Relevance of Prehospital Stroke Code Activation for Acute Treatment Measures in Stroke Care: A Review

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Key Words

Acute management of stroke · Acute stroke therapy ·
Prehospital management of stroke · Stroke code ·
Prehospital delay

Abstract

Background: The use of emergency services with prehospital stroke assessment and early notification to the treatment hospital (stroke code) is a crucial determinant of delay time for acute stroke treatment. We reviewed and summarized the literature on prehospital stroke code system implementation. **Methods:** Two databases were explored (last update June 20, 2011) with 3 key words (stroke code, stroke prehospital management and stroke prehospital services). Inclusion criteria were: randomized and quasirandomized controlled trials, cohort and case-control studies, and hospital- and emergency-based registers, with no year or language restrictions. We examined the reference lists of all included articles. All potentially relevant reports and abstracts were

transcribed into a specifically designed data abstraction form. **Results:** Only 19 of the 680 studies which were initially retrieved, published from 1999 to 2011, fulfilled our inclusion criteria. One clinical trial was identified. Large differences in stroke code procedures and study designs within and across countries prohibited the pooling of the data. Most studies were carried out in urban areas. Assuming the rate of tissue-plasminogen activator treatment as the performance measure, most studies report a significant increase in the rate of treatment (increase between 3.2 and 16%) with only 1 study not reporting any increase. **Conclusions:** Despite its limitations, this review suggests that the use of prehospital stroke code is an important intervention to improve the accessibility of the benefits of thrombolysis, especially when implemented together with educational campaigns to optimize the awareness and behavior of patients and bystanders.

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¹ See Appendix.

Introduction

Rapid care for acute stroke patients not only increases eligibility for thrombolytic therapy, but also increases its benefits [1]. To minimize delays the American Stroke Association recommends rapid access to emergency services that use diagnostic algorithms to identify, triage and transport the patient with acute stroke to an appropriate center [2]. Once the medical assistance is solicited, the Emergency Medical Services (EMS) must react quickly in coordination with the assigned hospital center that has the resources to manage acute stroke patients. The adoption of a prehospital stroke code (SC) is reported to significantly reduce the time to treatment, in particular the EMS-dependent and in-hospital delays [3]. A comprehensive review of delay times in acute stroke care [4] indicates that the majority of delays in treatment continue to be attributable to prehospital delays. SC is a crucial element of a coordinated prehospital approach. Systematic reviews of prehospital SC have not yet been undertaken. We undertook this review with the aim of testing whether a prehospital SC can enhance time performance in stroke care. For the purpose of this review, we termed prehospital SC a written protocol for emergency services stroke recognition, transport of the patient to the proper center and hospital prenotification. Moreover, the rate of thrombolysis was chosen as the main parameter. We sought examples of where prehospital SC was implemented, how it had been evaluated and what factors assisted in its implementation.

Methods

We identified 3 key words related to the prehospital phase of stroke assistance (stroke code, prehospital management and prehospital services). Two databases, Embase and MEDLINE (MeSH terms), were explored from 1980 onwards (accessed June 20, 2011) with the following terms: ['Thrombolytic Therapy'(MeSH)] AND 'Stroke'(MeSH) AND 'Stroke Code'; ['Thrombolytic Therapy' (MeSH)] AND 'Stroke'(MeSH) AND 'prehospital management'; ['Thrombolytic Therapy'(MeSH)] AND 'Stroke'(MeSH) AND 'Prehospital Services'; 'Stroke Code'. Inclusion criteria were as follows: all randomized controlled trials (RCT), quasi-RCT, cohort and case-control studies, and hospital- and emergency-based registers, with no year or language restrictions. We examined the reference lists of all included articles for other relevant references. We included studies where prehospital SC procedures were administered in the field; studies were excluded if patients had been transferred from another hospital. The degree of comprehensiveness of the prehospital SC procedure was rated on a scale from 0 to 2, where 0 = not present, 1 = minimally present (e.g. lack of hospital prenotification) and 2 = present. A paper

Fig. 1. Selection process for the inclusion of published papers in the review search.

needed to score at least 1 to be included in this review. It must be acknowledged that SC is often implemented together with campaigns to educate the public regarding the signs and symptoms of stroke and the importance of calling for an ambulance, as well as with specific training of emergency department staff. Therefore, it is not possible to exclude the contribution of these other factors.

Preference was given to papers reporting some kind of evaluation data, while those that reported on a program, policy or services without data were classified as 'commentaries' and not included in the final review. Because of large variations across studies as to the reported components of prehospital delay (call to doctor, transport time, symptoms-to-needle time, etc.), we chose to extract and report here only the rates of t-PA administration, i.e. the proportion of ischemic stroke patients who received intravenous t-PA therapy. For intervention studies, pre- and postintervention data are reported in the review. The titles and abstracts of retrieved papers were independently screened for inclusion by two reviewers (M.B. and B.P.).

The papers included in the final review were examined for the presence of the following items according to a predetermined data abstraction form: definition of prehospital SC, key questions addressed, design and methods, degree of comprehensiveness of SC procedure, results and impacts.

Figure 1 shows the breakdown of the published references from retrieval to inclusion in the final review. Large differences in SC procedures and study designs within and across countries prohibited the pooling of the data.

Table 1. Sample, site, study design, degree of comprehensiveness (DOC), rate of t-PA treatment in reverse publication year order, 2011–1999

Reference	Site	Time period	Study design	Study sample	Results rate of t-PA	DOC
Patel et al. [19], 2011	North Carolina, USA 52 hospitals	24 months (2008–2009)	Hospital registers Retrospective	3,214 patients without prenotification vs. 4,380 patients with prenotification	Higher rates in those with prenotification, RR = 1.6 (95% CI, 1.4–2.0)	1
Geffner-Sclarsky et al. [5], 2011	Castellon province, Spain 1 hospital	12 months 2008 (SC activation) vs. previous 12 months	Hospital register Prospective Historical controls	265 strokes vs. 353 strokes (with SC activation)	Increase from 3.8 to 12.7%	2
Vilas et al. [6], 2010	Urban Barcelona, Spain	5 years	Emergency Service records of stroke patients Prospective	1,223 with SC activation	During weekend, prehospital times were similar with shorter door-to-needle delay (median 60 min weekday, 49 min weekends; $p < 0.001$); time from stroke onset to the first attention was longer when stroke onset was at night; ($p < 0.001$)	1
Verma et al. [14], 2010	Urban Toronto, Canada 3 stroke centers	February 2005–March 2007	Hospital registers Retrospective analysis of all the patients triaged as SC by the emergency services	726 with SC activation: 425 during online medical control vs. 301 offline	Rates similar between the 2 groups (34 vs. 33%)	2
Iguchi et al. [21], 2011	Kurashiki city, Japan 1 hospital	May 2005–November 2009	Hospital register Retrospective	256 patients with Kurashiki Prehospital Stroke Scale (KPSS) vs. 174 without	No significant difference between the 2 groups KPSS ≥ 4 51.7% t-PA KPSS < 4 13.9%	1
Reig et al. [8], 2010	Madrid, Spain All stroke centers	2 weeks in 2008 before introduction of other organizational strategies vs. 2 weeks in 2009	Hospital registers Retrospective	110 patients (2008) vs. 104 patients (2009)	Increase from 6.9 to 23.3% SC activations increased from 42.6 to 57.4% ($p = 0.027$)	2
De Luca et al. [23], 2009	Lazio region, Italy 6 EMS stations	6 months in 2005	Cluster RCT: intervention = training personnel to identify stroke symptoms and to refer patients to stroke unit Run sheets of 3 EMS stations (intervention group) vs. run sheets of 3 EMS stations (control group)	1,181 suspected strokes vs. 720 suspected strokes	18.2% in intervention group vs. 0% in control group	2
Gladstone et al. [15], 2009	Urban Toronto, Canada 1 stroke center	4 months before intervention (2004) vs. 4 months after intervention (2005)	Hospital register Retrospective analysis of stroke patients Top-down	217 vs. 290	Increased from 9.5 to 23.4%	2
Gomez-Angelats et al. [7], 2009	Urban Barcelona, Spain 1 hospital	October 2004–May 2005 vs. 12 months 2006 (SC activation)	Hospital register Retrospective	531 strokes without SC vs. 681 strokes with SC	No significant difference (5.6 vs. 6.7%, $p = 0.50$)	2
Chenkin et al. [16], 2009	Urban Toronto, Canada 1 stroke center	12 months before intervention (2004) vs. 4 months after intervention (2005)	Hospital register Retrospective analysis of stroke patients Top-down	325 acute strokes triaged by EMS	Increased from 5.9 to 10.1%	2
Quain et al. [17], 2008	Hunter region, Australia 1 hospital	6 months pre-SC vs. 6 months post-SC	Hospital register Prospective study and historical controls	205 pre-SC vs. 232 post-SC	Increased from 4.7 to 21.4%	2

Table 1 (continued)

Reference	Site	Time period	Study design	Study sample	Results rate of t-PA	DOC
Zarza et al. [9], 2008	Urban Madrid, Spain 1 university hospital	January 2004– December 2006	Hospital register Prospective	87 ischemic strokes t-PA treated	SC activation reduced door-to-needle time and door-to-CT time	1
Perez de la Ossa et al. [10], 2008	Urban Barcelona, Spain 1 hospital	November 2004– December 2006	Hospital register Prospective	262 ischemic strokes: 57 with SC activated by emergency services vs. 112 with SC activated by other hospital vs. 93 with SC activated by emergency department in hospital	Rate was higher (54%) in patients arriving via emergency service than those arriving on their own at emergency department (46%) or taken from other hospital (27%)	2
Abdullah et al. [20], 2008	Urban Boston, USA 1 hospital	15 months (March 2004–June 2005)	Retrospective analyses of ambulance databases and voices for stroke patients	44 with prenotification vs. 74 without	In the prenotification group the rate was twice that of the group without prenotification	1
Mosley et al. [18], 2007	Urban Melbourne, Australia	6 months 2004	Ambulance records of stroke patients Prospective open observational study Bottom-up	187 records	Stroke recognition and hospital prenotification were independent predictors of reduced prehospital and in-hospital delay	1
Lindsberg et al. [23], 2006	Urban Helsinki, Finland 1 hospital	1999–2005	Hospital register Retrospective	Around 1,000 stroke patients (1999) vs. 1,000 stroke patients (2005)	Increase from 17 to 183 patients (20%)	1
Belvis et al. [11], 2005	Urban Barcelona, Spain	April 2001–April 2002	Emergency service records of stroke patients Prospective	39 SC activated vs. 181 pre-SC	Rate in SC group 19% vs. 6.9% in non-SC group	2
Alvarez-Sabin et al. [12], 2003	Urban Barcelona, Spain 1 hospital	June 2000– December 2001	Hospital register Retrospective analysis categorized into three periods of 6 months each	48 ischemic strokes: 21 with SC vs. 27 pre- SC	In the SC group the rate increased from 30 to 57%	1
Alvarez-Sabin et al. [13], 1999	Urban Barcelona, Spain 1 hospital	10 months	Hospital register Retrospective analysis	108 ischemic stroke patients admitted <6 h from onset: 29 with SC vs. 79 without	44.8% (13 patients) in the SC group vs. 30.4% (24 patients) in non-SC group 50% reduction of pre- and in-hospital delay	1

Results

We found 19 studies published from 1999 to 2011 which contained data from prehospital SC regional experiences in Spain [5–13], Canada [14–16], Australia [17, 18], USA [19, 20], Japan [21], Italy [22] and Finland [23] (table 1).

Methods and Study Samples

Methodological issues and findings from each study are summarized in table 1. All studies were carried out from 1999 onwards, after the widespread implementation of t-PA treatments. Most of the studies assess the effec-

tiveness of a prehospital SC system compared to standard procedures on the delivery of patients with acute stroke to hospital care. A top-down approach, starting from treated/nontreated patients, with historical controls is the most frequent study design. Some studies [6, 10, 11, 18] employed a bottom-up design, starting from patients who sought medical attention for suspected stroke, but only 2 of them [11, 18] employed the EMS registers and not the hospital registers.

All studies were carried out in urban areas. Only 2 studies [5, 15] included in this review reported on the efficacy of educational campaigns to physicians, paramedics and the population concerning how to recognize

stroke and how to react. Both these studies reported the greatest increases in the rate of t-PA treatments. The only RCT was carried out in Rome, Italy, and compared stroke patient referrals by EMS and emergency room health professionals trained in a standardized clinical pathway with those of nontrained EMS and emergency room controls. It was possible to disentangle data from the EMS group. The EMS personnel in the intervention group were trained to identify stroke symptoms by using the Cincinnati Prehospital Stroke Scale [24] to register age and time of symptoms onset and to refer patients to the nearest stroke unit when appropriate. The EMS personnel in the control group did not receive any training and therefore managed suspected stroke patients as usual, without specific protocol and procedure.

There were no paper reports either on complications or deaths during transportation and referral.

Characteristics of prehospital SC procedures are summarized in table 2 and described in the following sections.

Screening Assessment

The prehospital stroke assessment instruments differ across studies. Some studies either do not employ or at least do not report to use any standardized screening instrument [5, 6, 10–13, 20, 23]. The Cincinnati Prehospital Stroke Scale [24] and modified versions, including the Ontario Prehospital Stroke Screening Protocol, were the most frequently used. Only 1 study [21] included a scale to estimate stroke severity under prehospital conditions soon after stroke occurrence had been suspected. This study reported no significant difference in t-PA rates between those who were evaluated for severity and those who were not. Nevertheless, among those evaluated, severity turned out to be an independent predictor of receiving t-PA treatment.

Time of onset is an essential component of prehospital stroke screening procedure and may determine triage and transport modality decisions. Every report in the present review includes a time limit criterion to activate the prehospital SC. That time limit is quite narrow (within 2 h from symptom onset) both in the Canadian [14–16] and in the Australian experience [17], the widest limit being within 6 h in other countries [6, 8–10, 12, 13, 20, 22].

Both the Canadian and the Australian experiences have introduced blood sugar levels as a further criterion aiming at excluding stroke mimics [14–17].

Moreover, most studies have adopted the prestroke disability level as an essential requirement to activate the prehospital SC [5–10, 14–17].

Communication with Receiving Hospitals

The early notification of an in-bound stroke patient has been included in all but one of the prehospital SC experiences [22]. Two papers are dedicated to evaluate the efficacy of prenotification by itself [19, 20], comparing the EMS arrivals of suspected stroke patients by whether the receiving hospital was prenotified or not. Both studies found that the rate of t-PA treatments was significantly higher in the prenotification group. Mosley et al. [18] found no significant difference in stroke care times between patient groups where stroke was not identified and where stroke was identified but not prenotified.

Rate of t-PA

All studies report a significant increase in the rate of t-PA treatments (increase between 3.2 and 16%), except for one [7]. In this paper, the prehospital SC group obtained a significant reduction of time, but t-PA could not be administered in many patients because they were too disabled. In the paper by Quain et al. [17], study investigators organized stroke education programs for paramedics and designed and implemented a prehospital protocol including an SC. Their protocol included the bypassing of nonstroke center hospitals and the transportation of patients directly to certified stroke centers. The administration rate of t-PA increased from 4.7 to 21.4%. In the cluster RCT [22], thrombolysis was performed only on patients referred by the EMS intervention subgroup and not on those referred by the EMS control group.

Discussion

A considerable amount of literature has been identified during the review process, but only 19 studies fulfilled our inclusion criteria. We think our search strategy was comprehensive.

Data on the use of prehospital SC consistently indicate the efficacy in terms of the increased rate of t-PA treatments. Data from most studies give some measures of efficiency of selected prehospital and hospital triage, but cannot indicate how the treatment is being delivered to the whole population, with the exception of 2 studies [8, 18] that evaluated all hospitals of well-defined geographical regions.

The paper by Quain et al. [17] shows how a well-organized and comprehensive stroke care system is highly effective. The study demonstrates that a closer hospital may be bypassed so that a stroke patient may be better evalu-

Table 2. Summary of the characteristics of the individual prehospital SC procedures

Reference	Prehospital stroke assessment	Time limits	Age limits	Blood sugar	Prestroke disability	Level of consciousness	Other exclusion criteria	Prenotification
Patel et al. [19], 2011	Not specified	No limits	≥18 years	No	No	No	No	Calling the hospital
Geffner-Scarsky, et al. [5], 2011	Focal neurological signs suggestive of acute stroke	≤3 h from onset	18–80 years	No	Modified Rankin ≤2	No	No	Not specified
Vilas et al. [6], 2010; Perez de la Ossa et al. [10], 2008	Focal neurological signs suggestive of acute stroke	<6 h from onset	<80 years	No	Modified Rankin ≤2	No	No	Calling the neurologist at the stroke center
Verma et al. [14], 2010; Gladstone et al. [15], 2009; Chenkin et al. [16], 2009	Ontario Prehospital Stroke Screening Protocol At least 1 of the following symptoms: unilateral arm/leg weakness or drift, slurred or inappropriate words or mute, facial drop	Within 2 h from onset	No limits	≤4 mmol/l	Terminally ill or palliative	Glasgow Coma Scale <10	Breathing or significant circulatory problem Seizure at onset Symptoms have resolved	Not specified
Iguchi et al. [21], 2011	Kurashiki Prehospital Stroke Scale (KPSS) It comprises 4 items: level of consciousness, consciousness disturbances, motor weakness, language The total score ranges from 0 to 13 (maximum severity)	Within 3 h from onset	No limits	No	No	Included in the KPSS	No	Calling the stroke neurologists at the hospital
Reig et al. [8], 2010; Zarza et al. [9], 2008	Any of the following: one-sided weakness or numbness of face, arm, or leg, language disturbances, sudden vision problem, intense headache, coordination, equilibrium, walking problems	Within 6 h from onset	No limits	No	Modified Rankin ≤2 Terminally ill and/or demented	Glasgow Coma Scale <9	Poor general clinical status with hemodynamic instability	Calling the hospital
De Luca et al. [22], 2009	Cincinnati Prehospital Stroke Scale	Within 6 h from onset	≤80 years	No	No	No	No	No
Gomez-Angelats et al. [7], 2009	Cincinnati Prehospital Stroke Scale	Within 3–4 h from onset	≤80 years	No	Modified Rankin ≤2 handicapped	No	Significant comorbidity	Calling the hospital
Quain et al. [17], 2008	Weakness of one arm and speech impairment	<2 h from onset	>18 years	4–17 mmol	Not previously wheelchair- or bed-bound	No	Symptoms improving	Calling the hospital
Abdullah et al. [20], 2008	Signs and symptoms suggestive of acute stroke	<6 h from onset	No limits	No	no	No	No	Calling the hospital
Mosley et al. [18], 2007	No specific instrument, only stroke recognition and triage by urgency level	No limits	>18 years	No	No	No	No	Calling the hospital
Lindsberg et al. [23], 2006	No specific instrument	<5 h from onset		No	No	No	No	Calling the hospital

Table 2 (continued)

Reference	Prehospital stroke assessment	Time limits	Age limits	Blood sugar	Prestroke disability	Level of consciousness	Other exclusion criteria	Prenotification
Belvis et al. [11], 2005	Signs and symptoms suggestive of acute stroke	<3 h from onset	>18 years	No	No	No	Stroke due to trauma, erythropoiesis stimulating agents, subdural hematoma, spinal cord vascular disease	Calling the neurologist at the hospital
Alvarez-Sabin et al. [12, 13], 2003, 1999	Signs and symptoms suggestive of acute stroke	<6 h from onset	No limits	No	No	No	No	Calling the neurologist at the stroke center

ated and treated at a stroke center, where the preexisting system facilitates the appropriate care of acute stroke patients. The investigators succeeded in integrating the involvement of the community, ambulance and hospital into the process of stroke care, with the prehospital SC being only a step in the comprehensive strategy to improve stroke outcomes. The increase in t-PA administration rate was among the highest, together with that reported by Gladstone et al. [15] in Toronto, Canada, where a television campaign accompanied the implementation of the prehospital SC. The finding of a better performance of prehospital SC when implemented together with an educational campaign was replicated also in a Spanish study [5]. In the Canadian experience reported by Verma et al. [14], online medical control of the prehospital SC was effective in reducing false-positive stroke patients, thus reducing the burden of care of stroke centers, but not in impacting the t-PA treatment rate.

The bottom-up approach of 2 studies [11, 18] must be underlined. In these studies, patients calling the emergency services with symptoms suggestive of stroke were followed up. The quality of these data is relevant and less likely to be biased than most of the other studies. In fact, a selection bias might have occurred in the studies carried out only on those patients who reached the hospital and received the proper medical attention. The efficacy of prehospital SC is estimated only on in-hospital patients, while information about patients who die during transportation is often lacking.

Because more severe strokes may have a shorter prehospital delay [25], a confounding effect by severity may have been introduced after t-PA treatment rates had been evaluated. Stroke severity was measured in only 1 study

[21] and turned out to be positively associated with higher rates of treatment.

Only 1 RCT was identified [22]; therefore, there is no definite evidence supporting the association between SC implementation and increased rates of t-PA. The design of randomized trials may not be suitable to address such a research question because of the ethical concern of randomizing very critical patients and the need for very large samples. In addition, studies are only from a limited number of geographical areas, therefore we must be cautious in generalizing results. The local context is a major source of heterogeneity, and local settings may differ in terms of regional health care management (both hospitals and emergency services), road networks, distances, traffic jams and population sociodemographic characteristics. Nevertheless, the prehospital SC procedure seems to work effectively in different areas, regardless of which stroke assessment instrument has been selected. The active interplay between the EMS and hospital staff, together with prenotification, may represent the strongest determinants of efficacy of any prehospital SC.

Implication for Practice

A fundamental principle of prehospital stroke management should be the empowerment of both the population and the EMS, with the knowledge necessary for stroke symptoms to be swiftly recognized and for actions to be taken, because only half of stroke patients use the EMS [4, 26]. Multifaceted programs are more likely to be successful in reducing delay to therapy, as reported by the PRACTISE study [27]. For instance, fast assessment and transportation by EMS staff may not influence the t-PA treatment if there is a substantial delay in CT scanning

[28]. A possible criticism of SC is that more patients with symptoms mimicking a stroke may overload the stroke unit personnel [22]. Increasing the number of treatment hospitals may be needed, but this is easily and effectively implemented. From 2006, the Catalan SC system, which was already operated by a few hospitals since the late 1990s [10, 11], was disseminated to cover the whole territory together with designation of new referral hospitals with no previous expertise in thrombolysis. The t-PA treatment proved safe and effective even among inexperienced hospitals [29]. The cost of setting up a prehospital SC protocol is reported to be minimal if the stroke team is already present in the hospitals [17].

Implication for Research

Further research is needed to identify cost-effective multifaceted strategies to improve acute stroke care, and should be able to evaluate the contribution of each component of the strategy. One strategy will not fit all sites because factors to be considered are the availability of human and operational resources across the continuum of acute stroke care.

In conclusion, prehospital SC positively affects both EMS-dependent and in-hospital delays. Its implementation is a necessary step required to improve stroke outcomes, has a pivotal role in integrating EMS activation and response within stroke systems of care, and could save lives and health care resources, especially when implemented together with educational campaigns to optimize the awareness and behavior of patients and bystanders.

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Appendix

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