

The Statistical Fragility of Platelet-Rich Plasma in Lateral Epicondylitis: A Systematic Review and Simulated Fragility Analysis of Randomized Controlled Trials

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INTRODUCTION:

Lateral epicondylitis (LE) is a common overuse injury that can lead to persisting physical disability and economic burden. By introducing high concentrations of platelets, cytokines, and growth factors, platelet-rich plasma (PRP) has been gaining popularity as a treatment of LE. However, randomized controlled trials (RCTs) have demonstrated varying support for the efficacy of PRP. Due to a small sample size in the literature and limitations of interpreting *P* values, we use a novel Continuous Fragility Index (CFI) and Quotient (CFQ) to assess the statistical robustness of PRP injections in the treatment of LE.

METHODS: RCTs comparing the outcomes of PRP injections to nonsurgical and surgical treatments were screened following PRIMSA guidelines. For studies reporting dichotomous outcomes, traditional fragility indices (FI) were calculated by using the Fisher exact test to determine reversal of significance ($\alpha=0.05$). For studies reporting continuous outcomes, data was simulated and the CFI was calculated by manipulating patient treatment assignments until statistical significance was reversed. CFQ and fragility index quotients (FQ) were determined by dividing the CFI and FI by corresponding sample size.

RESULTS: Of 485 studies screened, 20 RCTs representing 1,603 elbows were ultimately included in this analysis. In total, 83 outcome events were analyzed with 72 reporting continuous data. Of these, 21 were found to be statistically significant ($P<0.5$) with a median CFI of 7.4 and CFQ of 15.2%. Eleven outcome events utilized dichotomous data and it was determined that significant outcomes were statistically more fragile (median FI=3.7, FQ=3.6%) than non-significant outcomes (median FI=5.7, FQ=7.1%). Of 70 outcome events reporting lost to follow-up data, 16 (22.9%) had corresponding CFI or FI values that exceeded the number of patients lost.

DISCUSSION AND CONCLUSION: Our analysis suggests that RCTs evaluating the efficacy of PRP injections for management of LE may possess substantial fragility. Thus, measures of fragility should be interpreted alongside *P* values to aid in clinical decision making. The ability to simulate data in the setting of continuous outcomes markedly increased the scope of this analysis and facilitated broader conclusions regarding the fragility surrounding the efficacy of PRP in LE treatment.