Decrease in self-reported pain and dynamic knee instability mediates the association between wearing a soft knee brace and reduction in activity limitations in persons with knee osteoarthritis

Cudejko, Tomasz; van der Esch, Martin; Rijnhart, Judith J.M.; van den Noort, J.C.; van der Leeden, Marike; Roorda, Leo D.; Lems, Willem; Harlaar, Jaap; Dekker, Joost

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COMPARATIVE EFFICACY OF ECCENTRIC AND CONCENTRIC-FOCUSED RESISTANCE EXERCISE ON PAIN, LEG STRENGTH AND WALKING ENDURANCE IN KNEE OSTEOARTHRITIS

H.K. Vincent, T. Vasilopoulos, K.R. Vincent. *Univ. of Florida, Gainesville, FL, USA*

Purpose: Evidence from the Osteoarthritis Initiative shows that as knee osteoarthritis (OA) progresses and pain increases over time, knee flexor and extensor muscle strength decline linearly in both men and women. Strength improvements from various exercises are related to pain reduction and reduction of pain impact on physical function. What remains unclear is which strength training type may be more effective for knee OA pain symptoms and reversing the OA-related strength decline. The primary purpose of this study was to compare the effectiveness of eccentrically-focused resistance exercise (ECC RT) and concentrically-focused resistance exercise (CNC RT) on knee OA symptoms and leg muscle strength over four months. The secondary purpose was to determine whether reduction in knee pain severity was related to knee extensor or flexor strength gain.
Methods: 90 participants (60–85 yr, 61% women) were randomized to CNC RT, ECC RT or a wait-list no-exercise control group (CON). All participants completed a graded, Naughton treadmill walking test to exhaustion. Four months of supervised exercise training were completed using traditional weight machines (CNC RT), or modified matched machines that overloaded the eccentric action (ECC RT). Main outcomes included one-repetition maximal strength (1RM; leg extension, leg flexion and leg press), weekly rate of strength gain, Western Ontario McMaster University Osteoarthritis Index (WOMAC) total score and pain, stiffness and function subscores. General linear models with intervention group (ECC RT, CNC RT, CON) and baseline (pre) measures as independent variables, and post-invention measures as the dependent variables were run to assess group differences in change in strength and WOMAC score and to assess which gains in strength best explained improvements in WOMAC scores. Linear regression was used to determine the contribution of the variance in change in walking exercise time to changes in leg strength.
Results: Treadmill walking endurance time increased by 6.7%, 10% and 8.3% in the CON, CNC RT and ECC R, respectively. Both CNC RT and ECC RT groups showed an average of 16%–28% improvement relative to CON group ($P = 0.003–0.005$) for all leg strength measures. The rate of weekly strength gain was greater for CNC RT than ECC RT for leg press and leg curl (by 2.9%–4.8%; both $P < 0.05$), but not for leg extension (0.7%; $P = 0.38$). There were no significant differences in WOMAC total and subscores across groups over time. Of the three leg exercises, leg press strength change was the most significant contributor to change in WOMAC Total scores ($R^2 = 0.223$). The change in leg curl strength from baseline to month four was a significant predictor of the change in WOMAC pain subscore ($P = .032$). Variability existed in the pain responsiveness to training, such that some patients achieved clinically meaningful improvements to pain whereas others did not. Participants with WOMAC pain reduction of ≥30% from baseline to month four showed greater 13.8%–24.7% higher strength gains in all three exercises compared to participants with pain reduction <30%. The four-month changes in leg curl and leg press strength contributed 7.6%–16.7% to the model for walking exercise time ($P < 0.05$).
Conclusions: Both resistance training types were effective in increasing leg muscle strength and contributing to improvement in walking exercise endurance time. The degree of strength gain was associated with pain relief not resistance exercise type. The choice of which strengthening mode to use may be dependent on individual OA treatment goals and tolerance to the exercise.

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HIF-1α IN ARTICULAR CARTILAGE IS UP-REGULATED BY TREADMILL RUNNING *IN VIVO*

Y. Fujii †, H. Inoue †, Y. Arai ‡, S. Nakagawa ‡, S. Tsuchida †, S. Ichimaru †, S. Shimomura †, O. Mazda §, T. Kubo †. † *Dept. of Orthopaedics, Graduate Sch. of Med. Sci., Kyoto Prefectural Univ. of Med., Kyoto, Japan;* ‡ *Dept. of Sports and Para-Sports Med., Graduate Sch. of Med. Sci., Kyoto Prefectural Univ. of Med., Kyoto, Japan;* § *Dept. of Immunology, Graduate Sch. of Med. Sci., Kyoto Prefectural Univ. of Med., Kyoto, Japan*

Purpose: Articular cartilage is a specialized avascular tissue composed of a small number of cells and an extensive extracellular matrix. Due to its avascular structure, articular cartilage is physiologically hypoxic tissue. The transcription factor hypoxia-inducible factor-1 alpha (HIF-1α) represents one of the important elements in maintaining proper cellular functions under hypoxic condition. HIF-1α is also of great importance by promoting the synthesis of relevant extracellular matrix components in chondrocytes. On the other hand, heat shock protein (HSP) 70 is a member of a family of highly conserved proteins which are synthesized in cells after stress loading, and protects cells from various types of stress including hypoxia or mechanical stress. In our previous study, HSP70 induced by up-regulation of HIF-1α expression has chondroprotective effects under hypoxic condition *in vitro*. The purpose of this study was to investigate the relationship between mechanical stress and HIF-1α expression on rat articular cartilage.
Methods: We used treadmill apparatus as mechanical loading. Twelve-week-old male Wistar rats ran on a treadmill at 12 m/min as moderate treadmill exercise or 20 m/min as intense for 45-min at a single time (n = 16 in each group). Rats in control group were simply kept in their cage (n = 16). All were immediately sacrificed after running, and articular cartilage in right knee was removed from patellar, distal femur, and proximal tibia. The cartilage was homogenized, and total RNA was extracted. We analyzed gene expressions of sox9 as transcription factors, aggrecan and col2a1 as anabolic factors with quantitative reverse transcriptase polymerase chain reaction (RT-PCR). Left knees of rats in control group and the 20 m/min group were removed and stained with immunostaining for HIF-1α.
Results: Gene expression of sox9 was significantly higher in the 20 m/min group than the others. Gene expression of aggrecan was tended to increase in a speed dependent manner. There was no significant difference among all groups in gene expression of Col2a1. On immunological staining, HIF-1α in rat knee articular cartilage was more strongly stained in the 20 m/min running group than the control group. The staining of HIF-1α was no difference between medial and lateral sides of the knees. Furthermore, the staining of HIF-1α was particularly enhanced from the superficial to the middle zone of the knee articular cartilage.
Conclusions: We have reported that the expression of HSP70 is elevated in chondrocytes with heat stimulation and mechanical stress *in vitro*, and that the expression of HSP70 had an important role for proteoglycan(PG) and Col2a1 synthesis with heat stimulation in rabbit articular cartilage. In rabbits, we also clarified that HSP70 induced by up-regulation of HIF-1α expression has chondroprotective effects under hypoxic condition *in vitro*. HIFs which sense extracellular oxygen tension and regulate gene expression play important roles as transcription factors in hypoxic environments. HIF-1α is a transcription factor essential for chondrocyte differentiation and maturation, and for maintenance of chondrocyte phenotypes. On the other hand, the oxygen environment in the joint may change with exercise, because it is known that oxygen partial pressure in articular cartilage is decreased by mechanical stress. In present study, the 20 m/min running increased the expression of sox9. This result show that cartilage metabolism in the joint may be activated from the early stage with excessive exercise. In immunostaining, the expression of HIF-1α is enhanced in rat knee articular cartilage by treadmill running *in vivo*. These may be reflected to inducing hypoxic environment in joints due to treadmill running. In conclusion, moderate speed running may protect articular cartilage by inducing hypoxic environment in rats.

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DECREASE IN SELF-REPORTED PAIN AND DYNAMIC KNEE INSTABILITY MEDIATES THE ASSOCIATION BETWEEN WEARING A SOFT KNEE BRACE AND REDUCTION IN ACTIVITY LIMITATIONS IN PERSONS WITH KNEE OSTEOARTHRITIS

T. Cudejko †, M. van der Esch ‡, J. Rijnhart §, J. van den Noort †,‖, M. van der Leeden †,‡, L.D. Roorda ‡, W. Lems ¶,#, J. Harlaar †,††, J. Dekker †. † *VU Univ. Med. Ctr. Amsterdam, Amsterdam, Netherlands;* ‡ *Amsterdam Rehabilitation Res. Ctr., Reade, Amsterdam, Netherlands;* § *Dept. of Epidemiology and Biostatistics, VU Univ. Med. Ctr., Amsterdam, Netherlands;* ‖ *Dept. of Radiology and Nuclear Med., Musculoskeletal Imaging Quantification Ctr. (MIQC), Academic Med. Ctr., Amsterdam, Netherlands;* ¶ *Jan van Breemen Res. Inst., Reade, Amsterdam, Netherlands;* # *Amsterdam Rheumatology & immunology Ctr., Amsterdam Med. Ctr., Reade, VU Univ. Med. Ctr., Amsterdam, Netherlands;* †† *Delft Univ. of Technology, Delft, Netherlands*

Purpose: We have previously shown that wearing a soft knee brace reduces activity limitations in persons with knee osteoarthritis (OA). Several underlying mechanisms have been proposed via which a soft knee brace reduces activity limitations in persons with knee OA. However, to our knowledge, no study has identified mechanisms explaining this effect. Therefore, the aim of the study was to identify mechanisms explaining the beneficial effect of wearing a soft knee brace on activity limitations in persons with knee OA.
Methods: This was an exploratory analysis of data from 44 participants with knee OA from Amsterdam Osteoarthritis cohort, who enrolled in a single-session within-subject cross-over design study, comparing a soft brace with no soft brace, and comparing a non-tight soft brace with a tight soft brace. A mediation analysis was performed and the mediation effect was calculated based on the product of coefficients approach. Confidence intervals were calculated with a bootstrap procedure. The outcome measures were activity limitations assessed with the 10-meter walk test and the Get up and Go test. The studied mediators were the changes in: knee joint proprioception, self-reported pain, pressure pain threshold (PPT) and objective dynamic knee instability. Knee joint proprioception was assessed by the active movement extent discrimination assessment; self-reported pain with the Numeric Rating Scale (NRS); PPT with a hand-held pressure algometer, and dynamic knee instability with the Perturbation Response (PR) i.e., a biomechanics based measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation on the treadmill, standardized to the mean (standard deviation) varus-valgus angle during level walking.
Results: Both a decrease in self-reported pain during walking and a decrease in dynamic knee instability mediated the association between wearing a soft knee brace and reduction in time to complete both 10-m walk test and the GUG test ($P < 0.05$). Changes in proprioception and PPT did not mediate these associations ($P > 0.05$). Magnitudes of the mediation effects were similar for a non-tight and a tight soft knee brace.
Conclusions: The decrease in activity limitations in persons with knee OA who wear a soft knee brace might be explained by a decrease in self-reported pain and a reduction in dynamic knee instability.

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RELIABILITY ASSESSMENT OF A PATELLOFEMORAL ARTHROMETER USING A FEEDBACK DEVICE WITH SHEET-TYPE PRESSURE SENSORS

H. Ohko. *Seijoh Univ., Aiti, Japan*

Purpose: We reported that a reduced knee flexion angle was associated with reduced inferior patellar mobility in healthy elderly women in OARSI 2017. Using conventional measurement methods, the level of the pushing force on the patella (about 80 N) was confirmed subjectively before each test with a handheld dynamometer. However, there have been problems regarding inconsistent levels of pushing force measurements during patellar movements, even when obtained by the same examiner. This is associated with factors such as the examiner's clinical experience. This needs to be improved if the reliability of the PFA is to be increased. In addition, clinical applications for knee osteoarthritis (OA) patients are also needed. The objective of this study was to examine inter-examiner reliability when real-time feedback was provided on the pushing force during patellar displacement in young healthy people. In addition, preliminary research was performed to examine the classification and severity of OA using the Kellgren-Lawrence system, which correlates with patellar mobility and patellar flexion angle.
Methods: For reliability assessment, young healthy females (N = 10) and young healthy males (N = 10) were recruited from the Department of Rehabilitation and Care of Seijoh University (Table 1). For each participant, we randomly chose the right or left patella, and assessed patellar mobility. To assess the level of patellar mobility, a PFA equipped with a digital caliper was used. Throughout the sessions, the manual pushing force at the end of patellar displacement was confirmed by the measurements in real time using a thin sheet sensor stuck to the thumb, which were approximately 80 N. Patellar mobility was measured when the pushing force of the thumb on the patella reached 80 N. In all cases, measurements were obtained three times, with the final analysis performed using the mean of the three results. To assess the intra-tester reliability in quantifying patellar mobility, repeated measurements were obtained on two separate days. The testers were blinded to their own measurements. The standard error of the mean (SEM) was calculated using the following equation: SEM = SD × ($\sqrt{1}$-ICC). To further investigate the real change beyond the measurement error of patellar displacement, the smallest real difference (SRD) was used to indicate the magnitude of change that would exceed the expected trial-to-trial variability. SRD was calculated using the following equation: $1.96 \times \sqrt{2} \times$ SEM. intraclass correlation coefficients (ICC), SEM, and SRD were compared to patellar mobility measurements performed previously by another examiner without the use of the feedback device. The OA patients included two women receiving outpatient care for OA (case 1 age 68, case 2 age 74). Kellgren-Lawrence classification with X-P, patellar mobility, and knee flexion angle were measured.
Results: The intratester ICCs of the medial, lateral, and inferior patellar displacement measurements varied from 0.993 to 0.998, and the SEM of all measurements ranged from 0.15 to 0.22 mm. The SRD of all measurements ranged from 0.02 to 0.05 mm. In comparisons based on the presence or absence of real-time feedback of patellar pushing force, slight improvements in ICC and SEM were observed, and SRD improved considerably (Table 2). OA case 1 was diagnosed as Kellgren-Lawrence Grade II (Figure 1). Her knee flexion angle was 120° and patellar mobility was medial: 10.3 mm, lateral: 11.2 mm, superior: 9.8 mm, and inferior: 7.9 mm. OA case 2 was diagnosed as Kellgren-Lawrence Grade II (Figure 1). Her knee flexion angle was 105° and patellar mobility was medial: 8.6 mm, lateral: 10.4 mm, superior: 8.8 mm, and inferior: 5.9 mm.
Conclusions: A high level of reliability was obtained when using a patellofemoral arthrometer that provided real-time feedback on patellar pushing force. Going forward, we would like to clarify the associations between reduced knee flexion angle, patellar mobility, and Kellgren-Lawrence classification to determine cases of reduced patellar mobility that could be candidates for treatment.

Subject characteristics in reliability study

	Male ($n = 10$)	Female ($n = 10$)
Age (y)	21.9 ± 0.7	21.8 ± 0.4
Height (cm)	171.0 ± 5.2	157.3 ± 4.3
Weight (kg)	62.4 ± 6.6	48.3 ± 3.9
BMI (kg/m^2)	21.3 ± 1.8	19.5 ± 1.2

Reliability of patellar mobility measurements based on presence/absence of feedback

	No feedback ($n = 29$)					With feedback ($n = 20$)				
	Day 1 mean	Day 2 mean	ICC (95% CI)	SEM	SRD	Day 1 mean	Day 2 mean	ICC (95% CI)	SEM	SRD
MPD (mm)	16.2 ± 3.2	16.2 ± 3.3	0.994 (0.986–0.998)	0.26	0.71	14.2 ± 2.7	14.2 ± 2.6	0.993 (0.984–0.997)	0.22	0.05
LPD (mm)	16.2 ± 4.0	16.5 ± 4.4	0.991 (0.979–0.997)	0.42	1.15	15.5 ± 3.3	15.4 ± 3.4	0.998 (0.994–0.999)	0.15	0.02
IPD (mm)	17.8 ± 2.9	17.9 ± 3.2	0.991(0.979–0.997)	0.31	0.85	14.1 ± 3.5	14.0 ± 3.4	0.993 (0.983–0.997)	0.29	0.07