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Mechanical Thrombectomy After Inter-Hospital Transfer: A Narrative Review of Door-In-Door-Out Time as a Quality Measure

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Abstract

Most patients who need mechanical thrombectomy do not arrive at a hospital that can perform it. They arrive somewhere else first, and what happens in that first emergency department, between the doors, decides much of what the procedure can still achieve.

Objectives: *To review the published evidence on door-in-door-out time in acute stroke: how long it actually takes, how that compares with the recommended target, what determines it, who waits longest, and what the evidence establishes about its relationship to outcome.*

Material and Methods: *Narrative review of randomised trials, individual patient data meta-analyses, national registry analyses, single-network cohorts and society guidance indexed in PubMed and the major stroke and neurointervention journals. No new patient data were generated; every estimate quoted is one published by the original investigators.*

Results: *Across 108,913 transfers from 1925 hospitals, the median door-in-door-out time was 174 minutes (IQR 116 to 276) and only 27.3 per cent of patients met the recommended target of 120 minutes or less. Among patients transferred specifically for endovascular therapy the median was 132 minutes. Longer times were associated with age 80 or older (14.9 additional minutes), non-Hispanic Black ethnicity (8.2), Hispanic ethnicity (5.4) and female sex (5.2). Individual centres have reported medians of 86 minutes, and 59 minutes within working hours. Thrombectomy itself achieved functional independence in 46 per cent against 27 per cent with medical therapy alone within six hours.*

Conclusion: *The interval is long, highly variable, and demonstrably compressible, since some centres achieve less than half the national median with the same technology. It is also the part of the pathway with no clinical work in it: the decision has been made and the patient is waiting. Whether shortening it improves outcomes has not been tested randomly, and the observational evidence is confounded by severity in both directions.*

Abbreviations: *AIS – Acute Ischaemic Stroke, DIDO – Door-In-Door-Out, ED – Emergency Department, EVT – Endovascular Thrombectomy, LVO – Large Vessel Occlusion, mRS – Modified Rankin Scale, cOR – Common Odds Ratio, IQR – Interquartile Range.*

Keywords: *Acute Ischaemic Stroke; Mechanical Thrombectomy; Door-In-Door-Out Time; Interhospital Transfer; Stroke Systems of Care*

Introduction

Mechanical thrombectomy is among the most effective treatments in acute medicine. Pooled individual patient data from five randomised trials covering 1287 patients showed reduced disability at 90 days with an adjusted common odds ratio of 2.49 (95% CI 1.76 to 3.53), with functional independence in 46 per cent against 27 per cent under medical therapy alone [1]. Later trials extended eligibility to selected patients presenting between 6 and 24 hours [2,3,4], and to those with established large infarcts [5,6].

It is also among the most time-sensitive. In the same pooled dataset, the odds of a better outcome fell as the interval from symptom onset to arterial puncture lengthened, with a common odds ratio of 2.79 at three hours, and the benefit ceased to be statistically significant beyond 7.3 hours [7]. The treatment effect therefore decays while the patient is being moved.

Moving them is usually necessary. Thrombectomy requires an angiography suite, an interventional operator and a team, and most hospitals have none of these, so patients presenting to a non-capable centre must be transferred [8,9]. The interval between arriving at the first hospital and leaving it is called the door-in-door-out time, and it contains no treatment. This review examines what is known about it: its length, its determinants, its distribution across patients, and the strength of the evidence linking it to outcome.

Material and Methods

Search strategy: PubMed and the archives of the major stroke, neurology and neurointervention journals were searched for studies of interhospital transfer for thrombectomy. Search terms combined acute ischaemic stroke, large vessel occlusion and thrombectomy with door-in-door-out, interhospital transfer, drip and ship, mothership, transfer delay, workflow and systems of care. Reference lists of society guidance [8,9,10] were screened by hand for primary sources.

Eligibility: Studies were included if they reported door-in-door-out or equivalent transfer intervals, determinants of those intervals, or their relationship to treatment times or clinical outcome. Trials of thrombectomy itself are cited to establish efficacy and its time dependence, not as evidence about transfer, and are identified as such.

Data extraction and handling: Design, setting, sample size, the definition of the interval used and the reported estimate were extracted as published. Definitions of the transfer interval differ between studies, and the definition is reported alongside every figure. Whether an association was adjusted is stated, because confounding by stroke severity operates in both directions in this literature. No pooling or re-analysis was performed. Figures 1 to 4 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

How long it takes: The largest description comes from the Get With The Guidelines-Stroke registry, covering 108,913 patients transferred from the emergency departments of 1925 hospitals between 2019 and 2021. The median door-in-door-out time was 174 minutes (IQR 116 to 276), and only 27.3 per cent of patients were transferred within the recommended 120 minutes. The median differed by reason for transfer: 178 minutes for haemorrhagic stroke, 201 minutes for ischaemic stroke transferred for other reasons, and 132 minutes for ischaemic stroke transferred for endovascular therapy (Figure 1) [11]. The 120-minute benchmark itself originates in Brain Attack Coalition recommendations [12].

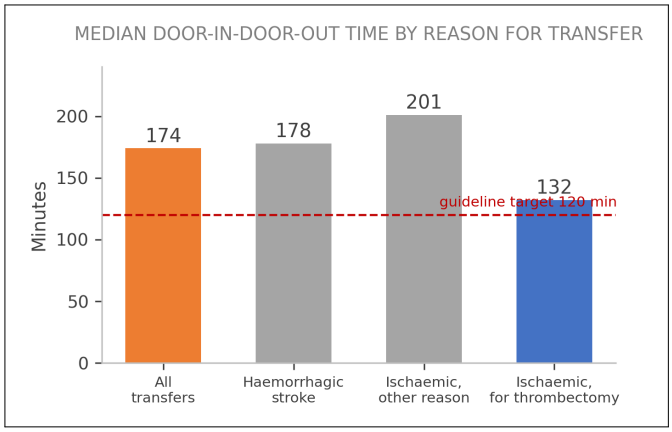

Figure 1: Median door-in-door-out time by reason for transfer, against the recommended target of 120 minutes [11,12]

How much shorter it can be: The national median is not a technical limit. A single primary stroke centre reported a median door-in-door-out time of 86 minutes (IQR 65 to 111) for patients transferred for thrombectomy, falling to 59 minutes (IQR 51 to 80) during working hours [13]. A large hub-and-spoke network reported a median of 120 minutes (IQR 97 to 149), with 18 per cent of transfers achieved within 90 minutes (Figure 2) [14]. The gap between 174 minutes and 59 minutes is not explained by imaging or by geography; it is explained by whether the receiving decision, the ambulance and the paperwork run in parallel or in series [15,16].

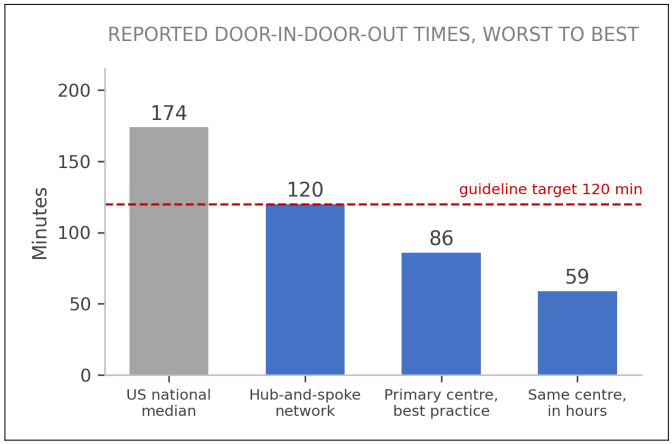

Figure 2: Reported door-in-door-out times from national registry, network and single-centre series [11,13,14]

Who waits longest: Delay is not evenly distributed. In the registry analysis, median door-in-door-out time was longer for patients aged 80 or older than for those aged 18 to 59 by 14.9 minutes (95% CI 12.3 to 17.5), for non-Hispanic Black compared with non-Hispanic White patients by 8.2 minutes (5.7 to 10.8), for Hispanic patients by 5.4 minutes (1.8 to 9.0) and for women by 5.2 minutes (3.6 to 6.9) (Figure 4) [11]. Individually these intervals are modest. Collectively they describe a system that is slower for the patients least able to advocate within it, and they compound the prehospital and diagnostic delays already documented in the same groups [17].

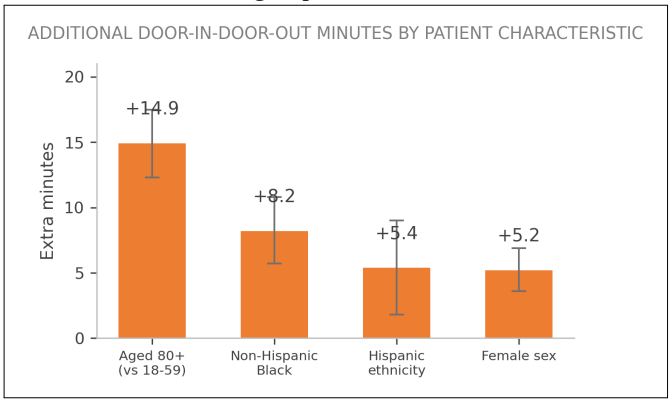

Figure 4: Additional median door-in-door-out minutes associated with patient characteristics, with 95% confidence intervals [11]

What the delay costs: The relationship between time and benefit is established for treatment, not for transfer specifically. In the pooled trial data the common odds ratio for reduced disability was 2.79 at three hours from onset to puncture and declined thereafter [7], and modelling of that decay has expressed it as roughly a week of healthy life lost per minute of delay at the population level [18]. Registry analysis of routine practice found the same time dependence outside trial conditions [19]. Transferred patients are treated later and do worse than those presenting directly, as reported in the STRATIS registry [20], and workflow analyses within the randomised trials showed outcome tracking the interval from imaging to reperfusion [21,22,23].

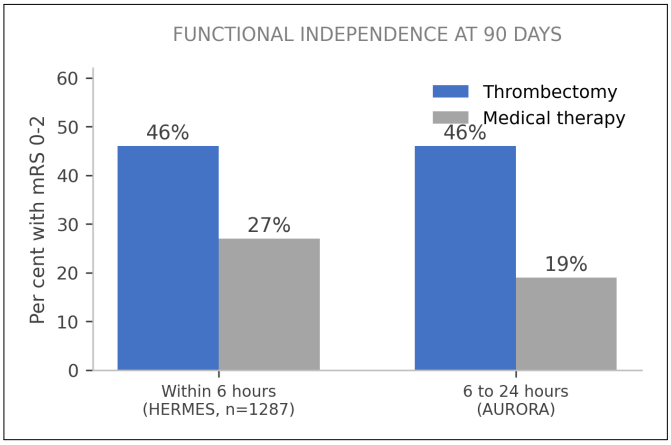

Figure 3: Functional independence at 90 days with thrombectomy against medical therapy, within six hours and in the 6 to 24 hour window [1,4]

Study	Design and cohort	Principal reported finding
Man et al. 2023 [11]	Registry, 108,913 transfers, 1925 hospitals	Median DIDO 174 min (IQR 116-276); only 27.3% within 120 min
Man et al. 2023 [11]	Same registry, subgroups	132 min for transfers for endovascular therapy; disparities by age, sex, ethnicity
Choi et al. 2019 [13]	Single primary stroke centre	Median DIDO 86 min; 59 min during working hours
Goyal et al. 2016 [1]	IPD meta-analysis, 1287 patients, 5 trials	Adjusted cOR 2.49 (1.76-3.53); functional independence 46% vs 27%
Saver et al. 2016 [7]	IPD meta-analysis, time to treatment	cOR 2.79 at 3 hours; benefit non-significant beyond 7.3 hours
Froehler et al. 2017 [20]	STRATIS registry	Transfer before thrombectomy: later treatment and worse outcome
Perez de la Ossa et al. 2022 [24]	RACECAT RCT, non-urban Catalonia	No difference between direct transport and local centre first

Table 1: Principal studies reviewed, with the finding as reported by the original investigators

Transfer or bypass: If the interval is the problem, one answer is to avoid it by taking suspected large vessel occlusion directly to a thrombectomy centre. Modelling suggested the best choice depends on travel times and on the probability of occlusion [25,26], and the question was tested directly in RACECAT, which randomised transport strategy in non-urban Catalonia and found no significant difference in functional outcome between direct transport and initial assessment at a local centre [24]. Observational comparisons of mothership against drip-and-ship have generally favoured direct transport while remaining vulnerable to selection [27,28]. Bypass also has a cost: patients taken past a closer hospital lose access to thrombolysis and to the diagnosis of conditions that are not occlusions, and futile transfers consume capacity in both directions [29,30].

What shortens it: The reported levers are procedural rather than technological. Determinant analyses identify repeat imaging at the receiving hospital, waiting for a formal report, sequential

rather than parallel activation of the ambulance, and out-of-hours presentation [31,32]. Interventions that have accompanied improvement include prehospital notification, a single telephone call to accept the patient, transfer protocols that begin before imaging is reviewed, and keeping the ambulance at the door [15,33]. One network dispatched interventional teams to the patient rather than the reverse [34]. Commentaries have cautioned that a single threshold applied to all transfers may distort priorities [35].

Determinant	Direction	Evidence
Repeat imaging at referring centre	Lengthens	Workflow analyses of transfer pathways [31,32]
Sequential ambulance activation	Lengthens	Deconstruction of transfer workflow [32]
Out-of-hours presentation	Lengthens	86 min overall vs 59 min in working hours [13]
Older age, female sex, ethnicity	Lengthens	Registry-wide disparities [11]
Prehospital notification	Shortens	Used in 43.9% of registry transfers [11,15]
Parallel protocol activation	Shortens	Single-centre and network series [13,14,33]
Bypass to thrombectomy centre	Avoids the interval	No outcome difference in RACECAT [24,25]

Table 2: Reported determinants of door-in-door-out time and the direction of their effect

Discussion

Three things are well established and one is not. It is established that thrombectomy works, that its benefit decays with time, and that the transfer interval is long and variable [1,7,11]. What is not established is that shortening the interval improves outcomes, because no trial has randomised it.

The observational evidence is genuinely difficult to interpret, and in an instructive way. Severity confounds the association in opposite directions depending on the population. A patient with a devastating occlusion is moved quickly because the urgency is obvious, which makes short transfer times look worse than they are. A patient who is stable enough to wait may also be stable enough to do well, which makes long transfer times look better than they are. This is visible in haemorrhagic stroke, where unadjusted analyses have found longer door-in-door-out times associated with better discharge outcomes, an association that disappears on adjustment [36]. Any claim that faster transfer causes better outcomes has to survive that objection, and at present it survives by mechanism rather than by direct evidence.

The mechanism is nonetheless strong. Treatment effect is a function of time from onset to reperfusion; the transfer interval is a component of that time; therefore reducing it moves patients into a window where the effect is larger. That chain does not require a separate trial to be plausible, though it does require honesty about what has been measured, which is the interval rather than the outcome.

What makes the metric worth keeping is the variation. A median of 174 minutes nationally against 59 minutes in working hours at a centre that organised itself around the problem is not a difference in patients or equipment [11,13]. It is a difference in whether the ambulance is called before or after the images are reviewed. That is unusually actionable for a quality measure, and it explains why door-in-door-out time has been adopted despite the absence of randomised support: it measures something a department can change this month without buying anything.

Study limitations

The limitations belong to the underlying literature. The largest dataset is a voluntary quality registry from a single country, and participating hospitals are plausibly better organised than non-participating ones, which would make 174 minutes an optimistic figure [11]. It covers 2019 to 2021, so pandemic disruption cannot be separated from baseline practice. Definitions of the interval vary between studies, and some measure door-in to door-out while others measure arrival to ambulance departure [31,32]. Single-centre reports of short times are subject to publication bias, since units with poor times rarely publish them [13]. The link to outcome is observational throughout and confounded by severity as described [36]. RACECAT was conducted in one region with particular geography and cannot settle the transport question generally [24]. And almost all of this evidence comes from high-income systems with functioning ambulance services [5,6].

Conclusion

Between arriving at one hospital and leaving it for another, a patient with a large vessel occlusion receives no thrombectomy, and the median duration of that interval is 174 minutes against a recommended 120. Only about one transfer in four meets the target. The interval is longer for older patients, for women, and for Black and Hispanic patients, which should be uncomfortable reading for any system that considers itself equitable. Whether compressing it improves outcomes has not been demonstrated directly and probably will not be, since the trial would be difficult to justify. What can be said is that the treatment loses effect with every hour, that the interval contains no treatment, and that centres which reorganised around it have halved it using the staff and equipment they already had.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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