Osteoarthritis and Cartilage



Brief Report

Trajectories of perceived exertion and pain over a 12-week neuromuscular exercise program in patients with knee osteoarthritis



C.A. Primeau $\dagger \ddagger \S \parallel$, T.B. Birmingham $\dagger \ddagger \S \parallel^*$, R.F. Moyer ¶, K.A. O'Neil \parallel , M.S. Werstine $\dagger \parallel$, G.K. Alcock $\dagger \parallel$, I.R. Giffin $\ddagger \S \parallel \#$

- † School of Physical Therapy, Faculty of Health Sciences, Western University, London, ON, Canada
- ‡ Bone and Joint Institute, Western University, London, ON, Canada
- § Wolf Orthopaedic Biomechanics Laboratory, Western University, London, ON, Canada
- || Fowler Kennedy Sport Medicine Clinic, Western University, London, ON, Canada
- School of Physiotherapy, Faculty of Health, Dalhousie University, Halifax, Nova Scotia, Canada
- # Department of Surgery, Schulich School of Medicine and Dentistry, Western University Ontario, London, ON, Canada

ARTICLE INFO

Article history: Received 10 February 2020 Accepted 31 July 2020

Keywords: Knee osteoarthritis Neuromuscular exercise Pain Perceived exertion RPF

SUMMARY

Background: Exercise programs rely on the overload principle, yet patients with knee osteoarthritis (OA) may not adequately progress exercises due to fear of exacerbating symptoms.

Objective: To describe trajectories for perceived exertion and exercise-induced knee pain during a neuromuscular exercise program for patients with knee OA.

Design: Participants with knee OA completed a 12-week neuromuscular exercise program consisting of weekly supervised sessions plus home exercises. During each supervised session, the Borg's rating of perceived exertion (RPE; 6 = no exertion, 20 = maximal exertion) and knee pain (pre, post, max) using Numeric Rating Scales (NRS; 0 = no pain, 10 = worst imaginable pain) were completed. Mean changes in RPE and pain from weeks 1–12 were calculated. Mixed effects regression was used to investigate trajectories over time (weeks) for RPE, and maximum pain (pre-to-max) and pain-change (pre-to-post) during exercise.

Results: 56 patients (95%) completed the program. From week 1–12, RPE increased by 2.6 (95%CI, 1.7 to 3.5), from 'somewhat hard' to 'very hard', while max pain decreased by 1.0 NRS (95%CI, 0.5 to 1.3) and pain-change decreased by 0.9 NRS (95%CI, 0.4 to 1.3). Linear mixed effects regression showed a quadratic increase for RPE over time until between weeks 9 and 10, then RPE plateaued. Maximum pain decreased linearly over time. Pain-change showed a quadratic decrease over time until approximately week 9, then pain-change plateaued.

Conclusions: In patients with knee OA participating in a 12-week neuromuscular exercise program, perceived exertion during exercise progressed from 'somewhat hard' to 'very hard' at 9 weeks, while exercise-induced knee pain decreased. Patients were able to work harder while experiencing decreases rather than increases in pain.

© 2020 Osteoarthritis Research Society International. Published by Elsevier Ltd. All rights reserved.

_ .

Introduction

Evidence-based guidelines recommend exercise as a first-line treatment for patients with knee osteoarthritis (OA)^{1,2}. Exercise programs require progressive increases in intensity to stimulate physiological changes, although the ability of patients with knee OA to adhere to this overload principle is unclear^{3,4}. For patients with knee OA, exercises are gradually increased in intensity and/or difficulty, as the progressive overload principle is thought to evoke optimal improvements^{5–8}. Paradoxically, activities similar to those

^{*} Address correspondence and reprint requests to: T. B. Birmingham, Fowler Kennedy Sport Medicine Clinic, University of Western Ontario, London, ON, N6A 3K7, Canada. Tel.: 519-661- 2111x81122.

E-mail addresses: cprimea@uwo.ca (C.A. Primeau), tbirming@uwo.ca (T.B. Birmingham), rebecca.moyer@dal.ca (R.F. Moyer), kyoung@uwo.ca (K.A. O'Neil), mmcalend@uwo.ca (M.S. Werstine), galcock@uwo.ca (G.K. Alcock), rgiffin@uwo.ca (J.R. Giffin).

during neuromuscular exercise programs can exacerbate knee symptoms⁹. Therefore, a balance is required between progressing exercises and limiting exercise-induced knee pain. Exercise progression while moderating pain is a well-accepted aspect of rehabilitation and its importance should not be underestimated. Kinesiophobia (fear of pain with movement) is common in OA and can present a considerable barrier to exercise prescription. Often. patients will avoid exercise in fear of exacerbating symptoms ¹⁰. It is therefore important to better understand the potential for increases in patient exertion levels, while monitoring knee pain. Previous research suggests knee pain during exercise programs can be managed with proper guidance 11,12. The ability for patients to simultaneously increase exertion levels throughout the program is less clear. The objectives of the present study were to describe the trajectories of perceived exertion and exercise-induced pain (during each exercise session) over a 12-week neuromuscular exercise program in patients with knee OA.

Methods

Participants

The first 59 patients who completed the neuromuscular exercise program as part of an ongoing prospective cohort study of interventions for knee OA were included. Inclusion criteria were diagnosis of symptomatic knee OA according to the American College of Rheumatology criteria¹³ and pain and radiographic disease primarily affecting the tibiofemoral rather than the patellofemoral joint. Patients with multiligamentous instability, infectious or inflammatory knee OA or pregnancy were excluded. The study was approved by the institution's Research Ethics Board for Health Sciences Research Involving Human Subjects and the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Neuromuscular exercise program

The goal of the exercise program was to improve pain and function by improving postural control, muscular strength and range of motion^{7,14}. The program was similar to those described as neuromuscular exercise where the majority of exercises target sensorimotor tasks and functional stabilization that are often compromised in patients with knee OA⁵. The program included one supervised session (completed in the clinic's physical therapy gym and using its exercise equipment) and three unsupervised sessions (completed at home, or at the patient's gym) per week for 12 weeks. During the first supervised session, patients were instructed how to perform the exercises, including potential variations, by one of two participating registered physiotherapists or one physiotherapy assistant, all with experience in therapeutic exercise prescription for patients with musculoskeletal conditions. The same therapists helped design the program. Emphasis was placed on maintaining alignment and functional stability during each exercise. Each session began with a 5-min warmup (e.g., cycling) followed by 6-to-13 exercises from a predetermined list of potential exercises prescribed by the therapist (Appendix A). Patients completed 2-to-3 sets of 10-to-15 repetitions of each assigned exercise. The first assessment provided a baseline for exercise ability. The therapist progressed the patient throughout the program by adding new exercises, adding resistance and/or increasing the difficulty of an existing exercise based on symptom response and quality of performance. We advised patients to expect some knee pain during exercise, but if the pain exceeded 5 on a 0-to-10 scale, to decrease the exercise difficulty or number of repetitions. During each of the 12 supervised in-clinic sessions we recorded patient attendance and asked patients to report the number of times they completed the home exercise program during the previous week. The program was provided as planned without modifications during the intervention period. Patients were instructed to continue the exercises on their own following the program three times per week, preferably with one day rest between sessions, but we did not monitor exercise adherence beyond the 12-week program.

Patient-reported measures

Perceived exertion

Patients completed the Borg Rating of Perceived Exertion (RPE) scale (Appendix B) after each supervised session. The RPE is a user-friendly numerical scale that evaluates an individual's self-reported level of effort, physical exertion and fatigue during exercise using a 15-point scale ranging from 6 (no exertion) to 20 (maximum exertion)¹⁵. The Borg RPE is suggested as a valid and reliable measure of exercise intensity^{15,16}.

Pain

Patients rated their knee pain before (pre) and after (post) each exercise session and reported the maximum level of pain experienced during the session using the Numeric Rating Scale (NRS) for pain¹⁷. We used an 11-point scale ranging from 0 (no pain) to 10 (worst imaginable pain) to investigate: 1) maximum pain during exercise (maximum minus pre), and 2) pain-change (post minus pre).

Statistical analysis

Baseline demographics were summarized using means for continuous data and frequencies for categorical data. We evaluated the sample mean change (95% confidence intervals [CI]) from week 1–12 for RPE, maximum pain and pain-change using dependent samples Student's t-tests and evaluated the trajectory of RPE and pain (outcomes) over time (predictor). Specifically, we performed linear mixed effects growth curve models between 1) RPE and time (in weeks), 2) maximum exercise-induced pain and time, and 3) pain-change and time (using the mixed function in Stata 16, StataCorp LLC, College Station, TX). Linear mixed effects models included all patients in the analyses by using restricted maximum likelihood estimation to accommodate missing data. In each model, time (weeks, re-scaled to range from 0 to 11) was entered as a continuous predictor variable for fixed effects. Random intercepts and slopes were specified by the participant ID and time terms. We tested the assumptions for linear mixed models; residuals were normally distributed and homoscedastic for all models. Likelihood ratio tests (LRTs) and Bayesian Information Criterion (BIC – lowest values preferred) were used to select the model covariance structure (to control for within-patient correlation) and to evaluate nonlinear relationships (Appendix C); maximum exercise-induced pain demonstrated a linear trajectory over time, whereas RPE and pain-change demonstrated quadratic trajectories. We identified the max/min of our polynomial function using the regression line derivative, solving for *X* when the slope was zero.

Results

Patients

Baseline characteristics are presented in Table I. 56 patients (95%) completed the program. Two patients were lost to follow-up (1 at week 3, 1 at week 6). One patient withdrew from the study for

unrelated reasons (week 3). 38 patients (64%) completed 12 inclinic sessions; the remaining 18 patients (31%) completed at least nine. The sample mean (standard deviation [SD]) days per week for sessions completed at home was 3 (2).

Perceived exertion and pain trajectories

Trajectories for exertion and pain are shown in Fig. 1(A). The mean increase in RPE from week 1–12 post-exercise was 2.6 (95%CI, 1.7 to 3.5). We observed a quadratic relationship between RPE and time. Linear mixed effects regression showed that RPE increased over time (from 13.5 [95%CI, 12.9 to 14.0] at week 1 to 16.1 [95%CI, 15.5 to 16.8] at week 9), then plateaued and remained constant until week 12 (15.9 [95%CI, 15.1 to 16.7]) [Fig. 1(B)]. Random effects suggested there was also evidence of variation in the intercept (SD = 1.8) and the slope across patients, but not for the rate of change in the slope.

Both measures of exercise-induced pain decreased from week 1–12. Maximum exercise-induced pain decreased by 1.0 NRS (95% CI, 0.5 to 1.3), while pain-change decreased by 0.9 NRS (95%CI, 0.4 to 1.3). We observed a linear relationship between maximum exercise-induced pain and time, and a quadratic relationship between pain-change and time. Linear mixed effects regression indicated maximum pain decreased, on average, by 0.08 NRS per week (95% creating pain decreased).

CI, 0.04 to 0.12) with evidence to suggest variation in the intercept across patients (SD = 1.5), but not the slope [Fig. 1(C)]. Linear mixed effects regression showed that pain-change decreased over time (from 0.9 [95%CI, 0.5 to 1.2] at week 1 to -0.1 [95%CI, -0.3 to 0.1] at week 9), then plateaued and remained constant until week 12 (0.0 [95%CI, -0.3 to 0.4]) [Fig. 1(B)]. Notably, pain-change with exercise reached approximately 0 by week 7 of the program. Random effects suggested there was also evidence of variation in the intercept (SD = 0.7), not slopes, across patients. Weekly descriptive statistics and regression coefficients are presented in Appendix C.

Discussion

Patients with knee OA participating in a supervised neuromuscular exercise program experienced a substantial increase (2.6 points on the RPE scale [95%CI, 1.7 to 3.5]) in perceived exertion during neuromuscular exercise, moving from the *somewhat hard* category at week 1 to the *hard/very hard* category by completion of the program (Fig. 1). Notably, the increase in perceived exertion followed a quadratic trajectory, such that RPE increased over the course of the program and began to plateau between weeks 9–10. According to the American College of Sports Medicine guidelines, the maximum exertion achieved in this sample (RPE = 16/17) is close to the suggested threshold for the limit of fatigue in healthy

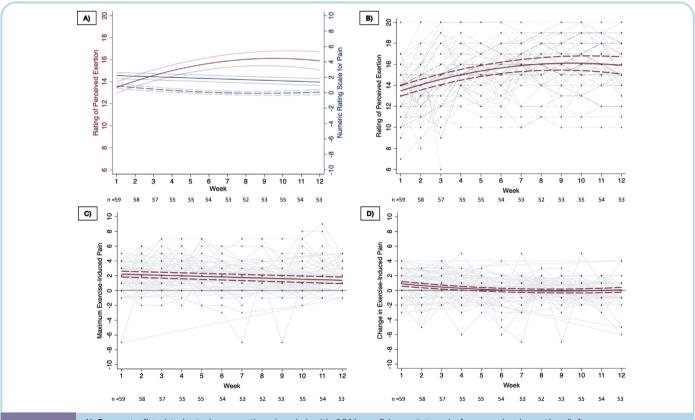


Fig. 1

A) Separate fitted trajectories over time (weeks) with 95% confidence intervals for perceived exertion (left axis; red line), exercise-induced maximum pain (right axis; max pain during exercise session minus pre; solid blue line) and pain-change (right axis; pain post-exercise session minus pre; dashed blue). Individual patient trajectories (blue dots with light blue lines) with the fitted trajectories (red lines with 95% confidence intervals) for B) perceived exertion, C) maximum exercise-induced pain and D) pain-change. The rating of perceived exertion was measured on a scale from 0 to 20. Joint pain was measured using a Numerical Rating Scale from 0 to 10. n = the number of patients with data available for each week.



individuals (RPE = 18/19 [i.e., very, very hard])¹⁶. Importantly, patients were able to increase RPE without increasing pain (Fig. 1). Consistent with previous research^{2,12}, pain decreased over the exercise program.

The Osteoarthritis Research Society International guidelines stress the importance of providing patients with necessary information about OA care and setting realistic/positive expectations from treatment¹. Results from this descriptive study suggest patients with knee OA, similar to the present sample, can strive for and expect to experience steady increases in perceived exertion over the first 9–10 weeks of neuromuscular exercise, ultimately reaching a hard/very hard level (Borg RPE of 16/17) without exacerbating symptoms. Given the relationship between RPE and exercise intensity^{15,16}, these findings suggest patients can meet the principles of progressive overload during neuromuscular exercise while also experiencing decreased pain. These results are consistent with observed improvements in isokinetic strength¹⁴ and

Age, years	55.2 ± 6.8
Sex, no. (%)	
Male	42 (71%)
Body mass index (kg/m²)	$30.7 \pm 4.9 \text{ kg/m}^2$
Duration of knee symptoms, years	7.3 ± 7.9
Kellgren & Lawrence Grade, no. (%) †	
0	_
1	8 (14%)
2	24 (41%)
3	27 (46%)
4	_
OARSI Medial Tibiofemoral Joint	
Space Narrowing Grade ‡	
0	_
1	11 (19%)
2	40 (68%)
3	8 (13%)
OARSI Lateral Tibiofemoral	
Joint Space Narrowing Grade ‡	
0	53 (90%)
1	6 (10%)
2	_
3	_
Self-reported activity level, no. (%)	
Low (i.e., sedentary)	12 (20%)
Moderate (i.e., normal activities)	31 (53%)
High (i.e., sports or mobile hobbies)	16 (27%)

All patients had clinical knee osteoarthritis according to the American College of Rheumatology Criteria. Clinical knee osteoarthritis is defined as exhibiting knee pain and 3 of any of the 6 following criteria: >50 years of age, morning stiffness <30 min, bony tenderness, bony enlargement, crepitus and/or no palpable warmth.

Radiographic severity gradings were from standing anteroposterior radiographs of the knee.

- * Values are reported as means with standard deviations unless otherwise specified.
- [†] Kellgren & Lawrence (KL) grade. Grade 1 indicates doubtful joint space narrowing and possible osteophytic lipping; grade 2 indicates possible joint space narrowing and definite osteophytes; grade 3 indicates definite joint space narrowing, multiple moderate osteophytes, some sclerosis and possible deformity of the bone contour.
- [‡] Osteoarthritis Research Society International (OARSI) Tibiofemoral Joint Space Narrowing grades. Medial and lateral compartments were graded from 0 (normal joint space) to 3 (total loss of joint space).

Table I

Baseline and clinical characteristics (n = 59)*



neuromuscular control⁷ in patients with knee OA completing the same exercise program. In line with previous studies^{11,12}, these results also provide evidence that exercise-induced pain can decrease over time with exercise programs. This information can help clinicians inform patients to expect some exercise-induced knee pain early on, but that the magnitude of pain will likely decrease gradually over time, to no knee pain in the later stages of the program.

There was no control group in this study and limitations that exist in observational studies must be acknowledged, including regression to the mean, natural variation in symptoms, social desirability and self-inclusion bias, among others. This study describes one trajectory based on 59 patients. There may also be differences in trajectories for subgroups of patients that would require a greater sample size to explore. Results of this study should be generalized to similar patients (Table I). Although all patients were referred to this tertiary care centre for unresolving knee pain and were diagnosed with knee OA by a clinician based on subjective and physical exam, the mean age was 55 years, all patients had a Kellgren & Lawrence grade less than 4 and 13% had less than grade 2. It is unclear whether older patients or those with greater radiographic disease experience similar changes in exertion and pain. There were more males (71%) than females referred to the present clinic and therefore recruited for this study. There may be differences in RPE and pain trajectories between males and females not evaluated in the present study. Notably, our results for pain are similar to those reported by Sandal et al. 12 in a sample with a greater proportion of females (60%). Linear mixed modelling assumes that missing data is at random. Three patients in the present sample withdrew from the study and did not complete the program. Although not stated by the participants, it is possible that reasons for withdrawal related to exertion or pain (i.e., were not random).

In conclusion, the present results suggest within-session perceived exertion during exercise increased while exercise-induced pain decreased over a 12-week neuromuscular exercise program for patients with knee OA. These results may provide important information for clinicians in educating patients with knee OA on expectations from therapeutic exercise programs.

Contributions

Conception and design: Primeau, Birmingham, Moyer, O'Neil, Werstine, Alcock, Giffin.

Collection and assembly of data: Primeau, Birmingham, Moyer, O'Neil, Werstine, Alcock, Giffin.

Analysis and interpretation of the data: Primeau, Birmingham, Moyer, O'Neil, Werstine, Alcock, Giffin.

Drafting and final approval of the article: Primeau, Birmingham, Moyer, O'Neil, Werstine, Alcock, Giffin.

Competing interests

The authors have no competing interests to disclose.

Role of the funding source

This study was supported in part from the Canadian Institutes of Health Research, the Arthritis Society of Canada, the Canada Research Chairs Program (T.B. Birmingham) and a Transdisciplinary Training Award from the Collaborative Training Specialization in Musculoskeletal Health, Bone and Joint Institute, Western University, ON, Canada (C.A. Primeau). Funders provided operating funds and salary support to the research team and were not involved in study design, analysis of the data, interpretation of the data or drafting of the manuscript.

Acknowledgements

We thank Celine Doiron, Jamie Wilson, and Nancy Adams for their assistance.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2020.07.011.

References

- 1. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, *et al.* OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage 2019;27(11):1578–89.
- 2. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. Cochrane Database Syst Rev 2015;1, Cd004376.
- 3. Bartholdy C, Juhl C, Christensen R, Lund H, Zhang W, Henriksen M. The role of muscle strengthening in exercise therapy for knee osteoarthritis: a systematic review and metaregression analysis of randomized trials. Semin Arthritis Rheum 2017;47(1):9–21.
- **4.** Schulz JM, Birmingham TB, Atkinson HF, Woehrle E, Primeau CA, Lukacs MJ, *et al.* Are we missing the target? Are we aiming too low? What are the aerobic exercise prescriptions and their effects on markers of cardiovascular health and systemic inflammation in patients with knee osteoarthritis? A systematic review and meta-analysis. Br J Sports Med 2020;54:771–5.
- Ageberg E, Roos EM. Neuromuscular exercise as treatment of degenerative knee disease. Exerc Sport Sci Rev 2015;43(1): 14–22.
- 6. Hellebrandt FA, Houtz SJ. Mechanisms of muscle training in man: experimental demonstration of the overload principle. Phys Ther Rev 1956;36(6):371–83.
- 7. Kanko LE, Birmingham TB, Bryant DM, Gillanders K, Lemmon K, Chan R, *et al.* The star excursion balance test is a reliable and valid outcome measure for patients with knee osteoarthritis. Osteoarthritis Cartilage 2019;27(4):580–5.
- 8. Skou ST, Roos EM. Good Life with osteoArthritis in Denmark (GLA:DTM): evidence-based education and supervised

- neuromuscular exercise delivered by certified physiotherapists nationwide. BMC Muscoskel Disord 2017;18(1):72.
- 9. Thorstensson CA, Roos EM, Petersson IF, Arvidsson B. How do middle-aged patients conceive exercise as a form of treatment for knee osteoarthritis? Disabil Rehabil 2006:28(1):51–9.
- **10.** Hurley M, Dickson K, Hallett R, Grant R, Hauari H, Walsh N, *et al.* Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. Cochrane Database Syst Rev 2018;4(4), Cd010842.
- **11.** Lee AC, Harvey WF, Han X, Price LL, Driban JB, Bannuru RR, *et al.* Pain and functional trajectories in symptomatic knee osteoarthritis over up to 12 weeks of exercise exposure. Osteoarthritis Cartilage 2018;26(4):501–12.
- **12.** Sandal LF, Roos EM, Bøgesvang SJ, Thorlund JB. Pain trajectory and exercise-induced pain flares during 8 weeks of neuromuscular exercise in individuals with knee and hip pain. Osteoarthritis Cartilage 2016;24(4):589–92.
- **13.** Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, *et al.* Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986;29(8): 1039–49.
- 14. Primeau CA, Birmingham TB, Thomas G, Olver T, Lorbergs AL, Moyer RM, *et al.* In: The Feasibility and Efficacy of a 12-week Body Re-composition and Neuromuscular Exercise Program in Patients with Knee Osteoarthritis 2019;vol. 27S497—8.
- **15.** Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377–81.
- Pescatello LS, Riebe D, Thompson PD. ACSM's Guidelines for Exercise Testing and Prescription. 9th edn. Lippincott Williams & Wilkins; 2014.
- 17. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). Arthritis Care Res 2011;63(Suppl 11):S240–52 (Hoboken).