

# Tennis Elbow, Study Protocol for Randomized Clinical Trial: Needling With and Without Platelet-Rich Plasma After Failure of Up-to-Date Rehabilitation

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## Study protocol

**Keywords:** Clinical Protocols, Double-Blind Method, Randomized, Research design, Tennis Elbow, Tendinopathy, Rehabilitation, Extracorporeal Shock Waves Therapy, Platelet-rich Plasma, Ultrasonography, Interventional.

**Posted Date:** August 5th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-53382/v1>

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**Version of Record:** A version of this preprint was published on October 7th, 2020. See the published version at <https://doi.org/10.1186/s13018-020-01998-8>.

# Abstract

**Background:** The conservative management of lateral epicondylitis is known to be a difficult-to-treat annoying condition. A treatment with platelet-rich plasma (PRP) is often performed, but its efficacy remains controversial.

**Methods:** This study is a single-center, randomized double-blind controlled trial, preceded by a case series.

This monocentric study including 232 patients will occur in two steps. During the first step, all patients will undergo an up-to-date rehabilitation, including epicondylar stretching and strengthening, periscapular tonification, epicondylar brace or taping, and focused extracorporeal shock waves therapy. Unsatisfied patients after the first step will be allocated for the 1:1 randomized trial of second step. Stratification is planned on age and lesion pattern. The masking will be quadruple (Participant, Care Provider, Investigator & Outcome Assessor). The patients will undergo ultrasound (US)-guided needling combined with either PRP (intervention group) or saline (Control group). Outcome data will be collected at -3, 0, 3, 6, and 12 months of the intervention.

The primary endpoint is the pain improvement between months 0 and 3 on a 0-10 visual analog scale (VAS) during a maximal strength isometric contraction of the extensor carpialis brevis muscle. The secondary endpoints include the proportion of patients for which the tendon needling is not necessary after rehabilitation protocol, pain changes on VAS at rest and during maximal strength isometric contraction, changes of Single Assessment Numeric Evaluation (SANE) score, changes of Patient-Rated Tennis Elbow Evaluation (PRTEE) score, changes of maximal grip strength on Jamar test, and changes of the US of the epicondylar tendons (i.e. Volume of the lesion in mm<sup>3</sup>; Doppler reaction classified at the proportion of the tendon marked with the Doppler signal; Solution of continuity in mm<sup>3</sup>; Tendon thickness in mm; Concomitant superficial lesion & volume in mm<sup>3</sup>; Pain on a 0-10 VAS scale during sonopalpation).

**Discussion:** The study results will provide insight into the effect of PRP as adjuvant therapy to tendon fenestration, and may contribute to identify the best preceding and concomitant rehabilitation protocol.

**Trial registration:** ClinicalTrials.gov: NCT03987256, registered 20 August 2019

## Administrative Information

### Note

the numbers in curly brackets in this protocol refer to the SPIRIT checklist item numbers. The items order has been modified to regroup similar items (see <http://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/>).

<b>Title {1}</b>	<b>Tennis Elbow, study protocol for randomized clinical trial: Needling With and Without Platelet-rich Plasma After Failure of Up-to-date Rehabilitation</b>
Trial registration {2a and 2b}.	Clinicaltrials.gov: NCT03987256, registered 20 August 2019, <a href="https://clinicaltrials.gov/ct2/show/NCT03987256">https://clinicaltrials.gov/ct2/show/NCT03987256</a>
Protocol version {3}	V1
Funding {4}	None
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Name and contact information for the trial sponsor {5b}	<p>Dr Adrien Schwitzguébel</p> <p>Hôpital de Providence</p> <p>Faubourg de l'hôpital 81</p> <p>2000 Neuchâtel</p> <p>032 720 32 75 / 079 762 05 62</p> <p>adrien.schwitzguebel@gmail.com</p>
Role of sponsor {5c}	Ultimate authority for: study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication

## Introduction

### Background and rationale {6a}

The conservative management of lateral epicondylitis is known to be a difficult-to-treat annoying condition. The first-line conservative management includes physical therapies, orthotics, (1) and extracorporeal shock waves therapy (ESWT). (2) The success rate of ESWT for lateral epicondylitis

depends mainly on the protocol used. Especially, poor results have been observed with too low energy. (3) Focused ESWT has been showed as being as effective as surgical tenotomy. (4)

Infiltrative therapies might be proposed in case of persistent symptoms. It has been well established that corticosteroids are efficient in the short-term but deleterious in the long-term (5, 6) likely for degenerative purposes. (7) Prolotherapy, autologous blood or botulinic toxin injections, and others infiltrative therapies are less studied and therefore not clearly supported by the current literature. (8-10) Stem cells might be an alternative in the future. (11)

Platelet-rich-plasma (PRP) is nowadays widely used for tendinopathies, considered as safe, and currently supported by the strongest scientific journals (12). However, the potential benefits of PRP are discordant, especially concerning the elbow. Even if the superiority of PRP over corticosteroids is well established (13), the superiority of PRP on tendon needling or peppering is still controversial. Martin et al. (14) found in a partially blinded randomized controlled trial (RCT) involving 71 patients no clinical differences at 6 months of follow-up between 2 sessions of peppering with saline + local anesthetic and PRP + local anesthetic. In a similar blinded RCT involving 50 patients, Schöffl et al. (15) found no clinical differences at 6 months of follow-up. Montalvan et al. (16) found in a RCT involving 50 patients between 2 infiltrations of PRP and saline no clinical differences at 6 months of follow-up. Rehabilitation was not allowed during the trial and the tendon was not peppered. Mishra et al. (17) found in a blinded RCT involving 119 patients a positive clinical effect of PRP over saline solution, using a single injection with peppering. Behera et al. (18) found similar results in a small RCT on 25 patients.

Some factors have been advocated to influence PRP outcomes. The most relevant ones are: direct mechanical action of the needle and fenestration (peppering) technique, number of PRP injections, cells count (platelets, white blood- and red blood cells), activation of the platelets, concomitant local anesthetic use, peri-interventional use of NSAIDs and corticosteroids, concomitant rehabilitation or a contrario immobilization. (19) Whether the positive results observed into the previous selected studies (17, 18) are due to either PRP, peppering (20), or any of the above-mentioned confounding factors remains debatable.

The first aim of this study is to determine the proportion of patients that would need an infiltrative technique after a proper rehabilitation protocol involving physical therapies, orthotics and ESWT. Our second aim is to establish whether PRP as adjuvant therapy to peppering would increase clinical outcomes.

## **Objectives {7}**

- The clinical efficacy of platelet-rich plasma as adjuvant therapy to tendon needling for patients suffering of epicondylar tendinosis managed with a first line up-to-date rehabilitation.
- The efficacy of platelet-rich plasma as adjuvant therapy to tendon needling on the epicondylar tendon repair.
- The clinical efficacy of the first-line rehabilitation

- The efficacy of the first-line rehabilitation on the epicondylar tendon repair

## **Trial design {8}**

This study will include 232 patients and takes place in two steps.

The first step consists in an observational case series. During this step, all patients will benefit from a proper rehabilitation including: epicondylar stretching and eccentric strengthening, periscapular and global tonification, postural adjustment, manual therapies including trigger points release, epicondylar taping or bracing, and focused shockwave therapy (**Additional file 1**).

The second step consists in a case-control superiority trial randomized 1:1 between PRP (intervention group) and saline (Control group) injections. A stratification is planned on age and lesion pattern.

At 3 months, after the rehabilitation, if patients are not satisfied, they will be allocated to the PRP or saline group. The follow-up will last one year after the intervention (intervention is month 0), with endpoints at -3, 0, 3, 6, and 12 months of follow-up.

## **Methods**

### **Participants, interventions and outcomes**

#### **Study setting {9}**

In this monocentric study, all patients will be recruited into the sports medicine division of La Providence Hospital, Neuchâtel, Switzerland.

#### **Eligibility criteria {10}**

The following inclusion criteria will be applied: (i) Lesion of the extensor carpalis radialis brevis (ECRB) tendon on ultrasonography; (ii) Age between 18 and 65 years old; (iii) Written consent obtained following adequate explanation of the study aims, design, and procedures.

The following exclusion criteria will be applied: (i) Presence of a concomitant pathology that can partially explain the symptoms; (ii) Diabetes, immunocompromised status, bleeding disorder, or other significant systemic disease; (iii) Corticoids or anticoagulants intake; (iv) Anticoagulation therapy; (v) Allergy to local anesthetics.

#### **Who will take informed consent? {26a}**

The informed consent will be obtained by the sponsor-investigator (AS).

#### **Additional consent provisions for collection and use of participant data and biological specimens {26b}**

Not applicable as no biological specimens were collected as part of this trial.

## **Interventions**

### **Explanation for the choice of comparators {6b}**

It is not clear whether PRP should be used or not as an adjuvant procedure to tendon needling. An injection of saline solution during the procedure as comparator seems the most logical, because (i) it allows a proper blinding of both patient and physician; (ii) has no deleterious effects on tendon repair (contrary to active products such as corticosteroids) and therefore no influence on clinical outcomes ; (iii) and has no potential side effects.

### **Intervention description {11a}**

In both groups, the intervention will occur under strict aseptic conditions as following:

First, a local anaesthetic blockade of the radial nerve under the arcade of Frohse will be performed under ultrasonographic control. Then, an ultrasound-guided needling of the ECRB tendon will be performed, using the peppering technique: 25 repetitions with a 20 gauge needle. During the procedure, the lesion will be fulfilled with either PRP (experimental group) or saline solution (control group).

The PRP (ACP Arthrex) will be prepared using a double syringe system under the manufacturer's recommendation. From 15 ml of peripheral blood, the PRP will be extracted on site using centrifugation (1500 rpm 5 minutes), as recommended by the manufacturer.

### **Criteria for discontinuing or modifying allocated interventions {11b}**

If the first 3 months of rehabilitation allow the symptom alleviation (i.e. the rehabilitation was successful), the intervention will not be performed. If, for any other reason, the intervention cannot be performed, the patient will be dropped out of the study.

### **Strategies to improve adherence to interventions {11c}**

No particular measures are planned to improve the adherence to the intervention. The adherence to the rehabilitation protocol will be optimized by the physician, because (i) he will encourage the patient and actively participate to the rehabilitation protocol (**Additional file 1**) during shockwaves sessions; (ii) at 6 weeks of rehabilitation, the patient will be asked to show the active auto-exercises learned to the physician.

### **Relevant concomitant care permitted or prohibited during the trial {11d}**

All patients should perform the rehabilitation protocol during the 3 months following the intervention (**Additional file 1**). After the intervention, the learned auto-exercises should be continued as long as necessary. The use of ice and pain medication with paracetamol or opioids (tramadol, codine) are used to manage the pain, if necessary.

Oral corticosteroids, aspirin, and non-steroid anti-inflammatory drugs must be avoided, in spite of their potential deleterious effect on focussed shockwaves and PRP.

### **Provisions for post-trial care {30}**

If patients remain symptomatic at the end of the trial, a second needling of the tendon with PRP as adjuvant therapy might be considered. If relevant, a surgical debridement of the lesion would be considered.

### **Outcomes {12}**

The primary endpoint is the pain improvement between months 0 and 3 on a 0-10 visual analog scale (VAS) during a maximal strength isometric contraction of the extensor carpialis brevis muscle.

Rationale: most specific clinical test in order to reproduce pain triggered by the tendon target of the intervention. Most clinical effects of the PRP used are awaited after 3 months of follow-up (18, 24).

Secondary endpoints (all values are compared with baseline at month 0):

- Proportion of patients for which the tendon needling is not necessary after rehabilitation protocol
- Clinical scores at -3, 0, 3, 6 and 12 months of follow-up: (i) Pain on a 0-10 visual analog scale (VAS) during a maximal strength isometric contraction at other timepoints; (ii) Pain on a 0-10 VAS scale at rest; (iii) Single Assessment Numeric Evaluation (SANE) score; (iv) Patient-Rated Tennis Elbow Evaluation (PRTEE) score; (v) Maximal grip strength on Jamar test.
- Ultrasonographic aspects of the epicondylar tendons at -3, 0, 3, 6 and 12 months of follow-up: (i) Volume of the lesion in mm<sup>3</sup>; (ii) Doppler reaction classified at the proportion of the tendon marked with the Doppler signal; (iii) Solution of continuity in mm<sup>3</sup>; (iv) Tendon thickness in mm; (v) Concomitant superficial lesion & volume in mm<sup>3</sup>; (vi) Pain on a 0-10 VAS scale during sonopalpation.

### **Participant timeline {13}**

Timelines are presented into **Table 1**. Baseline (month 0) is defined as the time of the intervention. The standardized rehabilitation occurs during the 3 months preceding the baseline.

### **Sample size {14}**

The sample size was calculated with the online calculator “sealed envelope” ([www.sealedenvelope.com](http://www.sealedenvelope.com)). 232 patients are required to have a 95% chance of detecting, as significant at the 5% level, a pain improvement difference of 10% between groups, considering a standard deviation of 10%, a success rate of the rehabilitation of 75% (i.e. for 4 patients included, one is expected to be randomized), and a dropout rate of 10%. The chosen pain improvement was of 50% into the control group and 60% into the

experimental group. The standard deviation of 10% was estimated under the basis of a previous study of Mishra et al. (16).

Because the estimated standard deviation is not fully reliable and the calculated sample size is relatively small, in order to avoid a potential lack of power ( $\beta$ ), the standard deviation will be re-evaluated and the sample size corrected accordingly if necessary. It would be performed when the primary outcome is evaluable on 40 patients.

### **Recruitment {15}**

Others physicians in La Providence Hospital and connected structures in Neuchâtel city (i.e. orthopaedists, general practitioners, physical therapists) are informed of the project. They are kindly requested to refer patients to the sports medicine department.

### **Assignment of interventions: allocation**

#### **Sequence generation {16a}**

The allocation will be performed using computer-generated random number by serials of 4 patients blocks on a 1:1 ratio. Four strata will be used: (i) Age 18-39 & absence of lesion on the superficial epicondylar tendon; (ii) Age 18-39 & concomitant lesion on the superficial epicondylar tendon; (iii) Age 40-65 & absence of lesion on the superficial epicondylar tendon; (iv) Age 40-65 & concomitant lesion on the superficial epicondylar tendon.

#### **Concealment mechanism {16b} & implementation {16c}**

The sponsor-investigator (AS) generated 10 computerized allocation sequences. The secretary selected randomly one of those sequences for the study.

The sponsor-investigator will enroll the participants. He will perform the intervention 3 months after the recruitment. Patients will be allocated to a group at the time of the intervention, and only if the rehabilitation process was not successful.

The unblinded co-investigator (MF) will access to the allocation on a sequentially numbered list and prepare the injection for the intervention in an opaque syringe (blinded content for AS). After this procedure, MF will not take care of the patients anymore.

### **Assignment of interventions: Blinding**

#### **Who will be blinded {17a}**

This study is quadruple-blinded. Blinding concerns the participants (i), and the principal investigator (AS) during the intervention (ii), the outcomes assessment (iii), and for the statistical analysis (iv).

A complete masking of the intervention will allow the blinding of the participant and the principal investigator for the intervention and the outcome assessment (i-iii). First, for all patients, the co-investigator (MF) will perform a blood puncture in room A. Then, MF will go in room B and, depending of the allocation, prepare the PRP or turn-on the centrifuge for 5 minutes (sham PRP preparation). After that, MF will prepare an opaque syringe containing either PRP or saline solution. In room A, AS will perform the ultrasound-guided fenestration of the ECRB tendon. During the fenestration, AS will use the opaque syringe and inject the blinded content into the ECRB tendon.

The statistical analysis (iv) will be performed by AS using a sham allocation list. When the statistical analysis is completed, the true allocation list will replace the same one.

### **Procedure for unblinding if needed {17b}**

Unblinding should not be necessary for the security of patients. Indeed, no adverse effects of the PRP (local pain and tenderness, infection) need unblinding for clinical management. Despite this, if unblinding is necessary in case of unexpected circumstance, MF will reveal the intervention for concerned patients.

### **Data collection and management**

#### **Plans for assessment and collection of outcomes {18a}**

All data collected in this trial will be recorded on standardized paper case report forms (CRF). The sponsor-investigator (AS) is responsible for ensuring that all parts of the CRFs are filled in correctly. The two used questionnaires, SANE score (21) and the PRTEE score (22) are commonly used validated tools. The principal investigator is responsible for ensuring that all parts of CRFs are filled in correctly. Any change or correction to a CRF should be dated and initialed. Each CRF must be signed at least once by the investigator.

#### **Plans to promote participant retention and complete follow-up {18b}**

The physician closely supervises the participants during rehabilitation visits in order to improve their compliance to the rehabilitation program (CF above). In case of missed appointment, a new date will be proposed by phone. If participants deviate from protocol, the remaining follow-up visits will still be performed and the corresponding data will be collected.

#### **Data management {19}**

All protocol-required information collected during the trial must be entered by the sponsor-investigator, or designated co-investigator, in the CRF. The CRF pages should be completed and signed the same day that a trial subject is seen for any of the trial procedures. For all CRF, a copy is immediately stored on the digital secured server of the principal investigator.

In order to ensure that the database reproduces the CRFs correctly, the sponsor-investigator, or designated representative, will perform a double entry of the data to CSV files on two distinct CSV. For each visit, a

different CSV file will be created. Then, the CSV files will be compiled on a database using “R” software (R Foundation for Statistical Computing, Vienna, Austria). The quality of the data entered is guaranteed using “R” software as follows: (i) the duplicate CSV for double entry are digitally compared, and discordant results identified; (ii) the completeness, validity, and plausibility of the data will be tested for each variable. In case of discordant data, the principal investigator will clarify or correct the problematic data. All eventual changes are recorded. If no further corrections have to be made in the database, the latter will be closed and used for statistical analyses.

All important trial documents (e.g., CRFs) are archived for at least 10 years after completion of the clinical trial.

### **Confidentiality {27}**

Trial data of the patient will be stored in a coded manner. The names of the patients will not be disclosed on CRF. A sequential unique patient number will be attributed to each patient into the trial and reported on the CRF. Identification of patients must be guaranteed at the centre. Identification of the patients will be stored on a sequential list stored in the principal investigator’s secured server. The principal investigator and designated representatives will have access to the coded dataset and the identification list during, at the end, and after the study.

Note: in order to insure the blinding of the principal investigator, the allocation list will only be accessible to the co-investigator (MF), or under request to the informatics crew for backup.

### **Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}**

Not applicable as no biological specimens were collected as part of this trial.

### **Statistical methods**

#### **Statistical methods for primary and secondary outcomes {20a}**

The difference in primary outcome (pain improvement from baseline to 3 months post-intervention) between the treatment and control groups will be evaluated using the unpaired Student T test (or the Wilcoxon rank test when appropriate). The difference in secondary outcomes (changes from baseline to other time points) between the treatment and control groups will be evaluated with the appropriate statistical test (Chi-squared, Fisher exact, Student, or Wilcoxon rank tests). All analyses will be performed with an intention-to-treat analysis. Estimates of effect, 95% confidence intervals and descriptive p-values will be reported whenever possible. In addition, graphs will be presented whenever possible.

#### **Interim analyses {21b}**

Because the intervention is not considered at risk, not interim analysis is planned. However, in order to re-adjust the sample size calculation, it is planned to re-assess the standard deviation of the primary

outcome for the 40 first allocated patients.

### **Methods for additional analyses (e.g. subgroup analyses) {20b}**

Not applicable as no additional analyses are planned for this trial.

### **Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}**

In case of missing data on the primary outcome, patients will be withdrawn. Patients with missing data for any of the secondary outcomes will be excluded from the analysis.

### **Plans to give access to the full protocol, participant level-data and statistical code {31c}**

It is not planned to grant a public access to the full protocol, participant-level dataset, and statistical code. However, if requested as example for reviewing or publication purposes, the first author (AS) will give access to any of the full protocol, the statistical code, or the anonymized participant-level dataset.

### **Oversight and monitoring**

#### **Composition of the coordinating center and trial steering committee {5d}**

A data safety monitoring committee is not needed, because the procedures involved in this study are the standard ones performed during the best clinical practice, and the PRP is considered safe.

#### **Composition of the data monitoring committee, its role and reporting structure {21a}**

Prof. Charles Benaim (CB), chief physician of the physical medicine & rehabilitation department of the Lausanne university Hospital will monitor this study, as follows: (i) At the beginning of the study, CB will ensure that the randomization and blinding procedure will be respected, first with a sham patient. He will then monitor the first injection procedure for the first patient, and ensure that the concealment of allocation is respected; (ii) The first 3 months, then every 3 months, CB will ensure that consent forms and CRF are correctly fulfilled and stored. He therefore also ensures that all data are available for the final data analysis; (iii) All kinds of adverse events must be transmitted to CB. He will manage or supervise reporting of adverse events and follow-up of concerned patients; (iv) CB will be advised of all withdrawals or discontinuations of patients; (v) CB will verify the reliability of the statistical analysis; (vi) If deemed necessary, CB will plan additional monitoring visits for either the intervention or the data collection.

#### **Adverse event reporting and harms {22}**

Adverse events and serious adverse events are recorded in the CRF. Serious adverse events are recorded in dedicated forms and reported to the ethical committee within 7 days. Adverse reactions or Suspected Unexpected Serious Adverse Reactions are recorded in dedicated forms and reported to the ethical committee within 7 days.

### **Frequency and plans for auditing trial conduct {23}**

Regular audits are not intended. For the purpose of onsite inspection or audit, the competent authorities or ethics committee may require access to all source documents, CRF, and other trial-related records. The principal investigator must ensure availability of these documents and support the work at any time.

### **Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}**

Eventual amendments require a positive assessment from the competent ethics committee.

### **Dissemination plans {31a}**

One unique publication of the results in a high-quality scientific journal.

## **Discussion**

The presented study design allows to assess the usefulness of PRP as adjuvant therapy to ECRB needling in case of tennis elbow. The procedure is debated and source of potential financial interests in spite of a common long-lasting musculoskeletal pathology. Moreover, the case series preceding the randomized controlled trial (RCT) allows to evaluate the effectiveness of combined rehabilitative therapies on symptoms relapse, as well as to standardize the studied population.

To precede the RCT by a case series for all the patients allows to better standardize the studied population, and thus strengthen the reproducibility of the results. Moreover, publishing both the case series and the RCT allows to establish a comprehensive complete management of the pathology, and therefore establish strong clinical recommendations. In the other hand, in case of mixed clinical outcomes, the presented study design could be reworked in spite of a future trial.

The most recent meta-analysis favors the use of PRP compared to others infiltrative therapies. (12, 23, 24) Many of the studies included comparisons between PRP and corticosteroids. (7, 25–28) Knowing that corticosteroid infiltrations have been shown as deleterious for epicondylitis (5), the authors consider that the potential benefits of the PRP observed could not support the use of the PRP itself in clinical practice, as in might be interpreted by reading the conclusion of the meta-analysis. This protocol has been thought to evaluate and validate the effect of the most recent conservative treatments, keeping in mind that the best-validated treatment regimen available should be used as comparator.

PRP is considered as a safe treatment, widely used in sports medicine and promoted by medical companies.. Financial interest might therefore easily influence the therapeutic decisions, even if the cost-effectiveness of PRP has never been clearly demonstrated for tendon use. (27, 29, 30) Therefore, even if the selected sample size is relatively small, authors consider that the chosen effect size of 10% of difference between the groups is small enough in order to detect a clinically relevant difference.

The results of this study will provide insights into the effect of PRP as adjuvant therapy to tendon fenestration, and may contribute to identify the best preceding and concomitant rehabilitation protocol.

## **Trial Status**

The trial is currently running. The protocol used is the 2nd version submitted to the ethical committee board (October 3, 2019). Recruitment and started in December 2019, and is planned to be completed in December 2023.

## **Abbreviations**

CRF Case Report Forms

ECRB Extensor Carpalis Radialis Brevis

ESWT Extracorporeal Shock Waves Therapy

PRP Platelet-Rich Plasma

PRTEE Patient-Rated Tennis Elbow Evaluation

RCT Randomized Controlled Trial

SANE Single Assessment Numeric Evaluation

VAS Visual Analog Scale

## **Declarations**

### **Acknowledgements**

Not applicable, because authors have nobody to acknowledge.

### **Authors' contributions {31b}**

AS & AL established the study design, AS wrote the draft of the manuscript, MF & FI contributes to the protocol conception and to the acquisition, analysis, and interpretation of the data, MB & VN designed the rehabilitation protocol. All authors read and approved the final manuscript.

### **Funding {4}**

The publication fees are assumed by AS.

### **Availability of data and materials {29}**

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

This study was approved by the Lausanne ethical committee, Switzerland (CER-VD; ID 2019-01621). All patients must have signed the informed consent form.

### **Consent for publication {32}**

Not applicable, because our manuscript does not contain data from any individual person.

### **Competing interests {28}**

The authors declare that they have no competing interests.

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## **References**

1. Coombes BK, Bisset L, Vicenzino B. Management of Lateral Elbow Tendinopathy: One Size Does Not Fit All. *J Orthop Sports Phys Ther.* 2015;45(11):938–49.
2. Thiele S, Thiele R, Gerdesmeyer L. Lateral epicondylitis: This is still a main indication for extracorporeal shockwave therapy. *Int J Surg.* 2015;24(Pt B):165–70.
3. Gerdesmeyer L, Mittermayr R, Fuerst M, Al Muderis M, Thiele R, Saxena A, et al. Current evidence of extracorporeal shock wave therapy in chronic Achilles tendinopathy. *Int J Surg.* 2015;24(Pt B):154–9.
4. Park JW, Hwang JH, Choi YS, Kim SJ. Comparison of Therapeutic Effect of Extracorporeal Shock Wave in Calcific Versus Noncalcific Lateral Epicondylopathy. *Ann Rehabil Med.* 2016;40(2):294–300.
5. Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials.

- Lancet. 2010;376(9754):1751–67.
6. Houck DA, Kraeutler MJ, Thornton LB, McCarty EC, Bravman JT. Treatment of Lateral Epicondylitis With Autologous Blood, Platelet-Rich Plasma, or Corticosteroid Injections: A Systematic Review of Overlapping Meta-analyses. *Orthopaedic journal of sports medicine*. 2019;7(3):2325967119831052.
  7. Gautam VK, Verma S, Batra S, Bhatnagar N, Arora S. Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation. *J Orthop Surg (Hong Kong)*. 2015;23(1):1–5.
  8. Dong W, Goost H, Lin XB, Burger C, Paul C, Wang ZL, et al. Injection therapies for lateral epicondylalgia: a systematic review and Bayesian network meta-analysis. *Br J Sports Med*. 2016;50(15):900–8.
  9. Sims SE, Miller K, Elfar JC, Hammert WC. Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials. *Hand (N Y)*. 2014;9(4):419–46.
  10. Lai WC, Erickson BJ, Mlynarek RA, Wang D. Chronic lateral epicondylitis: challenges and solutions. *Open Access J Sports Med*. 2018;9:243–51.
  11. Imam MA, Holton J, Horriat S, Negida AS, Grubhofer F, Gupta R, et al. A systematic review of the concept and clinical applications of bone marrow aspirate concentrate in tendon pathology. *SICOT J*. 2017;3:58.
  12. Fitzpatrick J, Bulsara M, Zheng MH. The Effectiveness of Platelet-Rich Plasma in the Treatment of Tendinopathy: A Meta-analysis of Randomized Controlled Clinical Trials. *Am J Sports Med*. 2017;45(1):226–33.
  13. Mi B, Liu G, Zhou W, Lv H, Liu Y, Wu Q, et al. Platelet rich plasma versus steroid on lateral epicondylitis: meta-analysis of randomized clinical trials. *Phys Sportsmed*. 2017;45(2):97–104.
  14. Martin JI, Atilano L, Merino J, Gonzalez I, Iglesias G, Areizaga L, et al. Platelet-rich plasma versus lidocaine as tenotomy adjuvants in people with elbow epicondylopathy: a randomized controlled trial. *J Orthop Surg Res*. 2019;14(1):109.
  15. Schoffl V, Willauschus W, Sauer F, Kupper T, Schoffl I, Lutter C, et al. Autologous Conditioned Plasma Versus Placebo Injection Therapy in Lateral Epicondylitis of the Elbow: A Double Blind, Randomized Study. *Sportverletz Sportschaden*. 2017;31(1):31–6.
  16. Montalvan B, Le Goux P, Klouche S, Borgel D, Hardy P, Breban M. Inefficacy of ultrasound-guided local injections of autologous conditioned plasma for recent epicondylitis: results of a double-blind placebo-controlled randomized clinical trial with one-year follow-up. *Rheumatology*. 2016;55(2):279–85.
  17. Mishra AK, Skrepnik NV, Edwards SG, Jones GL, Sampson S, Vermillion DA, et al. Efficacy of platelet-rich plasma for chronic tennis elbow: a double-blind, prospective, multicenter, randomized controlled trial of 230 patients. *Am J Sports Med*. 2014;42(2):463–71.
  18. Behera P, Dhillon M, Aggarwal S, Marwaha N, Prakash M. Leukocyte-poor platelet-rich plasma versus bupivacaine for recalcitrant lateral epicondylar tendinopathy. *J Orthop Surg (Hong Kong)*. 2015;23(1):6–10.

19. Kaux JF, Emonds-Alt T. The use of platelet-rich plasma to treat chronic tendinopathies: A technical analysis. *Platelets*. 2018;29(3):213–27.
20. Mattie R, Wong J, McCormick Z, Yu S, Saltychev M, Laimi K. Percutaneous Needle Tenotomy for the Treatment of Lateral Epicondylitis: A Systematic Review of the Literature. *PM R*. 2017;9(6):603–11.
21. Furtado R, MacDermid J. Clinimetrics: Single Assessment Numeric Evaluation. *J Physiother*. 2019;65(2):111.
22. Rompe JD, Overend TJ, MacDermid JC. Validation of the Patient-rated Tennis Elbow Evaluation Questionnaire. *J Hand Ther*. 2007;20(1):3–10. quiz 1.
23. Filardo G, Di Matteo B, Kon E, Merli G, Marcacci M. Platelet-rich plasma in tendon-related disorders: results and indications. *Knee Surg Sports Traumatol Arthrosc*. 2018;26(7):1984–99.
24. Johal H, Khan M, Yung SP, Dhillon MS, Fu FH, Bedi A, et al. Impact of Platelet-Rich Plasma Use on Pain in Orthopaedic Surgery: A Systematic Review and Meta-analysis. *Sports Health*. 2019;11(4):355–66.
25. Gosens T, Peerbooms JC, van Laar W, den Ouden BL. Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis: a double-blind randomized controlled trial with 2-year follow-up. *Am J Sports Med*. 2011;39(6):1200–8.
26. Krogh TP, Fredberg U, Stengaard-Pedersen K, Christensen R, Jensen P, Ellingsen T. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. *Am J Sports Med*. 2013;41(3):625–35.
27. Peerbooms JC, Sluimer J, Bruijn DJ, Gosens T. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double-blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. *Am J Sports Med*. 2010;38(2):255–62.
28. Yadav R, Kothari SY, Borah D. Comparison of Local Injection of Platelet Rich Plasma and Corticosteroids in the Treatment of Lateral Epicondylitis of Humerus. *J Clin Diagn Res*. 2015;9(7):RC05–7.
29. la Fleur P, Arguez C. Platelet-Rich Plasma Injections for Wound Healing and Tissue Rejuvenation: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines. *CADTH Rapid Response Reports*. Ottawa (ON)2017.
30. Samuelson EM, Odum SM, Fleischli JE. The Cost-Effectiveness of Using Platelet-Rich Plasma During Rotator Cuff Repair: A Markov Model Analysis. *Arthroscopy*. 2016;32(7):1237–44.

## Tables

Table 1  
participant timeline

STUDY PERIOD										
	Enrolment	Rehabilitation			Allocation		Post-allocation		Close out	
TIMEPOINT in months (Days)	-3 (-7d)	-3	-1.5	0	0	0	3	6	12	
							(+7d)			
<b>ENROLMENT:</b>										
Patient Information and Consent	x									
Informed consent collection		x								
Validation of inclusion & exclusion criteria		x								
Randomisation						x				
<b>INTERVENTIONS:</b>										
Organize rehabilitation		x								
Rehabilitation checkpoint			x	x			x	x		
Needling (with PRP or Saline)							x			
<b>ASSESSMENT:</b>										
Clinical evaluation	x	x								
Elbow echography	x			x			x	x		
Demographics		x								
Rehabilitation efficacy assessment				x						
Primary outcome assessment							x			
Clinical outcomes assessment		x		x			x	x	x	x
Concomitant Therapy, surgery			x	x			x	x	x	x

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [20200211ECRBRehabProtocol.docx](#)
- [Ethicalcommitteboardauthorization.pdf](#)

- [Funding.pdf](#)