REVIEW PROTOCOL

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1. ADMINISTRATIVE INFORMATION

Title

Virtual Tools for Total Knee Replacement Rehabilitation: a Protocol for a Systematic Review

Ethics and funding:

As this is a review of the existing literature, the informed consent of the participants is not required. The authors certify that they have no financial connection or commitment in any organization or entity with a direct economic interest in the matter or matters addressed in this work.
Protocol modifications

Any substantial modifications that occur in this protocol will be registered in PROSPERO and will be documented in the final publication.

Author’s contribution

JMB participated in the original idea, as well as in drafting of the manuscript, developed the selection criteria, developed the search strategy and provided the experience in rehabilitation of Total Knee Replacement (TKR) and made the methodological proposal for the review. AO and MCB will participate in the methodological quality assessment strategy, risk of bias assessment, data extraction and analysis. CI provides experience in physiotherapy of the aged for acceptance of the original idea, background and discussion, including writing and interpretation of results, as well as methodological criteria. All authors read, corrected, and approved the final protocol manuscript.

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2. INTRODUCTION

Rationale

The most common symptoms of knee osteoarthritis include joint pain, muscle atrophy, limited mobility, functional impairment and a deficit in the proprioceptive system [1]. In the more advanced stages of the condition, the solution usually consists
of a total knee replacement (TKR) procedure due to the benefits this entails [2]. In recent decades, TKR has become a common procedure and has also aroused the interest of researchers regarding patient outcomes after surgery. Indeed, more than 700,000 TKR interventions are performed every year in the United States of America [3], while the demand for TKR surgery is expected to exceed three million by year.

Rehabilitation following total knee replacement has been focused on reducing pain, restoring muscle and joint function through strengthening exercises and improving balance with balance and proprioceptive exercises [4]. In addition, it is possible to find studies in the literature evaluating task-oriented exercises including sensorimotor, neuromuscular or high intensity trainings [5].

In the last few years, technological devices, virtual reality tools and computer-based games have received growing interest from researchers and clinicians. Their application in different fields, including neuroscience, physical training and rehabilitation, has become more common. Focusing on the rehabilitation area, several studies have already evaluated and tested the effects of these technological devices for the training of neurological patients, for instance with Parkinson disease [6] and mainly after stroke [7] due to their specific capabilities for balance training, but also with other pathologies such as hemophilia [8]. Taking into consideration the high prevalence of TKR procedures, in this work it will be determined if the use of virtual tools are also reliable for the rehabilitation of orthopedic patients.

Virtual reality tools have been used because of their ability to provide a standardized, reproducible and controllable environment. Indeed, they may in fact be attractive and even amusing for patients. This could lead to a higher adherence to the rehabilitation program, with consequent benefits for the patient’s health. In addition to their entertaining and motivating properties, low-cost devices allow for easy access and
may be used at home, which may help to reduce the need for patients to go to hospital facilities [7]. This may be especially convenient for those patients with some degree of dependence or those living in rural areas and therefore far from hospitals. In addition, virtual tools would allow for training prior to surgery and also to keep the training program at home after traditional hospital rehabilitation. Importantly, all of the mentioned aspects may produce a consequent reduction in healthcare costs.

This systematic review aims to determine if the current literature demonstrates the effects and reliability of the use of virtual tools for the rehabilitation, treatment, training and assessment of patients with severe knee osteoarthritis that have undergone or will undergo TKR.

**Virtual Tools and Technology**

In this review, virtual tools refer to those hardware devices may or may not have been specifically designed for rehabilitation, training or assessment purposes (i.e. computers), but which include a software development presenting a simulated environment oriented towards interacting with the patient by means of a user interface. The software may be standardized, semi-custom or custom designed, but specifically used for rehabilitation, training or assessment purposes. Examples include well-known exercise-based games (exergames) adapted for this end, like Microsoft Kinect® or Nintendo Wii®.

**Other Reviews**

Several reviews have already assessed the use of virtual tools in different rehabilitation programs [7] [9]. This is the first review evaluating the use of such tools for the training and rehabilitation of patients with severe knee osteoarthritis that have undergone or will undergo TKR surgery.
**Review questions**

The present systematic review aims to answer the following questions.

Are virtual tools used for the training and rehabilitation of patients that have undergone or will undergo TKR? Are such virtual tools beneficial in the training methods of the patients mentioned? If so, what are the effects of these tools in TKR rehabilitation?

In addition, we wish to answer these questions: are they safe? And, may they be used to assess TKR outcomes?

**Objectives**

- Search and identify tools used for the training and rehabilitation of TKR patients.
- Determine if virtual tools may produce positive effects in the TKR patient recovery, in aspects like functionality, pain, balance, function, falls or quality of life.
- Determine if they a reliable and safe tools to be used with orthopedic patients, whether at hospitals or at home.
- Verify if these or other tools are being used to assess TKR outcomes.

3. **METHODS**

This review has been planned prospectively and will be carried out according to the proposed protocol methods in which all the items suggested in the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [10] have been collected. The results presentation will be done in accordance with the Main Item
Guidelines that should be reported for systematic reviews and meta-analysis (PRISMA) [11]

3.1 **Eligibility criteria**

- We will include participants with severe knee osteoarthritis that have undergone or will undergo TKR surgery.
- We will include studies with participants that took part in a rehabilitation training protocol with a virtual tool.
- We will include studies assessing the effects produced by training performed with a virtual tool.
- We will include studies assessing TKR outcomes with a virtual tool.
- No restriction about the age of participants will be made.
- We will include randomized clinical trials for quantitative synthesis.
- Observational studies may be considered to be included only for contextualization with contemporary literature, discussion and qualitative synthesis. Case reports will be excluded.
- Published from inception.
- Published in the English or Spanish language.
- No geographical considerations will be made.

3.2 **Information sources**

- Sources in the English language: Medical Literature Analysis and Retrieval System Online (MEDLINE), Web of Science (WOS), Physiotherapy Evidence Database (PEDro), Scopus, Embase and Cochrane.
- Sources in the Spanish language: Índice Médico Español (IME), Índice Bibliográfico Español en Ciencias de la Salud (IB ECS), Medicina en Español
(MEDES), base de datos de Enfermería, Fisioterapia y Podología (EnFisPo) and Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS)

- In addition, unpublished and ongoing trials (clinicaltrials.gov) and ongoing reviews (PROSPERO), as well as relevant record databases, and books will be searched and used.

3.3 **Search strategy**

The PICOs strategy will be used [12] to formulate the preliminary search strategy, that is, the conditions that the works must fulfil will respond to four aspects: Patients (P), Intervention (I), Control (C) and Outcomes (O), based on the criteria established in the corresponding section of this protocol.

- **P** (patient-participant): knee osteoarthritis, total knee replacement.
- **I** (intervention): TKR, virtual reality, tool, game, video, application, rehabilitation, and training.
- **C** (comparator): control group - no control group.
- **O** (outcomes): any outcome assessing the effects of the intervention in terms of functionality, self-reported functionality, balance, pain, anxiety, falls or quality of life.

3.4 **Study records**

**Data management**

Literature search results will be saved at Excel spreadsheet. Thus, duplicate articles will be removed. Zotero program (https://www.zotero.org) will be used to cite the reports.
Selection process

Two independent reviewers will screen the databases using the search strategies before mentioned. In a first stage articles that, based on the title and abstract, seems to meet inclusion criteria, will be pre-included and their full text version will be get. With the full text version, all the articles will be double-checked and those that do not meet inclusion criteria will be excluded. Once this stage has finished, the reviewers will put in common and discuss the results. In case of disagreement, a third author will be consulted.

Data selection process

The articles finally considered to be included will be collected in a common Excel spreadsheet. Relevant information about article will be shown in that document and all the authors of the review will be able to both consult and edit the document. In case of some relevant information of an article is missing, the author of the study will be contacted to resolve the questions and complete the missing information.

3.5 Data extraction and management

The texts will be screened first by title and abstract. Then they will be assessed for eligibility those selected after an in-depth reading. Two independent persons will put together results and compare. A standardized and predefined Excel spreadsheet will be used.

Articles finally included will be analyzed following structure: ID of the study, ID in PubMed or DOI, author, year, study design, intervention, control group training, and outcomes in balance and fall prevention.

We will seek to detect and quantify the virtual tools used to train and assess TKR patients. In addition relevant information will be collected. We understand for relevant
information that related to study and intervention design and outcomes, including the number of participants and sample descriptors, blinding, interventions and timeline, duration of the sessions and frequency, as well as assessment times, follow-up, and completion rate of the study. All the outcomes used by the trials to assess patients and progression will be extracted if they refer to functionality, pain, function, balance, strength or quality of life. All the results are planned to be drawn as the mean and the standard deviation with their level of significance, confidence intervals, or in case of they are marked as risk or odds ratios too. If effect sizes are available, or some information provided by the study deemed relevant, it will be extracted for the subsequent analysis and interpretation of results. Results obtained at each point of the study will be extracted.

It is planned to request not available data to the authors of the studies in the event that they are deemed necessary.

All data extracted will analyzed and discussed by 2 independent reviewers. One review author will extract the data from included studies and the second author will check the extracted data. Assessment and disagreements amongst reviewers will be resolved by consensus; if no agreement could be reached, a third author will decide.

3.6 Outcomes and prioritization

Primary outcome

One of the main objectives of TKR is to reduce pain and restore the patient’s knee functionality. Functionality is widely used to assess the achievement of complete rehabilitation, as well as an important predictor [13], especially taking into account the high percentage of patients showing functional impairments after surgery. In most of the
trials related to TKR, self-reported functionality is established as the primary outcome [14]

**Secondary outcomes**

Secondary outcomes that may be considered include physical function, balance, pain, quality of life, anxiety and incidence of falls.

In the case of the absence of results of some parameter, it must be reflected in the articles and with the reason explained. Parameters used to assess the outcomes will be critically evaluated by the two authors independently, considering that there exists evidence to support their validity and reliability. It is required for any outcome that the studies included in the review assessed those measures at least at two different times (baseline and endpoint). Results must have a comparison between the different groups and the differences among them.

**Outcomes description**

- Self-reported functionality: According to a recent review [14] this outcome may be reported with different scoring systems or scales, such as the Knee Society Score (KSS) [15] the Knee disability and Osteoarthritis Outcome Score (KOOS) and the Hip disability and Osteoarthritis Outcome Score (HOOS) activity daily live sub-scales (ADL), and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) functionality subscale [16]. For this reason, these shall be considered with results extracted regarding self-reported functionality.

- Balance: This outcome could be measured with different validated and reliable scales, according to different aspects in terms of balance [17]. Hence, results in balance will be considered when the patients’ performances are reported with validated scales to assess (1) the overall state of balance, (2) the static and (3) the dynamic balance
capabilities, or (4) as those balance performances measured with a dynamometric platform or virtual tools.

- Physical function: measured in terms of the joint range of movement (ROM) or muscle strength.

- Pain: this outcome may be considered when reported with the visual analogue scale (VAS). Pain subscales of the self-reported outcomes WOMAC, HOOS and KOOS [18] will be also considered.

- Incidence of falls: Articles reflecting the total number of falls during a specific period of time.

- Anxiety: Mainly related to preoperative expectations, for instance assessed in terms of the Euro Quality of Life Five Dimensions (E-QoL-5D) [19] anxiety dimension, a Visual Analog Scale or some validated procedure.

- Quality of life: This outcome will be considered when measured with validated self-reported health-related scales [20], for instance the 36-item short-form health survey (SF-36) or the WOMAC, HOOS, and KOOS quality of life sub-scales, as well as the Euro Quality of Life Five Dimensions.

3.7 **Risk of bias of individual studies**

To facilitate the assessment of possible risk of bias in individual studies we will use the Cochrane Risk of Bias Tool (http://methods.cochrane.org/bias/assessing-risk-bias-included-studies). The sources of bias assessed by this tool are: selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. A result table with the rationale and criteria for judgement will be reported or included in appendix. Studies will be catalogued as high, low or unclear risk of bias. This
judgement will be made independently by the two investigators, while a third investigator will be asked in case of disagreement. A table or appendix will be provided detailing the judgement criteria.

3.8 **Synthesis of results**

Results will be provided in a descriptive way. If there are sufficient included studies (randomize clinical trials), a traditional meta-analysis will be conducted. Comparisons of outcomes are planned to be done with the statistical methods like Mantel-Haenszel for random effects model, and the effect measure will be the mean, standard deviation and sample size with a confidence interval of 95% for each study. The summary value for each study will be given and represented in forest plots. Heterogeneity measures will be calculated with $I^2$ statistics. Meta-analysis is planned to be done for the primary outcome measures provided by the trials. If possible, subgroup analysis will be conducted with the outcomes more frequently reported, according to the outcome categories described in this protocol.

3.9 **Meta-biases**

Publication bias across studies is planned to be assessed with Funnel plots and Egger’s/Begg’s test [21], only if there are sufficient items to extract reliable results (i.e. over 5). Empirical methods may be used otherwise.

3.10 **Confidence in cumulative evidence**

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [22] might be used if deemed appropriated. This would aim to assign the quality of evidence of all outcomes. If the results are displayed, we will judge and fit them in one of the four grade scores reflecting the quality of the evidence: high,
moderate, low or very low-quality evidence [11]. The factors used to assign the results into one of these four grades will be: risk of bias, indirectness of evidence, inconsistency, imprecision of effect estimates and potential publication bias [23].

4. DISCUSSION

The results obtained from the selected works will be analyzed to extract conclusions that answer the questions formulated in the introductory section. Once the results are analyzed, they will be compared to similar studies in terms of findings agreement and disagreement. Differences will be explained and discussed.

Study aspects that may contribute with more reliability and validity will be reported. By contrast, those aspects that may be a source of bias will be also reported.

Based on the evidence obtained from the analyzed results, new recommendations for clinical applications will be presented.

5. REFERENCES


[18] G. H. Bock and e. al., "Osteoarthritis pain assessment in family practice."


