PERFEQTOS – Statistical Analysis Plan

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Introduction

This document summarizes the statistical analysis plan of the PERFEQTOS (Performance feedback on the quality of care in hospitals performing thrombectomy for ischemic stroke) trial. This document should be read as an adjunct to the study protocol, which has previously been published [1].

Aim of PERFEQTOS

This study aims to assess the extent to which performance feedback to healthcare providers in individual hospitals providing endovascular thrombectomy (EVT) for ischemic stroke, resulting in action plans and targets based on this feedback, reduces time from arrival at the hospital to initiation of EVT and thereby improves the quality of care.

Trial Design

PERFEQTOS is a stepped wedge cluster randomized trial (CRT) of performance feedback on the quality of care in hospitals performing EVT for ischemic stroke to determine the impact of a performance feedback intervention accompanying hospital-specific action plans and improvement targets. This is a specific RCT – design in which initially all clusters (in this study: hospitals) serve as controls. The intervention is randomly rolled out at different, prespecified time points, such that at the end of the study all clusters have crossed over to the intervention condition (Fig. 1)[2].

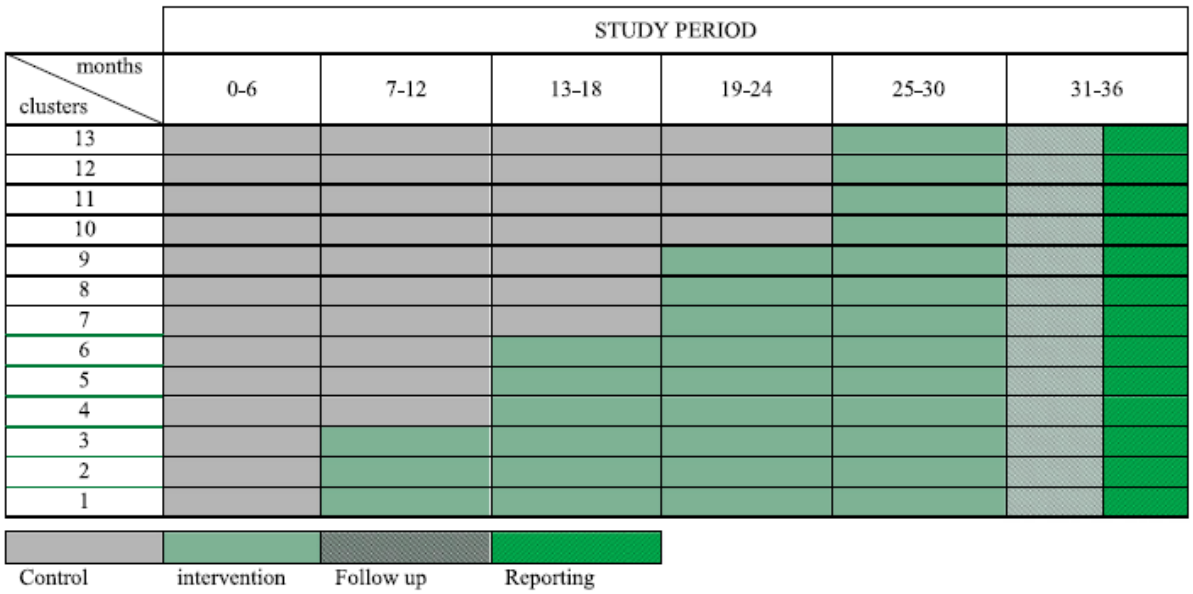

Fig. 1 SPIRIT figure. Schematic visualization of stepped wedge cluster randomized trial control and intervention allocation, follow-up, and reporting of the study

Intervention

The feedback intervention consists of a dashboard with quarterly reports on patient characteristics, structure, process, and outcome indicators related to patients with ischemic stroke treated with EVT. Hospitals can compare their present performance with their own performance in the past and with other hospitals. The performance feedback is provided to local quality improvement teams in each hospital, who define their own targets on specific indicators and develop performance improvement plans.

Study setting and participants

The study will be carried out in specialized hospitals performing EVT for ischemic stroke. In the Netherlands, EVT is concentrated in 17 such specialized hospitals [3]. All EVT hospitals are invited to participate in this trial with no specific inclusion or exclusion criteria. Thirteen out of these 17 hospitals agreed to participate in the study. The participating hospitals include all admitted adult patients with acute ischemic stroke who underwent EVT.

Data collection and management

Data on patient characteristics, care process, and outcomes are routinely collected in each hospital and reported to the Dutch Acute Stroke Audit (DASA) from the Dutch Institute of Clinical Auditing (DICA)[4]. DASA is the main prospective clinical auditing tool for stroke in The Netherlands since 2014, with the aim to assure the quality of patient care and to aid in improving outcomes.Hospitals participating in the DASA send their data to a trusted third party, the Medical Research Data Management (MRDM), which de-identify the data for DICA to comply with privacy legislation. For this study, the participating hospitals gave permission to the MRDM to provide de-identified data to the study coordinator.

Questionnaire

All Local Principal Investigators of the participating hospitals will be asked to fill out a questionnaire every 6 months. These questionnaires will summarize the activities of the quality improvement teams and help us understand how the dashboard has been used to formulate and implement improvement plans. The questionnaires will provide insight in the achieved contrast between intervention and control and will help to interpret the effect estimates of the intervention on the primary and secondary outcomes.

Outcomes

Primary outcome

The primary outcome is the door-to-groin time, which is defined as the time from arrival at the Emergency Room (ER) in the intervention hospital to groin puncture by the neurointerventionalist.

Secondary outcomes

The secondary outcomes are as follows:

- The door-to-needle time, which is defined as the time from arrival at the ER in the center of primary presentation to treatment with alteplase.
- The expanded treatment in cerebral infarction (eTICI) score assessed directly post-EVT on DSA imaging, where a higher score represents better reperfusion (0 no reperfusion – 3 complete reperfusion).
- Score on the National Institute of Health Stroke Scale (NIHSS) assessed at 24 hours, with a greater score representing more severe neurological deficit (0 no symptoms – 42 death).
- Score on the modified Rankin Scale (mRS) assessed at 3 months, with a higher score corresponding with less functional independence (0 no symptoms – 6 death).

These outcomes are collected for every individual patient. The analyses will provide insight on whether providing performance feedback results in faster treatment times and better radiological, clinical and functional outcomes.

Power calculation

The power calculation was based on mean differences in door-to-groin time as a primary outcome. We used a parametric power estimation methodology for stepped wedge designs put forward by Hemming and Girling [5] in the Stata function stepped wedge, derived from Hussy and Hughes [6]. We assumed 13 EVT centers were randomized in four clusters per time step (three clusters of three hospitals and one cluster of four hospitals) that treated an average of 30 patients per center per time period of 3 months [7]. We used a mean door-to-groin time of 77 min (standard deviation 47 min) and intra-cluster correlation (ICC) of 0.37, both obtained from the MR CLEAN Registry data [7, 8]. Assuming a significance level of 5%, this would result in 88% power to detect a clinically relevant reduction of door-to-groin time of 10 min.

Statistical analysis

The effect of the performance feedback intervention on the primary outcome will be estimated with a multivariable linear mixed model and expressed as beta and 95% confidence interval. This will allow us to account for the different observation cluster periods (both control and intervention) and the hierarchical structure of the data [6]. The model will contain fixed effects for intervention (yes/no), calendar time (month) to account for autonomous time trends, patient characteristics (i.e., patients' age, sex, NIHSS score at arrival, location of the proximal intracranial occlusion, and onset-to-door time) [6], and a random effect for the hospital. Adjusted and unadjusted effect estimates with corresponding 95% confidence intervals will be reported, with the adjusted effect as the primary effect parameter.

The same approach will be taken for the analysis of the secondary outcomes, using linear models for the continuous outcomes and generalized linear models for the ordinal outcomes.

Missing values will be imputed with multiple imputation with 5 iterations, using available data on patient characteristics, structure, and care processes.

Statistical analyses will be performed with R version 4.2.1. The lme4 package will be used for performing mixed modeling and the Hmisc package will be used for performing multiple imputations. A p value of less than 0.05 will be considered as statistically significant.

Database closure and time path of the analysis

Following completion of the trial, a 6-month period will be reserved for hospitals to report remaining 3-month mRS scores and other missing data. After this period, DICA/MRDM will hand over the database with de-identified data to Erasmus MC. After a final check, the database will be locked by study coordinator #1. The final analysis will be performed by study coordinator #1 under supervision of the study's methodologist and the principal investigator. A check for consistency and adherence to the study protocol and SAP will be done by the study coordinator #2. The final results will then be shared for consideration with the Steering Committee. Within six months after obtaining the final results, a manuscript describing the main results of the trial will be submitted for publication in a scientific medical journal. The syntax and output will be made available upon request.

References

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