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KNEE JOINT STABILIZATION THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF THE KNEE: A RANDOMIZED, CONTROLLED TRIAL

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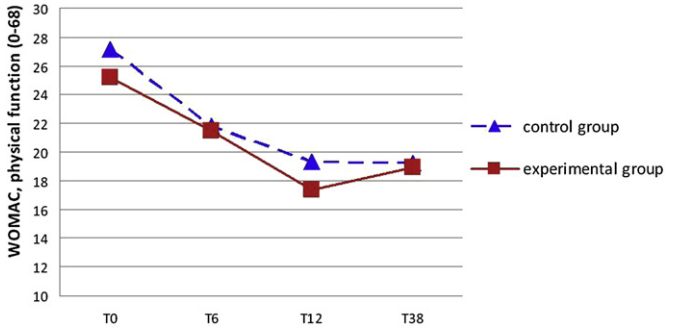
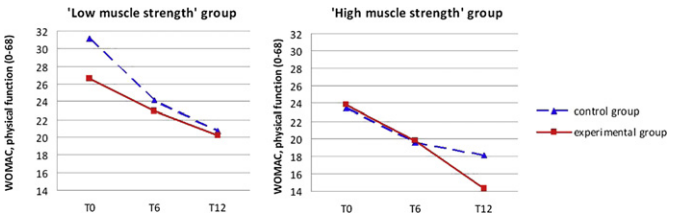
Purpose: To evaluate the effectiveness of additional knee joint stabilization therapy, prior to muscle strengthening and functional exercises in patients with knee osteoarthritis (OA) and instability of the knee joint.
Methods: Single-blind, randomized, controlled trial (NTR1475) involving 159 knee OA patients with self-reported or biomechanically assessed knee instability. Experimental treatment was a 12-week exercise program initially focusing on knee stabilization, prior to muscle strength and performance of functional activities. Control treatment was a 12-week exercise program consisting of muscle strengthening and functional exercises only. Primary outcome measure was self-reported activity limitations (WOMAC, subscale physical function), assessed at baseline, 6-week, 12-week and 38-week follow-up. Secondary outcome measures included pain, observed activity limitations and knee instability.
Results: Both treatment groups demonstrated large (~30-40%) and clinically relevant reductions in activity limitations, pain and knee instability, which were sustained six months post-treatment. Knee joint stabilization training did not show additional effect compared to the control treatment on primary outcome measure WOMAC, physical function (B (95% CI) = -0.01 (-2.58-2.57)) (see Figure 1) or secondary outcome measures, except for higher global perceived effect in the experimental group (p=.04). Subgroup analyses revealed an interaction (p=.02) between baseline upper leg muscles strength and treatment effect on WOMAC, physical function (see Figure 2).
Conclusions: Both exercise programs were effective in reducing activity limitations and pain and restoring knee stability. In the total group, initial knee joint stabilization training was not found to be effective in knee OA patients with instability of the knee, suggesting a dominant role of muscle function in knee joint stabilization. Results from subgroup analyses were indicative for an effect of additional knee joint stabilization training in persons with already high upper leg muscle strength.





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A RANDOMIZED, MULTICENTRE, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL OF ANTI TNF ALPHA (ADALIMUMAB) IN REFRACTORY HAND OSTEOARTHRITIS. THE DORA STUDY

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Purpose: Objective was to evaluate TNF blockers in patients with painful hand OA refractory to analgesics and NSAIDs.
Methods: This is a phase 3 randomized superiority, double-blind, placebo controlled, 26 weeks, multicenter trial, using TNF blocker adalimumab (2 sub cutaneous injections at week 0 and week 2). Patients meeting the ACR criteria for hand OA with pain above 40 mm, involving at least 3 painful interphalangeal joints, who did not respond to analgesics and NSAIDs, were recruited. The primary endpoint was the number of responders (more than 50% of improvement) at 6 weeks. Secondary outcomes were: number of painful joints and of swollen joints, morning stiffness, patient global assessments, functional index for hand OA. Consumption of analgesics was recorded (acetaminophen up to 3g/D as a rescue medication). Serum markers (COMP, PIIANP, HA, usCRP, cytokines level of TNF α, IL-6, IL-1) and urine level of CTX-II (corrected by creatinine) were measured at W0 and W6.
Results: On the 99 patients selected, 85 were randomized (42 placebo , 41 adalimumab). 78 patients with at least one injection were analyzed (37 placebo and 41 adalimumab) (mITT). Mean (SD) age was 62.5 (6.9), 85 % of women, mean (SD) level of pain was 65.4 (12.9) mm; mean (SD) number of painful IP joints: 11 (6). At W6, there was no difference between groups on the main outcome measure: 35.1% in the adalimumab group versus 27.3% in the placebo group (RR: 1.12 (95% CI: 0.82-1.54; p=0.48) corresponding to an intergroup difference of: -2.5 mm (95% CI, -14.0 to 9.0), p: 0.67. No statistically significant differences were found for any of the secondary outcomes. Analgesics use was similar between groups. There were no safety concerns. There was none variations of any biological markers between the 2 groups.
Conclusions: In a group of patients with refractory hand OA, TNFα blockers (adalimumab, 2 sc injections) failed to demonstrate any clinical improvement.
Trial registration clinicaltrials.gov Identifier: NCT00597623

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RECOVERY OF FUNCTION FOLLOWING HIP RESURFACING: A RANDOMISED CONTROLLED TRIAL COMPARING A TAILORED VERSUS STANDARD PHYSIOTHERAPY REHABILITATION PROGRAMME

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Purpose: To identify if a tailored rehabilitation programme is more effective than standard practice at improving function in patients

undergoing metal-on-metal hip resurfacing arthroplasty (MOMHRA). Currently there is little evidence-based guidance on the rehabilitation of patients with hip resurfacing. Previous work suggests that there is frequently persistent muscle weakness and poor functional mobility.
Methods: Single blinded randomised control trial. Setting: Hospital trust specialising in orthopedic surgery. Participants: 80 patients undergoing elective hip resurfacing arthroplasty(MOMHRA). Intervention: Physiotherapy exercise programme tailored to hip resurfacing, delivered in an out-patient setting. Comparison group of standard hip arthroplasty rehabilitation.
Main Outcomes: Oxford Hip Score (OHS), secondary measures of Hip disability and Osteoarthritis Outcome Score (HOOS), UCLA activity score, and EQ 5D. Hip range of motion, hip muscle strength and patient selected goals were also assessed. Measures were recorded at baseline and at 6, 16 and 52 weeks after surgery.
Results: Linear regression model, adjusted by baseline OHS, detected a 5.8 unit change in OHS at 52 weeks when the exposure group moved from control to treatment ($p=0.001$); effect size 0.76. There was a statistically significant increase in HOOS of 12.4 at 52 weeks ($p<0.0005$); effect size 0.76 when comparing the treatment and control groups. The UCLA activity score showed an increase of 0.66 ($p=0.019$); effect size 0.43 in favour of the treatment group at 52 weeks. The EQ5D summary index increased by 0.85 ($p=0.005$); effect size 0.76 at 52 weeks when moving from the control group to the treatment group. Hip flexion (increase of 17.9, $p<0.0005$) and hip extension (increase of 5.7, $p=.004$) also showed a marked improvement between the treatment group and the control group. Muscle strength improved more in the intervention group but was not statistically significant. Eighty percent (32 of 40) of the intervention group fully met their self-selected goal compared to 55% (22 of 40) of the control group.
Conclusions: A simple tailored exercise programme resulted in marked increases in hip range of motion and self reported function than the previous conventional rehabilitation programme. A change in the emphasis of post-operative rehabilitation could improve outcome for patients after hip resurfacing arthroplasty

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TISSUEGENE-C (TG-C) IN PATIENTS WITH OSTEOARTHRITIS: A PHASE IIB CLINICAL STUDY

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Purpose: TG-C is a cell mediated gene therapy that contains non-transduced (hChonJ) and transduced (hChonJb$^{\#}$7) human allogeneic chondrocytes. The hChonJb$^{\#}$7 cells were transduced with TGF-β1 gene-containing retroviral vector.
TG-C has been tested in Phase I and Phase IIa clinical studies in osteoarthritis patients and has proved its safety and efficacy in the patients.
Methods: In the current study, the placebo-controlled, randomized, single blind phase IIb trial was conducted to determine both safety and efficacy in patients with knee osteoarthritis. Participants ($n = 54$) with a confirmed diagnosis of knee osteoarthritis by X-ray and MRI were randomized into the treatment group (TG-C, $1.8x10^7$cells/knee, $n = 27$) and the placebo group (saline, $n = 27$). The primary evaluation parameter was International Knee Documentation Committee (IKDC) which measures pain, sports activities, and daily function. The secondary evaluation parameters were Western-Ontario and MacMaster University (WOMAC) score, Knee Injury and Osteoarthritis Outcome Score (KOOS), and 100 mm Visual Analogue Scale (VAS). These parameters were assessed at 12 and 24 weeks post treatment. Additionally, the changes in biomarkers were assessed in serum and urine samples. Safety measures, including physical exams, complete blood count, and serum chemistry were included up to 6 months post treatment. Blood samples were screened to detect the replication competent retrovirus, TGF-β1 DNA and protein starting from 2 weeks up to 6 months post treatment.
Results: TG-C treatment group showed improvement in IKDC, WOMAC, KOOS and 100 mm VAS scores compared to placebo group as shown in table 1.
Conclusions: In summary, the current Phase IIb study indicated that TG-C treatment improved the evaluation criteria for pain, sports activities, and quality of daily life in patients with knee osteoarthritis when compared to the placebo group.

Table 1
Changes in Scores of the Primary and the Secondary Evaluation Parameters at 6 months post t.

	TG-C	Placebo	P values
IKDC	18.1±14.3	8.5±11.0	p<0.01
WOMAC	-15.4±16.7	-6.9±13.6	p<0.06
KOOS	-25.6±23.6	-14.3±18.1	p<0.02
VAS	-27.3±25.6	-11.7±18.0	p<0.05

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DIFFERENT RECOVERY GROUPS 2 YEARS AFTER TOTAL KNEE ARTHROPLASTY

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Purpose: Patients early after total knee arthroplasty (TKA) have performance-based activity limitations. Performance-based measures are more responsive to change than patient-reported outcomes; No studies have investigated clinically significant change relative to return to normal ranges and minimal amount of change. The purpose of this study was to quantify clinical significant change in the Timed Up and Go (TUG) and Stair Climbing Test (SCT) up to two years after TKA.
Methods: One hundred twenty-one patients (40% women) started a progressive quadriceps strengthening program four weeks after TKA. All patients received 6 weeks of physical therapy. Patients completed the TUG and SCT after the intervention (baseline) and one and two years after TKA. ANOVA was used to determine change over time. Using healthy age- and sex-based normative data for the TUG and SCT, patients were classified into different recovery groups based on the Jacobson method: "Recovered"-exceed the age- and sex-based cutoff for knee function within normal ranges at baseline and maintained this at 2 years, "Improved to Recovered"-exceed the cutoff score at 2 years and had a reliable change index (RCI) greater than or equal to 1.96 for the change in Z-scores from baseline to 2 years, "Improved"-RCI was greater than or equal to 1.96 but they did not exceed the cutoff score, "Unchanged" -did not exceed the cutoff score and their RCI was between 1.96 and -1.96, and "Deteriorated" -did not exceed the cutoff score and their RCI was less than -1.96.
Results: TUG and SCT scores improved over time ($p<.001$) (Table 1). For the TUG and SCT, between 34.8-39.7% of patients were classified as either "Recovered" or "Improved to Recovered" two years after TKA (Table 2). However, between 46.8-52.0% did not improve or deteriorated two years after TKA (Table 2). Interestingly, for the TUG, the "Deteriorated" group was stable up to one year but worsened between one and two years (Figure A). The "Improved" group had significant changes between 3 months and one year and then plateaued (Figure A). A different pattern was seen for the SCT. The "Deteriorated" times slowed at each time period, whereas, the "Improved" group times were faster at each time period (Figure B).
Conclusions: A substantial number of patients had clinically significant improvement or had scores within the healthy range two years after TKA. However, close to half the patients did not improve or deteriorated by two years. Factors such as increased BMI or symptoms in the nonsurgical limb may contribute to the lack of improvement or decline in function in some individuals.