**STATISTICAL ANALYSIS**

Statistical analysis will be performed using Rstudio software. Descriptive analysis will be carried out for baseline characteristics: age, gender, ASA-classification, intoxications and co-morbidities. Also length of surgery and used anaesthetic technique of both groups will be described. Nominal and ordinal data will be presented by number and percentage. Continuous data will be presented depending on normal distribution with either mean and standard deviation or (in case of no normal distribution) median with range.

Inferential statistics will be performed for both primary and secondary outcomes. We will determine if data is normally distributed or not and do statistical analysis accordingly. In case of normal distribution we will use an unpaired t-test. In case of a non normal distribution we will perform a log transformation on the data, however, if still no normal distribution we will use the non parametric test Mann Whitney U (Wilcoxon rank sum). P values <0.05 will be considered significant. P values will be calculated with various tests depending on presence of normal distribution or not.

Statistical analysis will be based on an intention-to-treat analysis.

Missing data will be described thoroughly, and will be investigated on whether it is missing completely at random (MCAR), missing at random (MAR) or not missing at random (NMAR). In case patients received treatment the data known will be used in analysis. We expect to not have many missing data due to the follow up by phone. We expect that in case of missing data this will be completely at random. Therefore, we chose not to use imputating techniques but listwise deletion in case of missing data. In case there is more missing than 5% or a suspicion of MAR, we will rethink the use of imputating techniques.

**Primary study parameter(s)**

The primary outcome will be the mean VAS (1-100) between the two groups at day 1 after surgery. Pain scores are ordinal data and therefore a non parametric test should be used. However, one can discuss whether the VAS can’t be interpreted as continuous data, and therefore (if normally distributed) parametric tests can be used with more statistical power. Here we decided to treat VAS as continuous data and therefore use parametric test, the unpaired t-test..
**Secondary study parameter(s)**

- Pain scores (VAS 1-100) direct postoperatively, before discharge and in following 3 days postoperative. Ordinal data, but like with the primary outcome we will treat VAS as continuous data and therefore in case of normal distribution unpaired t test. Time to first necessity of pain medication after surgery. Continuous data, two groups; depending on normal distribution unpaired t test or Mann Whitney U.
- Cumulative consumption of in hospital opiates. Continuous data, two groups; depending on normal distribution unpaired t test or Mann Whitney U.
- Time to discharge. Continuous data, two groups; time to event; Kaplan Meier analysis.
- Analgesic medication taken at home by patient. Continuous data, two groups; depending on normal distribution unpaired t test or Mann Whitney U.
- Adverse effect of analgesic medication (nausea, obstipation, sedation) Dichotomous data, unpaired and 2 groups; Fisher exact.
- Safety of intravenous NAC 150 mg/kg in terms of nausea, vomiting, anaphylactoid or allergic reactions (presenting as dyspnea, urticaria)

**Interim analysis (if applicable)**

there will be no interim analysis.