ARTICLE

Neuromuscular Exercise as Treatment of Degenerative Knee Disease

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AGEBERG, E. and E.M. ROOS. Neuromuscular exercise as treatment of degenerative knee disease. *Exerc. Sport Sci. Rev.*, Vol. 43, No. 1, pp. 14–22, 2015. *Exercise is recommended as first-line treatment of degenerative knee disease. Our hypothesis is that neuromuscular exercise is feasible and at least as effective as traditionally used strength or aerobic training but aims to target more closely the sensorimotor deficiencies and functional instability associated with the degenerative knee disease than traditionally used training methods.*
Key Words: exercise therapy, knee joint, osteoarthritis, patient-reported outcomes, performance-based measures

INTRODUCTION

The term *osteoarthritis* (OA) describes a common, age-related, heterogeneous group of disorders characterized pathologically by focal areas of loss of cartilage in synovial joints, associated with varying degrees of osteophytic formation, subchondral bone change, and synovitis (10). The prevalence of OA, however, depends on the definition, with radiographic case definition representing the highest prevalence estimates (~53%), whereas self-reported and symptomatic OA definitions have lower but similar estimates (~24%) (25).

OA develops slowly across decades, making it amenable to prevention and early intervention, at least in terms of reducing symptoms and improving physical function, comparable to other chronic diseases (36). Radiographically visible structural changes of OA can be viewed as an end result of a degenerative process starting much earlier. A frequent early sign of this process is the degenerative meniscal tear in middle-aged individuals (12). In young people, a traumatic knee injury constitutes the highest risk factor for developing early-onset OA (22). To acknowledge the slowly developing disease process, the different definitions used, and the desire to intervene at all stages of the disease, we use the term *degenerative knee* to encompass both early and late stages of the disease, from onset of an identifiable risk factor, such as joint injury, via signs such as pain and a degenerative meniscal tear to radiographically verified stages of OA.

Pain is the chief complaint in patients with degenerative knee disease, but patients also report functional limitations in daily and/or sport and recreation activities, and they are less physically active than the general population. It is nowadays suggested that both self-reported and objective measures of function be used to obtain a complete picture of function in patients with OA.

A combination of patient education, exercise, and weight loss is recommended in evidence-based guidelines as first-line treatment of degenerative knee disease (see, for example, (15)). General exercise, such as aerobic training, and local exercise, such as strength training, show positive effects in terms of reduced pain and improved physical function (37). Because physical activity also has beneficial effects on general health, it's essential to provide appropriate recommendations regarding exercise for people with degenerative knee disease. Specific exercises to improve range of motion and flexibility usually are included in various training programs (15), but there are differences between types of exercise with regard to components such as goal and principles.

Available guidelines for aerobic and strengthening exercise, developed by the American Geriatrics Society (2001) for older people with OA and by the American College of Sports Medicine for healthy adults (2009), are used currently also for people with different stages of degenerative knee disease. Strength training has formed the cornerstone of specific training because muscle weakness of the lower extremity is common in people with OA (7), with most research focusing on quadriceps strengthening. Findings from recent studies and reviews

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suggest that besides muscle weakness, patients with degenerative knee disease have impairments such as reduced proprioceptive acuity and muscle activation deficiency (28). They also report functional knee instability (16).

From this perspective, it can be argued that training programs should address several aspects of sensorimotor function and functional stabilization to improve objective function and alleviate symptoms. In young people with knee injuries, at high risk of early-onset knee OA (22), neuromuscular training programs have been developed specifically to target the sensorimotor deficiencies and functional instability associated with knee injury (1). Because people with degenerative knee disease have similar deficiencies in sensorimotor function and also perceive functional instability, one could assume that they would benefit from this form of exercise therapy.

Our hypothesis is that neuromuscular exercise is feasible and at least as effective in reducing symptoms and improving physical function as traditionally used strength or aerobic training but aims to target more closely the sensorimotor deficiencies and functional instability associated with the degenerative knee disease than traditionally used training methods.

RATIONALE FOR NEUROMUSCULAR EXERCISE

Underlying Mechanisms for Sensorimotor Deficiency

The sensorimotor deficiencies observed in young and middle-aged people at high risk of degenerative knee disease (1,13) and in those with degenerative knee disease (7,28) suggest that impairments are present at different levels of the sensorimotor system — from sensory input through integration and processing of information in the central nervous system to motor output to perform voluntary movements and maintain postural control. This sensorimotor dysfunction also may play a role in the development and progression of degenerative knee disease.

Rice and McNair (26) summarize the neural mechanism involved in inhibition of the quadriceps muscle in different knee joint pathologies, such as anterior cruciate ligament (ACL) injury, meniscal damage, and OA. Neural inhibition caused by factors such as pain, swelling, inflammation, joint laxity, and damage to sensory receptors in the joint prevents the muscle to be activated fully likely through altered excitability of spinal and supraspinal pathways (26). This inability to activate voluntarily a muscle completely (arthrogenic muscle inhibition) is considered a potential contributing factor to the quadriceps weakness associated with ACL injury (24), and weak knee extensor strength may increase the risk of structural and symptomatic knee OA, particularly in women (7). There still is conflicting evidence for the role of muscle strength in OA progression, although higher strength may be related to slower progression in women and at the patellofemoral joint (7).

Although research on neural inhibition has focused on the quadriceps, other muscles in the lower extremity, such as the gastrocnemius, hamstrings, and hip abductors, also are important for stabilizing the knee joint. For example, weaker quadriceps, hamstrings, and hip abductor muscles and poorer knee joint proprioception are related to a greater functional decline in OA progression (7). Furthermore, not only strength but also muscle activation patterns and coordinated timing of muscles during movements influence knee joint load (7).

The understanding of the impairments present at all levels of the sensorimotor system led to the development of neuromuscular training programs in patients with ACL injury (1) and meniscal damage (13), with the aim of improving sensorimotor control and achieving functional stability. Neuromuscular training programs are found effective in improving function and reducing symptoms in people with knee injury (40) at high risk of early-onset OA. To reduce the number of severe traumatic knee injuries, there have been an emerging number of studies the past decade on prevention of such injuries. Today, there is strong evidence from well-designed, randomized, controlled trials that neuromuscular training programs are effective in reducing knee injuries (19). Recently, we found exercise according to the principles of neuromuscular training to be feasible and to relieve symptoms in people with degenerative knee disease (2,3,29,38), although there is today not enough knowledge to indicate whether neuromuscular training is sufficiently effective in the prevention and treatment of structural signs of OA (Fig. 1).

Relating Different Types of Exercise to Available Definitions of Physical Activity

We could relate current exercise forms that are used for people with degenerative knee disease to available definitions of physical activity, physical fitness, exercise, and exercise therapy, respectively, as follows: according to the World Health Organization, *physical activity* is defined as "any bodily movement produced by skeletal muscles that requires energy expenditure"; *physical fitness* is the characteristic people have or can achieve through physical activity or exercise (9); *exercise* is a Medical Subject Headings (MeSH) term defined as

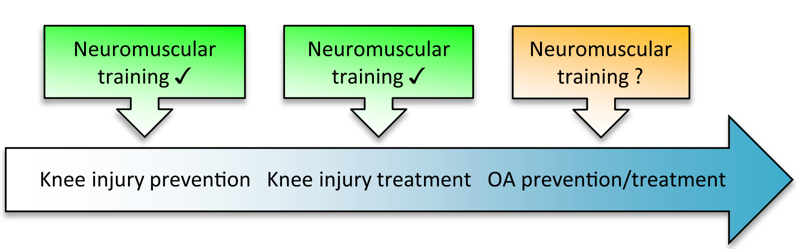


Figure 1. Neuromuscular training as prevention and treatment of knee injury and degenerative joint disease with the end-stage knee osteoarthritis (OA).

"physical activity which is usually regular and done with the intention of improving or maintaining physical fitness or health"; and *exercise therapy* is a MeSH term defined as "a regimen or plan of physical activities designed and prescribed for specific therapeutic goals. Its purpose is to restore normal musculoskeletal function or to reduce pain caused by diseases or injuries." For a person with or at high risk of knee injury/OA, aerobic training may be regarded as a form of *physical activity*, strength training as a form of *exercise*, and neuromuscular training as *exercise therapy*. More specifically, in this context, a person with OA walking performs aerobic training (defined as *physical activity* when walking at slow speed and defined as *exercise* when the intention is to improve physical fitness), doing exercises in weight machines performs strength training (exercise), and performing specific exercises aiming at relearning stair climbing with good sensorimotor control and without pain from the joint performs neuromuscular training (exercise therapy).

In Table 1, the differences in such as goals, principles, and structure between neuromuscular exercise, strength training, and aerobic exercise are given. In the following sections, focus will be on the sensorimotor deficiency observed in people with or at high risk of degenerative knee disease, serving as the basis for using neuromuscular exercise as treatment.

Sensorimotor Deficiency in People at High Risk of Degenerative Knee Disease

Knee injury is the major risk factor for early-onset OA in the young to middle-aged people, "Young patients with old knees" (22). Approximately 50% of these individuals have OA after 10 to 15 yr, that is, when they are approximately 30 to 40 yr old and still have high demands on the joints for work and recreation requiring physical activity. Particular focus is on severe traumatic knee injuries because such injuries often lead to several months of absence from physical activity and requires long-term exercise therapy with or without additional surgical treatment (17). The knowledge on the sensory role of ligaments reported in the 1990s led to a shift from strength-based training programs to neuromuscular training programs for patients with knee injury. It was found that the ligaments not only are crucial for passive joint stability but also are involved in functional joint stabilization. Thus, not only the mechanical aspects but also sensorimotor integration through motor learning were thought to be important in training to effectively use afferent neural input and improve sensorimotor function.

Sensorimotor deficiency in terms of reduced strength of muscles in the lower extremity, reduced functional performance, altered muscle activation patterns and timing, proprioceptive deficiency, and impaired postural control, as well as perceived functional instability, were reported in several studies (1). Sensorimotor deficiencies also were found in the noninjured leg compared with controls possibly because of factors such as physical inactivity after the injury, inherently poor function, and/or disturbed sensory feedback from the injured joint with an inhibitory effect of muscle activation also on the noninjured side. Neuromuscular training programs

TABLE 1. Neuromuscular exercise compared with strength training and aerobic exercise

Exercise Type	Goal	Rationale	Sensorimotor Deficiency Target(s)	Principles of Exercise	Type of Exercises	Level and Progression of Training
Neuromuscular exercise	Improve sensorimotor control and obtain functional joint stabilization	Sensorimotor deficiencies, symptoms (pain, functional instability), and functional limitations	Postural control (postural stability and orientation), proprioception, muscle weakness, muscle activation patterns, coordination, functional performance	Biomechanical and neuromuscular principles, specifically developed for patients with knee injury	Functional exercises involving multiple joints and muscle groups, mostly performed in closed kinetic chains in various positions (lying, sitting, standing) to achieve the desired requirement of postural activity	Guided by patient's sensorimotor control and quality of movement. Progression by varying number of, direction, and velocity of the movements; increasing load; changing support surface and/or using unexpected movements
Strength training	Increase strength and muscle mass	Muscle weakness	Muscle weakness	65%–70% of 1 RM, 2–3 times per week, according to guidelines for healthy adults	Muscle-strengthening exercises using free weights and/or weight machines involving one or more muscle groups in open and/or closed kinetic chains	1 RM, "plus-two-rule", *i.e.*, if the patient is able to add at least two extra repetitions to the last set, the load is increased at the next training session.
Aerobic exercise	Improve cardiovascular fitness	Low physical activity	Not specified, aims to target general fitness	20–30 min, 2–5 times per week, according to guidelines for older people with or without chronic disease	Walking, cycling, aquatic exercise	Low to moderate (corresponding to 12–14 according to Borg's RPE scale)

RPE indicates rating of perceived exertion.

are nowadays integrated and successfully used in the treatment of knee injuries (40).

Sensorimotor Deficiency in People with Degenerative Knee Disease

Patients with degenerative knee disease have sensorimotor deficiencies in terms of sensory dysfunction (28), lower limb muscle weakness (7), altered muscle activation patterns (7), and reduced functional performance (28). These sensorimotor deficiencies are reported not only for the affected leg compared with the unaffected leg but also compared with a reference group from the population (3). Given that these sensorimotor deficiencies are comparable to those observed in young people with knee injury, we applied the principles of neuromuscular training to middle-aged people with degenerative knee disease (13,27,30–32) and to older people with established OA (2,3,6,29,39).

The functional instability of the knee that many patients with OA perceive limits their ability to perform functional tasks (16). In Figure 2, we provide novel data from several of our cohorts, suggesting that patients with a degenerative meniscal tear or moderate to severe OA perceive functional knee instability corresponding to that reported by patients with ACL injury. Hallmarks of ACL rupture are increased mechanical sagittal instability and functional instability (give way) during activity (Fig. 2A). From our preexercise-postexercise therapy data, it seems like neuromuscular training can lead to improvement in knee confidence (Fig. 2B).

PRINCIPLES OF NEUROMUSCULAR EXERCISE

There is no uniform definition of neuromuscular exercise, and other terms such as functional exercise and proprioceptive, agility, or perturbation training are used in the literature. Neuromuscular exercises for the lower extremities typically involve multiple joints and muscle groups performed in functional weight-bearing positions. Emphasis is on the quality and efficiency of movement, as well as alignment of the trunk and lower limb joints.

The neuromuscular training method that we describe in this review is based on biomechanical and neuromuscular principles and aims to improve sensorimotor control and achieve compensatory functional stability (Table 1). Aerobic and strengthening exercise for people with OA follow guidelines for healthy or older people, while the neuromuscular training method was designed specifically to target the sensorimotor deficiencies and functional instability associated with knee injury (1,13). *Sensorimotor control* (also called *neuromuscular control*) is the ability to produce controlled movement through coordinated muscle activity, and *functional stability* (also called *dynamic stability*) is the ability of the joint to remain stable during physical activity. The neuromuscular training method was evaluated first in younger patients with ACL injury, summarized in a review (1), and later also in middle-aged patients with meniscectomy (13,27). The biomechanical and neuromuscular principles have been described in detail previously (1,13). These principles also apply to other knee injuries/diseases and to other joints in the lower extremities because the training aims at resembling conditions in daily life and more strenuous activities (1).

In summary, the principles include the following: *Active movements in synergies* of all the joints in the injured extremity are included. The movements start with the uninjured extremity initiating the normal movement and applying *bilateral transfer effect of motor learning* to the injured leg. To improve sensorimotor control, exercises are performed mainly in *closed kinetic chains* in different positions (*e.g.*, lying, sitting, standing) with the intention to obtain low, evenly distributed articular surface pressure by *muscular coactivation*. The model

Figure 2. A. Knee confidence (item Q3 from the knee-related quality of life subscale in the Knee injury and Osteoarthritis Outcome Score Questionnaire) reported by patients with anterior cruciate ligament (ACL) injury (17), severe primary knee osteoarthritis (OA) (3), degenerative meniscus tear (30), medial knee OA (6), and meniscectomy (13,27) at baseline before exercise therapy. The patients with severe primary OA were all on the waiting list for total knee replacement (3), patients with degenerative meniscus tear were all under consideration for arthroscopic surgery (30), patients with medial knee OA were recruited among community volunteers via advertisements (6), and patients with meniscectomy were recruited through the surgical code system (13,27). Thus, the different inclusion criteria in the studies may affect their knee symptoms and knee confidence. B. Self-reported knee confidence reported by patients at baseline and follow-up (Fup) after 12 wk (3,6,30) or 16 wk (13,27) of neuromuscular exercise.

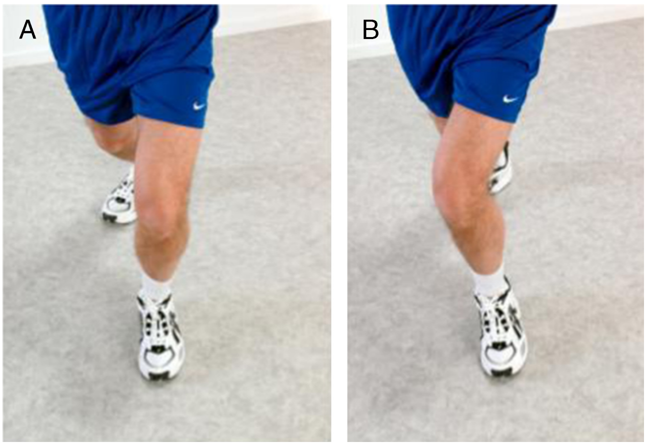


Figure 3. A. "Knee over toe position," that is, joints in lower extremity well aligned with appropriate position of knee over foot. B. "Knee medial to foot position," that is, joints in lower extremity not aligned; knee is placed inappropriately medial to foot.

emphasizes the enhancement of antigravity *postural functions* of weight-bearing muscles and the provocation of *postural reactions* (feed-forward and feedback control) in the injured leg by using voluntary movements in the other lower extremity, trunk, and arms. The *quality of the performance* in each exercise with an appropriate position of the joints in relation to each other (postural orientation), that is, with the hip, knee, and foot well aligned, is emphasized (Fig. 3).

The goal is to obtain equilibrium of loaded segments in static and dynamic situations and acquire postural control in situations resembling conditions of daily life and more demanding activities. Emphasis is put on efficiency and quality of movements of each exercise. Several aspects of sensorimotor function, such as strength, coordination, balance, and proprioception, are included in the exercises, but focus can be, for example, balance in one exercise and strength in another. To achieve the desired requirement of postural activity, patients perform exercises in various positions, that is, lying, sitting, and standing.

The training is individualized because symptoms and functional limitations are heterogeneous in people with an injury or disease. The level of training and progression is guided by the patient's sensorimotor function, taking into account various factors related to the individual (*e.g.*, symptoms, age, gender, previous and target activity level) and the injury/disease (*e.g.*, affected joint structures and type and severity of injury/disease). Progression is provided by varying the number of, direction, and velocity of the movements; increasing the load; changing the support surface; and/or using unexpected movements.

Training may take place in groups to use the positive effects of group training in terms of more effective learning compared with individual practice sessions. To ensure an appropriate level and progression, training takes place under the supervision of experienced physical therapists specializing in training of musculoskeletal disorders.

Because pain is a major symptom for patients with knee OA, we use a scale for monitoring pain during training. The patients are told that pain is allowed up to 5 on a 0-to-10 scale during and after the training session. They also are told that, the day after training, pain should subside to "pain as usual." If pain does not subside, the level of training is reduced. This pain-monitoring system is part of the NEMEX-TJR concept as described (see Additional file 1 in Ageberg *et al.* (2)).

We have named the neuromuscular training method NEuroMuscular EXercise (NEMEX). A suffix is added to indicate the group of patients to which that program applies; for example, NEMEX-TJR, where TJR stands for total joint replacement (2).

NEUROMUSCULAR TRAINING PROGRAMS

The principles of NEMEX have been applied to middle-aged people with degenerative knee disease (13,18,31) and for older people with end-stage OA (3,6,39). The complete NEMEX-TJR training program is given in the Additional file in Ageberg *et al.* (2), the NEXA training program in the Additional file in Bennell *et al.* (5), the neuromuscular and strength training program in the Appendix in Stensrud *et al.* (31), and the ALIGN program in Table 1 in Hall *et al.* (18). Examples of exercises with increasing level of difficulty are described and illustrated in Table 2.

FEASIBILITY AND EFFECTS OF NEUROMUSCULAR EXERCISE

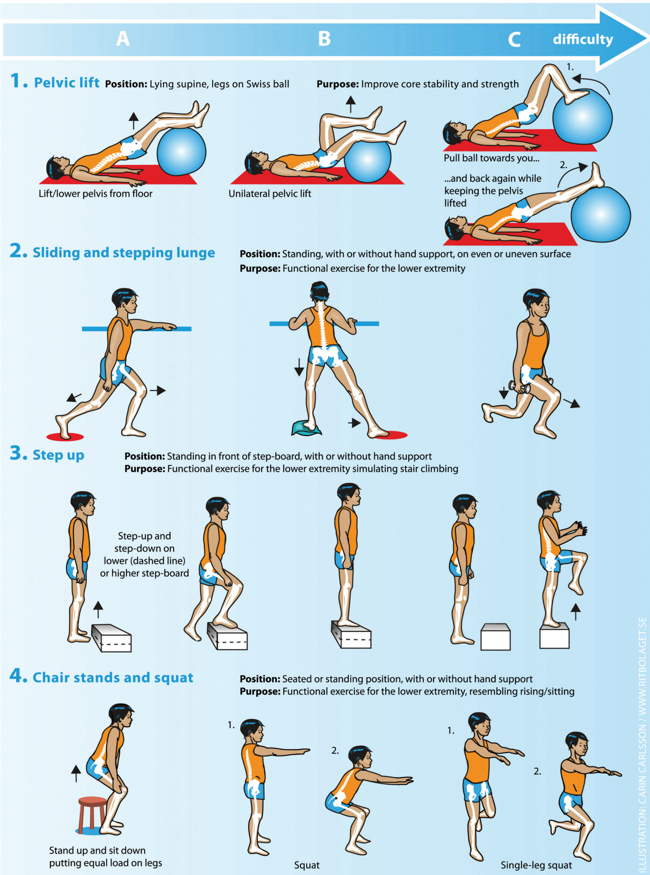
Feasibility

Two studies have reported on the feasibility of NEMEX (2,29). Seventy-six patients (mean, 69 yr; SD, 4.3) with severe primary knee (n = 38) or hip (n = 38) OA underwent supervised neuromuscular training (NEMEX-TJR) in groups with individualized level and progression of training for a median of 11 wk before they had a total joint replacement. The training program was found feasible in terms of reduced or unchanged pain during the training period, few joint-specific adverse events, and achieved progression of training level during the training period (2). Reductions in pain also were observed in a pilot study including 27 patients (mean age, 59 yr; range, 56–65 yr) with clinical knee OA who had two sessions of patient education and 6 wk of NEMEX-TJR (29). In succession of the second pilot study and the effect studies described below, physical therapists in Denmark currently are educated in delivering NEMEX for patients with knee and hip OA. In the first 15 months of the program (Good Life with Arthritis in Denmark, GLA:D), more than 200 physical therapists have learned the concept and trained more than 1700 patients in clinical practice (www.glaid.dk). The results of these studies indicate that neuromuscular training is feasible in patients at different stages of degenerative knee disease, and that it can be taught and implemented nationwide for patients with degenerative knee and hip disease.

Effects on Sensorimotor Function

In a first controlled before-and-after study, 87 patients with severe knee (n = 49) or hip OA (n = 38) had neuromuscular training (NEMEX-TJR) for a mean of 12 wk before they underwent TJR (3). The improvements obtained in

TABLE 2. Examples of exercises adapted from neuromuscular training programs (4,35,40), here shown with an increasing level of difficulty (from A to C). In all exercises, patients are encouraged to maintain a knee-over-foot position and to perform each exercise with good quality.



In all exercises, patients are encouraged to maintain a knee-over-foot position and to perform each exercise with good quality.

patient-reported outcomes (Knee injury and Osteoarthritis Outcome Score/Hip disability and Osteoarthritis Outcome Score (KOOS/HOOS)), performance-based measures (chair stands, 20-m walk test), and knee extensor strength (3) indicated that effects from neuromuscular training could be seen even in patients with severe OA about to have TJR. The feasibility of 8 wk of NEMEX-TJR was confirmed recently in a randomized controlled trial (RCT) in 164 patients before they had TJR (38). Immediately after the intervention, the 81 patients with knee disease who underwent neuromuscular exercise therapy improved in all self-reported outcomes, in most performance-based measures (chair stands, 20-m walk self-chosen speed, number of knee bends every 30 s), and in muscle power, measuring both force and velocity (*e.g.*, single-joint hip abduction) compared with the control group receiving an educational package (care-as-usual) (38). At 3 months after surgery, improvements were maintained in most functional tasks (chair stands, 20-m walk test, number of knee bends in 30 s), and in muscle power measures (knee extension, hip extension, hip abduction, multijoint leg extension), but only the improvement for hip abduction was large enough to show differences compared with the control group (data provided in supplementary Table S1 in Villadsen *et al.* (39)).

In a small RCT on middle-aged patients with meniscectomy (13,27), improvements were observed for hop performance (single-leg hop for distance), quadriceps endurance, and hamstring muscle strength after 16 wk of neuromuscular training compared with a control group without any intervention (13). However, no between-group differences were noted for hamstring muscle endurance or quadriceps strength. In a recent report on 20 middle-aged patients with degenerative meniscus tears included in an ongoing RCT (31), improvements were noted in both functional performance (single-leg hop for distance, 6-m timed hop, maximum number of knee bends in 30 s) and quadriceps and hamstring muscle strength by 12 wk of neuromuscular exercise (31). The same method for assessing knee muscle strength (isokinetic peak torque five repetitions at 60 degrees per second) was used in these two studies (13,31). Although both studies included supervised neuromuscular training with an individualized level and progression (13,31), the training program in the study by Stensrud *et al.* (31) also added single-leg concentric and eccentric exercises in both weight-bearing and non–weight-bearing positions in weight training machines. The addition of strength exercises to the neuromuscular training program may explain that Stensrud *et al.* (31) found the improvements in both quadriceps and hamstring muscle strength.

There currently is not enough data to indicate whether one exercise type is more beneficial than the other for people with degenerative knee disease (37). In a recent RCT comparing neuromuscular exercise (NEXA) with quadriceps strength (QS) (6), 12 wk of exercise provided similar improvements in both groups in knee and hip muscle strength and in performance-based measures (timed stair climb, sit-to-stand test, balance test, step test, and four square step test). However, it could be that different exercises target different symptoms and functional limitations. A secondary analysis from this trial showed that NEXA resulted in greater pain reduction than QS in patients with varus thrust, visually observed during walking, whereas effects were opposite for nonthrusters. This suggests that neuromuscular exercise may be the best type of exercise for pain relief in those with varus thrust (4).

EVALUATION TOOLS AND OUTCOMES IN NEUROMUSCULAR EXERCISE TRIALS

From the patient's perspective, it is most important to evaluate the effect from exercise on perceived pain and functional limitations. Patients with degenerative joint disease who seek medical care most often do so because of pain and other symptoms. Commonly, they also report difficulty with physical function, and objective testing reveals impairments related to muscle strength and sensorimotor control, resulting in activity limitations measured as decreased walking speed and worse performance during functional tests. Meta-analyses including data from patients with knee OA included in exercise trials reveal a moderate effect on pain and functional limitations, an effect size that was established already in 2004 and practically has been unchanged by additional studies since (37). The effect from neuromuscular exercise on pain and function (3,6,39) is comparable to the effects seen from other forms of exercise.

Functional tests are recommended to assess more complex activities of daily living and sport in those with or at risk of degenerative knee disease (11,21). Functional tasks measured in distance, height, or frequency usually are used. However, the quality of movement also may be important such as observing and scoring the position of the knee relative to the foot during the performance of functional tasks. Results indicate that tests of movement quality can be used to discriminate healthy versus those with a knee injury (34) and that such assessments seem to measure aspects of sensorimotor function that are not captured in the more commonly used measures of function and strength (35). However, it is still unknown to what extent movement quality performance is responsive to change from neuromuscular exercise.

On a population level, the correlation between structural changes of degenerative knee disease (meniscal tears on magnetic resonance imaging (MRI) and radiographic changes of OA) and perceived symptoms is poor (12,25), indicating structural changes being of no or little importance to patients' perceptions. Despite the correlation to symptoms improving with increasing degree of radiographic disease, interestingly and importantly, the degree of radiographic changes of OA was found not to impact on the effect seen from exercise, indicating patients benefitting to a similar degree from exercise, despite the severity of radiographic changes (20). Taken together, from the patients' perspective, it is most relevant to assess the impact from exercise on pain and function.

From a disease modification perspective, it is however of interest to evaluate the effect of exercise on joint structure. This approach is associated with a number of methodological difficulties, and no study has this far been able to combine successfully a rigorous study design with a large-enough number of patients, sufficient adherence to exercise, a long-enough follow-up time, and a sensitive outcome method to assess structural changes of the joint. The possible effect of exercise on joint structure is, therefore, still not well understood. The few studies that have attempted to research the question have showed either no effect or positive effect using a variety of outcomes. A few studies have addressed the question in relation to neuromuscular exercise. The hypothesized underlying mechanism would be that neuromuscular exercise improves functional (dynamic) stability and, thus, contributes to a reduced or more evenly distributed joint load across the weight-bearing surfaces.

A first RCT in middle-aged patients having had a partial medial meniscectomy, and, therefore, at high risk of future OA, found that the cartilage matrix quality was improved significantly after four months of supervised neuromuscular exercise compared with a no-intervention control group (27). In this study, delayed gadolinium-enhanced MRI of the cartilage (dGEMRIC) was used to assess indirectly the glucosaminoglycan content of the femoral weight-bearing cartilage. The patient is injected with gadolinium 2 h before MRI, and the dGEMRIC value is a function of the relaxation time that is inversely related to the glucosaminoglycan content of the cartilage. The improvement in cartilage matrix quality was paralleled by improved functional performance, but no improvements in quadriceps strength or aerobic capacity were detected (13). These findings have two important implications, the first being that neuromuscular exercise seems to improve function through mechanisms other than those commonly addressed with strength training and aerobic exercise, and the second being that neuromuscular exercise seems to improve cartilage quality. In an 11-yr follow-up of the same subjects, it was reported that a worse dGEMRIC value at baseline was associated with greater radiographic joint space narrowing at follow-up (23), indicating dGEMRIC being an important evaluation method in those at risk of future OA. It also was found that greater quadriceps strength at baseline (before exercise) protected from development of radiographic OA (14).

A noninvasive evaluation method is three-dimensional movement analysis, including the use of reflective markers and an 8 to 16 infrared camera system coupled with one or several force platforms. Inverse dynamics is used to calculate moments of all three movement planes related to the knee. The most commonly used outcome is the knee adduction moment (KAM), a measure of mediolateral force distribution across the knee that has been shown to predict radiographic OA development. In a first uncontrolled pilot study, 8 wk of neuromuscular exercise was found to decrease KAM by 13% in middle-aged patients with mild radiographic OA (33). A later RCT comparing the effect from 8 wk of neuromuscular exercise and quadriceps strengthening in patients with severe OA and malalignment found similar improvements in self-reported pain and function but failed to show any difference in KAM between groups or any improvements in KAM within groups (6). Recent studies suggest extensor and flexor moments being of, at least, similar importance as the KAM when used for evaluation of treatment effects from biomechanical interventions in knee OA (8).

SUMMARY AND FUTURE DIRECTIONS

In this review, we argue that neuromuscular exercise is feasible and at least as effective as traditionally used strength or aerobic exercise for people with degenerative knee disease and should, therefore, be part of the physical rehabilitation for this population. Data also suggest that neuromuscular training targets the functional knee instability that many patients perceive. The neuromuscular training method that we describe is based on biomechanical and neuromuscular principles and aims to improve sensorimotor control and achieve compensatory functional stability. The training method was developed specifically to target the sensorimotor deficiencies and functional instability associated with knee injury in young people. Because people with degenerative knee disease have similar deficiencies in sensorimotor function and perceive functional instability, neuromuscular training also may be a relevant exercise therapy for them. We have applied the principles of neuromuscular training to middle-aged people with degenerative knee disease and to older people with established OA, with promising results with regard to reduced pain and improvements in self-reported outcomes, sensorimotor function, and functional stability. However, so far, neither neuromuscular nor strengthening exercises seem sensitive to changes in lateral-to-medial knee joint load. A challenge for future studies is to explore the best type of exercise therapy for improving sensorimotor function, alleviating symptoms, and possibly slowing the disease process in different subgroups of patients with degenerative knee disease.

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