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Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

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1. Title: Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial

1a.Short title: Cost-utility of open and arthroscopic rotator cuff repair

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2.Abstract

Introduction: Rotator cuff injuries account for up to 70% of pain in the shoulder girdle. However, there is still no consensus on the best surgical treatment of patients with rotator cuff injuries, regarding the cost-effectiveness and cost-utility analysis between the open and arthroscopic methods of rotator cuff repair. The objective of this trial is to compare the efficacy, cost-effectiveness and cost-utility of open and arthroscopic procedure for rotator cuff repair.

Methods and Analysis: The trial is a two-group, parallel design, randomized controlled trial. A total of 100 patients with symptomatic rotator cuff lesion will be allocated in either open or arthroscopic technique in a 1:1 ratio, considering smoking (yes or no), lesion size (less than 3 cm or more than 3 cm) and diabetes (present or absent) as stratification factors. All patients will be included in the same rehabilitation program after the intervention. The primary outcome measure will be the Constant-

Murley score at 48 weeks post-surgery. Secondary outcomes include cost-effectiveness, cost-utility, pain, complications and clinical analysis, using the EuroQol 5-D3L, the simple shoulder test (SST), Visual Analogue Pain Scale (VAS), integrity of the repair evaluated through magnetic resonance imaging, complications and failures of the proposed methods. For the cost-effectiveness analyses, we will use the VAS and the Constant-Murley Score as measures of effectiveness; for the cost-utility analyses, we will use the EuroQol- 5D-3L as a measure of utility in terms of incremental cost per quality-adjusted life-years (QALY).

Ethics and Dissemination: the study is approved by Research Ethics Committee. The results will be published in a peer-reviewed journal.

Trial Registration Number: NCT04146987

Keywords: rotator cuff; surgery; arthroscopy; open repair; cost-effectiveness; QALY

Article Summary

- Few studies evaluate the cost-utility of rotator cuff repair surgery techniques
- This article will detail the protocol for a randomized controlled trial comparing the two techniques of rotator cuff repair.

Strenghts and limitations of this study

- This study is a prospective, randomized trial, that is the best design to address the study question.
- It will provide surgeons and healthcare providers with important information about the surgical techinique and the cost-effectiveness and cost-utility of these techniques
- The lack of blinding of the patient and surgeons is a limitation to the study design

4.Introduction

4a.Background and Rationale

Musculoskeletal injuries are a major cost to the healthcare system. In 2004, 30% of the North American population had some kind of musculoskeletal disorder that required medical treatment; between 2002 and 2004, the estimated cost of treating these changes was $510 billion. Shoulder diseases represent the third most common cause of these changes, behind only spinal and knee disorders [1], [2].

An evaluation of the primary health care system in Cambridge, United Kingdom, showed that the average frequency of shoulder pain was 9.5 per 1,000 individuals [3]. Of these, 86% had rotator cuff tendinopathy. North American data estimate that approximately 4.5

million patients annually seek medical attention due to shoulder pain; of these, two million have some symptoms related to the rotator cuff. About 250,000 rotator cuff repair surgeries are performed annually in the United States of America (US), and with the continued increase in life expectancy and aging, there is a tendency to increase this number [1], [2].

The rotator cuff is a group of four muscles and their tendons that act to stabilize the shoulder and allow for its extensive range of motion. Four muscles and their attached tendons make up the rotator cuff: the subscapularis, supraspinatus, infraspinatus, and teres minor. The long portion of the biceps tendon also contributes to cuff function, which is to stabilize the humeral head in the glenoid cavity, preventing superior migration of the humeral head [4].

The possible injuries range from tendon degeneration (tendinosis/tendinopathy), through partial tear (articular, interstitial or bursal), to complete tear. Diagnosis is made by associating history and physical examination along with imaging methods, and magnetic resonance imaging (MRI) is considered the method of choice [5]–[13].

Currently, the indication for surgical treatment is based on the persistence of symptoms and/or the degree of muscle weakness and/or size of the tear, after a time of conservative treatment.

In general, when opting for surgery, imaging can assist in the planning of surgical treatment, since it allows measuring the extent of the tear (partial or total) and discriminating which tendons are involved (supraspinatus, infraspinatus, etc.).

Treatment of rotator cuff tear depends on the type of injury, the patient's functional capacity, age, and the presence of symptoms. In general, tendon degeneration and partial tears are treated non-surgically, with physiotherapy, injections and analgesic medications. Complete and incomplete tears that did not respond well to conservative treatment, however, should be treated surgically [8], [14]–[16].

Among the surgical options, the open method is still considered the gold standard, with good or excellent results in over 90% of cases [17]–[19]. Due to arthroscopy and the evolution of arthroscopic instruments and implants in the last two decades, the arthroscopic repair technique has gained space and is widely used in our country. Some studies [17]–[20] did not show superiority of one technique over another in terms of clinical outcomes. On the other hand, since the cost of arthroscopic surgery is supposedly higher, due to the required equipment, it is important to establish which option has the best cost-utility ratio. Other published studies suggested that the open method is

superior than the arthroscopic method in relation to cost-utility [21]-[23].

4b.Objectives

Despite the high incidence of rotator cuff injury, there is no consensus about the best method of repair, neither which method has the cost-effectiveness and cost-utility ratio. Therefore, the present study aims to compare the open and arthroscopic methods for rotator cuff repair and determine which presents the best cost-effectiveness ratio.

5.Trial Design

The trial will be a prospective randomized controlled clinical trial.

6.Methods

This randomized controlled trial will follow the Consolidated Standards of Reporting Trials (CONSORT) Statement [24]; also the protocol was developed following the SPIRIT guidelines[25]. It will be performed at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil. The cost analysis will be performed by Hospital Israelita Albert Einstein team, São Paulo, Brazil.

The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert

Einstein (CAAE 19182619.3.1001.0071) and Hospital Alvorada Moema (CAAE 19182619.3.2002.5533).

All and any modifications in this study will be promptly reported to all Research Ethics Committee, all institutions, all investigators and all participants.

The project is registered in the ClinicalTrials.gov database (NCT04146987 https://clinicaltrials.gov/ct2/show/NCT04146987?term=NCT04146987&draw=2&rank=1).

The study is sponsored by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2019/02159-3) R. Pio XI, 1500 - Alto da Lapa - CEP 05468-901 São Paulo/SP - Brasil Tel: (+55) 11 3838-4000. This institution and the patients enrolled had and will have no role on study design, collection, management, analysis and data interpretation, writing the report and decision to submit the report for publication.

6a.Sample size

The sample size estimate was obtained to detect differences between the open and arthroscopic repair groups in relation to the primary outcome of the study, Constant-Murley Score (CM) instrument after the intervention. Kukkone's et al. 2013 study [26] estimated the clinically important minimal difference in CM

score in 10.4 points in patients with rotator cuff rupture after 3 months of surgical treatment by the arthroscopic method. The estimated sample size of 45 patients per group, total of 90 patients, would reach 90% power to detect a 10.4 difference between the groups in the CM instrument post-operative score with a standard deviation of up to 15 points with a significance level of 5% using a t-Student test. Predicting a loss of around 10% at 12 months of follow-up we aim to recruit 50 patients per group (PASS software [27]).

6b.Inclusion criteria

All patients eighteen years of age or older, presenting with complete rotator cuff injury or a high-grade partial rotator cuff injury, symptomatic, where conservative therapy failed (maintenance of pain and disability after conservative treatment), or the patient could not support the non-surgical treatment. All patients ought not to have any medical contraindications for surgery, have a good understanding of the Portuguese language, agree to participate in the study and sign the Informed Consent Form.

6c.Exclusion criteria

Patients with previous shoulder surgery, previous fractures in the affected shoulder, those with passive range of motion

limitation (joint stiffness with an elevation of 90 degrees or less), radiographic signs of glenohumeral osteoarthritis or neurologic injury will be excluded. Patients will also be excluded if they do not wish to participate or are unable to understand or sign the informed consent form (due to conditions such as cognitive impairment, or mental illness) or if there are any conditions that contraindicate any of the surgical methods.

6d.Randomization and allocation

After eligibility assessment, all patients will be informed about the nature and purpose of the study and will only be included after agreeing with the study and signing the informed consent form, that will be obtained by the surgeon that evaluated the patient and indicated the surgery. Patients will be consecutively allocated to one of two proposed treatment methods: open rotator cuff repair or arthroscopic rotator cuff repair (FIGURE 1). The software R was used to generate a randomization list, considering 100 patients to be included in the study and the same probability of allocation for both methods of surgery (open and arthroscopic repair). The variables will be: smoking (yes or no), the size of the lesion (≤ 3 cm or > 3 cm) and diabetes (present or absent). Randomization will be performed by the REDCap platform (Research Electronic Data Capture – Vanderbilt University)[28][29] after the patient is anesthetized and prepared for the surgery. A person not

associated with the study will open the software and acquire one of the two techniques possible and tell the surgeon who will perform the surgery.

6e.Recruitment

All patients that are already treated by the shoulder surgeons at at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil, will be enrolled in. this trial.

6f.Blinding

Due to the type of interventions, neither participants nor treatment providers can be blinded to treatment allocation. The outcome assessment of the primary and secondary outcomes (Constant-Murley; EuroQol; VAS and SST), patient-reported outcomes, will not be blind. One of the authors (RP) will assess all other clinical outcomes. All primary and secondary outcomes will be assessed at baseline, 6, 24 and 48 weeks, except for the VAS which will also be assessed at hospital discharge, 1, 2 and 4 weeks. The statisticians conducting the analyses will be blinded to the treatment status until the analyses are completed.

6g. Patient and Public Involvement

No patient involved

7.Intervention methods

Five surgeons with at least four years of surgical technique experience will participate in this study (EFC, MTCA, RP, BAM, VR). Also, the residents of shoulder and elbow surgery, as well as the residents of Orthopedics and Traumatology from Hospital Alvorada Moema and residents in shoulder and elbow surgery at Albert Einstein Hospital may participate in surgeries.

Open surgery: patients will be positioned in a beach chair position with the affected limb pending off the table, allowing manipulation and full range of motion range. After asepsis, antisepsis, and placement of sterile surgical fields, an anterolateral incision will be made in the shoulder in question; the deltoid muscle belly will be gently divided along its fibers until exposure of the subdeltoid / subacromial bursa, which will be partially excised for exposure of the subacromial space and rotator cuff tendons. After mobilization and release of the ruptured tendons and debridement of the rotator cuff footprint, the tendon repair to the bone will be performed using 5.5mm metal anchors, according to the preference and technique chosen by the surgeon. In all cases, the release of the coracoacromial ligament and acromioplasty will be performed.

Arthroscopic Technique: the patients will be positioned in lateral decubitus position, with the limb to be operated attached

to a skin traction device, which through a traction post and 7 kilograms (kg), will maintain the shoulder in the following position: abduction of 30 to 60 degrees and flexion of 20 to 30 degrees. After asepsis, antisepsis, and placement of impermeable sterile surgical fields, a posterolateral incision will be made in the shoulder for optic introduction, with a 50mmHg pressure pump and a 0.90 flow, and inspection of the glenohumeral joint. If necessary, an anterior accessory portal will be performed for intra articular instrumentation. After joint inspection, the optic will be introduced into the subacromial space with detachment of the subacromial and subdeltoid bursa with the trocar. After visualizing the lesion, an accessory lateral portal will be performed. With the use of shaver blades, partial bursectomy will be performed and any adherence to the tendon stumps will be released, as well as debridement of the rotator cuff footprint. The tendon will then be reinserted to the bone using metallic 5.5mm anchors, according to the preference of each surgeon. The technique used, as well as the suture configuration and type of knot used, will be defined by the surgeon, according to his preference. After tendon repair, the coracoacromial ligament will be released, as well as acromioplasty.

8.Postoperative rehabilitation

All patients will undergo the same postoperative rehabilitation protocol: use of Velpeau sling for 6 weeks; pendulum exercises from the second week; active movement and recovery of the range of motion from the sixth week and strengthening from the twelfth week.

The patients will be oriented to perform home exercises and, as well, to be assisted by a physiotherapist twice a week from the sixth week of surgery and on. It is expected at the end of treatment the need of about thirty sessions of physical therapy.

9.Outcomes assessment

Study data will be collected and managed using REDCap (Research Electronic Data Capture) hosted at Hospital Israelita Albert Einstein [28][29]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

All study participants will be evaluated preoperatively, at the hospital discharge and 1, 2, 6, 24 and 48 weeks after the

intervention. The Constant-Murley score, Visual Analogue Scale, EuroQol-5D-3L and the Simple Shoulder Test validated to the Portuguese language questionnaires will be filled out by the patient and assessed by evaluators to the assigned intervention.

To prevent loss of follow-up all the patients will be monitored by REDCap software and alerts will be sent to each patient near time points defined by the investigators. One week before every medical consultation and at the twelfth week, regarding the rehabilitation process. If the patient fails to fill any questionnaire or does not attend the medical consultations, he will be contacted by phone and e-mail.

10.Primary outcome

The Brazilian Portuguese Version of the Constant-Murley Score (CM) [30] will be measured preoperatively at 6, 24 and 48 weeks after the intervention. Research assistants (not blinded to the study aim) will ask the patients to fill in the validated CM form for the Portuguese language and measure the range of motion with a goniometer. The CM scale covers different domains of shoulder function (pain, activities of daily living, range of motion and power), punctuating each of them; it ranges from 0 to 100, with higher scores indicating better function.

10b.Secondary outcomes

EuroQol-5D-3L (European Quality of Life), a generic score developed to describe health-related quality of life [24] will also be assessed preoperatively, at 6, 24 and 48 weeks postoperatively. This score includes five health domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; each domain has 3 levels: no problem; some problems and extreme problems. In addition, the EuroQol-5D-3L has a visual analog scale where the participant assigns a value between zero and one hundred to his or her own health condition [31]. At the end of its application, EuroQol-5D-3L will provide a unique numerical value that can be used for longitudinal comparison between different time periods.

Clinical outcomes will also be assessed by the Simple Shoulder Test (SST), validated for Portuguese [32], preoperatively and at 6, 24 and 48 weeks after the procedure. SST is a simple, quick and widely used questionnaire for shoulder function measurement; it consists of 12 dichotomous questions answered by the patient himself. Each positive answer (yes) is given a score; at the end of the questionnaire the percentage of positive answers (score) is made, and the higher the percentage, the better the shoulder function. Other outcomes measured will be VAS (visual analogue pain scale) at hospital discharge, 1, 2, 6, 24 and 48 weeks after

the intervention. This scale allows pain intensity to be measured with maximum interobserver reproducibility; it consists of a 10 cm straight line with the ends determining the limits of pain sensation (no pain; worst pain ever experienced); the distance between zero (no pain) and the patient's demarcation defines the intensity of pain. Complications and failures of the proposed methods will also be assessed.

Failures will be characterized as the need for additional surgical procedures and/or change of the initially proposed procedure. Patients who, for any reason, demonstrate treatment failure or require additional interventions will be followed up and their results included in the group in which they were initially randomized, according to the intention to treat principle.

After the 48th week, all patients will be submitted to Magnetic Resonance Imaging (MRI) of the operated shoulder to evaluate the integrity and healing of the repair performed.

10c.Cost-effectiveness

Cost-effectiveness and cost-utility analyses will be assessed by the estimate of direct and indirect costs to the private

healthcare system at 48 weeks. The perspective adopted in the study will be the social costs, the direct and indirect medical costs. The set timeframe will be 48 weeks and a discount rate of 5% will be applied. The costs included in direct medical costs will be: hospitalization, medical fees, medication; the indirect costs: costs of absenteeism from work, which will be estimated by the patient-reported number of days away from work multiplied by the average wage rate of the current year. The costs will be converted from Brazilian Reais to US dollars and brought to the cost schedule of the current year, in order to avoid that the effect of inflation on the medical inputs influences the analysis. For the cost-effectiveness analyses, the VAS and the CM will be used as measures of effectiveness. For the cost-utility analyses, the EuroQOL-5D-3L will be used as a measure of utility. The timetable of outcomes assessment is described on Table 1.

Table1. Timetable of assessment

STUDY PERIOD

	Enrolment	Allocation	Post-Allocation					Close-Out
TIMEPOINT	**0**	**0**	Surgery	**1w**	**2w**	**6w**	**24w**	**48w**
ENROLMENT:								
Eligibility Screen	**X**							
Informed Consent	**X**							
CM; EQ-5D, SST; VAS	**X**							
Allocation	**X**							
INTERVENTIONS								
Open Repair			**X**					
Arthroscopic Repair			**X**					
ASSESSMENTS:								
CM; EQ-5D, SST;						**X**	**X**	**X**
VAS			**X**	**X**	**X**	**X**	**X**	**X**
MRI	**X**							**X**
Complications			**X**	**X**	**X**	**X**	**X**	**X**
Economics			**X**	**X**	**X**	**X**	**X**	**X**

11.Data analysis

The descriptive analyzes of variables will be based on the absolute frequencies and percentages for categorical variables and summary measures as means and standard deviations or medians and quartiles, as well as minimum and maximum values for numerical

variables [33]. Clinical scores will be represented by individual profile graphs separately by the surgical technique group.

The groups will be compared according to the presence of categorical clinical outcomes (failures, complications and healing integrity) by Chi-square or Fisher's exact tests, depending on the distribution observed after data collection.

For inferential analysis of numerical clinical outcomes, mixed models will be used and, if the normal distribution is not adequate, generalized mixed models will be used [34]. The models will have time effects (preoperative, 6, 24 and 48 weeks after intervention), surgical technique group (open repair or arthroscopic repair) and the interaction effect between time and group. The size of the lesion (smaller than three cm or larger than three cm) will also be included in the models as a control variable, seeking to avoid possible biases.

The analyzes will be performed with the aid of the SPSS program [35], considering a significance level of 5%.

12.Safety

There will be no benefit to the participant, beyond what is expected for the correction of the rotator cuff injury, expecting an improvement of pain and function of the affected shoulder. The

risks of the present study are those inherent in any surgical treatment and anesthetic procedure, such as surgical wound infection, scar formation, pain, shoulder range of motion, rotator cuff tear, neurovascular injury. If any complications occur, all patients will be treated by the same surgical team until the complication is healed.

Both surgical techniques have the same goal, that is, to repair the ruptured tendon to the bone. The open technique requires a larger incision, as well as greater surgical dissection and manipulation of the deltoid muscle, which may cause greater postoperative pain and weakness of this muscle, in addition to causing a slightly larger scar. However, it provides great visualization and manipulation and mobilization capability of the ruptured tendon, which provides a safer and tension-free repair.

The arthroscopic technique is performed with some point-shaped cuts in the shoulder, usually three or four; due to smaller incisions, it requires less muscle manipulation, which theoretically would cause less postoperative pain and less muscle weakness of the deltoid muscle, it also has minor scars. However, this technique requires more surgeon's experience and the mobilization of the ruptured tendon(s) is limited. Using a large amount of saline may cause edema in the operated shoulder, which is usually reversed after the first 12 hours of surgery.

Finally, there is a minimal risk of loss of data confidentiality, but the responsible researcher undertakes to do everything possible to maintain data confidentiality. One of the researchers will have access to all data during the entire trial period. Any adverse event will be reported to the researchers involved and communicated to the main investigator according to the Institutional Review Boards description.

13.Discussion

There is no consensus about the best cost-effectiveness of surgical treatment of patients with degenerative rotator cuff injuries. Several studies [21], [22], [36], [37] suggest that the open repair method is more cost-effective than the arthroscopic method, resulting in the same clinical outcome with lower cost. Adla, Deepthi N. et. al [21] in a prospective nonrandomized study, showed that both techniques lead to the same clinical outcomes. The costs of arthroscopic surgery were higher than the open surgery, mainly due to the costs of the suture anchors, which was used only in the arthroscopic group, is important to notice that in most of the open surgeries, the repair was performed through transosseous sutures. Köse, Kamil Çağri et. al [22], in a retrospective study, also demonstrated similar clinical outcomes, although the costs of arthroscopic procedure being much higher. Importantly, the open repair technique was performed using

transosseous sutures and the arthroscopic method using suture anchors and also, the open repair group required longer length hospital stay. Hui, Yik Jing et. al [36] in a retrospective cohort study, described a significantly higher cost for the arthroscopic procedure, compared to the open repair, evaluating only the in-hospital costs, but with the same clinical outcomes. However, it is important to emphasize that the open repair was performed using transosseous sutures, without suture anchors and that the arthroscopic group needed a longer surgery time. Churchill, R.S. et. al [37] using the New York Ambulatory Database System, with a total of 5,224 cuff repair surgeries, of which 1,334 open repair and 3,890 arthroscopic repair, showed that the mini-open rotator cuff repair costs significantly less than the arthroscopic repair and requires significantly less surgical time. However, no clinical outcomes have been analyzed in this study, making it impossible to determine the cost-effectiveness ratio. An elegant study Carr, A.J. et. al [38] carried out as a prospective multicenter randomized clinical trial, concluded that there is no difference in the effectiveness and cost-effectiveness between the open repair surgery and arthroscopic surgery after 24 months of follow-up, even with the higher initial costs in the arthroscopy surgery. An economic evaluation of the data from this study was carried out, showing that the Incremental Cost Effectiveness

(ICER) was uncertain and the arthroscopic repair surgery was slightly more costly and less effective than open repair surgery.

Thus, despite the high incidence of rotator cuff injury, there is insufficient evidence to determine the best method for treating these injuries. So, the present study proposes to answer the clinical question of which method, open or arthroscopic, presents the best cost-effectiveness in the surgical treatment of rotator cuff injury. Providing conclusive, good quality evidence for and contributing to the evidence base of methods used to treat rotator cuff injuries.

14.Trial status

Protocol Trial version: 3 Date: 07/24/2020

Recruitment Estimated Start Date: August/2020

Recruitment Estimated End Date: December/2021

Not yet recruiting.

15.Additional files

Table 1. Timetable of assessment

Figure 1. Flowchart of participants

Informed Consent

16.Abbreviations

CONSORT: Consolidated standards of reporting trials; VSA: Visual analogue scale; MRI: magnetic resonance imaging; QALY: quality-adjusted life years; CM: Constant-Murley Score; SST: Simple Shoulder Test

17. Declarations

17.1 Ethics Approval and Consent to Participate

The study has been approved by the local Research Ethics Committee (CAAE 19182619.3.1001.0071). Digital, informed consent to participate will be obtained from all participants through REDCAP.

17.2 Consent for Publication

Not Applicable

17.3 Availability of Data and Materials

The datasets used and/or analysed during the current study will be available from the corresponding author upon request.

17.4 Competing interests

The authors declare that they have no competing interests.

17.5 **Fundings**

This study is supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2019/02159-3).

17.6 Author contributions

ML is the Chief Investigator; he conceived the study, led the proposal and protocol development.

RP is the lead trial methodologist and helped in the study conceiving and development

EA contributed to study design and to development of the proposal.

IO contributes to study design related to QALY

IQC is responsible for cost-analysis

FM helped in the English translation and registration/publication of the trial

PF helped in the English translation and registration/publication of the trial

EFC helped in the study conceiving and development

BAM helped in the study conceiving and development

All authors read and approved the final manuscript.

17.7 Acknowledgements

Not applicable

18. Dissemination policy

All the authors are committed and agree to publish the full results of the research, despite the final results.

19. Data Monitoring Committee (DMC)

Since this trial have a short durations and both surgical techniques have known minimal risks, there is no need for such committee.

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TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Título do projeto*: Custo-Efetividade da Cirurgia de Reparo do Manguito Rotador Pelas Técnicas Aberta e Artroscópica. Ensaio Clínico Randomizado.*

Pesquisadores responsáveis: *Mario Lenza e Rafael Pierami*

O(a) Sr(a) está sendo convidado para participar, como voluntário, de uma pesquisa científica. O Termo de Consentimento Livre e Esclarecido tem por meta esclarecer esta pesquisa, explicando resumidamente seus objetivos, procedimentos, riscos e benefícios. Após ser esclarecido sobre as informações a seguir, e aceitar fazer parte do estudo, rubrique todas as páginas e assine ao final deste documento. Uma via será enviada para o(a) Sr(a) por e-mail.

Objetivo do estudo:

O objetivo deste estudo é avaliar o custo-efetividade (relação da melhora clínica com os custos dos procedimentos) de dois tipos de cirurgias para o reparo do manguito rotador: cirurgia aberta e cirurgia artroscópica.

Descrição do estudo:

A ruptura do manguito rotador, ou seja, o rompimento dos tendões do ombro é a principal causa de dor no ombro na população adulta, causando, além da dor, diminuição da força no ombro acometido e perda de qualidade de vida, devido a dor constante e piora na qualidade do sono causado pela dor. Existem duas técnicas cirúrgicas para

correção desta doença: a técnica cirúrgica aberta, realizada por uma incisão (corte) no ombro e visualização direta do tendão rompido; e a técnica cirúrgica artroscópica, realizada através de pequenos cortes no ombro, por onde são introduzidos uma câmera de vídeo, para visualização do tendão rompido e instrumentais para realização da cirurgia. Ainda não há uma definição se há diferença entre os resultados obtidos e as técnicas cirúrgicas utilizadas. O(a) Sr(a) está sendo convidado para participar deste estudo pois há indicação de cirurgia para o reparo do manguito rotador.

***Procedimentos a serem realizados*:**

O estudo terá dois grupos de pacientes: grupo que fará a reconstrução do manguito via técnica cirúrgica aberta e o grupo que fará a reconstrução via técnica cirúrgica artroscópica. A seleção dos voluntários será feita de forma randomizada, isto é, não saberemos em que tipo de cirurgia cada indivíduo será incluído. A duração total da pesquisa será de um (01) ano e a participação do Sr(a) será em responder questionários sobre a sua saúde antes da cirurgia, comparecer às consultas médicas, antes da cirurgia e após 6, 24 e 48 semanas da cirurgia e realizar os exames de Ressonância magnética antes da cirurgia e após 48 semanas da cirurgia. Caso o(a) Sr(a) concorde em fazer parte deste estudo, os dados preenchidos e coletados serão utilizados para fins de pesquisa. Importante informar que os pacientes de ambos os tipos de cirurgia receberão os mesmos cuidados e os mesmos seguimentos e que não serão necessários exames de imagem ou laboratoriais adicionais àqueles rotineiramente utilizados para pacientes com lesão do manguito rotador. Como tratamento habitual após a cirurgia de lesão do manguito, o(a) Sr(a) será orientado a realizar um programa de reabilitação que inclui o uso de tipóia do tipo Velpeau por seis (06) semanas e um programa de exercícios pendulares orientados. Após, a tipóia será retirada e o(a) Sr(a) será orientado a realizar exercícios domésticos para ganho de movimento, além de duas sessões semanais de fisioterapia para analgesia e recuperação da amplitude de movimento do ombro. A partir da décima segunda semana (12ª) iniciarão os exercícios de fortalecimento muscular sob orientação de fisioterapeuta. No término do estudo será verificado se houve melhora na função do ombro, na qualidade de vida e na cicatrização do tendão reparado por meio de questionários de simples preenchimento e exame de ressonância magnética.

Possíveis riscos e desconfortos:

Os riscos do presente estudo são aqueles inerentes a qualquer tratamento cirúrgico e procedimento anestésico, como infecção da ferida operatória, formação de cicatriz, dor, limitação do arco de movimento do ombro, rerruptura do manguito rotador, lesão neurovascular. A técnica cirúrgica aberta pode provocar maior dor pós-operatória e fraqueza muscular, além de causar uma cicatriz pouco maior. A técnica cirúrgica artroscópica pode causar menos dor pós-operatória e menos fraqueza muscular; além disso, apresenta cicatrizes menores, mas pode causar edema no ombro operado, o que geralmente é revertido após as primeiras 12 horas da cirurgia.

Benefícios para o participante:

O(a) Sr(a) não terá benefício além do esperado para a operação de correção da lesão, esperando-se melhora da dor e função do ombro operado, independente do tipo de técnica cirurgia utilizada. A sua participação ajudará a entender qual das técnicas cirúrgicas apresenta o melhor custo-efetividade para o tratamento de lesão do manguito rotador e permitirá apresentar à comunidade médica informações sobre a melhor indicação cirúrgica de tratamento.

Direitos do participante:

Sua participação é voluntária e o(a) Sr(a) pode retirar seu consentimento ou ainda descontinuar sua participação em qualquer momento, se o assim o preferir, sem penalização e/ou prejuízo de qualquer natureza. Não haverá nenhum custo ao Sr(a) proveniente deste estudo, assim como não haverá qualquer tipo de remuneração pela sua participação.

Estou ciente que:

1. As informações obtidas serão analisadas em conjunto com as de outros voluntários, não sendo divulgada a identificação de nenhum participante.

2. As informações produzidas neste estudo serão mantidas em lugar seguro, codificadas e a identificação só poderá ser realizada pela equipe do projeto.

4. Em qualquer etapa do estudo, você terá acesso aos profissionais responsáveis pela pesquisa para esclarecimento de eventuais dúvidas. O coordenador do projeto é o Dr. Mário Lenza e o principal responsável pelo estudo é o Dr. Rafael Pierami. Os pesquisadores podem ser encontrados nos seguintes endereços: Dr. Mario Lenza –Av. Albert Einstein, 627 – bloco A1 – 3º andar – Programa Locomotor, Morumbi, São Paulo – CEP 05652-900: Tel: (11) 2151.1444; e-mail: mario.lenza@einstein.br; e Dr. Rafael Pierami –Avenida Ministro Gabriel Rezende de Passos, 550, 2º andar, Hospital Alvorada Moema – Centro de Excelência em Cirurgia de Ombro e Cotovelo, Moema, São Paulo – CEP 04521-022 – Tel: (11) 2186-9810 ou (11) 2186-9809; e-mail: rafael_pierami@hotmail.com.

Se você tiver qualquer dúvida ética em relação à pesquisa, entre em contato com:

Comitê de Ética em Pesquisa do Hospital Israelita Albert Einstein - Av. Albert Einstein 627/701, São Paulo/SP, fone 2151-3729, e-mail: cep@einstein.br. Reclamações, elogios e sugestões deverão ser encaminhados ao Sistema de Atendimento ao Cliente (SAC) por meio do telefone (11) 2151-0222 ou formulário identificado como fale conosco disponível na página da pesquisa clínica ou pessoalmente.

Comitê de Ética em Pesquisa em Seres Humanos do Hospital Pró-Cardíaco (CEP/HPC) - Tel: (21) 3289-3802 - Localizado na Rua Voluntários da Pátria, 435/8º andar – Botafogo, Rio de Janeiro/RJ, CEP: 22270-005. Horário de atendimento: de segunda à sexta-feira, das 09:00h às 16:00h.

Confirmo que li o conteúdo deste Termo de Consentimento Livre e Esclarecido e aceitei participar voluntariamente deste estudo. Ficaram claros para mim quais são os propósitos do estudo, os procedimentos a serem realizados, seus eventuais desconfortos e riscos, as garantias de confidencialidade e de esclarecimentos permanentes. Ficou claro também que minha participação é isenta de despesas e que tenho garantia do acesso a tratamento hospitalar quando necessário. Concordo voluntariamente em participar deste estudo, sabendo que poderei retirar o meu consentimento a qualquer momento, antes ou durante o mesmo, sem penalidades ou prejuízos ou perda de qualquer benefício que eu possa ter adquirido, ou no meu atendimento neste Serviço.

_____

Nome Completo do participante da pesquisa

_____ Data:___/___/___

Assinatura do participante da pesquisa

_____

Nome completo e legível do pesquisador responsável

_____ Data:___/___/___

Assinatura do pesquisador responsável

_____

Nome completo do representante legal

_____ Data:____/____/____

Assinatura do representante legal

_____

HOSPITAL ISRAELITA ALBERT EINSTEIN-SP

UNIFIED REVIEW – ETHICAL AND RESEARCH COMMITTEE

RESEARCH PROJECT DATA

Project title: Cost-effectiveness of rotator cuff repair surgery by open and arthroscopic techniques: a randomized control trial

Responsible researcher: Mario Lenza

Area:
Version: 2
CAAE: 19182619.3.1001.0071

Proponent institution: SOCIEDADE BENEF ISRAELITABRAS HOSPITAL ALBERT EINSTEIN

Main funding source: SOCIEDADE BENEF ISRAELITABRAS HOSPITAL ALBERT EINSTEIN

TECHNICAL REPORT INFORMATION

REVIEW #: 3.636.334

Project:

This is a randomized clinical trial that will be carried out in two health facilties (Hospital M'Boi Mirim e Hospital Alvorada. The objective is to compare method of repair of the shoulder rotator cuff, open or arthroscopic. The study will be funding by the São Paulo Research Foundation – FAPESP.

Objective of the study:

To compare open or arthroscopic method of repair of the rotator cuff, and determine which method has the best cost effectiveness ratio.

Risks and benefits Assessment:

To respond to the request by the Ethical and Research Committee, in this new version authors describe specific risks for each surgical technique that will be study in the project.

Continuing – report # 3.636.334

Comments and considerations on the study:

Authors have addressed all requested changes. We believe that there is not need to hire a specific insurance, present statement of all participating institutions. Authors will be the solely responsible to treatment of possible adverse events as a result of the study. We also did not included cost of arthroscopy material, once they would exceed the total funding received for this study. For this reason, although the cost of arthroscopy would be included in total of treatment for the responsible institution, there are not real ethical deviation that avoids project execution.

Considerations on mandatory terms and conditions:

Required terms were presented, including the agreeing term of co-participant institution.

The consent form was revised, now its language is clear, and risks for each surgery technique were clarified.

Recommendations:

ERC is responsible to "follow-up the development of projects by providing semester reports to researchers and other monitoring strategies, taking into consideration the risk of the study". For this reason, the researcher/responsible needs to forward to Einstein's ERC partial reports every 6 months and a final report of the project, up to 30 days after its conclusion.

Partial report, final report, or study withdrawal or closure:
https://www.einstein.br/pesquisa/servicos/comite-etica-em-pesquisa/relatorio-pesquisas-aprovadas

Following the CNS 466/2012 resolution, the responsible researcher must guarantee confidentially and anonymity of procedures, imaging rights, and non-stigmatization of participants of the study, guaranteeing the non-use of information that may harm people and/or communities, including in terms of self-esteem, prestige, and/or finance and economic aspects.

In case of severe adverse events, please consider the guidance in the link:
http://apps.einstein.br/forms/pesquisa/form-adve.html

If event related to procedure of the study occurs or medication in use, please, fulfil the Severe Adverse Event from CONEP at
http://conselho.saude.gov.br/web_comissoes/conep/aquivos/FORMULARIO_EAS_CONEP_2011.doc

Conclusion or pending and inadequacy list:

After analysis, the following documents were approved:

1 - Research project – version dated September 27, 2019.

2 - Consent Term – Version 2 dated September 25, 2019.

Continuing – report # 3.636.334

Final considerations and ERC's criteria:

DOCUMENTS APPROVED BY ERC OF THE HOSPITAL ISRAELITA ALBERT EINSTEIN IN A MEETING HELD IN OCTOBER 08, 2019.

This report was elaborated based on the following documents:

Document	File	Upload date	Author	Status
Basic information of the project	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1381072.pdf	27/09/2019 17:47:33		Accepted
Statement of Institution and Infrastructure	Declaracao_de_assistencia_e_resposabilidade_Mboi_Mirim.pdf	27/09/2019 17:45:37	Rafael Pierami	Accepted
Consent form / Absence justification	TCLE.docx	27/09/2019 17:37:41	Rafael Pierami	Accepted
Consent form / Absence of justification	TCLE_sem_demarcacoes.docx	27/09/2019 17:37:23	Rafael Pierami	Accepted
Statement of Institution and Infrastructure	Termo_de_anuencia_Alvorada.pdf	27/09/2019 17:37:03	Rafael Pierami	Accepted
Detailed Project/ Researcher's brochure	Projeto_ECR_Manguito_Aberto_vs_Artroscopico_sem_demarcacoes.docx	27/09/2019 17:35:44	Rafael Pierami	Accepted
Detailed Project/ Researcher's brochure	Projeto_ECR_Manguito_Aberto_vs_Artroscopico_27_09_19.docx	27/09/2019 17:35:30	Rafael Pierami	Accepted
Statement of Researchers	carta_resposta_CEP_HIAE.docx	27/09/2019 17:35:15	Rafael Pierami	Accepted
Statement of Researchers	carta_resposta_CEP_HIAE_assinada.pd f	27/09/2019 17:35:01	Rafael Pierami	Accepted
Statement of institution and infrastructure	declaracao_assistencia_alvorada.pdf	27/09/2019 17:34:39	Rafael Pierami	Accepted
Chronogram	cronograma.xlsx	27/09/2019 17:33:59	Rafael Pierami	Accepted
Statement of Researchers	Declaracao_Resp_Pesq_Mario.pdf	16/08/2019 15:50:58	LETICIA FONSECA DA COSTA	Accepted
Others	AnuenciaGestorAreaMario.pdf	16/08/2019 15:49:39	LETICIA FONSECA DA COSTA	Accepted
Title page	Folha_de_rosto_plataforma_Brasil_ECR_manguito.pdf	12/08/2019 19:08:38	Rafael Pierami	Accepted
Statement of institution and infrastructure	autarquia_mboi_mirim.pdf	12/08/2019 19:07:39	Rafael Pierami	Accepted
Statement of institution and infrastructure	Termo_anuencia_mboi_mirim.pdf	12/08/2019 19:06:09	Rafael Pierami	Accepted

Status of the report:

Approved

Documents requires CONEP evaluation:

No

October 11, 2019

Responsible signature:

Fabio Pires de Souza Santos (Coordinator)

Address: Av. Albert Einstein 627 - 2ss - Morumbi - SP – Zip Code: 05.652-000

Phone: (11)2151-3729

Fax: (11)2151-0273 **E-mail:** cep@einstein.br

DISPATCH

Grant number 2019/0259-3
Support type Regular programs / Research support / Research project / Research project – Regular – Continuous Flow
Status Ongoing
Term June 01, 2019 to May 31, 2021
Grantee Mário Lenza
Principal investigator Mário Lenza

DISPATCH PAGE OF THE INITIAL PROPOSAL - REGULAR RESEARCH PROJECT

Result
Granted

Dispatch date
May 24, 2019

Budgeted amount

Benefits	Requested (R$)	Dispatched (R$)
Funds		
Permanent material	0.00	0.00
Costs		
Transportation	0.00	0.00
Daily expenses	0.00	0.00
Consumption material	135,520.00	121,968.00
Third parties	0.00	0.00
Technical reserve for		
complementary benefits	16,000.00	16,000.00
Technical reserve for		
Infrastructure	20,328.00	18,295.20
Importing provisioning		
Total	171,848.00	156,263.20

Scholarship quotes

None requested

Project team

Members of the team – requested

Name	Position	Complementary benefits	Term
Mário Lenza	Principal researcher	Yes	April 1, 2019 – March 31, 2021
Mário Ferreti Filho	Associate researcher	-	April 1, 2019 – March 31, 2021
Isadora Orlando de Oliveira	Technical support	-	April 1, 2019 – March 31, 2021
Rafael Pierami	Technical support	-	April 1, 2019 – March 31, 2021
Ana Claudia Pereira Sanguin	Administrative staff	-	April 1, 2019 – March 31, 2021
Tania Oliveira Lopes	Administrative staff	-	April 1, 2019 – March 31, 2021

Members of the team – dispatched

Name	Position	Complementary benefits	Term
Mário Lenza	Principal researcher	Yes	June 1, 2019 – May 31, 2021
Mário Ferreti Filho	Associate researcher	-	June 1, 2019 – May 31, 2021
Isadora Orlando de Oliveira	Technical support	-	June 1, 2019 – May 31, 2021
Rafael Pierami	Technical support	-	June 1, 2019 – May 31, 2021
Ana Claudia Pereira Sanguin	Administrative staff	-	June 1, 2019 – May 31, 2021
Tania Oliveira Lopes	Administrative staff	-	June 1, 2019 – May 31, 2021

Project planning

Start date: June 1, 2019
Duration: 24 months
End date: May 31, 2021
Field of knowledge: Health
Scientific report (quantity): 2
Scientific report (submission date): May 30, 2020
June 30, 2021
Financial report (quantity): 2
Financial report (submission date): May 30, 2020
June 30, 2021
Category of the research: T/PP **[AUTOR, VERIFICAR ACRÔNIMO]**

Observations / Transcriptions / Statements

Observations to the responsible

I am pleased to inform that your research grant mentioned above, after careful analysis by the FAPESP committee, has been approved. Please be aware that items in your budget

were revised, and some were not approved, and others were approved but for reduced amount. An e-mail will be sent with instructions for you to confirm the interest in the grant.

The use of the grant must follow instructions of the guideline on the use of resources, financial report, and technical reserve.

Further information about this dispatch is available at "Sistema SAGe - www.fapesp.br/sage .

If you have any questions or need more information about this grant, please use the channel made available for this purpose at "Talk to FAPESP" - www.fapesp.br/converse.

Sincerely,

Carlos Henrique de Brito Cruz
Scientific director

Statements for the responsible

None

Review to the responsible of the proposal

General analysis of the proposal including 1 – applicant's academic experience, 2 – research project, 3 – budget.

This is a good proposal, although the final result of the study is predicted, considering finding of the published in the international literature concerning the costs for each type of surgery. That said, the current proposal can have a positive impact, considering that final result may provide guidance for decision making of future Brazilian surgeries, who may choose the lower cost procedure, however, this is not the only factor to take into account.
The applicant's academic experience is adequate, especially for his deeply experience with shoulder surgery that can be seen by the studies he published in the area. The project itself is fairly simple but well planned and written, in addition it involves a high number of patients (100 individuals) and surgeons. It is important to note that each surgeon's preference and bias should be considered, as well as final clinical result. This bias needs to be careful followed-up by the principal researcher in order to prevent high standard deviations.

Please analyze the applicant's academic experience by considering scientific/technological production.

As previously mentioned, the applicant's academic experience is fair. He holds a PhD from UNIFESP for 9 years now, and a post-doctoral degree from university in Australia in 2011. In addition, he is professor at Einstein Medical College for 6 or 7 years. The 10 scientific publications listed in his application are all relevant and involved topics of his specialty and correlated areas. The grantee also acts as supervisor in graduate program, including projects with FAPESP funding. His scientific production totalize 57 papers and

2 book chapters. Currently he supervises two PhD students, and he had completed the supervision of one master-degree student and two PhD student.

Please specify the applicant's experience with projects related to the area

After the analysis of the applicant's CV, I believe his is the leader in his research area at Einstein Medical College. His performance seems adequate, given the graduate supervisions he had completed.

Please analyze the applicant's ability to educate new researchers

As stated above, the applicant performance in this regard is adequate.

If applicable, please analyze the performance of applicant with previous funding requests submitted to FAPESP

Not applicable

Provide/analyze other relevant issue of the applicant's academic experience

None to report

Applicant's academic experience – Final assessment

( ) Excellent
(x) Very good
( ) Good
( ) Fair
( ) Inadequate

Please analyze research project, considering the following:

Originality and contribution to the research area

As stated above, the results of the present study are somewhat predictable, but the topic is relevant, especially for the focus on less costly surgical procedure that is adequate for the reality of our country.

Theoretical framework and methodology

The project is simple, perhaps, this is reason why the results will be efficient. Of note are the bias problem due to the personal preferences of surgeons, and the need to equalize as much as possible these preferences in order to prevent unnecessary deviations in cost of the procedures. Another issue is the type implants to be used. Implants need need to be the same to all patients, whenever possible.

Funding for technical training

None to report

Total funding requested justifies the scientific and technological relevance of the project

(x) Yes
( ) No

Project term is adequate for the project development

(x) Yes
( ) No

Infrastructure of the institution where the study will be conduct adequate

(x) Yes
( ) No

Project will include scientific initiation and graduate students

(x) Yes
( ) No

Final assessment of the project

( ) Excellent
(x) Very good
( ) Very good, but mild issues should be addressed
( ) Good
( ) Good, but it has limitations to be addressed
( ) Fair
( ) Seriously limited

Please analyze the budget, considering the following:

Permanent material and equipment (>R$20.000,00) are justified

(x) Yes
( ) No

The rationale of the proposal is adequate

(x) Yes
( ) No

Materials and equipment needed that FAPESP should and must request a partnership with third parties

Not applicable

Request for consumption items is adequate

The consumption items are crucial for development of the project.

Services and materials that needed to be requested from third parties

Not applicable

Services that should be provided by the institution of the study upon FAPESP request

Not applicable

Please provide, if any, value suggestions to be replace in the project in the following items:

National permanent items

None to report

International permanent items

None to report

National consumption items

As stated above, applicant requested implants

Third parties services

None to report

International services

None to report

National transportation

None to report

International transportation

None to report

National daily expenses

None to report

International daily expenses

None to report

National miscellaneous expenses

None to report

International miscellaneous expenses

None to report

Total funding requested in national currency

Adequate

Total funding requested in international currency

Adequate

Sponsorship – considering the analyses above, please suggest number of technical training, if any
Technical training I (TT-I)
Technical training II (TT-II)
Technical training III (TT-III)
Technical training IV (TT-IV)
Technical training IVa (TT-IVa)
Technical training V (TT-V)

Final assessment of the budget

(x) Adequate
( ) Adequate, but the suggestions above should be addressed
( ) Inadequate

Check inadequacies observed, if any, on the following items:

Applicant's academic experience

( ) Inadequate scientific/technological production for the development of the project
( ) Limited scientific/technological production
( ) Applicant lacks experience in the area of the project

Research project

( ) Objective of the project is unclear
( ) Objective of the project if limited for the complete development of the project
( ) Project lacks originality
( ) Limited theoretical framework/methodology
( ) Amount of work inadequate for the funding requested
( ) Project execution is questionable
( ) High cost considering the scientific relevance to the area

( ) Project's deadline is unrealistic

Budget proposal

( ) Total of items requested is unclear
( ) Overestimated budget

Other limitations, if any:

None to report

Statements related to the grant:

None to report

Detailed budget

Consumption item – National

Item	**Description**	**Requested**	**Dispatched**
		Amount (R$)	**Amount (R$)**
1	140 units – 5.0 FASTIN RC ANCHOR with ORThOCORd (#222993) - Johnson & Johnson	135,520.00	121, 968.00

Consumption item – National

Not applicable

Technical reserve – complementary benefits

Recipients	Responsible researcher (June 1, 2019 – May 31, 2021)
Currency	R$
Value (unit) - annual	8,000.00
Date	May 25, 2019
Amount of complementary benefits	R$16,000.00

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Title: Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	01
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	03
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	05
Protocol version	#3	Date and version identifier	17
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	18;19
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	01
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	06
Roles and responsibilities:	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee,	05

committees		data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3;4;5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3;4;5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5;6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6;7
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8;9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10;11

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10;11;12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	6
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7;8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7;8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7;8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8

Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10;11;12;13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10;11;12;13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10;11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and	20

		reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	20
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	5
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	6
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	10;12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	16
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	20
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	19;20
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	20
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	25;26;27;28
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

Notes:

- 18a: 10;11;12;13
- 18b: 10;11;12;13
- 32: 25;26;27;28 This checklist was completed on 24. July 2020 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Clinical Outcomes and Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

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Complete List of Authors:	Pierami, Rafael; Hospital Israelita Albert Einstein, Sistema Locomotor; Grupo de Ombro e Cotovelo do Hospital Alvorara Moema, Departamento de Ortopedia Lenza, Mario; Hospital Israelita Albert Einstein, Programa Locomotor Antonioli, Eliane; Hospital Israelita Albert Einstein, Orthopaedic Oliveira, Isadora; Hospital Israelita Albert Einstein, Sistema Locomotor Castro, Isabela; Hospital Israelita Albert Einstein, Sistema Locomotor Manente, Felipe; Hospital Israelita Albert Einstein, Sistema Locomotor Fairbanks, Paula; Hospital Israelita Albert Einstein, Sistema Locomotor Carrera, Eduardo; Hospital Israelita Albert Einstein, Departamento de Ortopedia Matsumura, Bruno; Hospital Israelita Albert Einstein, Departamento de Ortopedia
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Keywords:	Adult orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Elbow & shoulder < ORTHOPAEDIC & TRAUMA SURGERY, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Shoulder < ORTHOPAEDIC & TRAUMA SURGERY, Orthopaedic sports trauma < ORTHOPAEDIC & TRAUMA SURGERY

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1. Title: Clinical Outcomes and Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial

1a. Short title: Cost-utility of open and arthroscopic rotator cuff repair

1b. Authors: Rafael Pierami[1], Eliane Antonioli[2], Isadora Oliveira[2], Isabela Queirós Castro[2], Felipe Manente[3], Paula Fairbanks[3], Eduardo da Frota Carrera[1], Bruno Akio Matsumura[1], Mário Lenza[2]

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2.Abstract

Introduction: Rotator cuff injuries account for up to 70% of pain in the shoulder. However, there is still no consensus on the best surgical treatment of patients with rotator cuff injuries, regarding the cost-effectiveness and cost-utility analysis between the open and arthroscopic methods of rotator cuff repair. The objective of this trial is to compare the efficacy, cost-effectiveness and cost-utility of open and arthroscopic procedure for rotator cuff repair.

Methods and Analysis: The trial is a two-group, parallel design, randomized controlled trial. A total of 100 patients with symptomatic rotator cuff lesion will be allocated in either open or arthroscopic technique in a 1:1 ratio, considering smoking (yes or no), lesion size (less than 3 cm or more than 3 cm) and diabetes (present or absent) as stratification factors. All patients will be included in the same rehabilitation program after the intervention. The primary outcomes measure will be the Constant-Murley score and EuroQol 5-D-3L at 48 weeks post-surgery. Secondary outcomes include cost-effectiveness, cost-utility, pain, complications and clinical analysis, using the simple shoulder test (SST), Visual Analogue Pain Scale (VAS), integrity of the repair evaluated through magnetic resonance imaging, complications and failures of the proposed methods. For the cost-effectiveness analyses, we will use the VAS and the Constant-Murley Score as measures of effectiveness; for the cost-utility analyses, we will use the EuroQol- 5D-3L as a measure of utility in terms of incremental cost per quality-adjusted life-years (QALY).

Ethics and Dissemination: The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert Einstein and Hospital Alvorada Moema/ Hospital Pró-Cardíaco. The results will be published in a peer-review open access journal.

Trial Registration Number: NCT04146987

Keywords: rotator cuff; surgery; arthroscopy; open repair; cost-effectiveness; QALY

Strengths and limitations of this study

- This study is a prospective, randomized trial, that is the best design to address the study question. Its methodological analyses is the best option to determine cost-utility and will provide a strong evidence.
- It will provide surgeons and healthcare providers with important information about the surgical technique and the cost-effectiveness and cost-utility of these techniques
- This study will provide important information about rotator cuff healing, what is still not certain
- The lack of blinding of the patient and surgeons is a limitation to the study design

3. Introduction

3a. Background and Rationale

Musculoskeletal injuries are a major cost to the healthcare system. North American data estimate that approximately 4.5 million patients annually seek medical attention due to shoulder pain; of these, two million have some symptoms related to the rotator cuff. About 250,000 rotator cuff repair surgeries are performed annually in the United States of America (US), and with the continued increase in life expectancy and aging, there is a tendency to increase this number[1][2][3]. An evaluation of the primary health care system in Cambridge, United Kingdom, showed that the average frequency of shoulder pain was 9.5 per 1,000 individuals [4]. Of these, 86% had rotator cuff tendinopathy.

The rotator cuff is a group of four muscles and their tendons that act to stabilize the shoulder and allow for its extensive range of motion. Four muscles and their attached tendons make up the rotator cuff: the subscapularis, supraspinatus, infraspinatus, and teres minor. The long portion of the biceps tendon also contributes to cuff function, which is to stabilize the humeral head in the glenoid cavity, preventing superior migration of the humeral head [5].

The possible lesions range from tendon degeneration (tendinosis/tendinopathy), through partial tear (articular, interstitial or bursal), to complete tear. Its etiology is multifactorial and the main factors associated with tears are tendon degeneration related to aging, trauma, tendon insertion hipovascularity and genetic factors[6][7][8]. Since most lesions are caused by wear and degeneration related to aging, people over 40 years are at great risk[3]. Diagnosis is made by associating history and physical examination along with imaging methods, and magnetic resonance imaging (MRI) is considered the method of choice [9]–[17].

Treatment of rotator cuff lesion depends on the type of tear, the patient's functional capacity, age, and the presence of symptoms. In general, tendon degeneration and partial tears are treated non-surgically, with physiotherapy, injections and analgesic medications. Complete and incomplete tears that did not respond well to conservative treatment, however, might be treated surgically [12], [18]–[20][3][21][22].

Among the surgical options, the open method is still considered the gold standard, with good or excellent results in over 90% of cases [23]–[25]. Due to arthroscopy and the evolution of arthroscopic instruments and implants in the last two decades, the arthroscopic repair technique has gained space and is widely used. Some studies [23]–[26] did not show superiority of one technique over another in terms of clinical outcomes. On the other hand, since the cost of

arthroscopic surgery is supposedly higher, due to the required equipment, it is important to establish which option has the best cost-utility ratio. Other published studies suggested that the open method is superior than the arthroscopic method in relation to cost-utility [27]–[29]. To date, no study in our country has assessed the comparison of the cost-utility of the two techniques; considering that the open technique is being left behind, is important to determine if it remains a viable, reliable and cost-effective option for the treatment of rotator cuff tears.

3b. Objectives

Despite the high incidence of rotator cuff tears, there is no consensus about the best method of repair, neither which method has the best cost-effectiveness and cost-utility ratio. Therefore, the present study aims to compare the open and arthroscopic methods for rotator cuff repair and determine which presents the best cost-effectiveness ratio.

4. Trial Design

The trial will be a prospective randomized controlled clinical trial.

5. Methods

This randomized controlled trial will follow the Consolidated Standards of Reporting Trials (CONSORT) Statement [30]; also the protocol was developed following the SPIRIT guidelines[31]. It will be performed at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil. The cost analysis will be performed by Hospital Israelita Albert Einstein team, São Paulo, Brazil. The project was approved by both hospitals research ethics committee and registered in clinicaltrials.gov.

5a. Sample size

The sample size estimate was obtained to detect differences between the open and arthroscopic repair groups in relation to the primary outcome of the study, Constant-Murley Score (CM) instrument after the intervention. Kukkone's et al. 2013 study [32] estimated the clinically important minimal difference in CM score in 10.4 points in patients with rotator cuff rupture after 3 months of surgical treatment by the arthroscopic method. The estimated sample size of 45 patients per group, total of 90 patients, would reach 90% power to detect a 10.4 difference between the groups in the CM instrument post-operative score with a standard deviation of up to 15 points with a significance level of 5% using a t-Student test. Predicting a loss of around 10% at 12 months of follow-up we aim to recruit 50 patients per group (PASS software [33]).

5b. Inclusion criteria

All patients eighteen years of age or older, presenting with complete rotator cuff tear or a partial rotator cuff tear of at least 50% of tendon thickness, with symptoms (pain and/or weakness), where conservative therapy failed will be included. The tendon tear will be confirmed by a Magnetic Resonance Imaging (MRI).

5c. Exclusion criteria

Patients with previous shoulder surgery, previous fractures in the affected shoulder, those with passive range of motion limitation (joint stiffness with an elevation of 90 degrees or less), radiographic signs of glenohumeral osteoarthritis or neurologic injury will be excluded. Patients will also be excluded if they do not wish to participate or are unable to understand or sign the

informed consent form (due to conditions such as cognitive impairment, or mental illness) or if there are any medical conditions that contraindicate any of the surgical methods.

5d. Randomization and allocation

After eligibility assessment, all patients will be informed about the nature and purpose of the study and will only be included after agreeing with the study and signing the informed consent form, that will be obtained by the surgeon that evaluated the patient and indicated the surgery. Patients will be consecutively allocated to one of two proposed treatment methods: open rotator cuff repair or arthroscopic rotator cuff repair. The software R was used to generate a randomization list, considering 100 patients to be included in the study and the same probability of allocation for both methods of surgery (open and arthroscopic repair). A stratified randomization will be performed using the following variables (strata): smoking (yes or no), the size of the lesion (≤ 3 cm or > 3 cm) and diabetes (present or absent). Randomization will be performed by the REDCap platform (Research Electronic Data Capture – Vanderbilt University)[34][35] after the patient is anesthetized and prepared for the surgery. A person not associated with the study will open the software and acquire one of the two techniques possible and tell the surgeon who will perform the surgery.

5e. Recruitment

All patients that already would be treated by the shoulder surgeons at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil, will be enrolled in this trial.

5f. Blinding

Due to the type of interventions, neither participants nor treatment providers can be blinded to treatment allocation. The outcome assessment of the primary and secondary outcomes (Constant-Murley; EuroQol; VAS and SST), patient-reported outcomes, will not be blind. One of the authors (RP) will assess all other clinical outcomes. The statisticians conducting the analyses will be blinded to the treatment status until the analyses are completed.

5g. Ethics and Dissemination

This study was developed and will follow the International Conference Guideline for Good Clinical Practice (ICH GP) to assure that the data and results are credible and that the rights, integrity and confidentiality of the trial subjects are protected and respected[36][37].

All authors agreed to publish the results of the present study in a peer-reviewed open access journal, despite the results and conclusions found. All data will be available upon request.

5h. Patient and Public Involvement

The patients nor the public were involved on the design and development of this study. Their participation will first occur with the contact between the surgeon and patient, time which they will be informed about the study and will decide to participate or not. At this time, they will be informed about the purpose and importance of it. At all times during the follow-up the patients will be able to enquiry the researchers and surgeons about the project and to make suggestions and complaints about it.

All the outcomes measures will be self-reported. In case of doubts from the patients, they will be assisted by one member of the research team.

Since the authors agreed to publish the results of this research, patients will not be involved on the dissemination. However, they will be encouraged to disseminate the knowledge among the community.

6. Intervention methods

Five surgeons with at least four years of surgical technique experience will participate in this study (EFC, MTCA, RP, BAM, VR). Also, the residents of shoulder and elbow surgery, as well as the residents of Orthopedics and Traumatology from Hospital Alvorada Moema and residents in shoulder and elbow surgery at Albert Einstein Hospital may participate in surgeries.

Open surgery: patients will be positioned in a beach chair position with the affected limb pending off the table, allowing manipulation and full range of motion. After standard patient preparation, an anterolateral incision will be made in the shoulder; the deltoid muscle belly will be gently divided along its fibers until exposure of the subdeltoid / subacromial bursa, which will be partially excised for exposure of the subacromial space and rotator cuff tendons. After mobilization and release of the ruptured tendons and debridement of the rotator cuff footprint, the tendon repair to the bone will be performed using 5.5mm metal anchors ("Super Revo"-CONMED, USA), according to the preference and technique chosen by the surgeon. In all cases, the release of the coracoacromial ligament and acromioplasty will be performed.

Arthroscopic Technique: the patients will be positioned in lateral decubitus position, with the limb to be operated attached to a skin traction device, which through a traction post and 7 kilograms (kg), will maintain the shoulder in the following position: abduction of 30 to 60 degrees and flexion of 20 to 30 degrees. After standard patient preparation, a posterolateral incision will be made in the shoulder for optic introduction, with a 50mmHg pressure pump and a 0.90 flow,

and inspection of the glenohumeral joint. After establishment of all required arthroscopic portals, joint inspection will be performed and any, if present, associated pathologies will be addressed. With the use of shaver blades, partial bursectomy will be performed and any adherence to the tendon stumps will be released, as well as debridement of the rotator cuff footprint. The tendon will then be reinserted to the bone using metallic 5.5mm anchors ("Super Revo"-CONMED, USA), according to the preference of each surgeon. The technique used, as well as the suture configuration and type of knot used, will be defined by the surgeon, according to his preference. After tendon repair, the coracoacromial ligament will be released, as well as acromioplasty will be performed.

7. Postoperative rehabilitation

All patients will undergo the same postoperative rehabilitation protocol: use of Velpeau sling for 6 weeks; pendulum exercises from the second week; active movement and recovery of the range of motion from the sixth week and strengthening from the twelfth week.

The patients will be oriented to perform home exercises and, as well, to be assisted by a physiotherapist twice a week from the sixth week of surgery and on. It is expected at the end of treatment the need of about thirty sessions of physical therapy.

8. Outcomes assessment

Study data will be collected and managed using REDCap (Research Electronic Data Capture- "Vanderbilt University, Nashville, Tennessee, USA") hosted at Hospital Israelita Albert Einstein [34][35]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for

seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

All study participants will be evaluated preoperatively, at the hospital discharge and 1, 2, 6, 24 and 48 weeks after the intervention. The Constant-Murley score, Visual Analogue Scale, EuroQol-5D-3L and the Simple Shoulder Test questionnaires will be filled out by the patient and assessed by evaluators to the assigned intervention. The endpoint of cost-utility analysis will be 48 weeks; clinical outcomes will also be assessed at 6 and 24 weeks.

To prevent loss of follow-up all the patients will be monitored by REDCap software and alerts will be sent to each patient near time points defined by the investigators. One week before every medical consultation and at the twelfth week, regarding the rehabilitation process. If the patient fails to fill any questionnaire or does not attend the medical consultations, he will be contacted by phone and e-mail. If the patient became incommunicable, we will consider a lost follow-up scenario, where, in accordance with the intention to treat principle, appropriate statistical methods for data analysis, that consider unbalanced data and loss of follow-up, such as Generalized Estimating Equation Model (GEE), will consider all patients observations, even if they fail in some moment. Thereby, these patients will not be excluded, and all data will be considered.

9. Primary outcome

The Brazilian Portuguese Version of the Constant-Murley Score (CM) [38] will be measured preoperatively at 6, 24 and 48 weeks after the intervention. Research assistants (not blinded to the study aim) will ask the patients to fill in the validated CM form for the Portuguese language and measure the range of motion with an analogic goniometer. The CM scale covers

different domains of shoulder function (pain, activities of daily living, range of motion and power), punctuating each of them; it ranges from 0 to 100, with higher scores indicating better function[38].

EuroQol-5D-3L (European Quality of Life), a generic score developed to describe health-related quality of life [30] will also be assessed preoperatively, at 6, 24 and 48 weeks postoperatively. This score includes five health domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; each domain has 3 levels: no problem; some problems and extreme problems. In addition, the EuroQol-5D-3L has a visual analog scale where the participant assigns a value between 0 and 100 to his or her own health condition, where 100 means "the best imaginable health status" or "the best health state you can imagine" and 0 means "the worst imaginable health state" or "the worst health state you can imagine". This is used to obtain a respondent's stated preference values, not to record their own health state. [39]. At the end of its application, EuroQol-5D-3L will provide a unique numerical value that can be used for longitudinal comparison between different time periods.

9b. Secondary outcomes

Clinical outcomes will also be assessed by the Simple Shoulder Test (SST), validated for Portuguese [40], preoperatively and at 6, 24 and 48 weeks after the procedure. SST is a simple, quick and widely used questionnaire for shoulder function measurement; it consists of 12 dichotomous questions answered by the patient himself. Each positive answer (yes) is given a score; at the end of the questionnaire the percentage of positive answers (score) is made, and the higher the percentage, the better the shoulder function. Other outcomes measured will be VAS (visual analogue pain scale) at hospital discharge, 1, 2, 6, 24 and 48 weeks after the intervention. This scale allows pain intensity to be measured with maximum interobserver reproducibility; it

consists of a 10 cm straight line with the ends determining the limits of pain sensation (no pain; worst pain ever experienced); the distance between zero (no pain) and the patient's demarcation defines the intensity of pain[41].

Complications and failures of the proposed methods will also be assessed. Failures will be characterized as the need for additional surgical procedures and/or change of the initially proposed procedure. Patients who, for any reason, demonstrate treatment failure or require additional interventions will be followed up and their results included in the group in which they were initially randomized, according to the intention to treat principle.

At the final follow-up (forty-eight weeks), the integrity and healing of repaired rotator cuff will be assessed through Magnetic Resonance Imaging (MRI).

9c. Cost-effectiveness

Cost-effectiveness and cost-utility analyses will be assessed by the estimate of direct and indirect costs to the private healthcare system at 48 weeks. The perspective adopted in the study will be the social costs, the direct and indirect medical costs. The set timeframe will be 48 weeks and a sensitivity analysis will be performed with the costs data, considering 0% to 5% discount rate to define the optimal discount rate for the data, according to methodological Guidelines for Economic Evaluation of Health Technologies – Brazilian Ministry of Health[42], [43][44]. The costs included in direct medical costs will be: hospitalization, costs related to arthroscopic instruments (e.g. cannulas, shaver blades, suture passer, ablator) medical fees, medication; the indirect costs: costs of absence from work, which will be estimated by the patient-reported number of days away from work multiplied by the average wage rate of the current year. The costs will be converted from Brazilian Reais to US dollars and brought to the cost schedule of the current year,

in order to avoid that the effect of inflation on the medical inputs influences the analysis. For the cost-effectiveness analyses, the VAS and the CM will be used as measures of effectiveness. For the cost-utility analyses, the EuroQOL-5D-3L will be used as a measure of utility. The timetable of outcomes assessment is described on Table 1.

Table1. Timetable of assessment

STUDY PERIOD								
	Enrolment	**Allocation**	**Post-Allocation**					**Close-Out**
TIMEPOINT	**0**	**0**	Surgery	**1w**	**2w**	**6w**	**24w**	**48w**
ENROLMENT:								
Eligibility Screen	**X**							
Informed Consent	**X**							
CM; EQ-5D, SST; VAS	**X**							
Allocation		**X**						
INTERVENTIONS								
Open Repair			**X**					
Arthroscopic Repair			**X**					
ASSESSMENTS:								
CM; EQ-5D, SST; VAS						**X**	**X**	**X**
			X	**X**	**X**	**X**	**X**	**X**
MRI	**X**							**X**
Complications			**X**	**X**	**X**	**X**	**X**	**X**
Economics			**X**	**X**	**X**	**X**	**X**	**X**

10. Data analysis

The descriptive analyzes of variables will be based on the absolute frequencies and percentages for categorical variables and summary measures as means and standard deviations or medians and quartiles, as well as minimum and maximum values for numerical variables [45]. Clinical scores will be represented by individual profile graphs separately by the surgical technique group.

The groups will be compared according to the presence of categorical clinical outcomes (failures, complications and healing integrity) by Chi-square or Fisher's exact tests, depending on the distribution observed after data collection.

For inferential analysis of continuous variables clinical outcomes, mixed models will be used and, if the normal distribution is not adequate, generalized mixed models will be used [46]. The models will have time effects (preoperative, 6, 24 and 48 weeks after intervention), surgical technique group (open repair or arthroscopic repair) and the interaction effect between time and group. The size of the lesion (smaller than three cm or larger than three cm) will also be included in the models as a control variable, seeking to avoid possible biases.

The analyzes will be performed with the aid of the SPSS program (**SPSS** Inc., Chicago, Illinois, USA) [47], considering a significance level of 5%.

11. Safety

There will be no benefit to the participant, beyond what is expected for the correction of the rotator cuff tear, expecting an improvement of pain and function of the affected shoulder. The risks of the present study are those inherent in any surgical treatment and anesthetic procedure,

such as surgical wound infection, scar formation, pain, decrease in shoulder range of motion, rotator cuff tear, neurovascular injury. If any complications occur, all patients will be treated by the same surgical team until the complication is healed.

Both surgical techniques have the same goal, that is, to repair the ruptured tendon to the bone. The open technique requires a larger incision, as well as greater surgical dissection and manipulation of the deltoid muscle, which may cause greater postoperative pain and weakness of this muscle, in addition to causing a slightly larger scar. However, it provides great visualization and manipulation and mobilization capability of the ruptured tendon, which provides a safer and tension-free repair.

The arthroscopic technique is performed with some point-shaped cuts in the shoulder, usually three or four; due to smaller incisions, it requires less muscle manipulation, which theoretically would cause less postoperative pain and less muscle weakness of the deltoid muscle, it also has minor scars. However, this technique requires more surgeon's experience and the mobilization of the ruptured tendon(s) is limited. Using a large amount of saline may cause edema in the operated shoulder, which is usually resolved after the first 12 hours of surgery.

Finally, there is a minimal risk of loss of data confidentiality; all data will managed, stored and protected by REDCAP software[34], [35]. One of the researchers will have access to all data during the entire trial period. Any adverse event will be reported to the researchers involved and communicated to the main investigator according to the Institutional Review Boards description.

12. Discussion

There is no consensus about the best cost-effectiveness of surgical treatment of patients with degenerative rotator cuff injuries. Several studies [27], [28], [48], [49] suggest that the open

repair method is more cost-effective than the arthroscopic method, resulting in the same clinical outcome with lower cost. Adla, Deepthi N. et. al [27] in a prospective nonrandomized study, showed that both techniques lead to the same clinical outcomes. The costs of arthroscopic surgery were higher than the open surgery, mainly due to the costs of the suture anchors, which was used only in the arthroscopic group, is important to notice that in most of the open surgeries, the repair was performed through transosseous sutures. Köse, Kamil Çağri et. al [28], in a retrospective study, also demonstrated similar clinical outcomes, although the costs of arthroscopic procedure being much higher. Importantly, the open repair technique was performed using transosseous sutures and the arthroscopic method using suture anchors and also, the open repair group required longer length hospital stay. Hui, Yik Jing et. al [48] in a retrospective cohort study, described a significantly higher cost for the arthroscopic procedure, compared to the open repair, evaluating only the in-hospital costs, but with the same clinical outcomes. However, it is important to emphasize that the open repair was performed using transosseous sutures, without suture anchors and that the arthroscopic group needed a longer surgery time. Churchill, R.S. et. al [49] using the New York Ambulatory Database System, with a total of 5,224 cuff repair surgeries, of which 1,334 open repair and 3,890 arthroscopic repair, showed that the mini-open rotator cuff repair costs significantly less than the arthroscopic repair and requires significantly less surgical time. However, no clinical outcomes have been analyzed in this study, making it impossible to determine the cost-effectiveness ratio. An important study by Carr, A.J. et. al [50] carried out as a prospective multicenter randomized clinical trial, concluded that there is no difference in the effectiveness and cost-effectiveness between the open repair surgery and arthroscopic surgery after 24 months of follow-up, even with the higher initial costs in the arthroscopy surgery. An economic evaluation of the data from this study was carried out, showing that the Incremental Cost Effectiveness (ICER)

was uncertain and the arthroscopic repair surgery was slightly more costly and less effective than open repair surgery.

Thus, despite the high incidence of rotator cuff tear, there is insufficient evidence to determine the best method for treating these injuries. So, the present study proposes to answer the clinical question of which method, open or arthroscopic, presents the best cost-utility in the surgical treatment of rotator cuff tear. Providing conclusive, good quality evidence for and contributing to the evidence base of methods used to treat rotator cuff injuries.

13. Trial status

Protocol Trial version: 4 Date: 10/06/2020

Recruitment Start Date: August/2020

Recruitment Estimated End Date: December/2021

Recruiting

14. Additional files

Table 1. Timetable of assessment

Informed Consent

15. Abbreviations

CONSORT: Consolidated standards of reporting trials; VAS: Visual analogue scale; MRI: magnetic resonance imaging; QALY: quality-adjusted life years; CM: Constant-Murley Score; SST: Simple Shoulder Test

16. Declarations

16.1 Ethics Approval and Consent to Participate

The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert Einstein (CAAE 19182619.3.1001.0071) and Hospital Alvorada Moema/ Hospital Pró-Cardíaco (CAAE 19182619.3.2002.5533). Digital, informed consent to participate will be obtained from all participants trough software REDCAP[35][34].

All and any modifications in this study will be promptly reported to all Research Ethics Committee, all institutions, all investigators and all participants.

16.2 Consent for Publication

Not Applicable

16.3 Availability of Data and Materials

The datasets used and/or analyzed during the current study will be available from the corresponding author upon request.

16.4 Competing interests

The authors declare that they have no competing interests.

16.5 Funding

This study is supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2019/02159-3).

16.6 Registry

The project is registered in the clinicaltrials.gov database (NCT04146987 https://clinicaltrials.gov/ct2/show/NCT04146987?term=NCT04146987&draw=2&rank=1).

16.7 Author contributions

Mário Lenza (ML) is the Chief Investigator; he conceived the study, led the proposal and protocol development. He helped write the first draft of the manuscript and project grant (sponsor)

Rafael Pierami (RP) is the lead trial methodologist and helped in the study conceiving and development. He helped write the first draft of the manuscript and project grant (sponsor)

Eliane Antonioli (EA) contributed to study design and to development of the proposal. She He helped write the first draft of the manuscript and project grant (sponsor)

Isadora Oliveira (IO) contributes to study design related to QALY and cost-utility design. She also helped on the reviews and translation of the manuscript.

Isabel Queiros Castro (IQC) is responsible for cost analysis and cost-utility analysis. She also helped on the methodological development

Felipe Manente (FM) helped in the English translation and registration/publication of the trial. He also helped on the reviews and corrections of the manuscript.

Paula Fairbanks (PF) helped in the English translation and registration/publication of the trial. She also helped on the reviews and corrections of the manuscript.

Eduardo da Frota Carrera (EFC) helped in the study conceiving and development; he also helped on the manuscript corrections and reviews

Bruno Akio Matsumura (BAM) helped in the study conceiving and development; he also helped on the manuscript corrections and reviews

All authors read and approved the final manuscript.

16.8 Acknowledgements

Not applicable

17. Dissemination policy

All the authors are committed and agree to publish the full results of the research, despite the final results.

18. Data Monitoring Committee (DMC)

Since this trial have a short duration and both surgical techniques have known minimal risks, there is no need for such committee.

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TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

***Título do projeto**: Custo-Efetividade da Cirurgia de Reparo do Manguito Rotador Pelas Técnicas Aberta e Artroscópica. Ensaio Clínico Randomizado.*

***Pesquisadores responsáveis:** Mario Lenza e Rafael Pierami*

O(a) Sr(a) está sendo convidado para participar, como voluntário, de uma pesquisa científica. O Termo de Consentimento Livre e Esclarecido tem por meta esclarecer esta pesquisa, explicando resumidamente seus objetivos, procedimentos, riscos e benefícios. Após ser esclarecido sobre as informações a seguir, e aceitar fazer parte do estudo, rubrique todas as páginas e assine ao final deste documento. Uma via será enviada para o(a) Sr(a) por e-mail.

Objetivo do estudo:

O objetivo deste estudo é avaliar o custo-efetividade (relação da melhora clínica com os custos dos procedimentos) de dois tipos de cirurgias para o reparo do manguito rotador: cirurgia aberta e cirurgia artroscópica.

Descrição do estudo:

A ruptura do manguito rotador, ou seja, o rompimento dos tendões do ombro é a principal causa de dor no ombro na população adulta, causando, além da dor, diminuição da força no ombro acometido e perda de qualidade de vida, devido a dor constante e piora na qualidade do sono causado pela dor. Existem duas técnicas cirúrgicas para correção desta doença: a técnica cirúrgica aberta, realizada por uma incisão (corte) no ombro e visualização direta do tendão rompido; e a técnica cirúrgica artroscópica, realizada através de pequenos cortes no ombro, por onde são introduzidos uma câmera de vídeo, para visualização do tendão rompido e instrumentais para realização da cirurgia. Ainda não há uma definição se há diferença entre os resultados obtidos e as técnicas cirúrgicas utilizadas. O(a) Sr(a) está sendo convidado para participar deste estudo pois há indicação de cirurgia para o reparo do manguito rotador.

***Procedimentos a serem realizados*:**

O estudo terá dois grupos de pacientes: grupo que fará a reconstrução do manguito via técnica cirúrgica aberta e o grupo que fará a reconstrução via técnica cirúrgica artroscópica. A seleção dos voluntários será feita de forma randomizada, isto é, não saberemos em que tipo de cirurgia cada indivíduo será incluído. A duração total da pesquisa será de um (01) ano e a participação do Sr(a) será em responder questionários sobre a sua saúde antes da cirurgia, comparecer às consultas médicas, antes da cirurgia e após 6, 24 e 48 semanas da cirurgia e realizar os exames de Ressonância magnética antes da cirurgia e após 48 semanas da cirurgia. Caso o(a) Sr(a) concorde em fazer parte deste estudo, os dados preenchidos e coletados serão utilizados para fins de pesquisa. Importante informar que os pacientes de ambos os tipos de cirurgia receberão os mesmos cuidados e os mesmos seguimentos e que não serão necessários exames de imagem ou laboratoriais adicionais àqueles rotineiramente utilizados para pacientes com lesão do manguito rotador. Como tratamento habitual após a cirurgia de lesão do manguito, o(a) Sr(a) será orientado a realizar um programa de reabilitação que inclui o uso de tipóia do tipo Velpeau por seis (06) semanas e um programa de exercícios pendulares orientados. Após, a tipóia será retirada e o(a) Sr(a) será orientado a realizar exercícios domésticos para ganho de movimento, além de duas sessões semanais de fisioterapia para analgesia e recuperação da amplitude de movimento do ombro. A partir da décima segunda semana (12ª) iniciarão os exercícios de fortalecimento muscular sob orientação de fisioterapeuta. No término do estudo será verificado se houve melhora na função do ombro, na qualidade de vida e na cicatrização do tendão reparado por meio de questionários de simples preenchimento e exame de ressonância magnética.

Possíveis riscos e desconfortos:

Os riscos do presente estudo são aqueles inerentes a qualquer tratamento cirúrgico e procedimento anestésico, como infecção da ferida operatória, formação de cicatriz, dor, limitação do arco de movimento do ombro, rerruptura do manguito rotador, lesão neurovascular. A técnica cirúrgica aberta pode provocar maior dor pós-operatória e fraqueza muscular, além de causar uma cicatriz pouco maior. A técnica cirúrgica artroscópica pode causar menos dor pós-operatória e menos fraqueza muscular; além disso, apresenta cicatrizes menores, mas pode causar edema no ombro operado, o que geralmente é revertido após as primeiras 12 horas da cirurgia.

Benefícios para o participante:

O(a) Sr(a) não terá benefício além do esperado para a operação de correção da lesão, esperando-se melhora da dor e função do ombro operado, independente do tipo de técnica cirurgia utilizada. A sua participação ajudará a entender qual das técnicas cirúrgicas apresenta o melhor custo-efetividade para o tratamento de lesão do manguito rotador e permitirá apresentar à comunidade médica informações sobre a melhor indicação cirúrgica de tratamento.

Direitos do participante:

Sua participação é voluntária e o(a) Sr(a) pode retirar seu consentimento ou ainda descontinuar sua participação em qualquer momento, se o assim o preferir, sem penalização e/ou prejuízo de qualquer natureza. Não haverá nenhum custo ao Sr(a) proveniente deste estudo, assim como não haverá qualquer tipo de remuneração pela sua participação.

Estou ciente que:

1. As informações obtidas serão analisadas em conjunto com as de outros voluntários, não sendo divulgada a identificação de nenhum participante.

2. As informações produzidas neste estudo serão mantidas em lugar seguro, codificadas e a identificação só poderá ser realizada pela equipe do projeto.

4. Em qualquer etapa do estudo, você terá acesso aos profissionais responsáveis pela pesquisa para esclarecimento de eventuais dúvidas. O coordenador do projeto é o Dr. Mário Lenza e o principal responsável pelo estudo é o Dr. Rafael Pierami. Os pesquisadores podem ser encontrados nos seguintes endereços: Dr. Mario Lenza –Av. Albert Einstein, 627 – bloco A1 – 3º andar – Programa Locomotor, Morumbi, São Paulo – CEP 05652-900: Tel: (11) 2151.1444; e-mail: mario.lenza@einstein.br; e Dr. Rafael Pierami –Avenida Ministro Gabriel Rezende de Passos, 550, 2º andar, Hospital Alvorada Moema – Centro de Excelência em Cirurgia de Ombro e Cotovelo, Moema, São Paulo – CEP 04521-022 – Tel: (11) 2186-9810 ou (11) 2186-9809; e-mail: rafael_pierami@hotmail.com.

Se você tiver qualquer dúvida ética em relação à pesquisa, entre em contato com:

Comitê de Ética em Pesquisa do Hospital Israelita Albert Einstein - Av. Albert Einstein 627/701, São Paulo/SP, fone 2151-3729, e-mail: cep@einstein.br. Reclamações, elogios e sugestões deverão ser encaminhados ao Sistema de Atendimento ao Cliente (SAC) por meio do telefone (11) 2151-0222 ou formulário identificado como fale conosco disponível na página da pesquisa clínica ou pessoalmente.

Comitê de Ética em Pesquisa em Seres Humanos do Hospital Pró-Cardíaco (CEP/HPC) - Tel: (21) 3289-3802 - Localizado na Rua Voluntários da Pátria, 435/8º andar – Botafogo, Rio de Janeiro/RJ, CEP: 22270-005. Horário de atendimento: de segunda à sexta-feira, das 09:00h às 16:00h.

Confirmo que li o conteúdo deste Termo de Consentimento Livre e Esclarecido e aceitei participar voluntariamente deste estudo. Ficaram claros para mim quais são os propósitos do estudo, os procedimentos a

2

serem realizados, seus eventuais desconfortos e riscos, as garantias de confidencialidade e de esclarecimentos permanentes. Ficou claro também que minha participação é isenta de despesas e que tenho garantia do acesso a tratamento hospitalar quando necessário. Concordo voluntariamente em participar deste estudo, sabendo que poderei retirar o meu consentimento a qualquer momento, antes ou durante o mesmo, sem penalidades ou prejuízos ou perda de qualquer benefício que eu possa ter adquirido, ou no meu atendimento neste Serviço.

_____

Nome Completo do participante da pesquisa

_____ Data:___/___/___

Assinatura do participante da pesquisa

_____

Nome completo e legível do pesquisador responsável

_____ Data:___/___/___

Assinatura do pesquisador responsável

_____

Nome completo do representante legal

_____ Data:____/____/____

Assinatura do representante legal

_____

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Title: Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	01
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	03
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	05
Protocol version	#3	Date and version identifier	17
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	18;19
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	01
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	06
Roles and responsibilities:	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee,	05

committees		data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3;4;5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3;4;5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5;6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6;7
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8;9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10;11

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10;11;12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	6
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7;8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7;8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7;8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8

Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10;11;12;13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10;11;12;13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10;11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and	20

		reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	20
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	5
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	6
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	10;12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	16
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	20
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	19;20
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	20
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	25;26;27;28
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

Notes:

- 18a: 10;11;12;13
- 18b: 10;11;12;13
- 32: 25;26;27;28 This checklist was completed on 24. July 2020 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Clinical Outcomes and Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

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1. Title: Clinical Outcomes and Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial

1a. Short title: Cost-utility of open and arthroscopic rotator cuff repair

1b. Authors: Rafael Pierami[1,2], Eliane Antonioli[2], Isadora Oliveira[2], Isabela Queirós Castro[2], Felipe Manente[3], Paula Fairbanks[3], Eduardo da Frota Carrera[1,2], Bruno Akio Matsumura[1,2], Mário Lenza[2]

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2.Abstract

Introduction: Rotator cuff injuries account for up to 70% of pain in the shoulder. However, there is still no consensus on the best surgical treatment of patients with rotator cuff injuries, regarding the cost-effectiveness and cost-utility analysis between the open and arthroscopic methods of rotator cuff repair. The objective of this trial is to compare the efficacy, cost-effectiveness and cost-utility of open and arthroscopic procedure for rotator cuff repair.

Methods and Analysis: The trial is a two-group, parallel design, randomized controlled trial. A total of 100 patients with symptomatic rotator cuff lesion will be allocated in either open or arthroscopic technique in a 1:1 ratio, considering smoking (yes or no), lesion size (less than 3 cm or more than 3 cm) and diabetes (present or absent) as stratification factors. All patients will be included in the same rehabilitation program after the intervention. The primary outcomes measure will be the Constant-Murley score and EuroQol 5-D-3L at 48 weeks post-surgery. Secondary outcomes include cost-effectiveness, cost-utility, pain, complications and clinical analysis, using the simple shoulder test (SST), Visual Analogue Pain Scale (VAS), integrity of the repair evaluated through magnetic resonance imaging, complications and failures of the proposed methods. For the cost-effectiveness analyses, we will use the VAS and the Constant-Murley Score as measures of effectiveness; for the cost-utility analyses, we will use the EuroQol- 5D-3L as a measure of utility in terms of incremental cost per quality-adjusted life-years (QALY).

Ethics and Dissemination: The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert Einstein and Hospital Alvorada Moema/ Hospital Pró-Cardíaco. The results will be published in a peer-review open access journal.

Trial Registration Number: NCT04146987

Keywords: rotator cuff; surgery; arthroscopy; open repair; cost-effectiveness; QALY

Strengths and limitations of this study

- This study is a prospective, randomized trial, that is the best design to address the study question. Its methodological analyses are the best option to determine cost-utility and will provide a strong evidence.
- It will provide surgeons and healthcare providers with important information about the surgical technique and the cost-effectiveness and cost-utility of these techniques
- This study will provide important information about rotator cuff healing and retear rates, what is still unclear in the literature
- The lack of blinding of the patient and surgeons is a limitation to the study design

3. Introduction

3a. Background and Rationale

Musculoskeletal injuries are a major cost to the healthcare system. North American data estimate that approximately 4.5 million patients annually seek medical attention due to shoulder pain; of these, two million have some symptoms related to the rotator cuff. About 250,000 rotator cuff repair surgeries are performed annually in the United States of America (US), and with the

continued increase in life expectancy and aging, there is a tendency to increase this number[1][2][3]. An evaluation of the primary health care system in Cambridge, United Kingdom, showed that the average frequency of shoulder pain was 9.5 per 1,000 individuals [4]. Of those, 86% had rotator cuff tendinopathy.

The rotator cuff is a group of four muscles and their tendons that act to stabilize the shoulder and allow for its extensive range of motion. Four muscles and their attached tendons make up the rotator cuff: the subscapularis, supraspinatus, infraspinatus, and teres minor. The long portion of the biceps tendon also contributes to cuff function, which is to stabilize the humeral head in the glenoid cavity, preventing superior migration of the humeral head [5].

The possible lesions range from tendon degeneration (tendinosis/tendinopathy), through partial tear (articular, interstitial or bursal), to complete tear. Its etiology is multifactorial and the main factors associated with tears are tendon degeneration related to aging, trauma, tendon insertion hypovascularity and genetic factors[6][7][8]. Since most lesions are caused by wear and degeneration related to aging, people over 40 years are at greater risk[3]. Diagnosis is made by associating history and physical examination along with imaging methods, and magnetic resonance imaging (MRI) is considered the method of choice [9]–[17].

Treatment of rotator cuff lesion depends on the type of tear, the patient's functional capacity, age, and the presence of symptoms. In general, tendon degeneration and partial tears are treated non-surgically, with physiotherapy, injections and analgesic medications. Complete and incomplete tears that did not respond well to conservative treatment, however, might be treated surgically [12], [18]–[20][3][21][22].

Among the surgical options, the open method is still considered the gold standard, with good or excellent results in over 90% of cases [23]–[25]. Due to arthroscopy and the evolution of arthroscopic instruments and implants in the last two decades, the arthroscopic repair technique has gained space and is widely used. Some studies [23]–[26] did not show superiority of one technique over another in terms of clinical outcomes. On the other hand, since the cost of arthroscopic surgery is supposedly higher, due to the required equipment, it is important to establish which option has the best cost-utility ratio. Other published studies suggested that the open method is superior than the arthroscopic method in relation to cost-utility [27]–[29]. To date, no study in our country has assessed the comparison of the cost-utility of the two techniques; considering that the open technique is being left behind, is important to determine if it remains a viable, reliable and cost-effective option for the treatment of rotator cuff tears.

3b. Objectives

Despite the high incidence of rotator cuff tears, there is no consensus about the best method of repair, neither which method has the best cost-effectiveness and cost-utility ratio. Therefore, the present study aims to compare the open and arthroscopic methods for rotator cuff repair and determine which presents the best cost-effectiveness ratio.

4. Trial Design

The trial will be a prospective randomized controlled clinical trial.

5. Methods

This randomized controlled trial will follow the Consolidated Standards of Reporting Trials (CONSORT) Statement [30]; also the protocol was developed following the SPIRIT

guidelines[31]. It will be performed at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil. The cost analysis will be performed by Hospital Israelita Albert Einstein team, São Paulo, Brazil. The project was approved by both hospitals research ethics committee and registered in clinicaltrials.gov.

5a. Sample size

The sample size estimate was obtained to detect differences between the open and arthroscopic repair groups in relation to the primary outcome of the study, Constant-Murley Score (CM) instrument after the intervention. Kukkone's et al. 2013 study [32] estimated the clinically important minimal difference in CM score in 10.4 points in patients with rotator cuff rupture after 3 months of surgical treatment by the arthroscopic method. The estimated sample size of 45 patients per group, total of 90 patients, would reach 90% power to detect a 10.4 difference between the groups in the CM instrument post-operative score with a standard deviation of up to 15 points with a significance level of 5% using a t-Student test. Predicting a loss of around 10% at 12 months of follow-up we aim to recruit 50 patients per group (PASS software [33]).

5b. Inclusion criteria

All patients eighteen years of age or older, presenting with complete rotator cuff tear or a partial rotator cuff tear of at least 50% of tendon thickness, with symptoms (pain and/or weakness), where conservative therapy failed will be included. The tendon tear will be confirmed by a Magnetic Resonance Imaging (MRI).

5c. Exclusion criteria

Patients with previous shoulder surgery, previous fractures in the affected shoulder, those with passive range of motion limitation (joint stiffness with an elevation of 90 degrees or less), radiographic signs of glenohumeral osteoarthritis or neurologic injury will be excluded. Patients will also be excluded if they do not wish to participate or are unable to understand or sign the informed consent form (due to conditions such as cognitive impairment, or mental illness) or if there are any medical conditions that contraindicate any of the surgical methods.

5d. Randomization and allocation

After eligibility assessment, all patients will be informed about the nature and purpose of the study and will only be included after agreeing with the study and signing the informed consent form, that will be obtained by the surgeon that evaluated the patient and indicated the surgery. Patients will be consecutively allocated to one of two proposed treatment methods: open rotator cuff repair or arthroscopic rotator cuff repair. The software R was used to generate a randomization list, considering 100 patients to be included in the study and the same probability of allocation for both methods of surgery (open and arthroscopic repair). A stratified randomization will be performed using the following variables (strata): smoking (yes or no), the size of the lesion (≤ 3 cm or > 3 cm) and diabetes (present or absent). Randomization will be performed by the REDCap platform (Research Electronic Data Capture – Vanderbilt University)[34][35] after the patient is anesthetized and prepared for the surgery. A person not associated with the study will open the software and acquire one of the two techniques possible and tell the surgeon who will perform the surgery.

5e. Recruitment

All patients that already would be treated by the shoulder surgeons at Hospital Alvorada Moema (Shoulder and Elbow Surgery Center of Excellence), São Paulo, Brazil, will be enrolled in this trial.

5f. Blinding

Due to the type of interventions, neither participants nor treatment providers can be blinded to treatment allocation. The outcome assessment of the primary and secondary outcomes (Constant-Murley; EuroQol; VAS and SST), patient-reported outcomes, will not be blind. One of the authors (RP) will assess all other clinical outcomes. The statisticians conducting the analyses will be blinded to the treatment status until the analyses are completed.

5g. Ethics and Dissemination

The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert Einstein (CAAE 19182619.3.1001.0071) and Hospital Alvorada Moema/ Hospital Pró-Cardíaco (CAAE 19182619.3.2002.5533). Digital, informed consent (supplementary material) to participate will be obtained from all participants trough software REDCAP[35][34].

This study was developed and will follow the International Conference Guideline for Good Clinical Practice (ICH GP) to assure that the data and results are credible and that the rights, integrity and confidentiality of the trial subjects are protected and respected[36][37].

All authors agreed to publish the results of the present study in a peer-reviewed open access journal, despite the results and conclusions found. All data will be available upon request.

5h. Patient and Public Involvement

The patients nor the public were involved on the design and development of this study. Their participation will first occur with the contact between the surgeon and patient, when they will be informed about the study and will decide to participate or not. At that time, they will be informed about the purpose and importance of it. During the entire follow-up the patients will be able to enquiry the researchers and surgeons about the project and to make suggestions and complaints about it.

All the outcomes measures will be self-reported. The patients will be assisted by one member of the research team, if they have any questions or doubts.

Since the authors agreed to publish the results of this research, patients will not be involved on the dissemination. However, they will be encouraged to disseminate the knowledge among the community.

6. Intervention methods

Five surgeons with at least four years of surgical technique experience will participate in this study (EFC, MTCA, RP, BAM, VR). Also, the residents of shoulder and elbow surgery, as well as the residents of Orthopedics and Traumatology from Hospital Alvorada Moema and residents in shoulder and elbow surgery at Albert Einstein Hospital may participate in surgeries.

Open surgery: patients will be positioned in a beach chair position with the affected limb pending off the table, allowing manipulation and full range of motion. After standard patient preparation, an anterolateral incision will be made in the shoulder; the deltoid muscle belly will be gently divided along its fibers until exposure of the subdeltoid / subacromial bursa, which will be partially excised for exposure of the subacromial space and rotator cuff tendons. After mobilization

and release of the ruptured tendons and debridement of the rotator cuff footprint, the tendon repair to the bone will be performed using 5.5mm metal anchors ("Super Revo"-CONMED, USA), according to the preference and technique chosen by the surgeon. In all cases, the release of the coracoacromial ligament and acromioplasty will be performed.

Arthroscopic Technique: the patients will be positioned in lateral decubitus position, with the limb to be operated attached to a skin traction device, which through a traction post and 7 kilograms (kg), will maintain the shoulder in the following position: abduction of 30 to 60 degrees and flexion of 20 to 30 degrees. After standard patient preparation, a posterolateral incision will be made in the shoulder for optic introduction, with a 50mmHg pressure pump and a 0.90 flow, and inspection of the glenohumeral joint. After establishment of all required arthroscopic portals, joint inspection will be performed and any, if present, associated pathologies will be addressed. With the use of shaver blades, partial bursectomy will be performed and any adherence to the tendon stumps will be released, as well as debridement of the rotator cuff footprint. The tendon will then be reinserted to the bone using metallic 5.5mm anchors ("Super Revo"-CONMED, USA), according to the preference of each surgeon. The technique used, as well as the suture configuration and type of knot used, will be defined by the surgeon, according to his preference.

After tendon repair, the coracoacromial ligament will be released, as well as acromioplasty will be performed.

7. Postoperative rehabilitation

All patients will undergo the same postoperative rehabilitation protocol: use of Velpeau sling for 6 weeks; pendulum exercises starting on second week; active movement and recovery of the range of motion from the sixth week and strengthening from the twelfth week.

The patients will be oriented to perform home exercises and to be assisted by a physiotherapist twice a week from the sixth week of surgery and on. Approximately thirty sessions of physical therapy will be expected.

8. Outcomes assessment

Study data will be collected and managed using REDCap (Research Electronic Data Capture- "Vanderbilt University, Nashville, Tennessee, USA") hosted at Hospital Israelita Albert Einstein [34][35]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

All study participants will be evaluated preoperatively, at the hospital discharge and 1, 2, 6, 24 and 48 weeks after the intervention. The Constant-Murley score, Visual Analogue Scale, EuroQol-5D-3L and the Simple Shoulder Test questionnaires will be filled out by the patient and assessed by evaluators to the assigned intervention. The endpoint of cost-utility analysis will be 48 weeks; clinical outcomes will also be assessed at 6 and 24 weeks.

To prevent loss of follow-up all the patients will be monitored by REDCap software and alerts will be sent to each patient near time points defined by the investigators. One week before every medical consultation and at the twelfth week, during the rehabilitation process. If the patient fails to fill any questionnaire or does not attend the medical consultations, he will be contacted by phone and e-mail. If a patient becomes not reachable at any time of the follow-up, we will consider a lost follow-up scenario, where, in accordance with the intention to treat principle, appropriate

statistical methods for data analysis, that consider unbalanced data and loss of follow-up, such as Generalized Estimating Equation Model (GEE), will consider all patients observations, even if they fail in some moment. Thereby, these patients will not be excluded, and all data will be considered.

9. Primary outcome

The Brazilian Portuguese Version of the Constant-Murley Score (CM) [38] will be measured preoperatively at 6, 24 and 48 weeks after the intervention. Research assistants (not blinded to the study aim) will ask the patients to fill in the validated CM form in Portuguese and measure the range of motion with an analogic goniometer. The CM scale covers different domains of shoulder function (pain, activities of daily living, range of motion and power), punctuating each of them; it ranges from 0 to 100, with higher scores indicating better function[38]. The constant-Murley score is one of the most commonly used scores on shoulder scoring system and is considered the gold-standard in Europe[39][40]. It is reliable for detection of shoulder improvement after surgical procedures and its strong correlation with shoulder specific diseases, especially rotator cuff, and reliability makes it a good score system for a clinical research.

EuroQol-5D-3L (European Quality of Life), a generic score developed to describe health-related quality of life [30] will also be assessed preoperatively, at 6, 24 and 48 weeks postoperatively. This score includes five health domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; each domain has 3 levels: no problem; some problems and extreme problems. In addition, the EuroQol-5D-3L has a visual analog scale where the participant assigns a value between 0 and 100 to his or her own health condition, where 100 means "the best imaginable health status" or "the best health state you can imagine" and 0 means "the worst imaginable health state" or "the worst health state you can imagine". This is used to obtain

a respondent's stated preference values, not to record their own health state. [41]. At the end of its application, EuroQol-5D-3L will provide a unique numerical value that can be used for longitudinal comparison between different time periods.

9b. Secondary outcomes

Clinical outcomes will also be assessed by the Simple Shoulder Test (SST), validated for Portuguese [42], preoperatively and at 6, 24 and 48 weeks after the procedure. SST is a simple, quick and widely used questionnaire for shoulder function measurement; it consists of 12 dichotomous questions answered by the patient himself. Each positive answer (yes) is given a score; at the end of the questionnaire the percentage of positive answers (score) is made, and the higher the percentage, the better the shoulder function. Other outcomes measured will be VAS (visual analogue pain scale) at hospital discharge, 1, 2, 6, 24 and 48 weeks after the intervention. This scale allows pain intensity to be measured with maximum interobserver reproducibility; it consists of a 10 cm straight line with the ends determining the limits of pain sensation (no pain; worst pain ever experienced); the distance between zero (no pain) and the patient's demarcation defines the intensity of pain[43].

Complications and failures of the proposed methods will also be assessed. Failures will be characterized as the need for additional surgical procedures and/or change of the initially proposed procedure. Patients who, for any reason, demonstrate treatment failure or require additional interventions will be followed up and their results included in the group in which they were initially randomized, according to the intention to treat principle.

At the final follow-up (forty-eight weeks), the integrity and healing of repaired rotator cuff will be assessed through Magnetic Resonance Imaging (MRI).

9c. Cost-effectiveness

Cost-effectiveness and cost-utility analyses will be assessed by the estimate of direct and indirect costs to the private healthcare system at 48 weeks. The perspective adopted in the study will be the social costs, the direct and indirect medical costs. The set timeframe will be 48 weeks and a sensitivity analysis will be performed with the costs data, considering 0% to 5% discount rate to define the optimal discount rate for the data, according to methodological Guidelines for Economic Evaluation of Health Technologies – Brazilian Ministry of Health[44], [45][46]. The costs included in direct medical costs will be: hospitalization, costs related to arthroscopic instruments (e.g. cannulas, shaver blades, suture passer, ablator) medical fees, medication; the indirect costs: costs of absence from work, which will be estimated by the patient-reported number of days away from work multiplied by the average wage rate of the current year. The costs will be converted from Brazilian Reais to US dollars and brought to the cost schedule of the current year, in order to avoid that the effect of inflation on the medical inputs influences the analysis. For the cost-effectiveness analysis, the VAS and the CM will be used as measures of effectiveness. For the cost-utility analysis, the EuroQOL-5D-3L will be used as a measure of utility. The timetable of outcomes assessment is described on Table 1.

Table1. Timetable of assessment

STUDY PERIOD								
	Enrolment	Allocation	Post-Allocation					Close-Out
TIMEPOINT	0	0	Surgery	1w	2w	6w	24w	48w

ENROLMENT:								
Eligibility Screen	X							
Informed Consent	X							
CM; EQ-5D, SST;	X							
VAS	X							
Allocation		X						
INTERVENTIONS								
Open Repair			X					
Arthroscopic Repair			X					
ASSESSMENTS:								
CM; EQ-5D, SST;						X	X	X
VAS			X	X	X	X	X	X
MRI	X							X
Complications			X	X	X	X	X	X
Economics			X	X	X	X	X	X

292

293 **10. Data analysis**

294 The descriptive analyses of variables will be based on the absolute frequencies and
295 percentages for categorical variables and summary measures as means and standard deviations or
296 medians and quartiles, as well as minimum and maximum values for numerical variables [47].

Clinical scores will be represented by individual profile graphs separately by the surgical technique group.

The groups will be compared according to the presence of categorical clinical outcomes (failures, complications and healing integrity) by Chi-square or Fisher's exact tests, depending on the distribution observed after data collection.

For inferential analysis of continuous variables clinical outcomes, mixed models will be used and, if the normal distribution is not adequate, generalized mixed models will be used [48]. The models will have time effects (preoperative, 6, 24 and 48 weeks after intervention), surgical technique group (open repair or arthroscopic repair) and the interaction effect between time and group. The size of the lesion (smaller than three cm or larger than three cm) will also be included in the models as a control variable, seeking to avoid possible biases.

The analyzes will be performed with the aid of the SPSS program (**SPSS** Inc., Chicago, Illinois, USA) [49], considering a significance level of 5%.

11. Safety

There will be no benefit to the participant, beyond what is expected for the correction of the rotator cuff tear, expecting an improvement of pain and function of the affected shoulder. The risks of the present study are those inherent in any surgical treatment and anesthetic procedure, such as surgical wound infection, scar formation, pain, decrease in shoulder range of motion, rotator cuff tear, neurovascular injury. If any complications occur, all patients will be treated by the same surgical team until the complication is healed.

Both surgical techniques have the same goal, that is, to repair the ruptured tendon to the bone. The open technique requires a larger incision, as well as greater surgical dissection and

manipulation of the deltoid muscle, which may cause greater postoperative pain and weakness of this muscle, in addition to causing a slightly larger scar. However, it provides great visualization and manipulation and mobilization capability of the ruptured tendon, which provides a safer and tension-free repair.

The arthroscopic technique is performed with some point-shaped cuts in the shoulder, usually three or four; due to smaller incisions, it requires less muscle manipulation, which theoretically would cause less postoperative pain and less muscle weakness of the deltoid muscle, it also has minor scars. However, this technique requires more surgeon's experience and the mobilization of the ruptured tendon(s) is limited. Using a large amount of saline may cause edema in the operated shoulder, which is usually resolved after the first 12 hours of surgery.

Finally, there is a minimal risk of loss of data confidentiality; all data will be managed, stored and protected by REDCAP software[34], [35]. Only the main investigator will have access to all data during the entire trial period. Any adverse event will be reported to the researchers involved and communicated to the main investigator according to the Institutional Review Boards description.

12. Discussion

There is no consensus about the best cost-effectiveness of surgical treatment of patients with degenerative rotator cuff injuries. Several studies [27], [28], [50], [51] suggest that the open repair method is more cost-effective than the arthroscopic method, resulting in the same clinical outcome with lower cost. Adla, Deepthi N. et. al [27] in a prospective nonrandomized study, showed that both techniques lead to the same clinical outcomes. The costs of arthroscopic surgery were higher than the open surgery, mainly due to the costs of the suture anchors, which was used

only in the arthroscopic group, is important to notice that in most of the open surgeries, the repair was performed through transosseous sutures. Köse, Kamil Çağri et. al [28], in a retrospective study, also demonstrated similar clinical outcomes, although the costs of arthroscopic procedure being much higher. Importantly, the open repair technique was performed using transosseous sutures and the arthroscopic method using suture anchors and also, the open repair group required longer length hospital stay. Hui, Yik Jing et. al [50] in a retrospective cohort study, described a significantly higher cost for the arthroscopic procedure, compared to the open repair, evaluating only the in-hospital costs, but with the same clinical outcomes. However, it is important to emphasize that the open repair was performed using transosseous sutures, without suture anchors and that the arthroscopic group needed a longer surgery time. Churchill, R.S. et. al [51] using the New York Ambulatory Database System, with a total of 5,224 cuff repair surgeries, of which 1,334 open repair and 3,890 arthroscopic repair, showed that the mini-open rotator cuff repair costs significantly less than the arthroscopic repair and requires significantly less surgical time. However, no clinical outcomes have been analyzed in this study, making it impossible to determine the cost-effectiveness ratio. An important study by Carr, A.J. et. al [52] carried out as a prospective multicenter randomized clinical trial, concluded that there is no difference in the effectiveness and cost-effectiveness between the open repair surgery and arthroscopic surgery after 24 months of follow-up, even with the higher initial costs in the arthroscopy surgery. An economic evaluation of the data from this study was carried out, showing that the Incremental Cost Effectiveness (ICER) was uncertain and the arthroscopic repair surgery was slightly more costly and less effective than open repair surgery.

Thus, despite the high incidence of rotator cuff tear, there is insufficient evidence to determine the best method for treating these injuries. So, the present study proposes to answer the

clinical question of which method, open or arthroscopic, presents the best cost-utility in the surgical treatment of rotator cuff tear. Providing conclusive, good quality evidence for and contributing to the evidence base of methods used to treat rotator cuff injuries.

13. Trial status

Protocol Trial version: 5 Date: 12/11/2020

Recruitment Start Date: August/2020

Recruitment Estimated End Date: December/2021

Recruiting

14. Additional files (Supplementary Material)

Table 1. Timetable of assessment

Informed Consent

Ethical Committee Review

SPIRIT Checklist

15. Abbreviations

CONSORT: Consolidated standards of reporting trials; VAS: Visual analogue scale; MRI: magnetic resonance imaging; QALY: quality-adjusted life years; CM: Constant-Murley Score; SST: Simple Shoulder Test

16. Declarations

16.1 Ethics Approval and Consent to Participate

The study has been approved by the local Research Ethics Committee from both institutions: Hospital Israelita Albert Einstein (CAAE 19182619.3.1001.0071) and Hospital Alvorada Moema/ Hospital Pró-Cardíaco (CAAE 19182619.3.2002.5533). Digital, informed consent to participate will be obtained from all participants trough software REDCAP[35][34].

All and any modifications in this study will be promptly reported to all Research Ethics Committee, all institutions, all investigators and all participants.

16.2 Consent for Publication

Not Applicable

16.3 Availability of Data and Materials

The datasets used and/or analyzed during the current study will be available from the corresponding author upon request.

16.4 Competing interests

The authors declare that they have no competing interests.

16.5 Funding

This study is supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2019/02159-3).

16.6 Registry

The project is registered in the clinicaltrials.gov database (NCT04146987 https://clinicaltrials.gov/ct2/show/NCT04146987?term=NCT04146987&draw=2&rank=1).

16.7 Contributorship Statement

All listed authors had a substantial contribution to the conceptions and development of this study, revised, approved the final version and are accountable for all aspects of the study. We ensure that all questions related to the accuracy or integrity of any part of the project are appropriately investigated and resolved. Contributions were as follows:

ML is the Chief Investigator; he conceived the study, led the proposal and protocol development.

RP is the lead trial methodologist and helped in the study conceiving and development

EA contributed to study design and to development of the proposal.

IO contributes to study design related to QALY

IQC is responsible for cost-analysis

FM helped in the English translation and registration/publication of the trial

PF helped in the English translation and registration/publication of the trial

EFC helped in the study conceiving and development

BAM helped in the study conceiving and development

16.8 Acknowledgements

Not applicable

17. Dissemination policy

All the authors are committed and agree to publish the full results of the research, despite the final results.

18. Data Monitoring Committee (DMC)

Since this trial have a short duration and both surgical techniques have known minimal risks, there is no need for such committee.

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TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Título do projeto: *Custo-Efetividade da Cirurgia de Reparo do Manguito Rotador Pelas Técnicas Aberta e Artroscópica. Ensaio Clínico Randomizado.*

Prezado,

Você foi convidado a participar da pesquisa intitulada "Custo-Efetividade da Cirurgia de Reparo do Manguito Rotador Pelas Técnicas Aberta e Artroscópica. Ensaio Clínico Randomizado". Essas informações serão fornecidas por meio de sua participação voluntária neste estudo, com o objetivo de avaliar o custo-efetividade (benefícios e malefícios e os custos dos procedimentos) das intervenções: reparo aberto do manguito rotador e reparo artroscópico do manguito rotador.

A ruptura do manguito rotador, ou seja, o rompimento dos tendões do ombro é a principal de causa de dor no ombro na população adulta, causando, além da dor, diminuição da força no ombro acometido e diminuição na qualidade de vida do paciente, devido a dor constante e piora na qualidade do sono, causado pela dor. Existem duas técnica cirúrgicas para correção desta doença: a técnica aberta, realizada por uma incisão (corte) no ombro e visualização direta do tendão rompido; e a técnica artroscópica, realizada através de pequenos corte no ombro, por onde são introduzidos câmera de vídeo, para visualização do tendão rompido através de monitor, e instrumentais para realização da cirurgia. A motivação da realização deste estudo se deve ao fato de encontrarmos na literatura atual dúvidas sobre qual método de reparo do manguito rotador apresenta a melhora relação custo-efetividade. Acreditamos que o reparo aberto do manguito rotador apresente os mesmos resultados funcionais e de qualidade de vida que o reparo artroscópico do manguito rotador, além de apresentar um custo menor.

Procedimentos a serem utilizados:

O número de participantes estimado é de 100 indivíduos, divididos em dois grupos, 50 para o grupo de reparo aberto do manguito rotador e 50 para o grupo de reparo artroscópico do manguito rotador. A seleção será feita de forma randomizada, isto é, não saberemos onde cada indivíduo será incluído.

Os dois grupos de pacientes receberão os mesmos cuidados e os mesmos seguimentos. As avaliações serão realizadas por meio de exames clínicos e funcionais (realizados por um médico) no pré-operatório, 6, 24 e 48 semanas após o procedimento cirúrgico, exame de ressonância magnética no pré-operatório e 48 semanas após o procedimento. O programa de reabilitação após as intervenções de tratamento será idêntico em cada um dos grupos comparados. Todos os pacientes utilizarão tipóia do tipo Velpeau por seis semanas; depois de duas semanas da intervenção, você iniciará um programa de exercícios pendulares orientados pelo médico e após a sexta semana, a tipóia será retirada e você será orientado a realizar exercícios domésticos para ganho de arco de movimento (ADM), além de duas sessões semanais de fisioterapia para analgesia e recuperação da amplitude de movimento do ombro. Os exercícios de fortalecimento serão permitidos a partir da décima segunda semana, sob orientação de fisioterapeuta.

No término do estudo será verificado se houve melhora nas avaliações funcionais, de qualidade de vida e cicatrização do tendão reparado por meio de questionários de simples preenchimento e exame de ressonância magnética.

Você não terá benefício além do esperado para a operação de correção da lesão, esperando-se melhora da dor e função do ombro acometido. Os riscos do presente estudo são aqueles inerentes a qualquer tratamento cirúrgico e procedimento anestésico, como infecção da ferida operatória, formação de cicatriz, dor, limitação do arco de movimento do ombro, rerruptura do manguito rotador, lesão neurovascular. Ambas as técnicas cirúrgicas tem o mesmo objetivo, ou seja, reparar o tendão rompido ao osso. A técnica aberta necessita de uma incisão (corte) maior, além de maior dissecção cirúrgica e manipulação do músculo deltoide, o que pode provocar maior dor pós-operatória e fraqueza desse músculo, além de causar uma cicatriz pouco maior. Entretanto, ela provê uma grande visualização e capacidade de manipulação e mobilização do tendão rompido, o que proporciona um reparo mais

seguro e livre de tensão. Já a técnica artroscópica é realizada com alguns cortes puntiformes no ombro, geralmente três ou quatro; pelas incisões (cortes) menores, ela necessita de menos manipulação muscular, o que teoricamente causaria menos dor pós-operatória e menos fraqueza muscular do músculo deltoide; além disso, apresenta cicatrizes menores. No entanto, é uma técnica que demanda mais experiência do cirurgião e a mobilização do(s) tendão(ões) rompidos é limitada; a utilização de grande quantidade de soro fisiológico pode causar edema no ombro operado, o que geralmente é revertido após as primeiras 12 horas da cirurgia.

Trata-se de um estudo que testará a hipótese de que a cirurgia de reparo aberto do manguito rotador apresenta uma melhor relação custo-efetividade que a cirurgia de reparo artroscópico do manguito rotador. Somente no final do estudo poderemos determinar a presença de alguma diferença entre estes dois tipos de tratamento.

Em qualquer etapa do estudo, você terá acesso aos profissionais responsáveis pela pesquisa para esclarecimento de eventuais dúvidas. O coordenador do projeto é o Dr. Mário Lenza e o principal responsável pelo estudo é o Dr. Rafael Pierami, que podem ser encontrados: Dr. Mario Lenza – endereço Av. Albert Einstein, 627 – bloco A1 – 3º andar – Programa Locomotor, Morumbi, São Paulo – CEP 05652-900: Tel: (11) 2151.1444; e-mail: mario.lenza@einstein.br; e Dr. Rafael Pierami – endereço Avenida Ministro Gabriel Rezende de Passos, 550, 2º andar ,Hospital Alvorada Moema – Centro de Excelência em Cirurgia de Ombro e Cotovelo, Moema, São Paulo – CEP 04521-022 – Tel: (11) 2186-9810 ou (11) 2186-9809; e-mail: rafael_pierami@hotmail.com.

Se você tiver qualquer dúvida ética em relação à pesquisa, entre em contato com o **Comitê de Ética em Pesquisa do Hospital Israelita Albert Einstein -** Av. Albert Einstein 627/701, fone 2151-3729, e-mail: cep@einstein.br ou o **Comitê de Pesquisa do Hospital Alvorada-** Av. Ministro Gabriel de Rezende Passos, 550, 2º andar, telefones 2186-9810 ou 2186-9809, e-mail: rafael_pierami@hotmail.com ou ainda o Comitê de Ética em Pesquisa em Seres Humanos do Hospital Pró-Cardíaco (CEP/HPC), Tel: (21) 3289-3802, Localizado na Rua Voluntários da Pátria, 435/8º andar, Botafogo, Rio de Janeiro, CEP: 22270-005 - Horário de atendimento: de segunda à sexta-feira, das 09:00h às 16:00h.

Reclamações, elogios e sugestões deverão ser encaminhados ao Sistema de Atendimento ao Cliente (SAC) por meio do telefone (11) 2151-0222 ou formulário identificado como fale conosco disponível na página da pesquisa clínica ou pessoalmente.

Você pode retirar o seu consentimento a qualquer momento e deixar de participar do estudo, sem qualquer prejuízo à continuidade de seu tratamento na Instituição.

Suas informações serão analisadas em conjunto com as informações de outros pacientes voluntários e não será divulgada a identificação de nenhum paciente. Você tem o direito de ser mantido atualizado sobre os resultados parciais das pesquisas e de quaisquer resultados que sejam do conhecimento dos pesquisadores. Não haverá nenhuma despesa pessoal para você em qualquer fase do estudo, incluindo exames e consultas, assim como também não há compensação financeira relacionada à sua participação.

Se você sofrer algum dano, previsto ou não neste termo de consentimento e relacionado com sua participação no estudo, a equipe que realizou o procedimento custeará as despesas médicas necessárias e decorrentes do estudo.

O pesquisador se compromete a utilizar os dados e materiais coletado durante o estudo somente para esta pesquisa, como descrito previamente.

Eu discuti com o Dr. Mário Lenza e/ou Dr. Rafael Pierami e/ou qualquer membro autorizado da equipe desta pesquisa, sobre a minha decisão em participar nesse estudo. Ficaram claros para mim quais são os propósitos do estudo, os procedimentos a serem realizados, seus eventuais desconfortos e riscos, as garantias de confidencialidade e de esclarecimentos permanentes. Ficou claro também que minha participação é isenta de despesas e que tenho garantia do acesso a tratamento hospitalar quando necessário. Concordo voluntariamente em participar deste estudo e poderei retirar o meu consentimento a qualquer momento, antes ou durante o mesmo, sem penalidades ou prejuízo ou perda de qualquer benefício que eu possa ter adquirido, ou no meu atendimento neste Serviço.

ALBERT EINSTEIN
HOSPITAL ISRAELITA

Hospital Alvorada

_____

Nome Completo do participante da pesquisa

_____ Data:___/___/___

Assinatura do participante da pesquisa

_____

Nome completo e legível do pesquisador responsável

_____Data:___/___/___

Assinatura do pesquisador responsável

_____

Nome completo do representante legal

_____ Data:____/____/____

Assinatura do representante legal

_____

Relação do representante legal com o paciente

_____

Nome completo da testemunha imparcial

****para casos de voluntários menores de 18 anos, analfabetos, semi-analfabetos ou portadores de deficiência auditiva ou visual.**

_____ Data:____/____/____

Assinatura da testemunha imparcial

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Title: Cost-Utility of Rotator Cuff Repair Surgery by Open and Arthroscopic Techniques: Study Protocol for a Randomized Clinical Trial.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	01
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	03
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	05
Protocol version	#3	Date and version identifier	17
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	18;19
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	01
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	06
Roles and responsibilities:	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee,	05

committees		data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3;4;5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3;4;5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5;6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6;7
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8;9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	12
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10;11

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10;11;12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	6
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7;8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7;8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7;8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8

Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10;11;12;13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10;11;12;13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	10;11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and	20

		reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	20
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	5
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	6
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	10;12
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19

Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	16
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	20
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	19;20
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	20
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	25;26;27;28
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

Notes:

- 18a: 10;11;12;13
- 18b: 10;11;12;13
- 32: 25;26;27;28 This checklist was completed on 24. July 2020 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai