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Social factors influencing hospital arrival time in acute ischemic stroke patients

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Abstract
Introduction This is a multi-center, hospital-based study aiming to estimate social factors influencing pre-hospital times of arrival in acute ischemic stroke, with a perspective of finding ways to reduce arrival time and to augment the number of patients eligible for intra-arterial thrombolysis.
Methods Acute ischemic stroke patients who presented at the emergency units of four major general public hospitals were registered. We assessed information concerning demographics, time of presentation, clinical situation, imaging, treatment, and socioeconomic factors. The sample was divided in two sub-samples, based on the time of arrival since onset of symptoms, and was statistically analyzed.
Results During one calendar year (2005), 907 patients were registered. Among them 34.6% arrived in the first 6 h from symptom onset, 38.7% arrived between 6 and 24 h, 18.1% after 24 h and for 8.6% the time of onset was unknown. Younger age (P=0.007), transfer with ambulatory service (P=0.002), living with a mate (P=0.004), and higher educational level (P<0.005) were factors which correlated significantly with early arrival at the hospital.
Conclusions Instructing patients at high risk for stroke to live with a housemate appears beneficial for timely arrival at the hospital. The establishment of dedicated acute stroke call and transportation center should improve the percentage of early arrival. A national information campaign is needed to increase the level of awareness of the population concerning beneficial social behaviors and optimal reaction to symptoms of acute ischemic stroke.

Keywords Acute ischemic stroke · Thrombolysis · Window of opportunity · Pre-hospital delays · Early arrival

Introduction

Cerebral acute ischemic stroke is a major medical and social issue in the western societies. In the last 15 years, new therapeutic strategies have been developed [1], especially thrombolytic treatment, giving new boost in acute ischemic stroke management and directing the countries in establishing dedicated, multidisciplinary acute stroke units for optimal thrombolysis implementation. International studies and consensuses delineate the need and clinical value of such acute stroke units [2] and recent European Union declarations [3] stress the need to provide this kind of etiologic treatment for every patient in the Union by the year 2012.

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One of the most significant problems in the management of acute stroke patients is early arrival at the hospital, within 6 h from symptom onset, in order to be eligible for intra-arterial thrombolysis [4], or within 3 h [5] (or 4.5 h [6]), in order to benefit from intra-venous thrombolysis. The current sub-study, part of a larger project in the region of Attica, the capital region of Greece, aims at investigating various factors that could potentially contribute to early arrival of acute ischemic stroke patients, in order to delineate the optimal patient profile, as far as early arrival is concerned. Our goal is to develop, via these results, efficient strategies for augmentation of the number of patients that arrive early at the hospital, thus being able to benefit from recanalization therapies.

The further goal of the whole project is a reform of the management of acute ischemic stroke in the area, with the establishment of a multidisciplinary acute stroke unit and a stroke "circuit", which will redirect patients that are currently treated in hospitals of the area towards the stroke unit, with the possibility for every eligible patient to have access to endovascular recanalization treatments.

Materials and method

We performed a multi-centered, hospital-based study, which included four major general public hospitals of the Attica region, for the period of one calendar year (1st January 2005 to 31st December 2005).

The main inclusion criteria, concerning the hospitals implemented in the study, were the burden of emergency events received in general duties and the existence of well-organized Neurology Departments for the hospitalization of patients. We aimed to acquire a reliable picture of the extent and the characteristics of acute stroke incidences that address the emergencies of the area.

The sample included all the patients that were referred to the emergency departments of the hospitals and eventually were hospitalized on an emergency basis, with the diagnosis of acute ischemic stroke. Patients with hemorrhagic stroke, intracranial hematoma, and stroke mimics were excluded from the study. Ischemic strokes with hemorrhagic transformation were included in the study.

The data of the emergency departments were registered in an electronic database and were cross-checked with the medical file and the imaging examinations for each patient at the end of each hospitalization.

Clinical evaluation Clinical presentation was assessed by a specialist neurologist and was expressed with National Institute of Health Stroke Scale; clinical outcome and disability were expressed in modified Rankin scale. Continuous variables were expressed in a quantitative fashion for statistical reasons, for example time of arrival was expressed in appropriate time intervals.

Imaging evaluation

CT imaging Admission computed tomography (CT) imaging was performed with 16-row multidetector CT scan. Non-enhanced CT was performed from skull base to the vertex, with gantry angulation along the supraorbital line, in caudocranial direction. Technical features: 120 kV–450 mA, with 1 s rotation time, collimation 1 mm. Reconstruction settings were of 3 mm, with a window setting of 40–80 HU for skull the base region and 40–65 HU for the rest of cerebrum. Enhanced CT scans were obtained with the same parameters, via an 18-gauge venous catheter, usually via a median cubital vein.

CT Angiography Technical features: 120 kV–200 mA, rotation time 0.5 s 0.6 mm collimation, 0° of gantry angulation, with caudocranial direction. The injection was realized with a bolus of high-concentration contrast medium via power injector at a rate of 4 ml/s and with the use of a bolus-tracking system. Reconstruction thickness was of 1 mm and MIP as well as volume rendering technique was used for post-processing.

MRI imaging MRI investigation was performed with 1.5-T MR system. The protocol included axial FLAIR, T2*, 3DTOF, T1+Gd sequences.

DS Angiography Exploration of internal carotid artery (ICA) and vertebral arteries in a mono-plane angiography suite, on 4 or 5 French introducing sheath and appropriate catheters (4 or 5 F Vertebral or 5 F Simmons-2 in cases of proximal tortuous vessels. Guiding wire 0.035inch hydrophilic Terumo)

US investigation Investigation of color Doppler ultrasonography of carotid and vertebral arteries was performed systematically during hospitalization.

Determination of site of occlusion The site of occlusion was systematically determined by computed tomography angiography (CTA) as well as by analyzing size and location of infarction on CT. In cases where CTA was not performed, site of occlusion was confirmed either by DSA or by MRI imaging, with T2* and 3D TOF imaging included in the protocol.

Classification of site of occlusion Since the design of the larger study, part of which is the present work, aimed at estimating the potential population eligible for endovascu-

lar recanalization therapies, the classification of site of occlusion was made with main criterion the potential eligibility of patients for intra-arterial thrombolysis or thrombectomy. The site of occlusion was determined with CT imaging, as mentioned above, and was categorized in one of the following groups, accordingly:

Involving large-caliber vessel ICA, carotid T, M1, M2, A1, A2, basilar artery, P1

Involving small-caliber vessel Medial and lateral perforators (from A1 and/or M1) thalamoperforators, AchA, distal branches of MCA, ACA or PCA or watershed areas.

The overall amount of information included 21 elements, from clinical presentation and initial imaging findings to history, social, educational and arrival information, clinical outcome, and length of hospitalization. For the evaluation of factors influencing early arrival, the following data were utilized:

Study population data

Baseline characteristics Age, sex

Social factors:

- Educational status: university, college, basic education, illiterate
- Conditions of life: living in couple, living alone, taken care of by children/relatives, taken care of by house assistant, lining in institution

Arrival factors:

- Time of arrival after onset of symptoms: 0–3, 3–6, >6< 24, >24 h, unknown
- Hour of arrival: hour of day (1st, 2nd, 3rd, 4th….24th hour)
- Means of transportation: ambulance, private vehicle

Clinical data

Vascular territory involved by stroke, clinical condition upon arrival (NIHSS) and at discharge (mRS)

Statistical analysis

The sample was divided in two sub-groups, according to their time of arrival from symptom onset. Patients who arrived at the hospital within the first 6 h since onset of their symptoms, and thus could potentially be eligible for thrombolytic therapy, intra-venous or intra-arterial, were categorized as Group A, and patients who arrived after the first 6 h since onset of their symptoms were included in Group B. The sample was statistically analyzed and parameters of the two groups were statistically compared with appropriate statistical tests (*t* test, Fisher's exact test, χ^2). The level of statistical significance was determined as $p<0.05$.

The nominal variables that were found to be statistically significant in the univariate analysis were treated with a multivariate logistic regression model, in order to estimate the association of early arrival (<6 h from symptom onset), which was expressed as dichotomous, with those variables.

Results

During one calendar year (2005), 907 patients fulfilled the eligibility criteria and were registered in the database. The sample population had a mean age of 61.64 (±14.7)years and the percentage of males versus females was 55.7% versus 44.3%, respectively (Table 1). Vascular territories that were affected included anterior circulation in 69.2%, posterior circulation in 29.2% and unknown in 1.6% of the sample.

In 45.6% of the cases, the incidence was a first-ever cerebral ischemic stroke, in 37.1% it was a recurrent stroke, in 17.0% at least one previous transient ischemic attack was reported and in 0.4% of the cases the patients had been previously hospitalized for neurological reason other than ischemic cerebral vascular event (χ^2, *df*: 3, $P<0.0001$). In 34.8%, the stroke was of cardioembolic origin. The mean NIHSS score at admission was 8.81 (±5.60; median: 8.00) and the mean mRS at discharge was 3.06 (±1.54; median: 3.00). The mean length of hospitalization was 15.99 (±9.43) days.

A percentage of 12.1% of the patients arrived at the hospital within the first 3 h since onset of their symptoms, 22.5% arrived between the third and the sixth hours (8.7% of the study population arrived from 3 to 4.5 h), 38.7% arrived after the sixth hour, but within the first 24 h (11.8% of the study population arrived from 6 to 8 h), 18.1% arrived after 24 h since onset and in 8.6% of the population the time of symptom onset was unknown. In total, 34.6% of the patients arrived within the first 6 h since the onset of their symptoms.

The population of the study was divided in two sub-groups, according to the time elapsed from the symptom onset until the arrival at the hospital (Table 2). Group A (0–6 h) consisted of 308 patients, with a mean age of 59.2 (±12.9)years and a male to female ratio of 54.2/45.8. Group B (>6 h) included 599 patients, with a mean age of 62.6 (±15.4)years and a male to female ratio of 56.4/43.6. Mean NIHSS score for the patients of group A was 8.36 (±4.79; median, 8.00) and for the patients of group B was 9.02

Table 1 Baseline clinical characteristics of the study population at the time of presentation of patients at the emergency departments of hospitals

	Baseline characteristics	Stat
Population (*N*)	907	
Sex (M/F) (%)	55.7/44.3	χ^2, *df*: 2, $P<0.0001$
Mean age (arithmetic; ±SD)	61,64 (±14.7)	Normal distribution (Kolmogorov–Smirnov test, $P=0,108$)
Territory (anterior/posterior/unknown: %) multiple territories-embolic stroke	69.2/29.2/1.6	χ^2, *df*: 2, $P<0.0001$
Large/small vessel infarct/unknown (%)	42.6/55.8/1.6	χ^2, *df*: 2, $P<0.0001$
First ever/recurrent/TIA/HOE	45.6/37.1/17.0/0.4	χ^2, *df*: 3, $P<0.0001$
Cardioembolic stroke (%)	34.18	
NIHSS at arrival: mean (±SD), median	8.81 (±5.60), 8.00	Kolmogorov–Smirnov test
	95% CI for the mean=8.2540 to 9.3739	($P<0.001$)
mRS at discharge: mean (±SD) median	3.06 (±1.54), 3.00	χ^2 test (796.81) *df*=19 ($P<0.001$)
	95% CI for the mean=2.8925 to 3.2221	
Deficit-arrival time (0–3/3–6/6–24/>24 h/unknown: %)	12.1/22.5/38.7/18.1/8.6	χ^2, *df*: 4, $P<0,0001$
3–4.5, 6–8 h (%)	8.7/11.8	
Length of hospitalization (mean days±SD)	15.99 (±9.43)	Kolmogorov–Smirnov test ($P<0.001$)

TIA pre-existence of transient ischemic attack, *HOE* hospitalization for other etiology; NIHSS National Institute of Health Stroke Scale; *mRS* modified Rankin Scale

(±6.02; median, 9.00). Mean mRS score at discharge from hospital was 2.85 (±1.28; median, 3.00) and 3.01 (±1.58; median, 3.00) for groups A and B, respectively.

For 48.8% of patients of group A and for 45.1% of group B, the incidence was a first-ever stroke; for 33.3% of patients of group A and for 38.3% of group B, the incidence was recurrent. For 16.7% of group A and for 16.5% of group B, a transient ischemic attack (TIA) preceded the incidence and for 2.0% of group A the incidence occurred during hospitalization for neurologic etiology other than ischemic stroke. The stroke involved the anterior circulation in 56.8% of group A and in 50.0% of group B and the posterior circulation in 39.7% and 47.7%, respectively. Embolic stroke was found in 35.38% of group A and in 33.55% of group B. A proximal occlusion was present in 49.4% of the patients of group A and in 33.7% of group B. In 49.9% of group A and in 64.0% of group B the incidence involved a small-caliber arterial occlusion and for 1.2% of patients in group A as opposed to 2.2% of group B the exact site of occlusion was unknown.

The means of transportation was ambulance in 79.1% of patients in group A and in 20.9% in group B, while 67.8% of group A and 32.2% of group B arrived by private vehicle. Among the patients of group A, 20.1% were university graduates, 50.3% had received higher education, and 29.5% were in basic educational level. As for group B, 11.9% of patients possessed a university diploma, 35.1% were in a higher educational level, and 53.1% of them were in basic educational level.

The conditions of living for group A included 63.3% of patients who lived with a spouse or mate, 13.3% who lived alone at home, while 18.1% were taken care of by children or other relatives, who lived in co-habitation with them. A percentage (4.2%) of patients of group A were living with a professional housekeeper or a person hired to take care of them at home and 1.2% lived in an institution such as a nursing home or house for elderly. As far as group B was concerned, these percentages, respectively, were 45.4% for living with mate, 25.4% for living all alone, 22.3% for living with relatives, 6.2% for living with a hired assistant and 0.8% for living in institution.

The two groups were statistically correlated and compared with appropriate statistical tests. No statistically significant difference was found between the two groups, as far as sex was concerned. The territory involved did not correlate with early arrival, consequently patients with infarcts of anterior and of posterior circulation arrived within the first 6 h at equal percentages. Recurrent stroke or previous transient ischemic attack did not statistically correlate with early arrival. The clinical condition at arrival was not statistically significant concerning the time of arrival, neither was the clinical outcome at discharge (Table 2).

Table 2 Statistical comparison of the sample divided in two sub-groups, according to the time elapsed from onset of symptoms until arrival at the hospital

	Group A: 0–6 h	Group B: >6 h	Stat
Population (N)	308	599	
Sex (M/F) (%)	54.2/45.8	56.4/43.6	χ^2, P=0.67
Mean age (arithmetic mean ±SD)	59.2 (±12.9)	62.6 (±15.4)	t test, P=0.0073
First ever/recurrent/TIA/HOE (%)	48.8/33.3/16.7/2.0	45.1/38.3/16.5/0.0	χ^2, P>0.05
Large/small vessel/unknown (%)	49.4*/49.9/1.2	33.7*/64.0/2.2	χ^2, *P=0.05, P>0.05 for rest
NIHSS at arrival: mean (±SD), median	8.36 (±4.79), 8.00	9.02 (±6.02), 9.00	t test, P=0.09
mRS at discharge: mean (±SD), median	2.85 (±1.28), 3.00	3.01 (±1.58), 3.00	t test, P=0.12
Territory: anterior/posterior/unknown	56.8/39.7/1.2	50/47.7/2.2	χ^2, P=0.06
Multiple territories-embolic (%)	35.38	33.55	
Social situation-way of life (living in couple/alone/care by children/house assistant/institution %)	63.3*/13.3**/18.1/4.2/1.2	45.4*/25.4**/22.3/6.2/0.8	χ^2. *P=0.004, **P=0.04
Educational status (basic/higher/university)	29.5/50.3/20.1	53.1/35.1/11.9	χ^2, P<0.005
Transportation (ambulance/private vehicle %)	79.1/20.9	67.8/32.2	χ^2, P=0.002

Group A corresponds to the patients who arrived within 6 h from symptom onset and group B to those that arrived after 6 h

TIA pre-existence of transient ischemic attack, *HOE* hospitalization for other etiology, *NIHSS* National Institute of Health Stroke Scale, *mRS* modified Rankin scale

Statistically significant correlation was found between younger age and early arrival at the hospital. Patients that were transported by ambulance arrived earlier than those who were transported by private vehicle and the difference was statistically significant (X^2, P=0.002). Statistically significant difference was found in favor of the patients who lived with a mate/husband (X^2, P=0,004), compared to those who lived alone (X^2, P=0.04), as far as early arrival at the hospital was concerned. On the contrary, no statistically significant difference could be ascertained, as far as early arrival was concerned, regarding the patients who had a house assistant taking care of them at home and those who lived in an institution. Finally, patients with higher and highest educational level arrived earlier at the hospital, in statistically significant manner, compared with the patients with basic educational level.

The multivariate analysis for the factors that were statistically significant (Table 3) revealed that patients who lived with a mate, patients with highest or higher educational level, patients who lived with relatives and patients who were transported by ambulance had higher probability of arriving at the hospital within 6 h from symptom onset. On the contrary, patients with only basic educational level, those who lived alone and those who arrived with a private vehicle were less probable to arrive within the first 6 h from symptom onset.

Discussion

This is the first multicenter study conducted in Greece to evaluate factors influencing time of arrival at the hospital, for patients with hyperacute ischemic stroke. We present our results with view to a strategic plan aiming to augment the number of patients eligible to thrombolysis.

To the best of our knowledge, this is the first study to evaluate conditions of living as factors influencing early arrival and the first to propose consulting advice concerning

Table 3 Multivariate analysis of arrival at hospital in <6 h from symptom onset

Variable	O.R.	95% CI	P
HIGHEST_EDUCATIONAL_LEVEL	2.8540	1.8452 to 4.4142	0.0000
HIGHER_EDUCATIONAL_LEVEL	2.3995	1.7195 to 3.3483	0.0000
LIVING_WITH_MATE	2.2996	1.6110 to 3.2824	0.0000
LIVING_WITH_FAMILY_MEMBER	1.7262	1.1022 to 2.7035	0.0171
TRANSPORTATION_BY_AMBULANCE	1.7553	1.2615 to 2.4424	0.0008
BASIC_EDUCATIONAL_LEVEL	0.3643	0.2692 to 0.4930	0.0000
LIVING_ALONE	0.4022	0.2721 to 0.5946	0.0000
TRANSPORT_BY_PR._VEHICLE	0.6915	0.4925 to 0.9709	0.0332

Sample size: 907, cases with Y= 0: 599(66.04%), cases with Y= 1: 308 (33.96%)

living and housing conditions to patients with high risk of stroke in the future. Our sample is adequately large (N=907) and one of the largest published until present, concerning socioeconomic factors.

Although at the time of the study design (2004) the cut-offs for thrombolysis were 3 and 6 h for IV or IA thrombolysis, we reviewed our database in order to include in our results the percentage of patients who arrived in the time intervals of 3 to 4.5 and 6 to 8 h from symptom onset, as according to more recent studies on intra-venous [5] and mechanical thrombus disruption [7], respectively. As new treatment options emerge, the time windows may vary slightly; for example, the very recent attempt to evaluate intra-arterial thrombolysis within the first 3 h from symptom onset [8], but still the landmarks of 3 and 6 h remain important and give us an overview of the situation in the area concerning times of arrival.

Our results concerning educational status indicate that patients with higher or highest educational level have higher probability to arrive within the first 6 h than those with only basic educational background. On the contrary, previous experience with recurrent strokes does not improve the probability of arriving early at the region. These two results indicate that a higher general level of knowledge promotes the awareness for early response to stroke in areas with lack of dedicated acute stroke management, which is not necessarily the case in regions with well-established stroke management circuits [9]. Bibliographically, it seems that these disparities tend to fade with an intense dissemination of information [10] to the general public.

Although no specific information campaign has ever been undertaken before in Greece regarding the importance of early arrival, the percentage of arrival within 6 h is already acceptable, compared to the percentages published in the international literature [11]. Although the percentage of arrival at 0–3 h from symptom onset was relatively low, the percentage of 3–6 h was high, compared to the ones published in the literature [12, 13].

In 37.1% of the patients, the stroke was recurrent. Although one would expect to have a higher rate of early arrival in these patients, due to previous experience, this is something that was not observed. It is possible that this observation is relevant to lack of adequate patient counseling, on behalf of the medical and paramedical staff, concerning the need for early arrival and the recognition of the potential symptoms of acute ischemic stroke.

In a recent study [14], the authors found much lower early arrival than presumed in patients with recurrent TIAs or small infarcts, which did not correlate with age, sex, social and educational status of the patients. In our study age, social and educational status correlated in a statistically significant manner with early arrival, but this was true only for acute ischemic strokes and not for TIAs.

Although borderline (p=0.05), no positive correlation was found between early arrival and large vessel infarct. In the present study, younger age was positively related to early arrival for the area of Attica, unlike in other regions, as published in current literature, where age and early arrival were not correlated [12, 14].

In another study published in the literature [9], educational level did not play a role in early arrival. In the present study, higher and highest educational level positively correlated with early arrival. We attribute these differences to the fact that the existence of a well-organized, dedicated call center in a country with years of acute stroke unit management, improves the time of arrival, while in countries with no such organization, as in Greece, younger age and high educational level compensate for the lack of public awareness and evenly distributed knowledge, concerning the symptoms and the need to respond promptly to an acute cerebrovascular event.

Although no bibliographic reference was found with focus on living conditions influencing early arrival, a recent study [15] exists, which is in accordance with ours, concerning the correlation between early arrival and patients that were surrounded by familiar persons at the time of the incidence. In our study, a higher probability of arrival within the first 6 h was found for patients who lived with a mate and, on the contrary, reduced probability was observed for those who lived in a house alone. Conditions of living that include co-habitants with strong relationships (mate, family) promote the probability of arrival at the hospital within 6 h from symptom onset.

Our results concerning early arrival with transportation by ambulance, via the emergency call center, compared to use of private vehicle, support the rest of the literature available on this matter [16, 17]. The establishment of a dedicated call center and ambulatory service for acute stroke services in the Attica region seems reasonable in the context of establishing a circuit between the participating hospitals and a new multidisciplinary acute stroke unit.

Overall, our results support the hypothesis that younger age, lifestyle, especially educational level and conditions of living, play an important role on early arrival at the hospital, as does the use of an ambulance for transportation. We could outline the characteristics of a patient most probable to arrive early at the hospital as an active person, with good social background, and alert in terms of acquiring knowledge.

An extensive public informative campaign, both via the media as well as delivered by the healthcare professionals, is needed to augment public awareness and sensitivity on the matter and to alert the population on the need for urgent, prompt, and appropriate response to acute stroke. Such a policy would also alleviate the inequalities among different social sub-groups.

Conclusions/summary

Factors that were found to influence early hospital arrival of acute ischemic stroke patients included younger age, higher/highest educational status, living with a mate, and transportation by ambulance. The time of arrival could be improved by the establishment of a dedicated call and transportation center, with an appropriate information campaign towards the population and the healthcare professionals, as well as encouragement of patients with recurrent strokes to live with a housemate.

In order to improve management of acute stroke, it is important to develop a nationwide campaign in order to inform the population on the symptoms of stroke and on the necessary actions, on their behalf, in order to arrive at the hospital on time and profit from an up-to-date treatment.

An organized trend to instruct patients in high risk of stroke to live with a housemate, as part of the precautions from stroke recurrence, seems advisable. An organized plan on behalf of the social security system, concerning persons that live alone, should be reinforced.

Conflict of interest We declare that we have no conflict of interest.

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