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# Transferring neurointerventionalists saves time compared with interhospital transfer of stroke patients for endovascular thrombectomy: a collaborative pooled analysis of 1001 patients (EVEREST)

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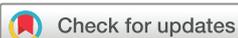
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## ABSTRACT

**Background** Interhospital transfer of stroke patients (drip and ship concept) is associated with longer treatment times compared with primary admission to a comprehensive stroke center (mothership concept). In recent years, studies on a novel concept of performing endovascular thrombectomy (EVT) at external hospitals (EXT) by transferring neurointerventionalists, instead of patients, have been published. This collaborative study aimed at answering the question of whether EXT saves time in the workflow of acute stroke treatment across various geographical regions.

**Methods** This was a patient level pooled analysis of one prospective observational study and four retrospective cohort studies, the EVEREST collaboration (EndoVascular thrombEctomy at Referring and External STroke centers). Time from initial stroke imaging to EVT (vascular puncture) was compared in mothership, drip and ship, and EXT concepts.

**Results** In total, 1001 stroke patients from various geographical regions who underwent EVT due to large vessel occlusion were included. These were divided into mothership (n=162, 16.2%), drip and ship (n=458, 45.8%), and EXT (n=381, 38.1%) cohorts. The median time periods from onset to EVT (195 min vs 320 min, p<0.001) and from imaging to EVT (97 min vs 184 min, p<0.001) in EXT were significantly shorter than for drip and ship thrombectomy concept.

**Conclusions** This pooled analysis of the EVEREST collaboration adds evidence that performing EVT at external hospitals can save time compared with drip and ship across various geographical regions. We encourage conducting randomized controlled trials comparing both triage concepts.

## INTRODUCTION

Several randomized controlled trials have shown that endovascular thrombectomy (EVT) is an effective treatment for large vessel occlusions.<sup>1</sup> As stated in the stroke guidelines by the American Heart Association and the American Stroke Association, this treatment requires the stroke patient to be at an experienced stroke center with rapid access to cerebral angiography, qualified neurointerventionalists, and a comprehensive periprocedural care team.<sup>2</sup> Area-wide coverage of this high level of expertise, especially the availability of neurointerventionalists,

remains variable.<sup>3</sup> A European survey of national scientific societies and stroke experts, for example, showed major inequalities in access to EVT between and within European countries.<sup>4</sup>

In most regional stroke networks there are two established triage concepts for EVT: first, stroke patients may be directly admitted to a comprehensive stroke center (CSC) (mothership (MS)), if this is the closest treatment option. Second, if the closest CSC is further away, stroke patients may be transported to the closest primary stroke center in order to avoid a delay of intravenous thrombolysis.<sup>5–7</sup> In the case of a large vessel occlusion, these patients are secondarily transferred to a CSC (drip and ship (DS)).

However, there are studies suggesting a worse outcome for DS patients compared with MS patients, secondary to time delays.<sup>8–11</sup> Some of these DS hospitals are sufficiently equipped with CT, MRI, an angiography suite, and stroke neurologists, as well as a stroke unit and an intensive care unit for postprocedural care. Generally, these hospitals are capable of performing EVT (thrombectomy capable stroke centers (TSCs)). They only lack a team of neurointerventionalists. Indeed, there is a lack of neurointerventionalists in acute stroke care, as reported by Bulwa and Chen.<sup>12</sup>

Since these TSCs have difficulties hiring neurointerventionalists, agreements between CSCs and TSCs in some stroke networks have been established. Instead of transferring a stroke patient with a large vessel occlusion from a TSC to a CSC, a neurointerventionalist is transferred to perform a thrombectomy at external hospitals (TSCs, EXT concept). The idea behind this triage option is that time can be saved in the acute treatment phase. Depending on the health-care and reimbursement system, there might also be a financial benefit for the TSC. In addition, this concept may reduce resource use from emergency medical services and stroke units of CSCs.

The results of this triage concept have been published under varying names, such as drip and drive, trip and treat, Mobile Interventional Stroke Team model, drive the doctor, and drive and retrieve.<sup>13–20</sup> These studies have demonstrated that EXT can save time compared with DS in those geographical regions.<sup>21</sup> However, the EXT concept has not been considered in national or international stroke guidelines.<sup>2 22</sup>

**Table 1** Studies included in this pooled analysis

Study, No of patients	Stroke networks	Triage concepts	Years of recruiting	Year published
Seker, n=126 <sup>15</sup>	Heidelberg, Germany	DS, EXT	2012–16	2018
Breckenfeld, n=74 <sup>13</sup>	Hamburg, Germany	DS, EXT	2016	2018
Osanai, n=133* <sup>14</sup>	Hokkaido, Japan	EXT	2015–19	2019
NEUROSQUAD, n=440 <sup>17</sup>	Heidelberg, Germany and Hamburg, Germany	DS, EXT, MS	2018	2020
Morey, n=228 <sup>19</sup>	New York City, USA	DS, EXT, MS	2016–18	2020

\*67 patients were included from the initial study, 66 patients were treated after publication of this study until December 2019.<sup>14</sup>  
DS, drip and ship; EXT, thrombectomy at external hospital; MS, mothership.

The purpose of this study was to pool patient data from five studies and to compare time metrics from initial stroke imaging to the initiation of EVT in DS and EXT in a large scale analysis. We hypothesize that EXT can save time compared with DS across various geographical regions.

## METHODS

### Study design and setting

The EVEREST (EndoVascular thrombEctomy at Referring and External STroke centers) collaborative group was established to compare the EXT concept with DS across various geographical regions. Four neurointerventional departments participated in this collaboration: Department of Neurosurgery, Icahn School of Medicine, Mount Sinai, New York City; Department of Neuroradiology, Heidelberg University; Department of Neurosurgery, Hokkaido University; and Department of Neuroradiology, University of Hamburg-Eppendorf. These departments provide EVT at their CSCs and at TSCs in metropolitan and/or rural areas. Details on these stroke networks are provided in the online supplemental file. These centers have published data on the EXT concept and compared this concept with DS and/or MS.<sup>13 14 17 19 23</sup> Data from these published studies were pooled for an analysis (table 1). Hokkaido University provided additional patients outside of their study. Details on each study are provided in the online supplemental material.

All data were deidentified and unlinked to any identifiers. The pseudonymized data of each study were sent to one author (FS) for statistical analysis. The institutional review board of each participating center approved the study and waived the need for patient consent. This manuscript was written according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

### Study cohort

All patients in the pooled analysis underwent thrombectomy and were treated according to national guidelines and the inhouse standards of each participating site. Intravenous thrombolysis was given according to national guidelines that were valid during the time of treatment. The occlusion sites were defined according to catheter angiography.

Patients in the included studies were pooled and classified as follows: DS, if the patient was transported to a primary stroke center first and secondarily transferred to a CSC for thrombectomy; and EXT, if the patient was transported to a TSC without on-site neurointerventionalists and thrombectomy was performed by a neurointerventionalist who was transferred from a CSC to this hospital. For comparison reasons, MS patients, that is, direct transport to a CSC with on-site neurointerventionalists, were also included. The main focus of this study was the comparison of DS and EXT.

### Outcome measures

The primary outcome measure was the time from stroke imaging (acquisition of the first image) to the start of EVT (ie, vascular puncture). Secondary outcome measures were time from onset or last seen well to initial stroke imaging and time from onset or last seen well to the start of EVT (ie, vascular puncture).

### Statistical analysis

Statistical analysis was performed using R V.3.6.2 and RStudio V.1.2.5033. Quantitative variables are expressed as means (SD) or median (IQR). Categorical variables are expressed as numbers (percentages). MS, DS, and EXT were compared using a Kruskal–Wallis test. The Conover test with Benjamini–Hochberg correction was used for post hoc group comparison. A p value <0.05 was considered statistically significant.

## RESULTS

In total, 1001 patients were included in this study. At one stroke network, data from three TSCs (n=53) were excluded because these TSCs left the network. This stroke network also excluded data from 10 MS and DS patients and has only provided data on EXT patients.

Of these 1001 patients, 162 (16.2%) were in the MS group, 458 (45.8%) were in the DS group, and 381 (38.1%) were in the EXT group.

Age, sex, stroke severity, and occlusion sites were similar among the groups. Intravenous thrombolysis was given less frequently in the MS group (MS 34% vs DS 58.3% and EXT 59.1%, p<0.001) (table 2).

Median time from imaging to thrombectomy was the shortest in the MS cohort (56 min). It was significantly shorter in the EXT cohort compared with the DS cohort (97 vs 184 min, p<0.001) (table 3, figure 1).

Median time from onset to imaging was shorter in the EXT cohort (93 min) compared with the MS (110 min, p=0.002) and DS cohorts (113 min, p<0.001). Median time from onset to thrombectomy was shorter in the EXT cohort (195 min) compared with the DS cohort (320 min, p<0.001) and similar to the MS cohort (180 min, p=0.27).

## DISCUSSION

The triage of stroke patients with large vessel occlusion has been of increasing interest in recent years.<sup>12</sup> It is well established that the transfer of stroke patients from primary stroke centers to a CSC is time consuming, given the required coordination of interhospital transport and patient preparation for the transfer.<sup>6 17 21 24–27</sup> The degree to which these activities prolong time to treatment are even more apparent for patients living in rural areas.<sup>9</sup>

**Table 2** Demographics

	MS (n=162)	DS (n=458)	EXT (n=381)	P value
Age (years) (mean (SD))	72.1 (12.4)	71.9 (13.8)	74.1 (12.7)	0.074
Women (n (%))	82 (50.6)	229 (50.0)	201 (52.8)	0.721
Baseline NIHSS (median (IQR))	15 (9–21)	16 (12–20)	16 (12–20)	0.361
Occlusion site (n (%))				
ICA	34 (21.0)	114 (24.9)	109 (28.6)	0.483
MCA	113 (69.8)	301 (65.7)	242 (63.5)	
BA	14 (7.4)	33 (7.2)	23 (6.0)	
Other	3 (1.9)	10 (2.1)	7 (1.8)	
Intravenous thrombolysis (n (%))	55 (34.0)	267 (58.3)	225 (59.1)	<0.001

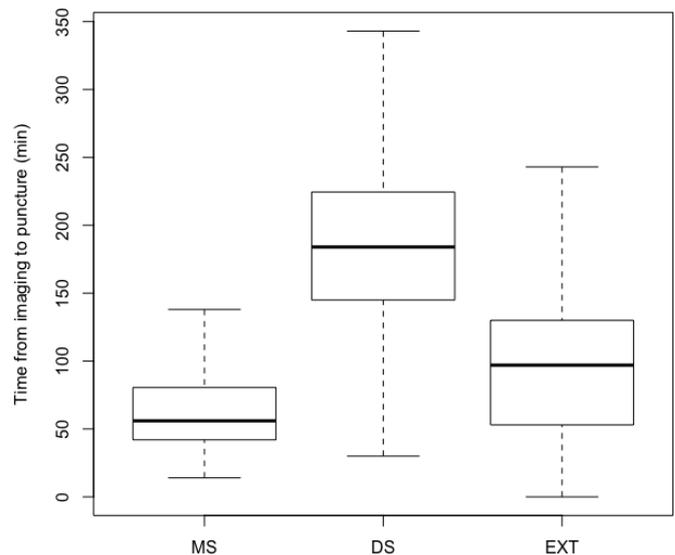
BA, basilar artery; DS, drip and ship; EXT, thrombectomy at external hospital; ICA, internal carotid artery; MCA, middle cerebral artery; MS, mothership; NIHSS, National Institutes of Health Stroke Scale.

The time delay present in the DS concept led to the idea of transferring neurointerventionalists from CSCs to perform EVT at external hospitals, which are thrombectomy capable (EXT concept). Eventually, compared with a patient, a neurointerventionalist can be transferred more easily to another hospital (eg, by driving or by taking a taxi). In a metro area such as New York City, even public transport can be faster than an ambulance.

Several retrospective single center studies, one prospective single center study, and one prospective bicenter study from the USA, Germany, and Japan have been published to date.<sup>13–15 17 19</sup> All of these studies reported that the EXT concept (under a variety of names) can save time in the acute phase in their respective geography. However, the logistics of these stroke networks are different. In the EVEREST collaboration, we have pooled our data to compare DS and EXT in a broader spectrum. To avoid confusion, we have chosen to use the abbreviation EXT (thrombectomy at external hospitals) for this triage concept in this study.

In this pooled analysis with 1001 patients, we showed that the EXT concept was time saving across various geographical regions. This concept has been implemented successfully in both metropolitan areas, New York City and Hamburg, that regularly deal with traffic congestion, and in rural areas around Hokkaido and Heidelberg. The results of this pooled analysis, therefore, confirm the previous publications of each individual stroke network, which were mostly single center analyses. This study adds evidence that the EXT concept may be a good alternative to the well established DS concept if certain requirements are met.<sup>28</sup> The EVEREST collaboration therefore encourages stroke networks to consider the EXT concept as a third triage pathway.<sup>29</sup>

The advantage of the EXT concept is that processes can be parallelized: during the transfer of the neurointerventionalist, the patient can be prepared in the angiography suite. This might explain why the time from imaging to thrombectomy was significantly shorter in the EXT cohort compared with the DS cohort.

**Figure 1** Box plot demonstrating time from stroke imaging to thrombectomy (vascular puncture) in the three cohorts: mothership (MS), drip and ship (DS), and thrombectomy at external hospital (EXT).

Some stroke networks use helicopters to transfer neurointerventionalists which may be even more time saving.<sup>30 31</sup> However, availability of helicopters is limited and not every neurointerventionalist might be willing to fly in a helicopter.

Despite the advantages of the EXT concept, there are several issues to consider. This triage concept is demanding in terms of human resources.<sup>32</sup> It requires at least two neurointerventionalists to be on call at the CSC, as there might be, for example, two simultaneous EVT cases. While one neurointerventionalist is treating a stroke patient at an external hospital, another neurointerventionalist needs to cover the CSC in the meantime. Therefore, not every CSC is capable of providing 24/7 EVT services for TSCs. In principal, it would be reasonable to employ one neurointerventionalist at a TSC to secure an EVT service. However, adding more neurointerventionalists at the CSC may be easier and more efficient than converting TSCs to CSCs because neurointerventionalists are generally more interested in working at a CSC due to the variety of neurointerventional cases and working in a larger and specialized team compared with a TSC. This may make TSCs less attractive for neurointerventionalists. Indeed, many TSCs have trouble finding neurointerventionalists willing to work under these difficult conditions, such as mostly working alone and not in a team, being solely responsible for EVT calls, having no back up in difficult cases, and no structured training. Therefore, converting TSCs to CSCs may not be a realistic option in many stroke networks.

**Table 3** Comparison of time metrics in the three triage concepts

	MS (n=162, 16.2%)	DS (n=458, 45.8%)	EXT (n=381, 38.1%)	P value*	P value† MS vs DS	P value† MS vs EXT	P value† DS vs EXT
Onset to imaging (min)	110 (69–313)	113 (65–265)	93 (57–171)	<0.001	0.742	0.002	<0.001
Onset to EVT (min)	180 (130–422)	320 (243–480)	195 (145–274)	<0.001	<0.001	0.27	<0.001
Imaging to EVT (min)	56 (42–80)	184 (145–225)	97 (53–130)	<0.001	<0.001	<0.001	<0.001

Time metrics given as median (IQR).  
\*Kruskal–Wallis test between MS, DS, and EXT.  
†Post hoc Conover test with Benjamini–Hochberg correction.  
DS, drip and ship; EVT, endovascular thrombectomy; EXT, thrombectomy at external hospital; MS, mothership.

Further concerns have been raised regarding the EXT concept.<sup>12,28</sup> Not every primary stroke center is qualified to be a TSC. We agree that TSCs need to be adequately equipped and staffed. It is not enough that TSCs are capable of performing EVT, but they need to be excellent, as correctly pointed out by Mack *et al* in the editor's column of *JNIS*.<sup>28</sup> Physicians performing EVT procedures at TSCs need to have sufficient neurointerventional training. Since the EXT concept is a team effort and relies not only on neurointerventionalists, but neurologists, anesthesiologists, nurses, and radiographers at these external hospitals also need to be trained to optimize the workflow. Furthermore, quality of care at TSCs needs to be adequately monitored.

Recent papers may have created the impression that there is an agenda of converting as many primary stroke centers as possible to TSCs and performing EVT at TSCs rather than at CSCs.<sup>12</sup> We would like to point out that this is not our intention. Offering EVT services at external hospitals is demanding in many ways, as explained above. EVT should only be performed at TSCs, if reasonable. This decision should be left to the discretion of the neurointerventional team and not be decided by hospital administrations or governmental institutions.

The strengths of this patient level pooled analysis are the large number of patients and its real world application. The main limitations of this study are its observational design and data selection from single centers. It cannot be excluded that structural advantages or disadvantages in certain regions may have influenced the results. Also, there might be selection bias, as patients were not selected consecutively. Each stroke network participating in this pooled analysis has published studies on the EXT concept with different study sizes. Hence the number of patients in this pooled analysis was not balanced among the stroke networks as this was not an a priori planned multicenter trial. For example, one of the four stroke networks provided about 40% of the data. Also, the time periods in which the patients were included might have varied. Therefore, some stroke networks might be underrepresented, which might have led to bias. The idea behind the DS concept is to reduce the time from onset to imaging for patients in rural areas. In our study, however, onset to imaging time was longer in DS compared with MS and EXT. This might be due to various reasons, such as geographical or logistical circumstances. Also, intravenous thrombolysis was less frequently given in the MS group (ie, the number of patients with contraindications for thrombolysis was presumably higher in this group). A possible explanation is that in these cases, emergency medical services may have decided to bypass primary stroke centers and go directly to the next CSC. Interestingly, the results of the recent RACECAT trial suggested that patients with certain prehospital clinical criteria bypass a primary stroke center if the next CSC is less than 30 min driving distance from the primary stroke center.<sup>33</sup>

## CONCLUSION

This pooled analysis adds evidence that performing thrombectomy in external hospitals (EXT concept) can save time compared with the drip and ship concept in both rural and metropolitan areas across various geographical regions.

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