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An 8-Week Neuromuscular Exercise Program for Patients With Mild to Moderate Knee Osteoarthritis: A Case Series Drawn From a Registered Clinical Trial

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Objective: To describe the feasibility of a neuromuscular exercise (NEMEX) program in patients with mild to moderate knee osteoarthritis (KOA).

Background: Neuromuscular exercise has been increasingly used in patients with osteoarthritis to achieve sensorimotor control and improved daily function.

Treatment: A study of the first 23 physically active patients (11 men, 12 women; age range = 48–70 years) who had mild to moderate KOA and were undergoing an 8-week, twice-weekly program, consisting of 11 exercises with 3 to 4 levels of difficulty, as part of an ongoing randomized controlled trial. The level of difficulty was noted for each exercise and session. We recorded exertion, pain, adverse events, and adherence. For the 18 patients who participated in 6 or more sessions, a progression of at least 1 level of difficulty (out of 3–4) was observed in half or more of the exercises. However, few patients progressed to jumping activities. Exertion ranged from light to very heavy. Four patients reported a clinically relevant increase in short-term pain after 1 to 2 of the 16 scheduled sessions. No adverse musculoskeletal events were reported. Notably, 3 patients dropped out due to increased (n = 2) or persisting (n = 1) knee pain. However, their pain ratings did not show worsening symptoms.

Uniqueness: This NEMEX-KOA program was designed for physically active middle-aged patients with mild to moderate KOA; therefore, it involved exercises and difficulty levels that were more challenging than a previously described NEMEX program for patients eligible for total joint replacement.

Conclusions: In patients with baseline mild to severe pain with activity, the NEMEX-KOA program was feasible. Progression was achieved with few incidents of clinically relevant increases in pain and no adverse events. However, jumping activities were not feasible. These findings hold promise for investigating the efficacy of the NEMEX-KOA program in individuals with mild to moderate KOA.

Key Words: physiotherapy, training, pain management

Key Points

- In patients with mild to moderate knee osteoarthritis, the neuromuscular exercise program was feasible for progression, exertion, pain, adverse events, and adherence but not for jumping activities.
- Most patients progressed to more complex neuromuscular exercises. Those who attended more sessions generally progressed to higher levels of difficulty.
- Temporary increases in exercise-related pain were limited, and no adverse musculoskeletal events occurred.
- Researchers should investigate the efficacy of this program on knee-joint loads, pain, and functional performance in patients with mild to moderate knee osteoarthritis.

Exercise effectively reduces knee pain and improves function in patients with knee osteoarthritis (KOA).[1] The mechanisms by which exercise reduces pain are poorly understood, and a variety of exercise interventions, ranging from aerobic exercise to isolated resistance training, have been used.[2] Unlike conventional strength training, neuromuscular exercise (NEMEX) is aimed at improving sensorimotor control and attaining functional joint stabilization by addressing the quality of movement in all 3 movement planes.[3] Researchers[1,4,5] have found that NEMEX feasibly and effectively relieves pain, improves function, alters knee biomechanics, and improves the muscle-activation patterns of the surrounding knee musculature in patients with severe KOA and degenerative meniscal tears. Furthermore, NEMEX has been shown to improve articular cartilage quality in middle-aged patients who have had meniscectomies and are at high risk of KOA.[6] These results indicate that NEMEX may have important implications for KOA treatment and benefit patients at risk for or with early-stage KOA. However, a detailed NEMEX treatment strategy for patients with mild to moderate KOA has not been described except in the protocol paper of our study.[7]

The primary aims of the NEMEX program, to improve sensorimotor control and functional joint stabilization (ie, quality of movement), differ from those of traditional

osteoarthritis programs, which have a main goal of improving cardiovascular output (ie, walking programs) or enhancing muscle strength (ie, strength training with machines).[3,8] The NEMEX-KOA program that we describe was designed for physically active, middle-aged patients with mild to moderate KOA; therefore, it involves exercises and difficulty levels that are more challenging than in the previously described NEMEX program for total joint replacement.[4]

In this study, we provide novel information on the progression of individual exercises, pain response, and perceived exertion. This information can help clinicians and researchers better understand patient responses, such as length of eventual pain flare and exertion from exercise, and the various mechanisms for progressing NEMEX. Thus, the purpose of this case series was to describe the feasibility of a progressive NEMEX therapy program aimed at improving postural control and functional performance in physically active, middle-aged patients with mild to moderate KOA. *Feasibility* was defined as progressions in the level of exercise difficulty, perceptions of exertion and pain from exercise, and adherence to exercise. To evaluate feasibility, we investigated the patients' responses to the program for (1) progression over time in each exercise, (2) exertion after individual sessions, (3) changes in pain before and after individual sessions, (4) adverse events, and (5) adherence to training.

CASE DESCRIPTION

The subsequent reporting follows the recommendations of the CAse REport (CARE) guidelines.[9] In this case series, we report on the first 23 patients (11 men, 12 women) who were randomized to exercise therapy in an ongoing randomized controlled trial (ClinicalTrials.gov Identifier: NCT01638962). To ensure continued blinding of study personnel, analysis of the primary outcome in the randomized controlled trial was conducted by a statistician who was masked to group allocation and was not directly involved in the study. All participants had mild to moderate KOA and were randomized to a supervised exercise program lasting 8 weeks, with 2 sessions weekly. They were recruited via general practitioners and the communities of Odense and Middelfart, Denmark. The inclusion criteria were, in summary, age from 40 to 70 years; persistent knee pain in accordance with the American College of Rheumatology criteria[10]; Knee injury and Osteoarthritis Outcomes Score (KOOS; http://www.koos.nu) pain subscale score of less than 80[11]; radiographic severity grade of 0 to 3 on the Kellgren and Lawrence scoring system[12]; body mass index (BMI) of less than 32. Exclusion criteria were leg surgery or trauma within the last 6 months or any contraindication to exercise, nonsteroidal anti-inflammatory drugs, or radiographs. The full list of inclusion and exclusion criteria is available from the published study protocol.[7] All participants provided written informed consent, and the study was approved by the regional Committee for Medical Research Ethics (project-ID: S-20110153) and the Danish Data Protection Agency (journal-ID: 2011-41-7045).

Initial Visit

At the initial visit, participants were screened for eligibility during a clinical examination (ie, KOA, BMI, and pain level) by the project manager (B.C.). Given the primary outcome of total knee-joint load for the randomized controlled trial, eligible patients were subsequently examined by radiographs to exclude those with greater lateral than medial joint space narrowing or a medial KOA Kellgren and Lawrence grade 4 (ie, large osteophyte, marked narrowing of the joint space, severe sclerosis, and definite deformity of the bone ends).[12]

Outcome Measures

Participant Characteristics. We recorded age, sex, and BMI at the initial visit. The University of California at Los Angeles (UCLA) Activity Score[13] and the KOOS were collected at a baseline examination that took place separately from the initial visit. The UCLA Activity Score assesses self-reported current activity level on a scale ranging from 1 (*wholly inactive, dependent on others, and cannot leave residence*) to 10 (*regularly participates in impact sports*).[13] The KOOS is a questionnaire that assesses self-reported outcomes for 5 subscales (pain, symptoms, activities of daily living, function in sport and recreation, and knee-related quality of life), with scores for each subscale ranging from 0 (*extreme symptoms*) to 100 (*no symptoms*).

The outcome measures were progression in the level of difficulty of the individual NEMEXs for each exercise and session, exertion after each exercise session, pain from exercise sessions and resting pain over the duration of the study, adverse events, and adherence to training. We defined *good feasibility* as progression in the level of difficulty for most exercises, increased perceived exertion with an increased level of exercise difficulty, no more than moderate pain after the absolute majority of exercise sessions, no serious adverse events, and at least moderate adherence to training (ie, having attended at least 6 of the 16 possible exercise sessions).

Registration of Progression of Individual Exercises. At each exercise session, the supervising physiotherapist recorded in an exercise diary the level of difficulty at which all specific exercises were performed. Exercises were categorized into 4 levels of difficulty (2 exercises included only 3 levels each). The difficulty increased with each level, and examples of how an increase was induced included changing to a softer, more challenging surface during a weight-bearing exercise or increasing load, or both. Whereas each level was associated with increased complexity, the increase in complexity might not be linear (ie, the increase from level 1 to level 2 was not necessarily similar to the increase from level 2 to level 3).

Registration of Exertion and Pain in Relation to the Individual Exercise Sessions. For each exercise session, the supervising physiotherapist instructed the patient to rate his or her exertion on the Borg[14,15] category ratio (CR-10) scale (0 = *nothing at all* to 10 = *extremely stong [almost maximal]*).

Pain from exercise was defined by the change in pain from before to after each exercise session. The supervising physiotherapist instructed the patient to orally rate his or her pain while looking at a numeric range scale (NRS; 0 = *no pain*, 10 = *pain as bad as it could be*). The scale was split into 3 sections. Pain up to 2 was considered *safe* and colored green; between 2 and 5, *acceptable* and colored

Table 1. Constructs Related to Exercise and Muscle Function

Constructs	Definition[3]
Strength gain	An increase in the amount of external force that a muscle can exert by increasing neural output or muscle mass
Postural control	The ability to perform voluntary movements without losing one's posture; includes postural stability and orientation, proprioception, muscle-activation patterns, coordination, and functional performance
Functional performance	The ability to perform a complex movement that challenges balance, coordination, postural control, and strength without losing quality of movement (eg, lower limb alignment during weight bearing). Correct functional alignment means that the knee is lined up over the second toe without tending to fall inward (medially) during knee flexion.
Closed kinetic chain exercise	Weight-bearing exercise with a distally situated axis of motion and movement occurring in several joints; the distal segment is usually fixed to a supporting surface (eg, squat)
Open kinetic chain exercise	Non–weight-bearing exercise with a proximally situated axis of motion and movement occurring at a single joint; the distal segment is free to move (eg, cable/elastic-band exercise)

yellow; and greater than 5, *avoid* and colored red.[4,16] Finally, *resting pain* over the duration of the study was calculated as the change in resting pain from before the first to before the last exercise session.

Registration of Adverse Events and Adherence. Adverse events were recorded using a nonleading questionnaire at separate test sessions at baseline and postintervention. Adverse events were coded according to the Medical Dictionary for Regulatory Activities,[17] as currently required by all regulatory authorities, including the US Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products.[18] In this report, we restricted adverse events to the musculoskeletal system because they are the most likely to result from exercise. An *adverse event* was defined as a change in the following symptoms: cramps, joint pain, back pain, swollen joints, or sciatic pain.

Adherence to the NEMEX-KOA for each patient was reported as the number of sessions attended during the intervention period, including the first and last sessions, out of a maximum of 16 sessions. Patients who exercised for less than 6 weeks (out of 8 weeks) were retrospectively asked about reasons for low attendance.

The Neuromuscular Exercise Program

We applied the principles of neuromuscular training described by Clausen et al[7] (Appendix). In brief, each exercise session consisted of warming up, NEMEXs, and cooling down.

Warming up involved ergometer cycling, treadmill walking, or stepping exercise for 10 minutes at a "rather strenuous" level.[15] *Neuromuscular exercises* comprised 11 exercises with the following key elements: functional performance, postural control, lower extremity muscle strength, balance, and functional stability of the trunk and knee. Definitions are provided in Table 1.[3] The exercises were mainly performed in a closed kinetic chain. Higher levels for some exercises included jumping; for the limping-cross and mini-trampoline exercises, all levels required jumping. Levels requiring jumping focused on a controlled takeoff and landing and not on jump height specifically. Each exercise was performed in 2 sets of 12 repetitions, with rest time corresponding to the duration of 1 set. The exercises were performed bilaterally but focused on the affected lower extremity. To allow for progression, 4 levels of difficulty were available for each exercise except for the kettlebell swing and cable/elastic-band exercises, which had 3 levels each. Patients progressed when the supervising physiotherapist deemed that an exercise was performed with good sensorimotor control and good quality (by visual inspection) and patients perceived that they could perform the movement with minimal exertion and with control of the movement. *Cooling down* included gait retraining (eg, walking in various ways, including backward with an emphasis on alignment) and stretching exercises for the lower extremity muscles (10 minutes).[4,5]

As described in the study protocol,[7] patients were offered two 60-minute supervised training sessions each week. Based on earlier studies,[4,19] the intervention period was set to 8 weeks, with 2 weekly sessions (maximum = 16 sessions). The training involved groups of up to 6 patients at a time and was conducted at 1 of 2 clinics under the supervision of 1 of 2 experienced physiotherapists specializing in the training of musculoskeletal disorders. All 4 supervising physiotherapists (2 per clinic) received education in the exercise program before the study started, were supervised by a colleague, and had regular meetings with the first author (B.C.) to ensure compliance with the study protocol and the exercise program. Each patient was monitored individually to ensure that the exercises were performed at a level consistent with his or her current level of neuromuscular function.

RESULTS

Patients

Participants consisted of 23 patients (11 men, 12 women; age range = 48–70 years; BMI range = 22.6–31.9 kg/m^2; Table 2). The KOOS pain scores ranged from 39 to 83, corresponding to mild to moderate or severe knee pain within the week before the study, and KOOS function in sport and recreation scores ranged from 10 to 85, corresponding to mild to extreme difficulty. The UCLA Physical Activity scores ranged from 4 to 10, with 21 of 23 participants regularly engaged in active events (ie, from light activities to sports). The KOOS subscale and UCLA Physical Activity scores are provided in Table 2.

Progression of Exercises

The 18 patients who participated in 6 or more sessions progressed to the more complex levels of difficulty in half or more of the NEMEXs, and overall, patients who performed more exercise sessions progressed to higher

Table 2. Descriptive Information and Outcomes for All Patients

Descriptive Information	Patient Identification																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Sex	F	F	F	F	F	M	F	F	M	M	M	M	M	F	F	F	M	M	M	F	F	M	M
Age, y	48	69	52	56	70	53	65	54	59	66	65	66	68	69	54	57	52	46	50	60	56	65	67
Body mass index, kg/m^2	25.1	25.7	22.9	31.6	27.3	26.7	24.4	24.9	24.1	22.6	30.4	30.1	24.4	25.0	26.1	26.7	25.7	27.8	25.3	28.9	30.9	31.9	26.3
Index knee[a]	L	R	L	L	R	L	L	L	R	R	R	L	L	R	R	R	R	L	R	L	L	R	L
No. of sessions attended[b]	2	2	2	3	5	6	6	7	7	7	8	11	11	12	12	12	12	13	13	13	14	14	16
Attendanced[c]	3	4	3	10	12	49	31	52	24	49	42	56	52	56	45	49	45	53	53	52	56	52	56
University of California at Los Angeles Physical Activity score[d]	10	7	4	8	8	9	7	8	7	7	7	10	8	7	9	7	9	9	9	10	5	8	8
Knee Injury and Osteoarthritis Outcome Score[e]																							
Pain	64	61	47	64	50	NA	58	67	72	78	56	69	67	42	78	39	83	72	61	75	69	61	64
Symptoms	64	82	54	71	71	93	71	68	75	89	54	82	75	71	86	79	79	68	71	75	54	71	NA
Activities of daily living	74	78	62	72	32	NA	75	69	84	97	59	75	71	47	88	68	94	79	62	93	56	71	76
Function in sport and recreation	10	65	15	20	25	80	50	45	20	70	10	75	15	15	55	55	70	35	50	85	15	45	30
Knee-related quality of life	44	63	38	44	38	50	50	25	44	75	44	75	31	13	75	63	69	69	44	44	31	44	50
Outcomes, numeric range scale[f]																							
Pain level before first exercise session	7	1	3	4	8	1	2	1	2	1	0	3	1	0	6	5	2	2	2	4	2	0	4
Pain level after exercise[g]	1–3	3–5	3–4	3–4	0–6	0–1	0–3	0–5	1–4	0–5	0–4	0–3	0–2	0–6	0–4	0–5	0–4	0–4	1–4	3–6	1–2	0–1	0–1
No. of sessions with pain after exercise >5	0	0	0	0	2	0	0	0	0	0	0	0	0	1	0	0	0	0	0	3	0	0	0

Abbreviations: F, female; L, left; M, male; NA, not available; R, right.

[a] Defined as the most painful knee or dominant lower extremity.
[b] Number of exercise sessions attended during the intervention period (maximum = 16 sessions).
[c] Number of days of attendance during the intervention period from the first to the last session (maximum = 56 days [8 weeks]).
[d] The 10-point scale included anchors of 1 (*wholly inactive, dependent on others, and cannot leave residence*) and 10 (*regularly participates in impact sports*).
[e] A score of 0 indicated *extreme symptoms*, and a score of 100 indicated *no symptoms*.
[f] The 10-point scale included anchors of 0 (*no pain*) and 10 (*pain as bad as it could be*).
[g] Range for all exercise sessions.

levels of difficulty. The progression for each exercise is described in this subsection.

Neuromuscular Exercises Focused on Strength Gain (Lunge, Squat, Step-Up, and Kettlebell Swing). Patients who participated in 6 or more exercise sessions progressed to a moderate level of difficulty; most commonly, the final level was reached after participating in half of the total number of sessions (Figure 1A through D). For the kettlebell-swing exercise, 9 patients progressed to the highest level of difficulty.

Neuromuscular Exercises Focused on Functional Performance (Weight Transfer, Mini-Trampoline, Cloth Under Foot, and Cable/Elastic-Band Exercise). All patients who participated in 6 or more sessions and 1 patient who participated in 3 sessions progressed to moderate to high levels of difficulty (ie, levels 2–4). Progression occurred gradually over 8 weeks (Figure 1E through H).

Neuromuscular Exercises Focused on Postural Stability (Side-Lying Jumping Jacks and Pelvic Lift). Only 6 of 23 patients progressed beyond the second level of difficulty for these exercises (Figure 1I and J).

Neuromuscular Exercises With Some Levels Including Jumps (All Levels of Limping Cross and Mini-Trampoline, Squat Levels 2 and 4, Step-Up Levels 3 and 4, and Weight Transfer Level 3). Fewer than half of the patients (n = 11) progressed and achieved exercise levels involving jumps on a firm surface (eg, wooden floor; Figure 1A, C, and K), although they were able to perform jumps on a soft surface (eg, trampoline or soft exercise mat; Figure 1E and G).

Exertion

Perceived exertion of the exercise program for each patient ranged from *weak (light)* to *very strong* (2 to 8 on CR-10; Figure 2). Our expectation that patients would report increased exertion after the level of difficulty increased was only partially met; 11 patients reported that the last exercise session was more strenuous than the first session. Nine of the 18 participants who attended 6 or more sessions reported that the last session was more strenuous than the first.

Pain

Pain From Exercise. Overall, we found few reports of a clinically relevant increase in pain from exercise and few reports of severe pain after exercise. Four patients reported a short-term clinically relevant increase in pain from exercise (defined as >2 NRS) after participating in 1 to 2 of 16 scheduled sessions.[16] The increased pain was temporary, and the patients continued the exercise program. After exercise, 3 patients reported a pain level greater than 5 NRS after 1, 2, and 3 sessions, respectively (Table 2).

Resting Pain. The resting pain before the first exercise session ranged from 0 to 8, with 4 patients reporting a pain level equal to or greater than 5 NRS; 3 of these patients reported decreased pain from exercise, and 1 reported no change in pain from exercise (Table 2). Resting pain levels before the last exercise session similarly ranged from 0 to 8, with 2 patients reporting a pain level equal to or greater than 5 NRS; both patients reported decreased pain from exercise (data not shown).

Adverse Events

No patient reported any treatment-specific adverse musculoskeletal events on the questionnaire.

Adherence

For the 8-week exercise program, attendance ranged from 2 to 16 sessions. The 23 patients attended a total of 208 exercise sessions out of 368 possible sessions over 3 to 56 days (Table 2). Seven patients attended for less than 6 weeks and gave the following reasons: increased knee pain (n = 2; patients 3 and 5); knee pain that was due to the original pain and disability and not necessarily aggravated by the exercise (n = 1; patient 4); and other reasons, such as work, transportation, and a cardiovascular procedure (n = 4; patients 1, 2, 7, and 9). Two of 3 patients who reported a high level of pain (>5 NRS) before the first session attended only 2 and 5 sessions, respectively, whereas 13 of 14 patients who reported a low level of pain (≤2 NRS) before the first session attended at least 6 sessions (Table 2).

DISCUSSION

In this case series, we provide a detailed description of a progressive NEMEX program specifically designed for physically active patients with mild to moderate KOA. The program is feasible because the majority of patients progressed to more complex levels of difficulty for most of the NEMEXs with few reports of short-term increased pain from exercise or temporary high levels of postexercise pain, no adverse musculoskeletal events, and moderate adherence to the exercise program. Notably, 3 patients with high levels of pain at baseline did not complete the 8-week program.

Neuromuscular Exercise and Other Types of Exercise

Exercise types that have been evaluated for efficacy as treatments for KOA include resistance, aerobic, and performance (proprioceptive, sensorimotor, balance, neuromuscular) exercises. These types of exercise differ in aims and content.[2] Whereas aerobic exercise is used to increase cardiac output and resistance training is used to increase the load a muscle can generate, performance exercise focuses on the knee joint and is used to improve postural control, dynamic joint stability, and functional performance of the lower extremity. In their meta-analysis, Juhl et al[2] observed similar effect sizes for pain with resistance, aerobic, and performance exercises in patients with KOA. In addition to reducing pain and symptoms, effective treatment approaches for KOA that can slow disease progression are needed.[20] Although we did not investigate this in our study, NEMEXs, which target the efficiency of lower limb movement and muscle-activation patterns, might effectively slow disease progression. In their randomized study, Roos and Dahlberg[6] found that 4 months of NEMEX were associated with increased proteoglycan content of the cartilage matrix immediately after an exercise intervention. Increased proteoglycan content translates into greater cartilage stiffness and a greater ability to withstand load. In a long-term follow-up of the same sample, Owman et al[21] found that a shorter relaxation time for delayed gadolinium-enhanced magnetic

resonance imaging of cartilage at baseline was associated with a higher grade of joint-space narrowing 11 years later, suggesting that lower proteoglycan content is an early marker of future osteoarthritis.

Method of Monitoring Progression

We presented each patient's progression in NEMEX exercises as the level of difficulty at which he or she exercised at the first, halfway or median point, and last exercise session.

Progression from the first to the last exercise session illustrates advancement through the complete intervention (up to 8 weeks). The halfway session shows the rate at which patients progressed and indicates whether an exercise had enough levels of difficulty or was associated with floor or ceiling effects. The reliability of the threshold for exercise progression is unknown. To improve the between-therapists agreement on threshold for progression, the 2 supervising physiotherapists from each clinic participated in familiarization sessions and discussions led by the project manager (B.C.).

Progression in Exercises

As expected, patients progressed differently through the individual exercises of the NEMEX-KOA program. Patients who attended 6 or more exercise sessions progressed to more complex levels of difficulty in most exercises (as seen in Figure 1: patients 1–5 performed exercises at lower levels of difficulty [ie, unfilled circles] compared with patients 6–23 [ie, increased fill of the circles]). Whereas methodologic differences exist, the literature[2,22] supports our findings, suggesting that greater exercise attendance is positively related to physical function.

For NEMEXs focusing on strength gain, patients progressed quickly to the levels of sufficient technique; however, they were less able to progress to the more advanced levels that challenge functional performance. Similar to resistance training,[23] a familiarization period with low loads seems to be needed for NEMEX-KOA until sufficient technique is learned. In the kettlebell-swing exercise, 9 patients progressed to the highest level of difficulty, indicating a ceiling effect for them. However, we observed a lack of progression to higher levels for most patients, which could be explained by upper extremity stress introduced in the kettlebell swing and lunge. In addition, the higher levels of difficulty for the squat, step-up, and limping cross included jumping, which clearly was a hindrance to progression. In an in vitro study, Nia et al[24] showed that cartilage in early-stage osteoarthritis is most sensitive to high loading rates (comparable with jumping activities). Consequently, exercises involving jumping should be performed only with great caution and under supervision.

For NEMEXs focused on functional performance, patients progressed throughout the duration of the exercise program, and most patients reached the most difficult levels. To reduce the risk of ceiling effects with long-term use, we recommend additional levels of high difficulty for progression in exercises with a focus on functional performance. An example is increasing the difficulty of the cloth-under-foot exercise (Figure 1H) by placing the weight-bearing foot on a balance pillow. For the exercises in which only a few patients progressed to the highest level of difficulty, we suggest adding intermediate levels that may promote progress. Examples include adding a level to the side-lying jumping-jack exercise (Figure 1J) to require that the position be maintained for 30 seconds in 3 sets and changing the surface used for the limping-cross exercise (Figure 1K) to a soft exercise mat with fingertip support on a railing or wall during jumping.

Exertion

We observed large variations in perceived exertion levels, and only half of the patients reported increased exertion with increased exercise difficulty. These findings are comparable with those reported for aerobic[25] and resistance training[26,27] in patients with KOA. We demonstrated no relationship between change in perceived exertion and exercise progression, pain from exercise, resting pain, and number of attended sessions, indicating that progression in the program and attendance did not depend on perceived exertion.

Pain

Three patients reported pain levels greater than 5 NRS after 1 or more exercise sessions, which is comparable with the results from 2 studies of NEMEX.[4,28] Ageberg et al[4] reported that 32% of patients with KOA noted a pain level greater than 5 NRS after 1 or more exercise sessions before total joint replacement. Stensrud et al[28] observed that 5% of patients with degenerative meniscal tears reported pain greater than 5 NRS after 1 or more exercise sessions. In terms of increased pain after an individual session, NEMEX-KOA was as safe as NEMEX for total joint replacement. For comparison, in studies of aerobic and resistance training, increased knee pain was reported by 8% to 18% of patients with KOA who performed aerobic[25] or resistance[26,29] training, respectively. In these studies, increased knee pain was measured with various methods, ranging from logbooks to documentation by instructors and reports of dropouts. Whereas a direct comparison with our study is difficult due to methodologic differences, NEMEX-KOA seems to be as safe as any other exercise intervention for patients with mild to moderate KOA.

Adverse Events

No treatment-specific adverse musculoskeletal events other than occasional pain flares were reported on the nonleading adverse-event questionnaire or in the exercise diary. Immediate adverse musculoskeletal events were recorded through a self-reported, nonleading questionnaire. In accordance with previous studies, serious adverse events were rare in patients with KOA when exercising. Serious adverse events have been reported in 2% to 4% of patients and were limited to fractures due to falling or dropping equipment.[30,31]

Adherence

Overall, we observed moderate attendance at the exercise program with large individual variations (2 to 16 sessions). We considered attendance of $\geq$6 sessions as acceptable, as long as low attendance was not due to treatment-related

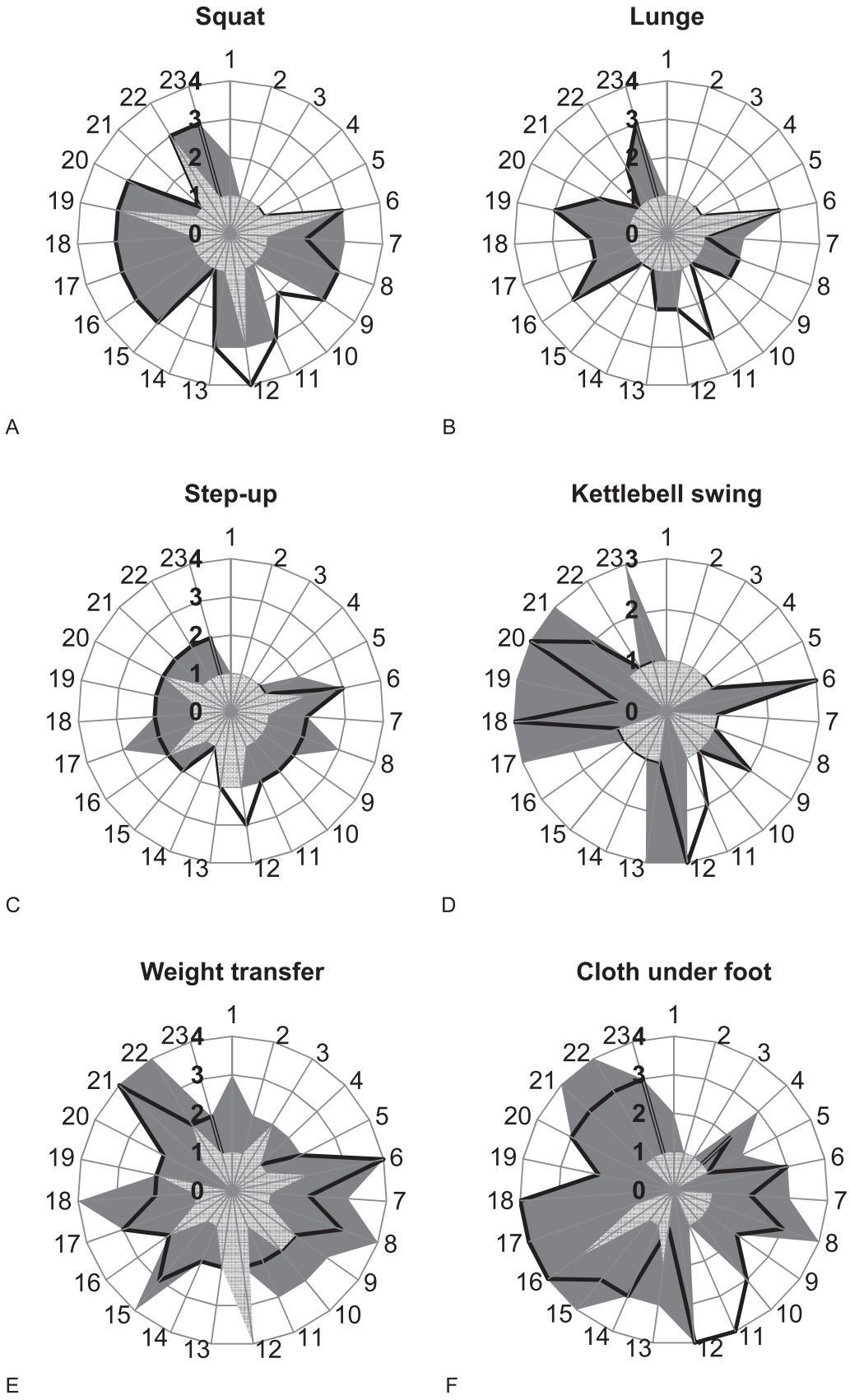

Figure 1. Level of difficulty at which each exercise was performed at the first, halfway, and last exercise sessions. Neuromuscular exercises focused on strength gain: (A) squat, (B) lunge, (C) step-up, and (D) kettlebell swing; functional performance: (E) weight transfer, (F) cloth under foot, (G) mini trampoline, (H) cable and elastics band; postural stability: (I) pelvic lift and (J) side-lying jumping jacks; and some levels containing jumps: (G) mini trampoline, (K) limping cross, (A) squat, levels 2 and 4, (C) step-up, levels 3–4, and (E) weight transfer, level 3. (Continued on next page.)

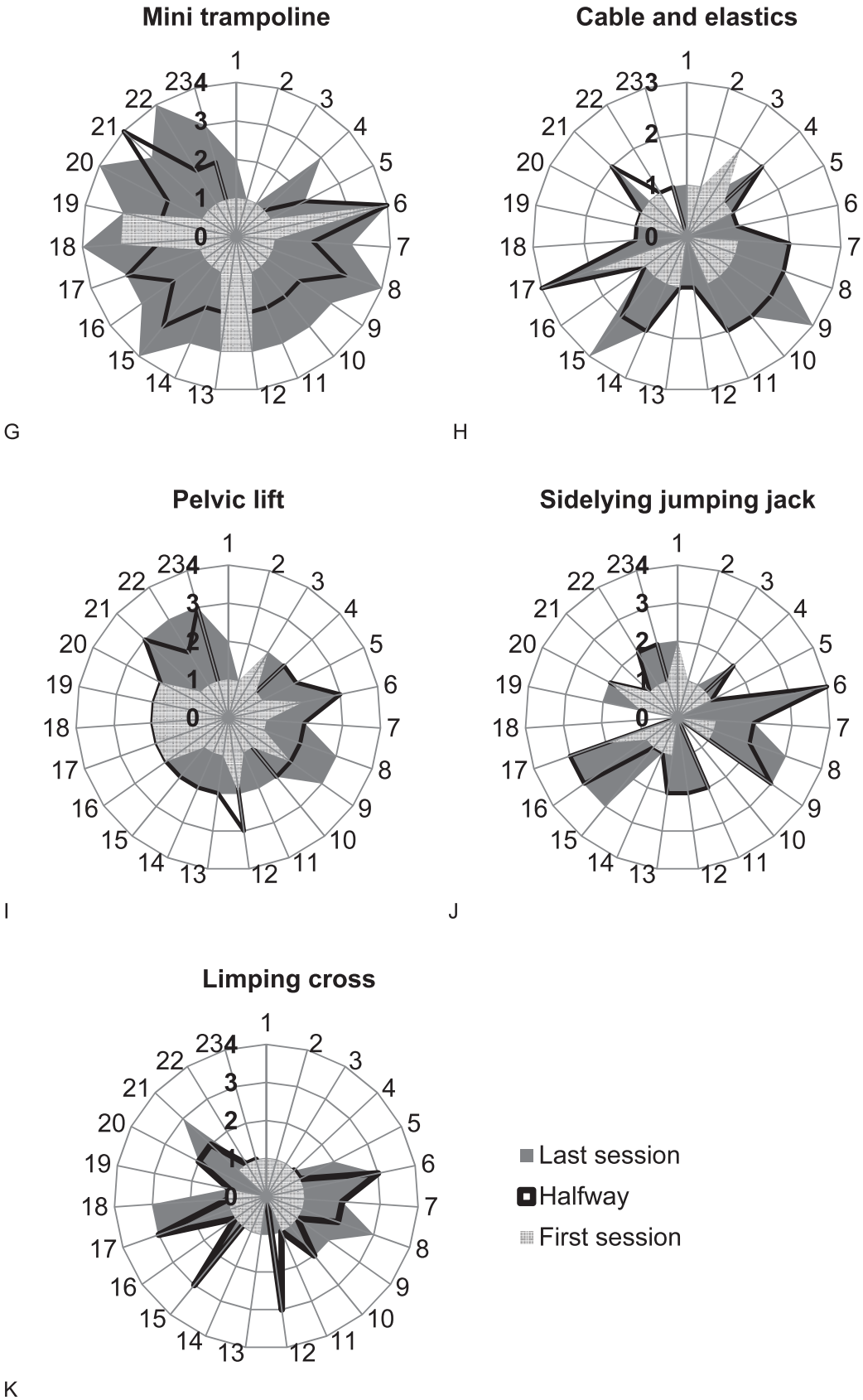

Figure 1. (Continued from previous page.) The numbers (0–3/4) from the center to the circumference corresponds to the level of difficulty, with 1 being the lowest. The numbers (1–23) around the circumference refer to the 23 individual patients. The light gray area indicates the level of difficulty for the patients at the first session. The black line indicates the level of difficulty for the patients at the halfway (median) session of the attended sessions. The dark gray area indicates the level of difficulty for the patients at the last session. Patients with identifications 1–5 attended 2–5 exercise sessions and those with identifications 6–23 attended 6–16 sessions.

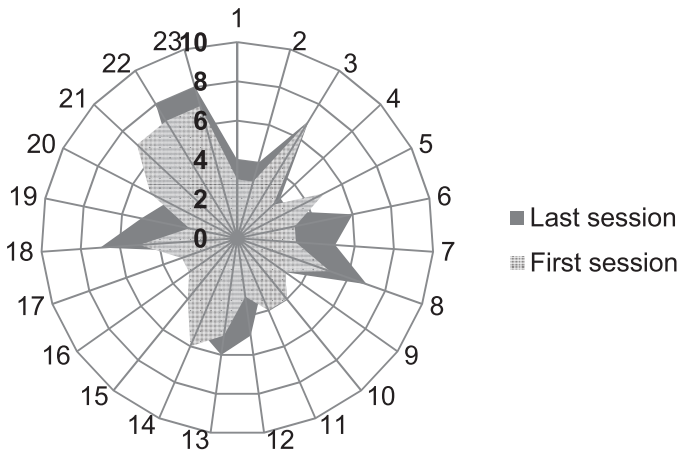

Figure 2. Perceived exertion after the first and last exercise sessions. The numbers (0–10) from the center to the circumference indicate exertion levels, with 0 representing *nothing at all* and 10 representing *extremely strong* (*almost max*). The numbers (1–23) around the circumference refer to the 23 individual patients. The light gray area indicates the perceived exertion level for the patients at the first session. The dark gray area indicates the exertion level for the patients at the last session. Patients with identifications 1–5 attended 2–5 exercise sessions and those with identifications 6–23 attended 6–16 sessions.

adverse events or increased pain. Three patients stated that they stopped exercise due to increased or persistent knee pain when performing the NEMEX-KOA. However, these oral statements were reflected only in the pain (>5 NRS after 2 exercise sessions) that 1 of these 3 patients (patient 5) reported. None of them described adverse events, including joint pain, on the self-reported adverse-events questionnaire. Similar dropout rates due to increased knee pain have been noted in other studies[5,26] testing NEMEXs for patients with severe KOA. Furthermore, comparable dropout rates (2%–12%) have been observed with resistance training in patients with moderate KOA.[26,29] Readers should consider that reported variations in dropout rates from countries around the world may be associated with cultural differences related to pain tolerance for both patients and physiotherapists and with other factors, such as differences in health care systems and recruitment strategies.

Limitations

Our study had limitations. Given the design, it was neither our aim nor possible to evaluate or compare the effects of the NEMEX therapy program with a control group. Instead, we described the NEMEX-KOA in detail and demonstrated its feasibility for progression, exertion, pain, adverse events, and adherence in patients with mild to moderate KOA.

CONCLUSIONS

We described a NEMEX program for mild to moderate KOA and demonstrated that it is feasible for progression, exertion, pain, adverse events, and adherence. Most patients progressed to more complex NEMEXs. Jumping activities, however, were generally not feasible. Patients who attended more exercise sessions were typically able to progress to higher levels of difficulty. We observed limited incidences of temporary increases in exercise-related pain and no reports of adverse musculoskeletal events. This case series holds promise for investigating the efficacy of the NEMEX-KOA program on knee-joint loads, pain, and functional performance in individuals with mild to moderate KOA.

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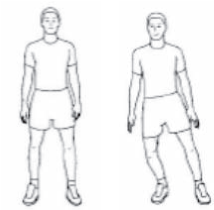
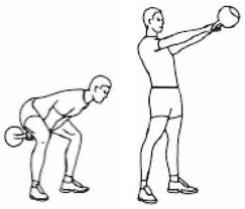
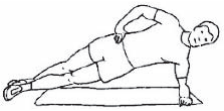
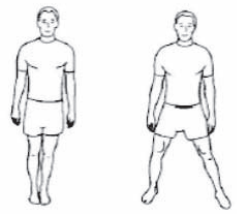
Appendix. NEMEX-KOA Training Program[a]

Exercise	Description	Amount	Figures
Warming up	Warming up should correspond to "moderate" on the CR-10[b] scale and have a duration of approximately 10 min. Warm up can be performed on a stationary bicycle, stepper, elliptical trainer, or treadmill or with skipping or running on a trampoline.	10 min	
Lunge	Stand with the feet a hip-width apart. Take a long step forward without lifting the toes of the rear foot. The landing must be controlled and done in 1 smooth motion. The body is lowered down so the rear knee almost touches the floor and the heel of the front foot remains on the floor. Level 1: No requirements; upper limbs can be used for balance. Level 2: This exercise is performed with a kettlebell in hands held in front of chest. Level 3: This exercise is performed as level 2; in end position, perform an upper body rotation in direction of the front knee. Level 4: This exercise is performed as level 3 with a kettlebell on each shoulder.	2 Sets of 12 repetitions	
Pelvic lift	Lie supine with the feet on a gymnasium ball (diameter 55–75 cm) with the knees extended to a maximum of 5° flexion. Level 1: With both feet on the ball, lift and lower the pelvis in a slow, controlled manner. Level 2: With both feet on the ball and the pelvis lifted, extend and flex the knees in a slow, controlled manner. Level 3: With 1 lower limb on the ball and the pelvis lifted during the whole exercise and with the hip extended, flex and extend the knee in a slow, controlled manner. The upper limbs are held to the sides for stability. Level 4: The exercise is performed as level 3 with upper limbs folded in front of the chest.	2 Sets of 12 repetitions	
Step-up	Stand with front to step bench. Height of step (13, 18, or 23 cm) is used for progression. Level 1: Step up with left foot first, put feet together, and step backward down with the right foot (in this way the left lower limb must control movement throughout the exercise). Repeat with the other limb. Level 2: Stand on 1 lower limb on the step bench. Alternate between touching the floor in front of and behind the bench with the heel and toes, respectively, by flexing the weight-bearing limb. Repeat with other limb.	2 Sets of 12 repetitions	

	Level 3: Stand on 1 limb on the step bench and jump down in front of the bench and land on the standing limb with a soft, controlled landing. Level 4: Stand on 1 limb on the step bench and alternate between jumping down in front of, to the side of, and behind the bench and land on the standing limb with a soft, controlled landing.		
Squat	Standing with the feet hip-width apart in front of a chair or stool, the knee shall be flexed to an extent so the buttocks just touch the chair without sitting down. Level 1: No requirements; and the upper limbs can be used for balance. Level 2: The exercise is performed with a jump at the end of the rise up. Bend knees to ensure a soft, controlled landing. Level 3: This exercise is performed as level 1 with a kettlebell in hands held in front of chest. Level 4: This exercise is performed as level 3, with jump on the rise-up. Bend the knees to ensure a soft, controlled landing.	2 Sets of 12 repetitions	
Weight transfer	Standing on a soft surface (thick mat or balance pillow) in broad standing with the knees bent, hips externally rotated, and knees well aligned over toes. Level 1: With the knees bent throughout the movement, move body weight from side to side without lifting the feet from the ground. Level 2: This exercise is performed as level 1. During the movement, lift the non–weight-bearing lower limb. Level 3: This exercise is performed as level 2 with an explosive jump on 1 limb. Land on both feet in a soft, controlled manner by bending in knees. Level 4: This exercise is performed as level 1 with rotation and a kettlebell on each shoulder.	2 Sets of 12 repetitions	
Mini trampoline	Standing on a trampoline (diameter 140 cm) in broad standing with the knees bent, externally rotated hips, and the knees well aligned over the toes. Level 1: Move body weight from side to side by alternating between lifting the non–weight-bearing lower limb. Level 2: In broad standing, alternate between jumping and landing on 1 lower limb with the lifted knee held high during the jump. Level 3: Stand on 1 lower limb and maintain balance for 30 s on each limb. Level 4: Jump on 1 limb. Switch limbs after 30 s.	2 Sets of 12 repetitions	

Limping cross	Stand on 1 lower limb in the middle of a cross. On 1 limb hop and land on the ends of the cross. Maintain balance between jumps. Next, jump is initiated only when balance is established and maintained. Level 1: Hop on 1 lower limb straight forward and backward in the cross; if possible, look directly ahead. Level 2: Hop on 1 lower limb from side to side in the cross; if possible, look directly ahead. Level 3: Hop on 1 lower limb in the cross 1 way and then the other; if possible, look directly ahead. Level 4: This exercise is performed as level 3 with eyes closed.	2 Sets of 12 repetitions	
Cloth under foot	Stand on a smooth surface with a piece of cloth under both feet. Stand with the weight on 1 lower limb and perform a 1-legged knee bend. Level 1: Perform with the non–weight-bearing lower limb sliding in abduction. To return to the standing position, use the hip adductors to pull the abducted limb back. Level 2: Perform with the non–weight-bearing lower limb sliding in extension. To return to the standing position, use the hip flexors to pull the extended limb back. Level 3: Perform with the non–weight-bearing lower limb sliding in big circles in both directions. Level 4: Perform with the non–weight-bearing lower limb sliding in large figure-of-eights in both directions and in horizontal and vertical.	2 Sets of 12 repetitions	
Kettlebell swing	In broad standing with externally rotated hips and a deep knee bending, swing the kettlebell between the lower limbs with extended upper limbs and a straight back. From here, swing it forward by using an explosive thrust in the knees and hips until it reaches eye level or higher. Level 1: Hold kettlebell in both hands. Level 2: Performed as level 1 with kettlebell held in 1 hand. Switch hands. Level 3: Performed as level 2, switching hands while the kettlebell is hanging in the air at eye level.	2 Sets of 12 repetitions	
Side-lying jumping jack	In side lying with weight on the forearm and hip and good alignment in the shoulder, spine, pelvis, and knees, raise and lower the pelvis in a slow, controlled manner. Level 1: Place the foot of the top lower limb in front of the other foot. Level 2: Place the feet side by side.	2 Sets of 12 repetitions	

	Level 3: Performed as level 2, fully abducting the top upper limb while the hip is lifted. Level 4: Performed as level 3, abducting the top lower limb while the hip is lifted and the upper limb is abducted.		
Cable/elastic band	Stand with straight lower limbs and the load on 1 lower limb. Perform the exercise in every direction: hip extension, hip and knee flexion, hip internal and external rotation, hip adduction and hip abduction. Perform every direction in 1 sequence without lowering the working leg. The most affected limb should always start as the weight-bearing limb. The focus of all exercises is good alignment of the weight-bearing limb. Level 1: Stand with both knees fully extended. Level 2: Stand with a small bend in the weight-bearing knee. Level 3: Stand on a soft surface (eg, mat or balance pillow).	2 Sets of 12 repetitions	
Gait retraining	Walk facing a mirror and focusing on high-quality gait. Herein, weight bearing during gait should be symmetric and uniform and can include walking and jogging forward, backward, sideways, or crossover.		
Stretching	Stretching is performed in a self-selected starting position in relation to the participant's performance level and can be accomplished while lying, sitting, or standing. The stretching should be performed after the hold-relax-contract method. Participants find a stretching position and make an isometric contraction for 12–15 s, followed by a 2–3-s relaxation, and then a 15–20-s stretch. Muscle groups to be stretched for both lower limbs include the hip flexors, hamstrings, quadriceps, hip abductors, and shank (triceps surae).		

[a] Participants performed 2 sessions per week. Progression was made when the supervising physiotherapist deemed that an exercise was performed with good sensorimotor control and good performance quality (by visual inspection) and the participant perceived that he or she could perform the movement with minimal exertion and control of the movement.
[b] The CD-10 scale ranging from 0 (*nothing at all*) to 10 (*extremely strong [almost max]*).