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Interfacility transfer for mechanical thrombectomy – Direct to neuroangiography or CT angiography first?

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ABSTRACT

Background and purpose: Faster time to mechanical thrombectomy (MT) improves outcome in stroke. In patients from other hospitals where a CT has ruled-out hemorrhage, transfer direct-to-angiography (DTA) may reduce door-to-groin time compared to transfer to CT angiography (CTA) +/− repeat CT first. However, this may result in unnecessary catheter angiography. We sought to determine how often CTA +/− CT changed the decision to proceed to MT.

Methods: Data on patients transferred to our comprehensive stroke center (CSC) from outside facilities for possible MT from 7/2016–5/2017 was extracted from a prospective database and supplemented with chart review.

Results: Of 170 patients transferred for MT undergoing CT +/− CTA on CSC arrival, MT was aborted in 108 (64%). Of these, 87 (81%) were aborted directly based on imaging findings, with absence of large vessel occlusion or occlusion too distal to be amenable to MT the most common reasons ($n = 76$), followed by extensive early CT changes ($n = 9$) and ICH post-tPA ($n = 2$). Even with NIHSS ≥10 on CSC arrival, MT was aborted based on imaging findings in 35% patients. Time from symptom onset dichotomized as early/late based on median onset-to-CSC arrival (253 min) was an important modifier of proceeding to MT in this group, with 71% of early presenters going to MT compared to 33% of late presenters ($p = .003$).

Conclusions: Transfer DTA may result in many patients who would have been excluded based on CT +/− CTA findings undergoing unnecessary catheter angiography. However, a target population for a DTA approach might be identifiable based on severity of deficit and time from onset.

1. Background

Mechanical thrombectomy (MT) improves outcomes in patients with stroke associated with large vessel occlusion (LVO), with faster treatment associated with better chances of recovery [1]. It is estimated that for every 4 min of delay from emergency department arrival to thrombectomy, 1 additional patient of every 100 will have increased disability. Many patients present initially to hospitals lacking endovascular or advanced imaging capabilities and are evaluated only with a non-contrast head CT; some will be treated locally with intravenous tPA. Potential candidates for MT then require urgent transfer to a comprehensive stroke center (CSC) capable of providing further evaluation and treatment. A common work-flow pathway for such transferred patients is to proceed immediately to multimodal CT on CSC arrival, including repeat non-contrast CT to assess for progression of infarction or hemorrhagic conversion, CT angiography (CTA) to assess for LVO, and in some cases, CT perfusion to optimize patient selection [2,3]. These studies consume valuable time even in high-volume centers with streamlined care processes. Recently, a "direct to angiography" (DTA) approach, bypassing CT and CTA on CSC arrival, has been proposed as a measure to substantially reduce treatment delays [4]. Such an approach depends on the clinical examination and referring hospital non-contrast head CT being sufficiently specific to identify patients with LVO to avoid a large number of unnecessary catheter angiograms. We sought to examine how often head CT and CT angiography performed at a CSC after inter-facility transfer changed the decision to pursue MT and whether specific factors associated with a change in decision could be identified.

2. Methods

We performed a retrospective review of a prospectively collected

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database of all subjects transferred to our comprehensive stroke center from an outside hospital for possible MT between July 2016 and May 2017. Our institution has a transfer protocol specifically for (and limited to) acute ischemic stroke patients being brought to our institution for possible MT. Such patients are transferred directly to the CT scanner and are met there by members of our team who perform a rapid clinical assessment and appropriate neuroimaging (typically non-contrast head CT and CT angiography during the period of this study). Patients appropriate for MT are then taken directly to the neuroangiography suite for intervention. Clinical and radiographic data which was not included in the prospectively collected database was extracted from the medical record using a standardized case report form. Reasons for deciding against MT were determined based on documentation in the medical record. This study was approved by our local institutional review board. The data that support the findings of this study are available from the corresponding author upon reasonable request.

2.1. Statistical analysis

Univariate analysis compared patients proceeding to MT with those in whom MT was aborted, with the analyzed population limited to the target population of patients undergoing CT +/− CTA on CSC arrival. Multivariable analysis of factors associated with MT was performed in this same population using logistic regression; age, baseline NIHSS, baseline ASPECTS, use of IV tPA, change in NIHSS from outside hospital to CSC, and time from symptom onset to CSC arrival were included in the model. As the goal was to identify factors independent of repeat imaging that might predict the need (or lack thereof) for such imaging, results of imaging at the CSC were not entered into the model. The effect of time from symptom onset on the decision to proceed to MT in specific subgroups was analyzed by dichotomizing into an “early” group with arrival time at the CSC below the overall median time, and a “late group” with time equal to or above the median time. Extensive early CT changes were considered present if the ASPECTS score was < 6. Analyses were performed using JMP version 14.0 (SAS Institute Inc., Cary, NC, USA).

3. Results

Of 187 patients with available data, 170 underwent CT +/− CTA on arrival, 5 went direct to angiography (DTA), and 12 were directly admitted without new imaging or intervention. Baseline characteristics of these patients are shown in Table 1. Overall, 67/187 (36%) patients proceeded to MT. In patients undergoing MT, time from CSC arrival to groin puncture tended to be shorter in the patients going DTA compared to CT +/− CTA (median 39 v 54 min, $p = .06$). Of the 12 patients directly admitted, five had complete clinical recovery on CSC arrival, review of outside hospital CTA indicated MT was either not feasible or not indicated in four, two were hemodynamically unstable, and one was diagnosed with stroke mimic on CSC arrival.

Table 1
Baseline characteristics of overall study population.

	$n = 187$
Age (mean ± SD)	68 ± 15
Female sex	84 (45%)
Atrial fibrillation	59 (32%)
Intravenous tPA given	84 (45%)
Prior anticoagulation use	28 (15%)
In-hospital stroke	20 (11%)
Baseline NIHSS, OSH, median (IQR)	11 (6–18)
ASPECTS, OSH, median (IQR)	9 (7–10)
CTA done at outside hospital	57 (30%)
Time from symptom onset to CSC arrival, min, median (IQR)	253 (198–397)

tPA: tissue plasminogen activator; NIHSS: National Institute of Health Stroke Scale; ASPECTS: Alberta Stroke Program Early CT Score; CTA: CT angiography; CSC: Comprehensive Stroke Center.

Among the 170 patients undergoing CT +/− CTA on CSC arrival, MT was aborted in 108 (64%) patients. Of these, 87 (81%) were aborted directly based on imaging findings, with absence of LVO or occlusion too distal to be amenable to MT being the most common reason ($n = 76$), followed by early CT changes felt to be too extensive ($n = 9$) and ICH post-tPA ($n = 2$). Study flowchart is illustrated in Fig. 1. Time from symptom onset to CSC arrival was associated with proceeding to MT; stratifying by the median time from onset (253 min), 46% of those presenting early proceeded to MT, compared to 26% of those presenting late ($p = .01$). In patients with outside hospital CTA demonstrating proximal LVO ($n = 49$), MT was aborted in 23 (47%) on CSC arrival, again primarily based on imaging findings ($n = 13$, 57%). These included absence of LVO or occlusion too distal to be amenable to MT ($n = 5$), ICH post-tPA ($n = 1$), early CT changes felt to be too extensive ($n = 6$), and presumed chronic cervical carotid artery occlusion (n = 1). Time from symptom onset to CSC arrival was an even more important factor in proceeding to MT in this group, with 79% of those presenting early proceeding to MT, compared to 35% of those presenting late ($P = .003$).

Univariate analysis of factors associated with proceeding to MT in the group of patients who underwent CT +/− CTA are shown in Table 2, and multivariate analysis in Table 3. In the latter, higher baseline NIHSS was associated with greater likelihood of proceeding to MT, and decrease in NIHSS (i.e. improvement) from initial to CSC examination was associated with a lower likelihood; other factors were not significantly associated with MT decision.

Further analysis using dichotomized NIHSS at thresholds indicative of severe stroke showed that, even in these patients, a substantial portion had MT aborted based on imaging findings. With NIHSS ≥10 on CSC arrival, MT was aborted based on imaging findings in 39 (35%) patients; in those with NIHSS ≥15, MT was aborted in 19 (26%) patients. In these subgroups, time from symptom onset was an important modifier of proceeding to MT. With NIHSS ≥10, 71% of those presenting earlier went to MT compared to 33% of those presenting later ($p = .003$); with NIHSS ≥15, it was 84% and 46%, respectively.

Restriticing analysis to patients presenting < 6 h from onset did not substantially change the results.

4. Discussion

We found that CT and CT angiography performed at a CSC after inter-facility transfer changed the decision to pursue MT a substantial portion of the time, even in patients with severe deficits on CSC arrival. The main reason for aborting MT in these cases was distal location or recanalization of vessel occlusion, followed by early extensive infarct changes on repeat CT. Not surprisingly, patients with severe deficit on CSC arrival were more likely to proceed to MT, particularly if there was a shorter interval between symptom onset and CSC arrival. Even in patients with a CTA at the outside hospital which demonstrated an LVO, re-scanning on arrival at the CSC resulted in a decision to abort MT in a significant number of patients, again mostly due to imaging findings.

Perhaps not surprisingly, we found that clinical improvement, as measured by a decrease in NIHSS between outside hospital and CSC arrival, was independently and robustly associated with a lower likelihood of proceeding to MT. The lack of an association with baseline ASPECTS score and the decision to pursue MT in multivariate analysis may seem counterintuitive at first examination, however this comparison is complex. On the one hand, while patients with a high ASPECTS score might be considered ideal candidates for MT, these patients are also more likely to have spontaneous recanalization, clinical improvement, or be a stroke mimic, resulting in aborting MT. Conversely, patients with lower ASPECTS scores, while more likely to have some irreversible brain infarction, are also more likely to have persistent severe deficit and proximal large vessel occlusion justifying proceeding to MT. While it might be expected that patients treated with IV tPA

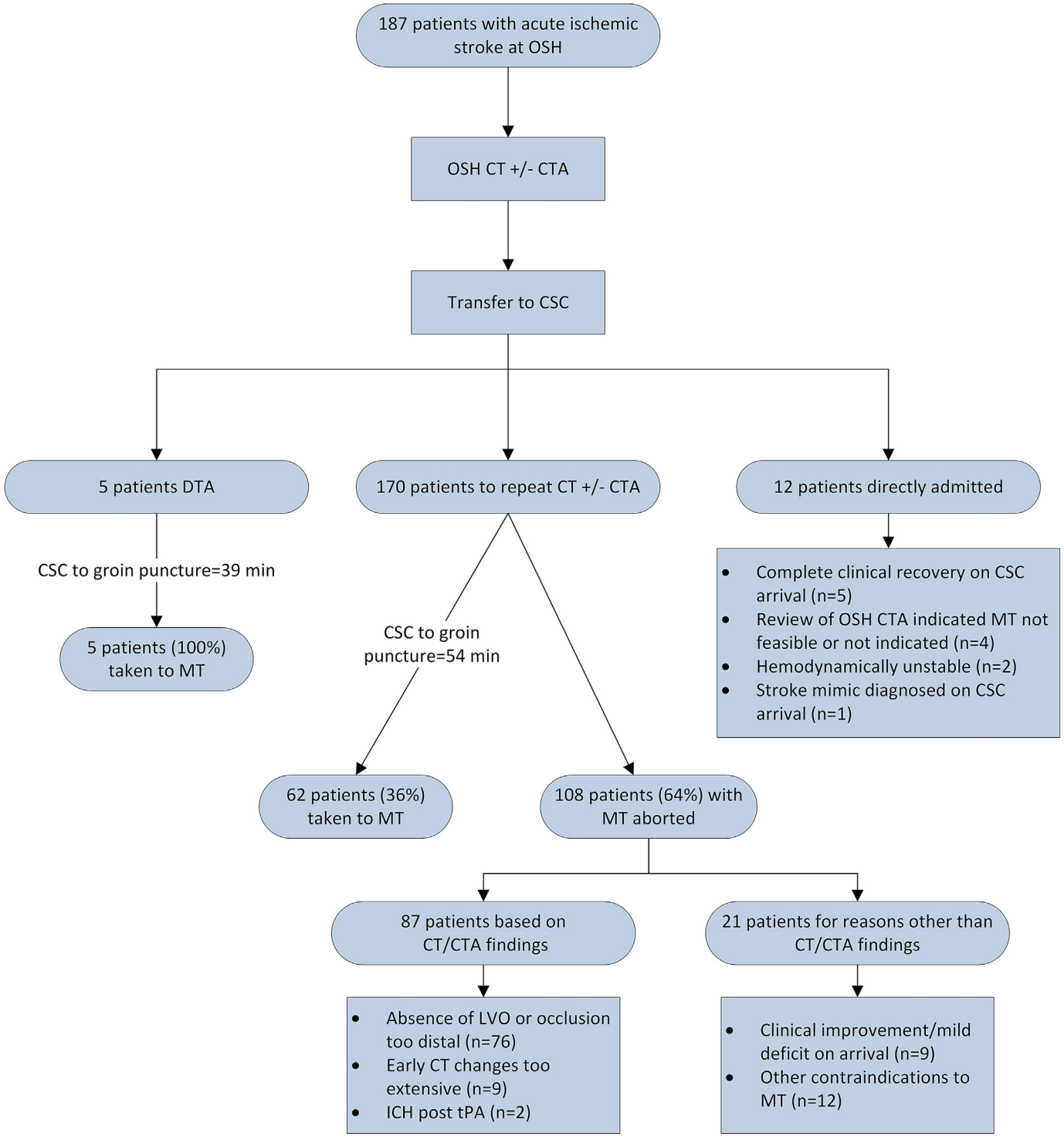

Fig. 1. Study flowchart.
OSH: outside hospital; CTA: CT angiography; CSC: Comprehensive Stroke Center; MT: mechanical thrombectomy; DTA: direct to angiography; tPA: tissue plasminogen activator;

would be more likely to have early recanalization and thus not need MT, we did not find a significant association between tPA use and MT. However, the confidence intervals are wide and the point estimate does not exclude an important effect of tPA in this respect, so this finding should be interpreted with caution.

In a single center study, a "direct to angiography" approach - bypassing CT/CTA- was shown to substantially reduce treatment times, with almost a 60 min reduction in door-to-groin puncture times, without any apparent safety concerns. [4] Our data suggest that a target population for a DTA approach might be identified based on clinical factors (severity of deficit and time from onset) in which the benefit from faster time to treatment outweighs the harm of unnecessary catheter angiography. However, it also argues against a blanket policy of taking all potential MT candidate direct to the neuroangiography suite. Furthermore, there may be additional benefits to performing CTA prior to catheter angiography which are harder to quantify, such as

Table 2
Factors associated with proceeding to MT in the group of patients who underwent CT +/− CTA on arrival at the comprehensive stroke center.

	No thrombectomy (n = 108)	Thrombectomy (n = 62)	p-Value
Age (mean ± SD)	67 ± 16	70 ± 14	0.24
Female sex	46%	42%	0.58
Atrial fibrillation	15%	13%	0.74
Baseline NIHSS, OSH, median (IQR)	9 (5–14)	17 (9–21)	< 0.0001
NIHSS on arrival at CSC, median (IQR)	9 (4–14)	20 (13–24)	< 0.0001
Intravenous tPA given	45%	52%	0.34
Prior anticoagulation use	15%	13%	0.74
In-hospital stroke	11%	10%	0.77
ASPECTS, OSH, median (IQR)	9 (7–10)	8 (7–10)	0.16
ASPECTS, CSC, median (IQR)	9 (8–10)	7 (6–9)	< 0.0001
Change in NIHSS from OSH to CSC, median (IQR)	0 (−3 to 3)	+4 (0–7)	0.002
Time from symptom onset to CSC arrival, min, median (IQR)	267 (204–437)	221 (181–315)	0.007
Time from OSH imaging to CSC imaging, min, median (IQR)	151 (127–192)	140 (121–174)	0.14

OSH: outside hospital; tPA: tissue plasminogen activator; NIHSS: National Institute of Health Stroke Scale; ASPECTS: Alberta Stroke Program Early CT Score; CSC: Comprehensive Stroke Center.

Table 3
Multivariate analysis of factors associated with proceeding to mechanical thrombectomy.

Characteristic	OR (95% CI)	p-value
Age, per year	0.99 (0.93–1.04)	0.70
Baseline NIHSS, per point	1.36 (1.16–1.64)	< 0.0001
Baseline ASPECTS, per point	1.36 (0.88–2.24)	0.17
Time onset to CSC arrival, per hour	0.80 (0.59–1.09)	0.12
NIHSS change, per point decrease	0.81 (0.69–0.91)	0.0004
IV tPA	0.33 (0.05–1.78)	0.20

NIHSS: National Institute of Health Stroke Scale; ASPECTS: Alberta Stroke Program Early CT Score; CSC: Comprehensive Stroke Center; tPA: tissue plasminogen activator.

identification of anomalous vasculature, severe atherosclerotic disease, or tandem occlusions that could inform the angiographic approach and risk of intervention.

Our study has limitations. First, the degree of early CT hypodensity which should exclude patients from MT is an unsettled question; at the time our data was collected, we generally considered an ASPECTS score < 6 as an exclusion. Recently, it has been suggested that even patients with more extensive CT changes might benefit from MT. [5] Second, we did not routinely pursue MT in patient with M2 branch occlusions unless there was a severe deficit and the M2 branch appeared unusually large. A more aggressive stance on pursuing more distal branch occlusions would clearly decrease the frequency with which CTA changed the MT decision and strengthen the argument for a DTA approach. Third, we had a small number of patients who underwent CT angiography at the initial hospital prior to CSC transfer; while we found repeating CT +/− CTA frequently changed the MT decision even in this group, the number of patients studied is small. Finally, the effect of time from symptom onset is clearly important; while the large majority of our patients arrived within 6 h of onset, time from initial to CSC imaging was quite prolonged.

Further studies should focus on identifying an optimal "high-yield" target population (e.g. NIHSS ≥15, time from onset < 4.5 h) in which repeat CT +/− CTA on CSC arrival (or CT angiography in those arriving directly to the CSC) could be deferred and time to thrombectomy acclerated. Given the marked time dependence of MT on outcome, this could substantially improve outcomes at the population level.

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Contributorship statement

KH- Substantially contributed to the conception and design on the project, data acquisition and analysis, and drafting of the mansucript.

MS- Substantially contributed to data acquisition and revision of the manuscript for important intellectual content.

EN - Substantially contributed to data acquisition and revision of the manuscript for important intellectual content.

BP- Substantially contributed to data acquisition and revision of the manuscript for important intellectual content.

BC -Substantially contributed to the conception and design on the project, data acquisition and analysis, and drafting and revising of the mansucript.

Data sharing

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

Declaration of Competing Interest

None of the authors have any competing interests to disclose.

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