

Protocol NCT02413996 clinicaltrials.gov

Document Date: March 6, 2014

Title: Effects of early Virtual Reality-based Rehabilitation in Patients with Total Knee Arthroplasty: a randomized controlled trial

AIM

We aim to compare the efficacy of early rehabilitation with virtual reality (VR) via the Virtual Reality Rehabilitation System (VRRS) versus traditional rehabilitation in improving functional outcomes after primary TKA.

METHODS

We will design a two-armed, single-blind, parallel, and superiority randomized controlled trial (RCT). The protocol is approved by the San Raffaele Hospital Ethic Committee in Milan (06/03/2014), registered with clinicaltrials.gov (NCT02413996) and strictly follow good clinical practice guidelines and the tenets of the Helsinki Declaration.

Informed, written consent will be obtained prior to participation. The study reporting followed the CONSORT statement and its extensions ^{1,3,4}.

Subjects will be allocated to treatment group according to a simple computer-generated randomization chart. An independent physician of the rehabilitation ward will assign the subjects to interventions. Assessors will be blinded to the interventions; due to the nature of the interventions, blinding of patients and physiotherapists will be impossible to maintain. An independent consultant will provide the statistical analysis.

We firstly expected to enroll 142 patients based on a pilot small study. However, in agree with our ethical committee, we subsequently amended the sample size according to a recent trial ⁵ based on a similar PICO (participants, interventions, comparisons, outcomes) methodology. The primary outcome will be the visual analogue scale (VAS) for pain score (0 to 100 points, wherein 0 denotes no pain). Based on an expected effect at 10 days in the control group of a reduction of 20.4 points on the VAS score, we assumed a common standard deviation (SD) of 25.8, a 5% type I error and a 10% type II error and a significant absolute difference of 20.3 points between the experimental and the control group while taking into account a 20% dropout rate from the whole sample. For this, a total sample size of 84 subjects will be planned.

Study setting and Participants

Participants will be recruited at the Rehabilitation Department, IRCCS Orthopedic Institute Galeazzi, Milan. Eligible participants will be adults between 45 and 80 years old who had undergone primary unilateral TKA for knee osteoarthritis and given written, informed consent to participate in the study. Exclusion criteria will be: previous orthopedic surgery on the same side (e.g., hip arthroplasty), unstable health condition (e.g., heart or lung disease), pregnancy, assumption of psychotropic drugs.

Interventions

Subjects will be randomly allocated 3-4 days after TKA to one of two rehabilitation groups: experimental (VR rehabilitation) or control (traditional rehabilitation). In addition, both groups will perform passive knee motion on a Kinetec® knee continuous passive motion system (Rimec, Chions, Italy) and functional exercises (stair negotiation and level walking) daily for 60 minutes on at least 5 days.

Outcomes

The primary outcome will be the absolute change in pain score as measured in 100 mm on a VAS ⁷. The secondary outcomes will be: knee disability as assessed by the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) ², which consists of 24 items divided into 3 subscales investigating pain, knee joint stiffness, and physical function; health-related quality of life (HRQoL) as assessed by the EuroQol five-dimensional (EQ-5D) questionnaire ⁸; the global perceived effect (GPE) as assessed by the GPE score ⁶; the Functional Independent Measure (FIM) as assessed by the FIM questionnaire ¹⁰; the frequency of medication assumption; the isometric strength of the quadriceps and hamstring muscles as assessed using a dynamometer, the knee active range of movement (ROM) measured by a goniometer and the proprioception assessed using the stabilometric platform of the Virtual Reality Rehabilitation System (VRRS). In particular, we will measure the percentage value of similarity between the trajectory points of an ideal healthy person's and the patient's center of pressure movement during the reaching test, a different task respect to the proprioceptive exercises proposed in the training of the experimental and control groups. All outcomes will be recorded at baseline and then at discharge (around 10 days after surgery).

Statistical methods

Demographic characteristics will report absolute and relative frequencies for categorical variables, and as mean with standard deviation (SD) for continuous variables. We plan to analyze continuous variables testing each outcome assessment with the Shapiro-Wilk test, and to use parametric methods for significance testing (i.e., t-test). Chi-square tests will be used to assess significant associations between categorical variables. In addition, we plan to apply a multivariate analysis of covariance (ANCOVA) with decrease in VAS as response variable to adjust for demographic characteristics (i.e., patient gender and age), and for baseline VAS pain scores. All analyses will be performed by an independent researcher using STATA statistical software, version 15⁹.

Role of the funding source

The funding sources has no controlling role in the study design, data collection, analysis, interpretation, or report writing. The corresponding author is responsible for the decision to submit the manuscript for publication.

Conflicting interests

The authors declare that they have no competing interests.

Funding

The work is supported by the Italian Ministry of Health for Conto Capitale 2012 (PCC-2012-2353895).

References

1. Altman, D.G., Schulz, K.F., Moher, D., *et al.* The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Annals of internal medicine* **134**, 663-694 (2001).
2. Bellamy, N., Buchanan, W.W., Goldsmith, C.H., Campbell, J. & Stitt, L.W. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *The Journal of rheumatology* **15**, 1833-1840 (1988).
3. Boutron, I., Altman, D.G., Moher, D., Schulz, K.F. & Ravaud, P. CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: A 2017 Update and a CONSORT Extension for Nonpharmacologic Trial Abstracts. *Annals of internal medicine* **167**, 40-47 (2017).
4. Boutron, I., Moher, D., Altman, D.G., Schulz, K.F. & Ravaud, P. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of internal medicine* **148**, 295-309 (2008).
5. Goto, K., Morishita, T., Kamada, S., *et al.* Feasibility of rehabilitation using the single-joint hybrid assistive limb to facilitate early recovery following total knee arthroplasty: A pilot study. *Assistive technology : the official journal of RESNA* **29**, 197-201 (2017).

6. Kamper, S.J., Ostelo, R.W., Knol, D.L., Maher, C.G., de Vet, H.C. & Hancock, M.J. Global Perceived Effect scales provided reliable assessments of health transition in people with musculoskeletal disorders, but ratings are strongly influenced by current status. *Journal of clinical epidemiology* **63**, 760-766 e761 (2010).
7. Norkin C, W.J. *Measurement of joint motion: a guide to goniometry*, (F. A. Davis Company, 1995).
8. Scalone, L., Cortesi, P.A., Ciampichini, R., *et al.* Italian population-based values of EQ-5D health states. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research* **16**, 814-822 (2013).
9. Stata-IC. Stata Statistical Software, v 15. College Station, TX: StataCorp LLC. (2017).
10. Tesio, L., Granger, C.V., Perucca, L., Franchignoni, F.P., Battaglia, M.A. & Russell, C.F. The FIM instrument in the United States and Italy: a comparative study. *American journal of physical medicine & rehabilitation* **81**, 168-176 (2002).