

Bloom JE, Rischin A, et al. Image-guided versus blind glucocorticoid injection for shoulder pain (Review). Cochrane Database of Systematic Reviews 2012, Issue 8, Art # CD009147.

Design: Meta-analysis of controlled clinical trials

PICOS:

- Patient population: patients of any age with rotator cuff disease or adhesive capsulitis
- Intervention: Image-guided (ultrasound, MRI, or arthrogram) subacromial and/or glenohumeral injections of corticosteroid
- Comparison: Injection using anatomic landmarks or injection of corticosteroid by intramuscular route
- Outcomes: Overall pain measured by numerical or categorical rating scales, function as measured by scales such as the Constant or the Shoulder Pain and Disability Index (SPADI)
 - o Trials which only looked at accuracy of the injections were not included
 - o Only short-term outcomes (up to 6 weeks) were reported, and only short-term outcomes were analyzed
 - Study types: Randomized clinical trials and controlled trials with quasi-randomization (such as date of birth or hospital record)

Study Selection:

- Databases included MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register, with additional screening of reference lists and the World Health Organization registry of ongoing trials through June 2011
- Two authors independently selected trials for inclusion, extracted data on trial characteristics, and assessed the risk of bias for each study using the Cochrane Risk of Bias tool (such as sequence generation, concealment of allocation sequence, blinding, incomplete outcome data, selective outcome reporting)
- The authors preferred, when possible, to use end of treatment scores, rather than change from baseline scores, and, when using dichotomous outcomes (such as success/failure), assumed that patients with missing data at the end of treatment did not have a positive outcome

Results:

- 574 records were screened, and 22 possibly eligible studies were assessed in full text; of these, 5 studies published between 2005 and 2009, with 290 participants, were selected for inclusion

- 3 of these studies were classified as randomized trials; one was classified as quasi-randomized (patients were alternately assigned to one treatment or the other), and one did not specify how patients were assigned to treatment
 - Four studies were categorized as having rotator cuff disease; the fifth was of patients with adhesive capsulitis
- Three of the rotator cuff studies used landmark-guided injection in the control groups; one used intramuscular injection of the upper gluteal region as the control injection, and the adhesive capsulitis study targeted the glenohumeral joint for the control injection
 - Four studies reported on pain, but no two studies measured pain in the same way (pain at rest and with activity versus pain in the daytime and before sleep versus pain in the previous week versus no specification of the type of pain)
 - Four studies reported on function, but no two studies used the same tool
 - All five trials reported some measure of range of motion, but measurements varied between trials
 - No study reported health-related quality of life or work disability
 - Only one study (Ekeberg 2009) was assessed as having a low risk of bias in all categories, and one study was assessed as overall low bias except for lack of blinding of patients; three studies were assessed as having a high risk of bias due to inadequate randomization methodology and allocation concealment as well as incomplete outcome data
 - The single trial which was free of bias (Ekeberg 2009) compared ultrasound-guided local rotator cuff injection with gluteal injection of systemic steroid, and this study reported no important differences between the two groups for any outcome
 - An attempt was made to pool results for short-term pain from the unbiased study with the results from the biased studies, but the results were highly heterogeneous, due to the fact that there was serious bias in the comparisons which favored ultrasound guidance of injections
 - No difference between injection approaches was found for shoulder function, although the results were statistically heterogeneous

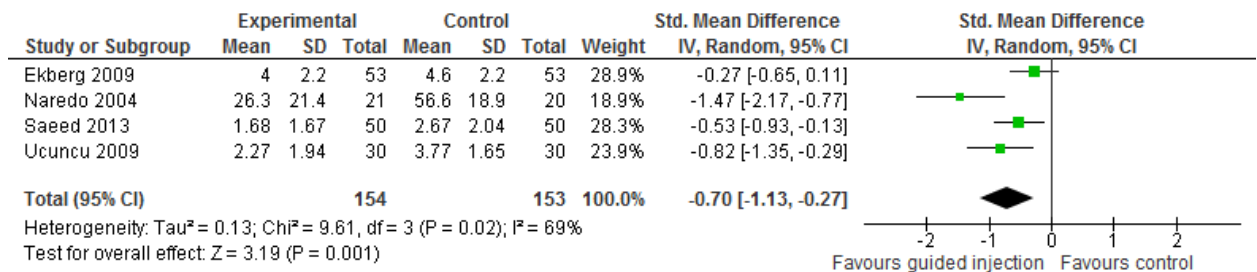
Authors' conclusions:

- Based only a single trial with a low risk of bias, current evidence does not confirm an advantage of ultrasound-guided imaging for improving the pain and functional outcomes of corticosteroid injections
- Studies with inadequate control of bias are likely to overestimate the treatment benefits of image-guidance of shoulder injections
- There is moderate quality evidence from one study that ultrasound-guided steroid injection is not superior to systemic injection of steroid in the gluteal region for relief of symptoms of rotator cuff disease

- A different systematic review (Soh 2011) of the same topic estimated that guided injection was superior to blinded injection for improving shoulder pain and function, but the authors excluded the highest-quality study (Ekeberg 2009) from their analysis, and pooled data from two unblinded studies with the risks of bias associated with lack of blinding, and this may have overestimated the benefit of guided injection

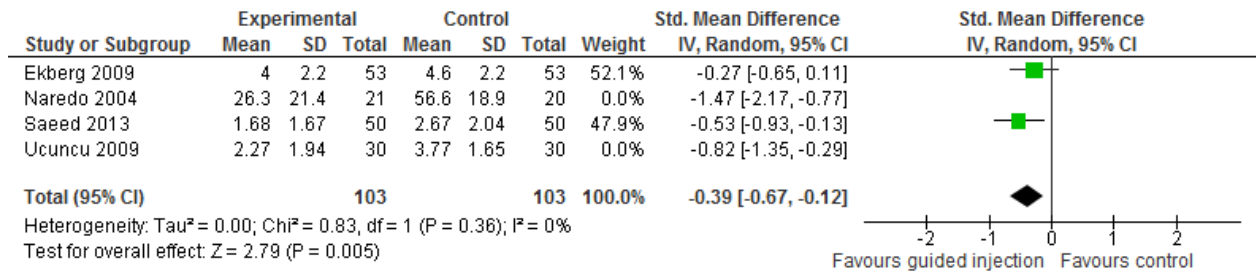
Comments:

- At the time of publication of this meta-analysis, a study of steroid injection for shoulder impingement pain (Saeed et al) was in progress but not yet published
- o In 2013, Saeed et al did publish their randomized trial, which compared ultrasound-guided with palpation-guided subacromial injection of 40 mg methylprednisolone acetate and 4 ml lidocaine HCl
- o This study had satisfactory randomization, allocation concealment, and blinded assessment of outcome, and would have qualified for inclusion in the Bloom meta-analysis as having low risk of bias
- o Saeed 2013 reported pain and function at 6 weeks for ultrasound-guided subacromial injection (n=50) and palpation-guided injection (n=50)
- o Saeed's data were analyzed with nonparametric methods, and used improvement from baseline rather than 6 week pain scores to compare groups
 - Saeed reported that ultrasound-guided injections led to greater improvement in pain and physician global assessment at 6 weeks compared to landmark-guided injections
- o Even though Saeed et al used nonparametric analyses to compare treatment groups, they did provide 6 week pain scores with standard deviations, making it possible to add their data to the forest plot in Analysis 1.1 on page 38, which reported a standardized mean difference of 0.80 standard deviations in favor of ultrasound guidance from the three studies with 6 week data; when Saeed is added to the analysis, the standardized mean difference is 0.70 standard deviations:



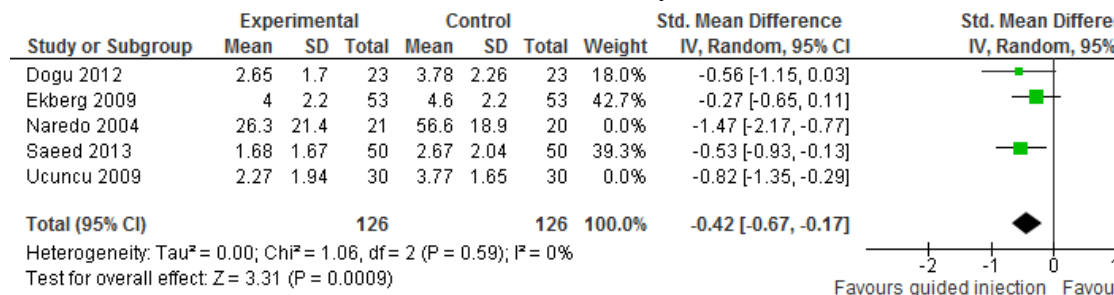
- o The data from Naredo 2004 and from Uncuncu 2009 were considered to be at high risk of bias due to lack of blinding; excluding these two studies and pooling only Ekberg 2009 and Saeed 2013 makes the standardized mean difference smaller, 0.39 SD instead of 0.70

SD:



- A pooled SMD of 0.39 is generally interpreted as a small to moderate effect size, and the pooling of data from only two studies leaves considerable uncertainty about the true effect size for ultrasound guidance
- Saeed did not report standard deviations for shoulder function scores at 6 weeks, meaning that they cannot be added to the forest plot in Analysis 1.2, which reported a statistically non-significant advantage for ultrasound guidance for that outcome
- Some other studies have been published more recently, including Dogu et al 2012, Sabeti-Aschraf et al 2011, Hashiuchi et al 2011, Zufferey et al 2012, and Hegedus et al 2010

- Dogu 2012 enrolled 46 patients with subacromial impingement syndrome, randomizing 23 to ultrasound-guided steroid injections and 23 to landmark-guided injections; both groups had gadolinium in the injectate to facilitate MRI ascertainment of accuracy of the injections; accuracy was equal in the two groups and no statistically significant differences were reported for pain at 6 weeks
- Although allocation concealment was unclear in Dogu 2012, outcome assessment was blinded, and it is likely that Dogu would meet inclusion criteria for this meta-analysis; if it is combined with Ekberg 2009 and Saeed 2013, it would yield a pooled SMD of 0.42 with similar 95% confidence intervals to the above analysis:



- Hegedus 2010 was a non-randomized observational study of the effect of glenohumeral joint injection accuracy on clinical outcomes of shoulder dysfunction, using contrast to ascertain the placement of the injected steroid in 103 patients, with a blinded radiologist classifying the injection as “in the joint” or “outside the joint;” the short-term pain relief was equal whether the injection was in the joint or outside it

- Because no ultrasound guidance was used, this study does not contribute to the meta-analysis, but does suggest that the benefits of glenohumeral steroid injection may not depend critically on the accuracy of the injection
- Hashiuchi randomized 30 patients to guided or unguided injection of the biceps tendon sheath; this study did not report on pain VAS or function, only on accuracy of the injection in the tendon sheath; they reported that injection of the tendon sheath of the long head of the biceps is more accurate with ultrasound than without it
- Sabeti-Aschraf reported on injection of 120 acromioclavicular joints of 60 cadavers, randomizing the joints to injection with or without ultrasound guidance, and reported that 25% of the blind injections were misplaced, but only 2% in the ultrasound injections were misplaced
- Zufferey 2012 randomized 70 patients with shoulder pain to ultrasound-guided or blind injection of steroid, reporting that the ultrasound group had lower daytime pain than the control group, which did not reach statistical significance; however, the actual data for daytime pain were not reported, and therefore cannot be pooled with the other studies
- Overall, it appears that there is considerable uncertainty concerning the effect of ultrasound guidance on the clinical outcomes of steroid injections; guidance is likely to increase the accuracy of the injections, but it is not clear whether the clinical outcomes are critically dependent on injection accuracy
- The pooled 6 week pain outcomes from Dogu, Saeed, and Ekeberg, with a standardized mean difference estimate of 0.42 SD with 95% confidence intervals between 0.17 and 0.67 SD, provide an uncertain estimate of a small to moderate advantage in pain relief at 6 weeks if ultrasound injection compared to landmark-guided injection of steroid

Assessment: Adequate for some evidence that ultrasound-guided injection of corticosteroid into the shoulder, while yielding a more anatomically accurate injection, is likely to have a small to moderate advantage over landmark-guided injection for pain relief at 6 weeks after the injection

References:

Dogu B, Yucel SB et al. Blind or Ultrasound-Guided Corticosteroid Injections and Short-Term Response in Subacromial Impingement Syndrome: A Randomized, Double-Blind, Prospective Study. *Am J Phys Med Rehabil* 2012;91:658-665.

Hashiuchi T, Sakuri G, et al. Accuracy of the biceps tendon sheath injection: ultrasound-guided or unguided injection? A randomized controlled trial. *J Shoulder Elbow Surg* (2011) 20, 1069-1073

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Saeed A, Khan M, et al. Impact of outpatient clinic ultrasound imaging in the diagnosis and treatment for shoulder impingement: a randomized prospective study. *Rheumatol Int* 2013; DOI 10.1007/s00296-013-2892-z

Sabeti-Aschraf M, Lemmerhofer B, et al. Ultrasound guidance improves the accuracy of the acromioclavicular joint infiltration: a prospective randomized study. *Knee Surg Sports Traumatol Arthrosc* 2011; 19:292–295

Zufferey P, Revaz S, et al. A controlled trial of the benefits of ultrasound-guided steroid injection for shoulder pain. *Joint Bone Spine* 2012;79:166-169.