Eitzen, I., Moksnes, H., Snyder-Mackler, L., Risberg, M. A. (2010). A progressive 5-week exercise therapy program leads to significant improvement in knee function early after anterior cruciate ligament injury. *Journal of Orthopaedic and Sports Physical Therapy*. 40(11), 705-721.

A progressive 5-week exercise therapy program leads to significant improvement in knee function early after anterior cruciate ligament injury

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The study was financed by RO1 HD 037985-04, RO1 HD 037985-05 and RO1 HD 037985-06 from The National Institutes of Health.

The study was approved by the Regional Ethical Committee, Health Region South-East, Norway (Institutional Review Board).

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ACKNOWLEDGEMENTS

We would like to acknowledge the physical therapists Ida Svege, Espen Selboskar, and Karin Rydevik for assistance in data collection, and Line Hagen in Exercise Organizer for providing illustrations for Appendix A.

ABSTRACT

Study design: Prospective cohort study without a control group.

Objectives: Firstly, to present our 5-week progressive exercise therapy program in the early stage after anterior cruciate ligament (ACL) injury. Secondly, to evaluate changes in knee function after completion of the program for patients with ACL injury in general and also when classified as potential copers or non-copers, and finally, to examine potential adverse events.

Background: Few studies concerning early stage ACL rehabilitation protocols exist. Consequently, little is known about the tolerance for and outcomes from short-term exercise therapy programs in the early stage after injury.

Methods: One-hundred patients were included in a 5-week progressive exercise therapy program within 3 months after injury. Knee function before and after completion of the program was evaluated from isokinetic quadriceps and hamstrings muscle strength tests, 4 single-leg hop tests, 2 different self-assessment questionnaires, and a global rating of knee function. A 2-way mixed analysis of variance (ANOVA) was conducted to evaluate changes from pre-to posttest for the limb symmetry index (LSI) for muscle strength and single-leg hop tests and the change in scores for the patient-reported questionnaires. In addition, absolute values and the standardized response mean (SRM) for muscle strength and single-leg hop tests were calculated at pre- and posttest for the injured and uninjured limb. Adverse events during the 5-week period were recorded.

Results: The progressive 5-week exercise therapy program led to significant improvements ($p<0.05$) in knee function from pre- to posttest both for patients classified as potential copers and non-copers. SRM values for changes in muscle

strength and single-leg hop performance from pre- to posttest for the injured limb were moderate to strong (0.49-0.84), indicating the observed improvements to be clinically relevant. Adverse events occurred in 3.9% of the patients.

Conclusion: Short-term progressive exercise therapy programs are well tolerated and should be incorporated in early stage ACL rehabilitation, either to improve knee function before ACL reconstruction or as a first step in further non-operative management.

Level of evidence: Therapy, 2b

Key words: ACL, adverse events, copers, hop tests, knee function, non-copers

Due to different clinical practice in the management of anterior cruciate ligament (ACL) ruptures, there is no universal agreement as to what is the ideal treatment algorithm for individuals with ACL injury.[6, 24, 43] In our outpatient clinic, our general recommendation to individuals with an acute ACL injury is to go through 10 sessions of a progressive exercise therapy program for a period of 5 weeks after initial impairments are resolved, before the final decision for either ACL reconstruction (ACLR) or further non-operative management is made. This is recommended independent of whether patients are classified as potential copers or non-copers.[45] Potential copers are characterized as having good knee stability and the ability to compensate well after injury, whereas non-copers have poor knee stability and less potential for compensation.[26]

Recent studies from our own research group have supported the underlying rationale for advising all patients with ACL injuries to perform a progressive exercise therapy program. Moksnes et al[45] demonstrated that patients with ACL injury who initially have poor knee function demonstrate good potential for functional improvement after rehabilitation. Further, Eitzen et al[19] found that pre-operative quadriceps strength both was the single most important predictor for knee function 2 years after ACLR, and that pre-operative deficits were persistent 2 years after surgery. These findings seem to be justification for postponing the decision for ACLR for a short period of time to optimize pre-operative knee function. Still, very few evidence-based protocols for early stage ACL injury management, including explicit descriptions of the rehabilitation programs and evaluation of outcome, exist.[12, 55, 65] As a consequence, little is known about the tolerance for and potential benefit from short-term progressive exercise therapy programs in the early stage after ACL injury.

In the present study, our purpose was to evaluate a 5-week progressive exercise therapy program either as a pre-operative optimization of knee function or as the first step in further non-operative management in patients with ACL injury. We wanted to examine changes in general, but additionally also analysis on individuals classified as potential copers or non-copers in accordance to the criteria described by Fitzgerald et al.[20] The first aim of the study was to present in detail our 5-week progressive exercise therapy program for patients with ACL injury. Secondly, to evaluate changes in isokinetic quadriceps and hamstrings muscle strength, single-leg hop tests, and self-assessment of knee function from pre- to posttest after completion of the exercise therapy program; included potential differences between patients classified as potential copers and non-copers. As the third and final aim, to examine the potential risk of adverse events for such an intensive program in the early stage after ACL injury. We hypothesized that:

1. Patients with ACL injury completing a 5-week progressive exercise therapy program in the early stage after injury will significantly improve knee function assessed from isokinetic muscle strength tests, single-leg hop tests and self-assessment questionnaires
2. Patients initially classified as non-copers will improve knee function assessed from isokinetic muscle strength tests, single-leg hop tests and self-assessment questionnaires significantly more than subjects classified as potential copers
3. Early after injury, patients with ACL rupture will tolerate a progressive exercise therapy program without adverse events

METHODS

Participants consisted of the first 100 included patients in an ongoing prospective cohort study. The patients were enrolled between January 2007 and August 2009. Patients were referred to our outpatient clinic from the emergency room, their physician or they came on their own initiative. To be considered eligible for inclusion, patients must have had a complete unilateral rupture of the ACL within the past 90 days. Complete rupture of the ACL was confirmed by both magnetic resonance imaging (MRI) and ≥ 3 mm bilateral difference using a KT-1000 knee arthrometer[70] (MED Metric, San Diego, California). Patients had to be between 13 and 60 years of age, participate regularly in pivoting sports equivalent to activity level I or level II as defined by Hefti et al[28] (TABLE 1) and be able to come to our clinic at least twice a week for conduction of the exercise therapy program. Patients were excluded if they had symptomatic meniscal injuries, range of motion (ROM) deficits that were not resolved within 90 days after the date of injury, a quadriceps muscle strength index ≤70%, grade III-IV injury to collateral ligaments, injury to the posterior cruciate ligament, previous injuries of any kind to the injured or uninjured knee, cartilage lesions affecting the subchondral bone (assessed from MRI), fractures, or if they did not agree to the compliance requirements of performing the exercise therapy program at least twice a week for 5 weeks.

The study was designed and carried out in accordance to the Declaration of Helsinki, and approved by the Regional Ethical Committee for Eastern Norway. Prior to inclusion all patients signed a written informed consent.

Outcome measures

Before testing, patients performed a standard 10 minutes warm-up on a stationary ergometer cycle. The test battery in this study included isokinetic muscle strength tests for quadriceps and hamstrings[29, 30, 36] (Biodex 6000, Biodex Medical Systems Inc., Shirley, New York), using 5 repetitions at 60° per second. This velocity is considered adequate for assessment of muscle strength after ACL injury.[15, 30, 39, 52] Patients performed 4 repetitions for practice for each limb before the test. Isokinetic absolute torque values were measured in Newton-Meters (N-M) for both peak torque and torque at 30° knee flexion angle[17] and expressed in Joule (J) for total work. Four single-leg hop tests[16, 20, 47] were included: The one-leg hop for distance (OLH), the triple cross-over hop for distance (TCH), the triple-hop for distance (TH), and the 6-meter timed hop test (6MTH). Patients performed 1 practice trial for each hop test on the uninjured and injured limb before the measured trials. A stop watch was used for timing the 6MTH. Single-leg hop tests have been considered to reflect both strength, coordination, and confidence after ACL injury.[37, 53] Patients performed 1 trial for each limb to familiarize themselves with the tests. Two trials were performed for each hop test and the average score of the 2 trials was used in the analyses. Absolute hop lengths were measured in centimeters, and time for the 6MTH in seconds. Immediately after the hop-tests patients answered 2 self-assessment questionnaires; the Knee Outcome Survey Activities of Daily Living Scale (KOS-ADLS)[35] and The International Knee Documentation Committee Subjective Knee Form (IKDC2000).[32] These 2 questionnaires were selected due to the previously shown reliability, validity and responsiveness for individuals with ACL injury.[32-35] Patients also stated their activity level, number of episodes of giving way, and a global rating of knee function from a numeric visual analogue scale (VAS).[22] Patients were classified as either

potential copers or non-copers according to the criteria described by Fitzgerald et al.[20] To fulfill the criteria of a potential coper, patients had to have ≥ 80 % score on the KOS-ADLS, a global rating numeric VAS score ≥ 60 %, single-leg hop performance on the 6MTH of ≥ 80 %, and maximum 1 episode of giving way since the injury.[20, 45]

Data collection procedures for the above tests are described in detail in a recent publication from our research group.[18] The baseline pretest including the screening examination for classification into potential copers and non-copers was performed as soon as initial impairments were resolved, whereas the posttest was to be performed within 6 weeks after the screening examination.

Exercise therapy program

ACL-rehabilitation in our outpatient clinic is divided into 3 subsequent phases, where the described progressive 5-week program represents phase 2. In the initial phase (phase 1), the goal is to resolve knee impairments related to swelling and ROM deficits. As soon as knee joint effusion is eliminated and full ROM is restored, phase 2 is initiated. Patients were excluded from this study if impairments were not eliminated within the first 3 months of phase 1 rehabilitation after their injury.

The primary aim of phase 2 rehabilitation is to restore muscle strength and adequate neuromuscular responses. Consequently, this phase emphasizes intensive muscle strength training, plyometric exercises,[10] and advanced neuromuscular exercises. Because specific evidence-based guidelines for strength training in the early stage after ACL injury do not exist, the strength training part of our phase 2 program is developed in correspondence with the principles outlined in the American College of Sports Medicine (ACSM) Position Stand for Progression Models for resistance training for Healthy Adults.[1] The strength training was standardized and

performed as multiple sets of exercises for a minimum of 2, maximum 4 sessions a week with maximal effort using 3 or 4 sets of 6 to 8 repetitions. These guidelines consistent with recent recommendations for training frequency, recovery, and exercise volume for recreational athletes at an intermediate level.[1, 50, 54, 69] Progression was guided by a dose-response theoretical framework where the absolute load is increased from a targeted repetition number in each set.[1] To assure progressive overload we used the "+2 principle". This principle implies that the patients are told to perform as many repetitions as they can manage in the last of the third or fourth sets. If they are able to add 2 extra repetitions, load will be increased in the next treatment session. Both single- and multiple-joint exercises, non-weight bearing and weight bearing exercises, as well as concentric, eccentric, and isometric strength exercises were included[1]. Non-weight bearing exercises have been shown to be of considerable importance for quadriceps strength improvement,[44, 62] and less threatening of unwanted anterior translation of the tibia than previously assumed.[41, 46, 49] Specific single limb exercises for the injured limb were performed on custom strength training equipments (Technogym®, Gambettola, Italy) using leg press, knee extension, and leg curl machines. The strength training program was individualized based on the specific needs of each patient. In addition to progressive strength training, plyometric exercises were included in the program for enhancement of neuromuscular performance and strength development.[10, 59] Plyometric exercises were performed through variations of single-legged hops and drills focusing on maintaining the knee over toe position with soft landings, to avoid landings with injurious dynamic loads.[48] Further, neuromuscular challenges were assured through balance and proprioception exercises like single-legged squats on balance pads or the BOSU balance trainer. The strength, plyometric and neuromuscular exercises

included in the program are presented in Appendix A. As a specific neuromuscular enhancement, a sequence of 10 sessions with perturbation training was included in the program. Perturbation training included balance- and stability exercises on custom-made rollerboard, rockerboard and platform, and involved perturbation of the support surface that allowed altered forces and torques to be applied to the injured limb in multiple directions in a controlled manner.[9] Progression of the perturbation training sessions was based on the guidelines from the University of Delaware,[21] and is presented in Appendix B and in instructional videos that recently have been published online.[27] Rehabilitation programs including perturbation training has previously been shown to enhance coordinated muscle activity and thus improve the dynamic stability of the knee early after injury.[9, 21, 26]

All patients were supervised at least twice a week throughout the program to assure that the intended quality of performance and correct level of difficulty was achieved, as well as to perform the perturbation sessions. Because patients were not supervised continuously during each session, compliance was additionally monitored through exercise diaries and medical records. Each training session was intended not to exceed 75 minutes, including a 10 to 15 minute warm up on a stationary ergometer cycle, treadmill or ellipse walker. Complications and adverse events were reported to the 2 supervising physical therapists (IE or HM) and noted in the medical records of each subject.

After completion of the progressive 5-week exercise therapy program, patients went through post testing and the final decision for reconstructive surgery or further non-operative management was addressed. The majority of the patients in our cohort had a preference for surgery, based on their desire to return to pivoting sports. The posttest results were incorporated when treatment options were discussed with the

patients, but not used as cut-off criteria in the final decision making for surgery or further non-operative management. Patients that were not referred to surgery continued rehabilitation in phase 3, whereas patients awaiting ACLR continued progressive rehabilitation in phase 2 with restrictions against participation in pivoting sports. Of the 100 included patients, 64 went through ACLR within the first 6 months after the posttest, and 36 continued non-operative management.

Data analyses

Descriptive data characterizing the cohort was calculated from frequencies and mean values with standard deviations (SD). Changes in muscle strength and hop performance limb symmetry index (LSI) from pretest to posttest were compared using a 2-way mixed analysis of variance (ANOVA). LSI was expressed as the side-to-side difference in percent using the uninjured limb as control. The ANOVA was also utilized for calculation of changes in score from pretest to posttest for the KOS-ADLS, IKDC2000 and VAS. The main effect evaluated changes over time from pretest to posttest. Further, potential interaction effects between groups (potential coper/non-coper) and time, as well as potential differences in the observed changes between potential copers and non-copers were calculated. Additionally, we calculated the percentage changes from pretest to posttest using the mean absolute values of the isokinetic muscle strength tests and the single-leg hop tests. To evaluate whether percentage changes could be regarded as clinically relevant, the standardized response mean (SRM) was calculated for changes in absolute torque values, hop lengths (OLH, TCH, TH) and time (6MTH) from pre- to posttest. The SRM was computed by dividing the mean change (posttest score minus pretest score) by the SD of the change.[11] SRMs were regarded as moderate between 0.5 and 0.8, and

large above 0.8.[5, 11] The number of adverse events was registered in the medical records for all patients.

RESULTS

Characteristics of the cohort

A flow chart of the study is presented in FIGURE 1. To include 100 patients, 211 were considered eligible for inclusion, and 111 were excluded. Reasons for exclusion are given in FIGURE 1. There were no significant differences in age, gender, body mass index (BMI), or pre-injury activity level between the included and excluded patients. The mean number of days from injury to the baseline pretest screening examination for the included patients was 60.4 (range 23-96) days, while the mean number of days from the baseline pretest screening examination to posttest was 34.9 (range 15-58) days. The exercise therapy program incorporated 10 sessions, and the mean number of completed sessions of the 98 patients that were included at follow-up was 9.7 (range 8-10) sessions. The sessions were completed within a mean time frame of 5 weeks. Subject characteristics are presented in TABLE 2. There were no significant baseline differences on age, gender, pre-injury activity level, KT-1000 static knee laxity, BMI, which side was injured, activity while injured, days from injury to pretest screening or days from pre- to posttest between patients classified as potential copers or non-copers. Further, there were no significant baseline differences between those who later opted to have ACLR (64%) and those who continued non-operative management (36%), except for age ($p=0.005$) and activity level ($p=0.003$). Those who opted for surgery were younger, with a mean age of 24.5 years compared to 29.0 year for those who elected not to have surgery. Among those who were surgically treated, 81% were active at level I and 19% at level II; whereas the activity level was

equally distributed with 50% at both level I and II among those who continued non-operative management.

Two patients were lost-to-follow up at posttest (FIGURE 1). One subject did not show for his appointments week 2 after pretest screening, then came back 6 weeks later, after he had reconstructive surgery at another clinic. The other subject was involved in a traffic accident and consequently did not complete the posttest. Both these patients were classified as potential copers at the pretest screening examination. Five additional patients have incomplete data from the hop-tests at posttest. Four of these experienced adverse events with swelling and pain during the 5-week exercise therapy program. The fifth had an episode of giving way during the TCH at posttest. However, this subject had completed the exercise therapy program without problems.

Quadriceps and hamstrings muscle strength

Changes from pre- to posttest for quadriceps and hamstrings muscle strength are shown in TABLE 3. There were no significant interaction effects between groups (potential copers/non-copers) and time. The main effect for time was significant for quadriceps muscle peak torque, 30° knee flexion and total work as well as hamstrings muscle peak torque and total work ($p<0.05$). The between-groups main effect was significant for all 3 quadriceps muscle strength outcome measurements ($p\leq0.01$; FIGURE 2), but non-significant for hamstrings muscle strength peak torque ($p=0.50$) and total work ($p=0.43$) (FIGURE 3).

Changes in percent of absolute torque values for quadriceps strength for the injured limb from pretest to posttest were between 8.2% and 11.1% for the 3 outcome measures with moderate corresponding SRM values (TABLE 4).

Single-leg hop tests

There were no significant interaction effects between groups (potential copers/non-copers) and time for the single-leg hop tests (TABLE 3). Further, no significant main effect for time was found for either of the single-leg hops. For the TH and the 6MTH, significant main effects for groups were present ($p<0.05$) (FIGURE 4).

Changes in percent of absolute hop length for the injured limb for the 4 hop tests were between 5.5% and 9.5%. The calculated SRM values were moderate for the OLH, TH, and 6MTH and large for the TCH (TABLE 5).

Self-assessment questionnaires

A significant interaction effect between groups (potential copers and non-copers) and time was evident for the KOS-ADLS ($p<0.01$; TABLE 6 and FIGURE 5), but not for the IKDC2000 or the VAS. Both the main effects for time and groups showed significant effects ($p<0.001$) for the IKDC2000 and the VAS (TABLE 6 and FIGURE 5).

Tolerance for the exercise therapy program

Two patients were lost to follow-up at posttest. Four of the remaining 98 patients (3.9%) experienced progressively more swelling and pain during the second or third week of the program, and had to reduce exercise intensity to the extent that they could not be considered compliant with the program. Swelling and pain occurred following the performance of plyometric exercises for all 4 patients. None of the patients reported pain during muscle strength exercises, balance and stability exercises, or perturbation sessions. Two of the 4 patients that had complications

during the plyometric exercises were non-copers and 2 were potential copers. These 4 individuals all later opted to have ACLR and also required a meniscus repair.

DISCUSSION

The purpose of this study was to investigate whether a progressive 5-week exercise therapy program in the early stage after injury before decision making for either ACLR or further non-operative management could improve knee function and was tolerated by patients with ACL injury. The overall results confirmed our first hypothesis; that a progressive exercise therapy program conducted within a mean time frame of 5 weeks leads to significantly improved knee function in patients with ACL injury. This was evident both for subjects initially classified as potential copers and non-copers. The second hypothesis, that non-copers would improve significantly more than potential copers, was not confirmed. An interaction effect implying larger improvement in non-copers compared to potential copers was only found for KOS-ADLS. Our third hypothesis, suggesting that there would be no adverse events among patients conducting the program, was partially confirmed with only 3.9% of the patients attending the posttest having progressive swelling and pain that required curtailing compliance with the 5-week program.

Currently, a clear consensus does not exist for the selection of exercises and exact dose-response in rehabilitation programs in the early stage after ACL injury. Our 5-week progressive program combines strength training, plyometric exercises, general exercises for balance and stability, and perturbation training. The strength training regimen is based on principles for heavy resistance strength training for healthy individuals with few repetitions in each series, in order to affect both the cross-sectional area of the muscle and the neuromuscular adaptation.[1] Both weight bearing and non-weight bearing exercises were included, as recent publications have

shown that non-weight bearing exercises are important to regain quadriceps muscle strength[41, 44] and also that non-weight bearing exercises can be conducted safely in patients with ACL injury.[44, 46, 49] The neuromuscular exercises in the program are intended to be of utmost challenge for the patient. Over the past few years, our exercise therapy program has evolved in the direction of higher loads, fewer repetitions, and less restrictions with regard to non-weight bearing exercises, as well as more challenging neuromuscular exercises.

LSI is commonly used to express both isokinetic muscle strength[61] and single-leg hop performance[3], and a LSI of ≥90% is often considered to indicate normal limb symmetry.[3, 25, 26, 61] However, the use of LSI alone may be ambiguous if the main purpose is to evaluate the response to exercise and improvement of knee function primarily in the injured limb. Using the uninjured limb as control has the methodological advantage that biological differences between patients are avoided. But, the potential disadvantage is that the status of the uninjured side may lead to misinterpretation of results[5, 8, 31] due to possible bilateral neuromuscular changes after injury.[2, 48] In addition to evaluation of the LSI, we performed supplementary evaluations of the absolute values for the uninjured and injured side and examined changes in percent from pre- to posttest for both isokinetic muscle strength torques and single-leg hop lengths (OLH, TCH,TH) and time (6MTH). These analyses revealed changes in both quadriceps and hamstrings muscle strength for the injured side (range from 8.2% to 11.1%); entailing a strength increase of 1.6% to 2.2% per week. The corresponding SRM values for the injured limb reflected changes of moderate clinical relevance (0.49-0.60), whereas the corresponding SRM values for the uninjured limb were low (0.13-0.40). Evaluation of absolute values (TABLE 5) for single-leg hop performance showed changes in percent in the injured limb from 5.5%

to 9.5%. The SRM values were moderate to strong (0.50-0.84) for all tests. Thus, analyses of the absolute values and corresponding SRMs for the injured leg revealed clinically interesting improvements that were concealed when evaluating only LSI. Without a control group, calculation of SRM values for pre- to posttest changes in the injured limb may be of particular clinical interest. While p-values reflect whether an observed change is statistically significant, SRM values express the magnitude of the observed changes.[5] Our SRM values emphasize that patients with ACL tears in the early stage after injury have potential for clinically relevant functional improvements, even from a short term exercise therapy program consisting of only 10 training sessions.

When comparing our muscle strength data to normative values presented by Phillips et al,[51] the mean posttest absolute peak torque values on the injured limb were equivalent to normative values from the dominant limb of healthy subjects (183.8 versus 180.3 N-M, respectively). But, the mean age of the subjects included in the normative study was higher than for our cohort (44.2 versus 26.1 years, respectively). However, Danneskiold-Samsøe et al[13] presented normative values for a cohort with patients age-matched to ours at 169.0 N-M, which further suggests that the patients in our cohort regained adequate muscle strength after the exercise therapy program. The limited amount of normative data for isokinetic knee muscle strength should, nevertheless, be addressed in future studies.

Previous studies from our group[17] and Shirakura et al[60] showed that there were larger differences in quadriceps strength at knee flexion angles less than 40°. Thus, quadriceps torque values at 30° knee flexion angle were included in the analyses. The results confirm previous findings that LSI differences were larger at angles closer to full knee extension (TABLE 1). This may have important clinical implications when

using quadriceps strength LSI in the evaluation of treatment outcome. However, when evaluating changes in absolute values and SRM values from pre- to posttest, the deficits at 30° demonstrated the highest percentage improvement (11.1%) and the highest SRM value (0.58) of the included strength measures. This indicates that even though larger at pretest, quadriceps muscle strength weakness in the injured limb at angles closer to full extension have good potential for improvement. As a consequence, knee extension exercises targeting strength deficits throughout the whole knee extension ROM should be included in early stage rehabilitation programs.

All self-assessments of knee function significantly improved from pre- to posttest ($p<0.001$). The KOS-ADLS showed a significant interaction effect, implying that non-copers improved significantly more than potential copers (FIGURE x). Significant main effects for time and groups were found for both the VAS and the IKDC2000 ($p<0.001$); revealing that both potential copers and non-copers improve but non-copers still have lower scores at posttest ($p<0.001$).

The IKDC2000 is used for assessment of knee function with regard to symptoms, function, and sports activity[4], and may thus be considered to be of particular relevance for our cohort of young, active individuals. The mean IKDC2000 score for our cohort at pre- and posttest was 69.7 and 77.8 points, respectively. According to the normative data for IKDC2000 published by Anderson et al[4], scores for subjects age-matched to our cohort indicate a mean score of approximately 89 points for men and 86 points for women. Previous studies have shown that ACL injury may lead to low self-efficacy[63] and that self-efficacy and mental preparedness before ACLR may influence the final outcome.[6, 64] The improvements in the IKDC2000 may suggest the potential importance of increased self-evaluation scores in the early stage after injury, before scheduled ACLR. This is of particular interest given the larger

improvements for non-copers, who from the original screening examination algorithm were not regarded as candidates for rehabilitation.[20] However, the IKDC2000 does not assess self-efficacy as such, and future studies investigating preoperative self-reported outcomes as predictors for postoperative outcome are needed to verify this suggestion.

Pre-operative quadriceps muscle strength deficits have previously been assessed from isokinetic measurements to be between 7 and 21%[14, 37-39, 56], and have also been shown to be persistent after ACLR.[19, 38, 68] As a consequence, there has been growing attention towards the importance of more aggressive strength training of the quadriceps muscle after ACL injury.[7, 26, 41] Ingersoll et al[31] suggested that strength deficits after ACL injury are the result of alterations to muscle activation patterns. The almost immediate development of weakness and the often observed persistency of the deficit despite rehabilitation suggest that arthrogenic muscle inhibition may play a major role in quadriceps atrophy after ACL injury.[48] Furthermore, individuals with ACL injury who have muscle strength deficits often have overall poor function.[62, 68] However, to what extent altered neuromuscular strategies [2, 7, 31, 48, 68] and proprioceptive deficits[23, 57] contributing to reduced function after ACL injury may be restored through rehabilitation is not well documented. Most systematic reviews and randomized controlled trials on ACL-injuries focus on individuals post ACLR. In 2 systematic reviews, Cooper et al[12] and Risberg et al[55] identified only a few high-quality studies on the effect of neuromuscular training programs for individuals with ACL-deficient knees, with variations both in exercises included and the duration of the programs. Still, it is concluded that exercises for proprioception and balance may improve dynamic knee stability and thus the functional ability of the patients. Further, there is some evidence suggesting that plyometric exercises will enhance muscular

strength and athletic performance[10, 59], and that rehabilitation programs including specific perturbation training may lead to beneficial neuromuscular adaptations.[21, 26, 42] Without a comparison group, we cannot state that our findings document that combined approaches of both neuromuscular exercises and strength training are superior to other exercise programs emphasizing separate elements. However, we can from our findings state that it is possible to achieve significant and clinically important improvements in both muscle strength and knee function even with a short-term exercise program, and that this is true both for subjects initially classified as potential copers and non-copers. Future studies including randomized controlled trials with groups that perform different exercise therapy programs are needed to verify the potential effectiveness of our program.

A crucial issue when introducing progressive exercise therapy programs is the tolerance for the training load. In this study 3.9% of the patients experienced adverse events during the period of conducting the program that prevented compliance with regard to progression of the plyometric exercises. Lack of tolerance demonstrated by progressively increasing symptoms of swelling and pain during or after training sessions. We attribute these complications to the performance of the plyometric exercises. Recent studies have emphasized the challenges related to the correct diagnosis of meniscus injuries.[40, 58, 67] We included both MRI and a clinical examination when evaluating individuals eligible for inclusion in the study. Our definition of a symptomatic meniscus injury implied that patients should reveal symptoms during hopping exercises, and/or have evident knee joint effusion, and/or ROM deficits that were not resolved within 3 months after the date of injury. The 4 patients that experienced adverse events all later opted to have ACLR and were found to require a concomitant meniscus repair. All patients in the study were advised

not to participate in any pivoting activities during phase 2. Further, they were monitored at least twice a week and any complications and adverse events were registered. No episodes of giving way were reported. Thus, it is unlikely that any of the 4 patients had new injuries within the 5-week period, and their symptoms were most probably related to the increased demands posed on the knee during phase 2 of the rehabilitation program. The remaining 94 patients were compliant with the demands for progression and exercises in the program. Our results indicate that the majority of patients with isolated ACL-injuries are able to comply with progressive exercise therapy programs. However, our results suggest that adverse events can be expected to occur in 1 out of 25 patients. Thus, the responsible physical therapist must monitor eventual adverse events closely on an individual basis, and never hesitate to adjust the program if undesired symptoms appear. Based on our findings, symptoms of pain and swelling during the rehabilitation program may be an indicator of other intra-articular pathology like a meniscus tear.

Limitations

Due to the inherent limitations of a study design without comparison groups, we cannot document superior effects of our program compared to other rehabilitation programs, but are restricted to report the observed changes in outcome measures from pre- to posttest and discuss the outcome in comparison to other studies.

Patients were instructed and regularly reminded to update a personal written exercise diary during the 5-week exercise therapy program. However, the compliance of the patients to fill in these self-reported data was not satisfactory. We did not register this information systematically when monitoring the patients, and as a consequence, data showing exact progression during each session throughout the

exercise period cannot be provided. Future studies should include closer monitoring of dose-response and progress for each separate exercise that is included in the exercise therapy program, both for muscle strength and neuromuscular exercises. From our experience this should be registered as part of the patient monitoring at each session and not be based on self-reporting.

Our cohort consisted of patients with isolated ACL-tears, including asymptomatic meniscus lesions. A considerable amount of patients with ACL injury have additional injuries to the menisci and/or collateral ligaments and related symptoms[66], which is also reflected in the number of individuals excluded from our cohort. Our results can therefore not be generalized to patients with symptomatic concomitant injuries. Our high tolerance rate for the progressive exercise therapy program must be interpreted within this context.

Finally, the patients included in this study were young, active individuals who may have had higher motivation for exercise and rehabilitation than other subgroups of patients with ACL injury. Our results are thus dependent on high compliance to and low drop-out rates from the exercise therapy program.

CONCLUSION

This study showed that a progressive rehabilitation program conducted within a mean time frame of 5 weeks with emphasis on heavy resistance strength training and challenging neuromuscular exercises led to significantly improved knee function in the early stage after ACL injury. It is therefore suggested to incorporate a short-term period of intensive exercise in ACL injury management, either before scheduled ACLR, or as a preparation for further non-operative management before returning to pre-injury activity without surgery.

KEY POINTS

Findings

A 5-week progressive exercise therapy program in the early stage after ACL injury led to significantly improved knee function before the decision making for reconstructive surgery or further non-operative management. The compliance to and tolerance for the program was high, with few adverse events.

Implication

Short-term progressive exercise therapy programs should be incorporated in the early stage after ACL injury, in order to optimize knee function before ACLR or as a first step in the preparation to return to previous activity without surgery.

Caution

The participants in this study had an ACL tear with no symptomatic concomitant injuries; therefore results cannot be generalized to all patients with ACL injury. The results in this study are further dependent on motivated patients with high compliance to the exercise therapy program.

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TABLE 1. Classification of activity level*.

Level	Sports activity	Occupational activity
I	Jumping, cutting, pivoting (soccer, basketball, American football)	Demands comparable to level I sports activities
II	Lateral movements (skiing, tennis)	Heavy manual labor, working on uneven surfaces
III	Light activity (running, weight-lifting)	Light manual labor
IV	Sedentary activity (housework, activities of daily living)	Comparable to activities of daily living

*In accordance with Hefti et al.[28]

TABLE 2. Characteristics of the cohort.

Subject characteristics	
Gender (males/females) (%)	44 /56
Age; mean and range (years)	26.1 (14-47)
Body mass index females; mean and range (kg/m^2)	23 (20-27)
Body mass index males; mean and range (kg/m^2)	24 (20-36)
Classification (potential coper/non-coper) (%)	52/48
KT-1000 static laxity; mean and SD	5.6 (2.3)
Injured side (left/right) (%)	53/47
Activity level prior to injury (I/II) (%)	70/30
Activity when injured (number of subjects)	
Soccer	33
Team handball	22
Alpine skiing	22
Basketball	5
Martial arts	4
Other	14

TABLE 3. Changes from pre- to posttest for limb symmetry indexes; isokinetic muscle strength and single-leg hop tests.

	LSI pretest (mean/SD)	LSI posttest (mean/SD)	Difference pre-posttest
Quadriceps PT[1]	88.6% (9.7)	92.6% (9.8)	4.0 % (9.4)
Quadriceps torque 30° flex[1]	84.4% (15.7)	92.5% (17.8)	8.1% (15.4)
Quadriceps TW[1]	88.4% (11.7)	92.0% (11.6)	3.6% (10.7)
Hamstrings PT[1]	94.0% (9.7)	96.9% (9.8)	2.9% (12.8)
Hamstrings TW[1]	92.8% (14.6)	96.0% (9.8)	3.2% (15.3)
OLH[2]	90.4% (9.4)	90.0% (18.6)	-0.4% (18.6)
TCH[2]	90.5% (13.3)	90.6% (17.9)	0.1% (16.5)
TH[2]	89.5% (12.6)	90.9% (18.3)	1.4% (14.8)
6MTH[2]	90.5% (15.6)	92.2% (17.9)	0.3% (18.4)

No interaction effects were established for any of the variables.
[1]Significant main effect for time was found for all strength outcomes ($p \leq 0.001$-0.04) with large effect sizes for quadriceps strength outcomes (0.15-0.22). Between groups (PC/NC) effects were significant for quadriceps strength outcomes ($p<0.01$) and for the TH and 6MTH ($p=0.02$), with moderate to large effect sizes (0.06-0.16).
[2]No main effect for time were found for the single-leg hop tests ($p>0.05$).

PC= Potential copers
NC= Non-copers
LSI = Leg symmetry index (side to side percentage differences, injured versus uninjured leg)
PT= Peak torque
TW= Total work
OLH= One-leg hop test for distance
TCH= Triple cross-over hop test for distance
TH= Triple hop test for distance
6MTH= 6-meter timed hop test

TABLE 4. Muscle strength torque improvement (%) from pre- to posttest.

	UNINJURED LIMB				INJURED LIMB			
	Pretest	Posttest	Change (%)	SRM	Pretest	Posttest	Change (%)	SRM
Quadriceps PT (N-M)	192.5 (51.6)*	200.1 (56.8)$^{+}$	3.9%	0.27	169.8 (45.8)*	183.8 (52.5)$^{+}$	8.2%	0.49
Quadriceps 30° flex (N-M)	118.8 (30.9)*	121.2 (32.7)$^{+}$	0.2%	0.13	100.9 (34.7)*	112.1 (36.2)$^{+}$	11.1%	0.58
Quadriceps TW (J)	887.8 (237.2)*	934.3 (266.6)$^{+}$	5.2%	0.35	784.1 (225.8)*	856.4 (264.0)$^{+}$	9.3%	0.53
Hamstrings PT (N-M)	96.8 (27.1)*	103.2 (29.8)$^{+}$	6.6%	0.37	90.4 (25.6)*	99.7 (29.3)$^{+}$	10.2%	0.53
Hamstrings TW (J)	545.1 (165.8)*	591.8 (182.3)$^{+}$	8.6%	0.40	499.8 (148.9)*	564.7 (170.5)$^{+}$	12.9%	0.60

Torque values and percentage changes are reported as mean values and standard deviation: Mean (SD)

SRM= Standardized response mean
PT= Peak torque
TW= Total work
N-M = Newton-Meter
J = Joule
* n=100
$^{+}$ n=98

TABLE 5. Hop performance improvement (%) from pre- to posttest.

	UNINJURED LIMB				INJURED LIMB			
	Pretest	Posttest	Change (%)	SRM	Pretest	Posttest	Change (%)	SRM
OLH (cm)	139.8 (26.6)*	145.1 (31.5)$^{+}$	3.8%	0.27	126.9 (25.0)*	136.0 (28.2)$^{+}$	7.2%	0.71
TCH (cm)	416.5 (92.7)*	451.8 (86.2)$^{+}$	8.5%	0.51	387.1 (78.5)*	423.9 (86.9)$^{+}$	9.5%	0.84
TH (cm)	460.3 (100.9)*	481.9 (84.6)$^{+}$	4.7%	0.32	423.5 (82.9)*	449.3 (87.7)$^{+}$	6.1%	0.69
6MTH (sec)	1.84 (0.29)*	1.79 (0.27)$^{+}$	2.7%	0.29	2.00 (0.38)*	1.89 (0.32)$^{+}$	5.5%	0.50

Hop lengths, time in seconds and percentage changes are reported as mean values and standard deviation: Mean (SD)

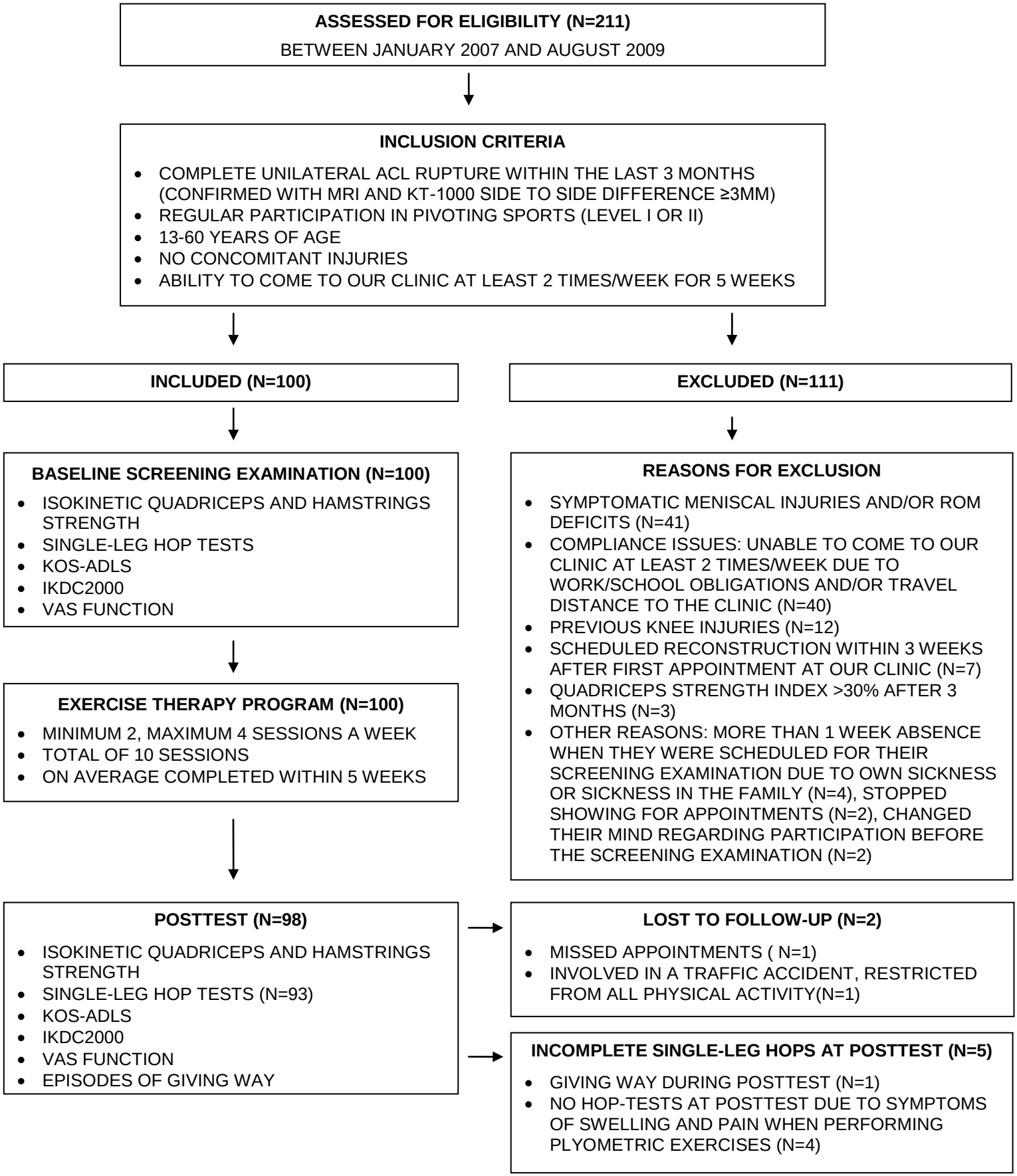
OLH = One-leg hop test for distance
TCH = Triple cross-over hop test for distance
TH = Triple hop test for distance
6MTH = 6-meter timed hop test
SRM = Standardized response mean
* n=100
$^{+}$ n=93

TABLE 6. Changes from pre- to posttest for self-assessment questionnaires.

	Main effect (time)	ES main effect (time)	Between-groups effect (PC/NC)	ES between-groups effect (PC/NC)	Interaction effect
KOS-ADLS	p<0.001	0.28	p<0.001	0.30	<0.01
IKDC2000	p<0.001	0.35	p<0.001	0.27	0.09
VAS	p<0.001	0.16	p<0.001	0.18	0.35

ES= Effect size
PC= Potential copers
NC= Non-copers
KOS-ADLS = Knee Outcome Survey Activities of Daily Living Scale
IKDC2000=-The International Knee Documentation Committee Subjective Knee Form
VAS= Global rating of knee function on a visual analogue scale

FIGURE 1: Flowchart of the study.



ABBREVIATIONS: ACL = Anterior cruciate ligament; IKDC2000 = International knee documentation committee knee evaluation form 2000; KOS-ADLS = Knee Outcome Score Activities of Daily living; MRI = magnetic resonnance imaging; VAS = visual analogue scale.

FIGURE 2: Main group and interaction effects between copers and non-copers, quadriceps strength.

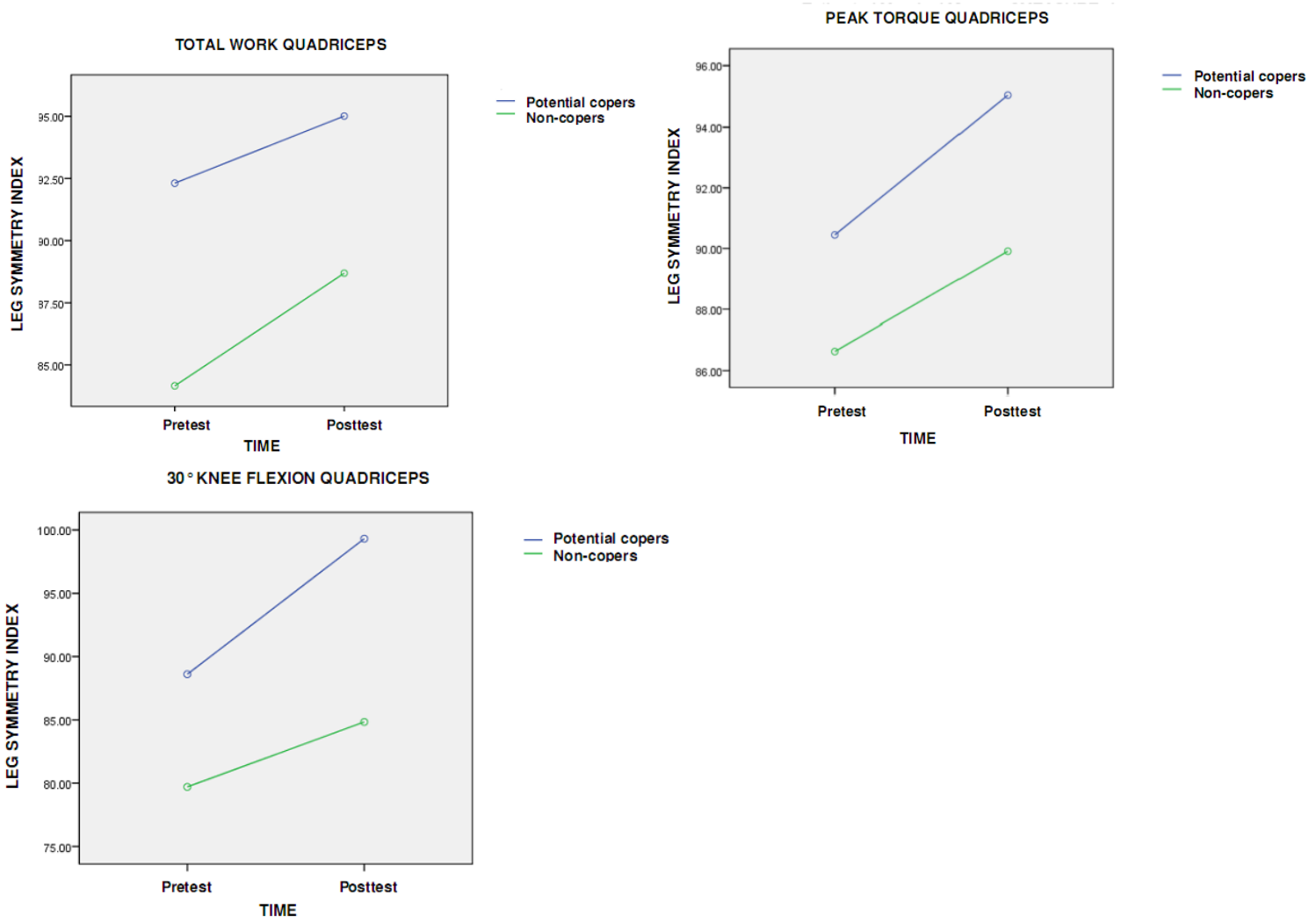


FIGURE 3: Main group and interaction effects between copers and non-copers, hamstrings strength.

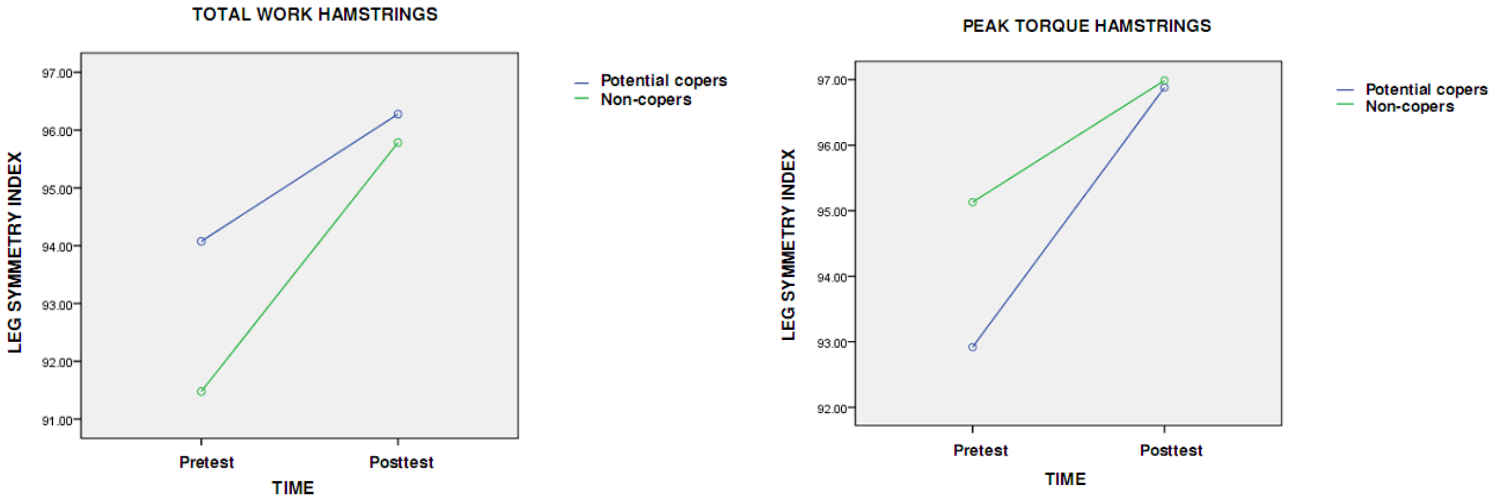


FIGURE 4: Main group and interaction effects between copers and non-copers, single-leg hop tests.

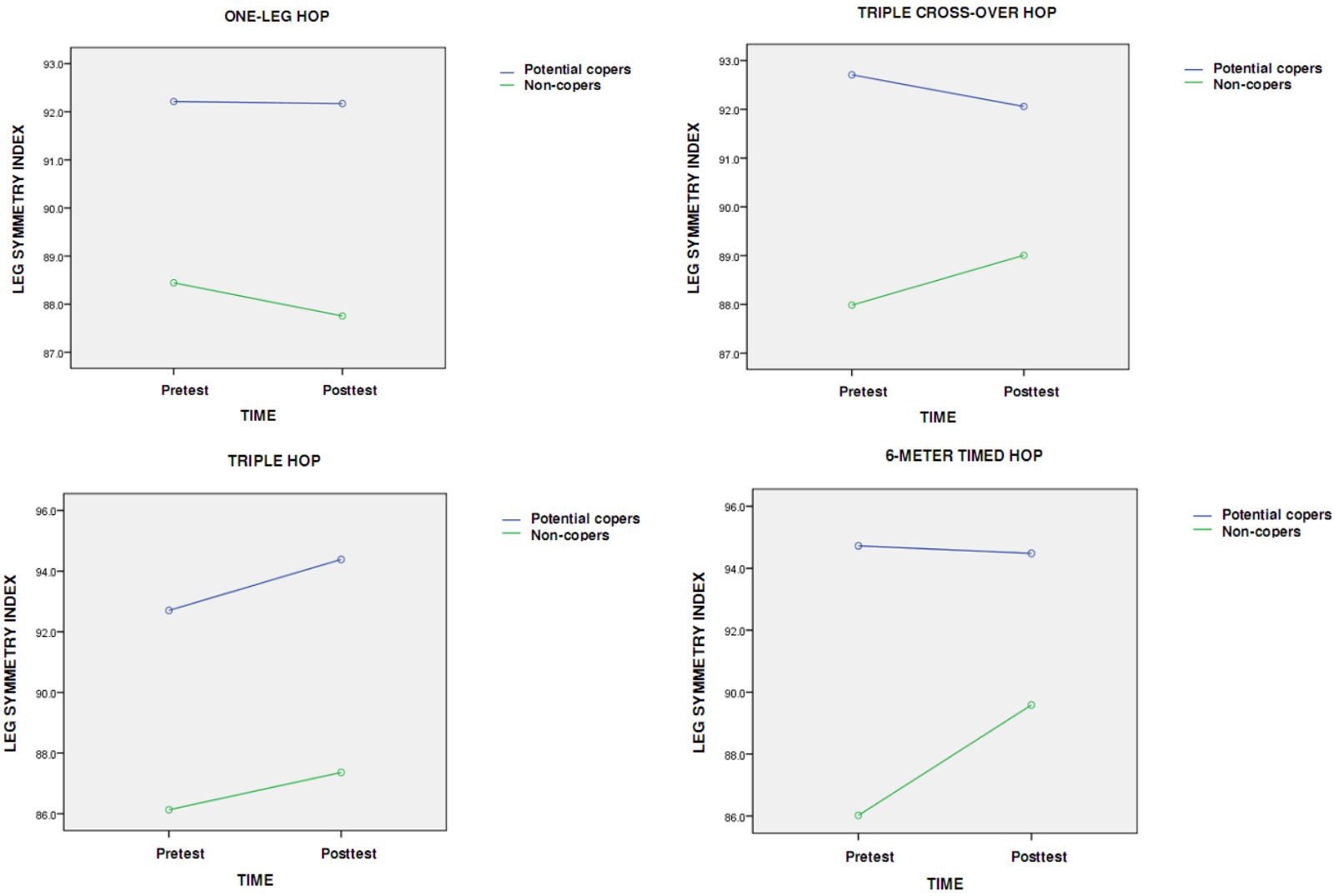
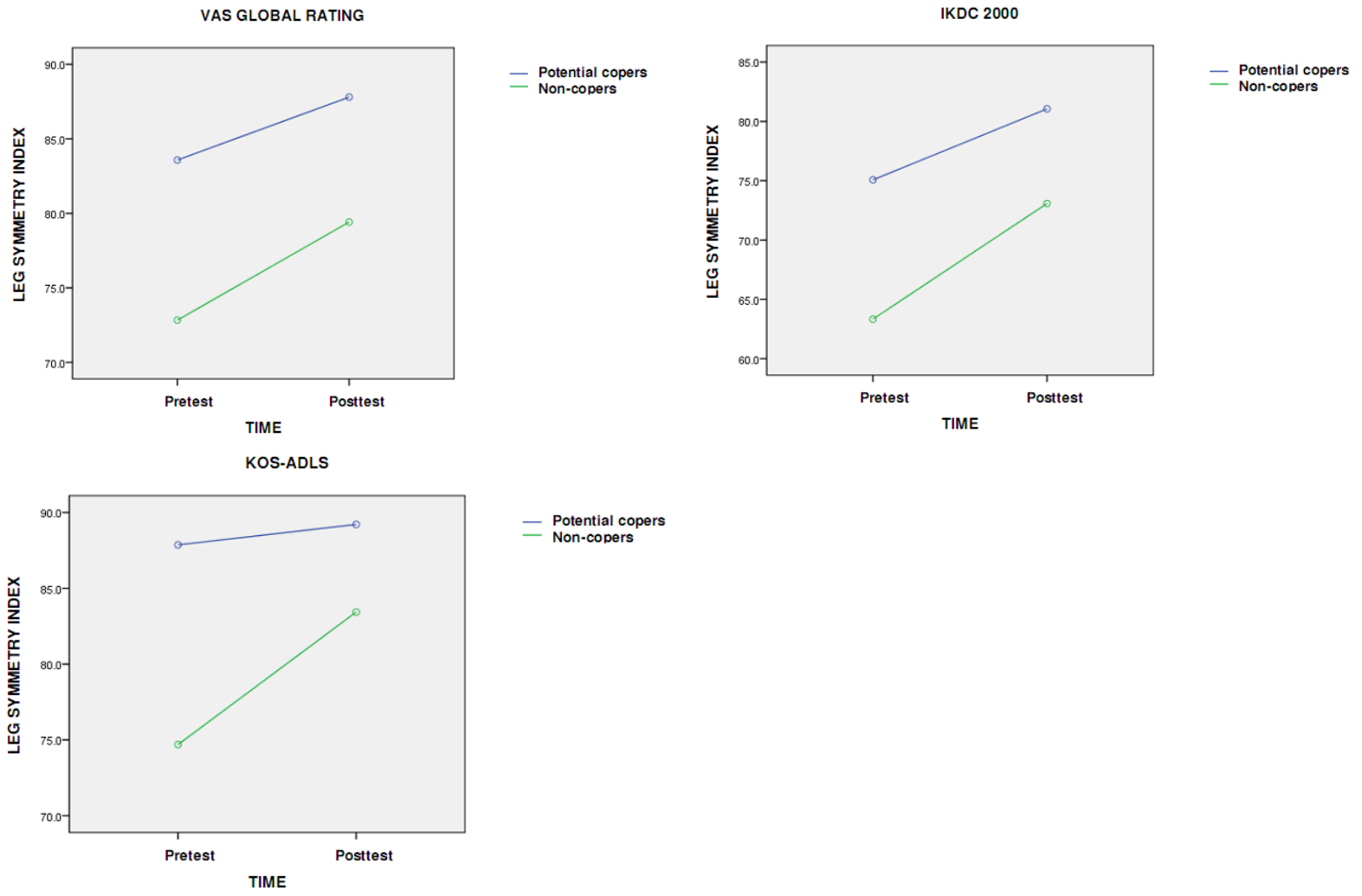
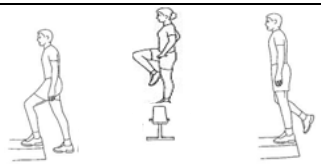
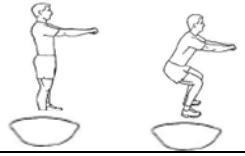
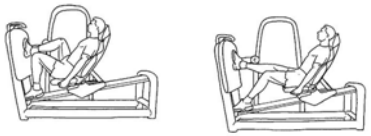
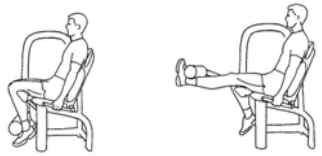
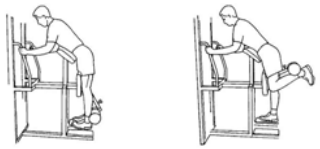
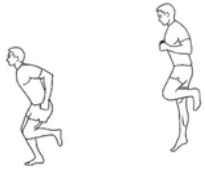


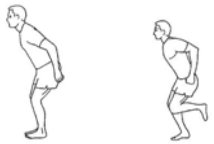
FIGURE 5: Main group and interaction effects between copers and non-copers, self-reported knee function.



APPENDIX A

Exercise		Set x Reps	Description
Stationary cycle		10 min	Continous warm-up at your preferred resistance
Treadmill		10 min	Continous warm-up at your preferred speed
Elliptical trainer		10 min	Continous warm-up at your preferred resistance
Single limb squat		3 x 8	Maintain knee over toe position
Step-up		2 x 10	Maintain knee over toe position
Squat on BOSU		2 x 20	Maintain knee alignment and core stability. Squat quickly down and up.

Single limb legpress		3 x 6 (+2)	Start in 90° knee flexion
Single limb knee extension		4 x 6 (+2)	Start in 90° knee flexion
Squats		3 x 8 (+2)	Squat slowly down to 90° knee flexion - stop - lift quickly up again
Leg curl		3 x 8 (+2)	Lift quickly up - stop - and then slowly down to full extension
Hamstring on Fitball		3 x 6	One foot on top of the ball - lift back and pelvis up - pull ball towards you
Single-leg hop		1 x 15	Hop up on step - stop - continue down and directly one hop forward with a soft controlled landing
Sideways single-leg hop		3 x 15	Start on 1 side of a board. Hop quickly sideways and stop after 3 hops. Continue and stop 5 times.

"Skating"		2 x 20	Start on 1 leg - hop sideways, perform a soft, deep and steady landing on 1 leg - hop back to the other side

All exercises are to be performed at each training session. 2-3 series in each session. Training sessions minimum 2, maximum 4 times a week. Progression from increasing loads on the strength exercises and for higher steps, longer/higher jumps, movement in several directions and more wobbly surfaces for the neuromuscular and plyometric exercises.

APPENDIX B
PERTURBATION TRAINING PROTOCOL NAME:

A/P = Anterior/posterior direction; M/L = Lateral/medial direction; ROT = rotation

SESSION	ACTIVITY		
	Rockerboard	**Rollerboard/platform**	**Rollerboard**
Session 1-4: Early phase. Progression by adding perturbations in all directions + minimizing of verbal cues			
1	▪ Bilateral stance ▪ Two sets, A/P ▪ Two sets, M/L	▪ Two sets with injured limb on rollerboard, A/P ▪ Two sets with uninvolved limb on rollerboard, A/P	▪ Bilateral stance ▪ Two sets A/P
2	▪ Unilateral stance ▪ Two sets A/P direction ▪ Two sets M/L direction	▪ Two sets with injured limb on rollerboard, A/P + M/L ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L	▪ Unilateral stance ▪ Two sets A/P
3	▪ Unilateral stance ▪ Two sets M/L direction ▪ Two sets diagonal direction	▪ Two sets with injured limb on rollerboard, A/P + M/L+ ROT ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L + ROT	▪ Unilateral stance ▪ Two sets A/P + M/L
4	▪ Unilateral stance ▪ Two sets M/L direction ▪ Two sets diagonal direction	▪ Two sets with injured limb on rollerboard, A/P + M/L+ ROT ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L+ ROT	▪ Unilateral stance ▪ Two sets A/P + M/L+ROT
Session 5-7: Middle phase. Progression by adding light sport specific activity during perturbations			
5	▪ Unilateral stance ▪ Two sets A/P direction ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball against wall	▪ Two sets with injured limb on rollerboard, A/P + M/L+ ROT ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L+ ROT ▪ Ball against wall	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball against wall
6	▪ Unilateral stance ▪ Two sets A/P direction ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball against wall/floor	▪ Two sets with injured limb on rollerboard, A/P + M/L ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L ▪ Ball against wall/floor	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball against wall/floor
7	▪ Unilateral stance ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball thrown by other	▪ Two sets with injured limb on rollerboard, A/P + M/L ▪ Two sets with uninvolved limb on rollerboard, A/P + M/L ▪ Ball thrown by other	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball thrown by other
Session 8-10: Late phase. Progression by adding sport-specific stances combined with sport specific activity			
8	▪ Unilateral stance ▪ Two sets A/P direction ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities	▪ Two sets with injured limb on rollerboard, A/P+M/L+ROT ▪ Two sets with uninvolved limb on rollerboard, A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities
9	▪ Unilateral stance ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball ▪ Other individually adjusted relevant sport specific activities	▪ Two sets with injured limb on rollerboard, A/P+M/L+ROT ▪ Two sets with uninvolved limb on rollerboard, A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities
10	▪ Unilateral stance ▪ Two sets M/L direction ▪ Two sets diagonal direction ▪ Ball ▪ Other individually adjusted relevant sport specific activities	▪ Two sets with injured limb on rollerboard, A/P+M/L+ROT ▪ Two sets with uninvolved limb on rollerboard, A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities	▪ Unilateral stance ▪ Two sets A/P+M/L+ROT ▪ Ball against wall/floor, thrown by other ▪ Other individually adjusted relevant sport specific activities