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Four-year Experience of Intravenous and Endovascular Treatment in Acute Ischemic Stroke: A Single Center Study

Akut İskemik İnmede İntravenöz ve Endovasküler Tedavi Deneyimlerimiz: Dört Yıllık Tek Merkez Çalışma

Zeynep Özdemir[1], Gülşah Zorgör Dindar[2], Sena Aksoy[1], Erkan Acar[3], Hakan Selçuk[4], Batuhan Kara[4], Aysun Soysal[1]

[1]Istanbul Bakirkoy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital, Clinic of Neurology, Istanbul, Turkey

[2]University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital, Clinic of Neurology, Istanbul, Turkey

[3]Acibadem Mehmet Ali Aydinlar University Faculty of Medicine, Department of Neurology, Istanbul, Turkey

[4]University of Health Sciences Turkey, Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Clinic of Radiology, Istanbul, Turkey

Abstract

Objective: Acute ischemic stroke (AIS) is a major cause of mortality and morbidity throughout the world. Intravenous thrombolysis (IVT) and endovasculary treatments (EVT) are recomended currently in eligible patients admitted within the therapeutic window. In this study, the data of AIS patients who were treated with intravenous and EVT methods in Istanbul Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital between 2017-2020 were evaluated retrospectively.

Materials and Methods: Five hundred and ninety patients who received IVT and/or EVT were included in the study. Demographic, clinical, radiological characteristics, risk factors and post-treatment clinical characteristics of these patients were analyzed.

Results: Of the 590 patients, 324 (54.9%) underwent IVT, 164 (27.8%) EVT and 102 (17.3%) combined IVT+EVT. The median National Institutes of Health Stroke Scale (NIHSS) scores were 9 (1-21) in the iv tPA group, 13 (3-27) in the EVT group, 12 (4-23) in the combined treatment group at admission In the IVT group, 220 patients had no artery occlusion (67.9%), M2 segment of the middle cerebral artery (MCA) was found to be the most frequently occluded artery with 32 patients (9.9%). In the EVT and combined IVT+EVT groups, the M1 segment of the MCA had the highest occlusion rate [76 (44.2%), 49 (45%), respectively]. Asymptomatic hemorrhage rate was higher in the EVT group than the other groups. Symptomatic hemorrhage rate was lower in the IVT group compared to the other groups. A total of 182 (56.2%), 67 (39%) and 53 (48.6%) patients in the IVT, EVT and combined IVT+EVT groups had good outcome, respectively.

Conclusion: Acute stroke treatment has been proven to significantly reduce the serious burden of stroke on patients, caregivers and society. For this reason, the societal awareness of the importance of urgent admission to emergency departmentsand the number and capacity of centers that provide AIS treatments should be increased.

Keywords: Acute stroke, acute stroke treatment, iv tPA, endovascular treatment

Öz

Amaç: Akut iskemik inme (Aİİ) tüm dünyada önemli bir mortalite ve morbidite nedenidir. Terapötik pencerede başvuran akut inmeli hastalara intravenöz tromboliz (İVT) ve endovasküler tedaviler (EVT) önerilmektedir. Bu çalışmada İstanbul Bakırköy Prof. Dr. Mazhar Osman Ruh ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi'nde 2017-2020 yılları arasında İVT ve EVT yöntemleri ile tedavi edilen Aİİ hastasının verileri retrospektif olarak değerlendirildi.

Gereç ve Yöntem: Bu çalışmaya intravenöz ve/veya EVT uygulanan 590 hasta dahil edilmiştir. Bu hastaların demografik, klinik, radyolojik özellikleri, risk faktörleri ve tedavi sonrası klinik özellikleri analiz edilmiştir.

Bulgular: Beş yüz doksan hastanın 324'üne (%54,9) İVT, 164'üne (%27,8) EVT ve 102'sine (%17,3) kombine İVT+EVT uygulandı. Başvuruda medyan National Institutes of Health Stroke Scale (NIHSS) skorları iv tPA grubunda 9 (1-21), EVT grubunda 13 (3-27), kombine tedavi grubunda 12 (4-23) idi. İVT grubunda 220 hastada endovasküler girişim gerektirecek arter tıkanıklığı yoktu (%67,9), 32 hasta (%9,9) ile MCA M2 segmenti en çok tıkanan arter olarak bulundu. EVT ve kombine İVT+EVT gruplarında, MCA'nın M1 segmenti en yüksek oklüzyon oranına sahipti [sırasıyla 76 (%44,2), 49 (%45)]. EVT grubunda

Address for Correspondence/Yazışma Adresi: Zeynep Özdemir, Istanbul Bakirkoy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital, Clinic of Neurology, Istanbul, Turkey
Phone: +905372816513 E-mail: zynp.ozdemir@hotmail.com ORCID: orcid.org/0000-0002-6403-4133
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asemptomatik kanama oranı diğer gruplara göre daha yüksekti. Semptomatik kanama oranı İVT grubunda diğer gruplara göre daha düşüktü. İVT, EVT ve kombine İVT+EVT gruplarında sırasıyla 182 (%56,2), 67 (%39) ve 53 (%48,6) hastada iyi sonuç alındı.

Sonuç: İnme tüm dünyada mortalitenin en önde gelen sebeplerinden biri olmakla birlikte, sağkalım sonrası çoğu hastada sekelli iyileşme yüzünden yüksek oranda morbiditeye neden olmaktadır. Aİİ tedavisinin inmenin hastalar, bakım veren kişiler, ve topluma oluşturduğu yükü önemli oranda azalttığı kanıtlanmıştır. Bu nedenle toplum acil başvuru konusunda daha bilinçli hale getirilmeli ve doğru tedaviyi uygulayan merkezlerin sayı ve kapasiteleri artırılmalıdır.

Anahtar Kelimeler: Akut inme, akut inme tedavisi, iv tPA, endovasküler tedavi

Introduction

Stroke is the most important cause of mortality and morbidity in adults after heart diseases and cancer, according to the data of the World Health Organization (1). Progress has been made in reducing mortality and morbidity with the use of intravenous thrombolysis (IVT) and endovascular treatments (EVT), which have become quite widespread in recent years in acute ischemic stroke (AIS) patients.

Intravenous tissue plasminogen activator (iv tPA), which was proven to be effective in 1996 when applied in the first 3 hours after stroke onset, was started to be used in selected patients who were admitted within the first 4.5 hours after The European Cooperative Acute Stroke Study (ECASS3) in 2008 (2,3). In addition, EVT was included in the treatment guideline by the American Heart Association (AHA) with a class 1 recommendation and evidence level A, in line with the positive results of the the MR CLEAN study in 2015 and the many studies supporting its positive results (4,5). With increased experience, standardizations in stroke treatment are made according to the AHA and the American Stroke Association guidelines, which are constantly updated.

IVT and EVT methods have been performed in Istanbul Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital Neurology Clinics since 2010 and satisfactory results have been obtained in a wide patient population. In this study, it was aimed to evaluate the data of patients who were treated for AIS in our hospital and to discuss them in light of the current literature, and to share the experiences of specific patient subgroups.

Materials and Methods

Istanbul Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital is one of the top referral hospital in Istanbul, Turkey. In our hospital, there is a neurology emergency service, which is open 24 hours a day, that allows patients with stroke to be first evaluated by neurologists at admission, thus preventing delays. After a rapid evaluation of the patients who are predicted to have hyperacute stroke, we call for "T-CODE" which has been developed to speed stroke management. In this organization, the residents of the neurology emergency service, nurses, patient transporters, radiographers, laboratory workers work together and simultaneously. The patient who is examined by the neurologist, is firstly evaluated with a cranial computed tomography (CT), and after hemorrhage is ruled out, if there are no contraindications, diffusion-weighted and cranial magnetic resonance (MR) angiography (MRA) for neurovascular examination are performed. In addition, for the patients with unknown-onset such as wake-up stroke, FLAIR MR imaging sequence is performed, as perfusion imaging is not available.

In this study, we retrospectively studied a database of patients with AIS admitted to the neurology emergency service of our hospital who received IVT and/or EVT between January 2017 and October 2020. The patients determined to be eligible for IVT were those in whom IVT was initiated within 4.5 hours of symptom onset. Endovascular thrombectomy was considered in the patients with Alberta Stroke Program Early CT score ≥6. Whether the patients were administered IVT did not affect the decision to perform EVT. The evaluation of vascular images before IVT and EVT was performed by one of 3 experienced interventional radiologists.

All variables, including demographic characteristics, risk factors, stroke severity National Institutes of Health Stroke Scale (NIHSS) score, laboratory tests, CT images, neurovascular images, symptom-to-door, door-to-needle, symptom-to-needle times, and door-to-puncture times and, modified thrombolysis in cerebral infarction (mTICI) scores were recorded. The recanalization rate was determined with mTICI scores of 0-2a, and 2b-3. Twenty-four hours after the procedure, CT was performed to evaluate post-procedure bleeding. Hemorrhagic transformation was classified as symtomatic or asymptomatic according to the ECASS III classification system. During the hospitalization of all patients, electrocardiogram, echocardiography, tests for lipid profile and glycosylated hemoglobin test (A1c), and vascular imaging were conducted. Stroke etiologies were classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. Length of stay was recorded. The low NIHSS score cut-off value was determined as ≤6 for this study. Modified Rankin scale (mRS) score at 90 days was determined as the primary outcome. Good outcome at 90 days was considered as having mRS ≤2. NIHSS score at admission was recorded by the neurologists. The 90-day mRS scores were recorded by the same neurologist.

The study was carried out in accordance with the ethical standards of the Declaration of Helsinki and the ethics committee approval was obtained from the Ethics Committee of the Clinical Studies Ethics Committee of University of Health Sciences Turkey, Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital, with the number of 2021/246.

Statistical Analysis

Firstly, we checked the assumption of normal data distribution using Kolmogorov-Smirnov test and the statistical analysis involved non-parametric tests. The variables were presented as median, interquartile range (IQR) or as percentages. The chi-squared test and Fisher's exact test were performed to compare categorical parameters between groups. Continuous variables with asymmetric distribution were compared between 2 groups using Mann-Whitney U and between more than 2 groups using Kruskal-Wallis test. Post-hoc analysis was used for comparing multiple categorical variables. For all analyses, a p-value of less than 0.05 was accepted as statistically significant.

Results

Patient Population

In this single center study, T-CODE was given in a total of 2001 patients between January 2017 and October 2020; 401, 565, 710 and 335 in each year, respectively. A total of 590 patients, comprising 279 females (47.3%) and 311 males (52.7%) were included in this study. The median age of all patients was 65 years (IQR, 56-77); the median age of female patients was 72.5 (IQR, 62-80), whereas the median age of male patients was 62 (IQR, 54-73) (p<0.001). Of 590 patients, 324 (54.9%) underwent IVT, 164 (27.8%) EVT and 102 (17.3%) combined IVT+EVT. The median age among all groups was highest in the IVT group (p<0.001).

The three groups were similar, in terms of comorbidities [hypertension (HT), diabetes mellitus, hyperlipidemia, atrial fibrillation, coronary artery disease and prior stroke). The median baseline NIHSS score of 590 patients was 11 (IQR, 7-15). The patients in the IVT group had lower baseline NIHSS score than those in the other treatment groups (p<0.001). The median symptom-to-door time of EVT group was longer than the other treatment groups (p<0.001). There was no significant difference in terms of door-to-needle time between the IVT and the combined IVT+EVT groups (p=0.125). The median door-to-puncture time was longer in the combined IVT+EVT group than in the EVT group (p=0.001). Succesful recanalization (mTICI 2b-3) rate was higher in the only EVT group with no significant difference (p=0.191)

In the IVT group, 220 patients had no artery occlusion (67.9%), M2 segment of the middle cerebral artery (MCA) was found to be the most frequently occluded artery [n=32 patients, (9.9%)]. In the EVT and the combined IVT+EVT groups, the M1 segment of the MCA had the highest occlusion rate [n=72 (%43,9) and n=48 (%47,1), respectively]. In all treatment groups, cardioembolism was the most common etiology among the determined etiologies. Large artery atherosclerosis rate was lower in the IVT group than in the other two groups (p<0.001). Small vessel occlusion and unknown etiology rates were higher in the IVT group than in the other two groups (p<0.001 and p=0.009, respectively) (Table 1).

Outcome Measures

Twenty four hours after the procedures, complications associated with the procedures were assessed. There was a significant difference between groups in terms of all types of hemorrhage (p<0.001). Asymptomatic hemorrhage rate was higher in the EVT group than in the other groups (p<0.001). Symptomatic hemorrhage rate was lower in the IVT group compared with the other groups in unadjusted analysis (p<0.001). In adjusted analysis, patients in the IVT group had a 62% lower risk of symptomatic hemorrhage 24 hours after procedure compared to the combined IVT+EVT group. The patients in the EVT group had a 17% decrease in the odds of symptomatic hemorrhage compared to the combined IVT+EVT group [95% confidence interval (CI): 0.45-1.54]. Patients in the EVT group had a significantly higher median 24-hour NIHSS score than those in the other groups (p<0.001) and, significantly longer median length of stay compared with the IVT group (p=0.002) (Table 1).

With regard to functional outcome, patients in the IVT group had lower median mRS score <2 (IQR, 0-4) at 90 days compared with EVT and the combined IVT+EVT groups. But the difference was significant only when compared with the EVT group (p<0.001). A total of 182 (56.2%), 62 (37.8%) ve 48 (47.1%) patients in the IVT, EVT and the combined IVT+EVT groups had good outcome, respectively. Patients in the EVT group had significantly lower rates of good outcome compared with the IVT group (p=0.001). In adjusted analysis, patients in the IVT group showed a 7% (95% CI: 0.55-1.57) lower chance of good outcome, and patients in the EVT group had an 18% (95% CI: 0.40-1.29) lower chance of good outcome compared to the combined IVT+EVT group. In unadjusted analysis, the rate of mortality was significantly lower in the IVT group (13.3%) compared with the other groups (p=0.006) (Table 1). In adjusted analysis, patients in the IVT group had a 40% (95% CI: 0.31-1.14) lower risk of mortality compared to the combined IVT+EVT group. Patients in the EVT group had a 10% (95% CI: 0.57-2.12) higher risk of death within 90 days after the index stroke compared to the combined IVT+EVT group.

In patients with low NIHSS score and LVO, the MCA M2 artery was the most occluded artery with a rate of 38.2%. Internal carotid artery was the most frequently occluded artery in the EVT group and MCA was the most frequently occluded artery in the combined IVT+EVT group. There was no statistically significant difference between the treatment groups in terms of occluded arteries (p=0.757). Baseline NIHSS score did not differ between the treatment groups (p=0.921). A statistically significant difference was not found between the groups in terms of hemorrhage rates (p=0.678). Patients in the IVT group had a significantly higher 90-day median mRS score (p=0.006), no significantly lower rate of good functional outcome (p=0.086), and no significantly higher rate of mortality (p=0.194) (Table 2).

Outcome by Years

Overall, the number of patients within the database did not significantly differ from 2017 to 2020 according to the procedure applied, however it was lowest in 2020. The symptom-to-door durations were longest in 2018 in the EVT group (p=0.006), in 2020 in the EVT group (p=0.064), and in 2019 in the combined IVT+EVT group (p=0.430). The door-to-needle durations in the IVT and the combined IVT+EVT groups were significantly longer in 2020 (p<0.001). The door-to-puncture duration was longest in both EVT and the combined IVT+EVT groups in 2020 (p=0.004, and p=0.540, respectively). No statistically significant difference was found when treatment groups were compared in terms of outcomes from 2017 to 2020 in terms of bleeding, mRS score at 90 days, and death within 90 days (Table 3) (Figure 1).

Discussion

Immediate admission directly to an acute stroke unit improves outcome and decreases mortality and morbidity caused by stroke. It is thought that more patients reach our hospital every year, both by outpatient and emergency ambulance services because of two reasons. One reason is that our center is a reference center and the second reason is that the society's awareness of stroke has increased in time. The significant decrease in the number of patients in 2020 compared to previous years is thought to be largely related to the coronavirus disease-2019 (COVID-19) pandemic and the inclusion of patients admitted until October 2020. Approximately two-thirds of the patients in whom T-CODE was given were not treated either with IVT or EVT because of several reasons such

Table 1. Comparision of baseline characteristics of patients treated with IVT, EVT, and combined IVT+EVT

Variable	IVT (n=324)	EVT (n=164)	IVT+EVT (n=102)	Test used	p-value
Age, year; median (IQR)	70 (59-80)*	66 (55-75)	62.5 (54-72)	KW	<0.001
Sex, female	152 (46.9)	82 (50)	45 (44.1)	χ^2	0.633
Comorbidities					
HT	216 (66.6)	108 (65.9)	75 (73.5)	χ^2	0.369
DM	121 (37.3)	54 (32.9)	38 (37.3)	χ^2	0.572
Hyperlipidemia	194 (59.8)	88 (53.6)	60 (58.8)	χ^2	0.430
Atrial fibrillation	94 (29)	62 (37.8)	30 (29.4)	χ^2	0.104
CAD	78 (24.1)	46 (28)	30 (29.4)	χ^2	0.451
Prior stroke	53 (16.3)	33 (20.1)	18 (17.6)	χ^2	0.798
Periprocedure					
Baseline NIHSS score ‖					
Median (IQR)	9 (6-13)*	13 (11-15.7)	13 (9-16)	KW	<0.001
Range	1-21	3-27	4-23		
Symptom-to-door, min; median (IQR)	77.5 (49-129.5)	167.5 (60-246.7)*	63.5 (45-121)	KW	<0.001
Door-to-needle, min; median (IQR)	60 (46-80)	-	55.5 (45-69.2)	MW	0.07
Door-to-puncture, min; median (IQR)	-	105 (77.2-136)	120 (99.7-145.5)	MW	0.004
Final TICI flow				χ^2	0.152
0-2a	-	56 (34.4)	44 (43.6)		
2b-3	-	107 (65.6)	57 (56.4)		
Site of vascular occlusion				χ^2	<0.001
ICA	26 (8)*	30 (18.3)	17 (16.7)	χ^2	0.002
ICA-Tandem	6 (1.9)*	25 (15.2)	12 (11.8)	χ^2	<0.001
MCA M1	29 (9)*	72 (43.9)	48 (47.1)	χ^2	<0.001
MCA M2	32 (9.9)	25 (15.2)	20 (19.6)§	χ^2	0.024
Basilar artery	3 (0.9)	10 (6.1)§	4 (3.9)	χ^2	0.004
Vertebral artery	4 (1.2)	1 (0.6)	1 (1.0)	FE	0.809
PCA	4 (1.2)	0	0	FE	0.191
Stroke etiology by TOAST					
Large artery atherosclerosis	40 (12.3)*	54 (32.9)	30 (29.4)	χ^2	<0.001
Cardioembolism	112 (34.6)	68 (41.5)	40 (39.2)	χ^2	0.300
Small vessel occlusion	49 (15.1)*	0	0	χ^2	<0.001
Other etiology	6 (1.9)	5 (3.0)	2 (2.0)	χ^2	0.685
Unknown etiology	117 (36.1)	37 (22.6)§	30 (29.4)	χ^2	0.009
Hemorrhage (all types)	46 (14.2)*	75 (45.7)	39 (38.2)	χ^2	<0.001
Symptomatic	30 (9.3)*	44 (26.8)	29 (28.4)	χ^2	<0.001
Asymptomatic	16 (4.9)	31 (18.9)*	10 (9.8)	χ^2	<0.001
24 h NIHSS					
Median (IQR)	6 (2-10)*	11 (5.7-16)*	8 (2-14)*	KW	<0.001
Range	0-27	0-39	0-37		
Length of stay (days), median (IQR)	11 (8-16)	14 (9-25.7)§	12 (8-22)	KW	0.002
mRS at 90 days					
Median (IQR)	2 (0-4)	3 (1-5)§	3 (0-5)	KW	<0.001

mRS dichotomized				χ^2	0.001
mRS 0-2	182 (56.2)	62 (37.8)§	48 (47.1)		
mRS >2	142 (43.8)	102 (62.2)§	54 (52.9)		
Death	43 (13.3)*	39 (24.1)	24 (23.5)	χ^2	0.006

Values are N (%), median (IQR)

χ^2 test was used for categorical variables, the Kruskal-Wallis test was used to compare 3 non-parametric variables, and the Mann-Whitney test was used to compare 2 non-parametric variables.

*Indicates a significant difference compared with any other groups,

§Indicates a significant difference compared with first group,

‖National Institutes of Health Stroke Scale (NIHSS) scores range from 0 to 42, with higher scores indicating greater neurologic deficit.

¶Indicates significant differences compared with second group.

CAD: Coronary artery disease, DM: Diabetes mellitus, FE: Fisher's exact test; HT: Hypertension, ICA: Internal carotid artery, IQR: Internal quartile range, KW: Kruskal-Wallis test, LACI: Lacunar infarct, MCA: Middle cerebral artery, MW: Mann-Whitney test, min.: Minute, mRS: Modified Rankin scale, OCSP: The Oxfordshire community stroke project, PACI: Partial anterior circulation ınfarct, PCA: Posterior cerebral artery, POCI: Posterior circulation infarct, TACI: Total anterior circulation infarct, TICI: Thrombolysis in cerebral infarction, TOAST: Trial of Org 10172 in Acute Stroke Treatment, IVT: Intravenous thrombolysis, EVT: Endovasculary treatments

Table 2. Baseline characteristics and outcome analysis of patients with LVO and low NIHSS score

	n	IVT (n=21)	EVT (n=15)	IVT+EVT (n=11)	Test used	p-value
Site of vascular occlusion					χ^2	0.757
ICA	12	6 (28.6)	5 (33.3)	1 (9.1)		
ICA-Tandem	4	1 (4.8)	2 (13.3)	1 (9.1)		
MCA M1	11	3 (14.3)	4 (26.7)	4 (36.4)		
MCA M2	18	11 (52.4)	4 (26.7)	3 (27.3)		
Basilar artery	2	0	0	2 (18.2)		
Baseline NIHSS, median (IQR)		5 (4.5-6)	5 (4-6)	5 (4-6)	KW	0.921
Hemorrhage (all types)					FE	0.678
Symptomatic		2 (9.6)	2 (13.3)	0	FE	1.00
Asymptomatic		0	2 (13.3)	0	FE	0.495
mRS at 90 days, median (IQR)		1 (0.5-3)*	0 (0-1)	0 (0-1)	KW	0.006
mRS 0-2		14 (66.7)	13 (86.7)	10 (90.9)	FE	0.086
Mortality		2 (9.5)	0	0	FE	0.194

Values are n (%), median (IQR)

*Indicates a significant difference compared with any other groups

FE: Fisher's exact test, ICA: Internal carotid artery, IQR: Internal quartile range, KW: Kruskal-Wallis test, LVO: Large vessel occlusion, MCA: Middle cerebral artery, mRS: Modified Rankin scale, NIHSS: National Institutes of Health Stroke Scal, IVT: Intravenous thrombolysis, EVT: Endovasculary treatments

as unknown symptom onset time, inappropriate NIHSS score, hemorrhage detected in inital cranial CT, suspicion of an intracranial mass, presence of resistant hypertension, rapidly resolving deficit, presence of medication contraindicated for treatment, and the lack of consent from the patient's relatives. Although a clear limit was not determined for the NIHSS score in studies, in the American Food and Drug Administration approval, a caution was put in place in the case of NIHSS score >22, and in the instructions for use of tPA in our country, NIHSS score >25 is accepted as severe stroke and in patients with NIHSS >25 tPA administration is not recommended (3). In our center, iv tPA treatment was administered in patients with a NIHSS score between 1 and 42 without contraindications. However, in mild stroke (NIHSS score ≤6), iv tPA was given when isolated speech disorder, vision loss or extremity paresis was detected, which might cause significant functional disability in daily activities.

There is a linear relationship between stroke risk and hypertension, which is one of the most important modifiable risk factors in stroke etiology (6). In our study, HT was detected in most of the patients, which was consistent with the literature. Diabetes, which causes microvascular complications in particular, is a known risk factor for stroke. Considering hyperlipidemia as an important risk factor for stroke, although only 91 (15%) patients had the diagnosis of hyperlipidemia at admission, 251 (42.5%) patients were diagnosed and treated during hospitalization. The high rate of diagnosis of hyperlipidemia at hospitalization suggests that high cholesterol is not given enough attention in our country, awareness is low and preventive health services are not adequately implemented.

The reason for the significantly lower median NIHSS score in the IVT group compared to the EVT groups in the study analysis could be explained by the worse clinical condition of patients with large vessel occlusion at presentation. Therefore, the 24th hour NIHSS score of the EVT group was found to be similarly high. However, the higher 24th hour NIHSS score detected in the EVT group was ascociated with the late symptom onset-door time

Table 3. Overall characteristics and outcomes of patients between 2017 and 2020

Variable	2017 (12 months) (n=158)	2018 (12 months) (n=169)	2019 (12 months) (n=173)	2020 (10 months) (n=90)	Test used	p-value
IVT	93 (58.9)	83 (49.1)	92 (53.2)	56 (62.2)	χ^2	0.185
Symptom-to-door, min; median (IQR)	78 (44.5-120)	100 (55-162)	60 (45-120)†	66 (50.7-120)	KW	0.006
Door-to-needle, min; median (IQR)	58 (45.5-70)	51 (41-72)	60 (45.7-81)	76 (60-105)*	KW	<0.001
Hemorrhage	17 (19.3)	10 (12)	16 (17.3)	3 (5.4)	χ^2	0.114
Symptomatic	9 (9.6)	6 (7.2)	12 (13)	3 (5.4)	χ^2	0.390
mRS at 90 days median (IQR)	3 (1-4)	1 (0-3)	2 (0-4)	1 (0-4)	KW	0.169
Death within 90 days	11 (11.8)	6 (7.2)	15 (16.3)	11 (19.6)	χ^2	0.141
EVT	37 (23.4)	50 (29.6)	52 (30.1)	25 (27.8)	χ^2	0.402
Symptom-to-door, min; median (IQR)	166 (45-223)	165 (60-244)	129.5 (60-240)	240 (114-448.5)	KW	0.064
Door-to-puncture, min; median (IQR)	90 (64.5-120)	103 (70-120)	112 (80-154.5)	136 (87.5-200)†	KW	0.004
Hemorrhage	19 (51.4)	25 (50)	20 (38.5)	11 (44)	χ^2	0.578
Symptomatic	7 (18.9)	18 (36)	13 (25)	6 (24)	χ^2	0.319
mRS at 90 days median (IQR)	3 (1.5-6)	3 (1-5.2)	3 (1.2-5)	3 (1-5.5)	KW	0.924
Death within 90 days	10 (27)	12 (24)	11 (21.2)	6 (24)	χ^2	0.948
IVT+EVT	28 (17.7)	36 (21.3)	29 (16.8)	9 (11.5)	χ^2	0.241
Symptom-to-door, min; median (IQR)	60 (44.2-108.7)	64 (56.7-127.7)	90 (45-142.5)	58 (35.5-90)	KW	0.430
Door-to-needle, min; median (IQR)	57.5 (44.7-108.7)	50.5 (37-60)	58 (50-72)	70 (64.5-95)†	KW	<0.001
Door-to-puncture, min; median (IQR)	119 (97.5-140)	120 (103.5-148.7)	119 (85-152.5)	130 (114-162.5)	KW	0.540
Hemorrhage	11 (39.3)	14 (38.9)	10 (34.5)	4 (44.4)	χ^2	0.952
Symptomatic	8 (28.6)	10 (27.8)	7 (24.1)	4 (44.4)	χ^2	0.704
mRS at 90 days median (IQR)	3 (0-6)	1 (0-5)	3 (0-5.5)	3 (0-4)	KW	0.762
Death within 90 days	9 (32.1)	8 (22.2)	7 (24.1)	0	χ^2	0.265

Values are n (%), median (IQR)
*Indicates a significant difference compared with any other group,
†Indicates a significant difference compared with second group,
‡Indicates a significant difference compated with first group.
IQR: Interquartile range, KW: Kruskal-Wallis test, mRS: Modified Rankin scale, IVT: Intravenous thrombolysis, EVT: Endovascular treatments

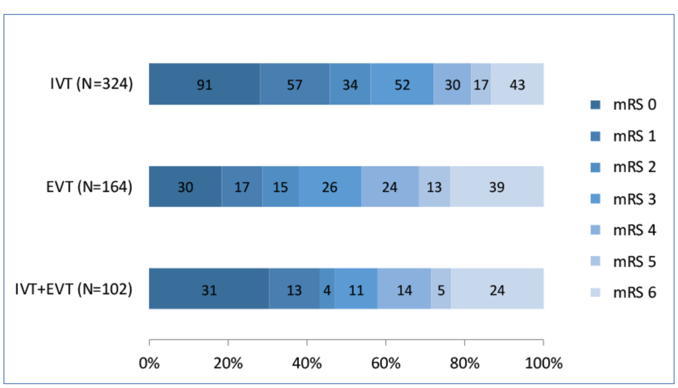

Figure 1. Modified Rankin scale score at 90 days in treatment groups

than the bridging therapy group. This suggests that it is directly related to the low rate of functional independence in the EVT group. There are variable results regarding bridging therapy in the literature, but there is no significant difference in recanalization rates in general (7-11). In our study, no difference was found between the mTICI recanalization rates of patients who were tretaed with and without bridging theraphy. The reason for the statistically low rate of symptomatic intracranial bleeding in the IVT group and higher rate in the EVT group could be explained by the high complication rate of EVT modalities, in line with the literature (12,13). However, contrary to large-scale studies (11), the rate of asymptomatic bleeding was higher in the EVT group without bridging theraphy (14). The reason for this might be the possible high number of passes in this patient group who were admitted outside the thrombolytic treatment window, but the lack of detailed data on this was one of the weakness of our study. The mortality rate was lower in the IVT group than others. This could be explained by the fact that patients who had already undergone IVT alone had lower clinical baseline NIHSS scores than the other groups, and intracranial hemorrhage rates were lower in the IVT group.

There are different results in the literature on bridging therapy. There are studies showing that bridging therapy provides better clinical outcome, lower mortality and more successful recanalization (15-17), besides there are studies showing that the outcomes are not different (14,18) and even that intracranial hemorrhage is at a higher rate (19,20). In a few randomized controlled studies on the subject, it was concluded that bridging therapy in the anterior circulation did not make a significant difference in clinical outcome or that EVT alone was non-inferior to IVT+EVT (7,11,21). In three studies on this subject, bridging treatment in the anterior circulation did not make a significant difference on the clinical outcome, and two studies suggested that EVT alone was non-inferior to IVT+EVT. In a review by Chen et al. (14), it was concluded that bridging therapy had no effect on clinical outcome. Similar to this review, in our study, when bridging therapy applied in patients admitted within the first 4.5 hours and EVT alone groups were compared, there was no statistically significant difference in both symptomatic hemorrhage rates and independent functional outcome at 3 months (p=0.77, p=0.13). Likewise, administration of IVT before EVT did not affect recanalization rates (p=0.13). Considering that the EVT+IVT has no effect on functionality and recanalization success, and considering the potential financial burden it creates, applying it only to a selected patient group may increase cost effectiveness (22,23). However, more randomized controlled studies are needed on this subject.

According to the TOAST classification, which isa reliable and frequently used classification in the etiology of stroke, most of the patients were classified as having cardioembolic stroke. Compared to the literature, it was thought that the reason why small vessel disease was less common in our patient group was that patients with lacunar infarction presented with mild symptoms or outside the therapeutic window (24). The rate of large vessel occlusion among treatment groups was lower in the IVT group, as expected.

One of the most important factors affecting the outcome in the treatment of AIS is time. The median admission time to the hospital was recorded as 90 minutes. Our center being a referral center, referral of some of the patients, and city traffic in individual admissions might be the environmental factors affecting the length of the symptom-to-door time. However, the most important factor influencing the length of this period is the lack of awareness of stroke symptoms in the society, the expectation that these symptoms resolve on their own, and the lack of awareness that it is a situation that requires urgent intervention. Our study showed that there were still delays in the management of cerebrovascular diseases in which every minute isimportant. A very good organization is required in every step from admission to the hospital to the beginning of treatment.

In our center, the median door-to-needle time was recorded as 59 minutes. Similarly, in patients receiving EVT, the door-to-puncture time was 112 minutes. Shorter duration between symptom onset and iv tPA was associated with better clinical outcome, less length of hospital stay, and a greater number of functionally independent patients (25). The most important factor prolonging this period was that both CT and diffusion MR and MRA imagings were performed in our center before treatment. Making a treatment decision with faster imaging techniques such as CT-CT angiography may play a role in shortening this period. Although the physical conditions of our hospital and the difficulties related to the patient/patient's relatives are important factors in the prolongation of this period, it needs to be improved. In terms of years, door-to-needle times in the IVT group, symptom-door and door-puncture times in the EVT group, and door-to-needle times in the combined IVT+EVT group were significantly longer in 2020 compared to other years. It is thougt to be related with the individual delay of patients in admitting to the hospital during the COVID-19 pandemic, the increase in the number of patients in need of ambulance services compared to the non-pandemic times and the precautions taken in isolation conditions of in-hospital transfer.

Considering the disability caused by stroke, 49.5% of the patients were mobilized independently, regardless of the treatment method. This rate was 56.2% in the group receiving IVT, 37.8% in the EVT group and 48.1% in the combined treatment group. The most important reason for this result was that the group receiving EVT had a higher admission NIHSS score and therefore had more severe stroke. For the same reason, mortality was higher in the group treated with EVT alone or combined with IVT (23.8% and 24,1%, respectively). Early physical therapy and rehabilitation for patients with mRS 3 and 4 may play a role in reducing long-term disability.

Study Limitations

There were some limitations of this study. There were missing data due to the retrospective nature of the study and the data records were not digitized in our hospital.

Conclusion

Stroke is one of the important causes of mortality and morbidity in adults all over the world, and its consequences create an economic burden in the individual and social sense. It was also seen in our study that the procedures applied in the treatment of acute stroke significantly reduced the mortality and morbidity caused by stroke. With the right selection of patient and treatment methods, almost half of the patients can continue their lives independently. Strategies should be developed to raise public awareness about the urgency and importance of early hospital admission.

Ethics

Ethics Committee Approval: The ethics committee approval was obtained from the Ethics Committee of the Clinical Studies Ethics Committee of University of Health Sciences Turkey, Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital, with the number of 2021/246.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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