BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

A comparative study of three treatment interventions for chronic patellar tendinopathy: a protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034304
Article Type:	Protocol
Date Submitted by the Author:	13-Sep-2019
Complete List of Authors:	Lopez-Royo, Maria Pilar Gómez-Trullén, Eva Maria Ortiz-Lucas, Maria Galán-Diaz, Rita Maria Bataller-Cervero, Ana Vanessa Al-bolushi, Zaid Hamam-Alcober, Yasmina Herrero, Pablo; San Jorge Univ, Physiotherapy
Keywords:	Eccentric Exercise, Chronic Patellar Tendinopathy, Tendinopathy, Percutaneous Needle Electrolysis, Dry Needling

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A comparative study of three treatment interventions for chronic patellar tendinopathy: a protocol for a randomized controlled trial

López-Royo MP[a,b], Gómez-Trullén EM[b], Ortíz-Lucas M[a], Galán-Díaz RM[a], Bataller-Cervero AV[a], AL-boloushi Z, Hamam-Alcober Y[a], Herrero P[a *]

AFFILIATIONS

A. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, Spain.

B. Universidad de Zaragoza. Facultad de Ciencias de la Salud. Dpto. de Fisiatría y Enfermería. C/ Domingo Miral s/n, 50009 - Zaragoza, Spain.

***CORRESPONDENCE TO:**

Dr. Pablo Herrero. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov A23, Km 299, 50830 Villanueva de Gállego, Zaragoza, Spain. Tel.: (+34) 976 060 100 Fax: 976 077 581. Email: pherrero@usj.es

ADDITIONAL AUTHOR INFORMATION

Maria Pilar López Royo. Emails: mplopez@usj.es

Eva María Gómez Trullén. Email: evagomez@unizar.es

María Ortíz Lucas. Email: mortiz@usj.es

Rita María Galán Díaz. Email: rmgalan@usj.es

Ana Vanessa Bataller-Cervero. Email: avbataller@usj.es

Yasmina Hamam-Alcober. Email: yhamam@usj.es

Zaid AL-boloushi. Email: boloushi@gmail.com

For peer review only

ABSTRACT

Introduction: Chronic patellar tendinopathy is a degenerative disease of the patellar tendon, which affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The aim of this study is to compare the effectiveness of needling therapies in order to determine the most effective treatment protocol of chronic patellar tendinopathy.

Methods and analysis: This study is a randomized controlled trial with blinded participants. Measurements will be carried out by a specially trained blind assessor. A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study for a minimum of three months and will be divided into three treatment groups. Eligible participants will be randomly allocated to receive either: (a) treatment group with Percutaneous Needle Electrolysis, (b) treatment group with Dry Needle or (c) treatment group with placebo needling and all of the them realized eccentric exercise. Functionality and muscle strength parameters, pain, histological changes and patient perceived quality of life shall be evaluated by Visa-p, jumps, VAS, US images and SF-36, respectively. Follow-up measurements will take place two and 12 weeks after the final treatment. The expected findings could be a breakthrough for the treatment of this injury as they would allow to define the most effective treatment protocol to deal with this disease and avoid the consequences that derive from it, reflecting all of this in a new relapse prevention.

Ethics and dissemination: This protocol has been approved by Ethics Committee of Aragon (Nº PI15/0017). The trial will be conducted in accordance with the Declaration of Helsinki.

Trial Registration Number: NCT02498795.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Strengths and limitations of this study

- This randomised clinical trial will report the effects in functionality and pain of three different treatments at short and long term.
- The double-blinded and placebo-control design improve the objectivity and help reduce bias.
- The effects between two minimally invasive treatments in physical therapy will be compared for the first time in patellar tendinopathy.

INTRODUCTION

Chronic patellar tendinopathy (CPT), also known as jumper´s knee, is a degenerative disease of the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella. This disorder has similar histologic findings to other tendon disorders characterized by an increased thickness of the tendon and changes in vascularity, and cellularity, with incompletely healed tendon micro-ruptures and disturbed collagen distribution [1].

This disorder affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The overall prevalence of CPT in non-elite players is 8.5%, although this figure increases in sports that place high demands on the patellar ligament, increasing up to 14.2% in volleyball athletes. Among elite volleyball and basketball players, a prevalence of 45% and 32%, respectively, has been reported. In addition, jumper's knee is almost twice as common among male non-elite athletes when compared with female athletes [2].

The diagnosis is typically based on the clinical history and symptomatic findings. Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) may represent the best combinations to confirm clinically diagnosed

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

CPT. The GS-US has higher sensitivity than magnetic resonance imaging (MRI). Therefore, ultrasound (US) techniques are more accurate than MRI for confirming clinically diagnosed CPT [3].

Treatments used for CPT fall into two major groups. On the one hand, medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection [4], polidocanol [3] and autologous growth factors [5]. On the other hand, physical therapies, including both conservative and invasive approaches (needling techniques).

Conservative therapies are generally accepted as the first line approach for managing CPT, with eccentric exercise (EE) considered the gold standard [6, 7]. In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including CPT, and there was a greater likelihood of clinical improvement when performed on a declined surface [6,8]. In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc [9].

Physical therapy approaches for CPT continue to evolve and a number of innovative treatment options are now available, such as dry needling (DN) [10], electrotherapeutic invasive modalities (e.g. electrolysis) [11-13] and extracorporeal shockwave (ECSW) therapy [14]. Recently, research has focused on regenerative therapies with high expectations of success because many of these techniques achieve a rapid regeneration of the injured tendon. However, evidence-based regenerative therapies are limited and there is no agreement to date regarding which of these is the most effective [15]. Dry needling consists of the insertion of a needle (filiform and solid, non-beveled) with the aim of provoking a local injury leading to an inflammatory response and the subsequent regeneration of the injured area in approximately one week. A study performed by Abat et al. reported that DN induced histological and mechanical changes in rat Achilles

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

tendons at week one, with changes persisting at week four [16]. Percutaneous Needle Electrolysis (PNE) is an ultrasound guided technique used by physiotherapists consisting of causing localized lysis in the damaged and/or degenerated tissue by means of a galvanic current transmitted through an acupuncture needle. This technique may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area in rats [16]. James et al.[10] carried out a cohort study in humans analyzing one group treated with DN and another treated with autologous blood injections. In both cases, they found improvements with regard to the beginning of the treatment, however failed to find differences between them, concluding that both technologies were equally effective. In relation to PNE, a study [13] analyzed the treatment effect of electrolysis applied once a week in a group of patients without any control or comparative group, reporting that patients obtained statistically and clinically significant improvements with regard to the baseline measurements. In another study [17] this technology was compared with other conventional treatments (US and currents), showing that PNE treatment was more effective than conventional treatment.

From a biological point of view, it seems reasonable to ascertain that a patient will obtain benefits thanks to the mechanical effects provided by the needle, and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle.

Therefore, the aim of this study is to know whether invasive techniques has additional effects for the treatment of CPT when compared with only EE, and if the application of PNE provides any additional benefits aside from only performing DN, in the short and long term.

METHODS AND ANALYSIS

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Study design

The trials is designed as a randomized, controlled, participant, investigator and outcomes assessor blinded, experimental study, whose purpose is to compare three protocols in which different physiotherapy protocols are applied in three intervention groups with CRT patients. Randomization will be performed as block randomization with a 1:1 allocation.

This protocol follows the standards of the Helsinki Convention of good clinical practices. The Ethics Committee of Aragon (CEICA) has evaluated the project and has given its favorable opinion and support, Nº PI15/0017 (Appendix A).

The study has been carried out following the SPIRIT statement for clinical trial protocol and a SPIRIT Checklist has been included (Appendix D).

Studying sitting

After reviewing the literature and observing the high incidence of this pathology in young adults who perform sports and more specifically, jump sports, the search of patients has been carry out in sports clubs of basketball, football, volleyball, CrossFit, handball, running clubs and some gyms in the city. It is decided to carry out the study in X, where the university is located as well as the laboratory that will be made use for assessments and treatments.

The assessments will be conducted at the Motion Analysis laboratory of X, and the treatment will be performed at two different sites depending on the availability both of spaces and of schedules, albeit the same material shall always be used.

Participants

Inclusion criteria

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants eligible for inclusion in this study must meet the following criteria: 1. History of CPT and pain at the level of the patellar tendon for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the patellar tendon; 4. A score below 80 on the VISA-P questionnaire.

Exclusion criteria

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Injection with corticosteroids within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs).

Methodology

In the first session, all participants will be instructed how to perform a daily home program of EE. This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol [18].

For the interventions, the participants will be placed in a supine position with a pillow under the knee (approximately 20º of knee flexion). The area will be cleansed with an antiseptic solution (70% Propan-2-ol, Skin-des). An ultrasound probe cover will be used during the intervention for infectious control. To determine the relevant treatment area, two factors will be considered: 1) Palpation of the areas exhibiting higher sensitivity and that reproduce the patient's symptoms; 2) Tendon areas showing degenerative changes assessed under ultrasound. Each group will receive a total of four sessions distributed throughout eight weeks of treatment, once every two weeks.

G-DN and G-PNE

Specific DN needles will be used during needling treatments, (Agu-punt, Spain). Considering the thickness of the tendon and the approach, we shall use needles measuring 0.25 x 25 mm. The procedure will be guided by US to ensure the specificity of application

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

on the injured area and to guarantee that the procedure is safe for the patient. The DN needle shall reach the relevant treatment area (areas with degenerative CPT changes). Each session will consist of three needle insertions lasting three seconds each. In G-PNE applications, an intensity of 3 mA galvanic current will be used during the three seconds that the procedure lasts. The dose of 3 mA has demonstrated to be effective in the treatment of tendinopathy injuries in animal models [12].

GC

A sham needle will be placed upon the treatment zone, simulating the same procedure as the rest of participants enrolled in the other groups. The needle will be placed in a specific holder and will be manipulated during the intervention to simulate a real treatment. This holder will have a cover over the bottom part of the same in order to avoid the needle contacting the skin.

Outcomes

Baseline data

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and infiltrations. A blinded observer will assess all participants at baseline, 10 weeks and 22 weeks after baseline.

Primary outcome measure

Participants will complete the VISA-P questionnaire at baseline. The VISA-P questionnaire is designed to measure the severity of CPT. VISA-P score is the primary outcome variable. This scale consists of eight questions, the first six questions of which employ an analogical visual scale in order to assign a score of 0 to 10, where 10 represents the optimum state, for the purpose of quantifying pain and function in different activities,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

whereas the last two questions assess the level of functionality and ability to perform physical activity.

Secondary outcome measure

At the first evaluation, participants will complete the Visual Analogical Scale (VAS), considering the level of pain they feel while practicing their sport's activity. Participants will be explained that a score of 0 indicates the absence of pain whereas a score of 10 represents the maximum tolerable pain. They will also complete a questionnaire to assess their quality of life (SF-36) [19].

In order to assess tendon structure, a US evaluation using ultrasound equipment (Logic S7 Expert, General Electric Healthcare) and a linear probe (MLG-15 5–10 MHz) will be used. The ultrasonographic assessment protocol will be carried out according to the Musculoskeletal Ultrasound Technical Guidelines: Knee, defined by the European Society of Musculoskeletal Radiology [20]. The ultrasonographic assessment will consist of a longitudinal sequence from the tendon origin to the insertion and transverse sections on the pole of the patella, the tendon body and its insertion on the tibial tuberosity, with the subject in supine position, with 20º knee flexion, and a pillow under the knee. The presence of degenerative signs compatible with the medical diagnosis of CPT (thickness of the tendon, hypoechoic areas, irregularities affecting the cortical bone, calcifications) that could be relevant for the selection of the target area will also be assessed. In addition, CD-US assessment will be carried out to detect the presence of hypervascularization, with the subject in supine position and with the knee relaxed in full extension, in order to obtain further information to specifically define the target area.

Upon completion of the evaluation, a jump test will be carried out, measured with a force platform (FP4060-10-2000, Bertec Corporation). In this evaluation, subjects will perform three different jumps on the platform to analyze the maximum height of the jump, the

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

eccentric power and the maximum concentric force performed. The protocol followed is described in the Table A.

Participant timeline

The study design will be a double-blind randomized controlled trial. The flow chart of the trial is shown in Figure A.

Sample size

Regarding the sample size, a calculation of statistical power was made prior to the study. Accepting an alpha risk of 0.05 and a beta risk in a bilateral contrast, 17 subjects are needed in every treatment group to detect a difference equal or superior to 15 points on the Visa-P scale [21], and assuming a standard deviation of 13.2 [22]. The estimated rate of loss to follow-up is 20%.

Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media.

The interested subjects will receive an e-mail explaining the inclusion and exclusion criteria, as well as the purpose of the study. If they meet the defined criteria, they will be invited to send us their medical diagnosis.

Recruitment

Participants will be recruited in sports clubs by the physiotherapist or the coach. There have been conversations with various traumatologists, so that when they make a diagnosis

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

in their examination room of this pathology they can refer us to the patients and begin to be part of the study.

Allocation

Participants will be randomly assigned to either GC or G-DN or G-PNE with a 1:1:1 allocation through opaque envelope.

Sealed opaque randomization envelopes with a study-specific participant number will be supplied by an external statistician. A colleague not involved in the research study will take the sealed opaque numbered envelopes in order, by number, and deliver the correct envelope to the treating physical therapist. The envelope will contain a piece of paper, which will be labelled with the same participant specific number, plus the group assignment (G-PNE, G-DN or GC).

Participants who fulfill the inclusion criteria will receive the standardized oral and written information, and, once they grant their consent to take part in the trial, they will be randomized into either a combined intervention with electrolysis along with EE (G-PNE), a DN intervention combined with EE (G-DN) or sham needling with EE (GC).

Blinding

Assessments regarding clinical recovery will be conducted by an assessor blind to treatment allocation. Due to the nature of the intervention, participants can be blinded to allocation. To the other hand, the physiotherapist that do the intervention cannot be blinded, but are strongly inculcated not to disclose the allocation status of the participant at the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyse data without having access to information about the allocation.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Data collection methods

For the data collection of the participants, an oral questionnaire is carried out in which questions are asked to collect baseline data and about the pathology. Appendix B. Different questionnaires and assessment scales (VISA-p, VAS, SF-36) in Spanish version will be given to the participant when they go to the evaluation in paper and all the time necessary to complete them will be left. Appendix C.

Data management and statistical analysis

In this study, all data will be entered electronically in the assessment room.

Originals scales and questionnaires will be entered and kept on file at the participating site locked.

Participant files are to be stored in numerical order and stored in a secure and accessible place and manner. Participant files will be maintained in storage for a period of 2 years after completion of the study.

The statistical analysis will be carried out by an intention-to-treat analysis. Variables will be described in number (percentage) and average (standard deviation) or median (interquartile range) attending to their distribution. Quantitative variables will be analyzed with the Shapiro Wilk test in order to confirm their distribution and to determine correct statistical tests according to these results.

Outcomes will be analyzed using mixed linear and logistic regression models considering participants as a random effect and group of treatment as fixed factors. Baseline characteristics will be introduced in the model as covariance. Numbers needed to treat index will also be calculated. The primary aim of the analysis will be to calculate the difference obtained in the Visa–P score after the intervention (final measurement - initial

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

measurement). Finally, the magnitude of the effect of the result shall be calculated and therefore its clinical importance, by means of the following formula:

$$r=\sqrt{\frac{F(1,dfR)}{F(1,dfR)+dfR}}.$$

The significance level set for all the analysis will be $p \leq 0.05$.

ETHICS AND DISEMINATION

The study design, procedures and informed consent procedure were approved and consequently the study will be carried out in compliance with the Helsinki Declaration of Human Rights. All participants will have to provide written Spanish informed consent. Appendix A.

The trial's results will be published in peer-reviewed international journals or otherwise made publicly available and will be presented at national and international conferences and symposiums irrespective of the outcomes.

Any modifications to the protocol, which may impact on the conduct of the study, potential benefit of the patient or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendment will be approved by the Ethics Committee prior to implementation and notified to the health authorities in accordance with local regulations.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored identified by code number. All local databases will be secured with password-protected access systems.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Availability of data and material: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

DISCUSSION

The study expects to investigate the effects of physiotherapy puction techniques on pain, functionality and quality of life in CPT.

CPT is a common cause of knee pain in which there is a degenerative disease of the patellar tendon. Among the causes of CPT, extrinsic factors (eg, patellar tendon loading with exercise) and intrinsic factors (eg, malalignment, high patella, imbalances) have been proposed.[23] Traditionally the focus has been on strengthening through EE of the quadriceps and many reviews have shown that the effect of the treatment could be estimated to give the patients a 50-70% change of improvement on pain and functionality.[6,24,25]

With regard with punction treatment, previous studies have shown a great improvement in CPT using PNE in combination with EE and all patients of these studies report an improvement after at least one month of treatment.[11-13,16,17] This time is less than the minimum three months needed to improve symptoms by applying other conventional techniques (pharmacological and biological treatments, cold/heat techniques, shock waves, etc.) Additionally, in a long-term study, in 2013, it could demonstrated that improve symptoms quickly and steadily for at least 10 years [16]. This fact demonstrates that this technique ensures that patients remain pain-free for a long period. Furthermore, only 5 articles[11-13,16,17] addressed the application of PNE for the recovery of CPT have been found, but none of the articles studied were RCTs, which entail limited evidence of the effectiveness of this technique.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

On the other hand, there are no standardized protocols for the application of PNE, which explains the great variability in the number of sessions and application time according to the literature. Therefore, this study aims to facilitate clinical practice and combine criteria of methodology to use this technique with a promising future.

Regarding DN, the literature shows many similarities with the PNE, since there is only one RCT that compares the improvement of functionality with patients who have received PRP. In this study, it was reflected that at short term PRP had better results at pain and functionality, however, DN was more effective than PRP after 6 months.[26]

In these two puncture techniques US is usually used to be able to observe in the first instance how the tendon is presented, and later to be able to observe the needle and be much more specific in the treatment. However, the US has disadvantages include its operator dependence and the limited ability to rule out intra-articular disease with this modality. The sensitivity and specificity of ultrasonography for patellar tendinopathy are 58% and 94%, respectively.[27]

There are several highlights to this study. First, we are going to evaluate two techniques that do not have strong evidence yet, contributing in this way with new knowledge in the field of the recovery of musculoskeletal injuries. Second, the role of invasive techniques willl be determinate by comparing the effects between these techniques and a control group, being able to obtain reliable data since patients, like the assessor will be blinded. Third, a sub-analysis with US will be performed to investigate changes in presence of calcifications, cortical irregularities, neovascularization, thickness, eco-intensity, eco-variation and eco-texture of the patellar tendon.

These findings could be a breakthrough for the treatment of this injury as they would allow to define the most effective treatment protocol to deal with this disease and avoid

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

the consequences that derive from it, reflecting all of this in a new relapse prevention and the potential impact on the musculoskeletal system.

REFERENCES

1. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. Journal of orthopaedic surgery and research. 2008;3:18. Doi: 10.1186/1749-799X-3-18.
2. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of Jumper's Knee Among Nonelite Athletes From Different Sports A Cross-Sectional Survey. American Journal of Sports Medicine. 2011;39(9):1984-8. Doi: 10.1177/0363546511413370.
3. Hoksrud A, Oehberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. American Journal of Sports Medicine. 2006;34:1738. Doi: 10.1177/0363546511415225.
4. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A Systematic Review of the Use of Platelet-Rich Plasma in Sports Medicine as a New Treatment for Tendon and Ligament Injuries. Clinical Journal of Sport Medicine. 2011;21(4):344-52. Doi: 10.1097/JSM.0b013e31821d0f65.
5. Andres BM, Murrell GAC. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clinical Orthopaedics and Related Research. 2008;466(7):1539-54. Doi: 10.1007/s11999-008-0260-1.
6. Larsson MEH, Kall I, Nilsson-Helander K. Treatment of patellar tendinopathy-a systematic review of randomized controlled trials. Knee Surgery Sports Traumatology Arthroscopy. 2012;20(8):1632-46. Doi: 10.1007/s00167-011-1825-1.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

7. Murtaugh B, Ihm JM. Eccentric Training for the Treatment of Tendinopathies. Current Sports Medicine Reports. 2013;12(3):175-82. Doi: 10.1249/JSR.0b013e3182933761.
8. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. British Journal of Sports Medicine. 2005;39(2):102-5. Doi: 10.1136/bjsm.2003.010587.
9. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symCPTomatic shoulder impingement or lateral epicondylar tendinopathy: A systematic review. J Sci Med Sport. 2016;19(6):438-53. Doi: 10.1136/bjsports-2016-096794.
10. James SLJ, Ali K, Pocock C, Robertson C, Walter J, Bell J, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine. 2007;41(8):518-21. Doi: 0.1136/bjsm.2006.034686.
11. Abat F DW, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibañez JM. Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up. Muscles Ligaments Tendons J. 2014;14(4):188-93.
12. Valera Garrido F, Minaya Muñoz F, JM SI. Effectiveness of electrolysis percutaneous intratisular (EPI®) in chronic insertional patellar tendinopathy. Trauma Fund MAPFRE. 2010;21(4):227-36.
13. Sánchez-Ibáñez J, Alves R, Polidori F, Valera F, Minaya F, Valles-Martí S, et al. Effectiveness of ultrasound-guided percutaneous electrolysis intratendon (EPI) in the treatment of insertional patellar tendinopathy in soccer players. Br J Sports Med. 2013;47(e2).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

14. Zwerver J, Verhagen E, Hartgens F, van den Akker-Scheek I, Diercks RL. The TOPGAME-study: effectiveness of extracorporeal shockwave therapy in jumping athletes with patellar tendinopathy. Design of a randomised controlled trial. Bmc Musculoskeletal Disorders. 2010;11:6. Doi: 10.1186/1471-2474-11-28.

15. Krey D, Borchers J, McCamey K. Tendon needling for treatment of tendinopathy: A systematic review. Physician and Sportsmedicine. 2015;43(1):80-6. Doi: 10.1080/00913847.2015.1004296.

16. Abat F, Valles S-L, Gelber P-E, Polidori F, Jorda A, Garcia-Herreros S, et al. An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI technique. BMC sports science, medicine and rehabilitation. 2015;7:7-. Doi: 10.1007/s00167-014-2855-2.

17. Sánchez Sánchez J. Estudio comparativo de un tratamiento fisioterápico convencional con uno que incluye la técnica de electrolisis percutánea intratisular en pacientes con tendinopatís crónica del tendón rotuliano [dissertation]. Salamanca; 2011.

18. Alfredson H, Pietila T, Jonsson P, Lorentzon P. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. American Journal of Sports Medicine. 1998;26(3):360-6. Doi: 10.1177/03635465980260030301.

19. Alonso J, Prieto L, Anto JM. The spanish version of the SF-36 health survey- A measure of clinical outcomes. Medicina Clinica. 1995;104(20):771-6.

20. Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights into imaging. 2010;1(3):99-141.

21. Stasinopoulos D, Stasinopoulos L. Comparison of effects of exercise programme, pulsed ultrasound and transverse friction in the treatment of chronic patellar tendinopathy. Clinical Rehabilitation. 2004;18(4):347-52. Doi: 10.1191/0269215504cr757oa.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

22. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural Adaptation of VISA-P Score for Patellar Tendinopathy in Spanish Population. Journal of Orthopaedic & Sports Physical Therapy. 2011;41(8):581-91. 10.2519/jospt.2011.3613.

23. Figueroa D, Figueroa F, Calvo R. Patellar tendinopathy: diagnosis and treatment. J Am Acad Orthop Surg. 2016 Dec;24(12):e184-92. Doi: 10.5435/JAAOS-D-15-00703.

24. Lian OB, Engebretsen L, Bahr R (2005) Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. Am J Sport Med 33:561–567. Doi: 10.1177/0363546504270454.

25. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. Br J Sports Med. 2007 Apr;41(4):217-23. Doi: 10.1136/bjsm.2006.032417.

26. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. American Journal of Sports Medicine. 2014;42(3):610-8. Doi: 10.1177/0363546513518416.

27. Warden SJ, Brukner P: Patellar tendinopathy. Clin Sports Med 2003;22(4):743-759.

AUTHOR'S CONTRIBUTIONS

MPL, EMG and PH conceived of the idea, and developed the intervention. MPL and PH wrote the article. MPL, MO, RMG, AVB, ZA, YH and PH developed the design of the trial. MO were involved in development of the statistical analysis of the trial and contributed to the content of the article. AVB contributed to the design and writing of the jump test protocol. All authors have read and approved the final manuscript.

FUNDING STATEMENT

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTEREST STATEMENT

The authors declare that they have no competing interests.

WORD COUNT: 3431words.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLES

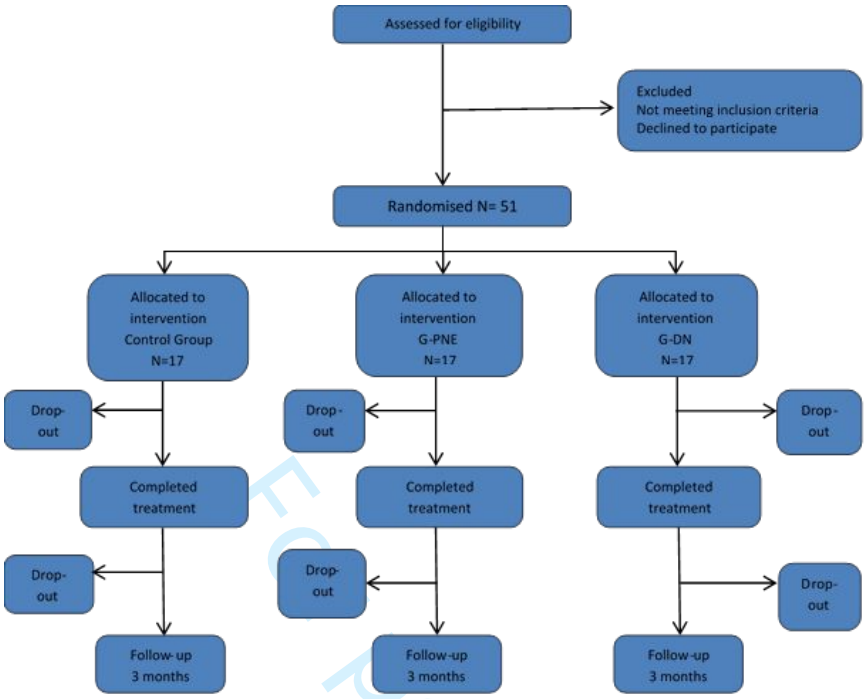
Table A. Jump test protocol.

JUMP TEST PROTOCOL	
5-minute warm-up consisting of steady jogging on a treadmill	
Dynamic Stretches lasting 5 minutes, as instructed by the physical therapist	Psoas Quadriceps Gluteus maximus Gastrocnemius Hamstring muscles
Three jump tests are performed - 3 jumps off the ground for 3 times for the patient to become familiar with the tests - The subject is placed on the platform and asked to perform each test 3 times, with 60 seconds rest between the different tests	Abalakov test Countermovement jump test Squat jump
The highest jump is selected for the study	

FIGURES

Figure A. Flow diagram. Randomized controlled trial design.

For peer review only



G-PNE: Percutaneous Needle Electrolysis Group. G-DN: Dry Needle Group.

Figure B. Schedule of enrolment, interventions, and assessments.

	Enrolment	Allocation	Close-out			
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control group			←	→		
G-PNE			←	→		
G-DN			←	→		
ASSESSMENTS:						
Baseline demographic information	X					

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

VISA-P	X		X		X	X
VAS			X		X	X
SF-36			X		X	X
Tendon structure US			X		X	X
Jump test			X		X	X

Schedule for enrolment and intervention per cluster. -t1: baseline; t1–t2: intervention period; t2: 8 weeks after baseline; t3: 10 weeks after baseline; t4: 3 month after baseline. G-PNE: Percutaneous Needle Electrolysis Group; G-DN: Dry Needle Group; US: ultrasound.

Appendix A. Informed Consent.

DOCUMENTO DE INFORMACIÓN AL PACIENTE

Fecha:

Título del proyecto: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Investigador principal:

Doña: Mª Pilar López Royo

Este estudio se basa en el estudio comparativo de tres tratamientos que utilizan distintas técnicas de fisioterapia invasiva junto con un programa de ejercicio excéntrico para el tratamiento de la tendinopatía rotuliana. Por medio del tratamiento se produce una disminución del dolor asociado a esta patología y un aumento de la fuerza de la pierna, lo que a su vez hace que mejore la funcionalidad en las actividades de la vida diaria y mejore la calidad de vida.

PROCESO DE SELECCIÓN DE PACIENTES

Criterios de inclusión:

- Edad comprendida entre 18 y 40 años.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- Practicar cualquier deporte de forma habitual.
- Pacientes con diagnóstico médico de tendinopatía rotuliana crónica con un mínimo de 3 meses de evolución y con sintomatología.
- Dolor a la palpación del tendón en el polo inferior de la rótula y durante el entrenamiento o competición.
- Puntuación del cuestionario VISA-P menor de 80 (el resultado obtenido de rellenar el cuestionario tiene que ser menor de 80 puntos de los 100 posibles para poder participar en el estudio).

Criterios de exclusión:

- Paciente operado de la rodilla afectada en los últimos 6 meses.
- Infiltraciones en la rodilla afectada en los últimos 3 meses.
- Paciente que ha recibido tratamiento farmacológico o fisioterápico en las últimas 48 horas o durante el estudio.
- Patología con menos de 3 meses de evolución.
- Presentar tendinopatía rotuliana bilateral.
- Puntuación del cuestionario VISA-p mayor o igual de 80 (el resultado obtenido de rellenar el cuestionario no puede ser igual o superar los 80 puntos de los 100 posibles, sino no podrá participar en el estudio).
- Imposibilidad para aplicar alguna de las técnicas de tratamiento o valoración por contraindicación absoluta o relativa.

PROCEDIMIENTO

El tratamiento consiste en realizar un protocolo de ejercicios excéntricos de cuádriceps que realizará en casa de forma diaria, y que serán revisados con el fisioterapeuta para valorar su correcta realización. Se complementará el tratamiento con la aplicación de una técnica de punción según el protocolo de tratamiento propuesto de forma totalmente **aleatorizada** y según los criterios diagnósticos específicos de la misma, siguiendo las indicaciones, criterios de aplicación y criterios diagnósticos.

Son técnicas de punción cuyo objetivo es producir una respuesta inflamatoria aguda que active los mecanismos fisiológicos de regeneración del tejido y mejorar el dolor y la funcionalidad en la articulación de la rodilla, se realiza con agujas de punción seca,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

similares a las agujas de acupuntura y sin infiltrar ningún tipo de sustancia dentro del organismo.

Los registros serán realizados en el Espacio de Valoración Funcional de la Universidad San Jorge, en la Facultad de Ciencias de la Salud, Edificio III.Se pondrá a su disposición la posibilidad de utilizar el autobús que utiliza el personal y alumnado de la universidad (en el horario que éste esté disponible).Las fechas y horarios serán convenidas con cada participante en función de su disponibilidad y la de los investigadores, buscando la conformidad de todos.La duración aproximada del estudio para cada paciente será de 30 minutos, aunque este horario podrá variar en función de los acontecimientos.

Será recibido por los miembros del equipo de investigación y una vez allí, se le realizará un primer análisis fisioterápico, rellenará una encuesta, una escala analógica visual (EVA) del dolor y el cuestionario Visa-p en el que se valorará la funcionalidad de la rodilla.

Tras éste primer registro se le colocará un marcador pasivo en el pantalón. Se le pedirá que realice el siguiente protocolo:

- Calentamiento de 5 minutos en cinta a ritmo constante.
- Estiramientos dinámicos de psoas, cuádriceps, glúteo, gastrocnemios, isquiotibiales durante 5 minutos instruidos por el fisioterapeuta.
- Realización de los 3 saltos fuera de la plataforma durante 3 veces para que se familiarice con los tests.
- En la plataforma de fuerzas realizará 3 test de salto: el test de Abalakov (ABK), el test de salto con contramovimiento (CMJ) y el squatjump (SJ).

Se colocará en la plataforma y realizará 3 saltos de cada uno de los test con una separación entre ellos de 60 segundos.

Se valora el tendón por ecografía, y se recogen datos por medio de personal adiestrado y se envía a personal especialista en radiodiagnóstico.

Tras los registros de los saltos se dará por finalizada la valoración.

Tras la 1ª valoración, se realizará una división en tres grupos de los pacientes de forma aleatorizada.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Se le realizará el protocolo de tratamiento de fisioterapia invasivaque le haya correspondido. Realizará una sesión del tratamiento cada 14 días, y se realizará la 2º valoración 1 semana más tarde de la 4º sesión de punción para valorar los cambios que se hayan producido tras el tratamiento, repitiéndose de nuevo el proceso de recogida de datos realizado al inicio del estudio. Se realizará un seguimiento a los tres meses de la valoración post-tratamiento para valorar la eficacia de la técnica a largo plazo del tratamiento.

El procedimiento se realizará guiado ecográficamente para asegurar la especificidad de aplicación sobre la zona relevante de tratamiento y garantizar la seguridad de la técnica. Se hace posterior a esta intervención una serie de ejercicios excéntricos de cuádriceps. El tratamiento se realizará durante 4 sesiones (a razón de una sesión cada 14 días).

RIESGOS

La aplicación de las técnicas de punción utilizadas no han demostrado tener ningún efecto secundario hasta la fecha, aunque el paciente puede experimentar dolordurante y tras la punción, generalmente de uno o dos días de duración.

RESPONSABILIDADES DEL PARTICIPANTE

La información que usted posea sobre su estado de salud o sobre sensaciones previas anormales al realizarle una punción, puede afectar la seguridad o el valor de estas pruebas. La rápida comunicación por su parte de las sensaciones que experimenta al realizar esta prueba es también de gran importancia. Usted es responsable de revelar esa información al personal de la prueba cuando se le pregunte.

PREGUNTAS

Le animamos a que haga cualquier pregunta sobre los procedimientos seguidos o sus resultados en la prueba. Si tiene alguna preocupación o pregunta, por favor pídanos más información, para ello le dejamos un correo electrónico mapilr86@hotmail.com y un número de teléfono móvil: 616102365.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

LIBERTAD PARA DAR EL CONSENTIMIENTO

Usted participa en el estudio de manera voluntaria, pudiendo abandonarlo en el momento que considere oportuno, sin que esto conlleve ninguna repercusión negativa para usted.

Los datos obtenidos en el estudio serán confidenciales y únicamente se hará uso de ellos para el cumplimiento de los objetivos planteados en la investigación. No se cederán estos datos a terceros sin el consentimiento expreso de los sujetos participantes a quienes pertenezcan los datos.

En esta investigación se garantizará el anonimato de los sujetos que aportan los datos, estableciendo un código disociado para identificarlos que sólo será conocido por los responsables de la realización del trabajo de campo.

Fdo: Mª Pilar López Royo

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- **MODELO DE CONSENTIMIENTO INFORMADO**

Título del PROYECTO: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Doña: Mª Pilar López Royo (mapilr86@hotmail.com)

Departamento de Fisiatría y Enfermería

UNIVERSIDAD DE ZARAGOZA

Yo, ... (nombre y apellidos del participante)

He recibido suficiente información en relación con el proyecto, he leído la hoja de información que se me ha entregado y he podido hacer preguntas sobre el proyecto, recibiendo respuestas satisfactorias.

Entiendo que la participación es voluntaria y que puedo abandonar el proyecto:

. Cuando lo desee

. Sin tener que dar explicaciones

. Sin que esto repercuta en mis cuidados médicos

He sido claramente informado de forma clara y precisa del tratado que recibirán mis datos personales que se contienen en este proyecto, sabiendo que los datos serán tratados y custodiados bajo mi intimidad y a la vigente normativa de la protección de datos, y que sobre estos datos me asisten los derechos de rectificación, acceso y oposición comunicándolo al investigador principal que figura en este consentimiento.

Declaro que presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Así pues, acepto que las muestras derivadas de este proyecto puedan ser utilizadas en futuras investigaciones siempre y cuando están relacionadas con ésta.

Por lo tanto, doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es revocable.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del proyecto al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Consentimiento informado estudio_____

Versión_____, fecha_____

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Appendix D. Checklist SPIRIT

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1-2
	2b	All items from the World Health Organization Trial Registration Data Set	1-2
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	19-20
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	19
	5b	Name and contact information for the trial sponsor	19
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-5
	6b	Explanation for choice of comparators	3-5
Objectives	7	Specific objectives or hypotheses	5

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6-7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8-10
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	10
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	10-11
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	11
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	11

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	11
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	11
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	11
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	12
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	12
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12-13
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12-13
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	-
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	13
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	14
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	-
	31b	Authorship eligibility guidelines and any intended use of professional writers	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	23-29
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

8

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034304.R1
Article Type:	Protocol
Date Submitted by the Author:	17-Nov-2019
Complete List of Authors:	Lopez-Royo, Maria Pilar; Universidad San Jorge Facultad de Ciencias de la Salud; Universidad de Zaragoza, Facultad de Ciencias de la Salud Gómez-Trullén, Eva Maria; Universidad de Zaragoza, Facultad de Ciencias de la Salud Ortiz-Lucas, Maria; Universidad San Jorge Facultad de Ciencias de la Salud Galán-Diaz, Rita Maria; Universidad San Jorge Facultad de Ciencias de la Salud Bataller-Cervero, Ana Vanessa; Universidad San Jorge Facultad de Ciencias de la Salud Al-Boloushi, Zaid; Universidad de Zaragoza Facultad de Ciencias; Kuwait Ministry of Health Hamam-Alcober, Yasmina; Universidad San Jorge Facultad de Ciencias de la Salud, Fisioterapia Herrero, Pablo; Universidad San Jorge Facultad de Ciencias de la Salud
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Sports and exercise medicine
Keywords:	Eccentric Exercise, Tendinopathy, Percutaneous Needle Electrolysis, Dry Needling

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

López-Royo MP[a,b], Gómez-Trullén EM[b], Ortíz-Lucas M[a], Galán-Díaz RM[a], Bataller-Cervero AV[a], Al-Boloushi Z[b,c], Hamam-Alcober Y[a], Herrero P[a *]

AFFILIATIONS

A. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, Spain.

B. Universidad de Zaragoza. Facultad de Ciencias de la Salud. Dpto. de Fisiatría y Enfermería. C/ Domingo Miral s/n, 50009 - Zaragoza, Spain.

A. Ministry of Health, State of Kuwait. Jamal Abdulnasser Street, Al Solaibeykhat Area 5. Kuwait City. Safat 13001.

***CORRESPONDENCE TO:**

Dr. Pablo Herrero. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov A23, Km 299, 50830 Villanueva de Gállego, Zaragoza, Spain. Tel.: (+34) 976 060 100 Fax: 976 077 581. Email: pherrero@usj.es

ADDITIONAL AUTHOR INFORMATION

Maria Pilar López Royo. Emails: mplopez@usj.es

Eva María Gómez Trullén. Email: evagomez@unizar.es

María Ortíz Lucas. Email: mariaortizlucas@gmail.com

Rita María Galán Díaz. Email: rmgalan@usj.es

Ana Vanessa Bataller-Cervero. Email: avbataller@usj.es

For peer review only

Yasmina Hamam-Alcober. Email: yhamam@usj.es

Zaid AL-boloushi. Email: boloushi@me.com

WORD COUNT: 3924words.

ABSTRACT

Introduction: Patellar tendinopathy is a degenerative disease of the patellar tendon, which affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The aim of this study is to compare the effectiveness of needling therapies in order to determine the most effective treatment protocol of patellar tendinopathy.

Methods and analysis: This study is a randomized controlled trial with blinded participants. Measurements will be carried out by a specially trained blinded assessor. A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups. Eligible participants will be randomly allocated to receive either: (a) treatment group with Percutaneous Needle Electrolysis, (b) treatment group with Dry Needling or (c) treatment group with placebo needling. In addition, all groups will perform eccentric exercise. Functionality and muscle strength parameters, pain, ultrasound appearances and patient perceived quality of life shall be evaluated using the VISA-p, jump test, VAS, US images and SF-36, respectively. Participants will be assessed at baseline, at 10 weeks and at 22 weeks after baseline. The expected findings will allow us to advance in the treatment of this injury as they will help determine whether a needling intervention has additional effects on an eccentric exercise program and whether any of the needling modalities is more effective than the other.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Ethics and dissemination: This protocol has been approved by the Ethics Committee of Aragon (Nº PI15/0017). The trial will be conducted in accordance with the Declaration of Helsinki.

Trial Registration Number: NCT02498795.

Strengths and limitations of this study

- This randomized clinical trial will report the effects on functionality and pain of three different treatment interventions in both the short and long term.
- The double-blinded and placebo-control design will enhance objectivity and help reduce bias.
- The effects of two minimally invasive treatments in physical therapy will be compared for the first time in patellar tendinopathy.

INTRODUCTION

Patellar tendinopathy (PT), also known as jumper´s knee, is a degenerative condition affecting the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella. This disorder has similar histologic findings to other tendon disorders characterized by an increased thickness of the tendon and changes in vascularity, and cellularity, with incompletely healed tendon micro-ruptures and disturbed collagen distribution(1).

This degenerative condition affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The overall prevalence of PT in non-elite players is 8.5%, although this figure increases in sports that place high demands on the patellar ligament, increasing up to 14.2% in volleyball athletes. Among elite volleyball and basketball players, a prevalence of 45% and 32%, respectively, has been

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

reported. In addition, jumper's knee is almost twice as common among male non-elite athletes when compared with female athletes(2).

The diagnosis is typically based on the clinical history and symptomatic findings. Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) can be used for the assessment of the patellar tendon to clinically confirm the diagnosis(3).

Treatments used for PT fall into two major groups. The first group comprises medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection(4) and autologous growth factors(5). The second group consists of physical therapies, including both conservative and invasive approaches (needling techniques).

Conservative therapies are generally accepted as the first line of approach for managing PT(6, 7), considering exercise as the gold standard of treatment, either eccentric exercise (EE) or high slow resistance training programs. Both had demonstrated similar effectiveness in the treatment of PT(6-8). In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including PT, and there was a greater likelihood of clinical improvement when performed on a declined surface(6, 8, 9). In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc.(10).

Physical therapy approaches for PT continue to evolve and a number of innovative treatment options are now available, such as dry needling (DN)(11), electrotherapeutic invasive modalities (e.g. electrolysis)(12-14) and extracorporeal shockwave (ECSW) therapy(15). Recently, research has focused on regenerative therapies with high expectations of success because some of these techniques seem to achieve a rapid

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

regeneration of the injured tendon(11, 12, 16). However, evidence-based regenerative therapies are limited and there is no agreement to date regarding which of these is the most effective(17). DN consists of the insertion of a needle (filiform and solid, non-beveled) with the aim of provoking a local injury leading to an inflammatory response and the subsequent regeneration of the injured area in approximately one week. A study performed by Abat et al. reported that DN induced histological and mechanical changes in rat Achilles tendons at week one, with changes persisting at week four(18). Percutaneous Needle Electrolysis (PNE) is an ultrasound-guided technique used by physiotherapists consisting of causing localized lysis in the damaged and/or degenerated tissue by means of a galvanic current transmitted through an acupuncture needle. This technique may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area in rats(18). James et al.(11) carried out a cohort study in humans analyzing one group treated with DN and another treated with autologous blood injections. In both cases, they found improvements compared to the baseline measurements. However, this study failed to find differences between the different treatments, concluding that both techniques were equally effective. In relation to PNE, a former study(14) analyzed the treatment effect of electrolysis applied once a week in a group of patients without any control or comparative group, reporting that patients obtained statistically and clinically significant improvements compared to baseline measurements.

From a biological point of view, it seems reasonable to hypothesize that a patient will obtain benefits thanks to the mechanical effects provided by the needle, and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle(16).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Therefore, the aim of this study is to determine whether invasive techniques have additional effects for the treatment of PT when compared with EE alone, and whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term.

METHODS AND ANALYSIS

Study design

The trial is designed as a randomized, controlled, participant, investigator and outcomes assessor blinded, experimental study, aimed at comparing three different physiotherapy protocols applied in three intervention groups of PT patients. Randomization will be performed as block randomization with a 1:1:1 allocation.

This protocol follows the standards of the Helsinki Convention of good clinical practices. The Ethics Committee of Aragon (CEICA) has evaluated the project and has given its favorable opinion and support, Nº PI15/0017 (Appendix 1).

The study has been carried out following the SPIRIT statement for clinical trial protocol and a SPIRIT Checklist has been included (Appendix 2).

Study setting

After reviewing the literature and observing the high incidence of this pathology in amateur young adults who perform sports and more specifically, jump sports, the search of patients has been performed in sports clubs of basketball, football, volleyball, CrossFit, and handball, together with running clubs and several gyms located in the city. A decision was made to conduct the study in X, where the university is located, as well as the laboratory to be used for assessments and treatments.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The assessments will be conducted at the Motion Analysis laboratory of X, and the treatment will be performed at two different sites depending on the availability of both spaces and of schedules. Nonetheless, the same material will always be used.

Participants

Inclusion criteria

Participants eligible for inclusion in this study must meet the following criteria: 1. History of PT and anterior knee pain located on the inferior pole of the patella for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the superior insertion of the patellar tendon; 4. A score below 80 on the VISA-p questionnaire.

Exclusion criteria

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Corticosteroid injection in the patellar tendon within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs); 6. Any other concomitant treatment for PT.

Methodology

In the first session, all participants will be instructed on how to perform a daily home program of EE. This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol(19) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale(20), and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

For the interventions, the participants will be placed in a supine position with a pillow under the knee (approximately 20º of knee flexion). The area will be cleansed with an

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

antiseptic solution (70% Propan-2-ol, Skin-des). An ultrasound probe cover will be used during the intervention for infectious control. To determine the relevant treatment area, two factors will be considered: 1) Palpation of the areas exhibiting higher sensitivity and that reproduce the patient's symptoms; 2) Tendon areas showing degenerative changes assessed under ultrasound. Each group will receive a total of four sessions distributed throughout eight weeks of treatment, once every two weeks.

DN intervention combined with EE (DN-G) and PNE intervention combined with EE (PNE-G)

Specific DN needles will be used during needling treatments, (Agu-punt, Spain). Considering the thickness of the tendon and the approach, we shall use needles measuring 0.25 x 25 mm. The procedure will be guided by US to ensure the specificity of application on the injured area and to guarantee that the procedure is safe for the patient. The DN needle will reach the relevant treatment area (areas with degenerative PT changes). Each session will consist of three needle insertions lasting three seconds each. In PNE-G applications, an intensity of 3 mA galvanic current will be used during the three seconds that the procedure lasts. The dose of 3 mA has demonstrated to be as effective as 6 mA in the treatment of tendinopathy injuries in animal models(18) as a result, the lower dose was selected for this study.

Control group (CG)

A sham needle will be placed upon the treatment zone, simulating the same procedure as the rest of participants enrolled in the other groups. The needle will be placed in a specific holder and will be manipulated during the intervention to simulate a real treatment. This

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

holder will have a cover over the bottom part of the same in order to avoid the needle contacting the skin.

Outcomes

Baseline data

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and previous rehabilitation treatments and infiltrations received. A blinded observer will assess all participants at baseline, 10 weeks and 22 weeks after baseline. Participants will be asked to inform the researchers if there were any changes in medication or if they are receiving any other treatment or infiltration during the study.

Primary outcome measure

Participants will complete the VISA-p questionnaire at baseline. The VISA-p questionnaire is designed to measure the severity of PT(21). The VISA-p score is the primary outcome variable. This scale consists of eight questions, the first six questions of which employ an analogical visual scale in order to assign a score of 0 to 10, where 10 represents the optimum state, for the purpose of quantifying pain and function in different activities, whereas the last two questions assess the level of functionality and ability to perform physical activity.

Secondary outcome measure

At the first evaluation, participants will complete the Visual Analog Scale (VAS), considering the level of pain they feel while practicing their sport's activity. Participants will be explained that a score of 0 indicates the absence of pain whereas a score of 10 represents the maximum tolerable pain. They will also complete a questionnaire to assess their quality of life (SF-36)(22).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

In order to assess tendon structure, an US evaluation using ultrasound equipment (Logic S7 Expert, General Electric Healthcare) and a linear probe (MLG-15 5–10 MHz) will be used. The ultrasonographic assessment protocol will be carried out according to the Musculoskeletal Ultrasound Technical Guidelines: Knee, defined by the European Society of Musculoskeletal Radiology(23). The ultrasonographic assessment will consist of a longitudinal sequence from the tendon origin to the insertion and transverse sections on the pole of the patella, the tendon body and its insertion on the tibial tuberosity, with the subject in supine position, with 20º knee flexion, and a pillow under the knee. The presence of degenerative signs compatible with the medical diagnosis of PT (thickness of the tendon, hypoechoic areas, irregularities affecting the cortical bone, calcifications) that could be relevant for the selection of the target area will also be assessed. In addition, CD-US assessment will be carried out to detect the presence of hypervascularization, with the subject in supine position and with the knee relaxed in full extension, in order to obtain further information to specifically define the target area.

Upon completion of the evaluation, a jump test will be carried out, measured with a force platform (FP4060-10-2000, Bertec Corporation). In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table 1)(24-26). The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed. The Abalakov jump will be performed with the subject standing in an upright

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

position with a full arm swing. A rapid downward movement will be immediately followed by a rapid upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, a Squat Jump will be performed with 90 degrees of flexion of the knee.

Participant timeline

The study design will be a double-blind randomized controlled trial. The flow chart of the trial is shown in Figure 1 and the check list SPIRIT schedule is shown in Figure 2.

'Patient and Public Involvement'

Patients who had PT were not involved in setting the research question or the outcome measures, however the concept of patient involvement translated to the execution phases of the research. Patients and their families were central to the dissemination of the information, which helped to recruit study participants. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Sample size

Regarding the sample size, a calculation of statistical power was made prior to the study. Accepting an alpha risk of 0.05 and a beta risk in a bilateral contrast, 19 subjects are needed in every treatment group to detect a difference equal or superior to 15 points on the VISA-p scale and assuming a standard deviation of 15 points(27). The estimated rate of loss to follow-up is 20%.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media.

The interested subjects will receive an e-mail explaining the inclusion and exclusion criteria, as well as the purpose of the study. *If they meet the* defined *criteria, they will be invited to send us their medical diagnosis.*

Recruitment

Participants will be recruited from sports clubs by the physiotherapist or the coach. Contact has been made with various orthopedists who will collaborate with recruitment, so that when they establish a diagnosis of this pathology in their examination room they can refer us to the patients for their recruitment to the study.

Allocation

Participants will be randomly assigned to either CG or DN-G or PNE-G with a 1:1:1 allocation using an opaque envelope, with a block size of fifteen participants (5 for each group).

Sealed opaque randomization envelopes with a study-specific participant number will be supplied by an external statistician. A colleague not involved in the research study will take the sealed opaque numbered envelopes in order, by number, and deliver the correct envelope to the treating physical therapist. The envelope will contain a piece of paper, which will be labelled with the same participant specific number, plus the group assignment (PNE-G, DN-G or CG).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants who fulfill the inclusion criteria will receive the standardized oral and written information, and, once they grant their consent to take part in the trial, they will be randomized into the three groups.

Blinding

Assessments regarding clinical recovery will be conducted by an assessor blinded to treatment allocation. Due to the nature of the intervention, participants can be blinded to allocation. Patients will be explained that they are going to receive a needling treatment, that it may be a bit painful, and that if at any moment they are unable to tolerate the pain they must inform the researcher to stop the intervention. In order to blind patients, all the interventions were made with the ultrasound and the PNE device connected to simulate the same intervention in all groups. In contrast, the physiotherapist performing the intervention cannot be blinded, however will be instructed not to disclose the allocation status of the participant at any time or during the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyze data without having access to information about the allocation.

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

Data collection methods

For the data collection of the participants, an oral questionnaire will be used containing questions targeted at collecting baseline data and information concerning the pathology.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Different questionnaires and assessment scales (VISA-p, VAS, SF-36) in Spanish will be given to each participant in paper when they attend the assessment, and they will be granted sufficient time to complete the same.

Data management and statistical analysis

In this study, all data will be entered electronically in the assessment room.

Original scales and questionnaires will be entered and kept on a locked file at the participating site.

Participant files are to be stored in numerical order and stored in a secure and accessible place and manner. Participant files will be maintained in storage for a period of 2 years after completion of the study.

The statistical analysis will be carried out by an intention-to-treat analysis. Variables will be described in number (percentage) and average (standard deviation) or median (interquartile range) attending to their distribution. Quantitative variables will be analyzed with the Shapiro Wilk test in order to confirm their distribution and to determine correct statistical tests according to these results.

Outcomes will be analyzed using mixed linear and logistic regression models considering participants as a random effect and group of treatment as fixed factors. Baseline characteristics will be introduced in the model as covariance. Numbers needed to treat index will also be calculated. The primary aim of the analysis will be to calculate the difference obtained in the VISA-p score after the intervention (final measurement - initial measurement). Finally, the magnitude of the effect of the result shall be calculated and therefore its clinical importance, by means of the following formula:

$$r=\sqrt{\frac{F(1,dfR)}{F(1,dfR)+dfR}}.$$

The significance level set for all the analysis will be $p \leq 0.05$.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ETHICS AND DISEMINATION

The study design, procedures and informed consent procedure were approved and consequently the study will be carried out in compliance with the Helsinki Declaration of Human Rights. All participants will have to provide written Spanish informed consent. Appendix A.

The trial's results will be published in peer-reviewed international journals or otherwise made publicly available and will be presented at national and international conferences and symposiums irrespective of the outcomes.

Any modifications to the protocol, which may impact the study procedures, potential patient benefits or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendments will be approved by the Ethics Committee prior to implementation and notified to the health authorities in accordance with local regulations.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored identified by code number. All local databases will be secured with password-protected access systems.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

DISCUSSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study seeks to investigate the effects of physiotherapy needling techniques on pain, functionality and quality of life in PT.

PT is a common cause of knee pain in cases of degeneration of the patellar tendon. Among the causes of PT, extrinsic factors (e.g., patellar tendon loading with exercise) and intrinsic factors (e.g., malalignment, high patella, imbalances) have been proposed(28). Traditionally, the focus has been on quadriceps strengthening exercises and many reviews have shown that the effect of the treatment could be estimated to give the patients a 50-70% change of improvement on pain and functionality(6, 29, 30).

Regarding needling treatment, previous studies have shown a great improvement in PT using PNE in combination with EE, with all patients reporting an improvement at least one month after treatment(12-14, 18). This is an improvement compared to the minimum three months needed to improve symptoms by applying other conventional techniques (pharmacological and biological treatments, cold/heat techniques, shock waves, etc.) Additionally, in a long-term study conducted in 2013, this technique was shown to improve symptoms quickly and steadily for at least 10 years(31). These findings demonstrate that this technique ensures that patients remain pain-free for a long period. Furthermore, we were only able to find four articles(12-14, 18) addressing the application of PNE for the recovery of PT, however, none of the articles studied were RCTs, which entail limited evidence of the effectiveness of this technique.

In addition, there are no standardized protocols for the application of PNE, which explains the great variability in the number of sessions and application time based on the literature. Therefore, this study aims to facilitate clinical practice and combine the available methodology criteria in the application of this promising technique.

Regarding DN, the literature shows many similarities with PNE, since there is only one RCT that compares functionality improvements among patients who have received PRP.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study reflected that in the short term PRP had better results for pain and functionality, however, DN was more effective than PRP after six months(32).

For the application of both needling techniques, US-guidance is normally used to be able to observe firstly the presentation of the tendon, and later to observe the needle and enable a much more specific treatment approach. However, US has disadvantages including its operator dependence and the limited ability to rule out intra-articular disease. The sensitivity and specificity of ultrasonography for patellar tendinopathy is between 58% and 94%, respectively(33).

Moreover, functionality of the tendon is usually measured with the VISA-p(34, 35), whereas jump tests (representing a similar action to that performed in subject's daily sports) are only evaluated in a few papers(25, 36). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men(37). Thus, we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

This study has several strengths. First, we will evaluate two techniques that currently lack strong evidence. However, in doing so, we are contributing to new knowledge in the field of the recovery of musculoskeletal injuries. Second, the role of invasive techniques will be determined by comparing the effects between these techniques and a control group. The reliability of data is ensured, as both patients and the assessor will be blinded. Third, a sub-analysis with US will be performed to investigate changes in the presence of calcifications, cortical irregularities, neovascularization, thickness, eco-intensity, eco-variation and eco-texture of the patellar tendon.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

The findings obtained may help advance the treatment of this injury by identifying the most effective treatment protocol and to avoid the associated consequences, such as the prevention of relapses and reducing the potential impact on the musculoskeletal system.

REFERENCES

1. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. Journal of orthopaedic surgery and research. 2008;3:18.
2. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of Jumper's Knee Among Nonelite Athletes From Different Sports A Cross-Sectional Survey. American Journal of Sports Medicine. 2011;39(9):1984-8.
3. Stenroth L, Sefa S, Arokoski J, Toyras J. Does Magnetic Resonance Imaging Provide Superior Reliability for Achilles and Patellar Tendon Cross-Sectional Area Measurements Compared with Ultrasound Imaging? Ultrasound Med Biol. 2019;45(12):3186-98.
4. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A Systematic Review of the Use of Platelet-Rich Plasma in Sports Medicine as a New Treatment for Tendon and Ligament Injuries. Clinical Journal of Sport Medicine. 2011;21(4):344-52.
5. Andres BM, Murrell GAC. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clinical Orthopaedics and Related Research. 2008;466(7):1539-54.
6. Larsson MEH, Kall I, Nilsson-Helander K. Treatment of patellar tendinopathy-a systematic review of randomized controlled trials. Knee Surgery Sports Traumatology Arthroscopy. 2012;20(8):1632-46.
7. Kongsgaard M, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scandinavian Journal of Medicine & Science in Sports. 2009;19(6):790-802.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

8. Murtaugh B, Ihm JM. Eccentric Training for the Treatment of Tendinopathies. Current Sports Medicine Reports. 2013;12(3):175-82.

9. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. British Journal of Sports Medicine. 2005;39(2):102-5.

10. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symptomatic shoulder impingement or lateral epicondylar tendinopathy: A systematic review. J Sci Med Sport. 2016;19(6):438-53.

11. James SLJ, Ali K, Pocock C, Robertson C, Walter J, Bell J, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine. 2007;41(8):518-21.

12. Abat F DW, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibañez JM. Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up. Muscles Ligaments Tendons J. 2014;14(4):188-93.

13. Valera Garrido F, Minaya Muñoz F, JM SI. Effectiveness of electrolysis percutaneous intratisular (EPI®) in chronic insertional patellar tendinopathy. Trauma Fund MAPFRE. 2010;21(4):227-36.

14. Sánchez-Ibáñez J, Alves R, Polidori F, Valera F, Minaya F, Valles-Martí S, et al. Effectiveness of ultrasound-guided percutaneous electrolysis intratendon (EPI) in the treatment of insertional patellar tendinopathy in soccer players. Br J Sports Med. 2013;47(e2).

15. Zwerver J, Verhagen E, Hartgens F, van den Akker-Scheek I, Diercks RL. The TOPGAME-study: effectiveness of extracorporeal shockwave therapy in jumping athletes with patellar tendinopathy. Design of a randomised controlled trial. Bmc Musculoskeletal Disorders. 2010;11:6.

16. Riggin CN, Chen M, Gordon JA, Schultz SM, Soslowsky LJ, Khoury V. Ultrasound-Guided Dry Needling of the Healthy Rat Supraspinatus Tendon Elicits Early Healing Without Causing Permanent Damage. J Orthop Res. 2019;37(9):2035-42.

17. Krey D, Borchers J, McCamey K. Tendon needling for treatment of tendinopathy: A systematic review. Physician and Sportsmedicine. 2015;43(1):80-6.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

18. Abat F, Valles S-L, Gelber P-E, Polidori F, Jorda A, Garcia-Herreros S, et al. An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI technique. BMC sports science, medicine and rehabilitation. 2015;7:7-.

19. Alfredson H, Pietila T, Jonsson P, Lorentzon P. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. American Journal of Sports Medicine. 1998;26(3):360-6.

20. Silbernagel KG, Crossley KM. A Proposed Return-to-Sport Program for Patients With Midportion Achilles Tendinopathy: Rationale and Implementation. J Orthop Sports Phys Ther. 2015;45(11):876-86.

21. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural Adaptation of VISA-P Score for Patellar Tendinopathy in Spanish Population. Journal of Orthopaedic & Sports Physical Therapy. 2011;41(8):581-91.

22. Alonso J, Prieto L, Anto JM. The spanish version of the SF-36 health survey- A measure of clinical outcomes. Medicina Clinica. 1995;104(20):771-6.

23. Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights into imaging. 2010;1(3):99-141.

24. Rodriguez-Rosell D, Mora-Custodio R, Franco-Marquez F, Yanez-Garcia JM, Gonzalez-Badillo JJ. Traditional vs. Sport-Specific Vertical Jump Tests: Reliability, Validity, and Relationship With the Legs Strength and Sprint Performance in Adult and Teen Soccer and Basketball Players. J Strength Cond Res. 2017;31(1):196-206.

25. Helland C, Bojsen-Moller J, Raastad T, Seynnes OR, Moltubakk MM, Jakobsen V, et al. Mechanical properties of the patellar tendon in elite volleyball players with and without patellar tendinopathy. Br J Sports Med. 2013;47(13):862-8.

26. Gual G, Fort-Vanmeerhaeghe A, Romero-Rodriguez D, Tesch PA. Effects of In-Season Inertial Resistance Training With Eccentric Overload in a Sports Population at Risk for Patellar Tendinopathy. J Strength Cond Res. 2016;30(7):1834-42.

27. Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.

28. Figueroa D, Figueroa F, Calvo R. Patellar Tendinopathy: Diagnosis and Treatment. J Am Acad Orthop Surg. 2016;24(12):e184-e92.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

29. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports - A cross-sectional study. American Journal of Sports Medicine. 2005;33(4):561-7.

30. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. British Journal of Sports Medicine. 2007;41(4):217-23.

31. Abat F, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibanez JM. Clinical results after ultrasound-guided intratissue percutaneous electrolysis (EPIA (R)) and eccentric exercise in the treatment of patellar tendinopathy. Knee Surgery Sports Traumatology Arthroscopy. 2015;23(4):1046-52.

32. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. American Journal of Sports Medicine. 2014;42(3):610-8.

33. Warden SJ, Kiss ZS, Malara FA, Ooi ABT, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. American Journal of Sports Medicine. 2007;35(3):427-36.

34. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural adaptation of VISA-P score for patellar tendinopathy in Spanish population. J Orthop Sports Phys Ther. 2011;41(8):581-91.

35. Andriolo L, Altamura SA, Reale D, Candrian C, Zaffagnini S, Filardo G. Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option: A Systematic Review and Meta-analysis. Am J Sports Med. 2019;47(4):1001-18.

36. de Vries A, Zwerver J, Diercks R, Tak I, van Berkel S, van Cingel R, et al. Effect of patellar strap and sports tape on pain in patellar tendinopathy: A randomized controlled trial. Scand J Med Sci Sports. 2016;26(10):1217-24.

37. Markovic G, Dizdar D, Jukic I, Cardinale M. Reliability and factorial validity of squat and countermovement jump tests. J Strength Cond Res. 2004;18(3):551-5.

AUTHOR'S CONTRIBUTIONS

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

MPL, EMG and PH conceived of the idea, and developed the intervention. MPL and PH

JUMP TEST PROTOCOL	
5-minute warm-up consisting of steady jogging on a treadmill	
Dynamic Stretches lasting 5 minutes, as instructed by the physical therapist	Psoas Quadriceps Gluteus maximus Gastrocnemius Hamstring muscles

wrote the article. MPL, MO, RMG, AVB, ZA, YH and PH developed the design of the trial. MO were involved in development of the statistical analysis of the trial and contributed to the content of the article. AVB contributed to the design and writing of the jump test protocol. All authors have read and approved the final manuscript.

FUNDING STATEMENT

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTEREST STATEMENT

The authors declare that they have no competing interests.

TABLES

Table 1. Jump test's protocol.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Three jump tests are performed - 3 jumps off the ground for 3 times for the patient to become familiar with the tests - The subject is placed on the platform and asked to perform each test 3 times, with 60 seconds rest between the different tests	Abalakov test Countermovement jump test Squat jump
The highest jump is selected for the study	

FIGURES

Figure 1. Flow diagram. Randomized controlled trial design.

G-PNE: Percutaneous Needle Electrolysis Group. G-DN: Dry Needle Group.

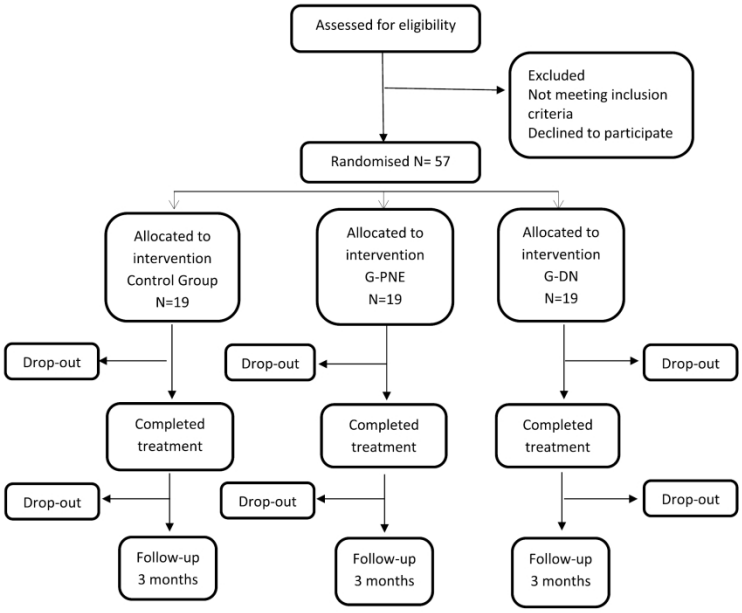
Figure 2. Schedule for the enrolment and intervention.

Schedule for enrolment and intervention per cluster. -t1: baseline; t1–t2: intervention period; t2: 8 weeks after baseline; t3: 10 weeks after baseline; t4: 3 months after baseline. G-PNE: Percutaneous Needle Electrolysis Group; G-DN: Dry Needle Group; US: ultrasound.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure 1. Flow diagram. Randomized controlled trial design.



210x297mm (300 x 300 DPI)

Figure 2. Schedule for enrolment and intervention.

	Enrolment	Allocation	Close-out			
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control group			⟷			
G-PNE			⟷			
G-DN			⟷			
ASSESSMENTS:						
Baseline demographic information	X					
VISA-P	X		X		X	X
VAS			X		X	X
SF-36			X		X	X
Tendon structure US			X		X	X
Jump test			X		X	X

215x279mm (300 x 300 DPI)

DOCUMENTO DE INFORMACIÓN AL PACIENTE

Fecha:

Título del proyecto: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Investigador principal:

Doña: Mª Pilar López Royo

Este estudio se basa en el estudio comparativo de tres tratamientos que utilizan distintas técnicas de fisioterapia invasiva junto con un programa de ejercicio excéntrico para el tratamiento de la tendinopatía rotuliana. Por medio del tratamiento se produce una disminución del dolor asociado a esta patología y un aumento de la fuerza de la pierna, lo que a su vez hace que mejore la funcionalidad en las actividades de la vida diaria y mejore la calidad de vida.

PROCESO DE SELECCIÓN DE PACIENTES

Criterios de inclusión:

- Edad comprendida entre 18 y 40 años.
- Practicar cualquier deporte de forma habitual.
- Pacientes con diagnóstico médico de tendinopatía rotuliana crónica con un mínimo de 3 meses de evolución y con sintomatología.
- Dolor a la palpación del tendón en el polo inferior de la rótula y durante el entrenamiento o competición.
- Puntuación del cuestionario VISA-P menor de 80 (el resultado obtenido de rellenar el cuestionario tiene que ser menor de 80 puntos de los 100 posibles para poder participar en el estudio).

Criterios de exclusión:

- Paciente operado de la rodilla afectada en los últimos 6 meses.
- Infiltraciones en la rodilla afectada en los últimos 3 meses.
- Paciente que ha recibido tratamiento farmacológico o fisioterápico en las últimas 48 horas o durante el estudio.
- Patología con menos de 3 meses de evolución.
- Presentar tendinopatía rotuliana bilateral.
- Puntuación del cuestionario VISA-p mayor o igual de 80 (el resultado obtenido de rellenar el cuestionario no puede ser igual o superar los 80 puntos de los 100 posibles, sino no podrá participar en el estudio).
- Imposibilidad para aplicar alguna de las técnicas de tratamiento o valoración por

For peer review only

contraindicación absoluta o relativa.

PROCEDIMIENTO

El tratamiento consiste en realizar un protocolo de ejercicios excéntricos de cuádriceps que realizará en casa de forma diaria, y que serán revisados con el fisioterapeuta para valorar su correcta realización. Se complementará el tratamiento con la aplicación de una técnica de punción según el protocolo de tratamiento propuesto de forma totalmente **aleatorizada** y según los criterios diagnósticos específicos de la misma, siguiendo las indicaciones, criterios de aplicación y criterios diagnósticos.

Son técnicas de punción cuyo objetivo es producir una respuesta inflamatoria aguda que active los mecanismos fisiológicos de regeneración del tejido y mejorar el dolor y la funcionalidad en la articulación de la rodilla, se realiza con agujas de punción seca, similares a las agujas de acupuntura y sin infiltrar ningún tipo de sustancia dentro del organismo.

Los registros serán realizados en el Espacio de Valoración Funcional de la Universidad San Jorge, en la Facultad de Ciencias de la Salud, Edificio III.Se pondrá a su disposición la posibilidad de utilizar el autobús que utiliza el personal y alumnado de la universidad (en el horario que éste esté disponible).Las fechas y horarios serán convenidas con cada participante en función de su disponibilidad y la de los investigadores, buscando la conformidad de todos.La duración aproximada del estudio para cada paciente será de 30 minutos, aunque este horario podrá variar en función de los acontecimientos.

Será recibido por los miembros del equipo de investigación y una vez allí, se le realizará un primer análisis fisioterápico, rellenará una encuesta, una escala analógica visual (EVA) del dolor y el cuestionario Visa-p en el que se valorará la funcionalidad de la rodilla.

Tras éste primer registro se le colocará un marcador pasivo en el pantalón. Se le pedirá que realice el siguiente protocolo:

- Calentamiento de 5 minutos en cinta a ritmo constante.
- Estiramientos dinámicos de psoas, cuádriceps, glúteo, gastrocnemios, isquiotibiales durante 5 minutos instruidos por el fisioterapeuta.
- Realización de los 3 saltos fuera de la plataforma durante 3 veces para que se familiarice con los tests.
- En la plataforma de fuerzas realizará 3 test de salto: el test de Abalakov (ABK), el test de salto con contramovimiento (CMJ) y el squatjump (SJ).

Se colocará en la plataforma y realizará 3 saltos de cada uno de los test con una separación entre ellos de 60 segundos.

Se valora el tendón por ecografía, y se recogen datos por medio de personal adiestrado y se envía

For peer review only

a personal especialista en radiodiagnóstico.
Tras los registros de los saltos se dará por finalizada la valoración.

Tras la 1ª valoración, se realizará una división en tres grupos de los pacientes de forma aleatorizada.
Se le realizará el protocolo de tratamiento de fisioterapia invasivaque le haya correspondido. Realizará una sesión del tratamiento cada 14 días, y se realizará la 2º valoración 1 semana más tarde de la 4º sesión de punción para valorar los cambios que se hayan producido tras el tratamiento, repitiéndose de nuevo el proceso de recogida de datos realizado al inicio del estudio. Se realizará un seguimiento a los tres meses de la valoración post-tratamiento para valorar la eficacia de la técnica a largo plazo del tratamiento.
El procedimiento se realizará guiado ecográficamente para asegurar la especificidad de aplicación sobre la zona relevante de tratamiento y garantizar la seguridad de la técnica. Se hace posterior a esta intervención una serie de ejercicios excéntricos de cuádriceps. El tratamiento se realizará durante 4 sesiones (a razón de una sesión cada 14 días).

RIESGOS

La aplicación de las técnicas de punción utilizadas no han demostrado tener ningún efecto secundario hasta la fecha, aunque el paciente puede experimentar dolordurante y tras la punción, generalmente de uno o dos días de duración.

RESPONSABILIDADES DEL PARTICIPANTE

La información que usted posea sobre su estado de salud o sobre sensaciones previas anormales al realizarle una punción, puede afectar la seguridad o el valor de estas pruebas. La rápida comunicación por su parte de las sensaciones que experimenta al realizar esta prueba es también de gran importancia. Usted es responsable de revelar esa información al personal de la prueba cuando se le pregunte.

PREGUNTAS

Le animamos a que haga cualquier pregunta sobre los procedimientos seguidos o sus resultados en la prueba. Si tiene alguna preocupación o pregunta, por favor pídanos más información, para ello le dejamos un correo electrónico mapilr86@hotmail.com y un número de teléfono móvil: 616102365.

LIBERTAD PARA DAR EL CONSENTIMIENTO

Usted participa en el estudio de manera voluntaria, pudiendo abandonarlo en el momento que considere oportuno, sin que esto conlleve ninguna repercusión negativa para usted.

Los datos obtenidos en el estudio serán confidenciales y únicamente se hará uso de ellos

For Peer review only

para el cumplimiento de los objetivos planteados en la investigación. No se cederán estos datos a terceros sin el consentimiento expreso de los sujetos participantes a quienes pertenezcan los datos.

En esta investigación se garantizará el anonimato de los sujetos que aportan los datos, estableciendo un código disociado para identificarlos que sólo será conocido por los responsables de la realización del trabajo de campo.

Fdo: Mª Pilar López Royo

For peer review only

MODELO DE CONSENTIMIENTO INFORMADO

Título del PROYECTO: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Doña: Mª Pilar López Royo (mapilr86@hotmail.com)
Departamento de Fisiatría y Enfermería
UNIVERSIDAD DE ZARAGOZA

Yo, ... (nombre y apellidos del participante)

He recibido suficiente información en relación con el proyecto, he leído la hoja de información que se me ha entregado y he podido hacer preguntas sobre el proyecto, recibiendo respuestas satisfactorias.

Entiendo que la participación es voluntaria y que puedo abandonar el proyecto:

. Cuando lo desee
. Sin tener que dar explicaciones
. Sin que esto repercuta en mis cuidados médicos

He sido claramente informado de forma clara y precisa del tratado que recibirán mis datos personales que se contienen en este proyecto, sabiendo que los datos serán tratados y custodiados bajo mi intimidad y a la vigente normativa de la protección de datos, y que sobre estos datos me asisten los derechos de rectificación, acceso y oposición comunicándolo al investigador principal que figura en este consentimiento.

Declaro que presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

Así pues, acepto que las muestras derivadas de este proyecto puedan ser utilizadas en futuras investigaciones siempre y cuando están relacionadas con ésta.

Por lo tanto, doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es

For peer review only

revocable.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del proyecto al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Consentimiento informado estudio_____

Versión_____, fecha_____

For peer review only

Appendix 2. Checklist SPIRIT

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1-3
	2b	All items from the World Health Organization Trial Registration Data Set	2-3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	22
	5b	Name and contact information for the trial sponsor	22
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-5
	6b	Explanation for choice of comparators	3-5
Objectives	7	Specific objectives or hypotheses	5-6

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12-13
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12-13

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	-
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	-
	31b	Authorship eligibility guidelines and any intended use of professional writers	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

8

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034304.R2
Article Type:	Protocol
Date Submitted by the Author:	08-Jan-2020
Complete List of Authors:	Lopez-Royo, Maria Pilar; Universidad San Jorge Facultad de Ciencias de la Salud; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Gómez-Trullén, Eva Maria; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Ortiz-Lucas, Maria; Universidad San Jorge Facultad de Ciencias de la Salud Galán-Diaz, Rita Maria; Universidad San Jorge Facultad de Ciencias de la Salud Bataller-Cervero, Ana Vanessa; Universidad San Jorge Facultad de Ciencias de la Salud Al-Boloushi, Zaid; Universidad de Zaragoza Facultad de Ciencias, Facultad de Ciencias de la Salud y del Deporte; Kuwait Ministry of Health Hamam-Alcober, Yasmina; Universidad San Jorge Facultad de Ciencias de la Salud, Fisioterapia Herrero, Pablo; Universidad San Jorge Facultad de Ciencias de la Salud
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Sports and exercise medicine, Pathology
Keywords:	Eccentric Exercise, Tendinopathy, Percutaneous Needle Electrolysis, Dry Needling

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

López-Royo MP[a,b], Gómez-Trullén EM[b], Ortíz-Lucas M[a], Galán-Díaz RM[a], Bataller-Cervero AV[a], Al-Boloushi Z[b,c], Hamam-Alcober Y[a], Herrero P[a *]

AFFILIATIONS

A. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, Spain.

B. Universidad de Zaragoza. Facultad de Ciencias de la Salud y del Deporte. Dpto. de Fisiatría y Enfermería. C/ Domingo Miral s/n, 50009 - Zaragoza, Spain.

A. Ministry of Health, State of Kuwait. Jamal Abdulnasser Street, Al Solaibeykhat Area 5. Kuwait City. Safat 13001.

***CORRESPONDENCE TO:**

Dr. Pablo Herrero. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov A23, Km 299, 50830 Villanueva de Gállego, Zaragoza, Spain. Tel.: (+34) 976 060 100 Fax: 976 077 581. Email: pherrero@usj.es

ADDITIONAL AUTHOR INFORMATION

Maria Pilar López Royo. Emails: mplopez@usj.es

Eva María Gómez Trullén. Email: evagomez@unizar.es

María Ortíz Lucas. Email: mariaortizlucas@gmail.com

Rita María Galán Díaz. Email: rmgalan@usj.es

Ana Vanessa Bataller-Cervero. Email: avbataller@usj.es

For peer review only

Yasmina Hamam-Alcober. Email: yhamam@usj.es

Zaid AL-boloushi. Email: boloushi@me.com

WORD COUNT: 3985 words.

ABSTRACT

Introduction: Patellar tendinopathy is a degenerative disease of the patellar tendon, which affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The aim of this study is to compare the effectiveness of three therapies in order to determine the most effective treatment protocol of patellar tendinopathy.

Methods and analysis: This study is a randomized controlled trial with blinded participants. Measurements will be carried out by a specially trained blinded assessor. A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups. Eligible participants will be randomly allocated to receive either: (a) treatment group with Percutaneous Needle Electrolysis, (b) treatment group with Dry Needling or (c) treatment group with placebo needling. In addition, all groups will perform eccentric exercise. Functionality and muscle strength parameters, pain, ultrasound appearances and patient perceived quality of life shall be evaluated using the VISA-p, jump test, VAS, US images and SF-36, respectively. Participants will be assessed at baseline, at 10 weeks and at 22 weeks after baseline. The expected findings will allow us to advance in the treatment of this injury, as they will help determine whether a needling intervention has additional effects on an eccentric exercise program and whether any of the needling modalities is more effective than the other.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Ethics and dissemination: This protocol has been approved by the Ethics Committee of Aragon (Nº PI15/0017). The trial will be conducted in accordance with the Declaration of Helsinki.

Trial Registration Number: NCT02498795.

Strengths and limitations of this study

- This randomized clinical trial will report the effects on functionality and pain of three different treatment interventions in both the short and long term.
- The double-blinded and placebo-control design will enhance objectivity and help reduce bias.
- The effects of two minimally invasive treatments in physical therapy will be compared for the first time in patellar tendinopathy.

INTRODUCTION

Patellar tendinopathy (PT), also known as jumper´s knee, is a degenerative condition affecting the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella. This disorder has similar histologic findings to other tendon disorders characterized by an increased thickness of the tendon and changes in vascularity, and cellularity, with incompletely healed tendon micro-ruptures and disturbed collagen distribution(1).

This degenerative condition affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The overall prevalence of PT in non-elite players is 8.5%, although this figure increases in sports that place high demands on the patellar ligament, increasing up to 14.2% in volleyball athletes. Among elite volleyball and basketball players, a prevalence of 45% and 32%, respectively, has been

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

reported. In addition, jumper's knee is almost twice as common among male non-elite athletes when compared with female athletes(2).

The diagnosis is typically based on the clinical history and symptomatic findings. Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) can be used for the assessment of the patellar tendon to clinically confirm the diagnosis(3).

Treatments used for PT fall into two major groups. The first group comprises medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection(4) and autologous growth factors(5). The second group consists of physical therapies, including both conservative and invasive approaches (needling techniques).

Conservative therapies are generally accepted as the first line of approach for managing PT(6, 7), considering exercise as the gold standard of treatment, either eccentric exercise (EE) or high slow resistance training programs. Both have demonstrated similar effectiveness in the treatment of PT(6-8). In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including PT, with a greater likelihood of clinical improvement when performed on a declined surface(6, 8, 9). In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc.(10).

Physical therapy approaches for PT continue to evolve and a number of innovative treatment options are now available, such as dry needling (DN)(11), electrotherapeutic invasive modalities (e.g. electrolysis)(12-14) and extracorporeal shockwave (ECSW) therapy(15). Recently, research has focused on regenerative therapies with high expectations of success because some of these techniques seem to achieve a rapid

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

regeneration of the injured tendon(11, 12, 16). However, evidence-based regenerative therapies are limited and there is no agreement to date regarding which of these is the most effective(17). DN consists of the insertion of a needle (filiform and solid, non-beveled) with the aim of provoking a local injury leading to an inflammatory response and the subsequent regeneration of the injured area in approximately one week. A study performed by Abat et al. reported that DN induced histological and mechanical changes in rat Achilles tendons at week one, with changes persisting at week four(18). Percutaneous Needle Electrolysis (PNE) is an ultrasound-guided technique used by physiotherapists consisting of causing localized lysis in the damaged and/or degenerated tissue by means of a galvanic current transmitted through an acupuncture needle. This technique may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area in rats(18). James et al.(11) carried out a cohort study in humans analyzing one group treated with DN and another treated with autologous blood injections. In both cases, they found improvements compared to the baseline measurements. However, this study failed to find differences between the different treatments, concluding that both techniques were equally effective. In relation to PNE, a former study(14) analyzed the treatment effect of electrolysis applied once a week in a group of patients without any control or comparative group, reporting that patients obtained statistically and clinically significant improvements compared to baseline measurements.

From a biological point of view, it seems reasonable to hypothesize that a patient will obtain benefits thanks to the mechanical effects provided by the needle(16), and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle(19).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Therefore, the aim of this study is to determine which intervention is the most effective, and whether invasive techniques have additional effects for the treatment of PT when compared with EE alone. Moreover, whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term.

METHODS AND ANALYSIS

Study design

The trial is designed as a randomized, controlled, participant, investigator and outcomes assessor blinded, experimental study, aimed at comparing three different physiotherapy protocols applied in three intervention groups of PT patients. Randomization will be performed as block randomization with a 1:1:1 allocation.

This protocol follows the standards of the Helsinki Convention of good clinical practices. The Ethics Committee of Aragon (CEICA) has evaluated the project and has given its favorable opinion and support, Nº PI15/0017 (Appendix 1).

The study has been carried out following the SPIRIT statement for clinical trial protocol and a SPIRIT Checklist has been included (Appendix 2).

Study setting

After reviewing the literature and observing the high incidence of this pathology in amateur young adult athletes who perform sports and more specifically, jump sports, patient recruitment has been performed in basketball, football, volleyball, CrossFit, and handball sports clubs, together with running clubs and several gyms located in the city. A decision was made to conduct the study in X, where the university is located, as well as the laboratory to be used for assessments and treatments.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The assessments will be conducted at the Motion Analysis laboratory of X, and the treatment will be performed at two different sites depending on the availability of both spaces and of schedules. Nonetheless, the same material will always be used.

Participants

Inclusion criteria

Participants eligible for inclusion in this study must meet the following criteria: 1. History of PT and anterior knee pain located on the inferior pole of the patella for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the superior insertion of the patellar tendon; 4. A score below 80 on the VISA-p questionnaire.

Exclusion criteria

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Corticosteroid injection in the patellar tendon within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs); 6. Any other concomitant treatment for PT.

Methodology

In the first session, all participants will be instructed on how to perform a daily home program of EE. This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol(20) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale(21), and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

For the interventions, the participants will be placed in a supine position with a pillow under the knee (approximately 20º of knee flexion). The area will be cleansed with an

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

antiseptic solution (70% Propan-2-ol, Skin-des). An ultrasound probe cover will be used during the intervention for infectious control. To determine the relevant treatment area, two factors will be considered: 1) Palpation of the areas exhibiting higher sensitivity and that reproduce the patient's symptoms; 2) Tendon areas showing degenerative changes assessed under ultrasound. Each group will receive a total of four sessions distributed throughout eight weeks of treatment, once every two weeks.

DN intervention combined with EE (DN-G) and PNE intervention combined with EE (PNE-G)

Specific DN needles will be used during needling treatments, (Agu-punt, Spain). Considering the thickness of the tendon and the approach, we shall use needles measuring 0.25 x 25 mm. The procedure will be guided by US to ensure the specificity of application on the injured area and to guarantee that the procedure is safe for the patient. The DN needle will reach the relevant treatment area (areas with degenerative PT changes). Each session will consist of three needle insertions lasting three seconds each. In PNE-G applications, an intensity of 3 mA galvanic current will be used during the three seconds that the procedure lasts(19). The dose of 3 mA has demonstrated to be as effective as 6 mA in the treatment of tendinopathy injuries in animal models(18,19). In humans, a study conducted in 2016 showed that a dose of 3 mA in PT generated structural changes compatible with tendon regeneration, together with improvement of functionality and pain (22). In contrast, the same study found that lower doses were effective only for the improvement of functionality and pain. As a result, a 3 mA dose was selected for this study.

Control group (CG)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

A sham needle will be placed upon the treatment zone, simulating the same procedure as the rest of participants enrolled in the other groups. The needle will be placed in a specific holder and will be manipulated during the intervention to simulate a real treatment. This holder will have a cover over the bottom part of the same in order to avoid the needle contacting the skin.

Outcomes

Baseline data

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and previous rehabilitation treatments and infiltrations received. A blinded observer will assess all participants at baseline, 10 weeks and 22 weeks after baseline. Participants will be asked to inform the researchers if there were any changes in medication or if they are receiving any other treatment or infiltration during the study.

Primary outcome measure

Participants will complete the VISA-p questionnaire at baseline. The VISA-p questionnaire is designed to measure the severity of PT(23). The VISA-p score is the primary outcome variable. This scale consists of eight questions, the first six questions of which employ an analogical visual scale in order to assign a score of 0 to 10, where 10 represents the optimum state, for the purpose of quantifying pain and function in different activities, whereas the last two questions assess the level of functionality and ability to perform physical activity.

Secondary outcome measure

During the first evaluation, participants will complete the Visual Analog Scale (VAS), considering the level of pain they feel while practicing their sport's activity. Participants

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

will be explained that a score of 0 indicates the absence of pain whereas a score of 10 represents the maximum tolerable pain. They will also complete a questionnaire to assess their quality of life (SF-36)(24).

In order to assess tendon structure, an US evaluation using ultrasound equipment (Logic S7 Expert, General Electric Healthcare) and a linear probe (MLG-15 5–10 MHz) will be used. The ultrasonographic assessment protocol will be carried out according to the Musculoskeletal Ultrasound Technical Guidelines: Knee, defined by the European Society of Musculoskeletal Radiology(25). The ultrasonographic assessment will consist of a longitudinal sequence from the tendon origin to the insertion and transverse sections on the pole of the patella, the tendon body and its insertion on the tibial tuberosity, with the subject in supine position, with 20º knee flexion, and a pillow under the knee. The presence of degenerative signs compatible with the medical diagnosis of PT (thickness of the tendon, hypoechoic areas, irregularities affecting the cortical bone, calcifications) that could be relevant for the selection of the target area will also be assessed. In addition, CD-US assessment will be carried out to detect the presence of hypervascularization, with the subject in supine position and with the knee relaxed in full extension, in order to obtain further information to specifically define the target area.

Upon completion of the evaluation, a jump test will be carried out, measured with a force platform (FP4060-10-2000, Bertec Corporation). In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table 1)(26-28).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed. The Abalakov jump will be performed with the subject standing in an upright position with a full arm swing. A rapid downward movement will be immediately followed by a rapid upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, a Squat Jump will be performed with 90 degrees of flexion of the knee.

Participant timeline

The study design will be a double-blind randomized controlled trial. The flow chart of the trial is shown in Figure 1 and the check list SPIRIT schedule is shown in Figure 2.

'Patient and Public Involvement'

Patients with PT were not involved in setting the research question or the outcome measures, however the concept of patient involvement translated to the execution phases of the research. Patients and their families were central to the dissemination of the information, which helped to recruit study participants. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Sample size

Regarding the sample size, a calculation of statistical power was made prior to the study. Accepting an alpha risk of 0.05 and a beta risk in a bilateral contrast, 19 subjects are needed in every treatment group to detect a difference equal or superior to 15 points on

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

the VISA-p scale and assuming a standard deviation of 15 points(29). The estimated rate of loss to follow-up is 20%.

Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media.

The interested subjects will receive an e-mail explaining the inclusion and exclusion criteria, as well as the purpose of the study. If they meet the defined criteria, they will be invited to send us their medical diagnosis.

Recruitment

Participants will be recruited from sports clubs by the physiotherapist or the coach. Contact has been made with various orthopedists who will collaborate with recruitment, so that when they establish a diagnosis of this pathology in their examination room they can refer us to the patients for their recruitment to the study.

Allocation

Participants will be randomly assigned to either CG or DN-G or PNE-G with a 1:1:1 allocation using an opaque envelope, with a block size of fifteen participants (5 for each group).

Sealed opaque randomization envelopes with a study-specific participant number will be supplied by an external statistician. A colleague not involved in the research study will take the sealed opaque numbered envelopes in order, by number, and deliver the correct envelope to the treating physical therapist. The envelope will contain a piece of paper,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

which will be labelled with the same participant specific number, plus the group assignment (PNE-G, DN-G or CG).

Participants who fulfill the inclusion criteria will receive the standardized oral and written information, and, once they grant their consent to take part in the trial, they will be randomized into the three groups.

Blinding

Assessments regarding clinical recovery will be conducted by an assessor blinded to treatment allocation. Due to the nature of the intervention, participants can be blinded to allocation. Patients will be explained that they are going to receive a needling treatment, that it may be slightly painful, and that if at any time they are unable to tolerate the pain they must inform the researcher to stop the intervention. In order to blind patients, all the interventions were made with the ultrasound and the PNE device connected to simulate the same intervention in all groups. In contrast, the physiotherapist performing the intervention cannot be blinded, however he/she will be instructed not to disclose the allocation status of the participant at any time or during the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyze data without having access to information about the allocation.

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

Data collection methods

For the data collection, an oral questionnaire will be used containing questions targeted at collecting baseline data and information concerning the pathology.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Different questionnaires and assessment scales (VISA-p, VAS, SF-36) in Spanish will be given to each participant in paper when they attend the assessment, and they will be granted sufficient time to complete the same.

Data management and statistical analysis

In this study, all data will be entered electronically in the assessment room.

Original scales and questionnaires will be entered and kept on a locked file at the participating site.

Participant files are to be stored in numerical order and stored in a secure and accessible place and manner. Participant files will be maintained in storage for a period of 2 years after completion of the study.

The statistical analysis will be carried out by an intention-to-treat analysis. Variables will be described in number (percentage) and average (standard deviation) or median (interquartile range) attending to their distribution. Quantitative variables will be analyzed with the Shapiro Wilk test in order to confirm their distribution and to determine correct statistical tests according to these results.

Outcomes will be analyzed using mixed linear and logistic regression models considering participants as a random effect and group of treatment as fixed factors. Baseline characteristics will be introduced in the model as covariance. Numbers needed to treat index will also be calculated. The primary aim of the analysis will be to calculate the difference obtained in the VISA-p score after the intervention (final measurement - initial measurement). Finally, the magnitude of the effect of the result will be calculated and therefore its clinical importance, by means of the following formula:

$$r=\sqrt{\frac{F(1,dfR)}{F(1,dfR)+dfR}}.$$

The significance level set for all the analysis will be $p \leq 0.05$.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ETHICS AND DISEMINATION

The study design, procedures and informed consent procedure were approved and consequently the study will be carried out in compliance with the Helsinki Declaration of Human Rights. All participants will have to provide written Spanish informed consent. Appendix 1.

The results for this trial will be published in peer-reviewed international journals or otherwise made publicly available and will be presented at national and international conferences and symposiums irrespective of the outcomes.

Any modifications to the protocol, which may impact the study procedures, potential patient benefits or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendments will be approved by the Ethics Committee prior to implementation and notified to the health authorities in accordance with local regulations.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored identified by code number. All local databases will be secured with password-protected access systems.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

DISCUSSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study seeks to investigate the effects of physiotherapy needling techniques on pain, functionality and quality of life in PT.

PT is a common cause of knee pain in cases of degeneration of the patellar tendon. Among the causes of PT, extrinsic factors (e.g., patellar tendon loading with exercise) and intrinsic factors (e.g., malalignment, high patella, imbalances) have been proposed(30). Traditionally, the focus has been on quadriceps strengthening exercises and many reviews have shown that the effect of the treatment could be estimated to give the patients a 50-70% change of improvement on pain and functionality(6, 32, 33).

Regarding needling treatment, previous studies have shown a great improvement in PT using PNE in combination with EE, with all patients reporting an improvement at least one month after treatment(12-14, 18). This is an improvement compared to the minimum three months needed to improve symptoms by applying other conventional techniques (pharmacological and biological treatments, cold/heat techniques, shock waves, etc.) Additionally, in a long-term study conducted in 2013, this technique was shown to improve symptoms quickly and steadily for at least 10 years(33). These findings demonstrate that this technique ensures that patients remain pain-free for a long period. Furthermore, we were only able to find four articles(12-14, 18) addressing the application of PNE for the recovery of PT, however, none of the articles studied were RCTs, which entail limited evidence of the effectiveness of this technique.

In addition, there are no standardized protocols for the application of PNE, which explains the great variability in the number of sessions and application time based on the literature. Therefore, this study aims to facilitate clinical practice and combine the available methodology criteria in the application of this promising technique.

Regarding DN, the literature shows many similarities with PNE, since there is only one RCT that compares functionality improvements among patients who have received PRP.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study reflected that in the short term PRP had better results for pain and functionality, however, DN was more effective than PRP after six months(34).

For the application of both needling techniques, US-guidance is normally used to be able to observe firstly the presentation of the tendon, and later to observe the needle and enable a much more specific treatment approach. However, US has disadvantages including its operator dependence and the limited ability to rule out intra-articular disease. The sensitivity and specificity of ultrasonography for patellar tendinopathy is between 58% and 94%, respectively(35).

Moreover, functionality of the tendon is usually measured with the VISA-p(36,37), whereas jump tests (representing a similar action to that performed in subject's daily sports) are only evaluated in a few papers(27,38). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men(39). Thus, we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

This study has several strengths. First, we will evaluate two techniques that currently lack strong evidence. However, in doing so, we are contributing to new knowledge in the field of the recovery of musculoskeletal injuries. Second, the role of invasive techniques will be determined by comparing the effects between these techniques and a control group. The reliability of data is ensured, as both patients and the assessor will be blinded. Third, a sub-analysis with US will be performed to investigate changes in the presence of calcifications, cortical irregularities, neovascularization, thickness, eco-intensity, eco-variation and eco-texture of the patellar tendon.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

The findings obtained may help advance the treatment of this injury by identifying the most effective treatment protocol and to avoid the associated consequences, such as the prevention of relapses and reducing the potential impact on the musculoskeletal system.

REFERENCES

1. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. Journal of orthopaedic surgery and research. 2008;3:18.
2. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of Jumper's Knee Among Nonelite Athletes From Different Sports A Cross-Sectional Survey. American Journal of Sports Medicine. 2011;39(9):1984-8.
3. Stenroth L, Sefa S, Arokoski J, Toyras J. Does Magnetic Resonance Imaging Provide Superior Reliability for Achilles and Patellar Tendon Cross-Sectional Area Measurements Compared with Ultrasound Imaging? Ultrasound Med Biol. 2019;45(12):3186-98.
4. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A Systematic Review of the Use of Platelet-Rich Plasma in Sports Medicine as a New Treatment for Tendon and Ligament Injuries. Clinical Journal of Sport Medicine. 2011;21(4):344-52.
5. Andres BM, Murrell GAC. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clinical Orthopaedics and Related Research. 2008;466(7):1539-54.
6. Larsson MEH, Kall I, Nilsson-Helander K. Treatment of patellar tendinopathy-a systematic review of randomized controlled trials. Knee Surgery Sports Traumatology Arthroscopy. 2012;20(8):1632-46.
7. Kongsgaard M, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scandinavian Journal of Medicine & Science in Sports. 2009;19(6):790-802.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

8. Murtaugh B, Ihm JM. Eccentric Training for the Treatment of Tendinopathies. Current Sports Medicine Reports. 2013;12(3):175-82.

9. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. British Journal of Sports Medicine. 2005;39(2):102-5.

10. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symptomatic shoulder impingement or lateral epicondylar tendinopathy: A systematic review. J Sci Med Sport. 2016;19(6):438-53.

11. James SLJ, Ali K, Pocock C, Robertson C, Walter J, Bell J, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine. 2007;41(8):518-21.

12. Abat F DW, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibañez JM. Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up. Muscles Ligaments Tendons J. 2014;14(4):188-93.

13. Valera Garrido F, Minaya Muñoz F, JM SI. Effectiveness of electrolysis percutaneous intratisular (EPI®) in chronic insertional patellar tendinopathy. Trauma Fund MAPFRE. 2010;21(4):227-36.

14. Sánchez-Ibáñez J, Alves R, Polidori F, Valera F, Minaya F, Valles-Martí S, et al. Effectiveness of ultrasound-guided percutaneous electrolysis intratendon (EPI) in the treatment of insertional patellar tendinopathy in soccer players. Br J Sports Med. 2013;47(e2).

15. Zwerver J, Verhagen E, Hartgens F, van den Akker-Scheek I, Diercks RL. The TOPGAME-study: effectiveness of extracorporeal shockwave therapy in jumping athletes with patellar tendinopathy. Design of a randomised controlled trial. Bmc Musculoskeletal Disorders. 2010;11:6.

16. Riggin CN, Chen M, Gordon JA, Schultz SM, Soslowsky LJ, Khoury V. Ultrasound-Guided Dry Needling of the Healthy Rat Supraspinatus Tendon Elicits Early Healing Without Causing Permanent Damage. J Orthop Res. 2019;37(9):2035-42.

17. Krey D, Borchers J, McCamey K. Tendon needling for treatment of tendinopathy: A systematic review. Physician and Sportsmedicine. 2015;43(1):80-6.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

18. Abat F, Valles S-L, Gelber P-E, Polidori F, Jorda A, Garcia-Herreros S, et al. An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI technique. BMC sports science, medicine and rehabilitation. 2015;7:7-.

19. Valera-Garrido, F, Minaya-Muñoz, F, Sánchez-Ibáñez, JM. Comparison of the acute inflammatory response and proliferation of dry needling and electrolysis percutaneous intratissue (epi) in healthy rat Achilles tendons. Br J Sports Med. 2013;47(9):e2-e2.

20. Alfredson H, Pietila T, Jonsson P, Lorentzon P. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. American Journal of Sports Medicine. 1998;26(3):360-6.

21. Silbernagel KG, Crossley KM. A Proposed Return-to-Sport Program for Patients With Midportion Achilles Tendinopathy: Rationale and Implementation. J Orthop Sports Phys Ther. 2015;45(11):876-86.

22. Padrón-Benítez, A, Rojas-Mederos, S. A comparative study between low and high intensity percutaneous needle electrolysis in patients with patellar tendinopathy: a structural and functional analysis. J Invasive Tech Phys Ther. 2016;1(1):10-17.

23. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural Adaptation of VISA-P Score for Patellar Tendinopathy in Spanish Population. Journal of Orthopaedic & Sports Physical Therapy. 2011;41(8):581-91.

24. Alonso J, Prieto L, Anto JM. The spanish version of the SF-36 health survey- A measure of clinical outcomes. Medicina Clinica. 1995;104(20):771-6.

25. Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights into imaging. 2010;1(3):99-141.

26. Rodriguez-Rosell D, Mora-Custodio R, Franco-Marquez F, Yanez-Garcia JM, Gonzalez-Badillo JJ. Traditional vs. Sport-Specific Vertical Jump Tests: Reliability, Validity, and Relationship With the Legs Strength and Sprint Performance in Adult and Teen Soccer and Basketball Players. J Strength Cond Res. 2017;31(1):196-206.

27. Helland C, Bojsen-Moller J, Raastad T, Seynnes OR, Moltubakk MM, Jakobsen V, et al. Mechanical properties of the patellar tendon in elite volleyball players with and without patellar tendinopathy. Br J Sports Med. 2013;47(13):862-8.

28. Gual G, Fort-Vanmeerhaeghe A, Romero-Rodriguez D, Tesch PA. Effects of In-Season Inertial Resistance Training With Eccentric Overload in a Sports Population at Risk for Patellar Tendinopathy. J Strength Cond Res. 2016;30(7):1834-42.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

29. Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.

30. Figueroa D, Figueroa F, Calvo R. Patellar Tendinopathy: Diagnosis and Treatment. J Am Acad Orthop Surg. 2016;24(12):e184-e92.

31. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports - A cross-sectional study. American Journal of Sports Medicine. 2005;33(4):561-7.

32. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. British Journal of Sports Medicine. 2007;41(4):217-23.

33. Abat F, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibanez JM. Clinical results after ultrasound-guided intratissue percutaneous electrolysis (EPIA (R)) and eccentric exercise in the treatment of patellar tendinopathy. Knee Surgery Sports Traumatology Arthroscopy. 2015;23(4):1046-52.

34. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. American Journal of Sports Medicine. 2014;42(3):610-8.

35. Warden SJ, Kiss ZS, Malara FA, Ooi ABT, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. American Journal of Sports Medicine. 2007;35(3):427-36.

36. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural adaptation of VISA-P score for patellar tendinopathy in Spanish population. J Orthop Sports Phys Ther. 2011;41(8):581-91.

37. Andriolo L, Altamura SA, Reale D, Candrian C, Zaffagnini S, Filardo G. Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option: A Systematic Review and Meta-analysis. Am J Sports Med. 2019;47(4):1001-18.

38. de Vries A, Zwerver J, Diercks R, Tak I, van Berkel S, van Cingel R, et al. Effect of patellar strap and sports tape on pain in patellar tendinopathy: A randomized controlled trial. Scand J Med Sci Sports. 2016;26(10):1217-24.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

39. Markovic G, Dizdar D, Jukic I, Cardinale M. Reliability and factorial validity of squat and countermovement jump tests. J Strength Cond Res. 2004;18(3):551-5.

AUTHOR'S CONTRIBUTIONS

MPL, EMG and PH conceived of the idea, and developed the intervention. MPL and PH wrote the article. MPL, MO, RMG, AVB, ZA, YH and PH developed the design of the trial. MO were involved in development of the statistical analysis of the trial and contributed to the content of the article. AVB contributed to the design and writing of the jump test protocol. All authors have read and approved the final manuscript.

FUNDING STATEMENT

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTEREST STATEMENT

The authors declare that they have no competing interests.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLES

Table 1. Jump test's protocol.

JUMP TEST PROTOCOL	
5-minute warm-up consisting of steady jogging on a treadmill	
Dynamic Stretches lasting 5 minutes, as instructed by the physical therapist	Psoas Quadriceps Gluteus maximus Gastrocnemius Hamstring muscles
Three jump tests are performed - 3 jumps off the ground for 3 times for the patient to become familiar with the tests - The subject is placed on the platform and asked to perform each test 3 times, with 60 seconds rest between the different tests	Abalakov test Countermovement jump test Squat jump
The highest jump is selected for the study	

FIGURES

Figure 1. Flow diagram. Randomized controlled trial design.

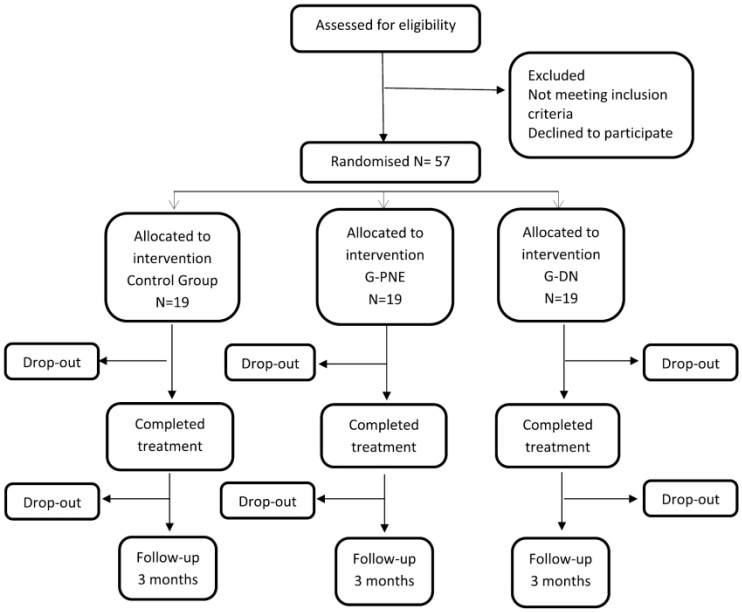
G-PNE: Percutaneous Needle Electrolysis Group. G-DN: Dry Needle Group.

Figure 2. Schedule for the enrolment and intervention.

Schedule for enrolment and intervention per cluster. -t1: baseline; t1–t2: intervention period; t2: 8 weeks after baseline; t3: 10 weeks after baseline; t4: 3 months after baseline. G-PNE: Percutaneous Needle Electrolysis Group; G-DN: Dry Needle Group; US: ultrasound.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure 1. Flow diagram. Randomized controlled trial design.



210x297mm (300 x 300 DPI)

Figure 2. Schedule for enrolment and intervention.

	Enrolment	Allocation	Close-out			
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control group			⟷			
G-PNE			⟷			
G-DN			⟷			
ASSESSMENTS:						
Baseline demographic information	X					
VISA-P	X		X		X	X
VAS			X		X	X
SF-36			X		X	X
Tendon structure US			X		X	X
Jump test			X		X	X

215x279mm (300 x 300 DPI)

DOCUMENTO DE INFORMACIÓN AL PACIENTE

Fecha:

Título del proyecto: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Investigador principal:

Doña: Mª Pilar López Royo

Este estudio se basa en el estudio comparativo de tres tratamientos que utilizan distintas técnicas de fisioterapia invasiva junto con un programa de ejercicio excéntrico para el tratamiento de la tendinopatía rotuliana. Por medio del tratamiento se produce una disminución del dolor asociado a esta patología y un aumento de la fuerza de la pierna, lo que a su vez hace que mejore la funcionalidad en las actividades de la vida diaria y mejore la calidad de vida.

PROCESO DE SELECCIÓN DE PACIENTES

Criterios de inclusión:

- Edad comprendida entre 18 y 40 años.
- Practicar cualquier deporte de forma habitual.
- Pacientes con diagnóstico médico de tendinopatía rotuliana crónica con un mínimo de 3 meses de evolución y con sintomatología.
- Dolor a la palpación del tendón en el polo inferior de la rótula y durante el entrenamiento o competición.
- Puntuación del cuestionario VISA-P menor de 80 (el resultado obtenido de rellenar el cuestionario tiene que ser menor de 80 puntos de los 100 posibles para poder participar en el estudio).

Criterios de exclusión:

- Paciente operado de la rodilla afectada en los últimos 6 meses.
- Infiltraciones en la rodilla afectada en los últimos 3 meses.
- Paciente que ha recibido tratamiento farmacológico o fisioterápico en las últimas 48 horas o durante el estudio.
- Patología con menos de 3 meses de evolución.
- Presentar tendinopatía rotuliana bilateral.
- Puntuación del cuestionario VISA-p mayor o igual de 80 (el resultado obtenido de rellenar el cuestionario no puede ser igual o superar los 80 puntos de los 100 posibles, sino no podrá participar en el estudio).
- Imposibilidad para aplicar alguna de las técnicas de tratamiento o valoración por

For peer review only

contraindicación absoluta o relativa.

PROCEDIMIENTO

El tratamiento consiste en realizar un protocolo de ejercicios excéntricos de cuádriceps que realizará en casa de forma diaria, y que serán revisados con el fisioterapeuta para valorar su correcta realización. Se complementará el tratamiento con la aplicación de una técnica de punción según el protocolo de tratamiento propuesto de forma totalmente **aleatorizada** y según los criterios diagnósticos específicos de la misma, siguiendo las indicaciones, criterios de aplicación y criterios diagnósticos.

Son técnicas de punción cuyo objetivo es producir una respuesta inflamatoria aguda que active los mecanismos fisiológicos de regeneración del tejido y mejorar el dolor y la funcionalidad en la articulación de la rodilla, se realiza con agujas de punción seca, similares a las agujas de acupuntura y sin infiltrar ningún tipo de sustancia dentro del organismo.

Los registros serán realizados en el Espacio de Valoración Funcional de la Universidad San Jorge, en la Facultad de Ciencias de la Salud, Edificio III.Se pondrá a su disposición la posibilidad de utilizar el autobús que utiliza el personal y alumnado de la universidad (en el horario que éste esté disponible).Las fechas y horarios serán convenidas con cada participante en función de su disponibilidad y la de los investigadores, buscando la conformidad de todos.La duración aproximada del estudio para cada paciente será de 30 minutos, aunque este horario podrá variar en función de los acontecimientos.

Será recibido por los miembros del equipo de investigación y una vez allí, se le realizará un primer análisis fisioterápico, rellenará una encuesta, una escala analógica visual (EVA) del dolor y el cuestionario Visa-p en el que se valorará la funcionalidad de la rodilla.

Tras éste primer registro se le colocará un marcador pasivo en el pantalón. Se le pedirá que realice el siguiente protocolo:

- Calentamiento de 5 minutos en cinta a ritmo constante.
- Estiramientos dinámicos de psoas, cuádriceps, glúteo, gastrocnemios, isquiotibiales durante 5 minutos instruidos por el fisioterapeuta.
- Realización de los 3 saltos fuera de la plataforma durante 3 veces para que se familiarice con los tests.
- En la plataforma de fuerzas realizará 3 test de salto: el test de Abalakov (ABK), el test de salto con contramovimiento (CMJ) y el squatjump (SJ).

Se colocará en la plataforma y realizará 3 saltos de cada uno de los test con una separación entre ellos de 60 segundos.

Se valora el tendón por ecografía, y se recogen datos por medio de personal adiestrado y se envía

For peer review only

a personal especialista en radiodiagnóstico.
Tras los registros de los saltos se dará por finalizada la valoración.

Tras la 1ª valoración, se realizará una división en tres grupos de los pacientes de forma aleatorizada.
Se le realizará el protocolo de tratamiento de fisioterapia invasivaque le haya correspondido. Realizará una sesión del tratamiento cada 14 días, y se realizará la 2º valoración 1 semana más tarde de la 4º sesión de punción para valorar los cambios que se hayan producido tras el tratamiento, repitiéndose de nuevo el proceso de recogida de datos realizado al inicio del estudio. Se realizará un seguimiento a los tres meses de la valoración post-tratamiento para valorar la eficacia de la técnica a largo plazo del tratamiento.
El procedimiento se realizará guiado ecográficamente para asegurar la especificidad de aplicación sobre la zona relevante de tratamiento y garantizar la seguridad de la técnica. Se hace posterior a esta intervención una serie de ejercicios excéntricos de cuádriceps. El tratamiento se realizará durante 4 sesiones (a razón de una sesión cada 14 días).

RIESGOS

La aplicación de las técnicas de punción utilizadas no han demostrado tener ningún efecto secundario hasta la fecha, aunque el paciente puede experimentar dolordurante y tras la punción, generalmente de uno o dos días de duración.

RESPONSABILIDADES DEL PARTICIPANTE

La información que usted posea sobre su estado de salud o sobre sensaciones previas anormales al realizarle una punción, puede afectar la seguridad o el valor de estas pruebas. La rápida comunicación por su parte de las sensaciones que experimenta al realizar esta prueba es también de gran importancia. Usted es responsable de revelar esa información al personal de la prueba cuando se le pregunte.

PREGUNTAS

Le animamos a que haga cualquier pregunta sobre los procedimientos seguidos o sus resultados en la prueba. Si tiene alguna preocupación o pregunta, por favor pídanos más información, para ello le dejamos un correo electrónico mapilr86@hotmail.com y un número de teléfono móvil: 616102365.

LIBERTAD PARA DAR EL CONSENTIMIENTO

Usted participa en el estudio de manera voluntaria, pudiendo abandonarlo en el momento que considere oportuno, sin que esto conlleve ninguna repercusión negativa para usted.

Los datos obtenidos en el estudio serán confidenciales y únicamente se hará uso de ellos

For Peer review only

para el cumplimiento de los objetivos planteados en la investigación. No se cederán estos datos a terceros sin el consentimiento expreso de los sujetos participantes a quienes pertenezcan los datos.

En esta investigación se garantizará el anonimato de los sujetos que aportan los datos, estableciendo un código disociado para identificarlos que sólo será conocido por los responsables de la realización del trabajo de campo.

Fdo: Mª Pilar López Royo

For peer review only

MODELO DE CONSENTIMIENTO INFORMADO

Título del PROYECTO: "ESTUDIO COMPARATIVO ENTRE 3 TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Doña: Mª Pilar López Royo (mapilr86@hotmail.com)
Departamento de Fisiatría y Enfermería
UNIVERSIDAD DE ZARAGOZA

Yo, ... (nombre y apellidos del participante)

He recibido suficiente información en relación con el proyecto, he leído la hoja de información que se me ha entregado y he podido hacer preguntas sobre el proyecto, recibiendo respuestas satisfactorias.

Entiendo que la participación es voluntaria y que puedo abandonar el proyecto:

. Cuando lo desee
. Sin tener que dar explicaciones
. Sin que esto repercuta en mis cuidados médicos

He sido claramente informado de forma clara y precisa del tratado que recibirán mis datos personales que se contienen en este proyecto, sabiendo que los datos serán tratados y custodiados bajo mi intimidad y a la vigente normativa de la protección de datos, y que sobre estos datos me asisten los derechos de rectificación, acceso y oposición comunicándolo al investigador principal que figura en este consentimiento.

Declaro que presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

Así pues, acepto que las muestras derivadas de este proyecto puedan ser utilizadas en futuras investigaciones siempre y cuando están relacionadas con ésta.

Por lo tanto, doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es

For peer review only

revocable.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del proyecto al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Consentimiento informado estudio_____

Versión_____, fecha_____

For peer review only

Appendix 2. Checklist SPIRIT

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1-3
	2b	All items from the World Health Organization Trial Registration Data Set	2-3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	22
	5b	Name and contact information for the trial sponsor	22
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-5
	6b	Explanation for choice of comparators	3-5
Objectives	7	Specific objectives or hypotheses	5-6

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12-13
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12-13

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	-
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	-
	31b	Authorship eligibility guidelines and any intended use of professional writers	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

8

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034304.R3
Article Type:	Protocol
Date Submitted by the Author:	17-Jan-2020
Complete List of Authors:	Lopez-Royo, Maria Pilar; Universidad San Jorge Facultad de Ciencias de la Salud; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Gómez-Trullén, Eva Maria; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Ortiz-Lucas, Maria; Universidad San Jorge Facultad de Ciencias de la Salud Galán-Diaz, Rita Maria; Universidad San Jorge Facultad de Ciencias de la Salud Bataller-Cervero, Ana Vanessa; Universidad San Jorge Facultad de Ciencias de la Salud Al-Boloushi, Zaid; Universidad de Zaragoza Facultad de Ciencias, Facultad de Ciencias de la Salud y del Deporte; Kuwait Ministry of Health Hamam-Alcober, Yasmina; Universidad San Jorge Facultad de Ciencias de la Salud, Fisioterapia Herrero, Pablo; Universidad San Jorge Facultad de Ciencias de la Salud
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Sports and exercise medicine, Pathology
Keywords:	Eccentric Exercise, Tendinopathy, Percutaneous Needle Electrolysis, Dry Needling

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

López-Royo MP[a,b], Gómez-Trullén EM[b], Ortíz-Lucas M[a], Galán-Díaz RM[a], Bataller-Cervero AV[a], Al-Boloushi Z[b,c], Hamam-Alcober Y[a], Herrero P[a *]

AFFILIATIONS

A. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, Spain.

B. Universidad de Zaragoza. Facultad de Ciencias de la Salud y del Deporte. Dpto. de Fisiatría y Enfermería. C/ Domingo Miral s/n, 50009 - Zaragoza, Spain.

A. Ministry of Health, State of Kuwait. Jamal Abdulnasser Street, Al Solaibeykhat Area 5. Kuwait City. Safat 13001.

***CORRESPONDENCE TO:**

Dr. Pablo Herrero. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov A23, Km 299, 50830 Villanueva de Gállego, Zaragoza, Spain. Tel.: (+34) 976 060 100 Fax: 976 077 581. Email: pherrero@usj.es

ADDITIONAL AUTHOR INFORMATION

Maria Pilar López Royo. Emails: mplopez@usj.es

Eva María Gómez Trullén. Email: evagomez@unizar.es

María Ortíz Lucas. Email: mariaortizlucas@gmail.com

Rita María Galán Díaz. Email: rmgalan@usj.es

Ana Vanessa Bataller-Cervero. Email: avbataller@usj.es

For peer review only

Yasmina Hamam-Alcober. Email: yhamam@usj.es

Zaid AL-boloushi. Email: boloushi@me.com

WORD COUNT: 3967 words.

ABSTRACT

Introduction: Patellar tendinopathy is a degenerative disease of the patellar tendon, which affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The aim of this study is to compare the effectiveness of three therapies in order to determine the most effective treatment protocol of patellar tendinopathy.

Methods and analysis: This study is a randomized controlled trial with blinded participants. Measurements will be carried out by a specially trained blinded assessor. A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups. Eligible participants will be randomly allocated to receive either: (a) treatment group with Percutaneous Needle Electrolysis, (b) treatment group with Dry Needling or (c) treatment group with placebo needling. In addition, all groups will perform eccentric exercise. Functionality and muscle strength parameters, pain, ultrasound appearances and patient perceived quality of life shall be evaluated using the VISA-p, jump test, VAS, US images and SF-36, respectively. Participants will be assessed at baseline, at 10 weeks and at 22 weeks after baseline. The expected findings will allow us to advance in the treatment of this injury, as they will help determine whether a needling intervention has additional effects on an eccentric exercise program and whether any of the needling modalities is more effective than the other.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Ethics and dissemination: This protocol has been approved by the Ethics Committee of Aragon (Nº PI15/0017). The trial will be conducted in accordance with the Declaration of Helsinki.

Trial Registration Number: NCT02498795.

Strengths and limitations of this study

- This randomized clinical trial will report the effects on functionality and pain of three different treatment interventions in both the short and long term.
- The double-blinded and placebo-control design will enhance objectivity and help reduce bias.
- The effects of two minimally invasive treatments in physical therapy will be compared for the first time in patellar tendinopathy.

INTRODUCTION

Patellar tendinopathy (PT), also known as jumper´s knee, is a degenerative condition affecting the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella. This disorder has similar histologic findings to other tendon disorders characterized by an increased thickness of the tendon and changes in vascularity, and cellularity, with incompletely healed tendon micro-ruptures and disturbed collagen distribution(1).

This degenerative condition affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The overall prevalence of PT in non-elite players is 8.5%, although this figure increases in sports that place high demands on the patellar ligament, increasing up to 14.2% in volleyball athletes. Among elite volleyball and basketball players, a prevalence of 45% and 32%, respectively, has been

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

reported. In addition, jumper's knee is almost twice as common among male non-elite athletes when compared with female athletes(2).

The diagnosis is typically based on the clinical history and symptomatic findings. Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) can be used for the assessment of the patellar tendon to clinically confirm the diagnosis(3).

Treatments used for PT fall into two major groups. The first group comprises medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection(4) and autologous growth factors(5). The second group consists of physical therapies, including both conservative and invasive approaches (needling techniques).

Conservative therapies are generally accepted as the first line of approach for managing PT(6, 7), considering exercise as the gold standard of treatment, either eccentric exercise (EE) or high slow resistance training programs. Both have demonstrated similar effectiveness in the treatment of PT(6-8). In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including PT, with a greater likelihood of clinical improvement when performed on a declined surface(6, 8, 9). In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc.(10).

Physical therapy approaches for PT continue to evolve and a number of innovative treatment options are now available, such as dry needling (DN)(11), electrotherapeutic invasive modalities (e.g. electrolysis)(12-14) and extracorporeal shockwave (ECSW) therapy(15). Recently, research has focused on regenerative therapies with high expectations of success because some of these techniques seem to achieve a rapid

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

regeneration of the injured tendon(11, 12, 16). However, evidence-based regenerative therapies are limited and there is no agreement to date regarding which of these is the most effective(17). DN consists of the insertion of a needle (filiform and solid, non-beveled) with the aim of provoking a local injury leading to an inflammatory response and the subsequent regeneration of the injured area in approximately one week. A study performed by Abat et al. reported that DN induced histological and mechanical changes in rat Achilles tendons at week one, with changes persisting at week four(18). Percutaneous Needle Electrolysis (PNE) is an ultrasound-guided technique used by physiotherapists consisting of causing localized lysis in the damaged and/or degenerated tissue by means of a galvanic current transmitted through an acupuncture needle. This technique may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area in rats(18). James et al.(11) carried out a cohort study in humans analyzing one group treated with DN and another treated with autologous blood injections. In both cases, they found improvements compared to the baseline measurements. However, this study failed to find differences between the different treatments, concluding that both techniques were equally effective. In relation to PNE, a former study(14) analyzed the treatment effect of electrolysis applied once a week in a group of patients without any control or comparative group, reporting that patients obtained statistically and clinically significant improvements compared to baseline measurements.

From a biological point of view, it seems reasonable to hypothesize that a patient will obtain benefits thanks to the mechanical effects provided by the needle(16), and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle(19).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Therefore, the aim of this study is to determine the additional effect of two interventions combined with EE and compare which one is the most effective at short and long-term follow-up for patients with PT.

METHODS AND ANALYSIS

Study design

The trial is designed as a randomized, controlled, participant, investigator and outcomes assessor blinded, experimental study, aimed at comparing three different physiotherapy protocols applied in three intervention groups of PT patients. Randomization will be performed as block randomization with a 1:1:1 allocation.

This protocol follows the standards of the Helsinki Convention of good clinical practices. The Ethics Committee of Aragon (CEICA) has evaluated the project and has given its favorable opinion and support, Nº PI15/0017 (Appendix 1).

The study has been carried out following the SPIRIT statement for clinical trial protocol and a SPIRIT Checklist has been included (Appendix 2).

Study setting

After reviewing the literature and observing the high incidence of this pathology in amateur young adult athletes who perform sports and more specifically, jump sports, patient recruitment has been performed in basketball, football, volleyball, CrossFit, and handball sports clubs, together with running clubs and several gyms located in the city. A decision was made to conduct the study in X, where the university is located, as well as the laboratory to be used for assessments and treatments.

The assessments will be conducted at the Motion Analysis laboratory of X, and the treatment will be performed at two different sites depending on the availability of both spaces and of schedules. Nonetheless, the same material will always be used.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants

Inclusion criteria

Participants eligible for inclusion in this study must meet the following criteria: 1. History of PT and anterior knee pain located on the inferior pole of the patella for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the superior insertion of the patellar tendon; 4. A score below 80 on the VISA-p questionnaire.

Exclusion criteria

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Corticosteroid injection in the patellar tendon within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs); 6. Any other concomitant treatment for PT.

Methodology

In the first session, all participants will be instructed on how to perform a daily home program of EE. This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol(20) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale(21), and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

For the interventions, the participants will be placed in a supine position with a pillow under the knee (approximately 20º of knee flexion). The area will be cleansed with an antiseptic solution (70% Propan-2-ol, Skin-des). An ultrasound probe cover will be used during the intervention for infectious control. To determine the relevant treatment area, two factors will be considered: 1) Palpation of the areas exhibiting higher sensitivity and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

that reproduce the patient's symptoms; 2) Tendon areas showing degenerative changes assessed under ultrasound. Each group will receive a total of four sessions distributed throughout eight weeks of treatment, once every two weeks.

DN intervention combined with EE (DN-G) and PNE intervention combined with EE (PNE-G)

Specific DN needles will be used during needling treatments, (Agu-punt, Spain). Considering the thickness of the tendon and the approach, we shall use needles measuring 0.25 x 25 mm. The procedure will be guided by US to ensure the specificity of application on the injured area and to guarantee that the procedure is safe for the patient. The DN needle will reach the relevant treatment area (areas with degenerative PT changes). Each session will consist of three needle insertions lasting three seconds each. In PNE-G applications, an intensity of 3 mA galvanic current will be used during the three seconds that the procedure lasts(19). The dose of 3 mA has demonstrated to be as effective as 6 mA in the treatment of tendinopathy injuries in animal models(18,19). In humans, a study conducted in 2016 showed that a dose of 3 mA in PT generated structural changes compatible with tendon regeneration, together with improvement of functionality and pain (22). In contrast, the same study found that lower doses were effective only for the improvement of functionality and pain. As a result, a 3 mA dose was selected for this study.

Control group (CG)

A sham needle will be placed upon the treatment zone, simulating the same procedure as the rest of participants enrolled in the other groups. The needle will be placed in a specific holder and will be manipulated during the intervention to simulate a real treatment. This

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

holder will have a cover over the bottom part of the same in order to avoid the needle contacting the skin.

Outcomes

Baseline data

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and previous rehabilitation treatments and infiltrations received. A blinded observer will assess all participants at baseline, 10 weeks and 22 weeks after baseline. Participants will be asked to inform the researchers if there were any changes in medication or if they are receiving any other treatment or infiltration during the study.

Primary outcome measure

Participants will complete the VISA-p questionnaire at baseline. The VISA-p questionnaire is designed to measure the severity of PT(23). The VISA-p score is the primary outcome variable. This scale consists of eight questions, the first six questions of which employ an analogical visual scale in order to assign a score of 0 to 10, where 10 represents the optimum state, for the purpose of quantifying pain and function in different activities, whereas the last two questions assess the level of functionality and ability to perform physical activity.

Secondary outcome measure

During the first evaluation, participants will complete the Visual Analog Scale (VAS), considering the level of pain they feel while practicing their sport's activity. Participants will be explained that a score of 0 indicates the absence of pain whereas a score of 10 represents the maximum tolerable pain. They will also complete a questionnaire to assess their quality of life (SF-36)(24).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

In order to assess tendon structure, an US evaluation using ultrasound equipment (Logic S7 Expert, General Electric Healthcare) and a linear probe (MLG-15 5–10 MHz) will be used. The ultrasonographic assessment protocol will be carried out according to the Musculoskeletal Ultrasound Technical Guidelines: Knee, defined by the European Society of Musculoskeletal Radiology(25). The ultrasonographic assessment will consist of a longitudinal sequence from the tendon origin to the insertion and transverse sections on the pole of the patella, the tendon body and its insertion on the tibial tuberosity, with the subject in supine position, with 20º knee flexion, and a pillow under the knee. The presence of degenerative signs compatible with the medical diagnosis of PT (thickness of the tendon, hypoechoic areas, irregularities affecting the cortical bone, calcifications) that could be relevant for the selection of the target area will also be assessed. In addition, CD-US assessment will be carried out to detect the presence of hypervascularization, with the subject in supine position and with the knee relaxed in full extension, in order to obtain further information to specifically define the target area.

Upon completion of the evaluation, a jump test will be carried out, measured with a force platform (FP4060-10-2000, Bertec Corporation). In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table 1)(26-28). The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed. The Abalakov jump will be performed with the subject standing in an upright

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

position with a full arm swing. A rapid downward movement will be immediately followed by a rapid upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, a Squat Jump will be performed with 90 degrees of flexion of the knee.

Participant timeline

The study design will be a double-blind randomized controlled trial. The flow chart of the trial is shown in Figure 1 and the check list SPIRIT schedule is shown in Figure 2.

'Patient and Public Involvement'

Patients with PT were not involved in setting the research question or the outcome measures, however the concept of patient involvement translated to the execution phases of the research. Patients and their families were central to the dissemination of the information, which helped to recruit study participants. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Sample size

Regarding the sample size, a calculation of statistical power was made prior to the study. Accepting an alpha risk of 0.05 and a beta risk in a bilateral contrast, 19 subjects are needed in every treatment group to detect a difference equal or superior to 15 points on the VISA-p scale and assuming a standard deviation of 15 points(29). The estimated rate of loss to follow-up is 20%.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media.

The interested subjects will receive an e-mail explaining the inclusion and exclusion criteria, as well as the purpose of the study. If they meet the defined criteria, they will be invited to send us their medical diagnosis.

Recruitment

Participants will be recruited from sports clubs by the physiotherapist or the coach. Contact has been made with various orthopedists who will collaborate with recruitment, so that when they establish a diagnosis of this pathology in their examination room they can refer us to the patients for their recruitment to the study.

Allocation

Participants will be randomly assigned to either CG or DN-G or PNE-G with a 1:1:1 allocation using an opaque envelope, with a block size of fifteen participants (5 for each group).

Sealed opaque randomization envelopes with a study-specific participant number will be supplied by an external statistician. A colleague not involved in the research study will take the sealed opaque numbered envelopes in order, by number, and deliver the correct envelope to the treating physical therapist. The envelope will contain a piece of paper, which will be labelled with the same participant specific number, plus the group assignment (PNE-G, DN-G or CG).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants who fulfill the inclusion criteria will receive the standardized oral and written information, and, once they grant their consent to take part in the trial, they will be randomized into the three groups.

Blinding

Assessments regarding clinical recovery will be conducted by an assessor blinded to treatment allocation. Due to the nature of the intervention, participants can be blinded to allocation. Patients will be explained that they are going to receive a needling treatment, that it may be slightly painful, and that if at any time they are unable to tolerate the pain they must inform the researcher to stop the intervention. In order to blind patients, all the interventions were made with the ultrasound and the PNE device connected to simulate the same intervention in all groups. In contrast, the physiotherapist performing the intervention cannot be blinded, however he/she will be instructed not to disclose the allocation status of the participant at any time or during the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyze data without having access to information about the allocation.

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

Data collection methods

For the data collection, an oral questionnaire will be used containing questions targeted at collecting baseline data and information concerning the pathology.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Different questionnaires and assessment scales (VISA-p, VAS, SF-36) in Spanish will be given to each participant in paper when they attend the assessment, and they will be granted sufficient time to complete the same.

Data management and statistical analysis

In this study, all data will be entered electronically in the assessment room.

Original scales and questionnaires will be entered and kept on a locked file at the participating site.

Participant files are to be stored in numerical order and stored in a secure and accessible place and manner. Participant files will be maintained in storage for a period of 2 years after completion of the study.

The statistical analysis will be carried out by an intention-to-treat analysis. Variables will be described in number (percentage) and average (standard deviation) or median (interquartile range) attending to their distribution. Quantitative variables will be analyzed with the Shapiro Wilk test in order to confirm their distribution and to determine correct statistical tests according to these results.

Outcomes will be analyzed using mixed linear and logistic regression models considering participants as a random effect and group of treatment as fixed factors. Baseline characteristics will be introduced in the model as covariance. Numbers needed to treat index will also be calculated. The primary aim of the analysis will be to calculate the difference obtained in the VISA-p score after the intervention (final measurement - initial measurement). Finally, the magnitude of the effect of the result will be calculated and therefore its clinical importance, by means of the following formula:

$$r=\sqrt{\frac{F(1,dfR)}{F(1,dfR)+dfR}}.$$

The significance level set for all the analysis will be $p \leq 0.05$.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ETHICS AND DISEMINATION

The study design, procedures and informed consent procedure were approved and consequently the study will be carried out in compliance with the Helsinki Declaration of Human Rights. All participants will have to provide written Spanish informed consent. Appendix 1.

The results for this trial will be published in peer-reviewed international journals or otherwise made publicly available and will be presented at national and international conferences and symposiums irrespective of the outcomes.

Any modifications to the protocol, which may impact the study procedures, potential patient benefits or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendments will be approved by the Ethics Committee prior to implementation and notified to the health authorities in accordance with local regulations.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored identified by code number. All local databases will be secured with password-protected access systems.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

DISCUSSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study seeks to investigate the effects of physiotherapy needling techniques on pain, functionality and quality of life in PT.

PT is a common cause of knee pain in cases of degeneration of the patellar tendon. Among the causes of PT, extrinsic factors (e.g., patellar tendon loading with exercise) and intrinsic factors (e.g., malalignment, high patella, imbalances) have been proposed(30). Traditionally, the focus has been on quadriceps strengthening exercises and many reviews have shown that the effect of the treatment could be estimated to give the patients a 50-70% change of improvement on pain and functionality(6, 31, 32).

Regarding needling treatment, previous studies have shown a great improvement in PT using PNE in combination with EE, with all patients reporting an improvement at least one month after treatment(12-14, 18). This is an improvement compared to the minimum three months needed to improve symptoms by applying other conventional techniques (pharmacological and biological treatments, cold/heat techniques, shock waves, etc.) Additionally, in a long-term study conducted in 2013, this technique was shown to improve symptoms quickly and steadily for at least 10 years(33). These findings demonstrate that this technique ensures that patients remain pain-free for a long period. Furthermore, we were only able to find four articles(12-14, 18) addressing the application of PNE for the recovery of PT, however, none of the articles studied were RCTs, which entail limited evidence of the effectiveness of this technique.

In addition, there are no standardized protocols for the application of PNE, which explains the great variability in the number of sessions and application time based on the literature. Therefore, this study aims to facilitate clinical practice and combine the available methodology criteria in the application of this promising technique.

Regarding DN, the literature shows many similarities with PNE, since there is only one RCT that compares functionality improvements among patients who have received PRP.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study reflected that in the short term PRP had better results for pain and functionality, however, DN was more effective than PRP after six months(34).

For the application of both needling techniques, US-guidance is normally used to be able to observe firstly the presentation of the tendon, and later to observe the needle and enable a much more specific treatment approach. However, US has disadvantages including its operator dependence and the limited ability to rule out intra-articular disease. The sensitivity and specificity of ultrasonography for patellar tendinopathy is between 58% and 94%, respectively(35).

Moreover, functionality of the tendon is usually measured with the VISA-p(36,37), whereas jump tests (representing a similar action to that performed in subject's daily sports) are only evaluated in a few papers(27,38). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men(39). Thus, we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

This study has several strengths. First, we will evaluate two techniques that currently lack strong evidence. However, in doing so, we are contributing to new knowledge in the field of the recovery of musculoskeletal injuries. Second, the role of invasive techniques will be determined by comparing the effects between these techniques and a control group. The reliability of data is ensured, as both patients and the assessor will be blinded. Third, a sub-analysis with US will be performed to investigate changes in the presence of calcifications, cortical irregularities, neovascularization, thickness, eco-intensity, eco-variation and eco-texture of the patellar tendon.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

The findings obtained may help advance the treatment of this injury by identifying the most effective treatment protocol and to avoid the associated consequences, such as the prevention of relapses and reducing the potential impact on the musculoskeletal system.

REFERENCES

1. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. Journal of orthopaedic surgery and research. 2008;3:18.
2. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of Jumper's Knee Among Nonelite Athletes From Different Sports A Cross-Sectional Survey. American Journal of Sports Medicine. 2011;39(9):1984-8.
3. Stenroth L, Sefa S, Arokoski J, Toyras J. Does Magnetic Resonance Imaging Provide Superior Reliability for Achilles and Patellar Tendon Cross-Sectional Area Measurements Compared with Ultrasound Imaging? Ultrasound Med Biol. 2019;45(12):3186-98.
4. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A Systematic Review of the Use of Platelet-Rich Plasma in Sports Medicine as a New Treatment for Tendon and Ligament Injuries. Clinical Journal of Sport Medicine. 2011;21(4):344-52.
5. Andres BM, Murrell GAC. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clinical Orthopaedics and Related Research. 2008;466(7):1539-54.
6. Larsson MEH, Kall I, Nilsson-Helander K. Treatment of patellar tendinopathy-a systematic review of randomized controlled trials. Knee Surgery Sports Traumatology Arthroscopy. 2012;20(8):1632-46.
7. Kongsgaard M, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scandinavian Journal of Medicine & Science in Sports. 2009;19(6):790-802.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

8. Murtaugh B, Ihm JM. Eccentric Training for the Treatment of Tendinopathies. Current Sports Medicine Reports. 2013;12(3):175-82.

9. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. British Journal of Sports Medicine. 2005;39(2):102-5.

10. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symptomatic shoulder impingement or lateral epicondylar tendinopathy: A systematic review. J Sci Med Sport. 2016;19(6):438-53.

11. James SLJ, Ali K, Pocock C, Robertson C, Walter J, Bell J, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine. 2007;41(8):518-21.

12. Abat F DW, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibañez JM. Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up. Muscles Ligaments Tendons J. 2014;14(4):188-93.

13. Valera Garrido F, Minaya Muñoz F, JM SI. Effectiveness of electrolysis percutaneous intratisular (EPI®) in chronic insertional patellar tendinopathy. Trauma Fund MAPFRE. 2010;21(4):227-36.

14. Sánchez-Ibáñez J, Alves R, Polidori F, Valera F, Minaya F, Valles-Martí S, et al. Effectiveness of ultrasound-guided percutaneous electrolysis intratendon (EPI) in the treatment of insertional patellar tendinopathy in soccer players. Br J Sports Med. 2013;47(e2).

15. Zwerver J, Verhagen E, Hartgens F, van den Akker-Scheek I, Diercks RL. The TOPGAME-study: effectiveness of extracorporeal shockwave therapy in jumping athletes with patellar tendinopathy. Design of a randomised controlled trial. Bmc Musculoskeletal Disorders. 2010;11:6.

16. Riggin CN, Chen M, Gordon JA, Schultz SM, Soslowsky LJ, Khoury V. Ultrasound-Guided Dry Needling of the Healthy Rat Supraspinatus Tendon Elicits Early Healing Without Causing Permanent Damage. J Orthop Res. 2019;37(9):2035-42.

17. Krey D, Borchers J, McCamey K. Tendon needling for treatment of tendinopathy: A systematic review. Physician and Sportsmedicine. 2015;43(1):80-6.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

18. Abat F, Valles S-L, Gelber P-E, Polidori F, Jorda A, Garcia-Herreros S, et al. An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI technique. BMC sports science, medicine and rehabilitation. 2015;7:7-.

19. Valera-Garrido, F, Minaya-Muñoz, F, Sánchez-Ibáñez, JM. Comparison of the acute inflammatory response and proliferation of dry needling and electrolysis percutaneous intratissue (epi) in healthy rat Achilles tendons. Br J Sports Med. 2013;47(9):e2-e2.

20. Alfredson H, Pietila T, Jonsson P, Lorentzon P. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. American Journal of Sports Medicine. 1998;26(3):360-6.

21. Silbernagel KG, Crossley KM. A Proposed Return-to-Sport Program for Patients With Midportion Achilles Tendinopathy: Rationale and Implementation. J Orthop Sports Phys Ther. 2015;45(11):876-86.

22. Padrón-Benítez, A, Rojas-Mederos, S. A comparative study between low and high intensity percutaneous needle electrolysis in patients with patellar tendinopathy: a structural and functional analysis. J Invasive Tech Phys Ther. 2016;1(1):10-17.

23. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural Adaptation of VISA-P Score for Patellar Tendinopathy in Spanish Population. Journal of Orthopaedic & Sports Physical Therapy. 2011;41(8):581-91.

24. Alonso J, Prieto L, Anto JM. The spanish version of the SF-36 health survey- A measure of clinical outcomes. Medicina Clinica. 1995;104(20):771-6.

25. Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights into imaging. 2010;1(3):99-141.

26. Rodriguez-Rosell D, Mora-Custodio R, Franco-Marquez F, Yanez-Garcia JM, Gonzalez-Badillo JJ. Traditional vs. Sport-Specific Vertical Jump Tests: Reliability, Validity, and Relationship With the Legs Strength and Sprint Performance in Adult and Teen Soccer and Basketball Players. J Strength Cond Res. 2017;31(1):196-206.

27. Helland C, Bojsen-Moller J, Raastad T, Seynnes OR, Moltubakk MM, Jakobsen V, et al. Mechanical properties of the patellar tendon in elite volleyball players with and without patellar tendinopathy. Br J Sports Med. 2013;47(13):862-8.

28. Gual G, Fort-Vanmeerhaeghe A, Romero-Rodriguez D, Tesch PA. Effects of In-Season Inertial Resistance Training With Eccentric Overload in a Sports Population at Risk for Patellar Tendinopathy. J Strength Cond Res. 2016;30(7):1834-42.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

29. Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.

30. Figueroa D, Figueroa F, Calvo R. Patellar Tendinopathy: Diagnosis and Treatment. J Am Acad Orthop Surg. 2016;24(12):e184-e92.

31. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports - A cross-sectional study. American Journal of Sports Medicine. 2005;33(4):561-7.

32. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. British Journal of Sports Medicine. 2007;41(4):217-23.

33. Abat F, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibanez JM. Clinical results after ultrasound-guided intratissue percutaneous electrolysis (EPIA (R)) and eccentric exercise in the treatment of patellar tendinopathy. Knee Surgery Sports Traumatology Arthroscopy. 2015;23(4):1046-52.

34. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. American Journal of Sports Medicine. 2014;42(3):610-8.

35. Warden SJ, Kiss ZS, Malara FA, Ooi ABT, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. American Journal of Sports Medicine. 2007;35(3):427-36.

36. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural adaptation of VISA-P score for patellar tendinopathy in Spanish population. J Orthop Sports Phys Ther. 2011;41(8):581-91.

37. Andriolo L, Altamura SA, Reale D, Candrian C, Zaffagnini S, Filardo G. Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option: A Systematic Review and Meta-analysis. Am J Sports Med. 2019;47(4):1001-18.

38. de Vries A, Zwerver J, Diercks R, Tak I, van Berkel S, van Cingel R, et al. Effect of patellar strap and sports tape on pain in patellar tendinopathy: A randomized controlled trial. Scand J Med Sci Sports. 2016;26(10):1217-24.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

39. Markovic G, Dizdar D, Jukic I, Cardinale M. Reliability and factorial validity of squat and countermovement jump tests. J Strength Cond Res. 2004;18(3):551-5.

AUTHOR'S CONTRIBUTIONS

MPL, EMG and PH conceived of the idea, and developed the intervention. MPL and PH wrote the article. MPL, MO, RMG, AVB, ZA, YH and PH developed the design of the trial. MO were involved in development of the statistical analysis of the trial and contributed to the content of the article. AVB contributed to the design and writing of the jump test protocol. All authors have read and approved the final manuscript.

FUNDING STATEMENT

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTEREST STATEMENT

The authors declare that they have no competing interests.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLES

Table 1. Jump test's protocol.

JUMP TEST PROTOCOL	
5-minute warm-up consisting of steady jogging on a treadmill	
Dynamic Stretches lasting 5 minutes, as instructed by the physical therapist	Psoas Quadriceps Gluteus maximus Gastrocnemius Hamstring muscles
Three jump tests are performed - 3 jumps off the ground for 3 times for the patient to become familiar with the tests - The subject is placed on the platform and asked to perform each test 3 times, with 60 seconds rest between the different tests	Abalakov test Countermovement jump test Squat jump
The highest jump is selected for the study	

FIGURES

Figure 1. Flow diagram. Randomized controlled trial design.

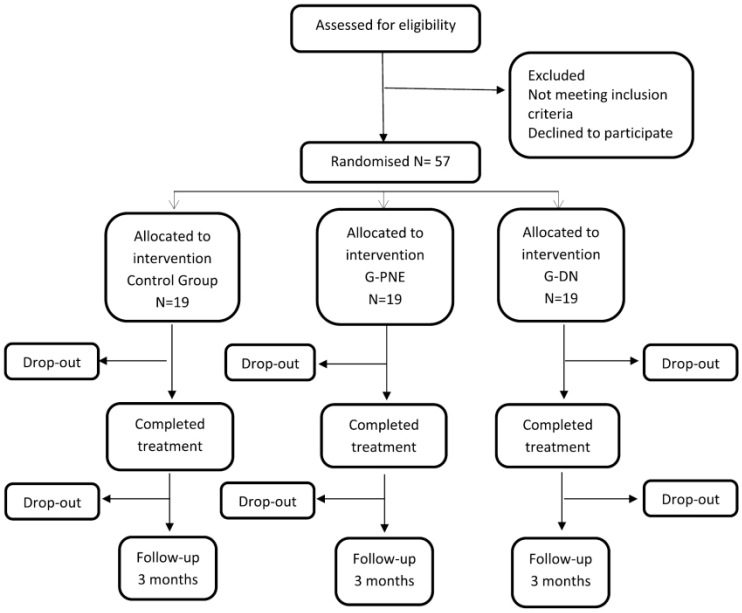
G-PNE: Percutaneous Needle Electrolysis Group. G-DN: Dry Needle Group.

Figure 2. Schedule for the enrolment and intervention.

Schedule for enrolment and intervention per cluster. -t1: baseline; t1–t2: intervention period; t2: 8 weeks after baseline; t3: 10 weeks after baseline; t4: 3 months after baseline. G-PNE: Percutaneous Needle Electrolysis Group; G-DN: Dry Needle Group; US: ultrasound.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure 1. Flow diagram. Randomized controlled trial design.



210x297mm (300 x 300 DPI)

Figure 2. Schedule for enrolment and intervention.

	Enrolment	Allocation	Close-out			
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control group			⟷			
G-PNE			⟷			
G-DN			⟷			
ASSESSMENTS:						
Baseline demographic information	X					
VISA-P	X		X		X	X
VAS			X		X	X
SF-36			X		X	X
Tendon structure US			X		X	X
Jump test			X		X	X

215x279mm (300 x 300 DPI)

DOCUMENTO DE INFORMACIÓN AL PACIENTE

Fecha:

Título del proyecto: "ESTUDIO COMPARATIVO ENTRE TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Investigador principal:

Doña: Mª Pilar López Royo

Este estudio se basa en el estudio comparativo de tratamientos que utilizan distintas técnicas de fisioterapia invasiva junto con un programa de ejercicio excéntrico para el tratamiento de la tendinopatía rotuliana. Por medio del tratamiento se produce una disminución del dolor asociado a esta patología y un aumento de la fuerza de la pierna, lo que a su vez hace que mejore la funcionalidad en las actividades de la vida diaria y mejore la calidad de vida.

PROCESO DE SELECCIÓN DE PACIENTES

Criterios de inclusión:

- Edad comprendida entre 18 y 40 años.
- Practicar cualquier deporte de forma habitual.
- Pacientes con diagnóstico médico de tendinopatía rotuliana crónica con un mínimo de 3 meses de evolución y con sintomatología.
- Dolor a la palpación del tendón en el polo inferior de la rótula y durante el entrenamiento o competición.
- Puntuación del cuestionario VISA-P menor de 80 (el resultado obtenido de rellenar el cuestionario tiene que ser menor de 80 puntos de los 100 posibles para poder participar en el estudio).

Criterios de exclusión:

- Paciente operado de la rodilla afectada en los últimos 6 meses.
- Infiltraciones en la rodilla afectada en los últimos 3 meses.
- Paciente que ha recibido tratamiento farmacológico o fisioterápico en las últimas 48 horas o durante el estudio.
- Patología con menos de 3 meses de evolución.
- Presentar tendinopatía rotuliana bilateral.
- Puntuación del cuestionario VISA-p mayor o igual de 80 (el resultado obtenido de rellenar el cuestionario no puede ser igual o superar los 80 puntos de los 100 posibles, sino no podrá participar en el estudio).
- Imposibilidad para aplicar alguna de las técnicas de tratamiento o valoración por

For peer review only

contraindicación absoluta o relativa.

PROCEDIMIENTO

El tratamiento consiste en realizar un protocolo de ejercicios excéntricos de cuádriceps que realizará en casa de forma diaria, y que serán revisados con el fisioterapeuta para valorar su correcta realización. Se complementará el tratamiento con la aplicación de una técnica de punción según el protocolo de tratamiento propuesto de forma totalmente **aleatorizada** y según los criterios diagnósticos específicos de la misma, siguiendo las indicaciones, criterios de aplicación y criterios diagnósticos.

Son técnicas de punción cuyo objetivo es producir una respuesta inflamatoria aguda que active los mecanismos fisiológicos de regeneración del tejido y mejorar el dolor y la funcionalidad en la articulación de la rodilla, se realiza con agujas de punción seca, similares a las agujas de acupuntura y sin infiltrar ningún tipo de sustancia dentro del organismo.

Los registros serán realizados en el Espacio de Valoración Funcional de la Universidad San Jorge, en la Facultad de Ciencias de la Salud, Edificio III.Se pondrá a su disposición la posibilidad de utilizar el autobús que utiliza el personal y alumnado de la universidad (en el horario que éste esté disponible).Las fechas y horarios serán convenidas con cada participante en función de su disponibilidad y la de los investigadores, buscando la conformidad de todos.La duración aproximada del estudio para cada paciente será de 30 minutos, aunque este horario podrá variar en función de los acontecimientos.

Será recibido por los miembros del equipo de investigación y una vez allí, se le realizará un primer análisis fisioterápico, rellenará una encuesta, una escala analógica visual (EVA) del dolor y el cuestionario Visa-p en el que se valorará la funcionalidad de la rodilla.

Tras éste primer registro se le colocará un marcador pasivo en el pantalón. Se le pedirá que realice el siguiente protocolo:

- Calentamiento de 5 minutos en cinta a ritmo constante.
- Estiramientos dinámicos de psoas, cuádriceps, glúteo, gastrocnemios, isquiotibiales durante 5 minutos instruidos por el fisioterapeuta.
- Realización de los 3 saltos fuera de la plataforma durante 3 veces para que se familiarice con los tests.
- En la plataforma de fuerzas realizará 3 test de salto: el test de Abalakov (ABK), el test de salto con contramovimiento (CMJ) y el squatjump (SJ).

Se colocará en la plataforma y realizará 3 saltos de cada uno de los test con una separación entre ellos de 60 segundos.

Se valora el tendón por ecografía, y se recogen datos por medio de personal adiestrado y se envía

For peer review only

a personal especialista en radiodiagnóstico.
Tras los registros de los saltos se dará por finalizada la valoración.

Tras la 1ª valoración, se realizará una división en tres grupos de los pacientes de forma aleatorizada.
Se le realizará el protocolo de tratamiento de fisioterapia invasivaque le haya correspondido. Realizará una sesión del tratamiento cada 14 días, y se realizará la 2º valoración 1 semana más tarde de la 4º sesión de punción para valorar los cambios que se hayan producido tras el tratamiento, repitiéndose de nuevo el proceso de recogida de datos realizado al inicio del estudio. Se realizará un seguimiento a los tres meses de la valoración post-tratamiento para valorar la eficacia de la técnica a largo plazo del tratamiento.
El procedimiento se realizará guiado ecográficamente para asegurar la especificidad de aplicación sobre la zona relevante de tratamiento y garantizar la seguridad de la técnica. Se hace posterior a esta intervención una serie de ejercicios excéntricos de cuádriceps. El tratamiento se realizará durante 4 sesiones (a razón de una sesión cada 14 días).

RIESGOS

La aplicación de las técnicas de punción utilizadas no han demostrado tener ningún efecto secundario hasta la fecha, aunque el paciente puede experimentar dolordurante y tras la punción, generalmente de uno o dos días de duración.

RESPONSABILIDADES DEL PARTICIPANTE

La información que usted posea sobre su estado de salud o sobre sensaciones previas anormales al realizarle una punción, puede afectar la seguridad o el valor de estas pruebas. La rápida comunicación por su parte de las sensaciones que experimenta al realizar esta prueba es también de gran importancia. Usted es responsable de revelar esa información al personal de la prueba cuando se le pregunte.

PREGUNTAS

Le animamos a que haga cualquier pregunta sobre los procedimientos seguidos o sus resultados en la prueba. Si tiene alguna preocupación o pregunta, por favor pídanos más información, para ello le dejamos un correo electrónico mapilr86@hotmail.com y un número de teléfono móvil: 616102365.

LIBERTAD PARA DAR EL CONSENTIMIENTO

Usted participa en el estudio de manera voluntaria, pudiendo abandonarlo en el momento que considere oportuno, sin que esto conlleve ninguna repercusión negativa para usted.

Los datos obtenidos en el estudio serán confidenciales y únicamente se hará uso de ellos

For Peer review only

para el cumplimiento de los objetivos planteados en la investigación. No se cederán estos datos a terceros sin el consentimiento expreso de los sujetos participantes a quienes pertenezcan los datos.

En esta investigación se garantizará el anonimato de los sujetos que aportan los datos, estableciendo un código disociado para identificarlos que sólo será conocido por los responsables de la realización del trabajo de campo.

Fdo: Mª Pilar López Royo

For peer review only

MODELO DE CONSENTIMIENTO INFORMADO

Título del PROYECTO: "ESTUDIO COMPARATIVO ENTRE TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Doña: Mª Pilar López Royo (mapilr86@hotmail.com)
Departamento de Fisiatría y Enfermería
UNIVERSIDAD DE ZARAGOZA

Yo, ... (nombre y apellidos del participante)

He recibido suficiente información en relación con el proyecto, he leído la hoja de información que se me ha entregado y he podido hacer preguntas sobre el proyecto, recibiendo respuestas satisfactorias.

Entiendo que la participación es voluntaria y que puedo abandonar el proyecto:

. Cuando lo desee
. Sin tener que dar explicaciones
. Sin que esto repercuta en mis cuidados médicos

He sido claramente informado de forma clara y precisa del tratado que recibirán mis datos personales que se contienen en este proyecto, sabiendo que los datos serán tratados y custodiados bajo mi intimidad y a la vigente normativa de la protección de datos, y que sobre estos datos me asisten los derechos de rectificación, acceso y oposición comunicándolo al investigador principal que figura en este consentimiento.

Declaro que presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

Así pues, acepto que las muestras derivadas de este proyecto puedan ser utilizadas en futuras investigaciones siempre y cuando están relacionadas con ésta.

Por lo tanto, doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es

For peer review only

revocable.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del proyecto al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Consentimiento informado estudio_____

Versión_____, fecha_____

For peer review only

Appendix 2. Checklist SPIRIT

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1-3
	2b	All items from the World Health Organization Trial Registration Data Set	2-3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	22
	5b	Name and contact information for the trial sponsor	22
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-5
	6b	Explanation for choice of comparators	3-5
Objectives	7	Specific objectives or hypotheses	5-6

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12-13
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12-13

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	-
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	-
	31b	Authorship eligibility guidelines and any intended use of professional writers	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

8

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034304.R4
Article Type:	Protocol
Date Submitted by the Author:	21-Jan-2020
Complete List of Authors:	Lopez-Royo, Maria Pilar; Universidad San Jorge Facultad de Ciencias de la Salud; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Gómez-Trullén, Eva Maria; Universidad de Zaragoza, Facultad de Ciencias de la Salud y del Deporte Ortiz-Lucas, Maria; Universidad San Jorge Facultad de Ciencias de la Salud Galán-Diaz, Rita Maria; Universidad San Jorge Facultad de Ciencias de la Salud Bataller-Cervero, Ana Vanessa; Universidad San Jorge Facultad de Ciencias de la Salud Al-Boloushi, Zaid; Universidad de Zaragoza Facultad de Ciencias, Facultad de Ciencias de la Salud y del Deporte; Kuwait Ministry of Health Hamam-Alcober, Yasmina; Universidad San Jorge Facultad de Ciencias de la Salud, Fisioterapia Herrero, Pablo; Universidad San Jorge Facultad de Ciencias de la Salud
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Sports and exercise medicine, Pathology
Keywords:	Eccentric Exercise, Tendinopathy, Percutaneous Needle Electrolysis, Dry Needling

SCHOLARONE™
Manuscripts

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

López-Royo MP[a,b], Gómez-Trullén EM[b], Ortíz-Lucas M[a], Galán-Díaz RM[a], Bataller-Cervero AV[a], Al-Boloushi Z[b,c], Hamam-Alcober Y[a], Herrero P[a *]

AFFILIATIONS

A. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, Spain.

B. Universidad de Zaragoza. Facultad de Ciencias de la Salud y del Deporte. Dpto. de Fisiatría y Enfermería. C/ Domingo Miral s/n, 50009 - Zaragoza, Spain.

C. Ministry of Health, State of Kuwait. Jamal Abdulnasser Street, Al Solaibeykhat Area 5. Kuwait City. Safat 13001.

***CORRESPONDENCE TO:**

Dr. Pablo Herrero. iPhysio Research Group. Universidad San Jorge. Campus Universitario, Autov A23, Km 299, 50830 Villanueva de Gállego, Zaragoza, Spain. Tel.: (+34) 976 060 100 Fax: 976 077 581. Email: pherrero@usj.es

ADDITIONAL AUTHOR INFORMATION

Maria Pilar López Royo. Emails: mplopez@usj.es

Eva María Gómez Trullén. Email: evagomez@unizar.es

María Ortíz Lucas. Email: mariaortizlucas@gmail.com

Rita María Galán Díaz. Email: rmgalan@usj.es

Ana Vanessa Bataller-Cervero. Email: avbataller@usj.es

For peer review only

Yasmina Hamam-Alcober. Email: yhamam@usj.es

Zaid AL-boloushi. Email: boloushi@me.com

WORD COUNT: 3967 words.

ABSTRACT

Introduction: Patellar tendinopathy is a degenerative disease of the patellar tendon, which affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The aim of this study is to determine the additional effect of two interventions combined with eccentric exercise and compare which one is the most effective at short and long-term follow-up for patients with patellar tendinopathy.

Methods and analysis: This study is a randomized controlled trial with blinded participants. Measurements will be carried out by a specially trained blinded assessor. A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups. Eligible participants will be randomly allocated to receive either: (a) treatment group with Percutaneous Needle Electrolysis, (b) treatment group with Dry Needling or (c) treatment group with placebo needling. In addition, all groups will perform eccentric exercise. Functionality and muscle strength parameters, pain, ultrasound appearances and patient perceived quality of life shall be evaluated using the VISA-p, jump test, VAS, US images and SF-36, respectively. Participants will be assessed at baseline, at 10 weeks and at 22 weeks after baseline. The expected findings will allow us to advance in the treatment of this injury, as they will help determine whether a needling intervention has additional effects on an eccentric exercise program and whether any of the needling modalities is more effective than the other.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Ethics and dissemination: This protocol has been approved by the Ethics Committee of Aragon (Nº PI15/0017). The trial will be conducted in accordance with the Declaration of Helsinki.

Trial Registration Number: NCT02498795.

Strengths and limitations of this study

- This randomized clinical trial will report the effects on functionality and pain of three different treatment interventions in both the short and long term.
- The double-blinded and placebo-control design will enhance objectivity and help reduce bias.
- The effects of two minimally invasive treatments in physical therapy will be compared for the first time in patellar tendinopathy.

INTRODUCTION

Patellar tendinopathy (PT), also known as jumper´s knee, is a degenerative condition affecting the patellar tendon resulting in anterior knee pain associated with focal and palpable tenderness at the inferior pole of the patella. This disorder has similar histologic findings to other tendon disorders characterized by an increased thickness of the tendon and changes in vascularity, and cellularity, with incompletely healed tendon micro-ruptures and disturbed collagen distribution(1).

This degenerative condition affects athletes from a variety of sports, and is especially predominant in sports involving high-impact jumping. The overall prevalence of PT in non-elite players is 8.5%, although this figure increases in sports that place high demands on the patellar ligament, increasing up to 14.2% in volleyball athletes. Among elite volleyball and basketball players, a prevalence of 45% and 32%, respectively, has been

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

reported. In addition, jumper's knee is almost twice as common among male non-elite athletes when compared with female athletes(2).

The diagnosis is typically based on the clinical history and symptomatic findings. Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) can be used for the assessment of the patellar tendon to clinically confirm the diagnosis(3).

Treatments used for PT fall into two major groups. The first group comprises medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection(4) and autologous growth factors(5). The second group consists of physical therapies, including both conservative and invasive approaches (needling techniques).

Conservative therapies are generally accepted as the first line of approach for managing PT(6, 7), considering exercise as the gold standard of treatment, either eccentric exercise (EE) or high slow resistance training programs. Both have demonstrated similar effectiveness in the treatment of PT(6-8). In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including PT, with a greater likelihood of clinical improvement when performed on a declined surface(6, 8, 9). In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc.(10).

Physical therapy approaches for PT continue to evolve and a number of innovative treatment options are now available, such as dry needling (DN)(11), electrotherapeutic invasive modalities (e.g. electrolysis)(12-14) and extracorporeal shockwave (ECSW) therapy(15). Recently, research has focused on regenerative therapies with high expectations of success because some of these techniques seem to achieve a rapid

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

regeneration of the injured tendon(11, 12, 16). However, evidence-based regenerative therapies are limited and there is no agreement to date regarding which of these is the most effective(17). DN consists of the insertion of a needle (filiform and solid, non-beveled) with the aim of provoking a local injury leading to an inflammatory response and the subsequent regeneration of the injured area in approximately one week. A study performed by Abat et al. reported that DN induced histological and mechanical changes in rat Achilles tendons at week one, with changes persisting at week four(18). Percutaneous Needle Electrolysis (PNE) is an ultrasound-guided technique used by physiotherapists consisting of causing localized lysis in the damaged and/or degenerated tissue by means of a galvanic current transmitted through an acupuncture needle. This technique may affect inflammatory mediators in damaged muscle tissue and influence the new vascularization of the injured area in rats(18). James et al.(11) carried out a cohort study in humans analyzing one group treated with DN and another treated with autologous blood injections. In both cases, they found improvements compared to the baseline measurements. However, this study failed to find differences between the different treatments, concluding that both techniques were equally effective. In relation to PNE, a former study(14) analyzed the treatment effect of electrolysis applied once a week in a group of patients without any control or comparative group, reporting that patients obtained statistically and clinically significant improvements compared to baseline measurements.

From a biological point of view, it seems reasonable to hypothesize that a patient will obtain benefits thanks to the mechanical effects provided by the needle(16), and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle(19).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Therefore, the aim of this study is to determine the additional effect of two interventions combined with EE and compare which one is the most effective at short and long-term follow-up for patients with PT.

METHODS AND ANALYSIS

Study design

The trial is designed as a randomized, controlled, participant, investigator and outcomes assessor blinded, experimental study, aimed at comparing three different physiotherapy protocols applied in three intervention groups of PT patients. Randomization will be performed as block randomization with a 1:1:1 allocation.

This protocol follows the standards of the Helsinki Convention of good clinical practices. The Ethics Committee of Aragon (CEICA) has evaluated the project and has given its favorable opinion and support, Nº PI15/0017 (Appendix 1).

The study has been carried out following the SPIRIT statement for clinical trial protocol and a SPIRIT Checklist has been included (Appendix 2).

Study setting

After reviewing the literature and observing the high incidence of this pathology in amateur young adult athletes who perform sports and more specifically, jump sports, patient recruitment has been performed in basketball, football, volleyball, CrossFit, and handball sports clubs, together with running clubs and several gyms located in the city. A decision was made to conduct the study in X, where the university is located, as well as the laboratory to be used for assessments and treatments.

The assessments will be conducted at the Motion Analysis laboratory of X, and the treatment will be performed at two different sites depending on the availability of both spaces and of schedules. Nonetheless, the same material will always be used.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants

Inclusion criteria

Participants eligible for inclusion in this study must meet the following criteria: 1. History of PT and anterior knee pain located on the inferior pole of the patella for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the superior insertion of the patellar tendon; 4. A score below 80 on the VISA-p questionnaire.

Exclusion criteria

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Corticosteroid injection in the patellar tendon within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs); 6. Any other concomitant treatment for PT.

Methodology

In the first session, all participants will be instructed on how to perform a daily home program of EE. This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol(20) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale(21), and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

For the interventions, the participants will be placed in a supine position with a pillow under the knee (approximately 20º of knee flexion). The area will be cleansed with an antiseptic solution (70% Propan-2-ol, Skin-des). An ultrasound probe cover will be used during the intervention for infectious control. To determine the relevant treatment area, two factors will be considered: 1) Palpation of the areas exhibiting higher sensitivity and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

that reproduce the patient's symptoms; 2) Tendon areas showing degenerative changes assessed under ultrasound. Each group will receive a total of four sessions distributed throughout eight weeks of treatment, once every two weeks.

DN intervention combined with EE (DN-G) and PNE intervention combined with EE (PNE-G)

Specific DN needles will be used during needling treatments, (Agu-punt, Spain). Considering the thickness of the tendon and the approach, we shall use needles measuring 0.25 x 25 mm. The procedure will be guided by US to ensure the specificity of application on the injured area and to guarantee that the procedure is safe for the patient. The DN needle will reach the relevant treatment area (areas with degenerative PT changes). Each session will consist of three needle insertions lasting three seconds each. In PNE-G applications, an intensity of 3 mA galvanic current will be used during the three seconds that the procedure lasts(19). The dose of 3 mA has demonstrated to be as effective as 6 mA in the treatment of tendinopathy injuries in animal models(18,19). In humans, a study conducted in 2016 showed that a dose of 3 mA in PT generated structural changes compatible with tendon regeneration, together with improvement of functionality and pain (22). In contrast, the same study found that lower doses were effective only for the improvement of functionality and pain. As a result, a 3 mA dose was selected for this study.

Control group (CG)

A sham needle will be placed upon the treatment zone, simulating the same procedure as the rest of participants enrolled in the other groups. The needle will be placed in a specific holder and will be manipulated during the intervention to simulate a real treatment. This

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

holder will have a cover over the bottom part of the same in order to avoid the needle contacting the skin.

Outcomes

Baseline data

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and previous rehabilitation treatments and infiltrations received. A blinded observer will assess all participants at baseline, 10 weeks and 22 weeks after baseline. Participants will be asked to inform the researchers if there were any changes in medication or if they are receiving any other treatment or infiltration during the study.

Primary outcome measure

Participants will complete the VISA-p questionnaire at baseline. The VISA-p questionnaire is designed to measure the severity of PT(23). The VISA-p score is the primary outcome variable. This scale consists of eight questions, the first six questions of which employ an analogical visual scale in order to assign a score of 0 to 10, where 10 represents the optimum state, for the purpose of quantifying pain and function in different activities, whereas the last two questions assess the level of functionality and ability to perform physical activity.

Secondary outcome measure

During the first evaluation, participants will complete the Visual Analog Scale (VAS), considering the level of pain they feel while practicing their sport's activity. Participants will be explained that a score of 0 indicates the absence of pain whereas a score of 10 represents the maximum tolerable pain. They will also complete a questionnaire to assess their quality of life (SF-36)(24).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

In order to assess tendon structure, an US evaluation using ultrasound equipment (Logic S7 Expert, General Electric Healthcare) and a linear probe (MLG-15 5–10 MHz) will be used. The ultrasonographic assessment protocol will be carried out according to the Musculoskeletal Ultrasound Technical Guidelines: Knee, defined by the European Society of Musculoskeletal Radiology(25). The ultrasonographic assessment will consist of a longitudinal sequence from the tendon origin to the insertion and transverse sections on the pole of the patella, the tendon body and its insertion on the tibial tuberosity, with the subject in supine position, with 20º knee flexion, and a pillow under the knee. The presence of degenerative signs compatible with the medical diagnosis of PT (thickness of the tendon, hypoechoic areas, irregularities affecting the cortical bone, calcifications) that could be relevant for the selection of the target area will also be assessed. In addition, CD-US assessment will be carried out to detect the presence of hypervascularization, with the subject in supine position and with the knee relaxed in full extension, in order to obtain further information to specifically define the target area.

Upon completion of the evaluation, a jump test will be carried out, measured with a force platform (FP4060-10-2000, Bertec Corporation). In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table 1)(26-28). The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed. The Abalakov jump will be performed with the subject standing in an upright

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

position with a full arm swing. A rapid downward movement will be immediately followed by a rapid upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, a Squat Jump will be performed with 90 degrees of flexion of the knee.

Participant timeline

The study design will be a double-blind randomized controlled trial. The flow chart of the trial is shown in Figure 1 and the check list SPIRIT schedule is shown in Figure 2.

'Patient and Public Involvement'

Patients with PT were not involved in setting the research question or the outcome measures, however the concept of patient involvement translated to the execution phases of the research. Patients and their families were central to the dissemination of the information, which helped to recruit study participants. We intend to disseminate the main results to trial participants and will seek patient and public involvement in the development of an appropriate method of dissemination.

Sample size

Regarding the sample size, a calculation of statistical power was made prior to the study. Accepting an alpha risk of 0.05 and a beta risk in a bilateral contrast, 19 subjects are needed in every treatment group to detect a difference equal or superior to 15 points on the VISA-p scale and assuming a standard deviation of 15 points(29). The estimated rate of loss to follow-up is 20%.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media.

The interested subjects will receive an e-mail explaining the inclusion and exclusion criteria, as well as the purpose of the study. If they meet the defined criteria, they will be invited to send us their medical diagnosis.

Recruitment

Participants will be recruited from sports clubs by the physiotherapist or the coach. Contact has been made with various orthopedists who will collaborate with recruitment, so that when they establish a diagnosis of this pathology in their examination room they can refer us to the patients for their recruitment to the study.

Allocation

Participants will be randomly assigned to either CG or DN-G or PNE-G with a 1:1:1 allocation using an opaque envelope, with a block size of fifteen participants (5 for each group).

Sealed opaque randomization envelopes with a study-specific participant number will be supplied by an external statistician. A colleague not involved in the research study will take the sealed opaque numbered envelopes in order, by number, and deliver the correct envelope to the treating physical therapist. The envelope will contain a piece of paper, which will be labelled with the same participant specific number, plus the group assignment (PNE-G, DN-G or CG).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Participants who fulfill the inclusion criteria will receive the standardized oral and written information, and, once they grant their consent to take part in the trial, they will be randomized into the three groups.

Blinding

Assessments regarding clinical recovery will be conducted by an assessor blinded to treatment allocation. Due to the nature of the intervention, participants can be blinded to allocation. Patients will be explained that they are going to receive a needling treatment, that it may be slightly painful, and that if at any time they are unable to tolerate the pain they must inform the researcher to stop the intervention. In order to blind patients, all the interventions were made with the ultrasound and the PNE device connected to simulate the same intervention in all groups. In contrast, the physiotherapist performing the intervention cannot be blinded, however he/she will be instructed not to disclose the allocation status of the participant at any time or during the follow up assessments. An employee outside the research team will feed data into the computer in separate datasheets so that the researchers can analyze data without having access to information about the allocation.

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

Data collection methods

For the data collection, an oral questionnaire will be used containing questions targeted at collecting baseline data and information concerning the pathology.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Different questionnaires and assessment scales (VISA-p, VAS, SF-36) in Spanish will be given to each participant in paper when they attend the assessment, and they will be granted sufficient time to complete the same.

Data management and statistical analysis

In this study, all data will be entered electronically in the assessment room.

Original scales and questionnaires will be entered and kept on a locked file at the participating site.

Participant files are to be stored in numerical order and stored in a secure and accessible place and manner. Participant files will be maintained in storage for a period of 2 years after completion of the study.

The statistical analysis will be carried out by an intention-to-treat analysis. Variables will be described in number (percentage) and average (standard deviation) or median (interquartile range) attending to their distribution. Quantitative variables will be analyzed with the Shapiro Wilk test in order to confirm their distribution and to determine correct statistical tests according to these results.

Outcomes will be analyzed using mixed linear and logistic regression models considering participants as a random effect and group of treatment as fixed factors. Baseline characteristics will be introduced in the model as covariance. Numbers needed to treat index will also be calculated. The primary aim of the analysis will be to calculate the difference obtained in the VISA-p score after the intervention (final measurement - initial measurement). Finally, the magnitude of the effect of the result will be calculated and therefore its clinical importance, by means of the following formula:

$$r=\sqrt{\frac{F(1,dfR)}{F(1,dfR)+dfR}}.$$

The significance level set for all the analysis will be $p \leq 0.05$.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

ETHICS AND DISEMINATION

The study design, procedures and informed consent procedure were approved and consequently the study will be carried out in compliance with the Helsinki Declaration of Human Rights. All participants will have to provide written Spanish informed consent. Appendix 1.

The results for this trial will be published in peer-reviewed international journals or otherwise made publicly available and will be presented at national and international conferences and symposiums irrespective of the outcomes.

Any modifications to the protocol, which may impact the study procedures, potential patient benefits or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendments will be approved by the Ethics Committee prior to implementation and notified to the health authorities in accordance with local regulations.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored identified by code number. All local databases will be secured with password-protected access systems.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

DISCUSSION

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study seeks to investigate the effects of physiotherapy needling techniques on pain, functionality and quality of life in PT.

PT is a common cause of knee pain in cases of degeneration of the patellar tendon. Among the causes of PT, extrinsic factors (e.g., patellar tendon loading with exercise) and intrinsic factors (e.g., malalignment, high patella, imbalances) have been proposed(30). Traditionally, the focus has been on quadriceps strengthening exercises and many reviews have shown that the effect of the treatment could be estimated to give the patients a 50-70% change of improvement on pain and functionality(6, 31, 32).

Regarding needling treatment, previous studies have shown a great improvement in PT using PNE in combination with EE, with all patients reporting an improvement at least one month after treatment(12-14, 18). This is an improvement compared to the minimum three months needed to improve symptoms by applying other conventional techniques (pharmacological and biological treatments, cold/heat techniques, shock waves, etc.) Additionally, in a long-term study conducted in 2013, this technique was shown to improve symptoms quickly and steadily for at least 10 years(33). These findings demonstrate that this technique ensures that patients remain pain-free for a long period. Furthermore, we were only able to find four articles(12-14, 18) addressing the application of PNE for the recovery of PT, however, none of the articles studied were RCTs, which entail limited evidence of the effectiveness of this technique.

In addition, there are no standardized protocols for the application of PNE, which explains the great variability in the number of sessions and application time based on the literature. Therefore, this study aims to facilitate clinical practice and combine the available methodology criteria in the application of this promising technique.

Regarding DN, the literature shows many similarities with PNE, since there is only one RCT that compares functionality improvements among patients who have received PRP.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

This study reflected that in the short term PRP had better results for pain and functionality, however, DN was more effective than PRP after six months(34).

For the application of both needling techniques, US-guidance is normally used to be able to observe firstly the presentation of the tendon, and later to observe the needle and enable a much more specific treatment approach. However, US has disadvantages including its operator dependence and the limited ability to rule out intra-articular disease. The sensitivity and specificity of ultrasonography for patellar tendinopathy is between 58% and 94%, respectively(35).

Moreover, functionality of the tendon is usually measured with the VISA-p(36,37), whereas jump tests (representing a similar action to that performed in subject's daily sports) are only evaluated in a few papers(27,38). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men(39). Thus, we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

This study has several strengths. First, we will evaluate two techniques that currently lack strong evidence. However, in doing so, we are contributing to new knowledge in the field of the recovery of musculoskeletal injuries. Second, the role of invasive techniques will be determined by comparing the effects between these techniques and a control group. The reliability of data is ensured, as both patients and the assessor will be blinded. Third, a sub-analysis with US will be performed to investigate changes in the presence of calcifications, cortical irregularities, neovascularization, thickness, eco-intensity, eco-variation and eco-texture of the patellar tendon.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

The findings obtained may help advance the treatment of this injury by identifying the most effective treatment protocol and to avoid the associated consequences, such as the prevention of relapses and reducing the potential impact on the musculoskeletal system.

REFERENCES

1. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. Journal of orthopaedic surgery and research. 2008;3:18.
2. Zwerver J, Bredeweg SW, van den Akker-Scheek I. Prevalence of Jumper's Knee Among Nonelite Athletes From Different Sports A Cross-Sectional Survey. American Journal of Sports Medicine. 2011;39(9):1984-8.
3. Stenroth L, Sefa S, Arokoski J, Toyras J. Does Magnetic Resonance Imaging Provide Superior Reliability for Achilles and Patellar Tendon Cross-Sectional Area Measurements Compared with Ultrasound Imaging? Ultrasound Med Biol. 2019;45(12):3186-98.
4. Taylor DW, Petrera M, Hendry M, Theodoropoulos JS. A Systematic Review of the Use of Platelet-Rich Plasma in Sports Medicine as a New Treatment for Tendon and Ligament Injuries. Clinical Journal of Sport Medicine. 2011;21(4):344-52.
5. Andres BM, Murrell GAC. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clinical Orthopaedics and Related Research. 2008;466(7):1539-54.
6. Larsson MEH, Kall I, Nilsson-Helander K. Treatment of patellar tendinopathy-a systematic review of randomized controlled trials. Knee Surgery Sports Traumatology Arthroscopy. 2012;20(8):1632-46.
7. Kongsgaard M, Kovanen V, Aagaard P, Doessing S, Hansen P, Laursen AH, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. Scandinavian Journal of Medicine & Science in Sports. 2009;19(6):790-802.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

8. Murtaugh B, Ihm JM. Eccentric Training for the Treatment of Tendinopathies. Current Sports Medicine Reports. 2013;12(3):175-82.

9. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. British Journal of Sports Medicine. 2005;39(2):102-5.

10. Ortega-Castillo M, Medina-Porqueres I. Effectiveness of the eccentric exercise therapy in physically active adults with symptomatic shoulder impingement or lateral epicondylar tendinopathy: A systematic review. J Sci Med Sport. 2016;19(6):438-53.

11. James SLJ, Ali K, Pocock C, Robertson C, Walter J, Bell J, et al. Ultrasound guided dry needling and autologous blood injection for patellar tendinosis. British Journal of Sports Medicine. 2007;41(8):518-21.

12. Abat F DW, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibañez JM. Effectiveness of the Intratissue Percutaneous Electrolysis (EPI®) technique and isoinertial eccentric exercise in the treatment of patellar tendinopathy at two years follow-up. Muscles Ligaments Tendons J. 2014;14(4):188-93.

13. Valera Garrido F, Minaya Muñoz F, JM SI. Effectiveness of electrolysis percutaneous intratisular (EPI®) in chronic insertional patellar tendinopathy. Trauma Fund MAPFRE. 2010;21(4):227-36.

14. Sánchez-Ibáñez J, Alves R, Polidori F, Valera F, Minaya F, Valles-Martí S, et al. Effectiveness of ultrasound-guided percutaneous electrolysis intratendon (EPI) in the treatment of insertional patellar tendinopathy in soccer players. Br J Sports Med. 2013;47(e2).

15. Zwerver J, Verhagen E, Hartgens F, van den Akker-Scheek I, Diercks RL. The TOPGAME-study: effectiveness of extracorporeal shockwave therapy in jumping athletes with patellar tendinopathy. Design of a randomised controlled trial. Bmc Musculoskeletal Disorders. 2010;11:6.

16. Riggin CN, Chen M, Gordon JA, Schultz SM, Soslowsky LJ, Khoury V. Ultrasound-Guided Dry Needling of the Healthy Rat Supraspinatus Tendon Elicits Early Healing Without Causing Permanent Damage. J Orthop Res. 2019;37(9):2035-42.

17. Krey D, Borchers J, McCamey K. Tendon needling for treatment of tendinopathy: A systematic review. Physician and Sportsmedicine. 2015;43(1):80-6.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

18. Abat F, Valles S-L, Gelber P-E, Polidori F, Jorda A, Garcia-Herreros S, et al. An experimental study of muscular injury repair in a mouse model of notexin-induced lesion with EPI technique. BMC sports science, medicine and rehabilitation. 2015;7:7-.

19. Valera-Garrido, F, Minaya-Muñoz, F, Sánchez-Ibáñez, JM. Comparison of the acute inflammatory response and proliferation of dry needling and electrolysis percutaneous intratissue (epi) in healthy rat Achilles tendons. Br J Sports Med. 2013;47(9):e2-e2.

20. Alfredson H, Pietila T, Jonsson P, Lorentzon P. Heavy-load eccentric calf muscle training for the treatment of chronic Achilles tendinosis. American Journal of Sports Medicine. 1998;26(3):360-6.

21. Silbernagel KG, Crossley KM. A Proposed Return-to-Sport Program for Patients With Midportion Achilles Tendinopathy: Rationale and Implementation. J Orthop Sports Phys Ther. 2015;45(11):876-86.

22. Padrón-Benítez, A, Rojas-Mederos, S. A comparative study between low and high intensity percutaneous needle electrolysis in patients with patellar tendinopathy: a structural and functional analysis. J Invasive Tech Phys Ther. 2016;1(1):10-17.

23. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural Adaptation of VISA-P Score for Patellar Tendinopathy in Spanish Population. Journal of Orthopaedic & Sports Physical Therapy. 2011;41(8):581-91.

24. Alonso J, Prieto L, Anto JM. The spanish version of the SF-36 health survey- A measure of clinical outcomes. Medicina Clinica. 1995;104(20):771-6.

25. Martinoli C. Musculoskeletal ultrasound: technical guidelines. Insights into imaging. 2010;1(3):99-141.

26. Rodriguez-Rosell D, Mora-Custodio R, Franco-Marquez F, Yanez-Garcia JM, Gonzalez-Badillo JJ. Traditional vs. Sport-Specific Vertical Jump Tests: Reliability, Validity, and Relationship With the Legs Strength and Sprint Performance in Adult and Teen Soccer and Basketball Players. J Strength Cond Res. 2017;31(1):196-206.

27. Helland C, Bojsen-Moller J, Raastad T, Seynnes OR, Moltubakk MM, Jakobsen V, et al. Mechanical properties of the patellar tendon in elite volleyball players with and without patellar tendinopathy. Br J Sports Med. 2013;47(13):862-8.

28. Gual G, Fort-Vanmeerhaeghe A, Romero-Rodriguez D, Tesch PA. Effects of In-Season Inertial Resistance Training With Eccentric Overload in a Sports Population at Risk for Patellar Tendinopathy. J Strength Cond Res. 2016;30(7):1834-42.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

29. Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.

30. Figueroa D, Figueroa F, Calvo R. Patellar Tendinopathy: Diagnosis and Treatment. J Am Acad Orthop Surg. 2016;24(12):e184-e92.

31. Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports - A cross-sectional study. American Journal of Sports Medicine. 2005;33(4):561-7.

32. Visnes H, Bahr R. The evolution of eccentric training as treatment for patellar tendinopathy (jumper's knee): a critical review of exercise programmes. British Journal of Sports Medicine. 2007;41(4):217-23.

33. Abat F, Gelber PE, Polidori F, Monllau JC, Sanchez-Ibanez JM. Clinical results after ultrasound-guided intratissue percutaneous electrolysis (EPIA (R)) and eccentric exercise in the treatment of patellar tendinopathy. Knee Surgery Sports Traumatology Arthroscopy. 2015;23(4):1046-52.

34. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-Rich Plasma as a Treatment for Patellar Tendinopathy A Double-Blind, Randomized Controlled Trial. American Journal of Sports Medicine. 2014;42(3):610-8.

35. Warden SJ, Kiss ZS, Malara FA, Ooi ABT, Cook JL, Crossley KM. Comparative accuracy of magnetic resonance imaging and ultrasonography in confirming clinically diagnosed patellar tendinopathy. American Journal of Sports Medicine. 2007;35(3):427-36.

36. Hernandez-Sanchez S, Hidalgo MD, Gomez A. Cross-cultural adaptation of VISA-P score for patellar tendinopathy in Spanish population. J Orthop Sports Phys Ther. 2011;41(8):581-91.

37. Andriolo L, Altamura SA, Reale D, Candrian C, Zaffagnini S, Filardo G. Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option: A Systematic Review and Meta-analysis. Am J Sports Med. 2019;47(4):1001-18.

38. de Vries A, Zwerver J, Diercks R, Tak I, van Berkel S, van Cingel R, et al. Effect of patellar strap and sports tape on pain in patellar tendinopathy: A randomized controlled trial. Scand J Med Sci Sports. 2016;26(10):1217-24.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

39. Markovic G, Dizdar D, Jukic I, Cardinale M. Reliability and factorial validity of squat and countermovement jump tests. J Strength Cond Res. 2004;18(3):551-5.

AUTHOR'S CONTRIBUTIONS

MPL, EMG and PH conceived of the idea, and developed the intervention. MPL and PH wrote the article. MPL, MO, RMG, AVB, ZA, YH and PH developed the design of the trial. MO were involved in development of the statistical analysis of the trial and contributed to the content of the article. AVB contributed to the design and writing of the jump test protocol. All authors have read and approved the final manuscript.

FUNDING STATEMENT

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTEREST STATEMENT

The authors declare that they have no competing interests.

Competing interest: None declared.

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLES

Table 1. Jump test's protocol.

JUMP TEST PROTOCOL	
5-minute warm-up consisting of steady jogging on a treadmill	
Dynamic Stretches lasting 5 minutes, as instructed by the physical therapist	Psoas Quadriceps Gluteus maximus Gastrocnemius Hamstring muscles
Three jump tests are performed - 3 jumps off the ground for 3 times for the patient to become familiar with the tests - The subject is placed on the platform and asked to perform each test 3 times, with 60 seconds rest between the different tests	Abalakov test Countermovement jump test Squat jump
The highest jump is selected for the study	

FIGURES

Figure 1. Flow diagram. Randomized controlled trial design.

G-PNE: Percutaneous Needle Electrolysis Group. G-DN: Dry Needle Group.

Figure 2. Schedule for the enrolment and intervention.

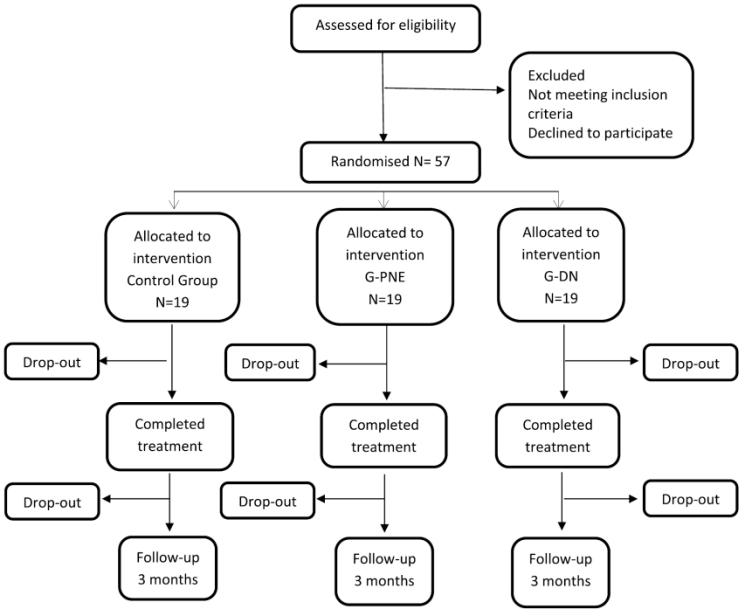
Schedule for enrolment and intervention per cluster. -t1: baseline; t1–t2: intervention period; t2: 8 weeks after baseline; t3: 10 weeks after baseline; t4: 3 months after baseline. G-PNE: Percutaneous Needle Electrolysis Group; G-DN: Dry Needle Group; US: ultrasound.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Figure 1. Flow diagram. Randomized controlled trial design.



210x297mm (300 x 300 DPI)

Figure 2. Schedule for enrolment and intervention.

	Enrolment	Allocation	Close-out			
TIMEPOINT**	$-t_1$	0	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Control group			⟷			
G-PNE			⟷			
G-DN			⟷			
ASSESSMENTS:						
Baseline demographic information	X					
VISA-P	X		X		X	X
VAS			X		X	X
SF-36			X		X	X
Tendon structure US			X		X	X
Jump test			X		X	X

215x279mm (300 x 300 DPI)

DOCUMENTO DE INFORMACIÓN AL PACIENTE

Fecha:

Título del proyecto: "ESTUDIO COMPARATIVO ENTRE TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Investigador principal:

Doña: Mª Pilar López Royo

Este estudio se basa en el estudio comparativo de tratamientos que utilizan distintas técnicas de fisioterapia invasiva junto con un programa de ejercicio excéntrico para el tratamiento de la tendinopatía rotuliana. Por medio del tratamiento se produce una disminución del dolor asociado a esta patología y un aumento de la fuerza de la pierna, lo que a su vez hace que mejore la funcionalidad en las actividades de la vida diaria y mejore la calidad de vida.

PROCESO DE SELECCIÓN DE PACIENTES

Criterios de inclusión:

- Edad comprendida entre 18 y 40 años.
- Practicar cualquier deporte de forma habitual.
- Pacientes con diagnóstico médico de tendinopatía rotuliana crónica con un mínimo de 3 meses de evolución y con sintomatología.
- Dolor a la palpación del tendón en el polo inferior de la rótula y durante el entrenamiento o competición.
- Puntuación del cuestionario VISA-P menor de 80 (el resultado obtenido de rellenar el cuestionario tiene que ser menor de 80 puntos de los 100 posibles para poder participar en el estudio).

Criterios de exclusión:

- Paciente operado de la rodilla afectada en los últimos 6 meses.
- Infiltraciones en la rodilla afectada en los últimos 3 meses.
- Paciente que ha recibido tratamiento farmacológico o fisioterápico en las últimas 48 horas o durante el estudio.
- Patología con menos de 3 meses de evolución.
- Presentar tendinopatía rotuliana bilateral.
- Puntuación del cuestionario VISA-p mayor o igual de 80 (el resultado obtenido de rellenar el cuestionario no puede ser igual o superar los 80 puntos de los 100 posibles, sino no podrá participar en el estudio).
- Imposibilidad para aplicar alguna de las técnicas de tratamiento o valoración por

For peer review only

contraindicación absoluta o relativa.

PROCEDIMIENTO

El tratamiento consiste en realizar un protocolo de ejercicios excéntricos de cuádriceps que realizará en casa de forma diaria, y que serán revisados con el fisioterapeuta para valorar su correcta realización. Se complementará el tratamiento con la aplicación de una técnica de punción según el protocolo de tratamiento propuesto de forma totalmente **aleatorizada** y según los criterios diagnósticos específicos de la misma, siguiendo las indicaciones, criterios de aplicación y criterios diagnósticos.

Son técnicas de punción cuyo objetivo es producir una respuesta inflamatoria aguda que active los mecanismos fisiológicos de regeneración del tejido y mejorar el dolor y la funcionalidad en la articulación de la rodilla, se realiza con agujas de punción seca, similares a las agujas de acupuntura y sin infiltrar ningún tipo de sustancia dentro del organismo.

Los registros serán realizados en el Espacio de Valoración Funcional de la Universidad San Jorge, en la Facultad de Ciencias de la Salud, Edificio III.Se pondrá a su disposición la posibilidad de utilizar el autobús que utiliza el personal y alumnado de la universidad (en el horario que éste esté disponible).Las fechas y horarios serán convenidas con cada participante en función de su disponibilidad y la de los investigadores, buscando la conformidad de todos.La duración aproximada del estudio para cada paciente será de 30 minutos, aunque este horario podrá variar en función de los acontecimientos.

Será recibido por los miembros del equipo de investigación y una vez allí, se le realizará un primer análisis fisioterápico, rellenará una encuesta, una escala analógica visual (EVA) del dolor y el cuestionario Visa-p en el que se valorará la funcionalidad de la rodilla.

Tras éste primer registro se le colocará un marcador pasivo en el pantalón. Se le pedirá que realice el siguiente protocolo:

- Calentamiento de 5 minutos en cinta a ritmo constante.
- Estiramientos dinámicos de psoas, cuádriceps, glúteo, gastrocnemios, isquiotibiales durante 5 minutos instruidos por el fisioterapeuta.
- Realización de los 3 saltos fuera de la plataforma durante 3 veces para que se familiarice con los tests.
- En la plataforma de fuerzas realizará 3 test de salto: el test de Abalakov (ABK), el test de salto con contramovimiento (CMJ) y el squatjump (SJ).

Se colocará en la plataforma y realizará 3 saltos de cada uno de los test con una separación entre ellos de 60 segundos.

Se valora el tendón por ecografía, y se recogen datos por medio de personal adiestrado y se envía

For peer review only

a personal especialista en radiodiagnóstico.
Tras los registros de los saltos se dará por finalizada la valoración.

Tras la 1ª valoración, se realizará una división en tres grupos de los pacientes de forma aleatorizada.
Se le realizará el protocolo de tratamiento de fisioterapia invasivaque le haya correspondido. Realizará una sesión del tratamiento cada 14 días, y se realizará la 2º valoración 1 semana más tarde de la 4º sesión de punción para valorar los cambios que se hayan producido tras el tratamiento, repitiéndose de nuevo el proceso de recogida de datos realizado al inicio del estudio. Se realizará un seguimiento a los tres meses de la valoración post-tratamiento para valorar la eficacia de la técnica a largo plazo del tratamiento.
El procedimiento se realizará guiado ecográficamente para asegurar la especificidad de aplicación sobre la zona relevante de tratamiento y garantizar la seguridad de la técnica. Se hace posterior a esta intervención una serie de ejercicios excéntricos de cuádriceps. El tratamiento se realizará durante 4 sesiones (a razón de una sesión cada 14 días).

RIESGOS

La aplicación de las técnicas de punción utilizadas no han demostrado tener ningún efecto secundario hasta la fecha, aunque el paciente puede experimentar dolordurante y tras la punción, generalmente de uno o dos días de duración.

RESPONSABILIDADES DEL PARTICIPANTE

La información que usted posea sobre su estado de salud o sobre sensaciones previas anormales al realizarle una punción, puede afectar la seguridad o el valor de estas pruebas. La rápida comunicación por su parte de las sensaciones que experimenta al realizar esta prueba es también de gran importancia. Usted es responsable de revelar esa información al personal de la prueba cuando se le pregunte.

PREGUNTAS

Le animamos a que haga cualquier pregunta sobre los procedimientos seguidos o sus resultados en la prueba. Si tiene alguna preocupación o pregunta, por favor pídanos más información, para ello le dejamos un correo electrónico mapilr86@hotmail.com y un número de teléfono móvil: 616102365.

LIBERTAD PARA DAR EL CONSENTIMIENTO

Usted participa en el estudio de manera voluntaria, pudiendo abandonarlo en el momento que considere oportuno, sin que esto conlleve ninguna repercusión negativa para usted.

Los datos obtenidos en el estudio serán confidenciales y únicamente se hará uso de ellos

For Peer review only

para el cumplimiento de los objetivos planteados en la investigación. No se cederán estos datos a terceros sin el consentimiento expreso de los sujetos participantes a quienes pertenezcan los datos.

En esta investigación se garantizará el anonimato de los sujetos que aportan los datos, estableciendo un código disociado para identificarlos que sólo será conocido por los responsables de la realización del trabajo de campo.

Fdo: Mª Pilar López Royo

For peer review only

MODELO DE CONSENTIMIENTO INFORMADO

Título del PROYECTO: "ESTUDIO COMPARATIVO ENTRE TÉCNICAS DE PUNCIÓN PARA EL TRATAMIENTO DE LA TENDINOPATÍA CRÓNICA DEL TENDÓN ROTULIANO"

Doña: Mª Pilar López Royo (mapilr86@hotmail.com)
Departamento de Fisiatría y Enfermería
UNIVERSIDAD DE ZARAGOZA

Yo, ... (nombre y apellidos del participante)

He recibido suficiente información en relación con el proyecto, he leído la hoja de información que se me ha entregado y he podido hacer preguntas sobre el proyecto, recibiendo respuestas satisfactorias.

Entiendo que la participación es voluntaria y que puedo abandonar el proyecto:

. Cuando lo desee
. Sin tener que dar explicaciones
. Sin que esto repercuta en mis cuidados médicos

He sido claramente informado de forma clara y precisa del tratado que recibirán mis datos personales que se contienen en este proyecto, sabiendo que los datos serán tratados y custodiados bajo mi intimidad y a la vigente normativa de la protección de datos, y que sobre estos datos me asisten los derechos de rectificación, acceso y oposición comunicándolo al investigador principal que figura en este consentimiento.

Declaro que presto libremente mi conformidad para participar en el estudio.

Deseo ser informado sobre los resultados del estudio: sí no (marque lo que proceda)

Así pues, acepto que las muestras derivadas de este proyecto puedan ser utilizadas en futuras investigaciones siempre y cuando están relacionadas con ésta.

Por lo tanto, doy mi conformidad para que mis datos clínicos sean revisados por personal ajeno al centro, para los fines del estudio, y soy consciente de que este consentimiento es

For peer review only

revocable.

Firma del participante: _____

Fecha: _____

He explicado la naturaleza y el propósito del proyecto al paciente mencionado

Firma del Investigador: _____

Fecha: _____

Consentimiento informado estudio_____

Versión_____, fecha_____

For peer review only

Appendix 2. Checklist SPIRIT

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1-3
	2b	All items from the World Health Organization Trial Registration Data Set	2-3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	22
	5b	Name and contact information for the trial sponsor	22
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3-5
	6b	Explanation for choice of comparators	3-5
Objectives	7	Specific objectives or hypotheses	5-6

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	11-12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	12
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12-13
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12-13

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	13
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	13
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	13
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	-
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	-
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	-
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	15
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	-
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	-
	31b	Authorship eligibility guidelines and any intended use of professional writers	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

8

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml