Endoscopic sinus surgery (ESS) to change quality of life for adults with recurrent rhinosinusitis

Statistical analysis plan

04.09.2020

Statistical methods for primary and secondary outcomes

To describe the data the following methods will be used. Data for normal distribution will be presented as mean and standard deviation (SD). Variables for skewed distributions will be described as median and interquartile range. Categorical variables will be expressed as frequencies with percentages.

The primary and secondary outcomes, measures and planned statistical analyses are displayed in Table 2. Our primary outcome is the difference between the average change in SNOT-22 scores from baseline to six months between the ESS and control groups. If the average baseline scores happen to be different between the two groups, comparison of the follow-up scores or change scores will lead to under- or overestimation of the treatment effect. Therefore, the analysis of covariance will be used where possible baseline imbalances are controlled for. The estimate for difference between the means will be calculated with 95% confidence intervals. Statistical significance will not be presented for secondary outcomes to avoid multicomparison problem.

Table 2. Variables, measures and planned statistical analyses. ESS= endoscopic sinus surgery, SNOT-22= Sinonasal outcome test quality of life questionnaire, RAND 36 = Research and Development 36 Item Health Survey, MIC = minimal clinically important change, CI = confidence interval, NNT= number needed to treat

Variable/Outcome	Hypothesis	Outcome measure	Method of analysis

Primary outcome	ESS improves outcome from baseline to 6 months	Difference between the mean SNOT-22 change scores of ESS and control group	Analysis of covariance, estimate for difference between means with 95% CI (adjusted age (≤50 vs. >50 years), sex and allergy status (yes vs, no))
Secondary outcomes			
General QoL change	Improvement occurs	Difference between the mean RAND-36 change scores of ESS and control group	Analysis of covariance
Proportion benefiting	Improvement occurs	Difference in proportions benefiting (SNOT-22 > MIC) in ESS and control group	Chi-squared test, Risk ratio with 95% CI, NNT
No. of episodes, visits, antibiotic courses, sick days	Improvement occurs	Difference in number of episodes, visits, antibiotic courses and sick days in ESS and control group	Difference in means with 95% CI
No. of symptomatic days	Improvement occurs	Difference in no. of days with nasal obstruction, nasal discharge, facial pain/pressure, and fever in ESS and control group	Difference in means with 95% CI
No. of postoperative complications	Improvement occurs	Frequency of postoperative synechia formations, infections, nasal pain, bleeding,	Number (%)

	and orbital and intracranial complications

Methods for additional analyses (e.g. subgroup and adjusted analyses)

We plan to conduct two subgroup analyses. We know that both age and sex will probably affect quality of life and medical care seeking. Firstly, we will compare the estimates for difference between the mean SNOT-22 scores between the ESS and control groups both in males and females. Secondly, we will do the same analysis in participants aged ≤50 and >50 years of age. We anticipate that the treatment effect will be larger among both females and younger participants.

If there is imbalance in baseline variables (age, sex, allergy status) between groups, we also perform adjusted analyses by including the following baseline variables in the analysis of covariance: age (≤50 vs. >50 years), sex, and allergy status (yes vs. no).

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data

An “as randomised” analysis is performed which retains participants in the group to which they were originally allocated (intention to treat principle). Outcome data obtained from all participants are included in the data analysis, regardless of protocol adherence. Per protocol analysis will be performed as sensitivity analysis. In case there is missing data on the primary outcome, a multiple imputation method will be used.