J Musculoskelet Neuronal Interact 2008; 8(1):35-42

Original Article

Hylonome

Pain and its relationship with muscle strength and proprioception in knee OA: Results of an 8-week home exercise pilot study

N. Shakoor[1], S. Furmanov[1], D.E. Nelson[2], Y. Li[3], J.A. Block[1]

[1]Section of Rheumatology, Rush Medical College of Rush University Medical Center, Chicago, IL, USA;
[2]Department of Nursing, Rush Medical College of Rush University Medical Center, Chicago, IL,USA;
[3]Rush Institute for Healthy Aging, Rush Medical College of Rush University Medical Center, Chicago, IL, USA

Abstract

Muscle strength and proprioception deficits have been recognized in knee OA. Pain is the symptomatic hallmark of knee OA. Indirect evidence suggests that muscle strength and proprioception deficits may be interrelated and that pain may have a confounding influence on the measurement of these factors in knee OA. However, these relationships have never been clearly evaluated. Therefore, the purpose of this investigation was to investigate relationships between pain, muscle strength, and proprioception in subjects with knee OA before and after an 8-week home exercise program. This study evaluated thirty-eight subjects with knee OA. Subjects were taught standard quadriceps strengthening exercises that were to be performed daily at home. Pain, muscle strength, and proprioceptive function were measured at baseline and after 8 weeks of therapy. Significant improvements in pain (42%, $p<0.001$) and quadriceps muscle strength (30%, $p<0.001$) were noted. Significant indirect associations were observed between pain and both muscle strength (rho=-0.39, $p=0.01$) and proprioceptive acuity (rho=-0.35, $p=0.03$) at baseline. Changes in pain were directly associated with changes in muscle strength (rho=0.45, $p=0.005$) and proprioceptive acuity (rho=0.41, $p=0.01$) with exercise. The association of pain with both muscle strength and proprioception should prompt future studies to consider and adjust for the influence of pain on neuromuscular factors in knee OA.

Keywords: Osteoarthritis, Exercise, Pain, Muscle Strength, Proprioception

Introduction

Osteoarthritis (OA) is the most common arthropathy worldwide and a major contributor to disability in the elderly. A majority of individuals over the age of 40 have radiographic evidence of OA and the prevalence of the disease increases with age[1]. Ten percent of the population will have symptomatic OA by the age of 70 and OA is the single most common indication for large joint arthroplasty[2].

Motor and sensory deficits can increase the risk of joint degeneration and have been associated with knee OA. For example, quadriceps weakness has been shown to be a predictor of the presence of both asymptomatic radiographic knee OA as well as symptomatic knee OA[3]. Therefore, previous studies have suggested that muscle weakness may be a primary risk factor for knee OA and not simply a consequence of advanced OA-induced pain and disuse.

Proprioception sense has been evaluated in OA as the awareness of limb position and movement in space. Knee proprioception so measured has been shown to decrease with increasing age and with the presence of knee OA[4-7]. Whether proprioceptive deficits initiate joint degeneration from abnormal neuromuscular control and harmful dissipation of knee loads or whether proprioceptive deficits in patients could be a *result* of damage to joint receptors from OA-associated degeneration is an unresolved issue.

Mechanoreceptors that provide proprioceptive function are located at the tendons, ligaments, meniscus, joint capsule and muscle[8-10]. Although specific associations between quadriceps muscle strength and proprioception have not

The authors have no conflict of interest.

Corresponding author: Najia Shakoor, M.D., Rush University Medical Center, 1725 West Harrison, Suite 1017, Chicago, IL 60612, USA
E-mail: najia_shakoor@rush.edu

Accepted 5 February 2007

been investigated in knee OA, there is some indirect evidence that suggests that muscle dysfunction may be associated with proprioceptive deficits in this disease[11-14].

Pain may be a factor affecting the evaluation of muscle strength and proprioceptive acuity[15,16]. Previous studies have shown a relationship between quadriceps strength and knee pain[17] as well as suggested that temporary pain reduction may improve maximum voluntary muscle contraction[15] and decrease abnormal involuntary muscular activation[16]. Conversely, the effect of pain on proprioceptive function has not been established. The minimal evidence that does exist is contradictory, suggesting that proprioceptive acuity may improve, decrease, or not change with improvements in pain[4,15,18,19].

Studies show that intervention with rehabilitation exercises can result in objective and subjective improvements in muscle strength and overall pain and function in subjects with symptomatic knee OA[20-24]. Some investigators have reported that training programs may influence proprioception at the knee[25] and more recently evidence has suggested that isokinetic muscle strengthening may improve joint position sense in subjects with patellofemoral pain syndrome[26]. However, little investigation has been done to evaluate the concomitant effects of muscle strengthening on proprioceptive acuity in subjects with knee OA[22].

The aim of this investigation was to evaluate for improvements in and relationships between pain, muscle strength, and proprioception in knee OA with an 8-week home exercise program. The corresponding hypotheses were that 1) pain would be indirectly associated with muscle strength and proprioception at baseline and changes in pain with exercise would correlate directly with changes in muscle strength and proprioception and that 2) muscle strength would be directly associated with proprioception at baseline and improvements in muscle strength with exercise would correlate directly to improvements in proprioceptive acuity.

Methods

This study was approved through the medical center's institutional review board for studies involving human subjects, and informed consent was obtained for all subjects. Thirty-eight subjects with symptomatic knee OA were recruited from the outpatient rheumatology clinics and through recruitment efforts of the Center for Clinical Studies in the Section of Rheumatology. Inclusion criteria included the presence of symptomatic OA of knee, which was defined by the American College of Rheumatology's Clinical Criteria for Classification and Reporting of OA of the knee and by the presence of at least 30 mm of pain (on a 100 mm scale) while walking (corresponding to question 1 of the visual analog format of the knee-directed Western Ontario and McMaster Universities Arthritis Index (WOMAC)[27,28]. All subjects had radiographic OA of the symptomatic knee documented within the preceding 6 months of greater than or equal to grade 1 out of a maximum 4 as defined by the modified Kellgren-Lawrence (KL) grading scale[29,30]. Subjects with pain in other joints were not excluded unless pain from other joints interfered with assessment procedures. However, the predominant complaint had to be of knee pain.

Subjects were excluded if they had received physical therapy for the knee within the preceding 6 months or an intra-articular injection for the knee within the preceding 3 months. Other exclusion criteria included: 1) the presence of systemic inflammatory arthropathy, such as rheumatoid arthritis, systemic lupus, or gout; 2) any history of knee or hip replacement, or history of trauma or surgical arthroscopy of either knee within the preceding 6 months; and 3) the presence of diabetes mellitus of greater than 10 years duration or evidence by history or physical exam of neurological disease or neuropathy.

The study was an 8-week prospective evaluation of a home exercise program. Subjects underwent a baseline evaluation for pain, muscle strength, and proprioception. They were taught three simple and common quadriceps strengthening exercises that were to be performed two times per day for 5 days of the week at home. They were asked to follow-up in 8 weeks to then be re-evaluated with the same protocol for pain, muscle strength, and proprioception testing. A follow-up phone call was made every 2 weeks after the initial visit to provide support and encouragement and to answer any questions or concerns about the exercises. Subjects taking analgesic medications were instructed to maintain their regimen, without making changes, throughout the course of the study. Patients were also asked to try not to make any other significant or purposeful changes in their level of physical activity.

Radiography. Any subject who had not had radiographs in the preceding 6 months to document OA underwent AP standing knee X-rays. Two trained and experienced rheumatologists independently evaluated the X-rays for KL grade. Secondary to the small number of subjects, for some analyses, the subjects were divided into 2 groups: "mild knee OA" (KL grades 1 and 2) and "severe knee OA" (KL grades 3 and 4).

Pain assessment. At each visit, subjects completed the WOMAC visual analog scale for evaluation of pain at the study knee. The WOMAC is the current standard in the analysis of pain and function in lower extremity OA[31-33] and site-directed adaptation of the WOMAC has proven useful and feasible[28,34]. The total WOMAC pain score is a scale of 0 to 500. Stiffness and function portions of the WOMAC were also completed (total maximum score of 200 and 1,700, respectively). Improvements in these measures were evaluated as the difference between baseline and follow-up scores.

Muscle strength analyses. Concentric and eccentric isokinetic strength of knee extensors and flexors were tested using a Biodex™ (Shirley, New York) isokinetic dynamometer. The measurements were performed with the patient in a seated position with the hip at a flexed angle of 90 degrees. Restraints were applied across the waist and an ankle strap proximal to the medial malleolus secured the tibial pad of the force transducer. The axis of rotation of the dynamometer was aligned with the axis of rotation of the knee. Subjects were instructed to fold their arms across their chest. Subjects underwent five maximal concentric and eccentric contractions for knee flexion and extension at a speed of 60°/sec with testing range of motion between 0° (full extension) and 80° of flexion. There was a rest period of 10 seconds between successive concentric and eccentric contractions. Peak torque measurements (ft-lbs) were used to represent maximum muscle strength and were divided by body weight (ft-lbs/BW). Since an appropriate assessment of muscle strength improvement was felt to be dependent on baseline muscle strength, a percentage improvement was calculated ((follow-up strength-baseline strength)/baseline strength). The reliability for muscle strength measurements (normal subjects tested on consecutive days) was high with an ICC of 0.95 to 0.99.

Proprioception analyses. Proprioception was evaluated at the knee with the passive extension-active replication method using the Biodex™ isokinetic dynamometer[35]. Subjects were asked to close their eyes. All subjects began at the semi-reclined position with the leg flexed at 90 degrees. Subjects had a handheld device with a red button. The subject's leg was *passively* extended by the technician, at a rate of approximately 10 degrees per second, to an index angle of 45 degrees flexion alternating with an index angle of 20 degrees flexion. The angle was maintained for 5 seconds and then the leg was returned passively to the starting position of flexion. The subject was asked to *actively* extend the leg to reproduce the index angle and press the red button on the handheld device when they felt they had reached the appropriate angle. The degrees difference between the starting index angle and the reproduced angle reflected the subject's ability to estimate angular motion accurately (lower number=better proprioceptive acuity). The subjects underwent 5 repetitions at each angle and the results were evaluated as the mean absolute error of the trials. Improvements in proprioception were calculated as the difference between baseline and follow-up measures. The reliability for proprioception measurements (normal subjects tested on consecutive days) was fair with an ICC of 0.67 to 0.73.

Exercise training/instruction. An exercise regimen for patients with knee OA was developed in consultation with a physical therapist and included quadriceps sets, straight leg raises, and knee flexions and extensions. Quadriceps sets were performed with the subject supine and both legs straight on the ground. They were instructed to push the back of the knees towards the ground, hold for 5 seconds and then relax. Straight leg raises were also performed supine. The normal knee was bent and the "affected knee" was straight on the ground. The "affected knee" was then raised to the level of the bent knee, held up for 5 seconds and then slowly returned to the ground. Knee flexion and extensions were performed while sitting in a chair. The leg was raised until straight (180 degrees), held for 5 seconds and then slowly brought to the ground. Each subject was individually taught the exercises by a trained co-investigator in the study.

Age (mean years±SD)	61±10
Gender (M/F)	10/28
BMI(mean kg/m^2±SD)	32.4±6.6
OA Severity (KL grade)	
KL 1	2
KL 2	16
KL 3	12
KL 4	8

Table 1. Baseline data on study subjects.

Exercises were demonstrated, and each subject practised performing them in the office until they were able to perform them correctly and safely. The subjects were provided with a detailed written description of the exercises. They were instructed to perform 30 repetitions of each exercise daily (3 sets of 10 repetitions). If the subjects were doing well with the exercises at the two-week phone call, they were asked to add a 5-pound ankle weight, which was provided to them at the initial visit.

Exercise diary/adherence. Each subject was provided with a detailed exercise diary in which to record performance of the exercises. Subjects recorded the number of repetitions of each exercise that were performed daily. Adherence was calculated by totaling the number of times the exercise was performed each day by the total number of repetitions prescribed per day.

Statistical analyses. Statistical analysis was performed using SAS software. A paired-samples t-test was used to evaluate improvements in muscle strength and WOMAC pain scores over the eight weeks. Correlations between baseline measures of all three factors and improvement in the factors were evaluated with Spearman and Pearson correlations. Relationships between radiographic severity and improvement in these factors were also evaluated using t-tests and Spearman correlations.

Power analysis. Based on previous randomized trials published in the literature, a moderate effect of exercise on pain and muscle strength was anticipated in this investigation. Little information was available about the effects of exercise on proprioception. However, Hurley and Scott had found significant improvements in proprioception with an exercise intervention[22]. Therefore, a study sample of thirty-two subjects was estimated to provide greater than 80% power to detect moderate effect sizes for the study's primary outcomes. For this analysis, "moderate" effect size was defined as greater than 0.5.

Results

Thirty-eight subjects were enrolled in the study. Four subjects did not follow-up for the second visit. Two of the sub-

	Baseline	Post-exercise
WOMAC (mm±SD)		
Pain	245±109	142±123*
Function	104±56	71±56*
Stiffness	840±416	495±428*
Quadriceps muscle strength (ft-lbs/BW±SD)	24.0±12.7	31.1±13.0*
Proprioception (degrees error±SD)	5.4±2.8	5.7±3.7
**p<0.05*		

Table 2. Baseline and post-exercise measurements.

jects claimed that they could not follow-up because of time constraints and the other two subjects did not provide reasons for discontinuing the study. These subjects were included in an intent-to-treat analysis with their initial observation carried forward. General demographic data on these subjects are outlined in Table 1. The mean age of the subjects was 61±10 years. There were 10 male subjects enrolled and 28 female subjects. The overall BMI was high in the study population with a mean of 32.4±6.6 kg/m^2. The radiographic severity of OA in the population varied with 2 subjects with KL grade 1 knee OA, 16 KL grade 2, 12 KL grade 3, and 8 KL grade 4.

Pre- and post-exercise values for the primary outcomes are summarized in Table 2. There were significant improvements observed in pain, stiffness and WOMAC function scores as well as quadriceps muscle strength between baseline and post-intervention evaluations. Pain improved by 42%. There were also significant improvements noted in both WOMAC stiffness (32%) and WOMAC function scores (41%). Quadriceps muscle strength improved by 30%. For the group as a whole, proprioception did not change significantly between baseline and follow-up exams.

At baseline, significant correlations were found between pain and muscle strength, and between pain and proprioception. Baseline pain was negatively correlated with baseline muscle strength (*rho*=-0.39, *p*=0.01). Thus, subjects with more severe pain demonstrated lower muscle strength. Baseline pain was also negatively correlated with baseline proprioceptive acuity (*rho*=-0.35, *p*=0.03). Therefore, increased pain was associated with worse proprioceptive acuity. After 8 weeks of exercise therapy, changes in pain were directly correlated with changes in muscle strength (*rho*=0.45, *p*=0.005, Figure 1). Similarly, changes in pain with exercise were directly associated with changes in proprioceptive acuity (*rho*=0.41, *p*=0.01, Figure 2). However, no significant correlation was found between muscle strength and proprioception. Correlations were also evaluated using percentage changes in proprioception and WOMAC pain scores, thereby accounting for baseline status. Correlation co-efficients changed minimally and remained statistically significant.

Subjects with "mild knee OA" experienced greater improvements in pain compared to the "severe knee OA" group, 58.5±29.1% (143±113 mm) vs. 27.1±56.4% (66.5±94.4 mm, *p*=0.03). Although proprioception acuity did not change significantly in the group as a whole, a significant direct correlation between the severity of knee OA and change in proprioception was observed (*rho*=0.32, *p*=0.05). There was no such correlation observed between severity of knee OA and change in muscle strength.

Overall, total average exercise adherence was 82.9±20% in this investigation. However, due to the small variation in adherence in the subjects and the small sample size, no significant correlations between adherence rate and improvements in pain, muscle strength or proprioception were observed.

Discussion

Significant improvements in knee pain, stiffness, and function were found in this study of subjects with knee OA who underwent 8 weeks of home exercise therapy. The results from this study support previous studies that have also found significant improvement in OA-related symptoms and muscle strength with exercise[20-24]. The degree of improvement in both pain and muscle strength have varied between studies. These differences may be attributable to variations in the intensity, type, and duration of the exercise intervention.

In contrast to the substantial improvements observed in pain and muscle strength, no significant differences were noted between proprioceptive acuity at baseline and post-intervention in this investigation. Few studies have evaluated the effects of exercise on proprioceptive acuity. Recently, Hazneci et al. noted significant improvement in knee joint position sense after 6 weeks of closed-chain exercises in subjects with patellofemoral pain syndrome[26]. The fact that this study was not able to observe a similar improvement in proprioception with exercise may be attributed to differences in the exercise regimen or differences in joint pathology in the subject groups. Patellofemoral pain syndrome is not felt to be associated with typical damage to joint structures as that seen in OA. Therefore, perhaps the proprioceptive deficits observed in those subjects are due to reversible factors while those in knee OA are secondary to irreversible damage to joint mechanoreceptors.

Hurley and Scott, to our knowledge, performed the only other investigation on the effects of exercise on proprioceptive acuity in knee OA[22]. They found that proprioception, measured also as joint position sense, improved significantly from baseline to post-intervention measurements. However, the control and treatment groups did not demonstrate significant differences in proprioceptive acuity. Furthermore, Hurley and Scott's study was a 6-month exercise study (5-weeks of structured rehabilitation followed by home exercise therapy for the remainder of the 6 months). Therefore, a pos-

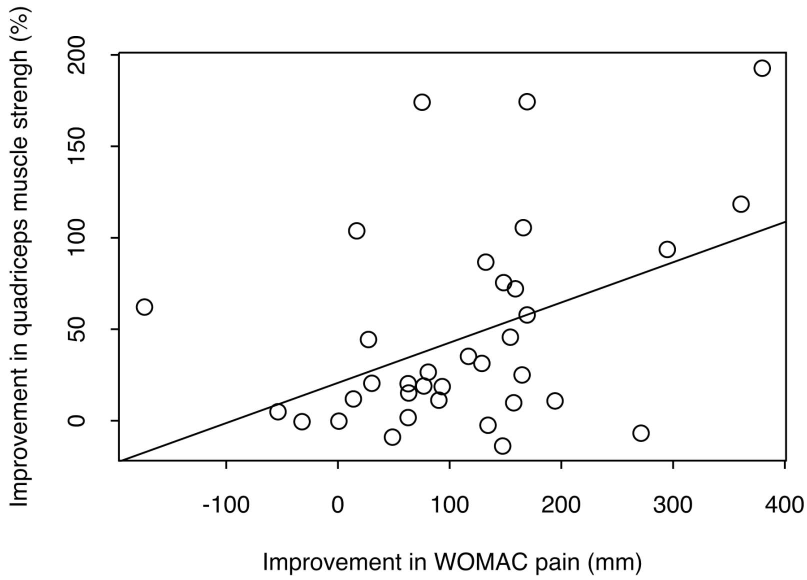

Figure 1. Correlation between change in pain and change in quadriceps muscle strength. Pain is expressed as the change in total WOMAC pain score in mm. Muscle strength is expressed as percentage change from baseline.

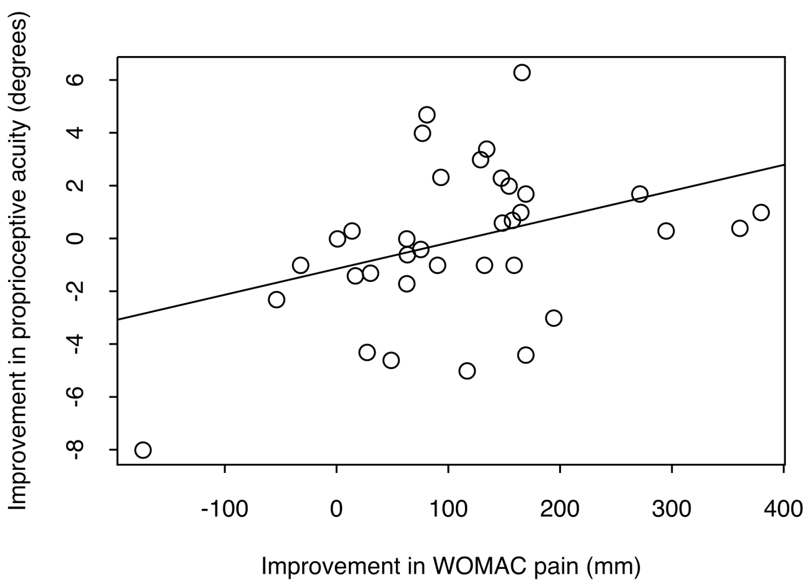

Figure 2. Correlation between change in pain and change in proprioceptive acuity. Pain is expressed as the change in total WOMAC pain score in mm. Proprioception is expressed as the degrees of change in angle reproducibility.

sibility for the differing results between the two studies is that this 8-week investigation may not have been of sufficient duration to detect significant improvements in a sensory function such as proprioception. Perhaps, despite the improvement in muscle strength, proprioceptive deficits take longer to recover.

To our knowledge, this is the first investigation to identify a negative relationship between baseline pain and proprioceptive acuity as well as the correlation between changes in proprioceptive acuity and changes in pain with exercise. Few studies have evaluated the relationship between pain and proprioception. Hassan et al. evaluated proprioception measured as both joint position sense and postural sway before and one hour after a saline or bupivacaine injection[15]. Postural sway did not change in either group. Joint position sense was shown to actually worsen in the bupivacaine group and not change in the saline group, despite the fact that both groups achieved some extent of pain relief. The authors suggested that the worsening in the bupivacaine group may be secondary to a direct effect of the anesthetic on neuroreceptors and that proprioceptive acuity was probably not related to pain. Similarly, Barrack et al. demonstrated that proprioception did not change in the presumably pain-free state after total joint arthroplasty for degenerative arthritis[19]. However, the authors did not specifically report pain measures before and after surgery. On the other hand, Barrett et al. performed a similar investigation and demonstrated that proprioception improved slightly after joint replacement surgery[4]. Again, specific associations with pain were not evaluated. It may be that the sensory functions of pain and proprioception are more intimately related than previously recognized. Therefore, perhaps the proprioceptive deficits previously observed in knee OA are substantially a consequence of pain at the joint or, conversely, perhaps proprioceptive acuity directly affects the degree of pain at the joint.

Similar to the relationship noted between pain and proprioception in this study, increased pain was associated with decreased muscle strength at baseline, and the changes in pain over 8 weeks correlated with changes in muscle strength. This negative association between pain and muscle strength detected in this investigation has some precedence in previous studies[15-17]. These studies have suggested that pain influences muscle activation as well as maximum voluntary muscle strength. O'Reilly et al. performed a cross-sectional investigation of 300 subjects with knee pain and 300 without knee pain[17]. They found a significant association between pain and the maximum muscle strength that was not entirely explained by lower quadriceps activation. Similarly, Hassan et al. evaluated muscle strength and function before and one hour after a saline or bupivacaine injection[15]. Temporary pain reduction was clearly associated with increased maximum muscle strength and muscle activation.

This study has three major limitations. The first limitation is the lack of an unexercised control group. Without such a group, it is difficult to assess the extent to which subjective improvements in pain and function were a result of patient prior expectations. Nevertheless, objective measurements of muscle strength were also shown to improve. And the correlations between improvements in pain with muscle strength and proprioception would be difficult to attribute entirely to a placebo response.

The second major limitation is that cause and effect cannot be established in this study. Therefore, the extent to which the presence of pain affects the measurements of proprioception and muscle strength in knee OA or chronic proprioceptive and muscle strength deficits lead to pain is still not clear. Nevertheless, this study has identified these correlations and future studies will be needed to further investigate the specific pathophysiologic relationships.

The third limitation is that few studies have evaluated the effects of exercise on proprioception. Therefore, with limited knowledge of previous effect sizes, this study may have been underpowered to detect a significant improvement in proprioception with exercise. In addition, it is possible that analgesic use by the subjects may have affected their performance on the pain scales without concomitant alteration in their proprioceptive acuity. However, subjects were advised to maintain constant regimens of analgesics throughout the study. Furthermore, if there was excessive analgesic use immediately prior to testing, it would be expected to weaken rather than to strengthen the negative association between pain and proprioception that we observed.

In summary, home exercise therapy can lead to significant improvements in pain and muscle strength in subjects with symptomatic knee OA. Pain, however, may be a mediating factor in the assessment of both muscle strength and proprioception in these subjects. The relationships between pain and proprioception observed in this study have not been previously reported. These relationships may provide significant insight into the pathophysiology of neuromuscular deficits in knee OA and need to be investigated further. Future studies should take into account the influence of pain on neuromuscular factors as well as attempt to further clarify the relationships between these factors.

Acknowledgements

The authors thank the Rush University Committee on Research and the Schweppe Foundation for their generous support of this work. The authors thank Todd Beck for his assistance in statistical programming and the Department of Physical Therapy at Rush University Medical Center for their assistance in developing an exercise program.

References

1. Peyron JG, Altman RD. The epidemiology of osteoarthritis. In: Moskowitz RW, Howell DS, Goldberg VM, Mankin HJ (eds) Osteoarthritis: Diagnosis and Medical/Surgical Management, 2nd Edition. Philadelphia: W.B. Saunders; 1992. p. 15-37.
2. Praemer A, Furner S, Rice DP. Musculoskeletal Conditions in the United States, 1st ed. American Academy of Orthopedic Surgeons, Park Ridge, Illinois; 1992.
3. Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, Wolinsky FD. Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med 1997;127:97-104.
4. Barrett DS, Cobb AG, Bentley G. Joint proprioception in normal, osteoarthritic and replaced knees. J Bone Joint Surg Br 1991;73:53-6.
5. Pai YC, Rymer WZ, Chang RW, Sharma L. Effect of

age and osteoarthritis on knee proprioception. Arthritis Rheum 1997;40:2260-5.
6. Skinner HB, Barrack RL, Cook SD. Age-related decline in proprioception. Clin Orthop 1984;184:208-11.
7. Sharma L, Pai YC, Holtkamp K, Rymer WZ. Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? Arthritis Rheum 1997;40:1518-25.
8. Brand RA. A neurosensory hypothesis of ligament function. Med Hypotheses 1989;29:245-50.
9. Hurley MV. The role of muscle weakness in the pathogenesis of osteoarthritis. Rheum Dis Clin North Am 1999;25:283-98.
10. O'Connor BL, Brandt KD. Neurogenic factors in the etiopathogenesis of osteoarthritis. Rheum Dis Clin North Am 1993;19:581-605.
11. Messier SP, Glasser JL, Ettinger WH Jr, Craven TE, Miller ME. Declines in strength and balance in older adults with chronic knee pain: a 30-month longitudinal, observational study. Arthritis Care Res 2002;47:141-8.
12. Barrack RL, Skinner HB, Brunet ME, Cook SD. Joint kinesthesia in the highly trained knee. J Sports Med Phys Fitness 1984;24:18-20.
13. Barrack RL, Skinner HB, Cook SD. Proprioception of the knee joint. Paradoxical effect of training. Am J Phys Med 1984;63:175-81.
14. Bernauer EM, Walby WF, Ertl AC, Dempster PT, Bond M, Greenleaf JE. Knee-joint proprioception during 30-day 6 degrees head-down bed rest with isotonic and isokinetic exercise training. Aviat Space Environ Med 1994;65:1110-5.
15. Hassan BS, Doherty SA, Mockett S, Doherty M. Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. Ann Rheum Dis 2002;61:422-8.
16. Brucini M, Duranti R, Galletti R, Pantaleo T, Zucchi PL. Pain thresholds and electromyographic features of periarticular muscles in patients with osteoarthritis of the knee. Pain 1981;10:57-66.
17. O'Reilly SC, Jones A, Muir KR, Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. Ann Rheum Dis 1998;57:588-94.
18. Ishii Y, Tojo T, Terajima K, Terashima S, Bechtold JE. Intracapsular components do not change hip proprioception. J Bone Joint Surg Br 1999;81:345-8.
19. Barrack RL, Skinner HB, Cook SD, Haddad RJ Jr. Effect of articular disease and total knee arthroplasty on knee joint-position sense. J Neurophys 1983;50:684-7.
20. Baker K, McAlindon T. Exercise for knee osteoarthritis. Curr Opin Rheumatol 2000;12:456-63.
21. Ettinger WH Jr, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, Shumaker S, Berry MJ, O'Toole M, Monu J, Craven T. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). JAMA 1997;277:25-31.
22. Hurley MV, Scott DL. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. Br J Rheumatol 1998;37:1181-7.
23. van Baar ME, Dekker J, Oostendorp RA, Bijl D, Voorn TB, Lemmens JA, Bijlsma JW. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. J Rheumatol 1998;25:2432-9.
24. Taaffe DR, Duret C, Wheeler S, Marcus R. Once-weekly resistance exercise improves muscle strength and neuromuscular performance in older adults. J Am Geriatr Soc 1999;47:1208-14.
25. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. Am J Sports Med 1982;10:329-35.
26. Hazneci B, Yildiz Y, Sekir U, Aydin T, Kalyon TA. Efficacy of isokinetic exercise on joint position sense and muscle strength in patellofemoral pain syndrome. Am J Phys Med Rehabil 2005;84:521-7.
27. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833-40.
28. McGrory BJ, Harris WH. Can the western Ontario and McMaster Universities (WOMAC) osteoarthritis index be used to evaluate different hip joints in the same patient? J Arthroplasty 1996;11:841-4.
29. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. Ann Rheum Dis 1957;16:494-502.
30. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, Levy D. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthritis Rheum 1995;38:1500-5.
31. Bellamy N. Pain assessment in osteoarthritis: experience with the WOMAC osteoarthritis index. Semin Arthritis Rheum 1989;18:14-7.
32. Theiler R, Sangha O, Schaeren S, Michel BA, Tyndall A, Dick W, Stucki G. Superior responsiveness of the pain and function sections of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) as compared to the Lequesne-Algofunctional Index in patients with osteoarthritis of the lower extremities. Osteoarthritis Cartilage 1999;7:515-9.
33. Stucki G, Sangha O, Stucki S, Michel BA, Tyndall A, Dick W, Theiler R. Comparison of the WOMAC (Western Ontario and McMaster Universities) osteoarthritis index and a self-report format of the self-administered Lequesne-Algofunctional index in patients with knee and hip osteoarthritis. Osteoarthritis Cartilage 1998;6:79-86.

34. Pincus T, Koch GG, Sokka T, Lefkowith J, Wolfe F, Jordan JM, Luta G, Callahan LF, Wang X, Schwartz T, Abramson SB, Caldwell JR, Harrell RA, Kremer JM, Lautzenheiser RL, et al. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. Arthritis Rheum 2001;44:1587-98.
35. Lephart SM. Proprioception and Neuromuscular Control in Joint Stability. Human Kinetics, Champaign, Illinois; 2000.