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Developing a Machine Learning Algorithm to predict retear probability in patients undergoing rotator cuff repair surgery: A protocol for a retrospective multicenter study.

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TITLE: Developing a Machine Learning Algorithm to predict retear probability in patients undergoing rotator cuff repair surgery: A protocol for a retrospective multicenter study.

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ABSTRACT

Purpose/Introduction: The effectiveness of rotator cuff tear repair surgery is influenced by multiple patient-related, pathology-centered and technical factors, which is thought to contribute to the reported retear rates between 17 and 94%. Adequate patient selection is thought to be essential in reaching satisfactory results. However, no clear consensus has been reached on which factors are most predictive of successful surgery. A clinical decision tool that encompassed all aspects is still to be made. Artificial Intelligence (AI) and machine learning algorithms use self-learning complex models that can be used to make patient-specific decision-making tools.

The aim of this study is to develop and train an algorithm that can be used as an online available clinical prediction tool, to predict the risk of retear in patients undergoing rotator cuff repair.

Methods: This is a retrospective multicenter cohort study. Patients undergoing rotator cuff repair and evaluated by advanced imaging for healing at a minimum of 6 months after surgery were included. This study consists of two parts. Part one: collecting all potential factors that might influence retear risks from retrospective multicenter data, aiming to include >1000 patients worldwide. Part two: combining all influencing factors into a model that can clinically be used as a prediction tool using machine learning.

Ethics and dissemination: For safe multicenter data exchange and analysis, our Machine Learning Consortium adhered to the World Health Organization (WHO) regulation "Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies." The study results will be disseminated through publication in a peer-reviewed journal. IRB approval does not apply to the current study protocol.

Trial registration: N/A

ARTICLE SUMMARY

- This study aims to calculate a patient-specific retear-chance after rotator cuff repair surgery.
- Creating an online-available tool that predicts retear chances can help both medical professionals and patients in clinical decision-making on rotator cuff repair surgery.
- Included data will be gathered from previously published databases of all authors included in the Machine Learning Consortium, aiming to include data from over 1000 patients.
- This study does have the limitation of being retrospective and therefore the study is dependent on the recordkeeping of each individual hospital.

INTRODUCTION

Despite technical advances of rotator cuff repair, the rate of unhealed or re-torn rotator cuff tears remains high, with percentages ranging between 17 and 94% (1). A myriad of patient-related (2), pathology-centered (3) and technical factors (4) influence this adverse outcome.

Patient selection is thought to be essential, however there is no consensus on which of the numerous potentially influential factors are most important for the prediction of satisfactory postoperative results (5). Furthermore, the value of preoperative optimization of potential comorbidities, metabolic deficiencies and intoxications remains questionable. Multiple leaders in shoulder surgery – convinced of patient-related influential factors – have implemented extensive preoperative screening and optimization programs prior to rotator cuff surgery. These include smoking cessation programs, diabetes control, use of statins in hyperlipidemia and vitamin D deficiency supplementing (2,6). However, a majority of shoulder surgeons – left daunted by the overwhelming and somewhat conflicting clinical evidence – seems to limit decision-making to more basic factors including age, functional demand and pathology-specific grading. Despite many different classification systems have been developed to facilitate decision making, a patient specific decision tool is still lacking (7,8).

Artificial intelligence and machine learning (ML) is believed to facilitate a more patient-specific approach and will allow us to move to the next level of evidence-based medicine: personalized patient-care. Clinical prediction tools, incorporating patient specific factors to predict outcome probabilities will provide guidance to both clinicians and patients (9–11). Within orthopedic (oncology) surgery, prediction tools based on ML algorithms, have already been successfully implemented to predict patient specific 5-year survival in patients with chondrosarcoma (12). Furthermore, based on a series of 422 patients undergoing lumbar discectomy, Staartjes et al. demonstrated deep learning algorithms to be superior to standard regression models in predicting patient-reported outcome measures (PROMs) (11).

The aim of this study is to develop and train a machine learning algorithm in order to create a clinical prediction tool to be used in clinical practice by predicting retear-chance of the rotator cuff based on preoperative patient data. The prediction tool will be free and online available.

METHODS AND ANALYSIS

This study consists of two parts

1. Collecting data
2. Creating an online clinical prediction tool

1. Collecting data

Step one involves collecting data from previously published studies in order to combine these into a central database. Included were all randomized controlled trials comparing any surgical technique, add-on biological intervention or rehabilitation protocols concerning rotator cuff surgery. In addition, cohorts evaluating risk factors of surgical techniques after rotator cuff repair were included. This retrospective review will therefore incorporate patients with all types of tears and concomitant procedures (e.g. biceps tenodesis or tenotomy and acromioclavicular resection). Exclusion criteria for all studies was the lack of postoperative evaluation by ultrasound, contrast-enhanced computed tomography or magnetic resonance imaging at minimally 6 months after surgery. Relevant studies have been identified using a systematic approach searching the online PubMed database according to the search terms found in supplement 1. We aim to include at least 1000 patients in the database, all centers worldwide will be able to contribute data.

2. Machine Learning

Training Data & Test Data

Eighty percent (80%) of all (>1000) patients included in the Machine Learning Consortium Database will be randomly allocated to the training dataset and 20% to the test dataset.

Outcome variables

Primary outcome measures (dichotomous)

- Rotator cuff retear rates at minimum 6 months follow-up (yes vs no, specified by Sugaya Classification (13)) as measured on magnetic resonance imaging, arthro-CT and/or ultrasound.
- Enduring satisfactory functional outcome defined as achievement (yes vs no) and maintenance (yes vs no) of the PROM-specific MCID (14) in numeric rating scales of PROMs from baseline at 2-5 years follow-up after repair (PROMs include the Constant-Murley score, ASES, UCLA, OSS, WORC, DASH).

Secondary outcome measures (categorical)

- Adverse events graded as the possibility of none/minor vs moderate/severe complication as defined in accordance to Felsch et al. and specified as infection, revision surgery or other (15).

Input Variables

For each respective primary outcome, a Random-Forest will be created based on all available data points in the Machine Learning Consortium Database to identify the variables with the highest predictive values. The data points available include patient demographic (sex, age), patient specific factors (BMI, dominance), pathology specific factors (e.g. tear size and location), surgical technique and add-on interventions. For a complete overview of all variables see supplement 2.

Machine learning algorithm: development and testing

Algorithms to be trained

Based on previous studies (16,17), the following algorithms are likely to result in accurate prediction models for our primary outcomes: 1) Bayes Point Machine 2) Boosted Decision Tree 3) Penalized Logistical Regression 4) Neural Network 5) Support Vector Machine. In order to recognize patterns related to each outcome, the machine learning algorithms will have to be trained separately for each outcome.

Assessing the performance of the algorithms on the test set

The test-set consisting of 20% of the remaining data will be used to assess the performance of these respective machine learning algorithms. The performance of the ML-algorithms will be assessed and compared based on 1) model discrimination 2) calibration and 3) overall model performance (Brier Score) according to Steyerberg's structured 'ABCD-methodology' for clinical prediction rules (18,19).

Accuracy, sensitivity, specificity and area under the ROC-curve are measures for a model's ability to distinguish patients with the primary outcome from those without.

Development decision rule

The best performing algorithm will be deployed as an open-access probability calculator and used to design a clinical decision rule. To simulate the clinical scenario to which a decision rule would be most applicable, thresholds shall be selected based on patients with clinical symptoms of a retear with an unsatisfactory functional outcome. The technical appendix and statistical code will be published.

Blinding of data and external validation

The researchers that will perform the statistical analysis and development of machine learning algorithms will be blinded of the origin of the data. Before incorporating the best performing algorithm will be externally validated. The same performance metrics will be calculated as described above.

Patients and public involvement

Patients and the public were not involved in the making of this protocol.

ETHICS AND DISSEMINATION

For safe multicentre data exchange and analysis, our Machine Learning Consortium adhered to the World Health Organization (WHO) regulation 'Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies' (20). As IRB has been acquired for each of the included studies and data are anonymized as in conventional meta-analyses, an additional IRB request does not apply to the current study protocol.

CURRENT STATUS

The study has currently entered the data-collection phase, which is expected to last until mid-2022. Re-evaluation of the data using machine learning algorithms to predict outcomes will start in September 2022, after which the algorithms can be externally validated. The expected time of completion is by the mid-2023.

DISCUSSION

Due to the wide variety of pathological factors at the origin of rotator cuff tears and the numerous surgical approaches to repair, optimal decision-making remains challenging. Smaller case series often provide heterogeneous data on this topic, however the largest and most recent meta-analysis to date including 2,611 patients with a mean follow-up of 25 months has somewhat demystified the matter. Patients with a full-thickness rotator cuff retear exhibited significantly lower functional outcome scores and strength compared with patients with an intact or partially torn rotator cuff (21). This is corroborated by the findings of rotator cuff repair with more than 10 years follow-up, showing clinical superiority of structural tendon integrity in partial cuff tears (22,23). Progressive osteoarthritic changes are significantly more common in patients with repair failures (23). The most recent RCT comparing surgical repair to conservative treatment for degenerative rotator cuff tears showed that only operated patients without retear had an improvement exceeding the minimal clinical important difference (MCID) in functional outcome at 1 year follow-up (24). Findings from the latest meta-analysis on this comparative topic conclude that as the success rate of conservative treatment may be high, judicious selection of patients who are most likely to benefit from surgery is key (25). It is extremely difficult to combine all these factors into a clinical decision related to one specific patient. Creating a free online available clinical prediction tool that takes all these factors into account will assist physicians in selecting which patients with rotator cuff tears will profit from a repair. In addition, the aimed size (more than 1000 patients) of the database that will be used to design and train the prediction tool might provide new insights on which biological or biomechanical factors influence retear risk the most. Awareness of these factors would be the essential first step to incorporating them in future treatment strategies and eventually improving outcomes. The main limitation of this study is that it is a retrospective, multicenter study. This means this study is dependent on the quality of recordkeeping in the different participating hospitals. This may lead to variance in recorded variables and therefore missing data.

AUTHOR STATEMENT

Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J van den Bekerom contributed to the conception, overall design and planning of the study. Laurent A.M. Hendrickx and Job N. Doornberg contributed to the conception and design of the methods section, primarily focussing on the machine learning section and data analysis. Alexander Lädermann, George S. Athwall, Thibault Lafosse and Laurent Lafosse contributed to the design of the methods section and primarily focussed on how the data should be collected and interpreted. Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J. van den Bekerom contributed to writing the protocol. All authors revised this version of the protocol and gave final approval for it to be published. All authors ensure that questions related to the accuracy or integrity of any part of this protocol are appropriately investigated and resolved.

CONTRIBUTOR STATEMENT

Vivek Pandey, Mats Ranebo, Martyn Snow and Riccardo d'Ambrosi have contributed by providing relevant feedback on the general design of the study.

CONFLICTS OF INTEREST

Dr Alexandre Lädermann is a paid consultant for Arthrex, Medacta and Stryker. He receives royalties from Stryker. He is the founder of BeeMed, Med4Cast and FORE. He owns stock options from Medacta. Dr. L. Lafosse is a consultant for Depuy Stryker, received royalties from Depuy. Dr. T. Lafosse is consultant for Depuy Mitek and Stryker. Dr. G.A. Buijze received consultancy fees from Depuy-Synthes and Research Funds from SECEC, Vivalto Santé. The remaining authors certify that neither he or she has funding or commercial associations that might pose a conflict of interest in connection with the submitted article.

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#1 subject
Rotator cuff tear/ injury

(rotator[tiab] AND cuff[tiab] AND injur*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND tear*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND repair*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND surg*[tiab])
OR
"Rotator Cuff Injuries"[Mesh]

#2.1 Intervention (RCT)
Repair

#2.2 Intervention (Cohort)

Repair

#3 Outcome
Retear rate measured by MRI ultrasound or arthro CT

(Retear[tiab] OR (re-tear)[tiab] OR healing[tiab])

OR

("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance"

OR

ultraso*[tiab] OR "Ultrasonography"[Mesh]

OR

"Arthrography"[Mesh] OR arthrography[tiab])

Search: **((Retear[tiab] OR re-tear[tiab] OR healing[tiab]) OR ("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance" OR ultraso*[tiab] OR "Ultrasonography"[Mesh] OR "Arthrography"[Mesh] OR arthrography[tiab])) AND ((rotator[tiab] AND cuff[tiab] AND injur*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND tear*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND repair*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND surg*[tiab]) OR "Rotator Cuff Injuries"[Mesh])** Filters: **Clinical Trial, Randomized Controlled Trial** Sort by: **Most Recent**

We will collect the following potential risk factors from the electronic medical records. The variables are mostly binary to make them compatible for all machine learning algorithms. Cut-off values will be used for the non-binary values. In case of doubt, overlap or less specific grouping than in this database, variables will be rounded up.

Patient characteristics

- Identification number
- Date of birth
- Sex
- Dominant side (yes/no)
- Chronicity of tear (<6 weeks / >6weeks)
  - Time from trauma to 1st treatment day
- ASA classification (1-4)

Biological factors

- Obesity (BMI <30 / ≥30)
- Cardiovascular disease incl. hypertension (yes / no)
- Smoking history (current smoker / non-smoker)
- Diabetes (yes/no; insulin dependent yes/no)
- Osteoporosis (yes/no)
- Hyperlipidemia (yes/no)
- Hypercholesterolemia (yes/no)
- Vitamin D deficiency (yes/no)
- NSAID use (yes/no)
- Thyroid dysfunction (no disease / hypothyroid / hyperthyroid)

Pathology characteristics (graded by by MRI or arthro CT)

- Tear location (posterolateral / anterosuperior)
- Size of tear (small (<1 cm), medium (1–3 cm), large (3–5 cm), or massive (>5 cm))
  - Size in the saggital oblique plane
- Fatty infiltration (Goutallier 0 - 4)
- Muscle atrophy as graded by tangent sign (yes / no)
- Tendon retraction (Patte 1 - 3)

Surgical Technique

- Single row (yes / no)
- Double row (yes / no)
- Suture bridge (yes no)
- Performing surgeon (surgeon / resident / fellow)

Rehabilitation protocol

- Timing of active mobilization (<6wks ≥ 6wks)

Add-on Intervention

- Biceps tenotomy/tenodesis (yes / no)
- Bone marrow stimulation by microfracturing footprint (yes/no)

- Steroid injections within year prior to surgery (0 / 1 / ≥2 injections)
- Augmentation with subacromial inflatable device (yes/no)
- Augmentation/bridging with patches/scaffolds/extracellular matrices (yes/no)
- Local injectable biologics (yes/no) including:
  - Platelet-rich plasma (P-PRP, L-PRP)
  - Leukocyte and platelet-rich fibrin (L-PRF)
  - Growth factors
  - Cell therapy (bone marrow stem cells / BMAC MSCs)
- Systemic drugs - Statins (yes/no)
- Systemic drugs - Vitamin D supplementation (yes/no)
- Systemic drugs - Vitamin C supplementation (yes/no)
- Systemic drugs – NSAIDs from >6 weeks postop (yes/no)

<u>Outcomes</u>

- Retear at minimum 6 months (yes no)
- Type of retear (Sugaya 1-5)
- Adverse event
  - None/mild (none reported) / Moderate/severe (reported adverse event)
  - Type of adverse event (Infection/revision/stiffness/other)
- PROMS
  - Type of PROM
  - Time of measurement (in days from surgery)
  - *Consistency of PROM (yes/no)*
    - *Will be seperatelly formulated per PROM based on MCID improvement/consistency*
    - *As the calculation of this variable will be greatly dependent on which PROMS and follow-up duration will be submitted by co-authors, we prefer to receive 'raw' data.*

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VERSION: 2.2

ABSTRACT

Purpose/Introduction: The effectiveness of rotator cuff tear repair surgery is influenced by multiple patient-related, pathology-centered and technical factors, which is thought to contribute to the reported retear rates between 17 and 94%. Adequate patient selection is thought to be essential in reaching satisfactory results. However, no clear consensus has been reached on which factors are most predictive of successful surgery. A clinical decision tool that encompassed all aspects is still to be made. Artificial Intelligence (AI) and machine learning algorithms use self-learning complex models that can be used to make patient-specific decision-making tools.

The aim of this study is to develop and train an algorithm that can be used as an online available clinical prediction tool, to predict the risk of retear in patients undergoing rotator cuff repair.

Methods: This is a retrospective multicenter cohort study. Patients undergoing rotator cuff repair and evaluated by advanced imaging for healing at a minimum of 6 months after surgery were included. This study consists of two parts. Part one: collecting all potential factors that might influence retear risks from retrospective multicenter data, aiming to include >1000 patients worldwide. Part two: combining all influencing factors into a model that can clinically be used as a prediction tool using machine learning.

Ethics and dissemination: For safe multicenter data exchange and analysis, our Machine Learning Consortium adhered to the World Health Organization (WHO) regulation "Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies." The study results will be disseminated through publication in a peer-reviewed journal. IRB approval does not apply to the current study protocol.

Trial registration: N/A

ARTICLE SUMMARY

Strengths and Limitations of this study

- This study aims to calculate a patient-specific retear-chance after rotator cuff repair surgery
- Creating an online-available tool that predicts retear chances can help both medical professionals and patients in clinical decision-making on rotator cuff repair surgery
- Included data will be gathered from previously published databases of all authors included in the Machine Learning Consortium, aiming to include data from over 1000 patients.
- This study does have the limitation of being retrospective and therefore the study is dependent on the recordkeeping of each individual hospital.

INTRODUCTION

Despite technical advances of rotator cuff repair, the rate of unhealed or re-torn rotator cuff tears remains high, with percentages ranging between 10 and 94% (1). A myriad of patient-related (2), pathology-centered(3) and technical factors(4) influence this adverse outcome.

Patient selection is thought to be essential, however there is no consensus on which of the numerous potentially influential factors are most important for the prediction of satisfactory postoperative results (5). Furthermore, the value of preoperative optimization of potential patient-related influential factors including comorbidities, metabolic deficiencies and intoxications remains questionable. The increasing worldwide interest in these factors is confirmed by development of preoperative screening and optimization programs aiming for smoking cessation, diabetes control, use of statins in hyperlipidemia and vitamin D deficiency supplementing (2,6). However, the majority of shoulder surgeons seems to limit decision-making to more basic, previously established predictive factors including age, functional demand and pathology-specific grading. Despite the many different classification systems that have been developed to facilitate decision making, a patient specific decision tool is still lacking (7,8). This, in combination with the fact that existing research commonly evaluates a single treatment option between homogenic groups, makes it almost impossible for surgeons to preoperatively indicate a reliable chance of satisfactory results.

Artificial intelligence and machine learning (ML) is believed to facilitate a more patient-specific approach and will allow us to move to the next level of evidence-based medicine: personalized patient-care. Clinical prediction tools, incorporating patient specific factors to predict outcome probabilities will provide guidance to both clinicians and patients (9,10). Within orthopedic (oncology) surgery, prediction tools based on ML algorithms, have already been successfully implemented to predict patient specific 5-year survival in patients with chondrosarcoma (11). Furthermore, based on a series of 422 patients

undergoing lumbar discectomy, Staartjes et al. demonstrated deep learning algorithms to be superior to standard regression models in predicting patient-reported outcome measures (PROMs)(9).

online available.

Aim of this study

The aim of this study is to develop and train a machine learning algorithm in order to create a clinical prediction tool to be used in clinical practice by predicting retear-chance of the rotator cuff as well as chance of clinical improvement based on preoperative patient data. The prediction tool will be free and online available

METHODS AND ANALYSIS

The primary and secondary outcome measures will be implemented as features for the prediction algorithm.

Primary outcome measures

- Rotator cuff retear rates at minimum 6 months follow-up as measured on magnetic resonance imaging, arthro-CT and/or ultrasound (yes vs no, defined by Sugaya grade 1-3 as no retear and grade 4-5 as retear (12)).
- Enduring satisfactory functional outcome defined as achievement (yes vs no) and maintenance (yes vs no) of the PROM-specific MCID(13) in numeric rating scales of PROMs from baseline at 2-5 years follow-up after repair (PROMs include the Constant-Murley score, ASES, UCLA, OSS, WORC, DASH).

Secondary outcome measures

- Adverse events graded as the possibility of none/minor vs moderate/severe complication as defined in accordance to Felsch et al. (14). Adverse events classify as moderate/severe from

Felsch class III onwards, which means when other surgical or radiologic intervention was needed or unexpected hospital admission was necessary. Adverse events will be differentiated into three groups; infection, revision surgery or other.

Model development

The development of the prediction model will be performed based on the steps described by Steyerberg et al (15):

1. Data collection
2. Data inspection
3. Coding of predictors
4. Model specification
5. Model estimation and performance
6. Model validation
7. Model presentation

1. Data collection

Step one will involve contacting authors from previously published studies in order to collect and combine their (raw) individual patient data into a central database. All randomized controlled trials comparing any surgical technique, add-on biological intervention or rehabilitation protocols concerning rotator cuff surgery will be included. In addition, cohorts evaluating risk factors of surgical techniques after rotator cuff repair will be included. This retrospective review will therefore incorporate patients with all types of tears and concomitant procedures (e.g. biceps tenodesis or tenotomy and acromioclavicular resection). Exclusion criteria for all studies will be the lack of postoperative evaluation by ultrasound, contrast-enhanced computed tomography or magnetic resonance imaging at minimally 6 months after surgery, or publication date from before 2005. Relevant studies will be identified using a

systematic approach primarily searching the online PubMed database according to the search terms found in supplement 1. As there is no golden standard for sample size or power calculations for prediction models, and we are fully dependent on contributed data, we aim to include at least 1000 patients word wide (15).

2. Problem definition and data inspection

All contributed data sets will be formatted into one central database. As data is commonly collected in .csv (Microsoft Excel) or .sav (SPSS) files, formatting will be performed with the dplyr package for R software. All raw data of the different variables will be separately reviewed for inaccuracies and other defects. This process will focus on uniformization of possible inconsistencies in the collected data, for example follow-up times into a standardized format as 'days after surgery'. Categorical data will be translated into English or corrected for typographs. Continuous variables will be screened for outliers by visualization in the ggplot package. Impossible values or uninterpretable syntax errors will be excluded from the central database.

3. Coding of predictors

For each primary outcome, a logistic regression will be performed including all available variables in the central database to identify the variables with the highest predictive values. The data points available include patient demographic (sex, age), patient specific factors (BMI, dominance, sport/activity level, workers compensation,), pathology specific factors (e.g. tear size and location), surgical technique and add-on interventions. For a complete overview of all variables see supplement 2. The variables with the highest predictive values will be used as the algorithms labels.

Missing data

As the main database will comprise data from multiple studies, we expect many cases of missing data. The approach to missing data will differ depending on the type of variable. Variables with less than 5% missing data will be replaced by imputation (16). Missing data on any surgical technique or add-on intervention is expectable as interventions outside the scope of a study would not be mentioned (or briefly mentioned in the exclusions part). Therefore this kind of missing data will be transformed to 'No'. Overall availability of variables will be presented according to current guidelines (17). Any variances between hospitals will be reported.

4. Model specification

Algorithms to be trained

Based on previous studies (18,19), the following algorithms are likely to result in accurate prediction models for our primary outcomes: 1) Bayes Point Machine 2) Boosted Decision Tree 3) Penalized Logistical Regression 4) Neural Network 5) Support Vector Machine. In order to recognize patterns related to each outcome, the machine learning algorithms will have to be trained separately for each outcome.

5. Model estimation and performance

Assessing the performance of the algorithms

The performance of the ML-algorithms will be assessed and compared based on 1) model discrimination; 2) calibration and 3) overall model performance (Brier Score) according to Steyerberg's structured 'ABCD-methodology' for clinical prediction rules (15,20).

The model's predicted probability is plotted against the actual observed probability to calculate calibration of a model. Perfect models will have calibration intercepts of 0, and calibration slopes of 1.27

The overall performance of the model will be assessed with the Brier-score. A perfect Brier score, indicating total accuracy, is a score of 0. The lowest possible score is a Brier score of 1.26. Accuracy, sensitivity, specificity and area under the ROC-curve are measures for a model's ability to distinguish patients with the primary outcome from those without.

6. Model validation

Internal validation

Internal validation of our algorithms will be performed by 10-fold cross validation. This means that instead of dividing the main data set into one training set and one testing set, this process will be 10 times randomly repeated and the results will be averaged. This has as main advantage that all individual patient records are used as training and testing data simultaneously, which results in higher accuracy of predictions as well as lower chance of bias. The cross validation will be performed using the trainControl() function from the Caret library for R.

External validation

Before incorporating the best performing algorithm, we aim to have the algorithm externally validated. The same performance metrics could be calculated as described above. However, this would involve collaboration with partners that have adequate data and are willing to share. As no agreements currently have been made, the external validation is outside the scope of this study.

7. Model presentation

The best performing algorithm will be deployed as an open-access probability calculator and used to design a clinical decision rule. To simulate the clinical scenario to which a decision rule would be most applicable, thresholds shall be selected based on patients with clinical symptoms of a retear or with an unsatisfactory functional outcome.

ETHICS AND DISSEMINATION

For safe multicentre data exchange and analysis, our Machine Learning Consortium adhered to the World Health Organization (WHO) regulation 'Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies.'(21) As IRB has been acquired for each of the included studies and data are anonymized as in conventional meta-analyses, an additional IRB request does not apply to the current study protocol. The technical appendix, statistical code and final dataset will be published with the original article.

PATIENT AND PUBLIC INVOLVEMENT

Patients and the public were not involved in the making of this protocol.

CURRENT STATUS

The study has currently entered the data-collection phase, which is expected to last until end-2022. Re-evaluation of the data using machine learning algorithms to predict outcomes will start in December 2022, after which the algorithms can be externally validated. The expected time of completion is by the mid-2023.

DISCUSSION

Due to the wide variety of pathological factors at the origin of rotator cuff tears and the numerous surgical approaches to repair, optimal decision-making remains challenging. Smaller case series often provide heterogeneous data on this topic, however the largest and most recent meta-analysis to date including 2,611 patients with a mean follow-up of 25 months has somewhat demystified the matter. Patients with a full-thickness rotator cuff retear exhibited significantly lower functional outcome scores and strength compared with patients with an intact or partially torn rotator cuff (22). This is corroborated by the findings of rotator cuff repair with more than 10 years follow-up, showing clinical superiority of structural tendon integrity in partial cuff tears(23–25). Progressive osteoarthritic changes are significantly more common in patients with repair failures.(24) The most recent RCT comparing surgical repair to conservative treatment for degenerative rotator cuff tears showed that only operated patients without retear had an improvement exceeding the minimal clinical important difference (MCID) in functional outcome at 1 year follow-up (26). Findings from the latest meta-analysis on this comparative topic conclude that as the success rate of conservative treatment may be high, judicious selection of patients who are most likely to benefit from surgery is key (27). It is extremely difficult to combine all these factors into a clinical decision related to one specific patient. Creating a free online available clinical prediction tool that takes all these factors into account will assist physicians in selecting which patients with rotator cuff tears will benefit from a repair. In addition, the aimed size (more than 1000 patients) of the database that will be used to design and train the prediction tool might provide new insights on which biological or biomechanical factors influence outcomes after rotator cuff repair the most. Awareness of these factors would be the essential first step to incorporating them in future treatment strategies and eventually improving outcomes. The main limitation of this study is that it is a retrospective, multicenter study. This means this study is dependent on the quality of recordkeeping in

the different participating hospitals. This may lead to variance in recorded variables and therefore missing data.

AUTHOR CONTRIBUTIONS

Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J van den Bekerom contributed to the conception, overall design and planning of the study. Laurent A.M. Hendrickx and Job N. Doornberg contributed to the conception and design of the methods section, primarily focussing on the machine learning section and data analysis. Alexander Lädermann, George S Athwal, Thibault Lafosse and Laurent Lafosse contributed to the design of the methods section and primarily focussed on how the data should be collected and interpreted. Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J. van den Bekerom contributed to writing the protocol. All authors revised this version of the protocol and gave final approval for it to be published. All authors ensure that questions related to the accuracy or integrity of any part of this protocol are appropriately investigated and resolved.

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CONFLICTS OF INTEREST

Dr Alexandre Lädermann is a paid consultant for Arthrex, Medacta and Stryker. He receives royalties from Stryker. He is the founder of BeeMed, Med4Cast and FORE. He owns stock options from Medacta. Dr. L. Lafosse is a consultant for Depuy Stryker, received royalties from Depuy. Dr. T. Lafosse is consultant for Depuy Mitek and Stryker. Dr. G.A. Buijze received consultancy fees from Depuy-Synthes and Research Funds from SECEC, Vivalto Santé. The remaining authors certify that neither he or she has funding or commercial associations that might pose a conflict of interest in connection with the submitted article.

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#1 subject
Rotator cuff tear/ injury

(rotator[tiab] AND cuff[tiab] AND injur*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND tear*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND repair*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND surg*[tiab])
OR
"Rotator Cuff Injuries"[Mesh]

#2.1 Intervention (RCT)
Repair

#2.2 Intervention (Cohort)

Repair

#3 Outcome
Retear rate measured by MRI ultrasound or arthro CT

(Retear[tiab] OR (re-tear)[tiab] OR healing[tiab])

OR

("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance"

OR

ultraso*[tiab] OR "Ultrasonography"[Mesh]

OR

"Arthrography"[Mesh] OR arthrography[tiab])

Search: **((Retear[tiab] OR re-tear[tiab] OR healing[tiab]) OR ("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance" OR ultraso*[tiab] OR "Ultrasonography"[Mesh] OR "Arthrography"[Mesh] OR arthrography[tiab])) AND ((rotator[tiab] AND cuff[tiab] AND injur*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND tear*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND repair*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND surg*[tiab]) OR "Rotator Cuff Injuries"[Mesh])** Filters: **Clinical Trial, Randomized Controlled Trial** Sort by: **Most Recent**

We will collect the following potential risk factors from the electronic medical records. The variables are mostly binary to make them compatible for all machine learning algorithms. Cut-off values will be used for the non-binary values. In case of doubt, overlap or less specific grouping than in this database, variables will be rounded up.

Patient characteristics

- Identification number
- Date of birth
- Sex
- Dominant side (yes/no)
- Chronicity of tear (<6 weeks / >6weeks)
  - Time from trauma to 1st treatment day
- ASA classification (1-4)
- Sport/activity level
- Receiving workers compensatioin (yes/no)

Biological factors

- Obesity (BMI <30 / ≥30)
- Cardiovascular disease incl. hypertension (yes / no)
- Smoking history (current smoker / non-smoker)
- Diabetes (yes/no; insulin dependent yes/no)
- Osteoporosis (yes/no)
- Hyperlipidemia (yes/no)
- Hypercholesterolemia (yes/no)
- Vitamin D deficiency (yes/no)
- NSAID use (yes/no)
- Thyroid dysfunction (no disease / hypothyroid / hyperthyroid)

Pathology characteristics (graded by by MRI or arthro CT)

- Tear location (posterolateral / anterosuperior)
- Size of tear (small (<1 cm), medium (1–3 cm), large (3–5 cm), or massive (>5 cm))
  - Size in the saggital oblique plane
- Fatty infiltration (Goutallier 0 - 4)
- Muscle atrophy as graded by tangent sign (yes / no)
- Tendon retraction (Patte 1 - 3)

Surgical Technique

- Single row (yes / no)
- Double row (yes / no)
- Suture bridge (yes no)
- Performing surgeon (surgeon / resident / fellow)

Rehabilitation protocol

- Timing of active mobilization (<6wks ≥ 6wks)

Add-on Intervention

- Biceps tenotomy/tenodesis (yes / no)
- Bone marrow stimulation by microfracturing footprint (yes/no)
- Steroid injections within year prior to surgery (0 / 1 / ≥2 injections)
- Augmentation with subacromial inflatable device (yes/no)
- Augmentation/bridging with patches/scaffolds/extracellular matrices (yes/no)
- Local injectable biologics (yes/no) including:
  - Platelet-rich plasma (P-PRP, L-PRP)
  - Leukocyte and platelet-rich fibrin (L-PRF)
  - Growth factors
  - Cell therapy (bone marrow stem cells / BMAC MSCs)
- Systemic drugs - Statins (yes/no)
- Systemic drugs - Vitamin D supplementation (yes/no)
- Systemic drugs - Vitamin C supplementation (yes/no)
- Systemic drugs – NSAIDs from >6 weeks postop (yes/no)

<u>Outcomes</u>

- Retear at minimum 6 months (yes no)
- Type of retear (Sugaya 1-5)
- Adverse event
  - None/mild (none reported) / Moderate/severe (reported adverse event)
  - Type of adverse event (Infection/revision/stiffness/other)
- PROMS
  - Type of PROM
  - Time of measurement (in days from surgery)
  - *Consistency of PROM (yes/no)*
    - *Will be seperatelly formulated per PROM based on MCID improvement/consistency*
    - *As the calculation of this variable will be greatly dependent on which PROMS and follow-up duration will be submitted by co-authors, we prefer to receive 'raw' data.*

BMJ Open

Developing a machine learning algorithm to predict probability of retear and functional outcomes in patients undergoing rotator cuff repair surgery: protocol for a retrospective, multicenter study

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Primary Subject Heading:	Surgery
Secondary Subject Heading:	Sports and exercise medicine, Medical publishing and peer review, Evidence based practice
Keywords:	ORTHOPAEDIC & TRAUMA SURGERY, Shoulder < ORTHOPAEDIC & TRAUMA SURGERY, Orthopaedic & trauma surgery < SURGERY

Developing a machine learning algorithm to predict probability of retear and functional outcomes in patients undergoing rotator cuff repair surgery: protocol for a retrospective, multicenter study

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ABSTRACT

Introduction: The effectiveness of rotator cuff tear repair surgery is influenced by multiple patient-related, pathology-centered and technical factors, which is thought to contribute to the reported retear rates between 17 and 94%. Adequate patient selection is thought to be essential in reaching satisfactory results. However, no clear consensus has been reached on which factors are most predictive of successful surgery. A clinical decision tool that encompassed all aspects is still to be made. Artificial Intelligence (AI) and machine learning algorithms use complex self-learning models that can be used to make patient-specific decision-making tools. The aim of this study is to develop and train an algorithm that can be used as an online available clinical prediction tool, to predict the risk of retear in patients undergoing rotator cuff repair.

Methods and analysis: This is a retrospective, multicenter, cohort study using pooled individual patient data from multiple studies of patients who have undergone rotator cuff repair and were evaluated by advanced imaging for healing at a minimum of 6 months after surgery. This study consists of two parts. Part one: collecting all potential factors that might influence retear risks from retrospective multicenter data, aiming to include >1000 patients worldwide. Part two: combining all influencing factors into a model that can clinically be used as a prediction tool using machine learning.

Ethics and dissemination: For safe multicenter data exchange and analysis, our Machine Learning Consortium adheres to the World Health Organization (WHO) regulation “Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies”. The study results will be disseminated through publication in a peer-reviewed journal. Institutional Review Board approval does not apply to the current study protocol.

ARTICLE SUMMARY

Strengths and limitations of this study

- This study aims to calculate a patient-specific retear-chance after rotator cuff repair surgery.
- Creating an online-available tool that predicts retear chances can help both medical professionals and patients in clinical decision-making on rotator cuff repair surgery.
- Included data will be gathered from previously published databases of all authors included in the Machine Learning Consortium, aiming to include data from over 1000 patients.
- This study does have the limitation of being retrospective and therefore the study is dependent on the recordkeeping of each individual hospital.

INTRODUCTION

Despite technical advances of rotator cuff repair, the rate of unhealed or re-torn rotator cuff tears remains high, with percentages ranging between 10 and 94% (1). A myriad of patient-related (2), pathology-centered(3) and technical factors(4) influence this adverse outcome.

Patient selection is thought to be essential, however there is no consensus on which of the numerous potentially influential factors are most important for the prediction of satisfactory postoperative results (5). Furthermore, the value of preoperative optimization of potential patient-related influential factors including comorbidities, metabolic deficiencies and intoxications remains questionable. The increasing worldwide interest in these factors is confirmed by development of preoperative screening and optimization programs aiming for smoking cessation, diabetes control, use of statins in hyperlipidemia and vitamin D deficiency supplementing (2,6). However, the majority of shoulder surgeons seems to limit decision-making to more basic, previously established predictive factors including age, functional demand and pathology-specific grading. Despite the many different classification systems that have been developed to facilitate decision making, a patient specific decision tool is still lacking (7,8). This, in combination with the fact that existing research commonly evaluates a single treatment option between homogenic groups, makes it almost impossible for surgeons to preoperatively indicate a reliable chance of satisfactory results.

Artificial intelligence and machine learning (ML) is believed to facilitate a more patient-specific approach and will allow us to move to the next level of evidence-based medicine: personalized patient-care. Clinical prediction tools, incorporating patient specific factors to predict outcome probabilities will provide guidance to both clinicians and patients (9,10). Within orthopedic (oncology) surgery, prediction tools based on ML algorithms, have already been successfully implemented to predict patient specific 5-year survival in patients with chondrosarcoma (11). Furthermore, based on a series of 422 patients

undergoing lumbar discectomy, Staartjes et al. demonstrated deep learning algorithms to be superior to standard regression models in predicting patient-reported outcome measures (PROMs)(9).

Aim of this study

The aim of this study is to develop and train a machine learning algorithm in order to create a clinical prediction tool to be used in clinical practice by predicting retear-chance of the rotator cuff as well as chance of clinical improvement based on preoperative patient data. The prediction tool will be free and online available.

METHODS AND ANALYSIS

This is a retrospective, multicenter, cohort study.

The primary and secondary outcome measures will be implemented as features for the prediction algorithm.

Primary outcome measures

- Rotator cuff retear rates at minimum 6 months follow-up as measured on magnetic resonance imaging, arthro-CT and/or ultrasound (yes vs no, defined by Sugaya grade 1-3 as no retear and grade 4-5 as retear (12)).
- Enduring satisfactory functional outcome defined as achievement (yes vs no) and maintenance (yes vs no) of the PROM-specific minimal clinical important difference (MCID) (13) in numeric rating scales of PROMs from baseline at 2-5 years follow-up after repair (PROMs include the Constant-Murley score, ASES, UCLA, OSS, WORC, DASH).

Secondary outcome measures

- Adverse events graded as the possibility of none/minor vs moderate/severe complication as defined in accordance to Felsch et al. (14). Adverse events classify as moderate/severe from

Felsch class III onwards, which means other surgical or radiologic intervention was needed or unexpected hospital admission was necessary. Adverse events will be differentiated into three groups: infection, revision surgery or other.

Model development

The development of the prediction model will be performed based on the steps described by Steyerberg et al (15):

1. Data collection
2. Data inspection
3. Coding of predictors
4. Model specification
5. Model estimation and performance
6. Model validation
7. Model presentation

1. Data collection

Step one will involve contacting authors from previously published studies in order to collect and combine their (raw) individual patient data into a central database. All randomized controlled trials comparing any surgical technique, add-on biological intervention or rehabilitation protocols concerning rotator cuff surgery will be included. In addition, cohorts evaluating risk factors of surgical techniques after rotator cuff repair will be included. This retrospective review will therefore incorporate patients with all types of tears and concomitant procedures (e.g. biceps tenodesis or tenotomy and acromioclavicular resection). Exclusion criteria for all studies will be the lack of postoperative evaluation by ultrasound, contrast-enhanced computed tomography or magnetic resonance imaging at minimally 6 months after surgery, or publication date from before 2005. Relevant studies will be identified using a

systematic approach primarily searching the online PubMed database according to the search terms found in supplement 1. As there is no golden standard for sample size or power calculations for prediction models, and we are fully dependent on contributed data, we aim to include at least 1000 patients worldwide (15).

2. Problem definition and data inspection

All contributed data sets will be formatted into one central database. As data is commonly collected in .csv (Microsoft Excel) or .sav (SPSS) files, formatting will be performed with the dplyr package for R software. All raw data of the different variables will be separately reviewed for inaccuracies and other defects. This process will focus on uniformization of possible inconsistencies in the collected data, for example follow-up times into a standardized format as 'days after surgery'. Categorical data will be translated into English or corrected for typographs. Continuous variables will be screened for outliers by visualization in the ggplot package. Impossible values or uninterpretable syntax errors will be excluded from the central database.

3. Coding of predictors

For each primary outcome, a logistic regression will be performed including all available variables in the central database to identify the variables with the highest predictive values. The data points available include patient demographic (sex, age), patient specific factors (BMI, dominance, sport/activity level, workers compensation), pathology specific factors (e.g. tear size and location), surgical technique and add-on interventions. For a complete overview of all variables see supplement 2. The variables with the highest predictive values will be used as the algorithms labels.

Missing data

As the main database will comprise data from multiple studies, we expect many cases of missing data. The approach to missing data will differ depending on the type of variable. Variables with less than 5% missing data will be replaced by imputation (16). Missing data on any surgical technique or add-on intervention is expectable as interventions outside the scope of a study would not be mentioned (or briefly mentioned in the exclusions part). Therefore, this kind of missing data will be transformed to 'No'. Overall availability of variables will be presented according to current guidelines (17). Any variances between hospitals will be reported.

4. Model specification

Algorithms to be trained

Based on previous studies (18,19), the following algorithms are likely to result in accurate prediction models for our primary outcomes: 1) Bayes Point Machine 2) Boosted Decision Tree 3) Penalized Logistical Regression 4) Neural Network 5) Support Vector Machine. In order to recognize patterns related to each outcome, the machine learning algorithms will have to be trained separately for each outcome.

5. Model estimation and performance

Assessing the performance of the algorithms

The performance of the ML-algorithms will be assessed and compared based on 1) model discrimination; 2) calibration and 3) overall model performance (Brier Score) according to Steyerberg's structured 'ABCD-methodology' for clinical prediction rules (15,20).

The model's predicted probability will be plotted against the actual observed probability to calculate calibration of a model. Perfect models will have calibration intercepts of 0, and calibration slopes of 1.27

The overall performance of the model will be assessed with the Brier-score. A perfect Brier score, indicating total accuracy, is a score of 0. The lowest possible score is a Brier score of 1.26. Accuracy, sensitivity, specificity and area under the ROC-curve will be measures for a model's ability to distinguish patients with the primary outcome from those without.

6. Model validation

Internal validation

Internal validation of our algorithms will be performed by 10-fold cross validation. This means that instead of dividing the main data set into one training set and one testing set, this process will be 10 times randomly repeated and the results will be averaged. This has as main advantage that all individual patient records are used as training and testing data simultaneously, which results in higher accuracy of predictions as well as lower chance of bias. The cross validation will be performed using the trainControl function from the Caret library for R.

External validation

Before incorporating the best performing algorithm, we aim to have the algorithm externally validated. The same performance metrics could be calculated as described above. However, this would involve collaboration with partners that have adequate data and are willing to share. As no agreements currently have been made, the external validation is outside the scope of this study.

7. Model presentation

The best performing algorithm will be deployed as an open-access probability calculator and used to design a clinical decision rule. To simulate the clinical scenario to which a decision rule would be most applicable, thresholds shall be selected based on patients with clinical symptoms of a retear or with an unsatisfactory functional outcome.

Patient and public involvement

None.

ETHICS AND DISSEMINATION

For safe multicenter data exchange and analysis, our Machine Learning Consortium adheres to the World Health Organization (WHO) regulation 'Policy on Use and Sharing of Data Collected by WHO in Member States Outside the Context of Public Health Emergencies'.(21) As Institutional Review Board (IRB) approval has been acquired for each of the included studies and data are anonymized as in conventional meta-analyses, additional IRB approval is not required for the current study protocol. The technical appendix, statistical code and final dataset will be published with the study results.

CURRENT STATUS

The study has currently entered the data-collection phase, which is expected to last until March 2023. Re-evaluation of the data using machine learning algorithms to predict outcomes will start in April 2023, after which the algorithms can be externally validated. The expected time for study completion is by late 2023.

DISCUSSION

Due to the wide variety of pathological factors at the origin of rotator cuff tears and the numerous surgical approaches to repair, optimal decision-making remains challenging. Smaller case series often provide heterogeneous data on this topic, however the largest and most recent meta-analysis to date including 2,611 patients with a mean follow-up of 25 months has somewhat demystified the matter. Patients with a full-thickness rotator cuff retear exhibited significantly lower functional outcome scores and strength compared with patients with an intact or partially torn rotator cuff (22). This is corroborated by the findings of rotator cuff repair with more than 10 years follow-up, showing clinical superiority of structural tendon integrity in partial cuff tears (23–25). Progressive osteoarthritic changes

are significantly more common in patients with repair failures (24). The most recent randomized controlled trial comparing surgical repair to conservative treatment for degenerative rotator cuff tears showed that only operated patients without retear had an improvement exceeding the MCID in functional outcome at 1 year follow-up (26). Findings from the latest meta-analysis on this comparative topic conclude that as the success rate of conservative treatment may be high, judicious selection of patients who are most likely to benefit from surgery is key (27). It is extremely difficult to combine all these factors into a clinical decision related to one specific patient. Creating a free online available clinical prediction tool that takes all these factors into account will assist physicians in selecting which patients with rotator cuff tears will benefit from a repair. In addition, the aimed size (more than 1000 patients) of the database that will be used to design and train the prediction tool might provide new insights on which biological or biomechanical factors influence outcomes after rotator cuff repair the most. Awareness of these factors would be the essential first step to incorporating them in future treatment strategies and eventually improving outcomes. The main limitation of this study is that it is a retrospective, multicenter study. This means this study is dependent on the quality of recordkeeping in the different participating hospitals. This may lead to variance in recorded variables and therefore missing data.

** ** **

CONTRIBUTORS

Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J van den Bekerom contributed to the conception, overall design and planning of the study. Laurent A.M. Hendrickx and Job N. Doornberg contributed to the conception and design of the methods section, primarily focussing on the machine learning section and data analysis. Alexander Lädermann, George S Athwal, Thibault Lafosse

and Laurent Lafosse contributed to the design of the methods section and primarily focussed on how the data should be collected and interpreted. Laurens J.H. Allaart, Sanne H. van Spanning, Geert Alexander Buijze and Michel P.J. van den Bekerom contributed to writing the protocol. All authors revised this version of the protocol and gave final approval for it to be published. All authors ensure that questions related to the accuracy or integrity of any part of this protocol are appropriately investigated and resolved.

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COMPETING INTERESTS

Dr Alexandre Lädermann is a paid consultant for Arthrex, Medacta and Stryker. He receives royalties from Stryker. He is the founder of BeeMed, Med4Cast and FORE. He owns stock options from Medacta. Dr. L. Lafosse is a consultant for Depuy Stryker, received royalties from Depuy. Dr. T. Lafosse is consultant for Depuy Mitek and Stryker. Dr. G.A. Buijze received consultancy fees from Depuy-Synthes and Research Funds from SECEC, Vivalto Santé. The remaining authors certify that neither he or she has funding or commercial associations that might pose a conflict of interest in connection with the submitted article.

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#1 subject
Rotator cuff tear/ injury

(rotator[tiab] AND cuff[tiab] AND injur*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND tear*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND repair*[tiab])
OR

(rotator[tiab] AND cuff[tiab] AND surg*[tiab])
OR
"Rotator Cuff Injuries"[Mesh]

#2.1 Intervention (RCT)
Repair

#2.2 Intervention (Cohort)

Repair

#3 Outcome
Retear rate measured by MRI ultrasound or arthro CT

(Retear[tiab] OR (re-tear)[tiab] OR healing[tiab])

OR

("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance"

OR

ultraso*[tiab] OR "Ultrasonography"[Mesh]

OR

"Arthrography"[Mesh] OR arthrography[tiab])

Search: **((Retear[tiab] OR re-tear[tiab] OR healing[tiab]) OR ("Magnetic Resonance Imaging"[Mesh] OR "MRI" OR "magnetic resonance" OR ultraso*[tiab] OR "Ultrasonography"[Mesh] OR "Arthrography"[Mesh] OR arthrography[tiab])) AND ((rotator[tiab] AND cuff[tiab] AND injur*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND tear*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND repair*[tiab]) OR (rotator[tiab] AND cuff[tiab] AND surg*[tiab]) OR "Rotator Cuff Injuries"[Mesh])** Filters: **Clinical Trial, Randomized Controlled Trial** Sort by: **Most Recent**

We will collect the following potential risk factors from the electronic medical records. The variables are mostly binary to make them compatible for all machine learning algorithms. Cut-off values will be used for the non-binary values. In case of doubt, overlap or less specific grouping than in this database, variables will be rounded up.

Patient characteristics

- Identification number
- Date of birth
- Sex
- Dominant side (yes/no)
- Chronicity of tear (<6 weeks / >6weeks)
  - Time from trauma to 1st treatment day
- ASA classification (1-4)
- Sport/activity level
- Receiving workers compensatioin (yes/no)

Biological factors

- Obesity (BMI <30 / ≥30)
- Cardiovascular disease incl. hypertension (yes / no)
- Smoking history (current smoker / non-smoker)
- Diabetes (yes/no; insulin dependent yes/no)
- Osteoporosis (yes/no)
- Hyperlipidemia (yes/no)
- Hypercholesterolemia (yes/no)
- Vitamin D deficiency (yes/no)
- NSAID use (yes/no)
- Thyroid dysfunction (no disease / hypothyroid / hyperthyroid)

Pathology characteristics (graded by by MRI or arthro CT)

- Tear location (posterolateral / anterosuperior)
- Size of tear (small (<1 cm), medium (1–3 cm), large (3–5 cm), or massive (>5 cm))
  - Size in the saggital oblique plane
- Fatty infiltration (Goutallier 0 - 4)
- Muscle atrophy as graded by tangent sign (yes / no)
- Tendon retraction (Patte 1 - 3)

Surgical Technique

- Single row (yes / no)
- Double row (yes / no)
- Suture bridge (yes no)
- Performing surgeon (surgeon / resident / fellow)

Rehabilitation protocol

- Timing of active mobilization (<6wks ≥ 6wks)

Add-on Intervention

- Biceps tenotomy/tenodesis (yes / no)
- Bone marrow stimulation by microfracturing footprint (yes/no)
- Steroid injections within year prior to surgery (0 / 1 / ≥2 injections)
- Augmentation with subacromial inflatable device (yes/no)
- Augmentation/bridging with patches/scaffolds/extracellular matrices (yes/no)
- Local injectable biologics (yes/no) including:
  - Platelet-rich plasma (P-PRP, L-PRP)
  - Leukocyte and platelet-rich fibrin (L-PRF)
  - Growth factors
  - Cell therapy (bone marrow stem cells / BMAC MSCs)
- Systemic drugs - Statins (yes/no)
- Systemic drugs - Vitamin D supplementation (yes/no)
- Systemic drugs - Vitamin C supplementation (yes/no)
- Systemic drugs – NSAIDs from >6 weeks postop (yes/no)

Outcomes

- Retear at minimum 6 months (yes no)
- Type of retear (Sugaya 1-5)
- Adverse event
  - None/mild (none reported) / Moderate/severe (reported adverse event)
  - Type of adverse event (Infection/revision/stiffness/other)
- PROMS
  - Type of PROM
  - Time of measurement (in days from surgery)
  - *Consistency of PROM (yes/no)*
    - *Will be seperatelly formulated per PROM based on MCID improvement/consistency*
    - *As the calculation of this variable will be greatly dependent on which PROMS and follow-up duration will be submitted by co-authors, we prefer to receive 'raw' data.*