

Original research

Intrinsic hospital factors: overlooked cause for variations in delay to transfer for endovascular thrombectomy

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ABSTRACT

Background Intrinsic hospital factors leading to time delay to inter-hospital transfer for endovascular thrombectomy (EVT) have not been adequately investigated, leading to uncertainty in generalizability of hub and spoke EVT services. We investigated the contribution of intrinsic hospital factors to variations in time delay in a multicenter, retrospective study.

Methods The setting was a hub and spoke EVT state-wide system for a population of 6.3 million and 34 spoke hospitals. We collected data on acute large vessel occlusion strokes transferred from spoke to hub for consideration of EVT between January 2016 and December 2018. The primary endpoint was the proportion of variability in delay-time in transfer cases contributed to by intrinsic hospital factors estimated through variance component analysis implemented as a mixed-effect linear regression model with hospitals as random effects.

Results We included 434 patients. The median age was 72 years (IQR 62–79), 44% were female, and the median baseline National Institutes of Health Stroke Scale (NIHSS) was 16 (IQR 11–20). The median onset to CT time was 100 mins (IQR 69–157) at the spoke hospitals and CT acquisition at the spoke hospital to time of transfer was 93 min (IQR 70–132). 53% of the observed variability in time from CT acquisition at the spoke hospital to transfer to the EVT center was explained by intrinsic hospital factors, as opposed to patient-related factors.

Conclusions Intrinsic hospital factors explained more than half of the observed variability in time from CT acquisition at the spoke hospital to departure for transfer. We recommend that the design of hub and spoke EVT services should account for intrinsic hospital factors to minimize hospital transfer delay.

INTRODUCTION

Endovascular thrombectomy (EVT) is the mainstay of treatment for large vessel occlusion.^{1–7} The American Stroke Association guidelines recommend that eligible patients should undergo EVT up to 24 hours from stroke onset, and the Australian Safer Care Victoria guidelines recommend immediate transfer to a center with EVT capabilities for eligible patients.^{8,9}

However, the maintenance of an EVT service is costly and requires 24 hour access to neuroimaging, a well-maintained angiographic suite, and

adequate staffing by specialized health professionals. This makes comprehensive strokes centers with EVT services a scarce resource, especially in geographically remote areas. To overcome this, the hub and spoke model is commonly used, which employs a ‘drip and ship’ system whereby patients are evaluated at a spoke hospital with imaging, receive thrombolysis, and are then transferred to a hub hospital for EVT.¹⁰

In the state of Victoria, Australia, a robust hub and spoke model has been instituted, with more than 99% of suspected stroke patients within a 60 min ambulance journey of a health service with capability to provide intravenous thrombolysis, and 97% within a 3 hour road journey from an EVT center.⁹ This allows for the whole state to be serviced by two comprehensive stroke centers with well-established EVT capabilities. This model, however, is based on travel time and does not take into account local hospital factors and potential inefficiencies at each spoke hospital that may result in additional delay.

Although intra-hospital sources of potential delay at the hub center have been elucidated, including lack of adequate personnel and arrival during non-regular hours, workflow efficiency at the spoke site has not been adequately elucidated, particularly post-CT acquisition and confirmation of stroke.^{11,12} It is possible that differences in workflow efficiency between spoke centers may be a source of delay that has been overlooked in the construction of the hub and spoke model.

While hub and spoke services are built on traveling time, this has not taken into account intrinsic hospital factors that may cause delay. In this study, we aim to estimate the proportion of variability in time, from acquisition of CT to departure for transfer to the comprehensive stroke center, contributed to by intrinsic spoke hospital factors. We hypothesize that intrinsic hospital factors will contribute to variability in time delay from CT acquisition to transfer between spoke centers, and thus should not be ignored in the hub and spoke system design.

METHODS

The Royal Melbourne Hospital (RMH) serves as one of two state-wide centers for EVT for multiple hospitals in the state of Victoria. Patients are selected for transfer for EVT based on the



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criteria defined by our state Acute Stroke Protocol.⁹ Patients are eligible for EVT if they have had an ischemic stroke with proven large vessel occlusion on imaging. This includes the internal carotid artery, middle cerebral artery (MCA), M1 segment between the carotid terminus and MCA bifurcation, proximal M2 segment with significant clinical deficit, and the basilar artery. Patients must have a premorbid modified Rankin Score (mRS) of 0–2. Basilar artery occlusion may be treated up to 24 hours after onset. Anterior circulation patients with favourable CT angiogram imaging may receive EVT up to 6 hours post onset, while those with favourable CT perfusion imaging should receive EVT between 6–24 hours after stroke onset. However, in select cases based on the decision by the interventionalist, ‘out of guidelines’ intervention may occur in patients with an mRS of 3 or a more distal occlusion.

The hub and spoke model in Victoria incorporates a system whereby at the nearest spoke center a stroke code is implemented and timely CT brain imaging is ordered. The images are then reviewed by a neurologist and a neurointerventionalist in order to guide the decision for thrombolysis and/or EVT. Thrombolysis is administered at the spoke and the patient is then transferred to the hub center for EVT whereby the hub neurointerventionalist, angiography suite staff and anesthetics team are pre-notified. This system services a population of 6.3 million over 34 spoke sites.

This multicenter retrospective study included patients who were 18 years or older and were transferred to RMH from a spoke hospital for consideration of EVT consecutively between January 2016 to December 2018. Only patients with adequate data including recorded time of brain CT, time of arrival at RMH, and National Institutes of Health Stroke Scale (NIHSS) on admission were included. Patients who did not have adequate data regarding imaging, time of admission to RMH or NIHSS were excluded. This project received institutional review board ethics approval (Project ID: QA2013072).

Two researchers independently performed the retrospective collection and recording of the time metrics. Critical time points for imaging were collected from the Synapse imaging software which included incorporated images from spoke hospitals. All other time metric data and patient characteristics were collected from the RMH electronic medical records (EMR).

Data collected included baseline patient characteristics and critical time metrics in code stroke workflow. Baseline characteristics included age, sex, vascular risk factors such as diabetes, atrial fibrillation, hypertension, hypercholesterolemia, ischemic heart disease, and previous stroke or transient ischemic attack (TIA). Markers of stroke severity and premorbid function included NIHSS and premorbid mRS. Angiographic factors included site of occlusion.

Time metrics recorded included time of onset, CT at spoke, thrombolysis administration, admission to hub, common femoral arterial puncture or radial artery puncture. The time metric of interest was duration of time (in minutes) between the initial CT imaging at the spoke center to the time of triage at the hub hospital (CT to ED (emergency department)). The time of CT imaging was standardised using the metric stamped on the CT brain report. The time of triage was determined by the RMH ED triage admission document on the EMR. The time taken to transfer via ambulance, or inter-hospital travel time, was then determined using Google maps data (Map Data 2020 Google) with an approximated travel time of a normal car at 3 am. This used the assumption that early am is the best standardized measure for little to no traffic, which simulates

the time it would take for an activated ambulance with sirens on to travel from site to site. For travel by air ambulance, data were acquired from travel times obtained from Flight Aware (2020 FlightAware). This travel time was then subtracted from the CT to ED triage time to determine the total time spent at the spoke hospital, from CT acquisition to commencement of transfer to spoke (CT to transfer).

Other time metrics calculated were time from onset to CT acquisition at spoke (onset to CT), time from arrival at hub emergency department to groin or radial puncture (hub ED to EVT), onset to administration of thrombolysis (onset to tPA (tissue plasminogen activator)), and onset to time of groin or radial puncture (onset to EVT). Time of groin or radial puncture was determined by the time stamp on the first image attained during the EVT procedure on the imaging report. Finally, CT acquisition to time of groin puncture for EVT (picture to puncture) was determined.

To elucidate underlying intrinsic factors that may contribute to this variability, spoke hospital characteristics were collected from our state-wide stroke service protocol website and spoke hospital websites.⁹ Data collected included attendance by a neurologist based at the spoke, the presence of a stroke unit as defined by our state-wide service protocol, and the presence of a stroke coordinator who liaises with our state’s stroke network. Additionally the number of stroke admissions per year at each institution was recorded and each hospital was designated as either a rural or metropolitan spoke center as per our state’s stroke network definitions.

Statistics

For baseline demographic and clinical data, a comparison was made between included and excluded patients to determine the potential extent of study selection bias. This analysis used the Mann-Whitney test for continuous variables and the χ^2 test for proportions data. This analysis was performed using SPSS software (IBM Corp, released 2017, IBM SPSS Statistics for Windows, version 25.0. Armonk, NY).

To estimate the amount of variability in time from CT acquisition to transfer at the spoke that can be attributed to the intrinsic hospital, rather than patient-specific factors, we used a variance component analysis implemented as a mixed effect linear regression model, with time from CT acquisition to transfer at the spoke as the dependent variable, patient age, sex and NIHSS as independent variables, and spoke hospitals as a random effect. Intraclass correlation coefficient (ICC) reported by this model estimates the between-hospital variability as a proportion of the total observed variability—that is, variability due to both between-hospital factors and due to individual patient differences. An ICC ranges from 0 to 1: an ICC close to 1 is indicative of almost all the variability in time at the spoke being attributed to intrinsic hospital factors, while an ICC close to 0 is indicative of individual patient factors contributing most of the observed variability in time at the spoke. This analysis was performed using STATA 15IC software (StataCorp, College Station, TX).

SPSS software was used to determine time metric data such as medians and IQRs.

To elucidate the underlying intrinsic hospital factors and their contributions to time delay, the number of cases in a spoke site attended to by a neurologist, equipped with a dedicated stroke unit and attended to by a stroke coordinator, was determined. The number of cases attended to in a rural spoke center and the number of cases attended to in a spoke site that admits ≥ 200 stroke consults and < 200 stroke consults were

calculated. These were then further subdivided into cases that took greater than or equal to, or less than the median CT to transfer time. An odds ratio was calculated to determine the relative contribution of intrinsic hospital factors to time delay.

We then determined whether the updated guidelines expanding the treatment window for EVT to 24 hours would impose an increased burden on the hub and spoke system. Median picture to puncture time was calculated for patients transferred for EVT before 1 January 2018 (pre DAWN and DEFUSE) and compared with those post.^{6,7} A Mann-Whitney U test was used to compare for a significant difference between groups.

RESULTS

Of 524 patients transferred to RMH for EVT in the time period, 434 met inclusion criteria and 90 were excluded. When comparing baseline characteristics between included and excluded patients, there was a significant difference in history of stroke or TIA (17% vs 8%, $p=0.025$) and tPA at spoke (64% vs 45%, $p=0.09$).

Of the included patients, the median age was 72 (IQR 62–79) and 192 (44%) were female.

On analysis of baseline cardiovascular risk factors, 90 (20%) patients had type 2 diabetes, 265 (61%) had hypertension, 149 (34%) had hypercholesterolemia, 181 (42%) had atrial fibrillation, 109 (25%) had ischemic heart disease, and 74 (17%) had a previous stroke or TIA.

Baseline median NIHSS was 16 (IQR 11–20) and median premorbid mRS was 0 (IQR 0).

The majority (260 (60%)) of patients presented with a middle cerebral artery occlusion; 277 (64%) patients received tPA at the spoke hospital (table 1).

Median time from onset to CT was 100 min (IQR 69–157). Median time from CT to transfer was 93 min (IQR 70–132). The spoke site with the longest median time was 304 min while the shortest median time was 82.5 mins. Median transport time was 18 min (IQR 16–60). Median time for hub ED to EVT was 28 min (IQR 20–43). Median time from CT to ED was 132 min (IQR 95–188). Median time from picture to puncture was 166 min (IQR 124–219). Median time from onset to EVT was 292 min (IQR 230–373) (figure 1).

The estimated ICC was 0.53, indicating that over half of the observed variability in time at the spoke center from CT to transfer could be attributed to hospital-specific (rather than patient-specific) factors. (figure 2).

In the analysis of the relative contributions of hospital intrinsic factors to time delay, only 400 patients were included due to unavailable data from two spoke sites. Two hundred and seven cases had a CT to transfer time of ≥ 93 min and 193 cases had a time of < 93 min. Factors including treatment in a hospital with a neurologist in attendance, the presence of a dedicated stroke unit, and the presence of a stroke coordinator were more likely to have reduced delay times when compared with the median time from CT to transfer. The respective odds ratios were: OR=5.06, 95% CI 2.61 to 9.82, $p<0.0001$; OR=5.20, 95% CI 2.36 to 11.46, $p<0.0001$; and OR=4.71, 95% CI 2.12 to 10.43, $p<0.0001$. Patients treated in a hospital with ≥ 200 stroke consults per year were also more likely to have reduced time delays compared with the median time from CT to transfer (OR= 5.27, 95% CI 2.65 to 10.47, $p<0.0001$) (table 2).

When comparing picture to puncture time for patients pre versus post the DAWN and DEFUSE era, median time pre was 169 min (IQR 128–226) while post was 165 min (IQR

Table 1 Baseline demographics

	Included (434)	Excluded (90)	P value
Age, median (IQR)	72 (62–79)	71 (60–78)	0.518
Gender (female), n (%)	192 (44)	42 (46)	0.673
Stroke risk factors, n (%)			
T2DM	90 (20)	15 (16)	0.365
HTN	265 (61)	51 (57)	0.395
Hypercholesterolemia	149 (34)	32 (36)	0.882
AF	181 (42)	33 (37)	0.350
IHD	109 (25)	16 (17)	0.129
Stroke/TIA	74 (17)	7 (8)	0.025
NIHSS			
Missing, n	0	45	
Median (IQR)	16 (11–20)	15 (12–20)	0.546
≤ 10 , n	102	10	
11–20, n	226	24	
> 20 , n	106	11	
mRS, median (IQR)	0 (0)	0 (0)	0.983
0	383	79	
1	27	9	
2	15	0	
3	9	2	
tPA at spoke, n (%)	277 (64)	41 (45)	0.09
Occlusion, n (%)			
MCA	260 (60)	40 (44)	
ICA	132 (30)	22 (24)	
Vert	6 (1)	7 (8)	
Basilar	30 (7)	19 (21)	
CCA	4 (0.9)	2 (2)	
ACA	1 (0.2)	0 (0)	
PCA	1 (0.2)	0 (0)	

ACA, anterior cerebral artery; AF, atrial fibrillation; CCA, common carotid artery; HTN, hypertension; ICA, internal carotid artery; IHD, ischemic heart disease; MCA, middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; T2DM, type 2 diabetes mellitus; TIA, transient ischemic attack; tPA, tissue plasminogen activator; Vert, vertebral arteries.

121–212). There was no significant difference ($p=0.299$) between the groups.

DISCUSSION

The design of the hub and spoke model is heavily dependent on travel time rather than taking into account potential inefficiency and time delay at spoke hospitals. Our study demonstrated that 53% of variability in time delay to transfer post CT acquisition is contributed to by hospital factors rather than patient characteristics. This strongly suggests that there are potentially hospital code stroke inefficiencies that interfere with speed of transfer.

Quality improvement measures in workflow have been critical in improving outcomes in other disease hub and spoke systems. For example, attempts to standardize and improve workflow among several rural hospital centers in hub and spoke systems for cardiac percutaneous intervention demonstrated significant benefit for 1 year mortality post implementation.¹³

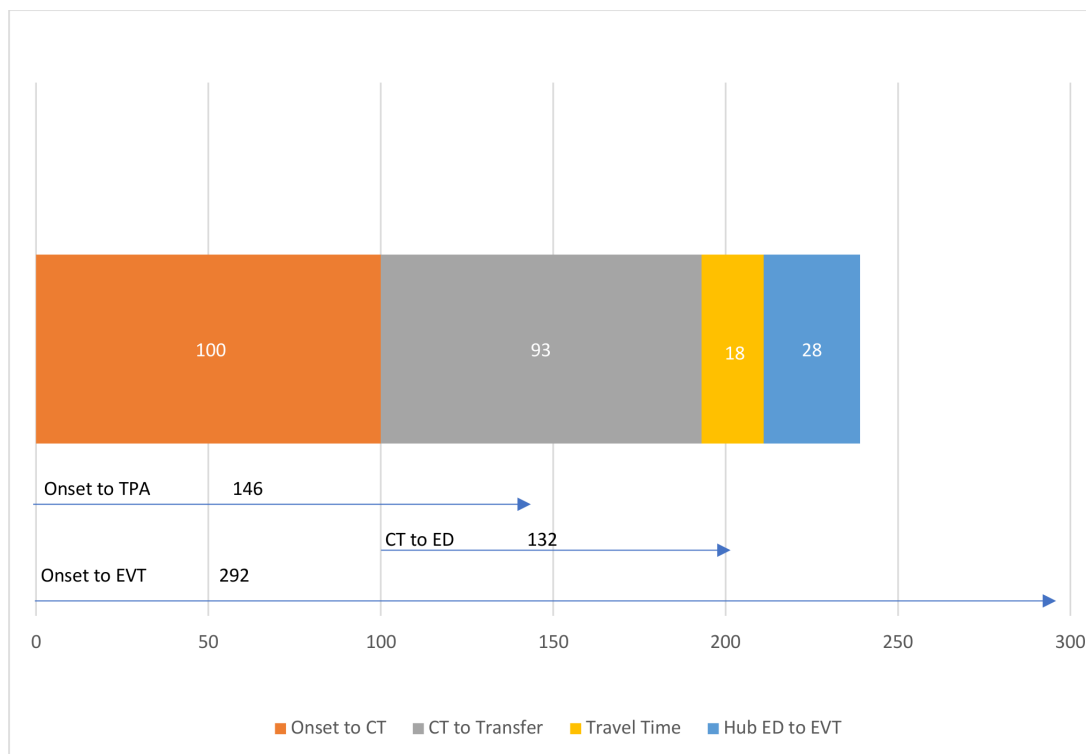


Figure 1 Median time for code stroke time metrics (minutes). ED, emergency department; EVT, endovascular thrombectomy; TPA, tissue plasminogen activator.

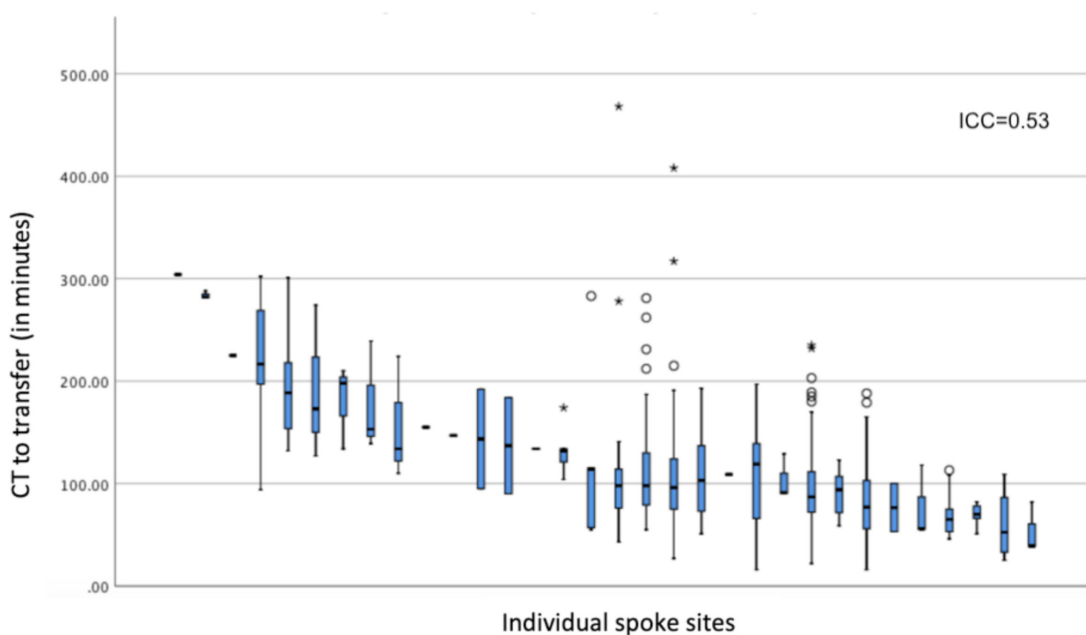


Figure 2 CT to transfer time for all 34 spoke sites. This box plot represents CT to transfer time (in minutes) by individual spoke site. The box represents the IQR. The whiskers extend from the upper and lower edge of the box to the highest and lowest values which are no greater than 1.5 times the IQR. The line across the box indicates the median. Outliers with values between 1.5 and 3 times the IQR are represented by \circ . Extremes are cases with values more than three times the IQR and are represented by $*$. A variance component analysis implemented as a mixed effect linear regression model with time from CT to transfer at the spoke as the dependent variable, patient age, sex and National Institutes of Health Stroke Scale (NIHSS) as independent variables and spoke hospitals as random effect was used. Intraclass correlation coefficient (ICC) reported by this model estimates the between-hospital variability as a proportion of the total observed variability—that is, variability due to both between-hospital factors and to individual patient differences. An ICC ranges from 0 to 1: an ICC close to 1 is indicative of almost all the variability in time at the spoke being attributed to intrinsic hospital factors, while an ICC close to 0 is indicative of individual patient factors contributing most of the observed variability in time at the spoke. An ICC of 0.53 means that 53% of the observed variability in time from CT acquisition at the spoke hospital to transfer to the endovascular thrombectomy (EVT) center was explained by intrinsic hospital factors, as opposed to patient-related factors.

Our state's trauma network provides a clear checklist for rural clinicians that ensures patient readiness for transfer in a timely manner.¹⁴ Such standardization and quality improvement for hospital factors that may delay time to transfer are crucial for ensuring a robust stroke hub and spoke service. Efficient workflow is critical as patients eligible for EVT stand to gain 4.2 days of health life for every minute of reduction in treatment delays.¹⁵

Another study of workflow in Georgia, USA has demonstrated an initial CT to hub center notification time of 66 min and a hub notification to emergency services arrival time of 35 min. While delays in inter-hospital transfer times were explored, the potential contribution of intrinsic hospital factors resulting in delay to hub notification was not elucidated.¹⁶ Our study demonstrated a median time for CT to transfer of 93 min, which may partially be explained by delay to notification of the hub center and time waiting for arrival of emergency services. In a study of rural Western Australia, the spoke CT to flight departure was 390 min. The authors discuss potential delay factors such as the Royal Flying Doctor service identifying suitable aircraft, but do not explore intrinsic hospital factors that may result in delay.¹⁷

Other studies have attempted to categorize intrinsic hospital factors that may result in workflow delay. A study of patients in a major Telestroke network in Texas demonstrated great inter-hospital variability in time from door to consultation with a Telestroke physician. Possible factors implicated in delay include lack of in-house neurology specialists and greater bed number.¹⁸ A wide range in door to page time (DTPT) among spokes was observed with a median DTPT of 19.5 min (IQR 11–34); however, a formal ICC was not performed. Our study

demonstrated that this variability still applies in the period between CT acquisition and transfer to a comprehensive stroke center, even after Telestroke has already been notified. Similar to this study, we identified that the lack of neurologist attendance was also a potential cause for delay. Additional intrinsic factors we identified associated with increased delays were the lack of a dedicated stroke unit, the lack of a stroke coordinator, and low volume centers that treat <200 stroke cases per year. The lack of staff specialized in efficient stroke care as well as a lack of specific infrastructure may contribute to inefficiencies in patient transfer. Additionally, centers that see a lower volume of stroke cases per year may have less experience in managing these patients. Interestingly rurality had minimal bearing on transfer time.

This degree of variability calls into question the efficiency of the hub and spoke model itself.

There exists a debate in the literature over whether direct transfer to a comprehensive stroke center or to hub and spoke results in better functional outcomes for patients.^{19,20}

Studies of this model in Alberta, Canada have demonstrated that due to spoke hospital time delay and inefficiency, patients who have had an ischemic stroke and are assessed at spoke within 45 min of the hub hospital may actually have improved 90-day mortality if admitted to the hub hospital directly.²¹ This study predicted that if the door to thrombolysis time was >30 min, the drip and ship model is only viable when the spoke hospital is geographically further away from the hub. While our study did not record spoke door to thrombolysis time, even median CT to tPA time far exceeded this with a median of 44 min. Other studies have demonstrated that prehospital triage and transfer directly to a hub capable of EVT rather than a spoke site may be beneficial for patients with a large vessel occlusion, even when travel to this center confers up to 45 min of additional travel time.²² While some studies have demonstrated faster time to EVT and reduced disability at 90 days for patients sent directly to the hub,²³ others have shown no difference in functional outcome.²⁴

Alternatives to the traditional hub and spoke model have been explored. This includes directly transferring a neuro-interventionalist to the spoke which was shown to reduce time from imaging to groin puncture (118 min when a neuro-interventionalist is transferred to spoke vs 172 min for drip and ship, $p < 0.001$). However, this study was performed in Germany and such a model may not apply over the large geographical distances present in the state of Victoria.²⁵ In a study comparing the California Kaiser Permanente and University of Texas hub and spoke catchment area, there was significant variability in transfer center acceptance to hub arrival and spoke departure to hub arrival with median combined times of 93 min ($p = 0.0118$) and 39 min ($p = 0.0042$), respectively. This study had similar patient baseline characteristics to ours, with age 66.4 years compared with 72 in our study, 43% female compared with 44% in our study, and a baseline NIHSS at spoke of 16 which was identical to our study. This study identified that transfer time from spoke to hub needs to be shortened.²⁶

A possible limitation of our study lies in its retrospective nature. Hospital records, particularly ambulance documentation for departure from spoke hospitals, were sparse. This resulted in travel time being determined via an ideal time calculated using Google Maps (Map Data 2020 Google) software which represents the fastest possible time that an ambulance could transfer the patient. Time at spoke was then determined using this ideal time. However, in reality factors such as road

Table 2 Spoke characteristics versus time delay

n=transfer cases analyzed for spoke characteristics	400		
Median time from CT to transfer (mins)	93		
Number of cases where CT to transfer time ≥ 93 min, n (%)	207 (51.7)		
Number of cases where CT to transfer time <93 min, n (%)	193 (48.2)		
Spoke characteristics	<93 min, n (%)	≥ 93 min, n (%)	OR (p value), 95% CI
Presence of neurologist			
Cases in spoke site with neurologist attendance	181 (94)	155 (75)	5.06 ($p < 0.0001$), 2.61 to 9.82
Presence of stroke unit			
Cases in spoke with stroke unit	185 (96)	169 (82)	5.20 ($p < 0.0001$), 2.36 to 11.46
Number of consults per year			
≥ 200 stroke cases per year	182 (94)	157 (76)	5.27 ($p < 0.0001$), 2.65 to 10.47
Rurality			
Cases in rural hospital	35 (18)	105 (50)	0.22 ($p < 0.0001$), 0.14 to 0.34
Cases in metropolitan hospital	158 (82)	102 (50)	
Stroke coordinator			
Cases with stroke coordinator present	185 (96)	172 (83)	4.71 ($p < 0.0001$), 2.12 to 10.43

closures and heavy traffic may result in longer travel times, making this ideal time an inaccurate metric in select situations. Additionally, time of entry to the spoke facility was not readily available for most patients on the EMR, therefore commonly used metrics such as door-in-door-out time, which have shown to be relevant in predicting patient outcomes, could not be calculated.²⁷ However, for the purposes of determining inter-hospital variability as well as intrinsic hospital factors, an analysis of delay once CT is acquired and stroke is confirmed is novel to our study.

Additionally, there was no significant difference in stroke risk factors between the included and excluded groups, except for previous stroke/TIA ($p=0.025$) and tPA at spoke ($p=0.09$). Perhaps in patients excluded due to vital missing data, such as lack of NIHSS data or incomplete imaging data, comprehensive medical histories were not fully available which could explain this difference. Another limitation is that the intubation status of patients with posterior circulation occlusions was often unavailable in the EMR, which, if accounted for, could have explained delays in transfer times.

Our study indicates that the future design of hub and spoke models must take into account potential inter-hospital variability and cannot be reliant on travel time as a tool for triaging. We demonstrate that as much as 53% of differences between spoke hospitals from CT to transfer is determined by intrinsic hospital factors, and this must be accounted for when constructing a robust system for time critical workflow.

CONCLUSION

We showed that intrinsic hospital factors explained over half of the observed variability in time from CT acquisition at the spoke hospital to departure for transfer. These intrinsic hospital factors have traditionally been overlooked in previous studies of code stroke time metrics. Since hub and spoke models heavily rely on travel time in their construction, it is clear from our study that intrinsic hospital factors can contribute to time delay. We suggest future studies whereby specific intrinsic hospital factors are explored further which can inform strict guidelines to prevent delays in patient transfer.

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