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Direct transfer of acute stroke patients to angiography suites equipped with flat-detector computed tomography: literature review and initial single-centre experience

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Background: Time is brain! This paradigm is forcing the development of strategies with potential to shorten the time from symptom onset to recanalization. One of these strategies is to transport select patients with acute ischaemic stroke directly to an angio-suite equipped with flat-detector computed tomography (FD-CT) to exclude intracranial haemorrhage, followed directly by invasive angiography and mechanical thrombectomy if large-vessel occlusion (LVO) is confirmed. *Aim:* To present existing published data about the direct transfer (DT) of stroke patients to angio-suites and to describe our initial experience with this stroke pathway. *Methods:* We performed a systematic PubMed search of trials that described DT of stroke patients to angio-suites and summarized the results of these trials. In January 2020, we implemented a new algorithm for acute ischaemic stroke care in our stroke centre. Select patients suitable for DT (National Institute of Health Stroke Scale score $\geq$10, time from symptom onset to door <4.5 h) were referred by neurologists directly to an angio-suite equipped with FD-CT. Patients treated using this algorithm were analysed and compared with patients treated using the standard protocol including CT and CT angiography in our centre. *Results:* We identified seven trials comparing the DT protocol with the standard protocol in stroke patients. Among the 628 patients treated using the DT protocol, 104 (16.5%) did not have LVO and did not undergo endovascular treatment (EVT). All the trials demonstrated a significant reduction in door-to-groin time with DT, compared with the standard protocol. This reduction ranged from 22 min (DT protocol: 33 min; standard protocol: 55 min) to 59 min (DT protocol: 22 min; standard protocol: 81 min). In three of five trials comparing the 90-day modified Rankin scale scores between the DT and standard imaging groups, this reduction in ischaemic time translated into better clinical outcomes, whereas the two other trials reported no such difference in scores. Between January 2020 and October 2021, 116 patients underwent EVT for acute ischaemic stroke in our centre.

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Among these patients, 65 (56%) met the criteria for DT (National Institutes of Health Stroke Scale score >10, symptom onset-to-door time <4.5 h), but only 7 (10.8%) were transported directly to the angio-suite. The reasons that many patients who met the criteria were not transported directly to the angio-suite were lack of personnel trained in FD-CT acquisition outside of working hours, ongoing procedures in the angio-suite, contraindication to the DT protocol due to atypical clinical presentation, and neurologist's decision for obtain complete neurological imaging. All seven patients who were transported directly to the angio-suite had LVOs. The median time from door-to-groin-puncture was significantly lower with the DT protocol compared with the standard protocol {29 min [interquartile range (IQR): 25–31 min] vs. 71 min [IQR: 55–94 min]; $P < 0.001$}. None of the patients had symptomatic intracranial haemorrhage in the DT protocol group, compared with 7 (6.4%) patients in the standard protocol group. Direct transfer of acute ischaemic stroke patients to the angio-suite equipped with FD-CT seems to reduce the time from patient arrival in the hospital to groin puncture. This reduction in the ischaemic time translates into better clinical outcomes. However, more data are needed to confirm these results.

Introduction

Mechanical thrombectomy is the treatment of choice for select patients with acute ischaemic stroke caused by large-vessel occlusion (LVO)[1-6] and has been recommended as the standard of care by the current guidelines.[7,8] The clinical efficacy of mechanical thrombectomy is highly dependent on the time duration between symptom onset and reperfusion.[9,10] This has driven efforts to shorten the delay caused by the pathway after hospital admission.

One of the strategies developed to bypass emergency and conventional imaging, including non-enhanced multidetector computed tomography (CT), a CT angiography, is direct transfer (DT). Direct transfer protocols for stroke patients were developed in several stroke centres with the aim to minimize the 'door-to-groin' time, i.e. the interval between patient arrival to the hospital and the mechanical thrombectomy procedure.

These protocols were used in patients presenting soon after symptom onset (to minimize the risk of large established ischaemia) and in those with severe neurological deficits (increased probability of LVO). Such patients are taken directly to angiography suites equipped with flat-detector computed tomography (FD-CT), which helps rule out intracranial haemorrhage and a large established infarct.[11-13] After the initial FD-CT, LVO can be diagnosed using a flat-detector angiography system immediately before arterial puncture, or directly using diagnostic invasive angiography.

The aim of this study was to perform a literature review of trials that included stroke patients transported directly to angio-suites equipped with FD-CT to evaluate the efficacy and safety of these protocols and to describe our initial experience with DT in stroke patients.

Methods

Literature review

We focused on clinical trials that described the logistics, efficacy, and safety of DT in stroke patients. We performed a systematic search on PubMed using the following keywords: 'direct transfer stroke', 'one-stop stroke management', 'flat-detector CT in stroke', and 'angio-suite transfer of stroke patients'. Among the 27 pre-screened papers, 7 met the inclusion criteria and were analysed.

Direct transfer protocol in our stroke centre

In the second part of the study, we report our initial experience with the DT protocol. In January 2020, we implemented a new algorithm for care of stroke patients treated in our comprehensive stroke centre. Patients who presented within 4.5 h of symptom onset and had severe neurological deficits [National Institutes of Health Stroke Scale (NIHSS) score ≥10] consistent with anterior circulation symptomatology were transferred directly to an angio-suite equipped with FD-CT (Philips Azurion 7 C20, Koninklijke Philips, Amsterdam, Netherlands). Flat-detector computed tomography scans were obtained, and if there were no signs of intracranial haemorrhage or large established ischaemia, invasive selective angiography of the supposedly occluded vessel was performed. If the angiography confirmed LVO, mechanical thrombectomy was performed.

Statistical analysis

Continuous variables were tested for normality using the Kolmogorov–Smirnov test and were presented as medians with interquartile range (IQR). Group differences were analysed using the Mann–Whitney *U*-test. Results were considered statistically significant at $P < 0.05$. All statistical analyses were performed using SPSS Statistics software (version 26; IBM Corp., Armonk, NY, USA).

Results

Literature review

Seven articles met the inclusion criteria[14-20] (*Table 1*), comprising five single-centre observational trials,[14-18] one single-centre prospective cohort study,[19] and one single-

Table 1 The overview of the trials describing direct transfer of acute stroke patients to angiography suites equipped with flat-detector computed tomography

			Ribo *et al.*[16]	Jadhav *et al.*[15]	Psychogios *et al.*[14]	Mendez *et al.*[17]	Psychogios *et al.*[18]	Bouslama *et al.*[19]	Requena *et al.*[20]
General	Type of study		Single-centre observational	Single-centre observational case-control	Single-centre observational	Single-centre observational case-control	Single-centre observational case-control	Single-centre prospective cohort	Single-centre randomized
Study population	Time from symptom onset		≤4.5 h	≤6 h	≤5 h	≤6 h	≤6 h	–	≤6 h
	Baseline stroke severity		RACE >4, NIHSS >10	NIHSS ≥ 9	NIHSS ≥ 10	RACE >4 NIHSS > 10	NIHSS ≥ 10 or ≥7 (from 2017)	–	RACE >4 NIHSS > 10
	Primary/secondary transports		Both	Secondary	Both	Both	Both	Secondary	Both
	Number of DT patients		40	111	30	97	230	61	89
	Number of DT without prior imaging		11	0	21	27	127	0	19
	Non-LVO DT patients (%)		16.4	6.3	40	18.6	27.8	8.2	16.9
Imaging protocol	NC FD-CT		Yes	Yes	Yes	Yes	Yes	Yes	Yes
	FD-CTA		No	No	LVO detection	No	LVO detection	LVO and collateral status study	No
Time metrics (min)	Onset to door	DT	182	303	105	207	160	227	233
		Control	160	304	Unknown	182	129	310	242
	Door to groin	DT	17	22	21	16	25	33	18
		Control	60	81	55	70	60	55	42
	Door to reperfusion	DT	73	66	65	70	68	85	57
		Control	114	125	106	111	102	111	84
Clinical outcomes	Dramatic recovery (%)	DT	48.6	–	–	50.6	–	–	33.8
		Control	27.4	–	–	31.7	–	–	28.8
	90 days % mRS 0-2	DT		43		41	58	45	43
		Control	–	44	–	28	33	41	27
	sICH (%)	DT	5	3	4	2.5	7	4.1	1.4
		Control	9.6	3	7	7.6	5	2	4.1

DT, direct transfer to flat detector computed tomography equipped angiography suite; RACE, Rapid Arterial Occlusion Evaluation Scale for Stroke; FD-CTA, flat-detector computed tomography angiography; LVO, large-vessel occlusion; mRS, modified Rankin Scale score; NC FD-CT, non-contrast-enhanced flat-detector computed topography; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial haemorrhage.

centre prospective randomized trial.[20] Altogether, the trials included 628 patients treated using DT protocols.

The inclusion criteria for DT were a symptom-onset-to-door interval <6 h in four trials,[15,17,18,20] <5 h in one trial,[14] and <4.5 h in one trial,[16] together with presence of a neurological deficit, defined as an NIHSS score ≥ 10 in five trials[14,16-20] and ≥ 9 in one trial.[15]

Five trials included both patients admitted directly to comprehensive stroke centres without prior imaging and patients who underwent initial neurological imaging at primary stroke centres. Two trials included only patients transported from other stroke centres, which did not provide endovascular treatment (EVT).[15,19] A total of 184 patients were admitted directly to comprehensive stroke centres without prior neurological imaging. Among the 628 patients treated using the DT protocol, 104 (16.5%) did not have LVOs and did not undergo EVT.

All trials used native FD-CT to exclude intracranial haemorrhage and large established ischaemia. The protocols used in two trials[14,18] also included FD-CT angiography to detect LVO, while another trial[19] used FD-CT angiography to evaluate the status of collaterals. All other trials used invasive angiography to confirm LVO.

All trials demonstrated a significant reduction in the door-to-groin time using the DT protocol compared with the standard protocol, which included complete neurological imaging. This reduction ranged from 22 min (DT protocol: 33 min; standard protocol: 55 min)[19] to 59 min (DT protocol: 22 min; standard protocol: 81 min).[15] The reduced ischaemic time translated into better clinical outcomes in three of five trials comparing the 90-day modified Rankin scale score between the DT and standard protocol groups.[15,17-20] Requena *et al.*,[20] Psychogios *et al.*,[18] and Mendez *et al.*[17] reported a significantly better 90-day modified Rankin scale score in patients transported directly to the angio-suite, compared with patients who underwent standard imaging, whereas Jadhav *et al.*[15] and Bouslama *et al.*[19] reported no such difference.

The risks of symptomatic intracranial haemorrhage and type 2 parenchymal haematoma, as the main safety endpoints, were not significantly higher in the DT protocol group in any of the trials.

Our experience with direct transfer

Between January 2020 and October 2021, 116 patients underwent EVT in our stroke centre, of whom 65 (56%) fulfilled the criteria for DT (time from symptom onset to door <4.5 h, NIHSS score ≥ 10, and anterior circulation symptoms); however, only 7 (10.8%) of these patients were treated using the DT protocol. The most common reasons why DT was not used in more patients included lack of personnel trained in FD-CT outside of working hours, other procedures taking place in the angio-suite, atypical clinical presentation (severe headache, severe impairment of conscious level, extreme hypertension or signs of cranial trauma) and the neurologist's decision to obtain complete neurological imaging (due to the atypical signs that increased probability of intracranial haemorrhage or stroke mimics). All patients treated using the DT protocol were admitted to our stroke centre primarily, without any previous neurological imaging. All seven patients treated using the DT protocol were diagnosed with LVO and underwent EVT, and only one patient (14.3%) underwent intravenous thrombolysis.

There was a significant reduction in the time interval between hospital arrival and groin puncture in DT patients compared with the 109 patients treated using the standard protocol [29 min (IQR: 25–31 min) vs. 71 min (IQR: 55–94 min); $P < 0.001$]. A borderline significant reduction in the interval between hospital arrival and recanalization was also observed with the DT protocol compared with the standard protocol [75 min (IQR: 65–102 min) vs. 113 min (IQR: 92–147 min); $P = 0.055$]. None of the patients had symptomatic intracranial haemorrhage in the DT protocol group, compared with 7 (6.4%) patients in the standard protocol group (*Table 2*).

Discussion

All the reviewed trials demonstrated that transport of selected stroke patients directly to the angio-suite equipped with FD-CT reduced in-hospital delays and resulted in quicker initiation of EVT and faster reperfusion. The faster reperfusion translated into better clinical outcomes in one randomized trial,[20] as well as some non-randomized trials that described clinical outcomes.[17,18]

The results of the reviewed studies suggested that there may be multiple reasons for the improved clinical outcomes in stroke patients treated using the DT protocol. The first and most obvious reason is that the effect of EVT in ischaemic stroke is highly time-dependent.[9,10,21] Ribo *et al.*[22] reported that the odds of functional independence decreased by $\sim$15% for every 30 min of delay in reperfusion. Therefore, decreasing the in-hospital delay increases the odds of good clinical outcomes. Second, the DT protocol prevents over-selection of patients for EVT. Even the benefits of EVT for patients with established ischaemic changes are uncertain, some trials have suggested that EVT may improve outcomes.[23,24] Requena *et al.*[20] reported that no patient with confirmed LVO in the DT protocol group was excluded from EVT, compared with 13% of patients in the standard protocol group, who were excluded because of large established ischaemia on CT. This absence of over-selection in patients undergoing less sensitive FD-CT may contribute to the clinical effects of the DT protocol.

However, some questions regarding the patients in the DT protocol group who did not undergo EVT (because of haemorrhagic aetiology of stroke or the absence of LVO) remain unanswered. No trial described the clinical outcomes of these patients, who represented 16.5% of the sample. Intravenous thrombolysis was allowed in all trials if intracranial haemorrhage was excluded on FD-CT. Thus, patients with ischaemic stroke without LVO were treated according to the guidelines, with no delay in treatment. Some delay in treatment may be expected in patients with haemorrhagic stroke requiring standard multi-detector CT. Nevertheless, the main safety parameters described in the trials (symptomatic intracranial haemorrhage or parenchymal haematoma type 2) were not any more common in the DT than standard protocol group. This suggests that DT may

Table 2 Comparison of time intervals between direct transfer and standard protocol

	Standard protocol	Direct transfer
Number of patients	109	7
Median time from hospital arrival to CT/FD-CT (IQR, h: min)	0:15 (0:11; 0:21)	0:19 (0:17; 0:24)
Median time from hospital arrival to groin puncture (IQR, h: min)	1:11 (0:55; 1:34)	0:29 (0:25; 0:31)
Median time from hospital arrival to achieving a TICI grade 2 b/3 (IQR, h: min)	1:53 (1:32; 2:27)	1:15 (1:05; 1:42)
Number of patients treated by systemic thrombolysis (%)	53 (48.6)	1 (14.3)
sICH, number (%):	7 (6.4)	0 (0)

CT, computed tomography; FD-CT, flat-detector computed tomography; IQR, interquartile range; sICH—symptomatic intracranial haemorrhage; TICI, thrombolysis in cerebral infarction classification.

be a safe protocol, which can slightly delay the treatment of a minority of patients with haemorrhagic stroke, probably without any impact on their outcomes, but it can significantly speed up the treatment of the majority of LVO patients and improve clinical outcomes.

Our own experience with DT concords with these findings. Unfortunately, we are struggling with wider and routine implementation of the DT protocol in our daily practice. The main reasons have been mentioned previously. The small number of patients treated using the DT protocol in our hospital prevented us from evaluating the clinical outcomes. Flat-detector computed tomography-equipped angio-suite in our centre is dedicated mainly to structural invasive cardiology procedures, and the machine is often occupied when a stroke patient suitable for DT needs it. Dedicated stroke FD-CT-equipped angio-suites may solve this problem. During off-hours, invasive radiologists/angiologists who perform EVT are on call, and not all neurologists are familiar with FD-CT acquisition. The time-saving benefit of DT would be lost if patients have to wait for FD-CT, and the standard protocol may be more effective in this scenario. Education of the medical staff present during off-hours (including all neurologist with help of angio-suite nurses) to perform FD-CT acquisition before interventional physician arrival may solve this issue. Lastly, this new algorithm of care has faced scepticism from the medical staff, mostly because of concerns about its safety. However, evidence regarding the safety and efficacy of this protocol is growing and will hopefully overcome this scepticism.

Conclusion

Direct transfer of select stroke patients to angio-suites reduces in-hospital delays, which allows to provide earlier the most effective care for a majority of these patients (EVT for patients with LVO). The DT protocol appears to lead to better clinical outcomes in stroke patients. However, further randomized multicentre studies are required.

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