Appendix 2 (as supplied by the authors): Information on sample size estimation, minimally important difference and application of cumulative distribution functions approach

Sample size estimation

According to a priori sample size estimation (80% power and 5% significant level), this trial could detect a difference of 0.3 or greater in the symptom severity scale (assumed Standard Deviation (SD) of 0.7) between the two groups when 156 patients were randomly assigned. We aimed to enrol 181 patients to compensate for withdrawals. Details are as follow:

The primary outcome measure was the final Symptom Severity Score (SSS) of Boston Carpal Tunnel Questionnaire (BCTQ) that range from 1 to 5. The primary analysis was to compare the SSS score between 1) the acupuncture and splinting arm and 2) waiting list plus splinting arm. We found no previous study that used the BCTQ as an outcome measure for evaluating the effect of electroacupuncture for CTS. Therefore we were unable to plan our sample size based on previous studies directly.

A recent systematic review suggested that splinting improves symptoms in a modest fashion at 4 weeks (weighted mean difference: -1.07, 95% CI: -1.29 to -0.85) (1). In two randomized trials that evaluated the effect of night splint with BCTQ, SSS change is found to be 0.33 (SD: 0.85) and 0.59 (SD: 0.51) respectively (2) (3). Thus, we may assume that a SSS score change ranging from 0.33 to 0.59 would represents a modest improvement in symptoms that is clinically relevant.

Conservatively speaking, if we assume that acupuncture would only exert a similarly modest improvement in symptoms, then we may expect that the SSS difference between night splint plus acupuncture group and night splint plus waiting list group would approximately be 0.30 at 17^{th} week, with a standard deviation of 0.70.

Consider 80% power to detect a 0.30 SSS score change with standard deviation 0.70 which is equivalent to a one-sided 5% level test by normal approximation, and a superiority margin of 0.02 (5% of the expected mean change) the calculated sample size is 91 per treatment arm after adjustments for a 15% expected drop-out rate. The total sample size for the whole study will therefore be 181 CTS patients (4):

Sample size calculation method

α: Type I error

β: Type II error

Appendix to: Chung VCH, Ho RST, Liu S, et al. Electroacupuncture and splinting versus splinting alone to treat carpal tunnel syndrome: a randomized controlled trial. *CMAJ* 2016. DOI:10.1503/cmaj.151003.
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1-β: Power
d: Value of allowable difference
δ: Superiority margin
σ: Expected standard deviation
r: drop out rate

Given $\alpha = 0.05$, $1-\beta = 0.80$, $d = 0.30$, $\delta = 0.02$ and $\sigma = 0.70$,

Sample size per group: $n = \frac{2(z_{1-\alpha} + z_{1-\beta})^2 \sigma^2}{(d-\delta)^2}$

which is equivalent to a two sample one-sided test at 5% significant level. Consider *r* = 15%, we multiplied a factor 1/(1-*r*) on sample size, finally we estimated that a total sample size of 181 was needed.

Statistical analysis

Baseline characteristics of participants were descriptively analysed by intervention groups. The 95% confidence intervals (CI) for the differences in mean score changes from baseline to different scheduled visits were drawn for the two treatment groups respectively. To investigate the treatment difference, the estimated effects (95% CI and two-sided p-values) on the scores were assessed by ANCOVA. Multiple imputations for missing data were employed for all inferential analyses (5). The level of significance was set as $p<0.05$. All analysis was carried out with the SAS software, version 9.4 (SAS Inc, Cary, NC). Previous acupuncture use was not controlled in the analysis as prevalence of acupuncture usage is very high among Chinese population, and they may have a different perception on acupuncture as compared to western population (6).

Minimally importance difference and application of cumulative distribution functions approach

When estimated using anchor based approaches, the minimally important difference of Symptom Severity Scale and Disabilities of the Arm, Shoulder and Hand Questionnaire for non-surgical treatment varies widely according to settings and treatment received (Symptom Severity Scale: 0.23 to 1.04; Disabilities of the Arm, Shoulder and Hand Questionnaire: 3.9 to 20). Also, minimally important difference values for Functional Status Scale and Dellon-Modified Moberg Pick-Up Test completion time was unavailable (7). Hence, a distribution based approach is followed (8), of which the minimally important differences of Symptom Severity Scale,

Functional Status Scale and Dellon-Modified Moberg Pick-Up Test completion time were set at half a standard deviation (SD) of their baseline values (9).

Cumulative distribution functions with x axis indicating Symptom Severity Scale, Functional Status Scale and Dellon-Modified Moberg Pick-Up Test completion time changes and y axis denoting the cumulative proportion of patients achieving such level of changes were plotted. This approach allowed us to illustrate the entire distribution of treatment effect across both groups by showing a continuous plot of the proportion of participants reaching a certain level of change or lower, including those reaching the minimally important difference. The cumulative distribution functions approach provides the benefit of visualizing separation between treatment and control group across all levels of change, and evidence for effectiveness is shown by larger separation of the cumulative distribution functions (10). The cumulative distribution functions approach was also used to illustrate changes in pain, maximal tip pinch strength and Semmes-Weinstein Monofilament Test. For pain, we followed the IMMPACT recommended minimally important difference of 2 on the Numerical Rating Scale (11). The minimally important difference for maximal tip pinch strength and Semmes-Weinstein Monofilament Test sensation diameter were set at 1.66 lbs and 0.3mm, respectively (7).

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