Contact Activation of Coagulation in Newly Inserted Central Venous Catheters (CAS-2) – a randomised controlled study

NCT number: NCT07014722

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STATISTICAL ANALYSIS PLAN FOR CAS-2

VERSION 2.1

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1. Study Design and Aims

This is a randomized, controlled trial evaluating coagulation activation in blood from four different central venous catheters (CVCs) using established laboratory methods. The primary aim is to investigate if four commonly used CVCs, with similar inner surface area, demonstrate different coagulation activation measured with clotting time (CT) in the ROTEM assay NATEM. Secondary aims include, but are not limited to, investigating if the four CVCs demonstrate different coagulation activation measured with additional ROTEM variables and coagulation markers, and if Sample 1 exhibits coagulation activation compared to Sample 2 within each CVC group, between CVC groups and in overall cohort. Blood samples will be drawn at two time points per catheter and analysed for coagulation markers. Sample 1 will be collected within seconds after the catheter insertion and Sample 2 after flush and discard of blood.

2. Study Groups

Participants will be randomized to receive one of four commonly used CVCs with similar inner surface area.

Each group will consist of 22 individuals based on sample size calculations.

3. Primary Outcome

- Change in CT (ΔCT) between Sample 1 and Sample 2 across the four CVCs.

4. Secondary Outcomes

- Change in additional ROTEM variables (Δadditional ROTEM variables) between Sample 1 and Sample 2 across the four CVCs.
- Change in additional coagulation markers (Δadditional coagulation markers) between Sample 1 and Sample 2 across the four CVCs.

- Differences between Sample 1 and Sample 2 for all ROTEM variables and coagulation markers within each CVC group and in the overall cohort irrespective of CVC group.

5. Sample Size Calculation

- Based on prior data (ΔCT = 450s, SD = 152s), a one-way ANOVA with assumed group means of 450s, 275s, 350s, and 400s required n = 17 per group for 80% power at $\alpha = 0.05$.
- To account for likely non-normality and analysis failure, the sample size was increased to n = 22 per group (total 88 individuals).

6. Statistical Methods

Analyses will be conducted according to the intention-to-treat principle. Continuous variables with a symmetrical distribution will be reported as mean (SD), whereas skewed variables will be summarized as median (IQR). Categorical variables will be presented as number (percentage).

Between-group comparisons, including differences in ΔCT and other coagulation markers among the CVC groups, will be analysed using the Kruskal–Wallis test with Dunn's post hoc test when data are not normally distributed. If normality is confirmed, a one-way ANOVA with Tukey's post hoc test will be applied.

Comparisons between Sample 1 and Sample 2 will be performed using the Wilcoxon matched-pairs signed-rank test for non-normally distributed data, and the paired t-test when data meet the assumption of normality

Data will be analysed using available cases. If appropriate, simple or multiple imputation methods may be applied, and any approach used will be reported in the final analysis.

For the primary outcome, a p-value < 0.05 will be considered statistically significant, as predefined in the sample size calculation. For secondary outcomes, correction for multiple testing will be performed. An adjusted significance level of $p < 0.01$ will be applied,

representing a modified Bonferroni correction that accounts for the fact that the tested variables are not fully independent of each other.

7. Software

- GraphPad Prism 10.2.2 for statistical analysis and visualization.
- SAS Proc Power (version 9.4) for sample size determination.
- REDCap (Research Electronic Data Capture) for data collection and randomization.