International Journal of Cardiology 215 (2016) 431–434

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Reducing time delays in the management of ischemic stroke patients in Northern Italy☆

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ARTICLE INFO

Article history:
Received 22 March 2016
Accepted 27 March 2016
Available online 8 April 2016

Keywords:
Avoidable delay
Stroke management
Thrombolysis

ABSTRACT

Background and purpose: Thrombolysis represents the best therapy for ischemic stroke but the main limitation of its administration is time. The avoidable delay is a concept reflecting the effectiveness of management pathway. For this reason, we projected a study concerning the detection of main delays with following introduction of corrective factors. In this paper we describe the results after these corrections.

Materials and methods: Consecutive patients admitted for ischemic stroke during a 3-months period to 35 hospitals of a macro-area of Northern Italy were enrolled. Each time of management was registered, identifying three main intervals: pre-hospital, in-hospital and total times. Previous corrective interventions were: 1.increasing of population awareness to use the Emergency Medical Service (EMS); 2.pre-notification of Emergency Department; 3.use of high urgency codes; 4.use of standardised operational algorithm. Statistical analysis was conducted using time-to-event analysis and Cox proportional hazard regression.

Results: 1084 patients were enrolled. EMS was alerted for 56.3% of subjects, mainly in females and severe strokes ($p < 0.001$). Thrombolytic treatment was performed in 4.7% of patients. Median pre-hospital and in-hospital times were 113 and 105 min, while total time was 240. High urgency codes at transport contributed to reduce pre-hospital and in-hospital time ($p < 0.05$). EMS use and high urgency codes promoted thrombolysis. Treatment within 4.5 hours from symptom onset was performed in 14% of patients more than the first phase of study.

Conclusions: The implementation of an organizational system based on EMS and concomitant high urgency codes use was effective to reduce avoidable delay and to increase thrombolysis.

1. Introduction

Stroke is a leading cause of mortality and the first cause of disability in adulthood [1]. For these reasons the main target of care in ischemic stroke is to reduce mortality and disability. In the last decades, scientific evidences have significantly contributed to change the cultural approach towards this disease and fundamental contribution came from the effectiveness of Stroke Units [2,3]. The best therapy now available in the acute phase of ischemic stroke is represented by the systemic thrombolysis, as reported in previous studies and registers [4–6]. Besides this therapeutic opportunity, the intra-arterial administration of thrombolytic drug is another possible procedure over 4.5 hours from symptom onset and up to 6 hours. Recent advances in acute treatment of ischemic stroke reported positive results in the use of mechanical thrombectomy in selected patients [7]. This therapeutical approach has been introduced in the last update international guidelines [8]. However, the main limitation of thrombolytic administration is the

☆ Drs Elio Agostoni and Simone Vidale had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Elio Agostoni.
Data collection, manuscript drafting and review: All Authors.
Analysis and interpretation of data: Elio Agostoni and Simone Vidale.
Obtained funding: Elio Agostoni.

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http://dx.doi.org/10.1016/j.ijcard.2016.03.232
0167-5273/

time. Indeed, few patients can receive the treatment because only 30% of all ischemic strokes arrive to the Hospital within 3 hours from symptom onset and only 25% of these patients meet the additional criteria to be treated. In our large geographical area, we projected a prospective study to improve the management of ischemic stroke patients in acute phase. In a previous paper we reported the temporal intervals in different phases of the stroke management [9]. In this paper we describe the delays after corrective interventions, coming from the previous survey.

2. Materials and methods

2.1. Study population

All patients admitted for stroke to the 35 hospitals of a large macroarea of Northern Italy, corresponding to 4 main Districts over a 3-months period were enrolled (during calendar year 2014). The study area covers a surface of about 6525 Km^2 and includes mountain territories (Sondrio), mostly hilly areas (Como, Lecco), and mostly plain areas (Varese and Milan). The entire area is populated by nearly 2.5 million inhabitants. In this analysis we considered only ischemic stroke patients. Study protocol with inclusion and exclusion criteria has been described in a previous paper [10].

2.2. Variables

For each patient a structured questionnaire was provided to the emergency medical services (EMS) and to the ED personnel to record age, gender, recruiting hospital, type of transportation to the hospital (private or by EMS), date and hour of symptom onset, time to EMS activation and arrival, transport code (Red, Yellow, Green), time to arrival to the ED, time to triage and assigned codes (Red, Yellow, Green), time of ED medical evaluation and to neurological consultation, time to CT scan and report, time to administration of appropriate therapy (rTPA, aspirin, heparin,…) and time to admission into the ward. Clinical data (stroke severity using NIHSS) and type of stroke (ischemic or haemorrhagic) were also recorded. We identified three main temporal intervals in the acute stroke pathway: pre-hospital (symptom onset-to-ED arrival) and in-hospital (ED arrival-to-treatment) phases and a total time (onset-to-needle time). Other than those times, we registered also temporal delays for imaging and neurological examination. The severity of stroke was classified in mild (NIH < 6), moderate (NIH: 6–11), severe (NIH: 12–19) and very severe (NIH > 19). Data about thrombolytic treatment were also collected.

2.3. Corrective interventions

The findings coming from the first phase of the study suggested three main limitations in acute stroke management: 1. low efficiency of the pre-hospital pathway, influenced by the interval between onset of symptoms-call to EMS; 2. a small access numbers to ED via EMS; 3. low efficiency of in-hospital course by a frequent inadequate assigned triage code. By these indications, corrective factors have been subsequently introduced in the second phase of the study: 1. need to call EMS achieved through cultural campaign of population; 2. pre-notification of ED of the receiving hospital by EMS; 3. grant assignment of specific disease code (stroke code) for the transport and at hospital triage; 4. continuous training of personnel concerning a new operational algorithm to stroke that considered time of symptom onset as main triage criteria.

2.4. Statistical analysis

Descriptive statistics were performed for subgroups defined by age, gender, mode of transportation and assigned codes. For continuous variables the analysis included median and interquartile range (IQR). The comparisons between the two study phases were calculated using the Student t test and analysis of variance (ANOVA) where appropriate. For categorical variables, the statistical significance was calculated using Pearson chi-square test. For all the above-mentioned variables, a univariate time-to-event analysis was performed, followed by a Cox proportional hazard regression, adjusted for age, clinical severity and gender. In order to determine the impact of corrective factors for the increase for thrombolytic procedures (outcome indicator), predictive value and estimation points with a concomitant range of 95% were also calculated, considering a probabilistic constant value. Statistical significance was set at the 5% level ($p < 0.05$). Statistical analysis was performed using SPSS 20 software.

2.5. Ethics

The study was approved by the Local Ethics Committee and by the hospitals' institutional review boards. Informed consent was released by patients or caregivers when appropriate. Data were treated in keeping with requirements of the Italian law concerning anonymity protection.

3. Results

A total of 1084 patients were recruited, excluding 170 cases with unknown onset time of symptoms (64% of them were awake strokes). Females were prevalent (63.2%) and the median of age was 78 (IQR: 69–84). The median of the NIH score was 7 (IQR: 3–13) and most of patients had a mild ischemic stroke (44%), while severe or very severe strokes were 19%. The EMS was alerted in more than half of subjects (56.3%). This service was activated more in female than male (58% vs 47%; $p < 0.001$) and in patients with more severe strokes (78% vs 37%; $p < 0.001$). We did not observe significant differences in the EMS use between ages or local geographical areas. Onset-to-needle time had a median value of 240 (160–390) minutes. Median times for pre-hospital and in-hospital pathway were 113 (IQR: 64–216) and 105 (63–179) minutes, respectively. In the pre-hospital time we observed a longer delay for the symptoms onset-to-EMS call (mean: 119 minutes; SD: 195). For the in-hospital pathway, the medical ED – neurologist evaluation delay was the longest lag-time (mean: 116 minutes; SD: 111). The differences between times and stroke severity depending on the EMS use are represented in Table 1. Yellow code was mostly applied (57%) in the transport to hospital and in 27% a high urgency code was used. This last contributed to a significant reduction both of the pre-hospital time ($p < 0.001$) and in-hospital time (p: 0.026). At the triage, a high urgency code was applied in 21% of the patients, while yellow code remained the most applied code (58%). Also in this setting, the high urgency code contributed to a significant reduction of the in-hospital time ($p < 0.001$). Thrombolytic treatment was performed in 51 patients (4.7%) and most of them were referred to hospital by EMS use (72%). The most frequent transport and triage codes in this subgroup of patients were yellows with 55.9% and 59.6%, respectively.

3.1. Comparison between the results of two phases

Age, gender, stroke severity and incidence were not significantly different in the two phases of the study. Considering temporal delays, the onset-to-needle time differed between the two phases with 60% of

Table 1
Breakdown times by EMS use.

	No EMS use	EMS use	p
Pre-hospital time	299 ± 403	157 ± 189	<0.001
Door-to-needle time	145 ± 137	139 ± 129	n.s.
Onset-to-needle time	419 ± 431	285 ± 211	<0.001
Door-to-imaging time	225 ± 346	161 ± 253	<0.001
Door-to-neurologist time	136 ± 184	103 ± 146	<0.001
NIHSS	6 ± 6	11 ± 7	<0.001