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Time of arrival and in−hospital evaluation processes among patients with acute ischemic stroke at Yozgat City Hospital in Turkey: A retrospective study

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ABSTRACT

Objective: To reveal the factors leading to delay in the evaluation processes of patients with suspected acute ischemic stroke at Yozgat City Hospital in Turkey and suggest potential solutions.

Methods: Patients who visited the emergency service of Yozgat City Hospital between 1 April 2017 and 1 July 2017 and those hospitalized with a diagnosis of ischemic stroke, were included in this retrospective study. The clinical information of the patients was collected *via* hospital files and telephone interviews. In addition, the potential association between arrival time and the clinical parameters was investigated.

Results: A total of 87 patients were included. The median arrival time to emergency service was 5 (IQR=9) h. Forty-four percent of patients arrived within the first 4.5 h from symptom onset. However, intravenous thrombolytic treatment was performed in only 7% of the patients. The median time from arrival to neuroimaging performing was 20.0 (IQR=34) min. Fifty-one percent of patients were screened within the first 20 min from arrival to emergency service. There was no association between arrival time and transfer method of the patients.

Conclusions: The main problem regarding acute stroke care in our region may be inefficient use of emergency ambulance. This study provides basis for measures to shorten the arrival time.

KEYWORDS: IV-tPA; Acute stroke care; Delay; Emergency ambulance; Turkey

1. Introduction

Time of symptom onset is a critical point for acute ischemic stroke treatment as intravenous thrombolytic treatment (IV-tPA) is acknowledged to be as an effective option within the only first 4 or 5 h after the clinical onset. In this context, a wide range of researches have been conducted to determine the ideal and applicable evaluation standards for patients with acute stroke[1-8]. However, as mentioned before[9,10], the optimum criteria and priorities should be probably changed according to ethnicity, sociocultural factors, hospital facilities, and many other factors, *etc*. In the light of these data, we think that the determination of the specific problems in acute ischemic stroke care in our province might provide substantial perspectives for making efficient stroke programs in our country. However, researches on this topic is very limited in Turkey[11-13]. We retrospectively investigated the arrival time and other clinical parameters which might influence the time from symptom onset to treatment initiation acute ischemic stroke patients in a secondary level hospital in Turkey. We aimed to reveal the factors leading to the delay in the evaluation procedures of patients with suspected acute ischemic stroke in our province and suggest potential solutions.

2. Materials and methods

2.1. Patients

Patients who visited the emergency service of Yozgat City Hospital between 1 April 2017 and 1 July 2017 and those hospitalized with

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the diagnosis of ischemic stroke were included in this retrospective study. Diagnosis of stroke was based on neurological examination that showed change in mental status, the weakness of the extremities, speech disturbance, paresthesia, vertigo and dizziness. The diagnosis was confirmed using computerized tomography (CT) to exclude neurological deficits other than stroke. The clinical onset of symptoms was obtained from the hospital files and telephone interviews (for the patient without documented data). In patients with wake-up stroke, the time of stroke onset was evaluated as the latest time the patient was seen as normal. Patients without reliable clinical data have been excluded from the study. Other clinical information including the arrival time of the patients, type of transportation to hospital (with ambulance or other facilities), time of the neuroimaging, duration from emergency service arrival to admission to neurology service or neuro-intensive care unit and some demographic data of patients were derived from the hospital's computer-based patient recording systems (AKGUN, PACS). We also investigated the potential association between arrival time and some clinical parameters including transfer method, admission unit (service or neuro-intensive care unit), hemispheric lateralization and age of the patients. Some of these analyses were also performed in the subgroup of patients with known stroke onset time (excluding patients with wake-up stroke).

2.2. Ethical approval

The necessary permissions and approval were received from the research ethics committee of Bozok niversity (Registration number 2017_KAEK_189_2019_11.27_23).

2.3. Statistical analysis

Statistical analysis was performed using the SPSS 20.0 package program. For data about arrival time to emergency service, duration from arrival to neuroimaging, and duration from arrival to hospitalization, median±interquartile ranges were used, and analyzed by non-parametric tests. The *Chi*-square test was used for comparison of categorical variables. The Student-*t* test was used for comparison of arrival time in patient with different facilities (ambulance/own facilities). In addition, odds ratios for clinical parameters associated with arrival time were calculated using binary logistic regression analyses. The significance level of the tests was set at α=0.05.

3. Results

Of the 111 stroke patients who were hospitalized within the identified time interval, 24 was excluded due to lack of the reliable clinical data. Overall, 87 patients were included. The demographic and clinical characteristics are given in Table 1. Mean age was (69.7±11.7) years old (female/male ratio: 40/47). A total of 33 patients had stroke lateralized to the right hemisphere; 45 patients had stroke in left

Table 1. Demographic and clinical characteristics of the patients.

Variables	n	Percentage (%)
Wake-up stroke	15	17.2
Arrival time to emergency service (h)		
0-3 h	25	28.7
3-6 h	20	23.0
6-12 h	17	19.5
12-24 h	14	16.1
>24 h	11	12.6
Duration from arrival to neuroimaging (min)		
0-15	27	31.0
15-30	29	33.3
>30	31	35.6

hemisphere. Nine patients were diagnosed with bilateral hemisphere stroke or diffusion negative stroke. The ambulance was used for the transfer of 57.5% of patients (*n*=50) whereas the remaining patients (*n*=37, 42.5%) was transferred to emergency service with their own facilities. Comorbid hypertension, diabetes mellitus, hyperlipidemia and coronary artery disease were present in 69%, 33%, 22%, 7% patients respectively.

The median duration from onset of symptoms to emergency service arrival was 5 (IQR=9) h. A total of 44% of patients had arrived within the first 4.5 h from symptom onset. The results showed that 28.7% (*n*=25) had arrived within 0-3 h and 23.0% (*n*=20) had arrived within 3-6 h. However, IV-tPA treatment had been performed in only 6.9% (*n*=6) of patients. A total of 17.2% of patients were evaluated as wake-up stroke (Table 1). Duration time from arrival to hospitalization was 124 (IQR=89) min. A total of 15 patients were transferred to intensive care unit.

In the sub-group of patients (83%) with known onset time, median arrival time was 4.45 (IQR=8.98), and no difference was found in terms of transfer style in this group (*P*=0.828). There was also no association between arrival time and transfer method of the overall patients (*P*=0.123, *t*-test). Furthermore, when analyses were repeated after classification as admission within 0-3 h and out of 3 h, again, no difference was found in terms of transfer method (*P*=0.107). Besides, no relationship between the previous history of stroke and arrival time was found (*P*=0.234) (Table 2). In addition, binary logistic regression analyses showed that no clinical parameters were found to be predictive for arrival within the first 3 h (Table 3).

Table 2. Association of clinical features with arrival time to emergency service.

Clinical features	Arrival time		*P*-value
	≤3 h (*n*=25)	>3 h (*n*=62)	
Transfer style to hospital			
Ambulance	11	39	0.107
Own facilities	14	23	
Hemispheric lateralization of stroke			
Right	9	24	0.864
Left	13	32	
Hospitalization type			
Service	20	52	0.665
Intensive care unit	5	10	
Previous history of stroke			
Yes	14	26	0.234
No	11	36	

Table 3. Regression analysis results.

Variables	B	S.E.	Wald	df	Sig.	exp(B)	95% *CI*	
							Lower	Upper
Hemispheric lateralization of stroke	-0.183	0.529	0.119	1	0.730	0.833	0.296	20.348
Transfer style to hospital	0.593	0.600	0.979	1	0.323	10.810	0.559	50.866
Hospitalization to intensive care unit or service	0.533	0.747	0.510	1	0.475	10.705	0.394	70.372
Previous history of stroke	-0.429	0.573	0.561	1	0.454	0.651	0.212	20.001
Constant	0.497	10.066	0.218	1	0.641	10.644		

The median duration from arrival to a neuroimaging (CT or MRI) was 20.0 (IQR=34) min. In 31% of the patients, neuroimaging was performed within the first 15 min while 33.3% during 15-30 min. Considering the recommendations in the latest guidelines, patients examined within the first 20 min after arrival were specifically investigated, and the results revealed that 45 of them (51.7%) were screened within the first 20 min. The mean time from emergency service arrival to hospitalization (service or intensive care unit) was 124 (IQR=89) min.

4. Discussion

The aim of stroke thrombolysis is to restore blood supply to the ischemic part of the brain before permanent damage occurring. Intravenous tissue plasminogen activator has been acknowledged as a vital treatment that reduces long term disability when administered early to eligible patients with acute ischemic stroke[1,3]. However, it has a major limitation of being applicable in a short therapeutic time window of up to 4.5 h. Remarkably, in a recent crucial review, it has been reported that only 6%–8% of patients presenting to the emergency department are eligible to receive IV-tPA, making it a highly underutilized therapy[14]. Besides its low rate of feasibility in the clinical practice, we know that earlier IV-tPA administration is also associated with lower risks for complications[4,5,8,14,15]. Because of the importance of rapid treatment, many programs and initiatives have focused on to develop the pre-hospital and in-hospitality evaluation processes for higher rates of earlier administration of IV-tPA in acute stroke patients. Based on these efforts, several proposals and recommendations regarding the pre-hospital care, urgent and emergency evaluation and treatment with intravenous and intra-arterial therapies, and in-hospital management processes have been proposed[1-3,6,7,16-18]. Some clinical remarks such as ideal neuroimaging time, CT interpretation time, neurology consultation and door-to-needle time have been formed. In the latest AHA/ASA guideline of 2018[7], use of emergency medical services by stroke patients was recommended as it has been independently associated with earlier arrival to the emergency department (Class 1, LOE B-NR). The personnel of emergency department service are recommended to provide pre-hospital notification to the receiving hospital that a suspected stroke patient is en route (Class 1, LOE B-NR). On the other hand, many other regional and individual factors might be efficient in outcomes of acute stroke. For instance, racial disparities and varying facilities have been several times emphasized to be efficient in clinical outputs making these factors vital ones to be kept in mind while constituting efficient stroke programs and initiatives[9,10,19]. In Turkey, a very limited number of studies have been conducted to investigate the basic problems impeding optimal administration of IV-tPA and the potential solutions[11-13]. Taken together, we think that the results of our study are strictly crucial since it has been rarely studied previously. We also think that these results may give valuable outcomes from the perspective of a distinct geography with differing health facilities.

We found that 29% of the patients with acute ischemic stroke had arrived to emergency department within the first 3 h from the onset of symptoms which was not an unfavorable ratio in comparison to the universal results[1-8,20]. However, a remarkable result of this study was that there was no difference in arriving time of the patients according to the transfer method to hospitalization (*P*=0.107). This was discordant with the general literature data[1,4]. Therefore, we particularly investigated the municipal working schedule of ambulance services to understand the problems. The total population of the province of Yozgat is estimated as 418 650 according to the latest measurements. The province includes 14 districts in which separate the ambulance service systems serve. In our ambulance services, paramedics usually represent the senior healthcare professional who determines the medical center the patient will be transported from the location of the event. On the other hand, there are only two medical centers where a full-time neurologist work and neuroimaging techniques including brain CT and MRI are available. Hence, IV-tPA treatment can be performed in only these centers, basically in our center due to factors such as localization, more advanced hospital facilities and intensive care support. Detailed discussions with command and control center of Yozgat emergency ambulance service and currently working paramedics were held to identify the problems in this regard. In conclusion, we have concluded that transports of these patients with suspected stroke were mainly made to the nearest medical center from the location of the incident, not to the nearest stroke center. Therefore, the transport of these patients with acute stroke to our center were mainly made from the regional hospitals (not from the location of the incident) which was the basic cause of arrival delay. Of note, prior to referring the patients, basic laboratory tests and cranial CT (if available) were usually performed in the local hospital which further delayed the arrival time. In the latest guidelines, it was recommended that patients with a positive stroke screen and/or a strong suspicion of stroke

should be transported rapidly to the closest healthcare facilities that can capably administer IV alteplase arrival (Class 1, LOE B-NR)[7]. However, in our province, transportation had been made to the closest healthcare facilities, ignoring its facilities to administer IV-tPA which constituted the major problem. Therefore, we have initially aimed to develop the quality of the referral chain in our province. In this setting, we planned to organize training programs for emergency medical technicians and paramedics. Among the previous studies from Turkey, Memis *et al.* determined that 68.4% of the patients arrived at the hospitals within three hours which was a higher rate reported in many other series from Western cities[13]. They associated this high rate of arrival time within the therapeutic window with some geographical and sociocultural features of the province Aydin being particularly a small, affluent city in Western Turkey with no traffic jams. Remarkably, they found a significant positive relationship between the use of ambulance transportation and earlier arrival times to the hospitals. On the other hand, another study by Kocak *et al.*, showed the primary barrier to the delivery of thrombolytic therapy for acute ischemic stroke was determined to be the delayed arrival of the patients to a hospital[12]. They found that only 15.2% of the patients could arrive within 2.5 h of symptom onset. Kocak *et al.* did not find a significant difference in terms of arrival times between the patients who came with their vehicles or those who came with the ambulance in their study conducted in a tertiary referral hospital in a province of Turkey in central Anatolia (Konya). In another report, Keskin *et al.*, the ratio of the patients examined within the 3 h after symptom onset was 49%[11]. Remarkably they also did not find a relationship between ambulance usage and arrival time of the patients in their referral center in Istanbul[11]. These results are also discordant with the literature data emphasizing emergency medical service usage was independently linked with earlier arrival to emergency department[7,9,21]. We think that negative results of associations in these studies might also be related with inappropriate evaluation processes in the emergency ambulances and initial transportation of the patients (as in our region) which were not mentioned in these previous studies[11,12].

On the other hand, when we classified the patients according to the arrival time, we have found that 29% of them had arrived in 0-3 h from the onset of symptoms. Arrestingly, it was found that 44% of patients had arrived within the 4.5 h of symptom onset. However, IV-tPA rate was determined to be 7%. These results also remark the problems during the in-hospital evaluation processes of these patients. The median value of duration from arrival to emergency service to a neuroimaging investigation was 20.0 (IQR=34) min. In 31% of them, neuroimaging was performed within the first 15 min. It has been recommended that brain imaging studies should be performed within 20 min of arrival in the emergency department in at least 50% of patients who may be candidates for IV tPA (Class 1, LOE B-NR)[7]. When the analyses were re-conducted, it was determined that 51.7 % of the patients were screened with a neuroimaging method within 20 min of arrival in the emergency department which is compatible with the universal recommendations. In the review by Jauch *et al.*, it was recommended that the brain imaging study should be interpreted within 45 min of patient arrival in the emergency department by a physician with expertise in reading CT and MRI of the brain parenchyma in patients with IV-tPA candidates[7]. In our routine practice, CT is generally interpreted by the emergency medicine physician within a few minutes soon after the recording and neurology specialist is informed by telephone interview immediately after. Cranial tomography is usually reported after two or three hours and the decision of IV-tPA treatment is based on the interpretation of emergency physician or neurology specialist. Due to the lack of a documented data, we could not evaluate the interpretation time of CTs; however, in the light of the abovementioned information, we think that CT interpretation time in our center coincides with the standards. On the other hand, unfortunately, we could not evaluate the clinical contraindications in these patients (due to insufficient documentation) that might be responsible for the low IV-tPA rates.

The main limitation of our study was its retrospective design didn't reveal the main causes underlying low rates of IV-tPA administrations. By this reason, we could not evaluate the impact of some clinical factors such as stroke severity, patient educational level, and some other individual factors in arrival time of patients and administration rates of IV-tPA. Besides, our study group involved a small number of patients which also attributed to another crucial limitation. However, considering that similar studies are strictly rare in our country and provinces socioeconomically similar to our region, we think that the results of our study may provide crucial perspectives to understand the basic problems in acute stroke care in regions with similar facilities and working schedules.

5. Conclusion

In conclusion, we remark the fact that the effectiveness of the ambulance transport system needs to be improved in our province. We think that the major problem was the initial transportation of patient with stroke was generally being to centers without stroke unit which causes a substantial delay in the arrival time. Hence, we aimed to conduct education programs to increase the awareness of acute stroke and the time dependence of the effective therapy of IV thrombolytics among paramedics to resolve the basic problem in this area. In addition, for improving the timely arrival, the intracommunity awareness of stroke and development of more rapid assessment modalities are warranted. The results of this study may provide substantial perspectives illustrating the evaluation procedures of acute stroke in a province possible representing the problem of several provinces (underdeveloped provinces) in Turkey in this regard. Future prospective studies are warranted to develop distinct policies to develop stroke care which probably should change according to the differing sociocultural and medical facilities.

Conflict of interest statement

The author reports no conflict of interest.

Authors' contribution

H.O. contributed to the data synthesis, study drafting, study design, study conceptualization, data collection, analysis or interpretation of the data, manuscript preparation, and manuscript revision.

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