The Efficacy of Cryoneurolysis on Chronic Pain in Patients with Knee Osteoarthritis; A Double-blinded Randomized Controlled Sham Trial

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Analysis plan

To assess the distribution of continuous outcomes, a visual inspection of the studentized residuals was performed to determine if the assumption of normality was appropriate. Both an Intention-To-Treat (ITT) analysis and a per-protocol (PP) analysis were conducted for all assigned patients. Mixed linear regression with the assumption of unstructured covariance was employed to model the effect of cryoneurolysis treatment over time, accounting for repeated measures by treating individuals as random variables. Fixed effects included time, treatment group, baseline pain levels, and the interaction between group and time, to estimate changes over time. The results are presented as predicted average values and predicted differences between groups, representing the estimated outcomes for each group while considering random effects and covariates included in the model. These are illustrated using marginal effects calculated with the margins command in Stata16. A P-value of less than 0.05 was considered statistically significant. For the primary outcome—average pain over 24 hours on the numeric rating scale—the p-value was adjusted for multiple comparisons (k=9) using the Holm-Bonferroni correction for the mixed effects model. Secondary outcomes were not adjusted, as these were exploratory in nature.