The Statistical Fragility of Platelet-Rich Plasma as Treatment for Plantar Fasciitis: A Systematic Review and Fragility-Analysis

Arjun Gupta, Carlos David Ortiz-Babilonia, Amy Li Xu, Davis Rogers, Ettore Vulcano, Amiethab Aiyer

INTRODUCTION:

Plantar fasciitis (PF) is estimated to account for 8% of all running-related injuries, affecting nearly 1 out of every 10 adults aged 50 and older. Recent randomized controlled trials (RCTs) suggest platelet-rich plasma (PRP) injection may be an effective nonsurgical treatment option for chronic, refractory PF. However, RCTs in general have come under scrutiny due to a frequent lack of reproducibility, which is largely attributable to shortcomings of the commonly used $p<0.05$ threshold for significance. Fragility indices may be an appropriate tool to gauge the clinical importance of RCT findings in these situations. In this study, we utilize the continuous fragility index (CFI) and continuous fragility quotient (CFQ) to determine the statistical robustness of data from RCTs evaluating PRP for PF.

METHODS:

RCTs comparing outcomes after PRP injection versus other conservative treatment in chronic PF patients were evaluated. Representative datasets were generated for each reported outcome event using summary statistics. The CFI was determined by manipulating each dataset until reversal of significance ($a=0.05$) was achieved. The corresponding CFQ was calculated by dividing the CFI by the sample size.

RESULTS:

Of 259 studies screened, 27 studies (59 outcome events) were included in this analysis. The median CFI for all events was 9 (CFQ=0.177), suggesting that altering the treatment of only 9 patients (or 17.7 out of 100) would be sufficient to reverse trial significance **(Table 1)**. Of the 36 outcome events reporting lost to follow-up data, 10 events (27.8%) lost ≥9 patients. Outcome events that were originally reported as significant ($p<0.05$) were considerably more fragile (CFI=5; CFQ=0.122) than events that were reported as nonsignificant (CFI=10; CFQ=0.179).

DISCUSSION AND CONCLUSION:

Fragility indices are a useful adjunct to p-values and provide an assessment of how easily statistical significance can be overturned. While there is some preliminary evidence supporting the clinical efficacy of PRP, our fragility analysis suggests that RCT findings may be underpowered in some cases. Over 27% of outcome events may have experienced a reversal of significance if the studies had simply maintained follow up. Given the importance of RCTs in clinical decision making, fragility indices should be reported alongside p-values to indicate the strength of statistical findings.

Table 1. Fragility Index and Quotient Data Based on Trial Characteristics

Characteristic	Events	Patients, n	Lost FU, n	CFI, Median (IQR)	CFQ, Median (IQR)
All trials	59	3539	255	9 (4.5–14)	0.177 (0.125–0.203)
Outcome					
VAS pain	20	1243	83	9 (4.75–14.25)	0.172 (0.121–0.213)
VAS function	1	36	0	7 (7–7)	0.194 (0.194–0.194)
AOFAS	9	624	66	9 (5–10)	0.150 (0.100–0.225)
PF thickness	6	296	22	6 (5–10)	0.128 (0.097–0.198)
FFI disability	7	423	45	14 (4–16)	0.200 (0.114–0.203)
FFI activity	6	369	35	12.5 (6.5–14.75)	0.185 (0.166–0.197)
FADI	1	28	4	3 (3–3)	0.107 (0.107–0.107)
R&M	4	220	0	10 (6.5–12.25)	0.181 (0.133–0.209)
HTI	1	60	0	12 (12–12)	0.200 (0.200–0.200)
FAI core scale	2	160	0	10 (10–10)	0.125 (0.125–0.125)
FHSQ	2	80	0	6.5 (5.25–7.75)	0.157 (0.145–0.168)
Reported p-value					
$p < 0.05$	20	1329	169	5 (3.75–14.5)	0.122 (0.062–0.241)
$p > 0.05$	39	2210	86	10 (5–14)	0.179 (0.133–0.201)

(FU: follow-up; CFI: continuous fragility index; CFQ: continuous fragility quotient; VAS: visual analogue scale; AOFAS: American Orthopedic Foot and Ankle Society score; PF: plantar fascia; FFI: foot function index; FADI: foot and ankle disability index; R&D: Roles and Maudsley scale; HTI: heel tenderness index; FAI: foot and ankle instrument; FHSQ: foot health status questionnaire)