ORIGINAL RESEARCH

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The Effect of Secondary Transfer Distance on Outcomes for Patients with Acute Ischemic Stroke: A Retrospective Cohort Study

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Abstract

Objective: The efficacy of mechanical thrombectomy (MT) and intravenous thrombolytic therapy (IVT) in patients with acute ischemic stroke (AIS) is time dependent. In this study, we investigated the effect of interhospital distance on outcomes for patients who received secondary transfer and were treated with MT and IVT to a comprehensive stroke center (CSC).

Materials and Methods: We included patients with AIS who were secondarily transferred by road to our center, which is considered a CSC, between January 7, 2023, and January 7, 2024. We compared patients based on their distance from the treatment facility: those who were closer or further than 30 km and those who were closer or further than 90 km, in terms of the treatment they received (MT/IVT), three-month mortality, intracranial hemorrhage within 36 hours, and good neurological outcome.

Results: The study included 259 patients who were secondarily transferred from 29 different hospitals. In the <30 km group, the number of patients who received at least one MT/IVT therapy was at least one MT/IVT therapy in the ≥30 km group, 11 patients (7.6%) received at least one MT/IVT therapy ($p=0.005$). In multivariate analysis, patients transferred within 30 km were twice as likely to receive IVT/MT, compared to those transferred from longer distances.

Conclusion: The need to travel greater distances in the secondary transfer of patients with AIS decreases the chance of these patients receiving MT/IVT. Although three-month mortality, intracranial hemorrhage within 36 hours, and a good neurological outcome did not differ between near and far patients, increasing the number of CSC centers will increase the number of stroke patients who can access MT/IVT treatment options.

Keywords: Acute ischemic stroke, thrombectomy, thrombolytic therapy, emergency medicine

Introduction

Time plays an important role in the treatment of acute ischemic stroke (AIS) as it determines treatment options, and timely access to treatment options for AIS patients is very important in reducing mortality and morbidity. Intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) are treatment options with proven benefits in patients with AIS [1,2]. For patients to benefit from IVT and MT, they need to arrive at the right center at the right time. Different management models are used to ensure that these treatments are provided at the appropriate time. Decisions are made to transfer a patient with suspected stroke to the nearest comprehensive stroke center (CSC) with MT facilities (the mothership model) to the nearest primary stroke

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center (PSC) with acute stroke care where IVT treatment can be administered and thentransfer MT candidates tsso the CSC (drip-and-ship model) [3].

It has not yet been determined which model is superior-the mothership model or the drip-and-ship model [4]. Both models have some disadvantages. While the mothership model creates a serious patient burden on the main center, in the drip-and-ship model, patients may be delayed in receiving MT [5]. Patient outcomes in both models depend on many factors, including the type of health insurance system, the geographical distribution of the population, geographical conditions, and the distance from and accessibility to stroke centers. Geographical constraints result in inequalities in access to centers where MT is available as patients in rural areas can be significantly disadvantaged [6].

Previous studies have compared the mothership and the drip-and-ship models. In this study, we aimed to investigate the effect of transfer distance on the treatment and outcomes of patients with AIS who were secondarily transferred to our CSC. We hypothesized that patients who were transferred to our CSC from more distant hospitals would show a lower rate of IVT and MT treatment and would have higher mortality.

Materials and Methods

Patients and Study Design

This is a single-center retrospective cohort study conducted in a tertiary care emergency department (ED). All patients over 18 years of age with a clinical and neuroimaging diagnosis of AIS who were secondarily transported by road from a PSC to our CSC between January 7, 2023, and January 7, 2024, were included in the study. The study was approved by the, University of Health Sciences Türkiye, Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (decision number: 2024-824, date: 04.09.2024). The study was conducted in accordance with the Declaration of Helsinki, and the patient data collected by the researchers were kept confidential. Pregnant patients, patients with missing data, and patients brought to the study center with cardiac arrest were excluded. Among cases of interhospital transfers, we excluded those who were diagnosed with AIS at the first facility but not at the CSC.

The ED of our 24-hour CSC hospital has a stroke unit and an intensive care unit with the capacity to provide emergency neuroimaging, IVT, and MT. The hospital is the most important and largest stroke center in the city. It is integrated into the country's healthcare system, and all healthcare services provided at the hospital are free of charge.

Stroke Management Strategy

The stroke management strategy used in our region is as follows. Patients with suspected stroke are brought to the nearest hospital. The patient with possible AIS is transferred to the CSC bypassing the nearest center if it will not lose more than 15 minutes of time. There is a pre-planned CSC center stroke on-call for each day, and patients are referred to the on-call CSC during off-hours. The stroke center where the study was conducted is considered a CSC and has 10-12 stroke on-call days per month. MT and IVT is not applied in the hospitals where patients are initially taken. Because the first hospitals patients entered were primary hospitals. In the secondary center where they are brought, IVT and/or MT are administered to eligible patients based on radiological imaging, clinical status, and the amount of time that has elapsed since the onset of symptoms. Patients are followed up in the stroke unit or ward after treatment.

Data Collection

Data were collected using the hospital's information system. Data including sociodemographic characteristics, neurologic complications, treatment modalities, stroke duration, and outcomes were collected. National Institutes of Health Stroke Scale scores (NIHSS) and modified rankin scores (mRS) were calculated using electronic patient records [7,8]. Three-month mortality, mRS after three months, and the day of the week when patients were transferred were recorded using the electronic patient records.

In addition, the hospitals from which the patients were also transferred to our CSC were recorded. Using the addresses of the hospitals and the Google Maps application programming interface, we calculated the distance in kilometers between these hospitals and our CSC.

Intracranial hemorrhage was defined as the occurrence of hemorrhagic transformation (parenchymal hematoma type 1-PH1 or type 2-PH2) within the first 36 hours, according to the ECASS II classification [9]. Good neurological outcome was defined as a 3-month mRS ≤2.

MT and IVT treatments were recorded independently of procedural success. Symptom onset to groin puncture and symptom onset to thrombolysis times were noted in minutes. For the MT procedure, the symptom-to-groin time was calculated as the time from symptom onset to the start of the procedure. Likewise, the symptom-to-needle time was calculated as the amount of time that elapsed from symptom onset to the time of the thrombolytic treatment. The time of symptom onset and the time of treatment initiation were taken from the electronic patient records.

Comparison Groups

After analyzing the distances between the hospitals from which the patients were transferred and the CSC, the patients were divided into the following groups: closer than 30 km and farther than 30 km, and closer than 90 km and farther than

90 km. The closer than 30 km and further than 30 km groups were compared with each other, and the closer than 90 km and further than 90 km groups were compared with each other.

Outcomes

The primary outcome of the study was the effect of administering IVT and MT therapies. The secondary outcomes included three-month mortality, intracranial hemorrhage within 36 hours, and good neurologic outcome.

Sample Size

To determine a significant difference in IVT treatment between patients transferred over different distances, a 5% margin of error and 95% power were required. Therefore, a total of 188 patients were included in the study: 94 patients who were transferred less than 50 km, and 94 patients who were transferred more than 50 km.

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences for Windows version 26 (IBM Corp., Chicago, Illinois, USA). The conformity of the data to normal distribution was evaluated using the Kolmogorov-Smirnov test and histograms. Normally distributed numerical data were presented as mean ± standard deviation, and non-normally distributed numerical data were presented as median and interquartile range (IQR) (25-75%). Categorical variables were presented as number (n) and frequency (%). Categorical variables were compared using the chi-squared test or Fisher's exact test. Continuous variables were compared with the Student's t-test or the Mann-Whitney U test. The statistical significance level was accepted as p<0.05 for all tests.

A multivariate logistic regression model was used to estimate the adjusted odds ratios (OR) and 95% confidence intervals (CI) for the association between the distance variable and outcome (MT, IVT, MT + IVT). The following covariates were included in the model based on their clinical relevance and potential for confounding: age, NIHSS, and a measure of 30 km. Statistical significance was determined using Wald tests, with a p-value <0.05 considered significant. The model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test and the akaike information criterion.

Results

Three hundred and ten patients met the inclusion criteria. After the exclusion of pregnant patients and patients with incomplete data, 259 patients were enrolled in the study. Of these patients, 144 (55.6%) were male. The median age of the patients was 68 years (IQR) 58-78. The median distance patients were transferred to the study center was 40 km (IQR 25-75; 15-80 km). Figure 1 shows the number of patients receiving IVT/MT according to the distance they were transferred.

When comparing patients who received thrombectomy (n=33) with those who did not (n=226), significant differences were observed in several key variables. Patients in the thrombectomy group were significantly younger, with a median age of 60 years (IQR: 54-71), compared to 69 years (IQR: 59-79) in the non-treated group (p=0.011).

Transfer distance significantly affected treatment rates. Treated patients had a median transfer distance of 18 km (IQR: 7-47), compared to 40 km (IQR: 17-81) in the non-treatment group (p=0.002). Thrombectomy was performed in 67% of patients transferred ≤30 km, versus 41% for those >30 km (p=0.005). Strikingly, none of the patients transferred from >90 km (p=0.004) received treatment, highlighting the negative impact of long transfer distances on timely intervention (Table 1). Age was significantly higher in the ≥30 km group than in the <30 km group, with a median age of 69 years (IQR 25-75; range 60-80 years) (p=0.030). Twenty-two patients in the <30 km group (19.3%) and 11 patients in the ≥30 km group (7.6%) (p=0.005) received at least one IVT or MT treatment. Other outcome parameters did not differ significantly between the groups.

The number of patients who received at least one IVT or MT treatment was 33 (15.6%) in the <90 km group, while no patients in the ≥90 km group received these treatments (p=0.004) (Table 2).

Multivariate regression analysis identified age, NIHSS score, and a transfer distance ≤30 km as independent predictors of receiving IVT/MT. Older age was associated with lower odds of treatment (OR=0.948, 95% CI: 0.917-0.980, p=0.002), while higher NIHSS scores increased the likelihood of thrombectomy (OR=1.083, 95% CI: 1.042-1.124, p<0.001). Patients transferred from within 30 km were more than twice as likely to receive IVT/MT than those from farther distances (OR=2.3, 95% CI: 1.02-5.187, p=0.045) (Table 3).

Discussion

The results of this study showed that patients who were transferred more than 30 km from a PSC to the CSC were less likely to receive IVT or MT than patients who were transferred less than 30 km. MT and IVT procedure onset times being similar between the groups seems to indicate the reduced chances of receiving IVT and MT treatments for patients who are transferred further than 30 km or 90 km, regardless of the time of the initiation of the procedure. It has been shown that patients living closer to the hospital are more likely to receive IVT than those living further away, and this cannot be explained by shorter arrival times [10]. This study also showed that patients whose transfer distance was more than 90 km had a lower chance of receiving IVT or MT treatment than patients with shorter transfer distances. Similarly, Khazen et al. [11] found that as the distance between PSC and CSC increases, the likelihood of receiving IVT decreases.

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Patients transferred to a location less than 30 km away were 2.3 times more likely to receive thrombectomy than those transferred further away. This highlights the critical role of proximity to a CSC in determining access to thrombectomy. These findings highlight the importance of optimising regional stroke networks to minimise secondary transfer delays and ensure equitable access to life-saving thrombectomy.

In the current study, which included only patients who were secondarily transferred from a PSC to the CSC, there was no difference in three-month mortality, intracranial hemorrhage, and neurological outcomes between patients transferred from nearby primary centers and those transferred from distant primary centers, although patients from remote areas had less chance of receiving IVT and MT. Similarly, a previous meta-analysis found no differences between patients transferred directly to the main center and those transferred secondarily [12]. Ader et al. [13] found that low socioeconomic status may be associated with delays in emergency medicine system (EMS) activation. In our patient population, the group of patients who were transferred more than 90 km to our CSC mostly reside in rural areas and have a low socioeconomic status. Delayed EMS activation for patients transferred from areas more than 90 km away reduces the chances of these patients receiving time-dependent treatments.

In a comprehensive study conducted in our country on patients with AIS, the rate of IVT was 12%, while the rate of MT was 8.3% [14]. In the current study, which included only secondarily transferred patients, the rate of MT was 8.4%, while the rate of IVT was 5.4%. This shows that in our transfer strategy, AIS patients lose the opportunity to receive IVT treatment for the possibility of MT. The low rate of IVT may be due to transfers from distant hospitals.

Interhospital transfer of AIS patients, even when the distance between the hospitals is short, has been shown to reduce the rate of MT administration [15]. However, unforeseen IVT will result in missed treatment time, creating a serious burden on CSCs. Therefore, algorithms that can predict large vessel occlusion early are being developed [16]. Video support for prehospital stroke consultation seems to be successful [17]. In regions where these facilities are not yet available, efforts should focus on ensuring the primary transfer of more patients to a CSC within the one-hour timeframe recommended by the American Heart Association guidelines for regional stroke plans in rural, suburban, and urban communities [18].

Table 1. Demographic and clinical characteristics of patients: a comparison between those who received IVT and/or MT and those who did not

Variables		Treatment+ n=33	Treatment- n=226	p
Age, years, median (IQR 25-75)		60 (54-71)	69 (59-79)	0.011*
Sex (male) n (%)		20 (60)	124 (55)	0.53
NIHSS[b], median (IQR 25-75)		15 (12-22)	8 (5-14)	<0.001*
mRS[c], median (IQR 25-75)		4 (4-5)	3 (2-4)	<0.001*
Good neurologic outcome, n (%)		13 (39)	140 (62)	0.014*
Poor neurologic outcome, n (%)		20 (61)	86 (38)	
Distance transferred, km, median (IQR 25-75)		18 (7-47)	40 (17-81)	0.002*
30 km	<30 km[a]	22 (67)	92(41)	0.005*
	>30 km	11 (33)	134 (59)	
90 km	<90 km	33 (100)	179 (80)	0.004*
	>90 km	0 (0)	47 (20)	
Needle onset time, median (IQR 25-75)		-	135 (120-180)	
Groin onset time, median (IQR 25-75)		-	240 (160-360)	
Emergency department outcome	Hospitalization, n (%)	32 (97)	223 (98)	0.422
	Exitus, n (%)	1 (3)	3 (2)	
Intracranial hemorrhage (36 saat), n (%)		3 (9)	2 (1)	0.016*
Length of ICU[d] stay, days, median (IQR 25-75)		6 (2-10)	0 (0-2)	<0.001*
Length of ward stay, days, median (IQR 25-75)		3 (0-7)	5 (3-7)	0.02*
mRS replacement		1 (0-2)	0 (0-1)	0.156
3[th] month mortality, n (%)		5 (15)	16 (7)	0.161

Treatment+: IVT and/or MT, Km[a]: Kilometers, NIHSS[b]: National Institutes of Health Stroke Scale scores, mRS[c]: Modified rankin scores, ICU[d]: Intensive care unit, IQR: Interquartile range

IVT: Intravenous thrombolytic therapy, MT: Mechanical thrombectomy

Table 2. Comparison of demographic and clinical characteristics between transferred kilometer groups

	<30 km[a] n=114	≥30 km n=145	p value	<90 km n=212	≥90 km n=47	p value
Age, years, median (IQR 25-75)	67 (56-75)	69 (60-80)	0.030	68 (58-77)	73 (58-83)	0.146
Gender, n (%) Female Male	43 (37.7) 71 (62.3)	72 (49.7) 73 (50.3)	0.055	94 (44.3) 118 (55.7)	21 (44.7) 26 (55.3)	0.966
NIHSS[b], median (IQR 25-75)	8 (5-16)	10 (5-15)	0.828	10 (5-16)	7 (5-11)	0.074
mRS[c], median (IQR 25-75)	3 (2-4)	3 (2-4)	0.963	3 (2-4)	3 (2-3)	0.040
Needle onset time, median (IQR 25-75)	130 (90-180)	180 (180-240)	0.126	135 (120-180)	-	-
Groin onset time, median (IQR 25-75)	300 (200-380)	220 (120-240)	0.209	240 (160-360)	-	-
IVT[d]/MT[e]	22 (19.3)	11 (7.6)	0.005	33 (15.6)	0 (0)	0.004
Intracranial hemorrhage	4 (3.5)	1 (0.7)	0.102	5 (2.4)	0 (0)	0.288
Good neurologic outcome	66 (57.9)	87 (60)	0.732	125 (59)	28 (59.6)	0.938
3 month mortality	13 (11.4)	8 (5.5)	0.085	18 (8.5)	3 (6.4)	0.632

Km[a]: Kilometers, NIHSS[b]: National Institutes of Health Stroke Scale scores, mRS[c]: Modified rankin scores, IVT[d]: Intravenous thrombolytic therapy, MT[e]: Mechanical thrombectomy

Table 3. Factors associated with treatment in univariate and multivariate models

Variable	Univariate OR (95% CI)	Univariate p-value	Multivariate OR (95% CI)	Multivariate p-value
Age	0.966 (0.940-0.993)	<0.01	0.948 (0.917-0.980)	<0.005
NIHSS[a]	1.060 (1.027-1.095)	<0.001	1.083 (1.042-1.124)	<0.001
<30 km[b]	2.91 (1.348-6.297)	<0.005	2.3 (1.02-5.178)	<0.05

NIHSS[a]: National Institutes of Health Stroke Scale scores, Km[b]: Kilometers

OR: Odds ratio, CI: Confidence interval

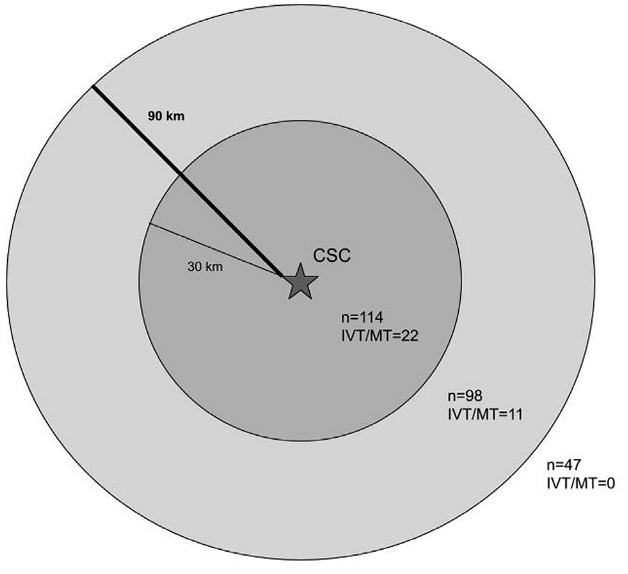

Figure 1. Number of patients treated with IVT/MT according to patients' secondary transfer distance from the CSC

IVT/MT: Intravenous thrombolytic therapy/mechanical thrombectomy, CSC: Comprehensive stroke center

In our region, if AIS patients who can reach the CSC within one hour were taken directly to the CSC, we think that they would have more opportunities to receive MT and IVT.

Study Limitations

Several possible limitations should be considered when interpreting the results of this study. First, the study is retrospective. Therefore, patients with missing data in their electronic patient records were excluded. Second, the management of AIS patients may be different in each country and in different regions within a country. Therefore, the results of this study may not be applicable to other countries or regions within our country. In addition, transfer times for patients may have been impacted by traffic density , indirectly affected the opportunities for patients to receive MT and IVT treatments. Finally, our study was conducted in a single center, and future studies should focus on multiple centers conduct more complex transfer analyses.

Conclusion

In patients with AIS who are secondarily transferred to a CSC, the rate of MT/IVT treatment decreases as transfer distance increases. However, there is no difference between patients whose transfer distances were shorter compared with those whose transfer distances were longer distances in terms of three-month mortality, intracranial hemorrhage, and good neurologic outcome. Our IVT administration rates are quite low for both groups, although our results revealed the negative impact of longer secondary transfers on the likelihood of patients receiving MT/IVT treatment. Increasing the number of centers where MT/IVT treatment is offered and CSCs to reduce secondary transfer distances will contribute to the stroke management strategy in our region.

Ethics

Ethics Committee Approval: The study was approved by the, University of Health Sciences Türkiye, Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee (decision number: 2024-824, date: 04.09.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.Ş., Concept: İ.Ş., E.A., İ.T., B.K.Z., Design: İ.Ş., T.S.M., İ.T., S.G.Ö., Data Collection or Processing: İ.Ş., E.A., T.S.M., Analysis or Interpretation: İ.Ş., E.A., T.S.M., S.G.Ö., Literature Search: İ.Ş., B.K.Z., S.G.Ö., Writing: İ.Ş., İ.T.

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