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IDENTIFYING SUBGROUPS OF AFRICAN AMERICAN PATIENTS WITH DIFFERENTIAL IMPROVEMENT FOLLOWING A PAIN COPING SKILLS TRAINING PROGRAM FOR OSTEOARTHRITIS

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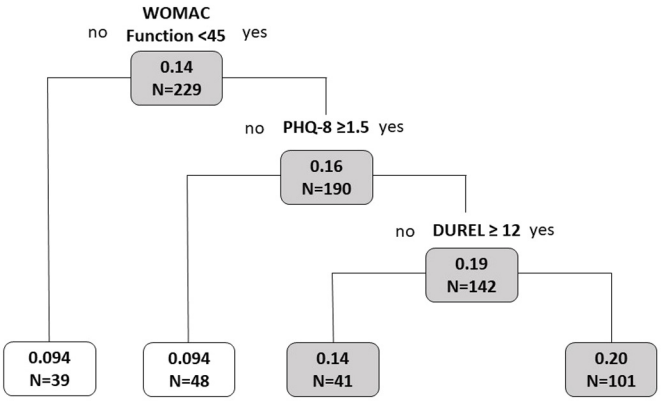
Purpose: To identify subgroups of African American patients with knee or hip osteoarthritis (OA) for which those randomized to a Pain Coping Skills Training (PCST) program have greater improvement than those randomized to wait list (WL) control group.
Methods: Participants were from a randomized clinical trial comparing a culturally tailored PCST program (N=124) with WL control group (N=124). Study sites were one Department of Veterans Affairs Medical Center and one university-affiliated health care system. The PCST program involved 11 weekly telephone calls delivered over about 3 months. This analysis used Virtual Twins (VT; VirtualTwins R package), a regression tree-based method that searches for cutpoints of predictor variables where the differential treatment effect exceeds a pre-specified threshold. We created a clinical improvement outcome by dichotomizing change in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score between baseline and 3-month follow-up based on achievement of a clinically relevant 10% improvement. In VT, we set 10% or greater threshold for difference in rate of improvement between PCST and WL for subgroup identification, minimum sample size of node to 30 and max depth of trees to 3. Empirical Bayes estimates from linear mixed effects models were used to generate dichotomous improvement outcome for participants with missing follow-up WOMAC pain scores. Baseline characteristics for potential subgroup identification were: study site, sex, age, marital status, education level (some college vs. lower) financial status (able to live comfortably vs. not), body mass index (BMI), number of comorbidities, WOMAC pain, WOMAC function, Duke University Religion Index (DUREL), depressive symptoms (Patient Health Questionnaire-8; PHQ-8), total coping attempts, pain catastrophizing, PROMIS pain interference and arthritis self-efficacy. Participants with missing baseline characteristics were excluded (n=19; n=8 in PCST and n=11 in WL).
Results: Participants were 49% female, the mean age was 59.0 years (standard deviation (SD)=10.3), and the baseline total WOMAC score was 53.0 (SD=17.8). Figure 1 shows subgroups identified by the VT method. Two subgroups were identified that met the 10% or greater threshold for difference in rate of improvement between PCST and WL. Both groups had WOMAC function scores <48 (indicating low to moderate functional limitations; maximum score=68) and PHQ-8 scores >1.5 (indicating having at least some self-reported depressive symptoms). The group with the largest difference in improvement between PCST and WL had higher (>12) scores on the Intrinsic Religiosity subscale of the DUREL (maximum score=15).
Conclusions: Multidimensional subgroups defined by baseline WOMAC function, depressive symptoms and religiosity predicted response to a PCST program among African Americans with OA. These exploratory analyses suggest that a "profile" of patients who may respond best to PCST have low to moderate functional limitations (vs. severe limitations), some depressive symptoms, and a higher degree of perceived intrinsic religiosity. However, a subgroup that had lower scores on perceived intrinsic religiosity also met the 10% or greater threshold for difference in rate of improvement between PCST and WL. These results are exploratory but suggest there may be subgroups of African American patients with OA who experience greater benefit from PCST. Further research in this area may help to guide targeted dissemination of PCST. In particular, it would be useful to understand more about why participants with lower physical function improved less and whether specific adaptations in pain CST programs may result in better response among individuals with the most severe functional limitations.



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RESPONDERS TO EXERCISE THERAPY IN PATIENTS WITH OSTEOARTHRITIS OF THE HIP: A SYSTEMATIC REVIEW AND META-ANALYSIS

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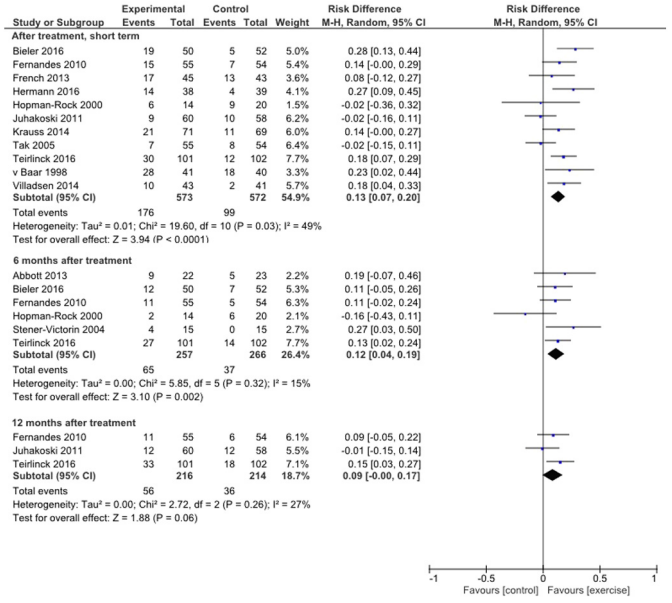
Purpose: The main aim of this study was to evaluate the effect of exercise therapy in patients with osteoarthritis of the hip, according to the response to therapy as formulated by the OMERACT-OARSI criteria.
Methods: This study is a secondary analysis of a meta-analysis of studies on the effect of exercise therapy in patients with osteoarthritis of the hip (hip OA). In 2016, our department was asked by the National Health Care Institute of the Netherlands to update the existing evidence of three Cochrane reviews on the effect of exercise therapy in patients with hip and knee OA. This because the Minister of Health, Welfare and Sports wanted to evaluate if exercise therapy for hip and knee OA should be added to the basic health insurance in the Netherlands. For the present study, we selected studies with adult patients with clinical and/or radiological hip OA. The studies compared exercise therapy by a physical therapist (not in combination with other interventions) to minimal or no treatment (usual care by a general practitioner, education, waiting-list, home-based exercises or no treatment). Other control treatments that were seen as 'active' physical treatments were excluded. Literature search was done using the search terms of the original Cochrane reviews from date of last search until the first of August 2016. Selection of studies, risk of bias assessment and data extraction was done by two review authors independently; a third review author was asked in case of no consensus. The Cochrane risk of bias tool was used in the risk of bias assessment. A standardized list was used to extract the data from each study. Data on pain, function, quality of life, total hip replacements, medication and adverse effects post-treatment and long-term (more than 6 months after treatment) were collected. In addition, we contacted all authors of included studies and ask them to calculate the number of responders and non-responders to treatment as defined in the OMERACT-OARSI criteria post-treatment and at 6 and 12 months after treatment. These data were used to perform a meta-analysis in Review Manager 5.3, using a random-effect model. Statistical heterogeneity was calculated with I^2 tests. A risk difference (RD) with a 95% confidence interval was calculated.
Results: Fifteen studies were included, of which one already reported the number of responders. All other authors were asked to calculate the number of responders in their data. Thirteen of them provided these data, so in total 14 studies could be included in our meta-analysis. Post-treatment, the RD of responders between the patients who received exercise therapy and the patients who received no or minimal intervention was 0.13 (95% CI 0.07, 0.20), (11 studies, 1145 patients; $I^2 = 49\%$). At 6 months after treatment, the RD = 0.12 (95% CI 0.04, 0.19), (6 studies; 523 patients, $I^2 = 15\%$), and at 12 months after treatment, RD = 0.09 (95%CI -0.00, 0.17), (3 studies; 430 patients, $I^2 = 27\%$).

Conclusions: For the outcome responders to therapy, defined by the OMERACT-OARSI criteria, a small and statistical significant effect was seen for exercise therapy compared to no or minimal intervention in patients with hip OA post-treatment. The risk difference of 0.13 means that 7.7 patients should receive exercise therapy to gain one responder. At 6 months after treatment this small effect was still visible, but no effect was seen anymore at 12 months after treatment. More (sensitivity)analyses will follow to gain more insight in the reasons for this small effect, like type of exercise therapy, compliance, patient selection, or the definition of responder criteria itself.



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CLINICAL-LIKE CRYOTHERAPY IMPROVES GAIT FUNCTION AND REDUCES SYNOVIAL INFLAMMATION IN RATS WITH KNEE OSTEOARTHRITIS

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Purpose: To evaluate the effects of clinical-like cryotherapy on gait function and synovial inflammation in rats with knee osteoarthritis (KOA) induced by anterior cruciate ligament transection (ACLT).
Methods: The experimental protocol was in accordance with the National Guide for the Care and Use of Laboratory Animals (National Research Council, 1996). All procedures were approved by the institutional Ethics Committee and conducted by trained professionals blinded to the identity of the experimental groups. Two-month-old male *Wistar*rats (n=32; 297±25 g) were studied. The animals were housed in pathogen-free conditions at 24ºC±1°C under a reverse light cycle (12/12 light/dark) with free access to standard rat chow and water. Animals were randomly allocated into four groups (n=8 per group): Control (without surgery and intervention); ACLT knee surgery (KOA); ACLT knee surgery submitted to ice pack (KOA+Cryotherapy), and ACLT knee surgery submitted to a sand pack (KOA+Placebo). An adapted ACLT-induced KOA model was used. The groups were analyzed one day before and 60 days after ACLT surgery from the least to the most stressful tests: skin temperature (thermography), gait test (paw print), thermal response threshold (hotplate) and swelling (digital caliper). Next, both the KOA+Cryotherapy and KOA+Placebo groups underwent the interventions (ice pack or sand pack) twice a day, for 20 min each, over five consecutive days (from the 61st to the 65th days). The four groups were then assessed on the 66th day, and after euthanasia, the synovial fluid (account of leukocytes and cytokine levels) and synovial membrane (histopathological analysis) were collected (Figure 1).
Results: Among the KOA groups, only the Cryotherapy group increased their paw contact area (P=0.004; 14%) after interventions, with no difference in relation to the Control group [Figure 2(A)]. Cryotherapy decreased the number of leukocytes (P<0.001; ≥95.0%; Figure 3) and cytokine levels (P<0.001; ≥55%; Figure 4) in synovial fluid in relation to the KOA and Placebo groups. There were no differences in synovial score and fibrosis in the synovial membrane of KOA groups.
Conclusions: Clinical-like cryotherapy improves the gait function and reduces the number of leukocytes and inflammatory cytokines in synovial fluid of rats with ACLT-induced KOA. These results provide new evidence of the beneficial effects of cryotherapy and suggest it can be used as a non-pharmacological and complementary treatment to control joint inflammation of KOA.