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A randomized clinical trial of glenohumeral joint steroid injection versus suprascapular nerve block in patients with frozen shoulder

A PROTOCOL FOR THE THERAPEUTIC INJECTIONS FOR FROZEN SHOULDER (TIFFS) STUDY

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Aims

Frozen shoulder is a common, painful condition that results in impairment of function. Corticosteroid injections are commonly used for frozen shoulder and can be given as glenohumeral joint (GHJ) injection or suprascapular nerve block (SSNB). Both injection types have been shown to significantly improve shoulder pain and range of motion. It is not currently known which is superior in terms of relieving patients' symptoms. This is the protocol for a randomized clinical trial to investigate the clinical effectiveness of corticosteroid injection given as either a GHJ injection or SSNB.

Methods

The Therapeutic Injections For Frozen Shoulder (TIFFS) study is a single centre, parallel, two-arm, randomized clinical trial. Participants will be allocated on a 1:1 basis to either a GHJ corticosteroid injection or SSNB. Participants in both trial arms will then receive physiotherapy as normal for frozen shoulder. The primary analysis will compare the Oxford Shoulder Score (OSS) at three months after injection. Secondary outcomes include OSS at six and 12 months, range of shoulder movement at three months, and Numeric Pain Rating Scale, abbreviated Disabilities of Arm, Shoulder and Hand score, and EuroQol five-level five-dimension health index at three months, six months, and one year after injection. A minimum of 40 patients will be recruited to obtain 80% power to detect a minimally important difference of ten points on the OSS between the groups at three months after injection. The study is registered under ClinicalTrials.gov with the identifier NCT04965376.

Conclusion

The results of this trial will demonstrate if there is a difference in shoulder pain and function after GHJ injection or SSNB in patients with frozen shoulder. This will help provide effective treatment to patients with frozen shoulder.

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Introduction

Frozen shoulder is a common condition causing severe pain and a reduced range of motion in the shoulder.[1] It can result in detrimental effects on quality of life and the ability to perform activities of daily living (ADLs).[2] It affects 2% to 5% of the global population and is more common in diabetic patients.[3] There are a variety of treatment options available for patients with frozen shoulder as part of the management ladder of interventions.[4] The UK FROST trial compared early structured physiotherapy, manipulation under anaesthesia (MUA), or arthroscopic capsular

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release.[5] It demonstrated that none of these options were superior in patient-reported pain and function at one year after treatment. These treatments were given alongside corticosteroid injections. Physiotherapy and the use of corticosteroid injections were shown to be the quickest to access and most inexpensive of the treatment arms, although a further analysis showed MUA is likely to be the most cost-effective option.[6] A review of the UK Frozen Shoulder Trial (FROST),[7] alongside existing evidence in the literature, confirmed these conclusions and the importance of injections alongside physiotherapy in the current treatment of frozen shoulder. Corticosteroid injections are often given into the glenohumeral joint (GHJ) when treating frozen shoulder. Another option is to give the corticosteroid injection as a suprascapular nerve block (SSNB). This has been shown through meta-analysis to significantly improve pain and ROM of patients with frozen shoulder.[8]

The use of SSNB is thought to be effective in shoulder pain as this nerve provides 70% of the sensory innervation of the shoulder and is used after shoulder surgery to provide effective pain relief.[9] It has also been hypothesized that the SSN is also involved in the pathogenesis of frozen shoulder, and therefore SSNB may be more effective than intra-articular injection.[10]

To our knowledge, there has been no previous trial in secondary care comparing the effect of a single GHJ corticosteroid injection versus SSNB in the treatment of frozen shoulder with the same corticosteroid and local anaesthetic mixture. A randomized controlled trial (RCT) has been performed previously comparing SSNB and intra-articular GHJ injection,[11] but did not standardize the treatments, using a different type and volume of local anaesthetic. The GHJ injection also included a large proportion of saline as opposed to local anaesthetic. In that trial the block was given at the suprascapular notch, which differs to the spinoglenoid location used in our trial. They gave the SSNB under ultrasound guidance but the GHJ injection was given without guidance. Although ultrasound-guided GHJ injection has been shown to be more accurate than the blind technique, it does not appear to affect functional outcomes at three months.[12] However, when comparing effectiveness of different treatments, it would be useful to ensure the treatment locations are known to allow conclusions to be drawn from the results. Parashar et al[11] reports improved pain and disability outcome scores at three months with SSNB which is promising, but further assessment of the two treatment methods is required with standardization of the guidance and pharmacological intervention to allow true comparison. Therefore, a RCT taking these changes into account in a UK population is required.

The aim of this study is to determine if there is any difference in terms of pain relief in patients with frozen shoulder when given a steroid injection as a SSNB compared to a GHJ intra-articular injection. The results of this trial will help to guide clinical practice. In particular, this trial may provide information to help effectively treat a patient's symptoms and improve resource allocation.

Methods

Study design. This is a single-centre, parallel, two-arm, randomized clinical trial. The trial is expected to take a total of three years with 12 to 18 months for patient recruitment and 12 months for follow-up, followed by six to 12 months for data collection, analysis, and publication. The trial started recruiting in January 2022. The trial takes place at a single-site NHS Foundation Trust. Trial management will be conducted by the local hospital research and development (R&D) team. The study is registered under ClinicalTrials.gov with the identifier NCT04965376.

Hypothesis. The null hypothesis is that there will be no differences in pain and ability to perform activities of daily living (ADLs) as measured by the Oxford Shoulder Score (OSS)[13] at three months, six months, and one year between a steroid injection as a SSNB compared to a GHJ intra-articular injection.

Eligibility. Patients will be screened against the following criteria. Inclusion criteria are patients diagnosed with unilateral frozen shoulder and age greater than or equal to 18 years. Diagnosis of frozen shoulder will be based on clinical examination (restriction of passive external rotation in the affected shoulder > 50% compared to opposite site), in the presence of normal plain radiographs (anteroposterior and axillary projections other than calcific tendinopathy). Exclusion criteria are age less than 18 years, lacking capacity/unable to give valid consent for participation, full-thickness rotator cuff tear diagnosed on either ultrasound scan or MRI, unable to complete follow-up, unable to speak or read English, allergy to corticosteroid or local anaesthetic, or simultaneous bilateral frozen shoulder.

Consent. Potential participants will receive a verbal explanation of the study by a suitably qualified member of the research team alongside an information leaflet. Participants will be given adequate time to read the information leaflet, digest the information provided and ask any questions they may have, as well as express their views and wishes.

Randomization and blinding. Patients will be allocated to each trial arm by means of an electronic randomizer, created in Excel (Microsoft, USA) and coded using Visual Basic (Microsoft). The order of randomization is predetermined using a mixed-block method, with blocks randomly created with sizes two, four, and six and treatments assigned in a 1:1 ratio. The electronic randomizer takes as inputs the patient details and date of consent, and allocates a unique trial ID and treatment arm to that patient, recording these automatically and such that no details can be altered or deleted except by the trial statistician;

past and future treatment allocations are not visible in order to preserve blinding until the point of randomization. Once randomized, neither patient nor clinician will be blinded to the treatment allocation in order to maintain a pragmatic approach to the patient's journey.

Post-recruitment withdrawals. During the study, the number of patients assessed for eligibility and reasons for any exclusion will be recorded. Participants will be free to withdraw from the study at any time without prejudice. The decision to decline to partake in the study or withdraw will not affect the standard of care the patient receives or availability of any treatment options. If participants withdraw from the study any information already obtained will be included in the final analysis of the study.

Treatment pathway

Pretreatment assessment. Diagnosis of frozen shoulder will be based on clinical examination, defined as restriction of passive external rotation in the affected shoulder > 50% compared to opposite site. Plain radiographs with anteroposterior and axillary projections will be obtained to exclude other pathology. Supplementary imaging will be used at the discretion of the treating clinician. Eligible participants will then be referred for their randomly allocated injection technique via ultrasound guidance on a separate day.

Trial intervention. Participants will be randomly allocated to one of two groups. Group 1 will consist of patients who undergo ultrasound-guided steroid injection into the GHJ (10 ml of 1% lidocaine with 40 mg depomedrone). Group 2 will consist of patients who undergo ultrasound-guided steroid injection as a SSNB at the spinoglenoid notch adjacent to the nerve as it traverses under the spinoglenoid ligament (10mls of 1% lidocaine with 40 mg depomedrone).

Physiotherapy rehabilitation. Following both injections, patients are taken through a protocol of physiotherapy for their frozen shoulder over the subsequent three months. A protocol is issued for guidance; however, therapists are allowed to use other methods as per their discretion. The physiotherapy protocol followed is that used in the UK FROST trial.[14] The frequency of appointments with physiotherapy will depend on the patient's symptoms as well as their progression. For study purposes, a frequency record of these meetings will be kept.

Follow-up. Participants will be seen back in the outpatient clinic three months after their injection to review their progress and collect follow-up data. These data will be collected by a clinician in the clinic who is seeing the patient. Further follow-up data will be collected by the completion of questionnaires via telephone appointment at six months and 12 months after the injection. This will be conducted by a member of the research team or clinician involved in the trial.

Adverse events. Safety reporting will be recorded for each participant starting at the time of the initial clinic visit up until the final follow-up date at 12 months after their injection. As both types of injection are commonly used in current NHS practice, serious adverse events are not expected. If an adverse event occurs in a trial participant, the principal investigator (PI) will review the adverse event and make a decision about the relatedness of the event to the intervention. Any serious adverse event thought to be related to the trial will be reported to the Research Ethics Committee.

Primary outcome measures. The primary outcome measure of this study is the OSS at three months post-injection. The OSS is a 12-item patient-reported outcome measure of the participants' subjective assessment of their pain and ability to perform ADLs.[13] Each symptom is graded from 1 (minimal symptoms) to 5 (severe symptoms), giving a minimum score of 12 and maximum score of 60, with a higher score indicating worse function. It is widely used in clinical studies to assess outcomes after surgical and non-surgical interventions and is considered reliable and valid. The questionnaire will be completed by the patient at three months after their injection in the outpatient clinic.

Secondary outcome measures. Secondary end points include OSS at six months and one year, pain using the Numeric Pain Rating Scale (NPRS)[15] at three months, six months, and one year, the abbreviated Disabilities of Arm, Shoulder and Hand (QuickDASH)[16] questionnaire at three months, six months, and one year, EuroQol five-level five-dimension health index (EQ-5D-5L)[17] at three months, six months, and one year, and range of shoulder movement at three months. The 11-item NPRS features a horizontal bar numbered 0 to 10 and requires the patient to select the whole number which best reflects the severity of their pain. This NPRS has been shown to be a reliable and valid measure of pain intensity in patients suffering from a large variety of conditions. QuickDASH features 11 questions assessing a person's subjective difficulty performing common everyday activities and the severity of their symptoms.[16] Eight questions assess the patient's ability to perform different activities over the previous week, scoring each from 1 (no difficulty) to 5 (unable to perform), and three questions assess symptom severity, scoring from 1 (none) to 5 (extreme or 'so much difficulty I can't sleep'). This is then calculated into a total score which gives a minimum score of 0 (least disability) and maximum score of 100 (most disability). The EQ-5D-5L is a measure of health-related quality of life. Outcome measures assessed at three months after injection will be recorded in the clinic. Questionnaires at six and 12 months after injection will be completed by telephone appointment with a member of the research team. Range of shoulder movement will be assessed in clinic by a clinician at three months. Movements will be

measured in degrees of motion at the GHJ alone and also as combined glenohumeral and scapulothoracic movements. Movements assessed will include forward elevation, abduction, external rotation, and internal rotation.

Power and sample size. Standard deviation (SD) for change in OSS at 12 weeks from baseline was obtained from a previous study of steroid injection for shoulder pain.[17] A total of 20 patients in each group are needed based on 80% power for an independent-samples *t*-test, detecting a minimally important difference of ten and a two-tailed significance level of 0.05 with a SD of 9.1. This accounts for 10% attrition between baseline and three months, as documented in the previous study.[18]

Statistical analysis. Baseline demographic and clinical variables will be reported using summary statistics. In terms of the primary outcome, the change in total Oxford Shoulder Score from baseline to three months post-injection will be compared between the two groups using either the independent-samples *t*-test or Mann-Whitney U test, with the final choice depending on an exploration of the data. The same approach will be adopted for secondary outcomes. All analysis will be performed according to the intention-to-treat principle.

Data management. Information about study subjects will be kept confidential and managed according to the requirements of the Data Protection Act and UK Policy Framework for Health and Social Care Research 2017.[19,20] Data recorded on encrypted memory stick will be stored securely until the study is published. This will be within a maximum of five years, after which all such data will be permanently destroyed.

Trial organization and oversight. The ongoing management of the trial will be the responsibility of the local R&D team with regular meetings to assess progress during the recruitment phase of the study. They will ensure that all staff involved will be adequately trained.

Quality control. The R&D team will continually monitor quality of all aspects of the study including the consenting process, and randomization and collection of data. The study will be conducted as per the study protocol, ethics committee, and Good Clinical Practice.[21] Approval of this trial has been confirmed by the Health Research Authority and Health and Care Research Wales.

Dissemination. Results of the study will be presented locally and at national and international meetings. Results will be published in a peer-reviewed journal and data from the study will be shared with patients in the future to help them decide between the different treatment options for frozen shoulder.

Take home message

- It is currently not known if glenohumeral joint injection or suprascapular nerve block provides better symptom relief in frozen shoulder patients.
- This trial aims to compare the clinical effectiveness of these injections.

References

1. **Hsu JE**, **Anakwenze OA**, **Warrender WJ**, **Abboud JA**. Current review of adhesive capsulitis. *J Shoulder Elbow Surg*. 2011;20(3):502–514.
2. **Fernandes MR**. Patient-reported measures of quality of life and functional capacity in adhesive capsulitis. *Rev Assoc Med Bras (1992)*. 2017;63(4):347–354.
3. **Zreik NH**, **Malik RA**, **Charalambous CP**. Adhesive capsulitis of the shoulder and diabetes: a meta-analysis of prevalence. *Muscles Ligaments Tendons J*. 2016;6(1):26–34.
4. **Charalambous CP**. Professionalism in Surgery. In: *Career Skills for Surgeons*. Cham, Switzerland: Springer, 2017: 5–46.
5. **Rangan A**, **Brealey SD**, **Keding A**, **et al**. Management of adults with primary frozen shoulder in secondary care (UK FROST): a multicentre, pragmatic, three-arm, superiority randomised clinical trial. *Lancet*. 2020;396(10256):977–989.
6. **Corbacho B**, **Brealey S**, **Keding A**, **et al**. Cost-effectiveness of surgical treatments compared with early structured physiotherapy in secondary care for adults with primary frozen shoulder : an economic evaluation of the UK FROST trial. *Bone Jt Open*. 2021;2(8):685–695.
7. **Rex SS**, **Kottam L**, **McDaid C**, **et al**. Effectiveness of interventions for the management of primary frozen shoulder : a systematic review of randomized trials. *Bone Jt Open*. 2021;2(9):773–784.
8. **Jump CM**, **Waghmare A**, **Mati W**, **Malik RA**, **Charalambous CP**. The impact of suprascapular nerve interventions in patients with frozen shoulder: a systematic review and meta-analysis. *JBJS Rev*. 2021;9(12):12.
9. **Ritchie ED**, **Tong D**, **Chung F**, **Norris AM**, **Miniaci A**, **Vairavanathan SD**. Suprascapular nerve block for postoperative pain relief in arthroscopic shoulder surgery: a new modality? *Anesth Analg*. 1997;84(6):1306–1312.
10. **Jump CM**, **Duke K**, **Malik RA**, **Charalambous CP**. Frozen shoulder: a systematic review of cellular, molecular, and metabolic findings. *JBJS Rev*. 2021;9(1):e19.
11. **Parashar A**, **Goni V**, **Neradi D**, **Guled U**, **Rangasamy K**, **Batra YK**. Comparing three modalities of treatment for frozen shoulder: a prospective, double-blinded, randomized control trial. *Indian J Orthop*. 2021;55(2):449–456.
12. **Cho C-H**, **Min B-W**, **Bae K-C**, **Lee K-J**, **Kim DH**. A prospective double-blind randomized trial on ultrasound-guided versus blind intra-articular corticosteroid injections for primary frozen shoulder. *Bone Joint* J. 2021;103-B(2):353–359.
13. **Dawson J**, **Fitzpatrick R**, **Carr A**. Questionnaire on the perceptions of patients about shoulder surgery. *J Bone Joint Surg Br*. 1996;78-B(4):593–600.
14. **Hanchard NCA**, **Goodchild L**, **Brealey SD**, **Lamb SE**, **Rangan A**. Physiotherapy for primary frozen shoulder in secondary care: developing and implementing stand-alone and post operative protocols for UK FROST and inferences for wider practice. *Physiotherapy*. 2020;107:150–160.
15. **Hawker GA**, **Mian S**, **Kendzerska T**, **French M**. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res (Hoboken)*. 2011;63 Suppl 11:S240–52.
16. **Beaton DE**, **Wright JG**, **Katz JN**, **Upper Extremity Collaborative Group**. Development of the QuickDASH: comparison of three item-reduction approaches. *J Bone Joint Surg Am*. 2005;87-A(5):1038–1046.
17. **Herdman M**, **Gudex C**, **Lloyd A**, **et al**. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–1736.
18. **Holt TA**, **Mant D**, **Carr A**, **et al**. Corticosteroid injection for shoulder pain: single-blind randomized pilot trial in primary care. *Trials*. 2013;14:425.
19. **No authors listed**. Data Protection Act 2018. GOV.UK. 2018. www.legislation.gov.uk/ukpga/2018/12/contents/enacted (date last accessed 7 March 2023).
20. **No authors listed**. UK Policy Framework for Health and Social Care Research 2017. NHS Health Research Authority. 2017. www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research (date last accessed 7 March 2023).
21. **No authors listed**. Good Clinical Practice. National Institute for Health and Care Research. www.nihr.ac.uk/health-and-care-professionals/learning-and-support/good-clinical-practice.htm (date last accessed 7 March 2023).

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