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STUDY PROTOCOL OF A MULTI-STAGE RANDOMISED CONTROLLED STUDY FOR THE ASSESSMENT OF POSTOPERATIVE THERAPEUTIC PROCEDURES AFTER TOTAL KNEE ARTHROPLASTY

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ABSTRACT

Background: There continues to be a lack of evidence to support physiotherapeutic rehabilitation measures after total knee arthroplasty (TKA), especially in the area of functional test procedures, which are indispensable for assessing perioperative physiotherapeutic interventions, including their efficacy.

Objective: A multi-stage randomized controlled study design is concerned with the establishment of an evidence-based perioperative physiotherapeutic treatment programme to evaluate physical functional test procedures with regard to their predictive value and the efficacy of physiotherapeutic interventions.

Setting: The RCT will be realized in a medical clinic in the department of orthopaedics, sports medicine and rehabilitation.

Participants: A first stage will include young, healthy subjects (Group A) and subjects who are due to undergo TKA and are then to be treated with a standard rehabilitation programme (Group B).

Design: Selected promising physical functional test procedures will be tested for their reliability. Inter-tester reliability will be determined in Group A. The test-retest reliability at different perioperative timepoints will be determined in Group B.

Measurements: The following test procedures will be investigated for reliability: 10-m walk test, timed up and go, three times sit to stand, the isometric maximal force of knee extension, stair climbing and the cumulative leg circumference. In addition, these test procedures will be correlated with each other and with the WOMAC and KSS for selected aspects of validity. In a second stage, the reliable test procedures will be applied to investigate selected promising physiotherapeutic interventions.

Conclusions: The investigation could change perioperative assessments and physiotherapeutic treatment in patients who have undergone TKA.

Keywords: Total Joint Replacement, knee, arthroplasty, Patient related outcomes, functional outcomes, trial.

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INTRODUCTION

The factors affecting the outcome of total knee arthroplasty are complex. Both patient-dependent and patient-independent factors determine the final result.

The connection between clinical course and mechanical functionality of the artificial joint is generally recognized. The association between the alignment of the implant components, on the one hand, and the probability of revision [1], joint stability [2], the postoperative pain level [3] and functionality [4], on the other, has been clearly demonstrated in numerous studies.

A global increase in total knee arthroplasty (TKA) is clearly apparent. An increase in total knee arthroplasties of 29-63 percent was observed in the member states of the OECD between 2005 and 2011, a trend that is likely to continue [5,6]. For the assessment of functional outcomes, questionnaires are used more often than motor tests, which measure the range of motion, but also provide test results for muscle strength, balance and walking capacity. Symmetry and balance, walking capacity, strength, and stair climbing are primarily used for the objective assessment of physical functions. They are referred to and applied as the gold standard [7,8]. Static or dynamic dual-scales tests are used for assessing symmetry.

Prosthesis alignment is an indicator for the survival of the prosthesis [9]. Sole assessment of static symmetry is only partially applicable to everyday functional aspects. Thus, a five-times-sit-to-stand test (FTSST) for assessing a dynamic balance distribution was taken from studies on balance disorders [10,11]. The time up and go test assesses balance during transfer from sitting to standing and walking capacity. It is very reliable [12]. For assessing walking capacity, the 4-meter, 10-metre, 2-minute or 6-minute walk test may be used. For patients who have undergone TKA, the 10-meter walk test shows very good reliability in the clinical rehabilitation process [13].

The quadriceps femoris muscle of the affected leg is already weakened before the operation, its strength dropping by a further 60 percent after surgery and only recovering again over the course of rehabilitation[14,15]. Diagnostic tests to determine the strength of the quadriceps femoris muscle are thus suitable for describing the course of rehabilitation, particularly since it has an influence on several of the above-mentioned functional test results[16]. Commonly used are isokinetic, isometric and isoinertial measuring procedures, which show good and very good reliability in the context of TKA[17]. As a result of their easy transportation and the clinical variability, handgrip dynamometers have become established in the clinical setting[18]. For the assessment of stair climbing, 10- to 15-step tests are applied. Stair climbing tests show very good reliability[19]. For all test procedures, reliability controls are only available at selective points and details of the positioning of the reliability control within the course of treatment are often lacking. This is of importance in order to be able to assess the entire course of perioperative rehabilitation in a reliable and valid manner. It is therefore vital to conduct reliability controls on commonly used and valid physical functional test procedures before, for example, perioperative exercise programmes or physiotherapeutic interventions can be reliably investigated for their efficacy with regard to physical functional aspects. The objective of the present study is to develop evidence-based perioperative physiotherapeutic support for TKA operations.

An initial step of this study will be concerned with assessing the reliability of the respective test procedures used at several different perioperative timepoints.

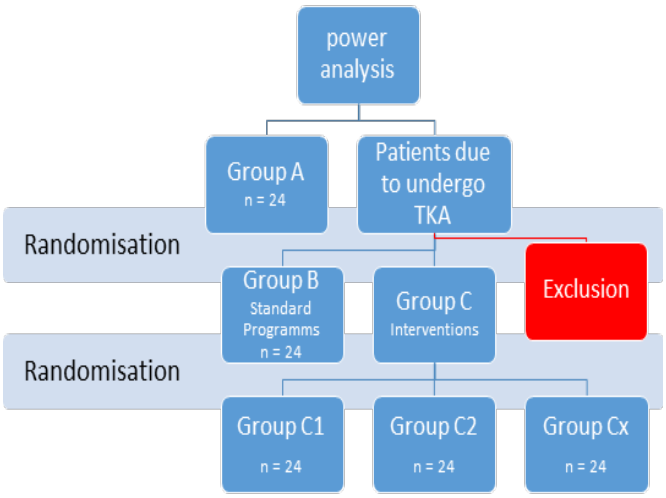
METHODS

Various different aspects of reliability will be elucidated to assess the respective test procedures used. The test-retest reliability also referred to as intra-tester reliability, will be determined for each test at every time point, as this is representative of the reliability of results. The results of the individual test procedures will be correlated. The correlation coefficients represent the parallel test reliability. This is interpreted as a criterion-related validity indicator, which permits conclusions to be drawn about the interchangeability of test procedures, thus answering the question of the transferability of physical functional test results among each other. The plan is to use those test procedures that are found to be reliable to assess the physical functional efficacy of promising interventions. This should help to standardize the perioperative physiotherapeutic process in routine clinical practice.

Design

A prospective randomized-controlled, triple-blind study design will be applied. In the first stage, the reliability control will be conducted. For this purpose, two groups of subjects will be recruited, young healthy subjects (Group A) and patients undergoing a TKA operation and then being put through the hospital's standard physiotherapy programme (Group B). This design is conceived to test the intra-individual reliability of the test procedures and to evaluate the levels of the test results over the course of treatment for differences. For this purpose, the selected tests will be performed with each subject on four measurement days at the same time: 1 day preoperatively, 5 days postoperatively, 9 days postoperatively and 6 weeks postoperatively. On each measurement day, each of the test procedures listed in Table 2 below will be performed twice. A complete pause will be observed between them. The measuring instruments to be applied are considered to be reliable. Insofar as there are doubts about the reliability of a measuring instrument, additional controls will be performed to determine device reliability. In the second stage, further groups with patients who will undergo TKA (Groups C_1, C_2 .. C_x) will be recruited, which will be treated differently from the standard physiotherapy programme. These groups will be evaluated for differences with regard to their physical functional development at the same perioperative measuring timepoints as Group B.

Table 1: Study design



Outcomes

The outcomes for stage 1 are the test-retest correlation coefficients, parallel test correlation coefficients between the data of individual measuring procedures and questionnaires at one time point and the development of the test results between the different perioperative timepoints. In the first stage, the parameters listed in Table 2 will be determined. For stage 2, the primary outcomes are the differences in performance development between the different groups (C_1, C_2 .. C_X), which will be evaluated on the basis of the differences of the means of the test procedures that are applied. The data will be evaluated and presented as an intention-to-treat and as a per-protocol analysis.

Table 2: Test procedures and parameters

Tests and assessments	Measuring instruments	Parameter
10-m walk test	Photoelectric sensors, stopwatch	Time in s
Time up and go	Stopwatch	Time in s
Three times sit to stand	Leonardo force measurement plate	Difference in kg
Isometric maximal force of knee extension	Microfet 2	Peak in N
Stair climbing	Stopwatch	Time in s
Cumulative leg circumference	Tape measure	Centimetres
Questionnaires used		
	WOMAC	Score
	KSS (FS / KS)	Score

Study population

For Group A, subjects aged between 22 and 27 years will be recruited at a university. The subjects may not have any restrictions on the function of their lower limbs. Subjects who report a medical history of injuries that might compromise symmetry will be excluded. These include fractures and cruciate ligament ruptures, but also other kinds of immobilization in the past 24 months, such as after supination trauma or acute pain in the past three months. They may not have any diseases that are associated with neurological symptom complexes, balance disorders or muscular dystrophies. Groups B .. X will be recruited at an orthopaedics department and will comprise subjects aged between 50 and 80 years who present at the department prior to a TKA operation that they are due to undergo. Subjects who cannot walk independently prior to surgery or who have serious neurological diseases or diseases of the vestibular system will be excluded.

Hypothesis

The hypotheses of stage 1 refer to Group A and B and propose that the physical functional tests: 10-m walk test, time up and go, three times sit to stand, isometric maximal force and stair climbing test, as well as the manual leg circumference measurement, are reliable test procedures. Further hypotheses in stage 1 refer to the validity of the test procedures. It will be tested whether the test procedures applied in stage 1 are capable of providing a differentiated picture of the patient's physical condition in the individual perioperative phases.

The hypotheses of stage 2 propose that the interventional groups (C .. X) will take a surgically significantly better physical-functional course in the short term than Group B.

Calculation of study group sizes

In order to detect mean effects of 0.5 in the second stage, in an ANOVA: Repeated measures, within factors, given four groups with four measuring timepoints, a maximum alpha error of five percent and a power 1-ß of 80 percent, at least 24 persons must be included in each group. An allocation ratio of 1:1 is planned.

Study quality, blinding and randomization

To secure study quality, the Consort Statement, the STARD checklist and the PEDro scale will be used for orientation during planning and conduct of the study. To begin with, a Clinical Study Steering Committee (CSSC) will be established, which will plan the study schedule and select the surgeons, therapists and study assistants involved. In an initial discussion, a Study assistant A will ask the subjects whether they are willing to take part in the study. The patients will be informed in advance that the study involves the evaluation of perioperative management. If subjects provide their voluntary consent, they will take part in the study. If a subject is included in the study, he or she will be allocated a subject number during the initial discussion. Study assistant A will conduct a randomized group allocation using a Microsoft Excel list. No further subjects will be included in a group once the planned number of 24 has been achieved. A second Study assistant B, who does not know the group allocation, will carry out the perioperative test procedures. The surgeon will not be given any information about the group allocation either. The subject will not be given any information about the part of the perioperative programme that is being evaluated in the study. The interventions will be carried out by physiotherapists of the university hospital, again without any information about which part is being evaluated. Subsequently, Study assistant B will forward the collected data without group allocation to the CSSC for blinded analysis. Since neither the testers, the persons carrying out the interventions, nor the evaluators have information about group allocation, this

results in a triple-blind design. The intermediate results will be confidential but will be accessible to an appointed study steering committee.

Definition of study timepoints

The screening day is defined as the day on which the subjects sign the declaration of consent and are randomly allocated. Measuring timepoint 1 (MP1) is scheduled one day before the operation. The day of surgery is defined as day 0. MP2 and MP3 are scheduled 5 and 9 days postoperatively. MP4 is scheduled for the 6th postoperative week. For stage 2, the intervention period is defined as the first ± 7 days postoperatively.

Accompanying care

All accompanying medical interventions will be documented in order to identify any systematic external influencing factors.

Publication

The study results will be published independently of the results in peer-reviewed international scientific journals. Anonymised patient data will be made available to the journals upon request. A copy of the protocol with a statistical analysis plan will be attached to the submitted manuscript if requested by the Journal.

Authorship

The recommendations of the International Committee of Medical Journal Editors are followed with regard to authorship. All authors accept responsibility for the submitted manuscripts. If necessary, an external scientific or medical writer will be contracted to improve the language quality of the manuscript. External professional writers and their financing will be declared. The CSSC is made up of the authors. No ghostwriters will be employed. Institutions do not appear on the original manuscript.

Study organization

No data and security committee will be appointed, as data reliability will be checked transparently in advance. The study steering committee is reliable for study design, quality assurance, as well as data analysis, writing, and publication. The committee will decide on statistical conclusions. With the exclusion of the statistician, the committee will be blind to group affiliation in statistical conclusions.

Data collection and data overview

Study assistant A, who will conduct the initial discussions, will arrange the follow-up appointments. This assistant will also distribute the questionnaires, collect them, and help with their completion if required. The other data will be collected by a Study assistant B, who will encode the data and enter them in Excel tables. External companies that are contracted for study monitoring/ management/ consultancy will be declared.

Adverse effects, device malfunctions

All adverse effects and device defects will be documented. Serious adverse effects will be reported to the ethics committee. Readmissions and a prolonged hospital stay of over 20 days, i.e. twice as long as normal, are examples of a serious adverse effect. All adverse effects will be pursued until they have disappeared or stabilized.

Ethics

The study conforms with the latest version of the World Medical Association Declaration of Helsinki. It has been examined and approved by the state medical association of Brandenburg, where it is registered under the number S3(a)/2017. Thus, all subjects will participate in the investigation voluntarily and can end their participation in the study at any time. Likewise, the investigator can terminate a subject's participation in the study, insofar as he or she has concerns about the subject's health. The responsible ethics committee has approved the study. The study is additionally registered in the German Clinical Trial Register under the. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. The Authors declare that there is no conflict of interest.

DISCUSSION

The focus on functional testing in perioperative patients who have undergone TKA contrasts with current practice, which is typically based on questionnaires. Those more objective evaluations of new treatment procedures will be implemented in the second stage of this study. The multi-stage design may provide fundamental evidence for functional testing and common therapeutic treatments. Therefore, the investigation could change perioperative assessments and physiotherapeutic treatment in patients who have undergone TKA. This study has a potential limitation. In order to ensure the blinding, the investigator can have hardly any contact to Study assistant A, the surgery team or the treating therapists.

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