SHORT COMMUNICATION

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Direct admission *versus* secondary transfer for mechanical thrombectomy: long-term clinical outcomes from a single Polish Comprehensive Stroke Centre

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ABSTRACT

Introduction. We aimed to compare 3-month clinical outcomes after mechanical thrombectomy (MT) in patients transferred directly to a comprehensive stroke centre ('mothership', MS) to the outcomes of patients transferred secondarily from primary stroke centres ('drip-and-ship', DAS) in Lubelskie province, the third largest province in Poland.

Material and methods. In a prospective stroke registry, all patients with large vessel occlusion in anterior circulation admitted within six hours of onset and treated with MT between 2017 and 2020 were retrospectively analysed.

Results. A total of 400 patients was evaluated: 267 treated with the MS approach and 133 with the DAS approach. Time from stroke onset to groin puncture was shorter in the MS group. There was a significant difference in 3-month excellent clinical outcomes (mRS 0–1) between these two groups (32.9% of MS patients *vs.* 22.5% of DAS patients, $p < 0.05$), but there was no difference if the 3-month endpoint was expressed as mRS ≤ 2 (42.3% of MS *vs.* 34.5% of DAS patients, $p = 0.13$). The rate of symptomatic intracranial haemorrhage and mortality was comparable in both groups.

Conclusions. Our study shows that direct admission to a comprehensive stroke centre resulted in more patients achieving excellent treatment outcomes (mRS 0–1). At the same time, the superiority of the MT model over the DAS model in obtaining mRS 0–2 was not unequivocally demonstrated. Further studies are needed to determine the best stroke model for patients potentially eligible for MT.

Key words: mothership, drip and ship, acute ischaemic stroke, mechanical thrombectomy, regional stroke care

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Introduction

Different prehospital referral systems have been proposed for patients with acute ischaemic stroke (AIS) who are potential candidates for mechanical thrombectomy (MT). The two most widely known are the drip-and-ship (DAS) and the mothership (MS) models [1].

The DAS model consists of transferring the patient to the nearest primary stroke centre (PSC), where thrombolysis therapy (IVT) is initiated, followed by a transfer of patients who are candidates for MT to a comprehensive stroke centre (CSC). The MS paradigm is direct transfer to a CSC, bypassing the nearest PSC. Both systems have been evaluated in a few observational studies, but as yet the results of only one randomised trial are available [2]. Recently published meta-analysis showed that patients with AIS eligible for reperfusion strategies might benefit more from the MS model than from the DAS model [3]. Furthermore, one recent study has demonstrated lower disability and mortality among patients with large vessel occlusion [LVO] who were directly transported to the CSC if the additional delay was < 30 minutes and < 50 minutes in urban and rural areas, respectively [4].

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On the other hand, the only completed randomised controlled trial (the RACECAT trial) does not support the hypothesis that direct triage of patients with symptoms of ischaemic stroke due to LVO to CSC leads to improved outcomes compared to the current practice of transferring all patients to the PSC [2].

This explains why the debate as to the best stroke strategy is ongoing, and why there are no clear recommendations in the current stroke guidelines.

The CSC located in the Public Clinic Hospital no. 4 (SPSK4) in Lublin, Poland forms a stroke network with 12 PSCs where only IVT is available. This study aimed to compare the onset-to-groin time, reperfusion rate, symptomatic intracranial haemorrhage (sICH) and mortality rate, as well as clinical outcome at 3 months after MT, in direct CSC admission AIS patients *vs.* secondarily transferred AIS patients.

Material and methods

In this single-centre study, we performed a retrospective analysis of prospectively collected data of 400 consecutive patients admitted with acute ischaemic stroke due to LVO of anterior circulation who underwent endovascular thrombectomy between January 2017 and November 2020. The first group included patients directly arriving at CSC at SPSK4 in Lublin (we called this the mothership model, MS), and the second group consisted of patients admitted to one of the above-mentioned hospitals with secondary transfer to the CSC (we called this the drip-and-ship model, DAS). Average distance from PSCs to CSC is 50 km.

The following inclusion criteria were applied: 1) LVO of anterior circulation confirmed by imaging examination (non-contrast CT and CT-angio and/or MRI) and treated with MT; 2) time from symptoms onset to reperfusion of no more than 6 h; 3) National Institute of Health Stroke Scale (NIHSS) score ≥ 6; 4) no prestroke dependency expressed as modified Rankin Scale (mRS) score 0–2.

Clinical data including age, sex, stroke risk factors, baseline medication, initial laboratory results, stroke severity as expressed by the NIHSS score, and time metrics were collected and evaluated. In accordance with the current Guidelines of the Polish Neurological Society for the Management of Patients with Ischaemic Stroke, intravenous thrombolysis (rt-PA) was administered if patients arrived in a window time < 4.5 h and where there was no contraindication [5]. An institutional review committee approved this study (approval number KE-0254/285/2019.). This study was conducted in accordance with the Declaration of Helsinki.

Endovascular thrombectomy

All procedures were performed under biplane angiography unit with 3D rotational angiography and with patients under conscious sedation or general anaesthesia. Mechanical thrombectomy was carried out with aspiration (ACE, Penumbra, Alameda), stent retriever (Solitaire, EV3, Irvine, CA, USA) or a combination of both (the Solumbra technique). Final recanalisation was assessed according to the Thrombolysis in Cerebral Infarction (TICI) classification. Good recanalisation was defined as TICI 2b and TICI 3. Complications related to the procedure were noted.

Follow-up

Routine non-contrast brain CT was performed 24 h after the procedure to evaluate brain infarction and assess the occurrence of intracranial haemorrhage (ICH) if available. ICH was classified as symptomatic according to the classification of the European-Australasian Acute Stroke Study (ECASS II) [6]. Clinical outcome was assessed based on the mRS score 90 days after the procedure. An excellent and a favourable result were defined as mRS 0–1 and mRS ≤ 2, respectively. Mortality rate was calculated.

Statistical analysis

Statistical analysis was conducted using a StatSoft Statistica 13.1PL package. The patients were classified into two groups (MS patients *vs.* DAS patients) and comparisons were made in terms of demographic data, initial NIHSS, risk factors, use of IVT, procedural details, and outcomes. Student's t-test, Mann-Whitney test and Chi-squared Pearson tests were used when appropriate. Statistical significance was defined as $p \leq 0.05$.

Results

During the study period (January 2017–November 2020), 400 AIS patients (267 MS patients and 133 DAS patients) with LVO in the anterior circulation were treated with MT. There was no significant difference between the groups with regards to baseline clinical characteristics or initial neurological deficit. Furthermore, IVT rate was comparable in both groups (74.5% in MS *vs.* 81.9% in DAS; $p = 0.09$). Time from picture-to-puncture and onset-to-groin puncture was significantly shorter in the MS group (61.5 ± 26.5 min for MS and 145.8 ± 67.0 min for DAS patients, $p < 0.001$ and 178.7 ± 64.5 min in MS patients *vs.* 263.7 ± 58.4 min in DAS patients, $p < 0.001$, respectively), whereas door-to-groin puncture time was shorter in the DAS group (median 35.4 ± 25.2 min *vs.* 85.9 ± 44.2 min, $p < 0.001$).

The rate of successful recanalisation (TICI 2b-3) as well as failed recanalisation (TICI 0) at the end of the procedure was similar in both groups (69.6% for MS patients *vs.* 68.4% for DAS patients; $p = 0.799$ for TICI 2b-3 and 10.4% for MS patients *vs.* 9.8% for DAS patients; $p = 0.825$ for TICI 0). The clinical and procedural details are set out in Table 1.

There was a significant difference in the 3-month excellent clinical outcomes expressed as mRS 0–1 between these two groups (32.9% of MS patients *vs.* 22.5% of DAS patients, $p < 0.05$). Similarly, a greater number of patients achieved mRS 0–2 in the MS model compared to the DAS model, although statistical significance was not reached (42.3% MS *vs.* 34.5%

Table 1. Baseline and treatment characteristics. Statistical significance marked in bold

Characteristic	MS group (n = 267)	DAS group (n = 133)	P-value
Baseline			
Males (n, %)	114 (42.7%)	66 (49.6%)	0.18
Age, y (mean)	73.7 ± 11.9	72.3 ± 12.5	0.16
mRS score = 0–1	211 (79.0%)	113 (85.0%)	0.15
mRS score = 2	56 (21.0%)	20 (15.0%)	015
Hypertension (n, %)	137 (51.3%)	59 (44.4%)	0.19
Diabetes (n, %)	75 (28.1)	41 (30.8%)	0.57
Atrial fibrillation (n, %)	56 (21.0)	30 (22.6)	0.72
Baseline NIHSS	18.2 ± 5.4	20.1 ± 4.1	0.11
IV-thrombolysis (n, %)	199 (74.5%)	109 (81.9%)	0.09
Time in min (mean ± SD)			
Picture-to-puncture	61.5 ± 26.5	145.8 ± 67.0	< 0.001
Onset-to-puncture	178.7 ± 64.5	263.7 ± 58.4	< 0.001
Door-to-puncture	85.9 ± 44.2	35.4 ± 25.2	< 0.001
Procedural results (n, %)			
Recanalisation (TICI 2b-3)	186 (69.6%)	91 (68.4%)	0.79
No recanalisation (TICI 0)	28 (10.4%)	13 (9.8%)	0.83
sICH	23 (8.5%)	11 (7.9%)	0.10
Clinical outcome (n, %)			
NIHSS at discharge	7.51	8.47	0.21
3-months mRS score = 0–1	88 (32.9%)	30 (22.5%)	< 0.05
3-months mRS score ≤ 2	113 (42.3%)	46 (34.5%)	0.13
3-months mortality rate	57 (21.4%)	31 (23.1%)	0.44

Used tests: Student's t-test, Mann-Whitney test, Chi-squared Pearson test

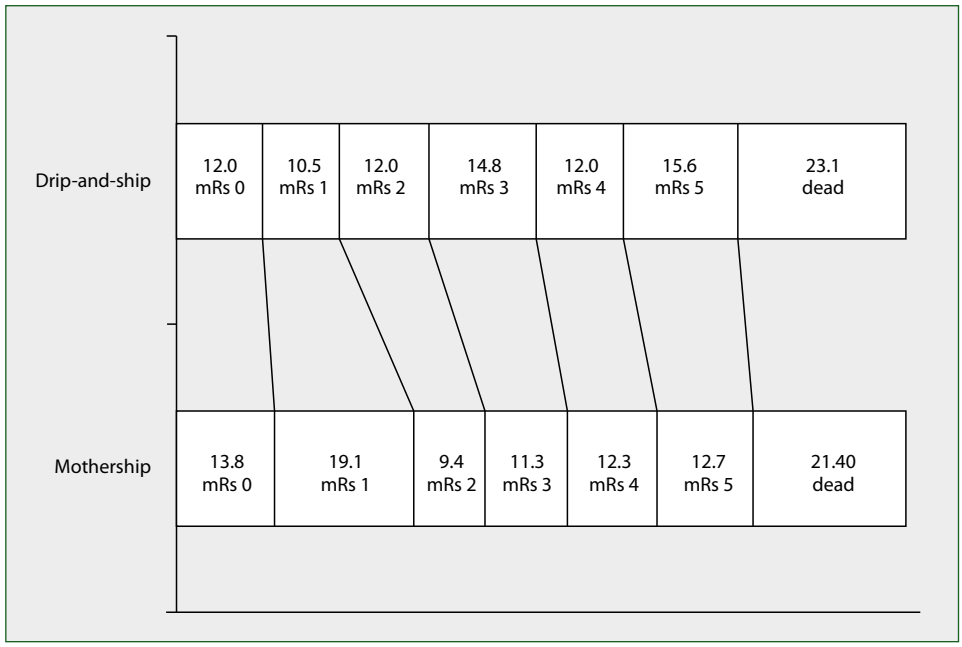

Figure 1. Percentage distribution of patients' modified Rankin scale scores at 3-month follow-up in compared groups

DAS, p = 0.136, Fig. 1). The rate of symptomatic intracranial haemorrhage and mortality was similar in both groups (8.5% in MS *vs.* 7.9% in DAS group, p = 0.101 and 21.4% in MS *vs.* 23.1% in DAS group, p = 0.44, respectively).

Discussion

The aim of this study was to evaluate whether the 'mothership' paradigm featuring direct admission of a stroke patient to the CSC without prior administration of IV thrombolysis in PSC results in a higher rate of favourable clinical outcomes, as it potentially shortens the time from onset to groin puncture and may result in earlier recanalisation. Several clinical trials focusing on endovascular therapy of ischaemic stroke have highlighted the importance of rapid treatment [7, 8]. Ota et al. [9] confirmed that onset-to-puncture time has an independent effect on functional outcomes after MT, and concluded that reducing this time metric is a key factor in successful endovascular therapy. In addition to this, the benefit of bridging IVT prior to MT is currently under discussion, and some studies have reported comparable thrombectomy outcomes with and without thrombolysis [10, 11].

The available studies comparing the results of MT in patients treated in the MS and DAS models do not clearly indicate an advantage for either of them. According to Garchenfeld et al., who compared both paradigms, there was no statistically significant difference either in terms of successful recanalisation or in long-term clinical outcome [14]. Similarly, the results of the RACECAT trial did not support the hypothesis that direct transfer of LVO suspected patients to CSC leads to improved outcomes [2].

On the other hand, Rinaldo et al., who reported clinical outcomes of 8,500 patients with LVO, showed that patients transferred from PSC have an increased risk of mortality compared to patients treated in CSC [12]. Recently published insights from the Ischaemic Stroke Registry in France showed that significantly more functional independence was achieved among MS patients compared to DAS patients [13].

This aligns with our findings. We observed a significant difference in 3-month excellent clinical outcomes expressed as mRS 0–1 between MS patients (32.9%) and DAS patients (22.5%). We also noticed that a greater number of patients achieved mRS 0–2 in the MS model (42.3%) compared to the DAS model (34.5%), although statistical significance was not reached. This result is most likely due to the significant onset-to-puncture time difference between the two groups (–85 min in MS patients *vs.* DAS patients), and was not abolished by significantly longer door-to-puncture time in the MS model compared to the DAS model.

We can assume that further acceleration of acute stroke patient management in CSCs and a 24-hour on-site angio suite team would significantly reduce the door-to-puncture time, resulting in even better treatment outcomes in the MS model. However, we should be aware that one limitation of the MS model is the possibility of overloading CSCs with stroke patients who will not be candidates for MT.

Our study has several limitations: a) the limited number of evaluated patients which limits the generalisability of our findings; b) the retrospective design of the study; c) the data collected in the tertiary hospital in the Lublin operational area and our findings may not be relevant to other regions; and d) our study does not take into account stroke-suspected patients transferred directly to CSC but who are eventually not eligible for MT.

Conclusions

Our study shows that patients with LVO transferred directly to a CSC (the MS model) achieved a better rate of excellent 3-month functional independence expressed as mRS 0–1 compared to the DAS paradigm. However, if the favourable clinical outcome is defined as mRS 0–2, the benefit of the MS approach was still not clearly demonstrated.

Clinical implications

The question of the overall best treatment paradigm for stroke patients remains unanswered. An effective and reliable pre-hospital assessment for LVO may condition the direct transport of the patient to the CSC, resulting in better clinical outcomes after MT. The use of the MS model or the DAS model should be flexible and based on the regional stroke service.

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