

## 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

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

## **eMethods.**

### *Quality criteria telestroke network TEMPiS*

The telestroke network provides 24 primary stroke centers with specialized stroke care. A 24/7 telemedical service is installed to conduct acute stroke examinations via bidirectional videoconference and give advice on further treatment. Each hospital receives audit visits by comprehensive stroke center staff to control for process and treatment quality. Medical audit visits: 2x/year, therapy visits (physiotherapy, occupational therapy and speech and language therapy): 1x/year each, nurse visits: 5x/year. Standard operating procedures on stroke care are created for the network and updated every 1-2 years. Data collection on treatment quality of all hospitals are gathered and analyzed 1x/year (external state-wide registry, network specific registry).

### *Requirements of flying intervention team hospitals*

Eligibility criteria for participating in flying intervention team service were the following:

#### Stroke Unit

- Hospitals had to be part of the TEMPiS network and fulfill the criteria set up by the network for high quality stroke care
- Hospitals had to have a Stroke Unit with monitoring units and non-monitoring beds, specialized nursing care, specialized therapists, telemedical assistance by a stroke physician, quality ensuring measures
- Hospitals had to have experience in treating stroke patients for at least 3 years
- TEMPiS network needed to approve participation based on annual results of external quality indicators of stroke unit treatment

#### Adjacent departments/expertise obligatory onsite:

- Emergency unit
- Intensive care unit
- Anesthesia, cardiology or internal medicine, radiology

#### Adjacent expertise onsite or in cooperation with other hospitals

- Vascular surgery
- Neurosurgery
- Stroke rehabilitation

#### Angiography suite

- Mono- or biplanar angiography
- DSA and/or road map function
- Size of suite suitable for intervention team and anesthesia team
- Availability of angiographic assistance from 8am-10pm
- Availability of anesthetist and anesthetic nurse from 8am-10pm

#### Helicopter pads.

- Helicopter pad at the hospital or nearby which was approved by “Bayerisches Luftamt Süd” (Bavarian air traffic authority) and fulfilled the criteria of a “public interest site” (PIS) or §6 helicopter pad and was therefore authorized to be used for helicopter emergency flight landings at all hours of the day
- Authorization by “Bayerisches Luftamt Süd” of the helicopter pad to be used for the flights within this project
- Availability of immediate transport of flying team from helicopter pad to hospital, if helicopter pad was not on hospital grounds (hospital private transfer)

### *Requirements for hospitals performing EVT for network patients*

Standards for regional EVT capable hospitals to qualify for patient transfer:

- Long lasting high quality stroke unit
- 24h EVT service
- > 60 EVT performed/year
- Intensive care unit with daily neurological ward round
- Anesthetic department
- CT, CT-A, CT-P
- Angiography suite
- Serving as region wide EVT provider
-

### *Requirements for Flying Interventionists*

Requirements were based on the criteria of the “German Society of Interventional Radiology and Minimal Invasive Therapy”, certification criteria module E:

- Radiology specialization
- Several years of experience in a center with neurointerventions
- > 100 vessel re-opening neurointerventions (of which at least 30 included mechanical thrombectomy)

### *Requirements for helicopter team*

Flights had to be performed prompt and at day- and night-time but no instrumental flights had to be provided in this project

- Position of helicopter/hangar had to be within short distance to the two comprehensive stroke centers pick up hospitals, so that team could be picked up within 15 minutes (defined as alarm of helicopter to start at comprehensive stroke center with flying intervention team on board)
- Technical equipment and pilot training sufficient for flights after dusk
- Flights always had to be performed by pilot and co-pilot
- Response time of call of <1 minute

### *Requirements for Flying Intervention Team deployment*

Luggage content, brought along with each deployment, included enough material to perform three interventions without returning home. It included (among others):

<b>Item:</b>	<b>Quantity</b>
Sheaths	8
Guide catheters	9
Balloons	4
Diagnostic catheters	6
Wires	14
Micro-catheter	6
Aspiration pump	1
Aspiration catheters	6
Stent retrievers	6
Puncture site closure system	4
<b>Rescue material:</b>	
Coils	5
Stents	9
<b>Medication:</b>	
Tirofiban, Heparin, Nimodipin	

**eFigure 1. Suitcase and traveling bags with interventional material brought along by the Flying Intervention Team with each deployment**



**eFigure 2. Angiography kit stored locally to be prepared by onsite staff before arrival of Flying Intervention Team**



### *Patient eligibility criteria for Flying Intervention Team deployment*

According to network standard operating procedures, patients with one or more of the following characteristics were not eligible for deployment of the flying team:

- age <18 or >85 years
- main target occlusion other than intracranial internal carotid artery, middle cerebral artery (M1 or proximal M2) or basilar artery
- presentation outside defined time window from stroke onset (>6h for anterior circulation occlusion without possibility of advanced imaging in primary stroke center, >24h for posterior circulation occlusion or anterior circulation with mismatch in advanced imaging)
- ASPECT-Score <6
- severely reduced life expectancy
- premorbid modified Rankin Scale (mRS) >3.

### *Standard operating procedures for EVT by Flying Intervention Team*

The following processes were standardized in protocols for primary stroke centers:

- Door to decision: examination, imaging, contact to teleconsultant, videoconference
- Decision to groin: team alarm, preparation of patient and of angiography room
- Groin to reperfusion: various support of intervention team
- Post-procedure: specific multidisciplinary stroke unit care, complication management

The following processes were standardized in protocols for teleconsultant team:

- First contact – decision: imaging recommendation, pre-alarm, videoconference, indication for EVT, documentation
- Decision to transfer of the flying team: notification of teams, organization of transfer
- Post-procedure: 24h teleconsultation, follow up

The following processes were standardized for Flying Intervention Team:

- Decision to groin: availability, technical equipment, conduct in helicopter, content of luggage, documentation

### *Standard operating procedures for interhospital transfer*

The following processes were standardized in protocols for primary stroke centers:

- Choice of referral center: a list of first choice and alternative choices of regional referral centers was established for each primary stroke center site allowing to use the referral center with the least expected time delay and allowing to rapidly choose alternatives in case of non-availability of the referral center.

Interhospital transfer: indication for transfer, mode and content of communication with EMS, including level of urgency, indications for medical supervision during transfer, preparation of patient before transfer, communication with referral center after departure

**eTable 1. Demographics and baseline characteristics for patients with endovascular thrombectomy**

<b>eTable 1. Demographics &amp; Baseline Characteristics in patients with EVT</b>		
	<b>Flying Team</b>	<b>Transfer</b>
No. of patients	60	57
<b>Demographics</b>		
Age, median (IQR), y	76 (68 to 82)	76 (67 to 79)
<b>Sex</b>		
Women, No. (%)	39 (65)	26 (46)
Men, No. (%)	21 (35)	31 (54)
<b>Medical history, No. (%)<sup>a</sup></b>		
Hypertension	37 (63)	40 (70)
Atrial fibrillation	20 (35)	16 (28)
History of stroke	14 (24)	12 (21)
Diabetes mellitus	12 (20)	11 (19)
History of myocardial infarction	4 (7)	7 (12)
<b>Index stroke</b>		
NIHSS, median (IQR) <sup>b</sup>	15 (10 to 18)	13 (9 to 16)
<b>NIHSS groups, No. (%)</b>		
Mild stroke (NIHSS ≤ 5)	5 (8)	4 (7)
Moderate stroke (NIHSS 5-15)	28 (47)	37 (65)
Severe stroke (NIHSS ≥ 15)	27 (45)	16 (28)
tPA treatment in primary stroke center, No. (%)	40 (67)	39 (68)
<b>Occlusion site, No. (%)<sup>c</sup></b>		
MCA, M1 segment	31 (52)	32 (56)
MCA, M2 segment	17 (28)	7 (12)
Basilar artery	6 (10)	10 (18)
ICA	4 (7)	8 (14)
ICA with M1 involvement ("Carotid T")	4 (7)	4 (7)
<b>Aetiology, No. (%)<sup>d</sup></b>		
Macroangiopathy	38 (63)	30 (53)
Cardiac embolism	11 (18)	13 (23)
Unknown source	10 (17)	13 (23)
Other known source	1 (2)	1 (2)
<b>Time intervals before EVT decision, median (IQR)</b>		
Symptom onset to arrival in primary stroke center	85 (62 to 162)	84 (58 to 132)
Arrival in primary stroke center to first imaging	10 (6 to 15)	13 (8 to 18)
First imaging to decision	39 (27 to 49)	37 (28 to 60)
<b>Straight-line distance, median (IQR), km</b>		
Distance between primary stroke center base of flying team and primary stroke center	50 (42 to 54)	
Distance between primary stroke center and receiving referral center		42 (34 to 50)
<b>Mode of patient transfer, No. (%)</b>		
Airborne transport		28 (51)
Ground transport		27 (49)

Table 1. Baseline characteristics.

Abbreviations: EVT, endovascular thrombectomy; SD, standard deviation; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; MCA, middle cerebral artery; ICA, internal carotid artery.

<sup>a</sup> Medical history was assessed by medical personnel during hospital stay.

<sup>b</sup> The NIHSS is a scale used for the evaluation of acute stroke. The score ranges from 0 to 42, with greater values indicating greater stroke severity.

<sup>c</sup> As multiple occlusion sites are possible, patients may occur in more than one category.

<sup>d</sup> Aetiology was determined by medical personnel during hospital stay.

**eTable 2. Clinical outcomes at 3 months**

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	Flying Team <sup>a</sup>	Transfer <sup>a</sup>	Absolute difference (95%-CI)	Unadjusted OR (95%-CI)	P value	Adjusted OR (95%-CI) (prespecified adjustment variables) <sup>b</sup>	P value	Adjusted OR (95%-CI) (post-hoc specified adjustment variables) <sup>c</sup>	P value
<b>All patients with follow-up</b>									
No. of patients	71	83							
<b>Outcome after 3 months</b>									
mRS score, median (IQR) <sup>d,e</sup>	3 (1 to 6)	3 (2 to 5)	0 (-1 to 2)	1.43 (0.81 to 2.52)	.21	1.91 (1.05 to 3.50)	0.04	2.21 (1.19 to 4.17)	.01
Good outcome (mRS 0-2), No. (%) <sup>f</sup>	32 (45)	32 (39)	6.5 (-8.8 to 21.6)	1.31 (0.69 to 2.50)	.4	1.62 (0.80 to 3.34)	0.19	1.70 (0.82 to 3.61)	.16
Death within 3 months, No. (%) <sup>f</sup>	18 (25)	18 (22)	3.7 (-9.6 to 17.2)	1.23 (0.58 to 2.60)	.59	1.06 (0.48 to 2.34)	0.88	0.99 (0.44 to 2.24)	.98
<b>Patients with EVT and follow-up</b>									
No. of patients	59	57							
<b>Outcome after 3 months</b>									
mRS score, median (IQR) <sup>d,e</sup>	3 (2 to 6)	3 (2 to 5)	0 (-1 to 2)	1.26 (0.66 to 2.41)	.49	1.91 (0.96 to 3.88)	.07	2.27 (1.10 to 4.79)	.03
Good outcome (mRS 0-2), No. (%) <sup>f</sup>	26 (44)	22 (39)	5.5 (-12.2 to 22.6)	1.25 (0.60 to 2.64)	.55	1.64 (0.72 to 3.72)	.24	1.72 (0.75 to 4.10)	.21
Death within 3 months, No. (%) <sup>f</sup>	15 (25)	11 (19)	6.1 (-9.1 to 21.0)	1.43 (0.59 to 3.51)	.43	1.14 (0.44 to 2.94)	.79	0.88 (0.30 to 2.47)	.80

eTable 2. Clinical outcomes at 3 months.

Abbreviations: OR, odds ratio; CI, confidence interval; mRS, modified Rankin Scale; EVT, endovascular thrombectomy.

Outcome was analyzed by using non-adjusted and adjusted ordinal logistic regression models. No missings were present in the baseline data used in the adjusted models.

<sup>a</sup> Missings due to follow-up: Flying Team: 1 in all patients, 1 in patients with EVT; Transfer: 2 in all patients.

<sup>b</sup> Prespecified adjustment variables: age, sex, NIHSS score.

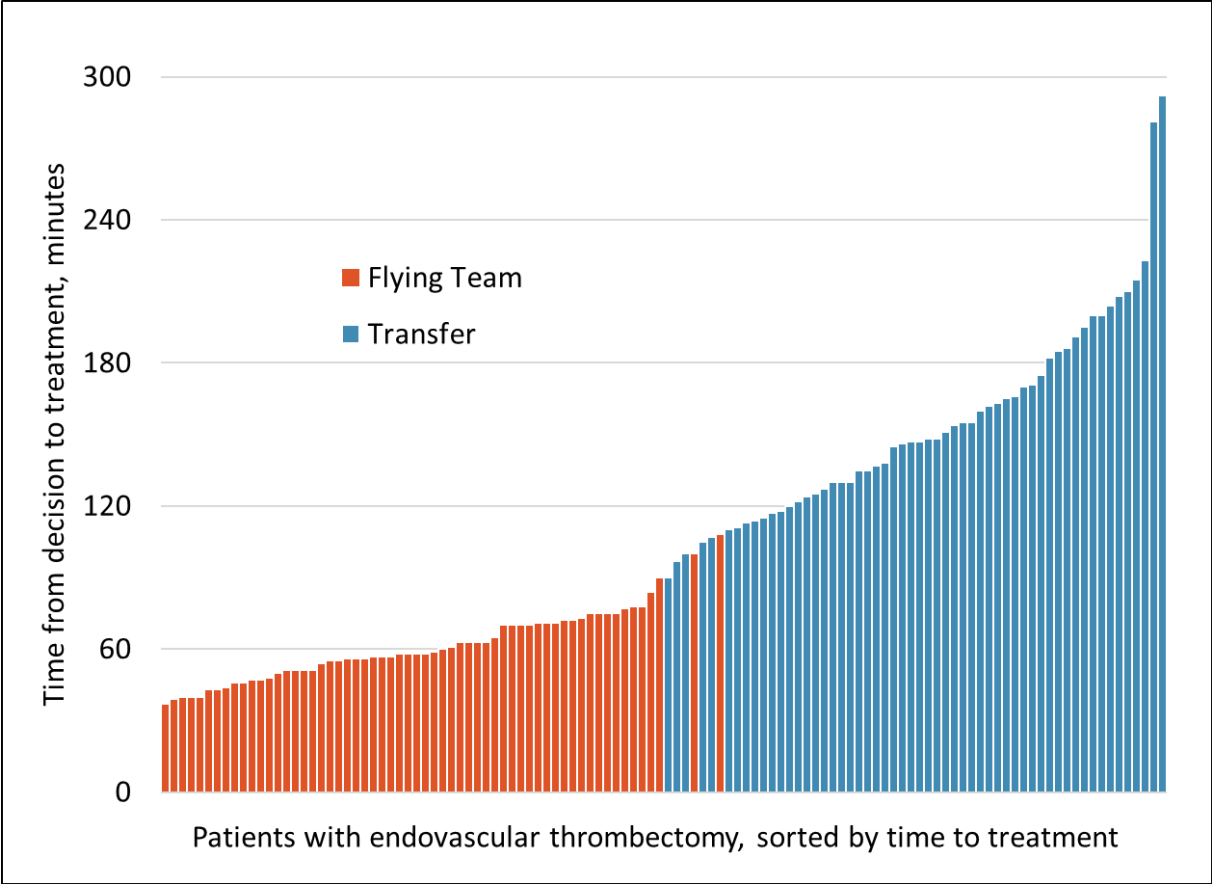
<sup>c</sup> Post-hoc specified adjustment variables: age, sex, NIHSS score, occlusion sites

<sup>d</sup> Scores on the modified Rankin Scale range from 0 to 6, with 0 indicating no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, 6 death. Severe disability (5) and death (6) were combined in a single worst category.

<sup>e</sup> The adjusted common odds ratio for a shift in the direction of a better outcome with the corresponding 95% confidence interval was presented as effect estimate.

<sup>f</sup> Unadjusted and adjusted odds ratio for good outcome and mortality was calculated by using binary logistic regression models.

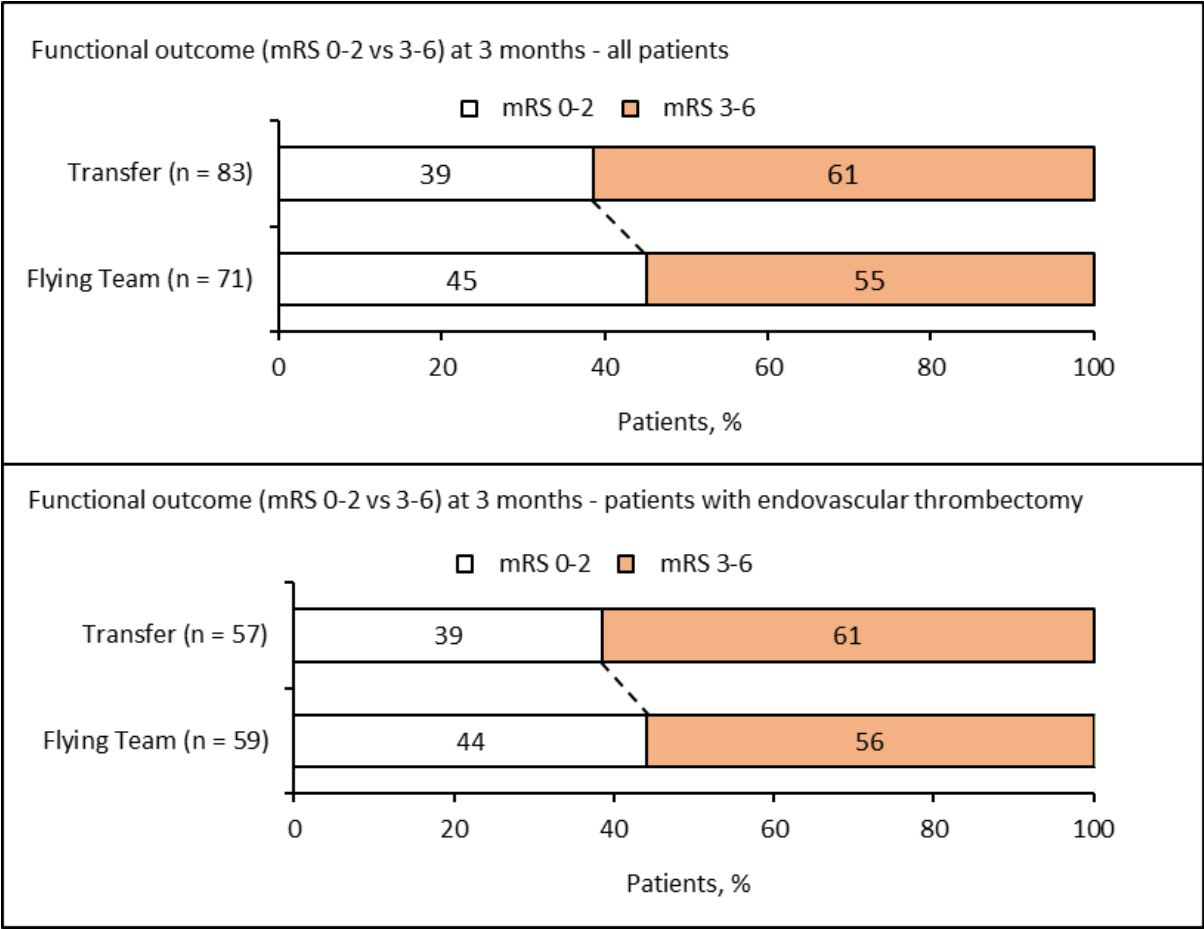
eFigure 3. Time from decision for EVT to groin puncture in ascending order



eFigure 3. Time from decision for EVT to groin puncture in ascending order. Flying team patients (n = 60) are shown in orange, transfer patients (n = 57) in blue. Median in the flying team group was 58 minutes (IQR, 51-71) vs 148 minutes (IQR, 124-177) in the transfer group (difference in medians, 90; 95% CI, 75 to 103).



**eFigure 4. Functional outcome at 3 months in flying team and transfer patients (mRS 0-2 vs. 3-6)**



eFigure 4. Functional Outcome at 3 months in flying team and transfer patients (mRS 0-2 vs. 3-6). Abbreviations: mRS, modified Rankin Scale. Scores on the modified Rankin Scale range from 0 (no symptoms) to 6 (death). Patients with mRS 0-2 after 3 months (“good outcome”) were compared to patients with mRS 3-6. Of all patients included, follow-up data were missing in 3 patients (2 in transfer, 1 in flying team). In patients with EVT, follow-up data was missing in 1 flying team patient. Adjusted odds ratio for good clinical outcome in the flying team group was 1.64 (CI 95% 0.72-3.72) in patients with endovascular thrombectomy and 1.62 (CI 95% 0.08-3.34) in all patients (including those who did not receive endovascular thrombectomy).