Analyzing Corticosteroid Injection Configuration to Optimize Outcomes in De Quervain's Tenosynovitis: A Systematic Review, Meta-Analysis, and Meta-Regression of Randomized Controlled Trials

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INTRODUCTION: Corticosteroid injections (CSIs) are amongst the first line treatments for De Quervain's tenosynovitis. Although prior meta-analyses have assessed CSI efficacy, most studies had some degree of heterogeneity in the results and noted a need to investigate injection details that could confound outcomes. Thus, this study aimed to investigate if CSI configuration affected outcomes and accounted for heterogeneity.

METHODS: PRISMA guidelines were followed; PubMed, Embase, and CENTRAL databases were searched for randomized controlled trials, where one arm received isolated CSI and the other received any other comparative treatment (has to be different than the first arm). Consistent with the previously validated methodology, the comparative treatments were controlled for in each analysis throughout the study to accurately understand the effect of the variable of interest. Demographics, number of injections administered, diabetes inclusion criteria, covariates (injection guidance, anesthetic dosage-per-injection, corticosteroid type, corticosteroid dosage-per-injection), pain improvement (PI) (pain at longest follow-up minus preoperative pain) via the Visual Analog Scale (VAS), and adverse events were collected. First, a meta-analysis was performed to validate the heterogeneity observed in prior literature. Then, four layers of analyses were done. [1] Primary (all studies that met inclusion criteria), [2] secondary (studies administering only 1 injection), [3] tertiary (studies with non- or controlled-diabetics), [4] and quaternary (only 1 injection and non- or controlled-diabetics. This stepwise analysis increases the robustness of results by reducing the confounding risk of number of injections administered and diabetes. Meta-regression was used to assess whether a covariate affected meta-analysis results and accounted for heterogeneity in that meta-analysis. When performing meta-regression in each layer of analysis, each covariate was first individually tested for an association with PI or adverse events; this was then repeated while controlling for comparative treatments. Only covariates significantly associated with PI or adverse events while controlling for the comparative treatments were progressed to multivariable analysis, where the effect of the variable of interest was assessed in the presence of other covariates. Meta-regression results were reported as effect estimate [95% confidence intervals], p-value, and the amount of heterogeneity accounted for from the original meta-analysis (R^2).

RESULTS: Sixteen studies with 943 total patients (mean follow-up: 7.7m, mean age: 40.8y, 78% females) were included. In meta-analysis, adverse events had insignificant heterogeneity (p=0.11) while PI had significant heterogeneity (I^2=92%, p<0.01), even when adjusted for comparative treatments. Primary, secondary, tertiary, and quaternary analyses included 16, 10, 14, and 9 studies, respectively. In meta-regression, injection guidance and corticosteroid type were not associated with adverse events or PI. Anesthetic dosage was associated with adverse events in primary analysis without adjusting for comparative treatments (p=0.035), but this did not hold in further analyses. Corticosteroid dosage was associated with PI in all four layers of analysis (adjusted for comparative treatment), accounting for 97-98% of heterogeneity in the original meta-analysis (p<0.001 for all). For example, in quaternary analysis, each 1 mg dosage increase was associated with a 0.12 point mean difference increase, indicating reduced CSI favorability over comparative treatment (Table 1). In multivariable analysis, corticosteroid dosage remained associated with PI in all four layers of analyses while controlling for comparative treatment and corticosteroid type, altogether accounting for 94-96% of heterogeneity (p<0.001 for all); other covariates could not be analyzed due to limited power.

DISCUSSION: Corticosteroid dosage-per-injection was associated with PI and accounted for heterogeneity in pooled results, with greater dose associated with reduced CSI favorability. This indicates that dosage could play a crucial role in outcomes, underscoring the need to optimize injection formulation. Notably, injection guidance, anesthetic dosage, and corticosteroid type were not independently associated with adverse events or PI. Future studies should directly investigate this dose-dependent relationship with sufficient power to conclu9sively determine the strength and degree of this association.

SIGNIFICANCE/CLINICAL RELEVANCE: This study assessed the effect of CSI configuration on outcomes for De Quervain's Tenosynovitis and investigated heterogeneity in prior literature. This study found higher corticosteroid dosage-per-injection to be associated with reduced CSI favorability.

IMAGES AND TABLES:

Table 1. Single covariate meta-regression investigating different covariates on pain improvement and adverse events.

	Without Adjusting for Comparative Treatment		Adjusting for Comparative Treatment	
Covariate	**Pain VAS Improvement**	**Any Adverse Events**	**Pain VAS Improvement**	**Any Adverse Events**
Primary Analysis				
Injection Guidance*	1.00 [-2.51-4.51], p=0.577, R^2=0%	-0.94 [-7.05-5.17], p=0.764, R^2=0%	NA	NA
Anesthetic Dosage per Injection (mg)	0.17 [-0.15-0.50], p=0.298, R^2=2%	**0.18 [0.01-0.35], p=0.035, R^2=100%**	NA	0.16 [-0.15-0.48], p=0.318, R^2=100%
Corticosteroid Name†	-0.25 [-2.51-2.01], p=0.826, R^2=0%	-0.24 [-2.31-1.83], p=0.820, R^2=0%	-1.07 [-4.02-1.88], p=0.476, R^2=24%	-2.99 [-6.05-0.07], p=0.056, R^2=100%
Corticosteroid Dosage per Injection (mg)	**0.09 [0.01-0.18], p=0.026, R^2=30%**	0.00 [-0.09-0.10], p=0.944, R^2=0%	**0.10 [0.06-0.14], p<0.001, R^2=98%**	0.00 [-0.16-0.16], p>0.99, R^2=54%
Secondary Analysis				
Injection Guidance	1.30 [-3.90-6.50], p=0.625, R^2=0%	-0.94 [-7.05-5.17], p=0.764, R^2=0%	NA	NA
Anesthetic Dosage per Injection (mg)	0.13 [-0.30-0.56], p=0.564, R^2=0%	NA	NA	NA
Corticosteroid Name	-0.03 [-2.71-2.65], p=0.980, R^2=0%	-0.65 [-3.72-2.41], p=0.676, R^2=0%	0.09 [-3.98-4.16], p=0.966, R^2=29%	-2.99 [-6.05-0.07], p=0.056, R^2=100%
Corticosteroid Dosage per Injection (mg)	0.09 [-0.00-0.18], p=0.053, R^2=26%	0.04 [-0.08-0.17], p=0.494, R^2=0%	**0.12 [0.06-0.18], p<0.001, R^2=98%**	0.00 [-0.18-0.18], p>0.99, R^2=0%
Tertiary Analysis				
Injection Guidance	1.00 [-2.51-4.51], p=0.577, R^2=0%	-0.94 [-7.05-5.17], p=0.764, R^2=0%	NA	NA
Anesthetic Dosage per Injection (mg)	0.17 [-0.15-0.50], p=0.298, R^2=2%	0.18 [-0.01-0.38], p=0.061, R^2=100%	NA	0.14 [-0.11-0.39], p=0.262, R^2=100%
Corticosteroid Name	0.15 [-2.26-2.57], p=0.901, R^2=0%	-0.54 [-2.64-1.57], p=0.618, R^2=0%	0.09 [-3.98-4.16], p=0.966, R^2=14%	-2.99 [-6.05-0.07], p=0.056, R^2=100%
Corticosteroid Dosage per Injection (mg)	0.11 [-0.01-0.23], p=0.062, R^2=22%	-0.00 [-0.10-0.09], p=0.951, R^2=0%	**0.12 [0.06-0.18], p<0.001, R^2=97%**	-0.00 [-0.16-0.16], p>0.99, R^2=21%
Sensitivity Analysis				
Injection Guidance	1.30 [-3.90-6.50], p=0.625, R^2=0%	-0.94 [-7.05-5.17], p=0.764, R^2=0%	NA	NA
Anesthetic Dosage per Injection (mg)	0.13 [-0.30-0.56], p=0.564, R^2=0%	NA	NA	NA
Corticosteroid Name	0.37 [-2.51-3.25], p=0.802, R^2=0%	-0.65 [-3.72-2.41], p=0.676, R^2=0%	0.09 [-3.98-4.16], p=0.966, R^2=31%	-2.99 [-6.05-0.07], p=0.056, R^2=100%
Corticosteroid Dosage per Injection (mg)	0.11 [-0.02-0.25], p=0.105, R^2=19%	0.04 [-0.08-0.17], p=0.494, R^2=0%	**0.12 [0.06-0.18], p<0.001, R^2=98%**	-0.00 [-0.18-0.18], p>0.99, R^2=0%

*Blind group used as reference for injection guidance
†Methylprednisolone acetate group used as reference for corticosteroid name
Significant findings are bolded. NA = Not Available.