european journal of neurology
the official journal of the european academy of neurology

ORIGINAL ARTICLE OPEN ACCESS

A Transfer Strategy Utilizing a Helicopter and a Ground Ambulance Together Does Not Prolong Door-In-Door-Out Times in Thrombectomy Patients: A Retrospective Analysis

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Received: 5 December 2024 | **Revised:** 25 March 2025 | **Accepted:** 27 March 2025

Funding: This work was supported by state funding for university-level health research, Tampere University Hospital, and the Wellbeing Services County of Pirkanmaa (9 AC011).

Keywords: door-in-door-out | helicopter emergency medicine service | large vessel occlusion | thrombectomy

ABSTRACT

Background: An interfacility transfer should commence immediately to a hospital with endovascular capability to perform mechanical thrombectomy when a patient is diagnosed with a large vessel occlusion (LVO) stroke. The turnaround time in the primary stroke center (PSC) is called door-in-door-out time (DIDO). We investigated DIDOs from two PSCs and how the implementation of a helicopter emergency medical service (HEMS) unit for patient transportation together with a ground ambulance affected the DIDO.

Methods: We retrospectively identified thrombectomy candidates transferred to Tampere University Hospital from two PSCs, Seinäjoki and Kanta-Häme Central Hospitals, from February 2019 until October 2022. A HEMS unit was dispatched to transport the patients from Seinäjoki after June 2020. Patient medical records and DIDOs were also analyzed and compared with ground transport and air transport between the two PSCs. Factors for faster DIDOs were determined by linear regression analysis.

Results: The DIDOs of 129 patients were analyzed. The median (interquartile range) DIDO in the total population was 50 (35–71) minutes, and the PSCs achieved equal DIDOs. The strongest factors of the DIDO were the prehospital prenotification ($B = -55.6$, $p < 0.001$), the same ambulance continuing the interfacility transport ($B = -33.8$, $p < 0.001$), and the patient's age ($B = 0.65$, $p = 0.039$). HEMS dispatch or transport was not associated with any delays in DIDO.

Conclusion: The prehospital prenotification of a stroke patient to a PSC should include a discussion of whether the patient is a thrombectomy candidate. The same ambulance should be engaged for the mission and continue with the same patient to the thrombectomy facility.

Abbreviations: CSC, comprehensive stroke center; CTA, computed tomography angiography; DIDO, door-in-door-out time; EMS, emergency medical service; HEMS, helicopter emergency medical service; IQR, interquartile range; LVO, large vessel occlusion; PSC, primary stroke center; SD, standard deviation.

1 | Introduction

Stroke triage experienced a revolution when mechanical thrombectomy with or without thrombolysis was introduced as the gold standard for large vessel occlusion (LVO) recanalization [1]. Increasing the time from the onset of stroke symptoms to the recanalization of the occluded artery decreases the probability of a favorable recovery [2]. Registry-based publications suggested that LVO stroke patients would benefit from primary stroke center (PSC) bypass and transport to the nearest comprehensive stroke center (CSC) [3, 4]. Interestingly, recent randomized trials could not show any health benefit in the directly transported patient groups [5, 6] although it might be reasonable to triage the late-presenting subset of patients to the CSC [7]. A greater percentage of patients receive thrombolysis when stroke patients are directed to the nearest stroke center, which, at least with an imaging protocol including computed tomography angiography (CTA) of the brain, relieves the burden on the emergency department in the CSC [5, 8].

Routing patients through PSCs challenges the stroke protocols in emergency departments. The American Heart Association Guidelines recommend implementing a protocol to identify thrombectomy candidates in the PSC's emergency department and commencing secondary transport as soon as possible [9]. Alberts et al. [10] recommended a 120-min door-in-door-out time (DIDO), but this recommendation also includes non-LVO stroke patients transferred from acute stroke-ready hospitals to PSCs. No international guideline states an exact goal in minutes for DIDO when the transfer process concerns LVO patients whose recovery is also time critical after thrombolysis has begun.

To our knowledge, Gaynor et al. [11] report the fastest median DIDO in their quality improvement study: 45 min. The majority of reported median DIDOs range from 60 to 150 min [12, 13]. Factors identified affecting the DIDO are, for example, patient age, stroke severity, imaging protocol, thrombolysis administration, time of day, dispatch protocol of the transferring ambulance, and the occluded artery's location. Some studies report utilizing air transfer to reach the CSC faster [5, 14–17]. The distance needed to travel by air to compensate for the waiting time increases if the patient waits for the air ambulance at the PSC [16].

We implemented a new transport protocol in June 2020 for thrombectomy candidates from our PSC, Seinäjoki Central Hospital, to the CSC, Tampere University Hospital [17]. Previously the patients were transported by ambulances to the CSC. The revised protocol stated that the secondary transport from the PSC begins as soon as possible, and the local helicopter emergency medical service (HEMS) unit picks up the patient at a rendezvous. We aimed in this study to report the effect of implementing a HEMS dispatch on the DIDO in Seinäjoki Central Hospital and to compare this DIDO to that of a similar PSC, Kanta-Häme Central Hospital, in our CSC's special responsibility area. We also compared the patients with a DIDO of less than 45 min to the others. Additionally, we aimed to compute the linear regression equation for the combined patient group's DIDO.

2 | Methods

2.1 | Design and Outcome

This is a retrospective chart review study of factors affecting the DIDO, that is, the time from when the ambulance stops moving at the PSC to when the secondary transport to the CSC begins. The main outcomes of interest were the DIDO and factors associated with its duration.

2.2 | Patients

We included thrombectomy candidates referred to Tampere University Hospital for mechanical thrombectomy from Seinäjoki Central Hospital and Kanta-Häme Central Hospital between February 13, 2019, and October 10, 2022. We excluded in-patient strokes.

2.3 | Setting

Tampere University Hospital is a comprehensive stroke center for over 900,000 people in its special responsibility area. The interventional radiology team is on call 24/7. They are able to arrive after office hours at the CSC within 30 min after the emergency medical services' (EMS's) special thrombectomy prenotification, which is based on the Finnish Prehospital Stroke Scale (FPSS, Table S1) [18] or according to the PSCs' imaging results. Approximately 200 mechanical thrombectomies are performed yearly.

Thrombectomy candidates from five different PSCs are referred to Tampere University Hospital. Two of these PSCs (Seinäjoki and Kanta-Häme Central Hospitals) belong to Tampere University Hospital's special responsibility area. Seinäjoki Central Hospital is the PSC in the South Ostrobothnia hospital district for 190,000 inhabitants. Kanta-Häme Central Hospital in Hämeenlinna is the PSC in Kanta-Häme hospital district for 170,000 people. The driving distance from Seinäjoki Central Hospital to Tampere University Hospital is 180 km and from Kanta-Häme Central Hospital it is 80 km. The EMS in both PSC hospital districts has the possibility of transporting a thrombectomy candidate directly to the CSC from the nearest neighboring areas when FPSS > 4 and after consulting the CSC neurologist by phone. They give a prehospital prenotification when the EMS transports a suspected stroke patient to the PSC. The stroke protocol in both hospitals begins with this prenotification if the patient is considered a candidate for recanalization. The patient is taken with the ambulance stretcher straight to the computed tomography imaging of the head. Thrombolysis commences in the radiology suite after noncontrast head imaging if there is no contraindication for thrombolysis, and CTA follows immediately. The CTA images are uploaded to the CSC's server immediately for all patients diagnosed with an LVO. The CSC's neurologist and neurointerventionalist are consulted if a mechanical thrombectomy is considered feasible. The same ambulance crew ideally waits for this decision and continues with the secondary transport as soon as the consultants confirm the patient's suitability for endovascular treatment at the CSC.

A publicly financed and prehospital physician-led HEMS unit, FinnHEMS 30, is located at Tampere-Pirkkala airport near Tampere University Hospital. It mainly responds to major trauma and out-of-hospital cardiac arrests. We implemented a thrombectomy candidates' transport protocol from Seinäjoki in June 2020 [17]. The accompanying EMS asks the Finnish Emergency Response Center Agency to dispatch the HEMS unit immediately when the CSC neurologist approves the transfer. The HEMS crew accepts the dispatch and attends the thrombectomy candidate's transport if the weather minima for flying are met and they are not engaged in a previous HEMS mission. The patient's transfer begins with an ambulance as soon as possible, and the HEMS unit picks up the patient at a rendezvous. If the HEMS unit is not able to take part in the thrombectomy candidate's transport, the patient is transported to the CSC by ground. This transport protocol was developed to minimize the transport time without affecting the DIDO in the Seinäjoki Central Hospital. This decreased the transport time from Seinäjoki Central Hospital to our CSC by 25 min but had no effect on the time from the onset of symptoms to recanalization [17]. A new HEMS unit, FinnHEMS 40, commenced operating from Seinäjoki airport in October 2022. The thrombectomy candidates' transport protocol was renewed at that time; therefore, the data acquisition for this study ended. The HEMS unit's dispatch protocol implementation had no effect on the Kanta-Häme Central Hospital's thrombectomy candidate protocol during the study time and all the thrombectomy candidates were transported with ground ambulances during the study.

2.4 | Data Acquisition

We used the Codea reporting portal (Codea Ltd, Porvoo, Finland), a web-based software, to obtain automatically saved timestamps and ambulance locations during the EMS missions. We accessed Tampere University Hospital's electronic patient records for specific data: age, sex, medical history, arrival time to the PSC emergency department, imaging modalities, choice of thrombolysis, stroke severity, and the occlusion site.

2.5 | Statistics

Mean with standard deviation (SD) as well as median with interquartile range (IQR) are presented when feasible. Chi-square test was used for the comparison of categorical variables. Continuous variables were compared either with a t-test or Mann–Whitney U-test. In stepwise linear regression, predictors were entered into the model if the probability of the F-statistic was less than 0.05 and removed if the probability exceeded 0.10. Analyses were completed with SPSS version 29 (IBM Corporation, Armonk, NY, USA), and statistical significance was set at $p \leq 0.05$.

2.6 | Ethics

The Ethics Committee of Tampere University Hospital approved the study design (ETL R20082R) and waived the need for informed consent from the patient or their relatives. Pirkanmaa Hospital District's research director granted access to view the patient records.

3 | Results

A total of 129 patients were included in the study. Fifty-eight (45%) referrals were from Seinäjoki Central Hospital Emergency Department, and of these patients, 43/58 (74%) were referred after the implementation of the hybrid transport protocol with HEMS. Seventy-two patients were referred from Kanta-Häme Central Hospital, but we were unable to find the DIDO for one patient, which leaves 71 (55%) patients for the analysis. Two (2.8%) patients arrived at the Kanta-Häme Central Hospital with private vehicles. The mean age of the thrombectomy candidates was 73 (SD 11) years, and 66 (51%) were male. Table 1 presents the patients' characteristics.

The median (IQR) DIDO in the study was 50 (35–71) minutes. There was no difference between the two hospitals. The median (IQR) DIDO in Seinäjoki Central Hospital was 51 (35–64) minutes, and in Kanta-Häme Central Hospital it was 48 (33–73) minutes ($p = 0.64$). The median (IQR) DIDO in Seinäjoki Central Hospital was 54 (41–64) when the HEMS unit was not dispatched, and after the transport protocol change with HEMS dispatch, the DIDO was 46 (35–65) minutes ($p = 0.46$).

The DIDO was faster than 45 min in 56 (43%) cases. Table 2 shows the differences between patients with DIDO < 45 and ≥ 45 min. Prehospital prenotification and the same ambulance crew continuing with the interhospital transport were more frequent in the faster DIDO group. Additional imaging at the PSC (any imaging modality in addition to noncontrast-computed tomography and CTA) and arrival at the PSC's emergency department at night (after 10 pm and before 6 am) were more frequent in the slower group. Chest X-ray ($n = 8$) and perfusion imaging of the brain ($n = 7$) were the most common additional imaging modalities.

The final regression equation was DIDO = 81.0–55.6* prehospital prenotification—33.8* the use of the same ambulance for the secondary transport +0.65*age. Prehospital prenotification and use of the same ambulance were highly significant ($p < 0.001$), and the patient's age had p value of 0.039. Pearson's correlation coefficients for Seinäjoki Central Hospital ($R = 0.02$, $p = 0.87$) and Kanta-Häme Central Hospital ($R = 0.13$, $p = 0.29$) showed no change in DIDO over time.

4 | Discussion

We learned in this study that the strongest factors for a swift LVO patient transport protocol are, first and foremost, EMS prenotification and that the same ambulance crew continues with the secondary transport. Dispatch of the HEMS unit or helicopter transport had no effect on the DIDO at Seinäjoki Central Hospital when the transport protocol emphasized the immediate start of the transport by ground.

Both PSCs in our study should be complimented for their DIDO performance. Gaynor et al. [11] present their quality

TABLE 1 | Patient characteristics according to the first hospital.

	All		Seinäjoki Central Hospital		Kanta-Häme Central Hospital		
	***N*=129**		***N*=58**		***N*=71**		***p*[a]**
Male, *n* (%)	66	(51)	33	(57)	33	(46)	0.28
Mean age [SD]	73	[11]	72	[11]	73	[12]	0.52
Any co-existing disease, *n* (%)	129	(100)	58	(100)	71	(100)	
Hypertension	91	(71)	37	(64)	54	(76)	0.10
Coronary disease	33	(26)	17	(29)	16	(23)	0.41
Atrial fibrillation	33	(26)	11	(19)	22	(31)	0.11
Diabetes	27	(21)	13	(22)	14	(20)	0.75
Chronic heart failure	17	(13)	9	(16)	8	(11)	0.50
Chronic pulmonary disease	16	(12)	7	(12)	8	(11)	0.89
Previous stroke	15	(12)	6	(10)	9	(13)	0.66
Occluded artery, *n* (%)							
Internal carotid artery	30	(23)	17	(29)	13	(18)	0.14
Middle cerebral artery, first branch	64	(50)	29	(50)	35	(49)	0.94
Middle cerebral artery, second branch	26	(20)	8	(14)	18	(25)	0.09
Basilar artery	7	(5.4)	3	(5.2)	4	(5.6)	1
Posterior cerebral artery	1	(0.8)	0		1	(1.4)	
Anterior cerebral artery	1	(0.8)	1	(1.7)	0		
Known-onset stroke	66	(51)	30	(52)	36	(51)	0.99
Patients treated with thrombolysis. *n* (%)	73	(57)	34	(59)	39	(55)	0.76
HEMS dispatch			43	(74)	0		
HEMS transport			28	(48)	0		
Door-in-door-out time, minutes, median [IQR]	50	[35–71]	51	[35–64]	48	[33–73]	0.64
Prehospital prenotification, *n* (%)	105	(81)	48	(83)	57	(80)	0.88
Same ambulance continues the secondary transport, *n* (%)	73	(57)	43	(74)	30	(42)	**< 0.001**
PSC arrival during office hours, *n* (%)[b]	51	(40)	23	(40)	28	(39)	0.96
PSC arrival at night, *n* (%)[c]	18	(14)	9	(16)	9	(13)	0.67
Additional imaging at the PSC[d]	20	(16)	13	(22)	7	(10)	0.06
NIHSS, *n* (%)							0.10
< 5	11	(8.5)	5	(14)	6	(8.5)	
5–15	60	(47)	32	(55)	28	(39)	
> 15	46	(36)	15	(22)	31	(44)	
NIHSS missing	12	(9.3)	6	(10)	6	(8.5)	

Note: Bold values are statistically significant ($p < 0.05$).
Abbreviations: DIDO, door-in-door-out time; HEMS, helicopter emergency medical service; IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale; PSC, primary stroke center; SD, standard deviation.
[a]*p* for comparison between the PSCs.
[b]Monday–Friday 08–16 (excluding public holidays).
[c]Every night 22–06.
[d]Any modality in addition to noncontrast and angiographic imaging of the head.

TABLE 2 | Patient characteristics in groups with door-in-door-out times < 45 and ≥ 45 min.

	DIDO < 45 min		DIDO ≥ 45 min		
	N = 56		N = 73		p
Male, n (%)	28	(50)	37	(51)	0.94
Mean age [SD]	72	[12]	73	[11]	0.64
Medical history, n (%)					
Hypertension	38	(68)	52	(71)	0.68
Coronary disease	14	(25)	18	(25)	0.96
Atrial fibrillation	17	(30)	15	(21)	0.20
Diabetes	11	(20)	16	(22)	0.75
Chronic heart failure	8	(14)	9	(12)	0.75
Chronic pulmonary disease	7	(13)	8	(11)	0.79
Previous stroke	6	(11)	9	(12)	0.78
Occluded artery, n (%)					0.14
Internal carotid artery	9	(16)	21	(29)	
Middle cerebral artery, first branch	33	(59)	31	(42)	
Middle cerebral artery, second branch	13	(23)	13	(18)	
Basilar artery	1	(1.8)	6	(8.2)	
Posterior cerebral artery			1	(1.4)	
Anterior cerebral artery			1	(1.4)	
Side of the paresis left, n (%)	26	(46)	32	(44)	0.77
Known-onset stroke, n (%)	33	(59)	33	(45)	0.12
Patients treated with thrombolysis. n (%)	33	(59)	40	(55)	0.64
HEMS dispatch, n (%)	20	(36)	23	(32)	0.62
HEMS transport, n (%)	15	(42)	13	(18)	0.22
PSC arrival during office hours, n (%)[a]	22	(39)	29	(40)	0.96
PSC arrival at night, n (%)[b]	4	(7.1)	15	(21)	**0.033**
Prehospital prenotification, n (%)	54	(96)	51	(70)	**< 0.001**
Same ambulance continues the secondary transport, n (%)	43	(77)	30	(41)	**< 0.001**
Additional imaging at the PSC, n (%)[c]	2	(3.6)	18	(25)	**0.001**
NIHSS, n (%)					0.43
< 5	5	(8.9)	6	(8.2)	
5–15	25	(45)	35	(48)	
> 15	25	(45)	21	(38)	
NIHSS missing	1	(1.8)	11	(15)	

Note: Bold values are statistically significant ($p < 0.05$).
Abbreviations: DIDO, door-in-door-out time; HEMS, helicopter emergency medical service; IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale; PSC, primary stroke center; SD, standard deviation.
[a]Monday–Friday 08–16 (excluding public holidays).
[b]Every night 22–06.
[c]Any modality in addition to noncontrast and angiographic imaging of the head.

improvement project with several adjustments made in their PSC's thrombectomy protocol. The 27 patients transferred after the protocol change had a median DIDO of 45 min, and 75% of patients had a DIDO of less than 55 min. Our PSCs' respective performance was a median DIDO of 50 min, and 75% of patients had a DIDO of less than 71 min. McTaggart et al. [19] claim that a 45-min DIDO is not achievable. Based on Gaynor et al.'s [11] and our results, we argue that a 45-min DIDO should indeed be set as the goal for ambitious PSCs. PSC stroke teams should especially strive to maintain their performance during out-of-office hours as well [12, 20, 21].

Prehospital prenotification proved to be highly valuable for a fast PSC process in our material. The EMS in both hospital districts can be considered proficient because 80% of the patients transferred for mechanical thrombectomy arrived at the PSCs' emergency departments with a prehospital prenotification. In comparison, Stamm et al. [21] report a prehospital prenotification rate of 63% for patients eligible for endovascular stroke treatment. They, correspondingly, highlight the importance of an appropriate prenotification to accomplish reasonable DIDOs.

Reducing the time from imaging to the hospital door has been increasingly emphasized in recent literature [22]. Gaynor et al. [11] were the first to suggest the utilization of the same ambulance crew for secondary transport to the CSC. This strategy has since been validated in multiple studies [12, 16, 20] demonstrating its association with reduced DIDO times, a finding that is also supported by our results.

Choi et al. [12] report that they were able to increase the percentage of the same crew continuing the transport up to 59% with their quality improvement program. Our respective percentage was 57% in total, but it has to be noted that the personnel in Seinäjoki Central Hospital were able to recruit the same ambulance in almost three-quarters of the cases. We consider this percentage should be set as a minimum for the thrombectomy transport protocols from the PSCs. It is inevitable that this increases the time the ambulance is engaged with stroke patients [11]. Using clinical scales to distinguish LVO and non-LVO strokes from one another by the EMS is not only for triaging LVO patients straight to the CSC. Using these scales when the drip and ship strategy is chosen is also important. Only those ambulances bringing stroke patients with a high clinical probability of an LVO stroke should remain engaged in the callout until there is a definitive decision on whether the patient is transferred to the CSC or not. Van de Wijdeven et al. [23] report a 24-min delay in ambulance requests after CTA and an additional 15-min delay in ambulance departure after the request. Ng et al. [20] showed that the ambulance request is the longest component of the DIDO and suggested commencing the interfacility transport before the patient's eligibility for endovascular treatment has been decided. Howell et al. [24] put this into effect and introduced an AutoLaunch protocol in their report. They dispatched the ambulance to the CSC before the patient's final acceptance. We dare to suggest that DIDOs could be cut down to the minimum if the patient is taken straight to the PSC imaging with the ambulance stretcher and immediately back to the same ambulance after imaging and initiation of thrombolysis. The same ambulance could even start driving toward the CSC without lights and sirens during the consultation call. The patient would be returned to the PSC if the patient is considered ineligible for endovascular treatment. Otherwise, after a radio transmitted approval of the transfer, the rest of the remaining interfacility transport would be driven with lights and sirens.

A predefined imaging protocol affects the DIDO. Both of our hospitals route suspected stroke patients straight to the radiology suite after a prehospital prenotification. Noncontrast-computed tomography is the first choice; if it shows no intracerebral hemorrhage or extensive and irreversible ischemic damage, CTA follows immediately or after the initiation of thrombolysis with alteplase. It was interesting to notice that although the ambulance crew in South Ostrobothnia stayed more frequently with the thrombectomy candidate, this time benefit might have been lost when acquiring additional imaging in the PSC. Al Kasab et al. [25] showed in their study that angiography causes an additional hour to the DIDO, but their imaging protocol included returning the patient to the emergency room for thrombolysis before proceeding to angiography. Flores et al. [26] concur that angiography is required to minimize unnecessary secondary transports. The role of perfusion imaging at the PSC is undefined. In metropolitan surroundings where the interfacility transfer is short, perfusion imaging at the PSC could be debatable. PSCs referring LVO patients to Tampere University Hospital are located 80–240 km away from the CSC. Angiography and perfusion imaging are acquired automatically at the CSC arrival to define the extent of salvageable brain tissue that might have decreased during the transport. We suggest all necessary imaging should be performed at once, unnecessary imaging modalities (such as chest X-ray) should be avoided, and back-and-forth in-hospital patient transfers should be minimized.

Interestingly, we found that thrombolysis had no effect on the DIDO. This is contrary to previous studies [13, 16, 27] that showed that thrombolysis is associated with a shorter DIDO. Warach et al. [28] showed that changing alteplase to tenecteplase expedites the PSC transport protocol even more. Tenecteplase was not in use for stroke in our hospitals during the study. A simple bolus instead of an infusion seems to be the optimal thrombolysis strategy when the patient continues from the PSC to the CSC for endovascular treatment [29].

Using an air ambulance for the LVO patient's transport inherently increases the DIDO if the HEMS unit is not already at the PSC. The patient does not benefit from fast air transport if the time from the onset of symptoms to recanalization does not decrease. Wong et al. [16] approximated that increasing DIDO is acceptable if the distance between the PSC and the CSC is 250 km or more. Almallouhi et al. [15] published a report with comparable DIDOs for HEMS and ground transports (median DIDO 101 and 111.5 min, respectively) but faster transport with HEMS. We showed in our previous article [17] that our hybrid transport protocol, that is, the transport begins with an ambulance, and the HEMS unit continues with the transport from a rendezvous, decreased the transport time from Seinäjoki Central Hospital to Tampere University Hospital by 25 min. However, there was no significant change in the time from the onset of stroke symptoms to recanalization. Now we have shown that this dispatch protocol did not have any effect on the DIDO at the PSC.

This study is limited by its retrospective design; yet, data from only one patient were not found, and the number of patients in total is comparable to previous studies. The number of patients is, however, too small to study whether DIDO has any effect on the patients' recovery [19, 30]. Existing flight regulations and geographical circumstances must be taken into account when considering the adoption of the air transport protocol presented in this study [31]. The strength of our data is that our software automatically saves the data of an ambulance's location, and we were able to accurately determine the time the patient truly stopped at the PSC.

5 | Conclusion

We conclude that the implementation of an HEMS unit to the transport protocol does not delay the DIDO of an LVO patient when the transport begins with an ambulance and the HEMS unit picks the patient up en route. EMS prehospital prenotification of a stroke patient should already include the discussion of whether the patient is a thrombectomy candidate and whether the same ambulance should be reserved for the interhospital transfer as well. A 45-min DIDO should be set as the goal for ambitious PSCs, and their stroke teams should also strive to maintain their performance during out-of-office hours.

Author Contributions

Pauli Vuorinen: conceptualization, investigation, visualization, formal analysis, methodology, data curation, writing – review and editing, writing – original draft. **Joonas Kiili:** writing – original draft, writing – review and editing, conceptualization, methodology. **Markku Grönroos:** writing – review and editing, data curation. **Ilkka Virkkunen:** writing – review and editing, data curation. **Heini Huhtala:** formal analysis. **Piritta Setälä:** writing – original draft, writing – review and editing, data curation, supervision, conceptualization. **Sanna Hoppu:** funding acquisition, writing – original draft, writing – review and editing, data curation, supervision, resources, conceptualization.

Ethics Statement

The study plan was supported by the Ethics Committee of Tampere University Hospital (IRB number ETL R20082R).

Consent

The Act on the Secondary Use of Health and Social Data (552/2019, § 38) in Finland allows secondary utilization of medical records in research without informed consent. The Ethics Committee of Tampere University Hospital waived the need for informed consent in their study approval.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.