### Accepted Manuscript

Title: <sup>☆</sup>Comparison of corticosteroid, autologous blood or sclerosant injections for chronic tennis elbow

Author: R. Branson K. Naidu C. du Toit A.H. Rotstein R. Kiss D. McMillan L. Fooks B.K. Coombes B. Vicenzino



PII:S1440-2440(16)30226-2DOI:http://dx.doi.org/doi:10.1016/j.jsams.2016.10.010Reference:JSAMS 1412To appear in:Journal of Science and Medicine in Sport

 Received date:
 6-3-2016

 Revised date:
 26-9-2016

 Accepted date:
 21-10-2016

Please cite this article as: Branson R, Naidu K, du Toit C, Rotstein AH, Kiss R, McMillan D, Fooks L, Coombes BK, Vicenzino B. & Comparison of corticosteroid, autologous blood or sclerosant injections for chronic tennis elbow. *Journal of Science and Medicine in Sport* http://dx.doi.org/10.1016/j.jsams.2016.10.010

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

# Title: Comparison of corticosteroid, autologous blood or sclerosant injections for chronic tennis elbow.

R Branson<sup>a</sup>, K Naidu<sup>a</sup>, C du Toit<sup>a</sup>, A.H Rotstein<sup>b</sup>, R Kiss<sup>b</sup> D McMillan<sup>a</sup>, L Fooks<sup>a</sup>, B.K Coombes<sup>c,d</sup>, B Vicenzino<sup>d</sup>

<sup>a</sup> Olympic Park Sports Medicine Centre, AAMI Park, Olympic Boulevard, Melbourne, Vic, Australia

<sup>b</sup> Victoria House Medical Imaging, MIA Radiology, 316 Malvern Road, Prahran, Vic, Australia

<sup>c</sup> University of Queensland, School of Health and Rehabilitation Sciences, Physiotherapy, Queensland, Australia.

<sup>d</sup> School of Biomedical Sciences, University of Queensland, Queensland, Australia

#### Address for correspondence/reprints:

Bill Vicenzino

School of Health and Rehabilitation Sciences: Physiotherapy

The University of Queensland, Building 84A, St Lucia QLD 4072

Phone: + 617 3365 2781 Fax: + 617 3365 1622 Email:

b.vicenzino@uq.edu.au

Word count 2578

1 Table, 2 Figures

#### Abstract

**Objectives:** To compare three different ultrasound-guided injections for chronic tennis elbow **Design:** Assessor-blinded, randomized controlled comparative trial **Methods:** 44 patients with clinically diagnosed tennis elbow, confirmed by Doppler ultrasound, received under ultrasound guidance, a single corticosteroid injection (n=14), or two injections (separated by 4weeks) of either autologous blood (n=14) or polidocanol (n=16). Clinical and ultrasound examination was performed at baseline, 4,12 and 26weeks. **Results:** Complete recovery or much improvement was greater for corticosteroid injection than autologous blood and polidocanol at 4weeks (p<0.001, number needed to treat 1 (95% CI 1 to 2). In contrast, at 26weeks corticosteroid was significantly worse than polidocanol (p=0.004, number needed to harm 2 (1 to 6). Recurrence after corticosteroid injection was significantly higher than autologous blood or polidocanol (p=0.007, number needed to harm 2 (1 to 4). Corticosteroid injection produced greater reduction in tendon thickness and vascularity than autologous blood at 4weeks only. Compared to autologous blood, polidocanol reduced tendon thickness at 4 and 12weeks and reduced echogenicity and hyperaemia after 12 or 26weeks respectively.

**Conclusions:** Injections of corticosteroid cannot be recommended over polidocanol or autologous blood, because despite beneficial short-term effect there were inferior long-term effects. Whether polidocanol or autologous blood injections are effective is unknown, especially as their global effect profiles are not unlike previously reported for wait-and-see. Trial registration: ACTRN12614000398606

#### Keywords

Lateral epicondylalgia, polidocanol, blood products, ultrasonography, colour doppler

#### Introduction

Tennis elbow affects approximately 1-3% of the general population<sup>1-3</sup> and leads to considerable morbidity and economic burden.<sup>4</sup> Corticosteroid injection has been in use since the 1950s and remains in widespread use,<sup>5</sup> despite evidence it may be harmful over longer periods.<sup>6, 7</sup> The last decade has seen the emergence of several novel injection therapies, including injection of the sclerosing agent, polidocanol<sup>8, 9</sup> and autologous blood derived growth factors, either by whole blood or platelet rich plasma injections.<sup>10-13</sup> There is little quality evidence to support of any of these injections over the others.<sup>14, 15</sup> This is compounded by a lack of understanding of the complex pathophysiology of tennis elbow and/or the mechanisms of action of such injections, including their effect on tendon thickness, hyperaemia or echogenicity. Advances in colour/power-Doppler ultrasound have focused on detecting and quantifying the presence of neovessels and accompanying nerves,<sup>16, 17</sup> with high diagnostic accuracy reported for tennis elbow.<sup>16</sup> Despite this, few studies of tennis elbow have adopted diagnostic Doppler ultrasound as an eligibility criteria.

We aimed to compare the effect of ultrasound-guided injections of corticosteroid, autologous blood and polidocanol on clinical outcomes, as well as musculoskeletal ultrasound examination findings in a population with unilateral tennis elbow with confirmed tendon neovascularity.

#### Methods

A randomized, assessor-blinded clinical trial was conducted within a community setting in Melbourne, Australia. Patients meeting a clinical diagnosis of tennis elbow and demonstrating neovascularisation on Doppler ultrasound were enrolled between January 2012 and September 2013. Randomisation was by computer generated sequence. Concealed allocation was performed by drawing from opaque envelopes by a trial nurse not involved in the trial.

Ethical approval was obtained from the University of Queensland. Trial registration: ACTRN12614000398606. No financial support was received for this study.

Patients with a provisional diagnosis of tennis elbow were referred to one of three private sports medicine clinics (Melbourne, Australia) from general practitioners, sport physicians and physiotherapists, or were self-referred after reading advertisements in the local paper. Potentially eligible patients underwent telephone and physical screening by one of the study sports physician registrars (R.B. or K.N.). Inclusion criteria were lateral elbow pain for more than 2 months, reproduced by resisted wrist and/or middle finger extension, tenderness over the lateral epicondyle and neovascularization on ultrasound examination. Exclusion criteria were bilateral elbow pain or clinical symptoms suggestive of radioulnar joint synovitis or osteoarthritis, neurological symptoms or cervical radiculopathy. Patients who had received any injections into the common extensor tendon within the previous three months were excluded.

Outcomes were assessed before randomisation, and at 4, 12 and 26weeks by assessors blinded to treatment. At each follow up, patients rated their Global Rating of Change (GROC) since baseline on a 6point Likert scale (completely recovered, much improved, improved, same, worse, much worse). Consistent with previous studies,<sup>6, 18, 19</sup> GROC scores were dichotomized (completely recovered or much improved versus improved, same, worse or much worse), while recurrence was defined as completely recovered or much improved at four weeks, but not at 12 or 26weeks.

Secondary outcomes included measures of pain and disability, pain free grip strength and ultrasound characteristics. The Patient Rated Elbow Evaluation (PREE), now refined into the Patient Rated Tennis Elbow Evaluation (PRTEE),<sup>20</sup> was used as a measure elbow pain and disability. It consisted of a series of questions on pain (5 items) and disability (15 items) experienced over the previous week rated on Likert scales. The total score out of 100 was

calculated by summing the pain items with the weighted disability score (15 items summed, divided by 3).

Pain free grip strength was measured over both arms using digital dynamometry (MIE, Medical Research, Leeds, UK), according to published protocols,<sup>21</sup> with established excellent reliability.<sup>22</sup> The patient (positioned in supine and arm resting in pronation) was asked to grip until the first onset of pain or the first increase in pain (if resting pain was experienced). The mean of three efforts with rest periods of 30 seconds was computed and expressed as a ratio of affected to unaffected side.

Ultrasound investigation was performed at Medical Imaging Australia (Melbourne, Australia) by a sonographer with 10years experience in musculoskeletal ultrasonography (R.K.) and reviewed by a musculoskeletal radiologist (A.R., P.S.). Ultrasound investigations were performed using GE Logiq E9 Ultrasound Machine (GE Healthcare UK) with Broadband Matrix Array Transducer (ML-6-15) operating at its highest frequency of 15MHz according to a standardised examination protocol.<sup>16</sup> The patient was scanned while sitting with their arm relaxed on the table in 90° flexion.

The common extensor tendon was first scanned in the longitudinal and transverse planes with B-Mode to record changes in overall echogenicity (classified on a four point scale as being normal, mild, moderate or severe) and the presence or absence of a tendon tear. Tendon thickness was measured in the longitudinal plane at the point of maximal tendon thickness at the epicondylar margin. This was followed by Colour Doppler imaging (pulse repetition frequency 10MHz, wall filter 75 Hz, colour gain of 86%). Care was taken to scan with light pressure in order to not compress the neovessels. The amount of colour doppler activity was quantified by the colour fraction, defined as the number of colour pixels divided by the total number of pixels in the region of interest.<sup>17</sup> The region of interest was a standard sized ellipse (155.5mm2) placed over the common extensor origin in the longitudinal plane. A sweep of

the tendon was performed to identify the maximum colour fraction without flash artifact. Previous studies have found acceptable reliability for measurement of tendon thickness (ICC>0.76) and colour fraction measurement of vascularity (ICC=0.964)<sup>23</sup> using similar techniques.

Following baseline examination, an experienced musculoskeletal radiologist (A.R., P.S.) performed one of the following ultrasound guided injections using a 25g needle: (a) Corticosteroid: 1ml Betamethasone (Celestone Chondrose) was injected into the abnormal tendon and along the superficial tendon surface; (b) Autologous blood: Multiple dry needling punctures of the abnormal tendon were performed to cause local bleeding. A second 25g needle was then used to inject 3ml of autologous blood targeting the abnormal tendon area. (c) Polidocanol: 3ml Lauromacrogol was injected superficial to the tendon, targeting regions of neovascularity from lateral to medial back to the normal artery. Prior to each injection, 3 ml of blood was drawn from a cubital fossa vein of the other elbow in all patients, regardless of the allocated injection. Blood that was not used for injection was disposed in a safe manner. The patient was blindfolded so they could not see the syringe contents. The skin was prepared with a chlorhexidine wash and neovascularity sites were marked on the skin with a texta pen. No local anaesthetic was injected in any injection option.

Following the injection all patients were seen by a physiotherapist who was unaware of the injection type. They were given an information sheet advising regarding general activity modification (e.g. avoidance of lifting objects with a pronated forearm), and taught an eccentric home exercise program. At the four week follow-up, patient reported outcomes and ultrasound examination were assessed by a radiographer who was not aware of the injection type. Following this, patients allocated to the autologous blood and polidocanol groups received a second ultrasound-guided injection. Patients were asked not to disclose the number of injections received to the physiotherapist or radiographer, who were both absent at the time of injection.

Analyses were performed using SPSS 20.0 on an intention-to-treat basis. Missing data for drop-outs were replaced with values carried forward. Binary outcomes were compared between groups using chi-squared statistics, with Bonferroni adjusted p-values. For continuous outcomes, change from baseline scores were computed and examined using analysis of variance, including time (within-subject) and treatment (between-subject) variables. Significant time by treatment interactions were present for all continuous outcomes (p<0.009), hence pairwise comparisons with Bonferroni correction are reported at each time point. P<0.05 was considered significant.

The following point estimates of effect were computed for pairwise differences between treatments using RevMan 5.0.<sup>24</sup> Relative risk (RR) was computed as the ratio of the risk of an event for two treatments. Standardized mean differences (SMD) expressed the size of the intervention effect relative to the variability. Effect sizes were considered large when absolute SMD was greater than 0.8 or RR was more than 2 or less than 0.5. Numbers needed to treat (NNT) or harm (NNH) were computed for primary outcomes to facilitate development of clinical guidelines for these treatments.

#### Results

Thirty-nine patients (88.6%) completed the trial. Additional information about study eligibility is provided in supplemental material. Five patients (11%), each receiving corticosteroid, withdrew from the study after the 12week follow up, because of condition deterioration, hence were considered not successful for the primary outcome. Participants who withdrew were comparable on baseline demographic and clinical characteristics to participants who completed the trial. No other adverse events were reported.

The groups were comparable at baseline on all demographic, clinical and ultrasound characteristics (Table 1). The study sample included 28 (64%) males, and had a mean (SD)

age of 48.0(7.5) years. The median (IQR) duration of symptoms was 5mths (4 -12) and mean (SD) PREE scores were 50.7 (16.5). Baseline ultrasound examination demonstrated moderate-severe changes in echogenicity and tendon tears in 27 (61%) and 15 (34%) patients respectively. Mean (SD) tendon thickness and colour fraction were 6.2(1.12)mm and 0.17(0.11) respectively. Changes in clinical and ultrasound outcomes are presented in figure 1 and table 2.

#### Primary outcomes

A significant effect of injection was found for ratings of complete recovery or much improvement at four weeks (p=0.002) and 26 weeks (p=0.01). Corticosteroid was superior to autologous blood and polidocanol at four weeks (RR >4.1, NNT 2). In contrast, after 26wks, corticosteroid was inferior to polidocanol (RR 0.4, NNH 2), while differences between corticosteroid and autologous blood neared significance (RR 0.4, p=0.058). No differences were seen between autologous blood or polidocanol at any time point.

There was also a significant effect of injection on recurrence rate (p=0.001). Sixty-four percent of patients (9/14) treated with corticosteroid injection experienced recurrence, significantly higher than autologous blood (2/14, 14%) or polidocanol (1/16, 6%) (RR 0.4, NNH 2). There were no differences in recurrence between autologous blood and polidocanol.

#### Secondary outcomes

A significant effect of injection was found for changes in pain and disability (PREE, p=0.004) and pain free grip ratio (p=0.008) at four weeks only (Table 2, figure 1). Pairwise comparison indicated corticosteroid produced significantly greater improvement in pain and disability (SMD > 1.1) and pain free grip ratio (SMD > 1.1) compared to autologous blood or polidocanol. No differences were seen between autologous blood and polidocanol.

A significant effect of injection was also found for changes in tendon thickness at 4 and 12weeks (p=0.004, 0.038 respectively), hyperaemia at 4 and 26weeks (p<0.001, 0.028

respectively) and echogenicity at 12 weeks (p=0.003). Pairwise comparison revealed corticosteroid and polidocanol had significantly greater reduction in tendon thickness than autologous blood at four weeks (SMD >|0.8|). Improvement in tendon thickness remained higher for polidocanol than autologous blood at 12 weeks (SMD -1.0). Corticosteroid also showed greater reduction in hyperaemia than autologous blood or polidocanol (SMD >0.9) at 4weeks. In contrast, polidocanol showed greater reduction in hyperaemia at 26 weeks than autologous blood (SMD -1.0). Polidocanol had a positive effect on echogenicity at 12weeks compared to corticosteroid or autologous blood (RR <0.5). There were no significant differences between treatments for ultrasound detection of tendon tears at any time point.

#### Discussion

This randomized controlled trial provides comparative efficacy and effect on ultrasoundderived features of tendinopathy of three different injections for tennis elbow, each performed in a blinded manner under ultrasound guidance. Based on the primary outcome of complete recovery or much improvement, corticosteroid was superior to both autologous blood and polidocanol at four weeks, but worse at 26weeks than polidocanol. Recurrence was significantly higher after corticosteroid injection. The efficacy of autologous blood or polidocanol cannot be concluded from this trial.

These data supports a previous meta-analysis,<sup>7</sup> which concluded that corticosteroid injection is beneficial in the short term but detrimental in the long term and is associated with high recurrence rates, ranging from 64% in the current study to 55-72% in previous trials. Mirroring the pattern of recurrence observed using patient reported outcomes, corticosteroid had a large short-term effect on tendon thickness and hyperaemia compared to autologous blood but benefits were not maintained. In contrast, the pattern of global recovery for autologous blood and polidocanol injections appears very similar to that of placebo injection<sup>6</sup> or a wait and see approach<sup>18</sup> demonstrated by previous studies of tennis elbow, and is in agreement with systematic reviews finding a lack of benefit on pain or overall recovery

following injections of polidocanol<sup>7</sup> and autologous blood<sup>25</sup> for tendinopathy. While autologous blood showed no improvement in tendon thickness or hyperaemia at any time point, polidocanol had a large effect on tendon thickness at 4 and 12weeks and produced superior improvements in echogenicity and hyperaemia after 12 and 26weeks respectively. Whether such response is linked to a clinically meaningful improvement remains to be determined.

The strengths of this study include the blinded design, use of ultrasound to standardise the enrolled patients and the precise localization of the injection, 100% compliance and 0% dropouts except at six months. There are also limitations that need to be considered. A lack of placebo group is considered the greatest weakness, particularly given the efficacy of autologous blood and polidocanol is unclear, while that of corticosteroid injection is variable. The number of participants was relatively small and some of the near statistical significant effects are likely real, especially when considering that we elucidated substantial differences at both short and longer follow up on a range of outcomes. Success in blinding was not examined. Differing injection techniques and numbers of injections may have led to unblinding. For example, patients received a single corticosteroid injection or two injections of either autologous blood or polidocanol (at baseline and four weeks), based on study protocol. Given that 100% of corticosteroid injected patients reported complete recovery or much improvement at four weeks, a second injection may not be deemed clinically appropriate, although we cannot exclude that it may have improved late outcomes, given drop-outs were exclusive and high (36%) within this group. No local anaesthetic was used in the trial, although it is recognized that this does not reflect usual clinical practice. Patients also received instruction by a physiotherapist on eccentric home exercise, although monitoring of compliance to exercise or other co-interventions was not undertaken and may have influenced outcomes. A recent trial showed that addition of physiotherapy consisting of exercise and elbow mobilization to corticosteroid injection, did not change the characteristic response to corticosteroid injection.<sup>6</sup>

This study provides meaningful information about the numbers needed to treat or harm to facilitate informed treatment decisions about the comparative efficacy of common injections for tennis elbow. More research is needed to ascertain whether autologous blood or poliodocanol is (are) effective and whether subgroups of individuals may have a better response to one injection than another. Comprehensive ultrasound examination may be used to better understand the complex nature and temporal sequence of changes accompanying tendon pathology.<sup>26</sup>

#### Conclusion

Corticosteroid injection remains the best short-term option, but produces inferior patient reported outcomes compared to polidocanol and possibly autologous blood after 6 months. Superior long-term improvements in tendon thickness, hyperaemia and structure were seen following polidocanol, but it is of unclear significance.

#### Practical implications

- Corticosteroid injection is better than autologous blood or polidocanol in the short term but worse than polidocanol in the long term when considering overall recovery.
- Corticosteroid injection produced only short-term benefit on tendon thickness and vascularity.
- Polidocanol injection reduces tendon thickness, echogenicity and vascularity, although changes take at least 12 weeks, but this is of unclear significance.
- While we did not use a placebo comparator, the use of polidocanol or autologous blood is questionable, given that their outcome trajectories parallel that of wait-and-see approach in previous trials.

#### Acknowledgements

The authors would like to thank Dr Peter Smith and the nursing staff of MIA Radiology for their help and contribution to the study.

No conflicts of interest are declared.

No financial support was received for this study

#### Statement of Contribution

RB was the primary investigator in the study and was involved in the design, ethics approval submission, participant recruitment, follow up and writing up of the paper for submission. KN was involved in participant recruitment and follow up and contributed to the write up of the study. NDT was the study supervisor and was involved in the design, ethics submission and writing up of the paper for submission. AHR was involved in design, ethics submission, radiology protocols, providing radiology services, interpreting ultrasound findings and performing the Ultrasound guided injections. RK was the sonographer who carried out ultrasound examinations on the participants as well as collecting and collating the ultrasound data. LF was involved and carried out baseline assessments, education sessions and follow up assessments of participants. DMcM carried out baseline assessments, education sessions and follow up assessments of participants. BKC contributed significantly in statistical analysis, interpretation, as well as writing up the study for publication. BV was involved in the conception, ethics application, design of the study, data interpretation and contributed to the final paper.

References

1. Walker-Bone K, Palmer KT, Reading I et al. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis Rheum.* 2004;51(4):642-51.

2. Walker-Bone K, Palmer KT, Reading I et al. Occupation and epicondylitis: a population-based study. *Rheumatology (Oxford)*. 2012;51(2):305-10.

3. Verhaar JA. Tennis elbow. Anatomical, epidemiological and therapeutic aspects. *Int Orthop.* 1994;18(5):263-7.

4. Coombes BK, Connelly L, Bisset L et al. Economic evaluation favours physiotherapy but not corticosteroid injection as a first line intervention for chronic lateral epicondylalgia: evidence from a randomised clinical trial. *Br J Sports Med.* accepted May 2015.

5. Titchener AG, Booker SJ, Bhamber NS et al. Corticosteroid and platelet-rich plasma injection therapy in tennis elbow (lateral epicondylalgia): a survey of current UK specialist practice and a call for clinical guidelines. *Br J Sports Med.* 2013.

6. Coombes BK, Bisset L, Brooks P et al. Effect of corticosteroid injection, physiotherapy or both on clinical outcomes in patients with unilateral lateral epicondylalgia. A randomized controlled trial. *JAMA*. 2013;309(5):461-9.

7. Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials. *Lancet*. 2010;376(9754):1751-67.

8. Zeisig E, Fahlstrom M, Ohberg L et al. Pain relief after intratendinous injections in patients with tennis elbow: results of a randomised study. *Br J Sports Med*. 2008;42(4):267-71.

9. Zeisig E, Ohberg L, Alfredson H. Sclerosing polidocanol injections in chronic painful tennis elbow-promising results in a pilot study. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(11):1218-24.

10. Connell DA, Ali KE, Ahmad M et al. Ultrasound-guided autologous blood injection for tennis elbow. *Skeletal Radiol*. 2006;35(6):371-7.

11. Kazemi M, Azma K, Tavana B et al. Autologous blood versus corticosteroid local injection in the short-term treatment of lateral elbow tendinopathy: a randomized clinical trial of efficacy. *Am J Phys Med Rehabil*. 2010;89(8):660-7.

12. Ozturan KE, Yucel I, Cakici H et al. Autologous blood and corticosteroid injection and extracoporeal shock wave therapy in the treatment of lateral epicondylitis. *Orthopedics*. 2010;33(2):84-91.

13. Creaney L, Wallace A, Curtis M et al. Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, single-blind, randomised trial of autologous blood injections versus platelet-rich plasma injections. *Br J Sports Med.* 2011;45(12):966-71.

14. Hegmann KT, Hoffman HE, Belcourt RM et al. ACOEM practice guidelines: elbow disorders. *J Occup Environ Med*. 2013;55(11):1365-74.

15. Krogh TP, Bartels EM, Ellingsen T et al. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network metaanalysis of randomized controlled trials. *Am J Sports Med.* 2013;41(6):1435-46.

 du Toit C, Stieler M, Saunders R et al. Diagnostic Accuracy Of Power-Doppler Ultrasound In Patients With Chronic Tennis Elbow. *Br J Sports Med.* 2008;42(11):572-6.

17. Schueller-Weidekamm C. Quantification of synovial and erosive changes in rheumatoid arthritis with ultrasound--revisited. *Eur J Radiol*. 2009;71(2):225-31.

 Bisset L, Beller E, Jull G et al. Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. *BMJ*. 2006;333(7575):939.

19. Smidt N, van der Windt DA, Assendelft WJ et al. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomised controlled trial. *Lancet*. 2002;359(9307):657-62.

20. Macdermid J. Update: The Patient-rated Forearm Evaluation Questionnaire is now the Patient-rated Tennis Elbow Evaluation. *J Hand Ther*. 2005;18(4):407-10.

21. Lim EC. Pain free grip strength test. *J Physiother*. 2013;59(1):59.

22. Smidt N, van der Windt DA, Assendelft WJ et al. Interobserver
reproducibility of the assessment of severity of complaints, grip strength, and pressure
pain threshold in patients with lateral epicondylitis. *Arch Phys Med Rehabil*.
2002;83(8):1145-50.

23. Terslev L, Ellegaard K, Christensen R et al. Head-to-head comparison of quantitative and semi-quantitative ultrasound scoring systems for rheumatoid arthritis: reliability, agreement and construct validity. *Rheumatology (Oxford)*.

2012;51(11):2034-8.

Higgins JPT, Green SE. Cochrane Handbook for Systematic Reviews of
Interventions Available from: <u>http://www.cochrane-handbook.org</u>. Accessed 2008
11.12.2015

25. de Vos RJ, van Veldhoven PL, Moen MH et al. Autologous growth factor injections in chronic tendinopathy: a systematic review. *Br Med Bull*. 2010;95:63-77.

26. Malliaras P, Purdam C, Maffulli N et al. Temporal sequence of greyscale ultrasound changes and their relationship with neovascularity and pain in the patellar tendon. *Br J Sports Med.* 2010;44(13):944-7.

#### Tables

Table 1 Baseline demographic, clinical and ultrasound measures for patients treated by corticosteroid injection (CSI), autologous blood injection (ABI) and polidocanol injection (POL).

	CSI n=14	ABI n=14	POL n=16	Total population n=44
Demographic characteristics				
Age (years)	48.1 (8.1)	47.9 (6.9)	47.9 (7.8)	48.0 (7.5)
Male n (%)	8 (57%)	10 (71%)	10 (63%)	28 (64%)
Clinical measures				
Duration (median IQR) (months) Pain and disability	4.5 (3.0, 7.5)	5.5 (3.0, 12.5)	5.0 (4.0, 12.0)	5 (4,12)
(PREE, 0-100)	48.5 (17.2)	52.0 (13.8)	51.0 (17.6)	50.7 (16.5)
PFG ratio (Affected/unaffected)	0.39 (0.21)	0.42 (0.26)	0.58 (0.32)	0.47 (0.28)
Ultrasound measures				
Tendon thickness (mm)	6.38 (1.16)	6.07 (0.90)	6.14 (1.29)	6.20 (1.12)
Hyperaemia colour fraction (0-1)	0.2 (0.11)	0.14 (0.09)	0.16 (0.11)	0.17 (0.11)
Tears (%)	6 (43%)	4 (29%)	5 (31%)	15 (34%)
Moderate-severe echogenicity (%)	10 (71%)	9 (64%)	8 (50%)	27 (61%)

Data represents mean (SD) or frequency (%), unless otherwise specified. No

significant differences were observed between groups at baseline. Abbreviations:

PREE Patient rated elbow evaluation; PFG pain free grip

#### Table 2 Effect of corticosteroid injection (CSI), autologous blood injection (ABI) and

					Between-group comparisons (SMD or RR, 95% CI)			
	CSI n=14	ABI n=14	POL n=16		CSI v ABI	CSI v POL	ABI v POL	
Primary	y outcome meas	sures						
Comple	ete recovery or	much impro	vement					
4wks	14 (100%)	3 (21%)	2 (13%)		4.1 (1.7, 10.4)*	6.6 (2.1, 20.7)*	1.7 (0.3, 8.8)	
12wks	6 (43%)	5 (36%)	6 (38%)		2 (1,1.8)* 1.2 (0.5,3.0)	2 (1,1.4)* 1.1 (0.5,2.7)	12 (2.8,-5.6) 1.0 (0.4, 2.5)	
12 WK3	0(4370)	5 (50%)	0 (3070)		14 (2.3,-3.5)	19 (2.5,-3.4)	NNH 56 (-2.8,3.1)	
26wks	4 (29%)	9 (64%)	13 (81%)		0.4 (0.2, 1.1)	0.4 (0.2, 0.8)*	0.8 (0.5, 1.3)	
_				NNH	3 (1.4,82.1)	2 (1.2,4.5)*	6 (-2.1,6.9)	
Recurr	ence § 9 (64%)	2 (14%)	1 (6%)	RB	0.4 (0.2, 0.9)*	0.4 (0.2, 0.8)*	0.9 (0.7, 1.2)	
	) (0470)	2(14/0)	1 (070)		2 (1.2,5.3)*	2 (1.2,3.3)*	13 (-3.3,7.2)	
	ary clinical out							
Improv	ement in pain	and disability	y (PREE, 0-10	)0)				
4wks	36.0 (19.6)	13.6 (21.5)	9.2 (20.7)	SMD	1.1 (0.2,1.9)*	1.3 (0.5,2.1)*	0.2 (-0.4,0.8)	
12wks	17.9 (22.5)	17.8 (18.3)	19.9 (22.7)	SMD	0.0 (-0.8,0.8)	-0.1 (-0.8,0.7)	-0.1 (-0.9,0.7)	
26wks	19.2 (23.1)	29.4 (22.5)	28.9 (21.2)	SMD	-0.4 (-1.3,0.4)	-0.4 (-1.2,0.3)	0.1 (-0.3,0.5)	
Improv	ement in pain	free grip rati	o (affected/ur	naffecte	d)			
4wks	0.49 (0.22)	0.16 (0.37)	0.17 (0.29)	SMD	1.1 (0.3, 1.9)*	1.2 (0.4, 2.0)*	-0.03(-0.8, 0.7)	
12wks	0.29 (0.29)	0.40 (0.28)	0.20 (0.34)	SMD	-0.4 (-1.1, 0.4)	0.3 (-0.5, 1.0)	0.6 (-0.1, 1.4)	
26wks	0.25 (0.34)	0.46 (0.20)	0.33 (0.35)	SMD	-0.7 (-1.5, 0.04)	-0.2 (-1.0, 0.5)	0.4 (-0.3, 1.2)	
Seconde	ary ultrasound o	outcome meas	ure					
Reduct	ion in tendon t	hickness (mn	ı)					
4wks	0.58 (0.66)	-0.21 (0.45)	0.23 (0.61)	SMD	1.4 (0.5, 2.1)*	0.6 (-0.2, 1.3)	-0.8(-1.5, -0.04)*	
12wks	0.06 (0.61)	-0.16 (0.35)	0.36 (0.60)	SMD	0.3 (-0.4, 1.1)	-0.6 (-1.3, 0.2)	-1.0 (-1.8, -0.2)*	
26wks	0.25 (0.55)	-0.20 (0.58)	0.27 (0.65)	SMD	0.7 (-0.04, 1.5)	-0.03 (-0.8, 0.7)	-0.8 (-1.5, -0.02)	
Reduct	ion in hyperae	mia (colour fi	raction)					
4wks	0.13 (0.13)	-0.03 (0.07)	0.03 (0.07)	SMD	1.5 (0.6, 2.3)*	0.9 (0.1, 1.7)*	-0.8 (-1.5,0.01)	
12wks	-0.01 (0.10)	-0.03 (0.06)	0.01 (0.08)	SMD	0.2 (-0.5. 1.0)	-0.2 (-1.0, 0.5)	-0.6 (-1.3, 0.2)	
26wks	-0.01 (0.09)	-0.04 (0.09)	0.05 (0.09)	SMD	-0.3 (-0.4, 1.4)	-0.7 (-1.5, 0.02)	-1.0 (-1.8,-0.2)*	
Echoge	enicity (modera	nte-severe) (%	<b>)</b>					
4wks	5/14 (36%)	9/14 (64%)	6/16 (38%)	RR	1.8 (0.8, 4.0)	1.0 (0.6, 1.8)	0.6 (0.3, 1.3)	
12wks	10/14 (71%)	8/14 (57%)	2/16 (13%)	RR	0.7 (0.2, 1.9)	0.3 (0.1, 0.8)*	0.5 (0.3, 0.9)*	
26wks	8/14 (57%)	6/14 (43%)	4/16 (25%)	RR	0.8 (0.4, 1.6)	0.6 (0.3, 1.1)	0.8 (0.5, 1.3)	
Tears (	%)							
4wks	8/14 (57%)	3/14 (21%)	7/16 (44%)	RR	0.6 (0.3, 1.1)	0.8 (0.4, 1.6)	1.4 (0.8, 2.3)	
12wks	5/14 (36%)	3/14 (21%)	4/16 (25%)	RR	0.8 (0.5, 1.3)	0.9 (0.5, 1.4)	1.1 (0.7, 1.6)	
26wks	4/14 (29%)	1/14 (7%)	3/16 (19%)	RR	0.8 (0.5, 1.1)	0.9 (0.6, 1.3)	1.1 (0.9, 1.5)	

polidocanol injection (POL) on primary and secondary outcomes.

Summary data are represented by no. events/total sample at each time point (%) or mean

change from baseline (SD), unless otherwise specified. Pairwise differences between treatments for categorical or continuous outcomes are represented by relative risk (RR) or standardized mean differences (SMD) respectively. RR>1 and SMD>0 represent differences

in favour of the first listed injection. NNT number needed to treat; NNH number needed to harm. Significant pairwise differences between treatments, as determined by Pearson chi-squared or univariate analysis of variance (p<0.05) are indicated by an asterisk. § Recurrence is defined as complete recovery or much improvement at four weeks, but not at either 12 or 26weeks. PREE Patient rated elbow evaluation.

**Figure 1:** Proportion of patients reporting complete recovery or much improvement at each timepoint. Mean (SE) change from baseline for continuous outcomes for the three treatments.

