steel instrument (Prestm, Dispis, Seoul, Korea) was placed on the subject's skin at an angle of approximately 45°, and continuous pressure was applied. IASTM was applied for 8 min,^{25,29,37} while the researcher made sure not to induce any discomfort by communicating with the subject. Figure 1 shows the application of IASTM.

Maximal isometric strength

MIS was measured by a strain gauge (Jackson Strength Evaluation System Model 32628CTL,



FIG. 1 IASTM application.

Lafayette Instrument Co., Lafayette, IN, USA) attached to a modified preacher curl machine. Each subject was asked to sit on the machine, place their arm on the pad, bend the elbow joint to 90°, and pull the pad toward themselves as hard as possible when told by the researcher. MIS was measured before and immediately after, and 24, 48, 72, and 96 h after exercise. Measurements were performed three times at each time point, and the mean value was recorded.

Muscle soreness

The visual analogue scale (VAS) was used to measure muscle soreness and was conducted on the elbow flexor muscle that performed the eccentric exercise. After each subject repeated flexion and extension of their exercised arm in a standing position, a perpendicular line was drawn on VAS, indicating the perceived pain at each measurement. VAS was measured before, and 24, 48, 72, and 96 h after exercise.

Creatine kinase

Serum was collected through blood samples to measure CK activity. The baseline blood collection was conducted between 8 and 9 a.m. by visiting the laboratory after 8 h of fasting. The blood sample was allowed to clot for at least 30 min, centrifuged at 2500–3000 rpm, transferred to a

microtube (MCT-150-C, Axygen, Inc., Union City, CA, USA), and stored at -80° until analysis. CK analysis was conducted using a kit (AceChem CK kit, YD-Diagnostics Corp., Yongin-si, Korea) and automated clinical chemistry analyzers (Miura One, I.S.E. S.r.l, Rome, Italy).

Transforming growth factor- β 1

Plasma TGF- β 1 was analyzed using a kit (ProcartaPlex® Multiplex Immunoassay, Thermo Fisher Scientific, Waltham, MA, USA) according to the manufacturer's guidelines. 1N HCL (100 mL) and 1.2N NaOH/0.5M HEPES (100 mL) were prepared for plasma TGF- β 1 analysis. The reagents were mixed well, and 11.9 g of HEPES was added and the solution was mixed again well. The final volume was made up to a 100 mL by adding deionized water. Plasma activation was analyzed as follows: 10 μ L of 1N HCL was added to the plasma, mixed well, and incubated for 10 min at room temperature. The sample was neutralized by adding 8 μ L of 1.2N NaOH/0.5M HEPES. All samples were analyzed using clinical diagnostics instruments (Luminex® 200 System, Luminex Corporation, Austin, TX, USA).

Statistical analysis

Statistical analysis software (SPSS ver. 21.0, IBM Corp., Armonk, NY, USA) was used for the analysis of study results. Values are presented as mean \pm standard deviation. Repeated-measure analysis of variance was used to analyze the group-by-time interactions followed by a post hoc test using Tukey's method when a significant main effect was found. Statistical significance was set at $P < 0.05$.

RESULTS

Changes in MIS in response to IASTM after eccentric exercise

Significant effects of time ($F=57.997$, $P < 0.001$), group ($F=5.035$, $P < 0.05$), and group-by-time interaction ($F=4.212$, $P < 0.05$) were observed for

MIS. The IASTM group demonstrated a faster recovery of MIS after eccentric exercise than the control group, and the difference between the two groups was highest at 96 h after exercise ($P < 0.001$; Figure 2).

Changes in muscle soreness in response to IASTM after eccentric exercise

A significant effect of time ($F = 21.656$, $P < 0.001$) was observed for muscle soreness. However, neither effects of group ($F = 0.066$, $P > 0.05$) nor group-by-time interaction ($F = 0.075$, $P > 0.05$) were significant. Changes in muscle soreness were noted to be similar between the two groups during the recovery period (Figure 3).

Changes in CK activity in response to IASTM after eccentric exercise

A significant effect of time ($F = 15.495$, $P < 0.001$) was observed for CK activity. However, no significant effects on group ($F = 0.023$, $P > 0.05$) and group-by-time interaction ($F = 0.561$, $P > 0.05$) were found. CK activity increased for 96 h after eccentric exercise in both groups (Figure 4).

Changes in TGF-β1 level in response to IASTM after eccentric exercise

Significant effects of time ($F = 16.000$, $P < 0.001$), group ($F = 14.789$, $P < 0.001$), and group-by-time interaction ($F = 11.954$, $P < 0.001$) were observed for TGF-β1 response. TGF-β1 level was lower in the IASTM group than in the control group during the recovery period, and the

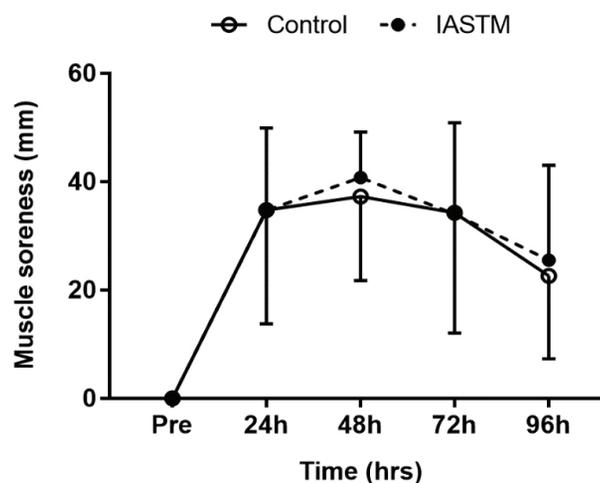


FIG. 3 Changes in muscle soreness in response to IASTM after eccentric exercise. Values are expressed as means ± SD.

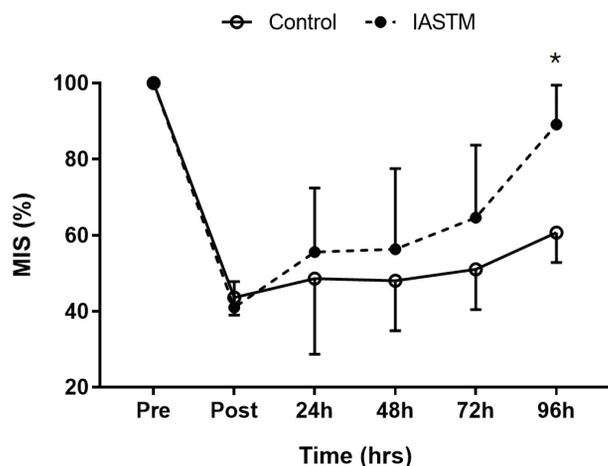


FIG. 2 Changes in MIS in response to IASTM after eccentric exercise. *Significant difference between groups ($P < 0.001$). Values are expressed as means ± SD.

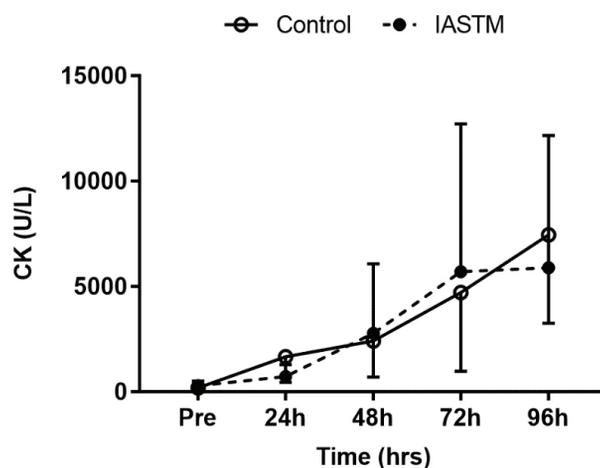


FIG. 4 Changes in CK activity in response to IASTM after eccentric exercise. Values are expressed as means ± SD.

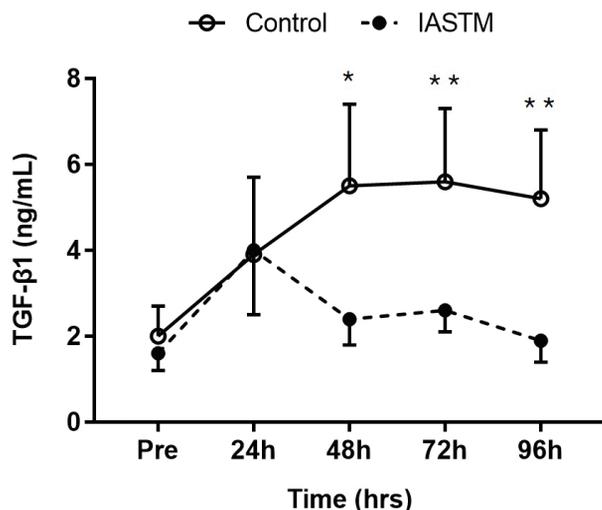


FIG. 5 Changes in TGF- β 1 level in response to IASTM after eccentric exercise.

*Significant difference between groups ($P < 0.01$); **significant difference between groups ($P < 0.001$). Values are expressed as means \pm SD.

difference between two groups was significant at 48, 72, and 96 h after exercise ($P < 0.05$; Figure 5).

DISCUSSION

The aim of this study was to investigate the effects of IASTM following eccentric exercise on changes in muscle damage and fibrotic factor. So far, IASTM has been studied primarily for chronic musculoskeletal injuries, but there is a lack of studies on how it affects acute muscle injury. To our knowledge, this is the first study to address the effects of IASTM on acute muscle injury caused by repeated eccentric exercise. The results in this study showed that IASTM following eccentric exercise reduced TGF- β 1 levels and improved strength recovery.

Scar tissue formation occurs when there is an excessive increase in the level of fibrotic factors, such as TGF- β 1, and it is well known to interfere with strength recovery.^{38,39} Gumucio et al.⁴⁰ reported that when a TGF- β 1-inhibiting drug was injected after eccentric muscle contraction, significant differences in strength recovery compared

with the control group were seen on days 3 and 7 after injury. In particular, when the injured tissues were analyzed at 3 days after injury, cellular infiltration by type 1 collagen was lower in the TGF- β 1-inhibited group than in the control group. Such results can be interpreted as TGF- β 1 inhibition reducing scar tissue formation by preventing excessive accumulation of type 1 collagen in the injured muscles, which may result in faster strength recovery.

This study also showed a similar increase in TGF- β 1 levels in both groups up to 24 h after exercise, but beyond that time-point, TGF- β 1 was reduced in the IASTM group only. In particular, TGF- β 1 levels were significantly decreased in the IASTM group compared with the control group after 48 h until 96 h after exercise, and changes during this period ultimately had a positive impact on strength recovery. In other words, it is believed that IASTM following an acute muscle injury might help reduce TGF- β 1 levels leading to scar tissue formation. However, the main difference between the research study conducted by Gumucio et al.⁴⁰ and this study is that his was an animal study and that the animals were treated with a drug to inhibit TGF- β 1 activity and ultimately prevent scar tissue formation after acute muscle injury. Another potential mechanism for rapid strength recovery after IASTM is considered to be a general massage. A massage is defined as providing mechanical manipulation to body tissues with rhythmic pressure and stroking.⁴¹ This is similar to the manipulation provided by IASTM. Potential mechanisms to increase muscle strength recovery by massaging include psychological changes, rearrangement of muscle fibers, and increased oxygen and nutrient supplies to damaged muscles.⁴² However, studies supporting these potential mechanisms are still limited.

A notable finding in this study was that despite IASTM being applied immediately after and 48 h after eccentric exercise, TGF- β 1 level

showed a significant difference between the two groups starting from 48 h after exercise. In addition, MIS showed a significant difference between the two groups only at 96 h after the exercise. These results suggest that IASTM at 48 h after exercise may be more effective in reducing scar tissue formation in injured muscle tissues than IASTM immediately after eccentric exercise. However, these explanations on such hypothesis based on the findings in this study alone are inadequate, and the effects based on intervention times are also unclear. Therefore, additional discussions on the appropriate timing of IASTM intervention for acute muscle injuries in future studies are essential.

In this study, IASTM following eccentric exercise did not have any impact on changes in muscle soreness. Contrary to the results of this study, Cheatham et al.⁴³ recently reported that IASTM after strenuous exercise had a positive effect on perceived pain reduction. However, there are several differences between the current study and Cheatham et al.,⁴³ such as the muscle type, protocol, and characteristics of the study subjects as well as exercise types that induced muscle soreness. In the investigation by Cheatham et al.,⁴³ muscle soreness was induced by 100 drop jumps from a box with a height of 0.5 m, and rectus femoris muscle area was the lesion to which IASTM was applied to with light pressure for 90 s. Also, Cheatham et al.'s study⁴³ included subjects with recreational fitness activities, both men and women. Several studies on the differences between males and females have reported that sex steroids such as estrogen, which is high in females, can act as a natural pain relief system.^{44,45} In summary, multiple factors that are presented above may be considered as reasons for the differences seen between the present study and the Cheatham et al.'s study.⁴³ Several studies have reported pain attenuation after applying IASTM, but these studies were performed on individuals with subacromial pain

syndrome or chronic lower back pain rather than acute injury.^{46,47} These differences make it difficult to explain the changes in muscle soreness in this study.

Meanwhile, CK is one of the blood markers, indicating cell membrane permeability after muscle damage is inflicted by eccentric exercise.⁴⁸ Although there was a steady increase in CK after eccentric exercise in this study, there was no significant difference between the IASTM and control groups. These results indicate that IASTM may not be an effective tool for reducing cell membrane damage.

This study has some limitations. We speculated that TGF- β 1 is an indicator of scar tissue formation leading to fibrotic response. Thus, reduction of TGF- β 1 following IASTM application may be related to blunted formation of scar tissue and faster recovery of strength. However, as we did not observe scar tissue formation in injured muscles by histological examination, it was difficult to determine whether IASTM reduced scar tissue formation. In this study, we made an estimation only with changes in muscle strength and TGF- β 1. These limitations should be addressed in future studies.

CONCLUSION

The results of this study showed that application of IASTM to muscles at a 45° angle for 8 min immediately after and 48 h after eccentric exercise reduced TGF- β 1 level and accelerated strength recovery. Such findings demonstrate that IASTM is an effective method for reducing fibrous scar tissue and restoring muscle function quickly after exercise-induced muscle damage. In future, additional studies on muscle function and metabolic responses to IASTM applied in combination with other treatments (e.g., icing and Kinesio taping) or nutritional supplements may be able to propose a more effective IASTM method for recovery from exercise-induced muscle damage.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

- Kim J, Lee J. The relationship of creatine kinase variability with body composition and muscle damage markers following eccentric muscle contractions. *J Exerc Nutrition Biochem* 2015;19(2):123–9. <https://doi.org/10.5717/jenb.2015.15061910>
- Chen HL, Nosaka K, Chen TC. Muscle damage protection by low-intensity eccentric contractions remains for 2 weeks but not 3 weeks. *Eur J Appl Physiol* 2012;12(2):555–65. <https://doi.org/10.1007/s00421-011-1999-8>
- Gao Y, Kostrominova TY, Faulkner JA, et al. Age-related changes in the mechanical properties of the epimysium in skeletal muscles of rats. *J Biomech* 2008;41(2):465–9. <https://doi.org/10.1016/j.jbiomech.2007.09.021>
- Vardiman JP, Siedlik J, Herda T, et al. Instrument-assisted soft tissue mobilization: Effects on the properties of human plantar flexors. *Int J Sports Med* 2015;36(3):197–203. <https://doi.org/10.1055/s-0034-1384543>
- Peake JM, Neubauer O, Della Gatta PA, et al. Muscle damage and inflammation during recovery from exercise. *J Appl Physiol* 2017;122(3):559–70. <https://doi.org/10.1152/jappphysiol.00971.2016>
- Mann CJ, Perdiguero E, Kharraz Y, et al. Aberrant repair and fibrosis development in skeletal muscle. *Skelet Muscle* 2011;1(1):21. <https://doi.org/10.1186/2044-5040-1-21>
- Chen X, Li Y. Role of matrix metalloproteinases in skeletal muscle: Migration, differentiation, regeneration and fibrosis. *Cell Adh Migr* 2009;3(4):337–41. <https://doi.org/10.4161/cam.3.4.9338>
- Garg K, Corona BT, Walters TJ. Therapeutic strategies for preventing skeletal muscle fibrosis after injury. *Front Pharmacol* 2015;6:87. <https://doi.org/10.3389/fphar.2015.00087>
- Jakeman JR, Byrne C, Eston RG. Efficacy of lower limb compression and combined treatment of manual massage and lower limb compression on symptoms of exercise-induced muscle damage in women. *J Strength Cond Res* 2010;24(11):3157–65. <https://doi.org/10.1519/JSC.0b013e3181e4f80c>
- Alves AN, Fernandes KP, Melo CA, et al. Modulating effect of low level-laser therapy on fibrosis in the repair process of the tibialis anterior muscle in rats. *Lasers Med Sci* 2014;29(2):813–21. <https://doi.org/10.1007/s10103-013-1428-9>
- Best TM, Loitz-Ramage B, Corr DT, et al. Hyperbaric oxygen in the treatment of acute muscle stretch injuries. Results in an animal model. *Am J Sports Med* 1998;26(3):367–72. <https://doi.org/10.1177/03635465980260030401>
- Cezar CA, Roche ET, Vandenburg HH, et al. Biologic-free mechanically induced muscle regeneration. *Proc Natl Acad Sci U S A* 2016;113(6):1534–9. <https://doi.org/10.1073/pnas.1517517113>
- Chan YS, Li Y, Foster W, et al. The use of suramin, an antifibrotic agent, to improve muscle recovery after strain injury. *Am J Sports Med* 2005;33(1):43–51. <https://doi.org/10.1177/0363546504265190>
- Nishizaki K, Ikegami H, Tanaka Y, et al. Effects of supplementation with a combination of β -hydroxy- β -methyl butyrate, L-arginine, and L-glutamine on postoperative recovery of quadriceps muscle strength after total knee arthroplasty. *Asia Pac J Clin Nutr* 2015;24(3):412–20.
- Nozaki M, Li Y, Zhu J, et al. Improved muscle healing after contusion injury by the inhibitory effect of suramin on myostatin, a negative regulator of muscle growth. *Am J Sports Med* 2008;36(12):2354–62. <https://doi.org/10.1177/0363546508322886>
- Piedade MC, Galhardo MS, Battlehner CN, et al. Effect of ultrasound therapy on the repair of gastrocnemius muscle injury in rats. *Ultrasonics* 2008;48(5):403–11. <https://doi.org/10.1016/j.ultras.2008.01.009>
- Laumonier T, Menetrey J. Muscle injuries and strategies for improving their repair. *J Exp Orthop* 2016;3(1):15. <https://doi.org/10.1186/s40634-016-0051-7>
- Tatsumi R, Sheehan SM, Iwasaki H, et al. Mechanical stretch induces activation of skeletal muscle satellite cells in vitro. *Exp Cell Res* 2001;267(1):107–14. <https://doi.org/10.1006/excr.2001.5252>

19. Huang D, Shen KH, Wang HG. Pressure therapy upregulates matrix metalloproteinase expression and downregulates collagen expression in hypertrophic scar tissue. *Chin Med J* 2013;126(17): 3321–4.
20. Best TM, Gharaibeh B, Huard J. Stem cells, angiogenesis and muscle healing: A potential role in massage therapies? *Postgrad Med J* 2013;89(1057):666–70. <https://doi.org/10.1136/postgradmedj-2012-091685rep>
21. Butterfield TA, Zhao Y, Agarwal S, et al. Cyclic compressive loading facilitates recovery after eccentric exercise. *Med Sci Sports Exerc* 2008;40(7): 1289–96. <https://doi.org/10.1249/MSS.0b013e31816c4e12>
22. Stupka N, Tarnopolsky MA, Yardley NJ, et al. Cellular adaptation to repeated eccentric exercise-induced muscle damage. *J Appl Physiol* 2001;91(4):1669–78. <https://doi.org/10.1152/jappl.2001.91.4.1669>
23. Kim J, Sung DJ, Lee J. Therapeutic effectiveness of instrument-assisted soft tissue mobilization for soft tissue injury: Mechanisms and practical application. *J Exerc Rehabil* 2017;13(1):12–22. <https://doi.org/10.12965/jer.1732824.412>
24. Kivlan BR, Carcia CR, Clemente FR, et al. The effect of Astym® Therapy on muscle strength: A blinded, randomized, clinically controlled trial. *BMC Musculoskelet Disord* 2015;16:325. <https://doi.org/10.1186/s12891-015-0778-9>
25. Laudner K, Compton BD, McLoda TA, et al. Acute effects of instrument assisted soft tissue mobilization for improving posterior shoulder range of motion in collegiate baseball players. *Int J Sports Phys Ther* 2014;9(1):1–7.
26. Davidson CJ, Ganion LR, Gehlsen GM, et al. Rat tendon morphologic and functional changes resulting from soft tissue mobilization. *Med Sci Sports Exerc* 1997;29(3):313–19. <https://doi.org/10.1097/00005768-199703000-00005>
27. Loghmani MT, Warden SJ. Instrument-assisted cross-fiber massage accelerates knee ligament healing. *J Orthop Sports Phys Ther* 2009;39(7):506–14. <https://doi.org/10.2519/jospt.2009.2997>
28. Blanchette MA, Normand MC. Augmented soft tissue mobilization vs natural history in the treatment of lateral epicondylitis: A pilot study. *J Manipulative Physiol Ther* 2011;34(2): 123–30. <https://doi.org/10.1016/j.jmpt.2010.12.001>
29. Papa JA. Conservative management of Achilles Tendinopathy: A case report. *J Can Chiropr Assoc* 2012;56(3):216–24.
30. Schaefer JL, Sandrey MA. Effects of a 4-week dynamic-balance-training program supplemented with Graston instrument-assisted soft-tissue mobilization for chronic ankle instability. *J Sport Rehabil* 2012;21(4):313–26. <https://doi.org/10.1123/jsr.21.4.313>
31. Hammer WI, Pfefer M. Treatment of subacute lumbar compartment syndrome using the Graston Technique. *J Manipulative Physiol Ther* 2005;28(3):199–204. <https://doi.org/10.1016/j.jmpt.2005.02.010>
32. MacDonald N, Baker R, Cheatham SW. The effects of instrument assisted soft tissue mobilization on lower extremity muscle performance: A randomized controlled trial. *Int J Sports Phys Ther* 2016;11(7):1040–7.
33. Cheatham SW, Lee M, Cain M, et al. The efficacy of instrument assisted soft tissue mobilization: A systematic review. *J Can Chiropr Assoc* 2016;60(3): 200–11.
34. Hammer WI. The effect of mechanical load on degenerated soft tissue. *J Bodyw Mov Ther* 2008;12(3):246–56. <https://doi.org/10.1016/j.jbmt.2008.03.007>
35. Clarkson PM, Hoffman EP, Zambraski E, et al. ACTN3 and MLCK genotype associations with exertional muscle damage. *J Appl Physiol* 2015;99(2):564–9. <https://doi.org/10.1152/jappphysiol.00130.2005>
36. Castellani JW, Zambraski EJ, Sawka MN, et al. Does high muscle temperature accentuate skeletal muscle injury from eccentric exercise? *Physiol Rep* 2016;4(9):12777. <https://doi.org/10.14814/phy2.12777>
37. Markovic G. Acute effects of instrument assisted soft tissue mobilization vs. foam rolling on knee and hip range of motion in soccer players. *J Bodyw Mov Ther* 2015;19(4):690–6. <https://doi.org/10.1016/j.jbmt.2015.04.010>

38. Delos D, Maak TG, Rodeo SA. Muscle injuries in athletes: Enhancing recovery through scientific understanding and novel therapies. *Sports Health* 2013;5(4):346–52. <https://doi.org/10.1177/1941738113480934>
39. Huard J, Li Y, Fu FH. Muscle injuries and repair: Current trends in research. *J Bone Joint Surg Am* 2002;84(5):822–32. <https://doi.org/10.2106/00004623-200205000-00022>
40. Gumucio JP, Flood MD, Phan AC, et al. Targeted inhibition of TGF- β results in an initial improvement but long-term deficit in force production after contraction-induced skeletal muscle injury. *J Appl Physiol* 2013;115(4):539–45. <https://doi.org/10.1152/jappphysiol.00374.2013>
41. Cafarelli E, Flint F. The role of massage in preparation for and recovery from exercise. An overview. *Sports Med* 1992;14(1):1–9. <https://doi.org/10.2165/00007256-199214010-00001>
42. Weerapong P, Hume PA, Kolt GS. The mechanisms of massage and effects on performance, muscle recovery and injury prevention. *Sports Med* 2005;35(3):235–56. <https://doi.org/10.2165/00007256-200535030-00004>
43. Cheatham SW, Kreiswirth E, Baker R. Does a light pressure instrument assisted soft tissue mobilization technique modulate tactile discrimination and perceived pain in healthy individuals with DOMS? *J Can Chiropr Assoc* 2019;63(1):18–25.
44. Kendall B, Eston R. Exercise-induced muscle damage and the potential protective role of estrogen. *Sports Med* 2002;32(2):103–23. <https://doi.org/10.2165/00007256-200232020-00003>
45. Thompson HS, Hyatt JP, De Souza MJ, et al. The effects of oral contraceptives on delayed onset muscle soreness following exercise. *Contraception* 1997;56(2):59–65. [https://doi.org/10.1016/S0010-7824\(97\)00093-0](https://doi.org/10.1016/S0010-7824(97)00093-0)
46. Coviello JP, Kakar RS, Reynolds TJ. Short-term effects of instrument-assisted soft tissue mobilization on pain free range of motion in a weightlifter with subacromial pain syndrome. *Int J Sports Phys Ther* 2017;12(1):144–54.
47. Lee JH, Lee DK, Oh JS. The effect of Graston technique on the pain and range of motion in patients with chronic low back pain. *J Phys Ther Sci* 2016;28(6):1852–5. <https://doi.org/10.1589/jpts.28.1852>
48. Brancaccio P, Maffulli N, Limongelli FM. Creatine kinase monitoring in sport medicine. *Br Med Bull* 2007;81–82:209–30. <https://doi.org/10.1093/bmb/ldm014>