

Supplemental Online Content

Hubert GJ, Hubert ND, Maegerlein C, et al. Association Between Use of a Flying Intervention Team vs Patient Interhospital Transfer and Time to Endovascular Thrombectomy Among Patients With Acute Ischemic Stroke in Nonurban Germany. *JAMA*. Published online May 5, 2022. doi:10.1001/jama.2022.5948

Supplement 2. **Statistical analysis plan**

This supplemental material has been provided by the authors to give readers additional information about their work.

Statistical Analysis Plan

“Flying Intervention Team for Endovascular Treatment of Acute Ischemic Stroke in Rural Areas”

1. Objective

The aim of the study is to determine whether endovascular therapy (EVT) after transfer to a primary stroke center by the Flying Intervention Team (FIT) can be initiated more quickly than EVT after interhospital transfer.

Analysis of the secondary endpoints will show whether there are relevant differences in clinical outcome at 3 months as well as differences in other procedural and safety parameters between the two systems of care.

2. Study population

a. FIT registry

All patients with acute ischemic stroke, admitted to one of the participating primary stroke centers who are

- approached by a Flying Intervention Team for the performance of EVT
- transferred to an intervention center for the performance of EVT
- transferred for perfusion or other advanced imaging (to establish eligibility for EVT)

are included in the FIT registry.

b. Inclusion and exclusion criteria

Patients enrolled in the FIT registry who also meet the following eligibility criteria are included in the study.

Inclusion criteria:

- i) Admission to participating primary stroke center between February 1, 2018 and October 24, 2019
- ii) Aged between 18 and 85 years
- iii) Evidence of vessel occlusion of the middle cerebral artery (M1 or proximal M2), intracranial internal carotid artery or basilar artery
- iv) Time window from symptom onset to decision for thrombectomy: 0-6h for anterior circulation occlusions, 0-24h for basilar artery occlusions, and 0-24h for anterior circulation occlusions with evidence of appropriate mismatch of on-site perfusion imaging
- v) Decision for thrombectomy between 8.00am and 10.00pm
- vi) Performance of EVT (use of at least one thrombectomy device)

Exclusion criteria:

- vii) ASPECTS < 6 (Alberta Stroke Program Early CT Score; scale of 0-10: 10 = irreversible damage not visible in any of the ten defined brain areas, 0 = irreversible damage visible in all ten defined brain areas)

- viii) Premorbid functional status (need of assistance in everyday life) or more specifically a score >3 on the modified Rankin Scale (mRS)
- ix) Severe pre-existing conditions with significantly increased mortality (acute myocardial infarction <7 days, severe heart failure, severe tumor disease, etc.)
- x) Transfer for advanced imaging
- xi) Scheduled system of care (Flying Intervention Team / interhospital transfer) not available

3. Groups / study arms

Patients who received EVT by a Flying Intervention Team at the primary stroke center are compared with patients who received EVT after secondary transfer to a comprehensive stroke center.

4. Variables of interest

Primary endpoint:

Time between decision for thrombectomy and groin puncture (decision to groin).

Secondary procedural outcomes:

- Time from onset or last seen well to groin puncture
- Time from arrival in primary stroke center to groin puncture
- Time from first imaging to groin puncture
- Time from onset or last seen well to recanalization
- Time from arrival in primary stroke center to recanalization
- Time from first imaging to recanalization
- Time from decision for thrombectomy to recanalization
- Time from groin puncture to recanalization

- Decision to groin puncture < 60 minutes
- Decision to groin puncture < 120 minutes
- Decision to groin puncture < 180 minutes
- Decision to groin puncture < 240 minutes

Secondary clinical outcomes:

- Successful recanalization (mTICI $> 2b$)

Periprocedural complications

- Intracranial perforation
- Distal embolisation
- Arterial dissection

In-hospital complications

- Symptomatic ICH
- Asymptomatic ICH
- Malignant brain swelling
- New ischemic stroke
- Extracranial hemorrhage
- Death or palliative care within 7 days

Outcome after 3 months

- modified Rankin scale after 3 months (Shift analysis)
- Good Outcome after 3 months (modified Rankin scale < 3)
- Mortality after 3 months

Baseline characteristics to be described

- Age
- Sex
- Atrial fibrillation
- Hypertension
- Diabetes mellitus
- History of stroke
- History of myocardial infarction
- NIHSS score
- tPA treatment in primary stroke center
- Occlusion site
- Aetiology
- Onset-Door
- Door-CT
- CT-Decision
- Distance to center

5. Biometrical evaluation

Baseline characteristics, process times as well as clinical and procedural outcomes are presented descriptively, stratified by system of care. Thereby, categorical variables are described by absolute and relative frequencies. Continuous variables are represented by median and 1st and 3rd quartiles.

Standard statistical procedures (χ^2 -test, Mann-Whitney U test) are used to examine whether patients differ in baseline data, process times (including primary endpoint), and other outcomes within the two systems of care.

To prevent bias due to a possible imbalance of relevant parameters, analyses of functional outcome (modified Rankin Scale at 3 months) and, if applicable, other clinical outcomes are performed with and without adjustment for relevant parameters (age, sex, NIHSS).

For analyzing the functional outcome (mRS), severe disability (5) and death (6) are combined in a single worst category. An ordinal logistic regression (SHIFT analysis) is performed, if the model assumptions ("proportional odds assumption") are fulfilled accordingly. Otherwise, a binary approach is used (logistic regressions with mRS cut-off at <2, <3, and <4).

P-values < 0.05 are considered significant.