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Review of external referrals to a regional stroke centre: it is not just about thrombectomy

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AIMS: To determine the experience of a regional stroke referral centre of external referrals for endovascular thrombectomy (EVT) in patients with symptoms of acute ischaemic stroke (AIS) and large vessel occlusion (LVO).

MATERIALS AND METHODS: Data were collected prospectively over two 4-month periods (2017–2018) on consecutive external referrals for EVT. Baseline demographics, imaging findings, and key time parameters were recorded. Reasons for not transferring patients and for not performing EVT were recorded. Key time intervals were calculated and compared between the transferred and non-transferred group with and without intracranial occlusion and between the transferred patients who underwent thrombectomy and those who did not.

RESULTS: Two hundred and sixty-two patients were referred. Sixty-one percent (n=159) were accepted and transferred for treatment. Of those transferred, 86% (n=136) had EVT. Fourteen percent (n=23) were unsuitable for EVT on arrival due to no vessel occlusion (48% n=11), poor Alberta Stroke Program Early CT Score (ASPECTS)/established infarct (30%, n=7) haemorrhage (9%, n=2), and clinical recovery (13% n=3). One hundred and three patients (39%) were ineligible for EVT following phone discussion due to absence of intracranial occlusion (59%, n=61), low ASPECTS (22%, n=23), distal occlusion (4%, n=4), low/improving National Institutes of Health Stroke Scale (NIHSS; 10.7%, n=11), and poor modified Rankin Scale (mRS) at baseline (3%, n=3). Patients with LVO but not transferred had longer onset to hospital arrival time compared with those transferred 151.5 versus 91 minutes ($p<0.005$), with a trend also toward a longer door to CT/CTA 40 minutes versus 30 minutes (p=0.142).

CONCLUSION: These data provide valuable insights into the service provision of a comprehensive stroke network. The present rates of EVT and futile transfers are modest compared to published data. Access to neuroradiology and specialised stroke assessment is crucial to optimise time to treatment.

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Introduction

Acute ischaemic stroke (AIS) is a leading cause of death and disability worldwide.[1] Approximately a quarter of strokes result from an intracranial large-vessel occlusion (LVO), the treatment of which is rapidly evolving, thereby placing new challenges upon service providers.[2–5] In recent years, EVT has become the standard of treatment for LVO in AIS with multiple recent randomised controlled trials and subsequent meta-analyses providing Class 1 level A evidence unequivocally supporting its efficacy and safety.[6–13] Subsequently, further research has been published showing significant benefit in appropriately selected patient's 6–24 hours following symptom onset.[14–17] The Interventional Neuroradiology Service, Beaumont Hospital (INS-BH) in Dublin is the only EVT centre in the Republic of Ireland operating around the clock. Referrals are accepted from 24 external centres throughout the country ranging from 5 to 244 km away serving a population of up to 4.5 million. A second institution in the south of the country provides EVT Monday–Friday during working hours. A drip and ship model is currently employed with patient's being evaluated in their local hospital and subsequent referral made by phone direct to neuroradiology. A full description of the service provided by the institution has already been published.[18]

The aim of the present study was to report the experience of a regional stroke referral centre with external referrals for EVT in patients with AIS and suspected LVO. Specifically, the additional workload regarding the referral process and patients who undergo thrombectomy are evaluated, and the reasons for unsuitability of patient transfer for intervention is considered.

Materials and methods

The data that support the findings of this study are available from the corresponding author upon reasonable request. Data were collected prospectively over two 4-month periods, from March to July 2017 and January to April 2018, on consecutive referrals from external hospitals for EVT of patients with symptoms of AIS and suspected LVO. Following an initial pilot period of data gathering regarding external referrals in 2017, this process was restarted in order to more fully understand practice in other institutions as part of a continuous national audit of the stroke service. Going forward, these data will be gathered prospectively and used to inform of the need for quality improvement (QI) as part of a national QI programme.

The decision pathway involves referrals coming directly from the clinical team managing the patient in the referring hospital to the neuroradiology service. Data were recorded by the interventional neuroradiologist or specialist registrar in radiology at the time of the phone referral. Patient details were recorded including baseline demographics, admission National Institutes of Health Stroke Scale (NIHSS), and intravenous thrombolysis administration. Details of the recommended standard approach imaging at the referring hospital (non-contrast computed tomography [CT] of the brain [CTB] and CT angiography [CTA]) and any further imaging in the centre were recorded, including time of imaging, Alberta Stroke Program Early CT Score (ASPECTS), occlusion location, and collateral grade. After the referral call is made, imaging was reviewed by the neuroradiology team in the endovascular hospital through the national PACS system. The timing of the call was recorded noting whether it was received in hours or out of hours. In hours included Monday to Friday 8.00 am to 6.00 pm, while out of hours included all times outside of this window, including weekends and public holidays. Key time parameters were recorded including time of symptom onset, time of presentation, time of referral, time of acceptance, and time of arrival at the stroke centre if transferred. Reasons for decision-making were also recorded, including reasons for patient ineligibility for EVT and reasons for not proceeding with EVT following transfer. Baseline characteristics and key time parameters in the transferred group were compared with the group that were not transferred with and without intracranial occlusion. Patients are accepted from 24 primary stroke centres (PSC) throughout the country. If transferred, the "drip, ship, retrieve, and leave model" is employed, whereby patients present directly to their PSC, they receive thrombolysis as appropriate, and are then transferred to the endovascular stroke centre (ESC). Depending on their distance from the ESC, they are either repatriated immediately post-procedure to their referring institution or are admitted to the acute stroke unit in the ESC. Patients are categorised into two groups: local region hospitals (within 90 minute drive of ESC) are repatriated immediately and the remote region hospitals (>90 minute drive from ESC) are admitted to the ESC stroke unit with the intention of being repatriated within 24 hours. The distance from the ESC in those transferred and not transferred was evaluated. In addition, baseline characteristics and key time parameters in the EVT group were compared with those transferred and subsequently deemed ineligible for EVT. As this was a study of current practice at the unit, and as it did not influence individual patient management, it was categorised as a service review and was exempt from requiring institutional ethics approval. The ongoing audit of the service is registered with the Institutional Quality and Standards Department. All data are given as median in minutes (IQR 25–75%). Mann–Whitney tests were used to test the difference between groups. The chi-squared test was used to assess the significance of distance (local or remote) and in/out of hours on referrals. Statistical significance was defined as $p \leq 0.05$.

Results

During the study period, there were a total of 262 referrals by phone to the centre from 23 external hospitals (Fig 1). This included long-distance referrals and local city referrals with hospitals ranging from 5 to 244 km from the centre. Of these, 159 patients (61%) were transferred to the institution and 136 patients (52%) had EVT. Twenty-three patients (9%) who were transferred to the centre did not undergo EVT. One hundred and three patients (39%) were deemed ineligible for EVT following phone discussion. Fifty-seven percent of patients (n=91) received thrombolysis in the group transferred compared to 26% (n=11) in the group not transferred with intracranial occlusion and 16% (n=10) in the group not transferred without intracranial occlusion. Age, sex, NIHSS, and ASPECTS are evaluated between the groups in Table 1. The site of occlusion on CT angiogram is displayed in Table 2. On review of the reasons for not accepting patients for EVT following phone referral, 85.4% of patients (n=88) were unsuitable based on review of imaging (Table 3). Of these, 59% (n=61) had no intracranial occlusion, 22.3% (n=23) had an ASPECTS of <5, 4% (n=4) had a distal occlusion not amenable to EVT; 10.7% (n=11) of patients were deemed unsuitable on account of mild or improving clinical symptoms and 3% (n=3) due to poor modified Rankin Scale (mRS) at baseline. Of the 23 patients who were transferred to the centre but did not undergo EVT, eight patients (35%) proceeded to catheter angiogram, but had resolution of occlusion. Nine patients (39%) underwent repeat imaging, which showed either a low ASPECTS/established infarct (30%, n=7) or haemorrhage (9%, n=2). Three patients (13%) did not have a CTA performed in their referring institution and so underwent CTA on arrival, which showed no intracranial occlusion. Three patients (13%) had resolution of symptoms. Two of the three had repeat CT and CTA on arrival (Table 3).

Median onset of symptoms to arrival at referring institution time in the transferred group was significantly shorter compared to the group not transferred, but with intracranial occlusion (91 versus 151.5 minutes, $p<0.005$; Table 4). The median time from arrival to referral was 70.5 minutes in the group that was transferred compared to 79.5 minutes in the group not transferred with intracranial occlusion (p=0.366). The median door to CTB and median door to CTA times were shorter in the transferred group, which was trending towards significance (30 versus 40 minutes, p=0.142 and 36.5 versus 47.5 minutes, p=0.063 respectively). Median time of CTA to time of contact was 27 versus 25 minutes in the group transferred compared to not transferred with intracranial occlusion (p=0.437). Time of contact to decision time was shorter in the transferred group (2 versus 8.5 minutes, $p<0.001$).

In the patients who were transferred, the median time of contact to arrival was 79 minutes (IQR, 27–261). There were no complications during inter-hospital transfers. The median presentation to groin puncture time was 147 (62–420) minutes and median presentation to reperfusion time was 187 (68–450) minutes. Median onset to groin puncture time was 254 (87–1392) minutes and onset to reperfusion 270 (128–1396) minutes.

The median distance from the ESC in those transferred was 90.4 km (5.1–244 km) compared to 123.5 km (5.1–244 km) for those not transferred. Overall, 73% of patients were referred from hospitals within a 90-minute drive of the ESC (local region group) versus 27% from institutions over 90 minutes away (remote region group). Of the 191 referrals from local region hospitals, 69% (n=132) of these were transferred to the ESC compared to 38% (n=27) of all the remote referrals (n=71; $p<0.001$). Eighty-seven percent of patients who were transferred from the local region group underwent thrombectomy compared to 70% in the remote region group (p=0.14).

Overall, 59% of referrals (n=154) were out of hours at the time of phone referral whereas 41% (n=108) were in hours. Of 108 in-hours referrals, 72% (n=78) were transferred versus 53% (n=81) of 154 referrals out of hours ($p<0.01$). Therefore, there are a higher number of referrals out of hours but a lower transfer rate.

Discussion

The present data offer an insight into the workload of a regional comprehensive stroke centre receiving referrals from multiple institutions and could assist in planning, allocation of resources, and service improvement. Figures from the Stroke Alliance for Europe (SAFE) Burden of Stroke report, estimate that the number of stroke cases will rise by approximately 58% over the next 10 years.[19] This is expected to lead to increased numbers of thrombectomy procedures per year. A previously published study in the UK estimated that 10% of all stroke admissions are eligible for thrombectomy, while a recent study in the USA estimated a current annual EVT rate of 3 per 100 000 people of the population.[20,21] If this were applicable to the ESC's population that would mean approximately 450 thrombectomies a year would be performed. The ESC performed 248 and 262 thrombectomies in 2017 and 2018, respectively, and 134 during the study period excluding those who presented directly to the ESC. This does not include the second

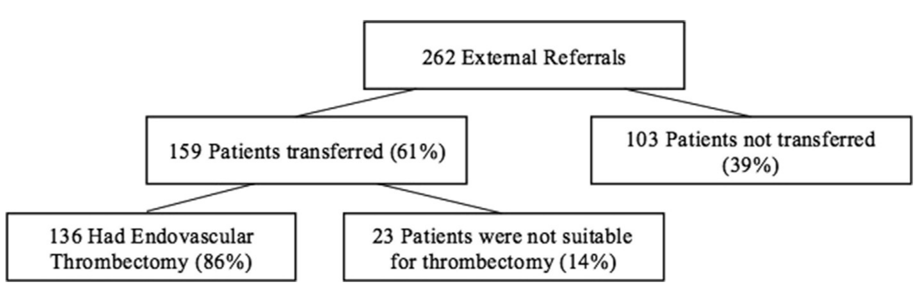

Figure 1 Breakdown of patient referrals. There were a total of 262 referrals from 23 external hospitals to Interventional Neuroradiology Service, Beaumont Hospital, Dublin, Ireland.

Table 1
Demographics Transferred vs not transferred with and without intracranial occlusion.

	Overall Transferred Treated	Not transferred with intracranial occlusion	Not transferred without intracranial occlusion	Transferred with no EVT
Number of referrals	136	42	61	23
Age	71 (25–94)	71 (32–92)	68 (36–90)	75 (55–94)
Male	70	18	30	12
Female	66	24	31	11
Inpatient at time of referral	15 (11%)	4 (9.5%)	6 (10%)	0
NIHSS *	14 (2–40)	13 (2–30)	6 (0–31)	14 (2–26)
IV Thrombolysis	79 (58%)	11 (26%)	10 (16%)	12 (52%)
ASPECTS †	9	9	10	9

*NIHSS, National Institutes of Health Stroke Scale.
†ASPECTS, Alberta Stroke Program Early CT Score.

Table 2
Vessel occlusion, overall vs not transferred with intracranial occlusion.

Vessel Occluded	Overall Transferred treated N = 136	Not transferred with intracranial occlusion N = 42	Transferred not treated N = 23
MCA, M1 **	83 (61%)	18 (43%)	12 (57%)
MCA, M2 **	14 (10.2%)	11 (26%)	4 (19%)
ICA	32 (23.5%)	6 (14.2%)	2 (9.5%)
Basilar	7 (5%)	3 (7%)	1 (4.7%)
Vertebral	0	3 (7%)	1 (4.7%)
PCA	0	1 (2.3%)	0

** MCA, Middle Cerebral Artery.

Table 3
Reasons for not accepting transfer/not proceeding to EVT.

Reason	Patients not accepted for transfer (%)	Not proceeding to EVT (%)
Low ASPECTS/Established infarct	23 (22.3%)	7 (30%)
No intracranial occlusion	61 (59%)	3 (13%)
Distal Occlusion	4 (4%)	N/A
Clinical Improvement/Low NIHSS	11 (10.7%)	3 (13%)
Poor Baseline	3 (3%)	
Haemorrhage on repeat imaging	N/A	2 (9%)
Recanalisation	N/A	8 (35%)

Table 4
Key time parameters between groups.

Variable	Transferred N = 159 [a]	Not transferred with intracranial occlusion N = 42 [b]	Statistical analysis Comparing transferred to not transferred with intracranial occlusion
Onset to arrival in referring hospital	91 (60–185.5)	151.5 (102.5–270)	N = 176, U = 1.788, p < 0.005
Door to CT	30 (20–40)	40 (21–62)	N = 176, U = 2.213, p = 0.142
Door to CTA ‡	36.5 (50–114.2)	47.5 (59.5–116.2)	N = 176, U = 2.073, p = 0.063
Door to contact	70.5 (23–330)	79.5 (20–265)	N = 176, U = 2.370, P = 0.366
CTA to contact	27 (15–51)	25 (14.5–37.5)	N = 176, U = 3.384, p=0.437
Contact to decision	2 (2–5.7)	8.5 (5–15)	N = 176, U = 1.485, p < 0.001
Contact to arrival at EVT § centre	79 (27–261)	N/A	N/A

‡ CTA, CT Angiography.
§ EVT, Endovascular Thrombectomy.
[a] Four inpatients.
[b] Six inpatients.
Data given as median in minutes (IQR 25–75%).
Mann–Whitney used to test difference between groups.

institution which provides an in hour endovascular thrombectomy service, performing 25 and 53 cases in 2017 and 2018 respectively. This figure has continued to rise year on year. Analysis of the present data shows a LVO rate of 40.2% in those with confirmed stroke diagnoses who undergo CTA and 18.4% of primary discharge diagnoses of stroke (who may or may not have had a CTA on admission). Although the present study reports EVT rates of 26% and 12% for those two groups respectively[22]; however, EVT rates tend to vary from study to study as different patient groups are used for analysis (e.g., estimated stroke incidence versus primary and secondary stroke diagnoses and TIAs as used in the studies mentioned above).

In thrombectomy patients, outcome is dependent on CT to reperfusion times rather than onset to CT times[7]; however, this does not reflect the number of patients who become unsuitable due to prolonged onset to imaging times. In the authors' experience, 23 of 42 patients with occlusion were unsuitable for transfer for thrombectomy based on established infarction. They presented to hospital much later (151.5 minutes) than those who were transferred (91 minutes). There were probably more patients than this, which the present study did not capture because the ESC was not notified. The ESC is working with all referring hospitals to improve data collection on all stroke patients that present even if they are not referred. Strategies to reduce this time include education of the public on the symptoms of stroke and importance of seeking prompt medical attention. Evidence shows that advertising campaigns increase the numbers of patients who present to hospital in a timely manner. The introduction of the F.A.S.T. campaign in Ireland showed a significant impact on patients presenting to Emergency Departments with symptoms of stroke ($p<0.001$).[23]

Patients with delayed onset to arrival times, from the remote region group or presenting out of hours are less likely to be transferred. It is not unexpected, that delayed arrival results in patients not being transferred. There is, however, no cut-off in terms of distance for rejecting a referral as all hospitals have access to the service; however, it is possible that there is a selection bias in accepting patients from further afield resulting in the transfer rate from the local region hospitals being higher than the remote region group (69% versus 38%). The reduced transfer rate out of hours likely reflects less experienced personnel in the referring hospital out of hours seeking expert opinion.

The drip and ship model, with the recommended pathway as employed in the ESC, leads to a rate of transfer of 61% per external referral, of which 91% were treated. This is quite high compared with published data.[24] The rate of futile inter-hospital transfer (transferred but no EVT) is significantly lower than rates others published.[24] This is due to most patients undergoing CTA prior to referral, therefore reducing unwarranted transfers. A recent study in a population where vascular imaging was not performed prior to transfer to EVT centre, demonstrated that with the availability of vascular imaging, 50% of transferred patients would have had EVT and 20% of futile transfers would have been prevented.[25] A Spanish study in 2015 showed a rate of futile transfer of approximately 41% with none of the baseline characteristics being able to predict which cases would not be suitable for EVT following transfer.[24] Despite the present low futile transfer rate, 85% of referrals were excluded based on imaging findings when reviewed by the neuroradiology department. Although this does not mean that the radiology report was incorrect, it highlights the varying degree of experience among clinicians making an inappropriate referral due to a lack of understanding in a developing service and the benefit of training all radiologists who report on acute stroke imaging in assessing patients for suitability for thrombectomy. Access to 24/7 neuroradiology and experienced stroke physicians perhaps by telemedicine would reduce this while also aiding junior personnel out of hours in the decision-making process and help to ensure a high rate of EVT while working towards a low rate of futile inter-hospital transfer.

Fourteen percent (n=23) of transferred patients with occlusion did not receive thrombectomy, 55% due to clinical improvement and 45% because of established infarct or haemorrhage. It is understood that some patients will recover even without thrombectomy, as in control arms of trials, but for the patients whose infarct becomes established, the system of care needs to be optimised to reduce the occurrence of this.

The median time of decision to accept to arrival was 79 minutes (IQR, 27–261). Delays in inter-hospital transfers reduce the likelihood of patients having thrombectomy. A recent study demonstrated 2.5% decrease in the chances of performing intra-arterial therapy for every minute of transfer time.[25] The actual travel time cannot be improved (unless helicopter deployed for longer trips) but efficiencies can be made in door in door out time (DIDO) times. Improving the DIDO time is crucial in each stroke centre. This includes the door to CT time, CT to contact, and contact to departure. It is hoped that ESC achieve a DIDO target of 30 minutes with option for ambulance crew to wait with the patient until a decision is made regarding transfer in order to then take the patient directly to thrombectomy centre. Making changes to the national infrastructure and providing resources and training to the National Ambulance Service (NAS) is crucial to decreasing both the onset to arrival time and transfer time to the ESC.

Future technological advances including computer-assisted interpretation of imaging and an automated decision-support tool may improve speed and accuracy of radiological and clinical decision-making in acute stroke patients, which potentially would improve clinical outcomes. They would also assist in the workload associated with the provision of the radiological support structure to non-endovascular centres, where the burden of the new radiological requirements in acute stroke imaging can have a significant impact on radiology departments.

In conclusion, the present data offer an insight into the workload of a regional comprehensive stroke centre and allows for informed policy and system improvements. The present EVT rate and futile transfer rate are good compared with published data. In addition, the present data highlight the importance of early presentation to the PSC as the treatment rate decreases for late presenters. As EVT firmly establishes itself as the reference standard in the management of LVO AIS, access to neuroradiology, specialised stroke assessment, possible future technological decision-support tools, and public awareness campaigns will be crucial for improving the referral process, decreasing the onset to presentation, and presentation to treatment time for patients resulting in improved patient outcomes.

Conflict of interest

The authors declare no conflict of interest.

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