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ORIGINAL COMMUNICATION

Intra-hospital delays in stroke patients treated with rt-PA: impact of preadmission notification

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Abstract Pre-hospital notification enhances thrombolysis rate and improves intra-hospital delays, but the impact of the notification to the neurologist by the emergency medical system (EMS) call centre remains unknown. Our objective was to compare pre-hospital and in-hospital delays in stroke patients treated by intravenous recombinant tissue plasminogen activator (rt-PA), with and without pre-hospital notification. We compared baseline characteristics and in-hospital delays in stroke patients treated by rt-PA with a high-level notification (call to EMS and EMS–neurologist discussion), a low-level notification (call to EMS without EMS–neurologist discussion) and no pre-hospital notification. Of 302 consecutive patients [165 women, 54.6 %; median age 74 years, interquartile range (IQR) 59–83], patients with high-level, low-level and no notification differed for the severity at admission (median National Institutes of Health Stroke Scale scores, respectively, of: 12, IQR 7–17; 9, IQR 6–15, and 8, IQR 6–14, $p = 0.029$). Patients with high-level notification had shorter (1) admission-to-completion of imaging times (27 min, IQR 14–35) than patients with low-level notification (35 min, IQR 17–54) or no notification (36 min, IQR 30–58) ($p < 0.01$); (2) door-to-needle times (49 min, IQR 39–62 vs. 57 min, IQR 39–81 vs. 63 min, IQR 51–97; $p = 0.003$); and (3) onset-to-needle times (140 min, IQR 110–175 vs. 155 min, IQR 106–230 vs. 182 min, IQR 131–234; $p < 0.001$). They did not differ for onset-to-admission time and imaging-to-needle time. Pre-hospital notification by the EMS reduces intra-hospital delays in patients eligible for rt-PA, but the benefit is higher in the case of discussion between the EMS and the neurologist before admission.

Keywords Thrombolysis · rt-PA · Stroke · Cerebral ischaemia · Emergency · Pre-hospital care · Notification · Stroke pathway

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Introduction

Intravenous (i.v.) recombinant tissue plasminogen activator (rt-PA), given within 4.5 h of symptom onset, decreases the proportion of ischaemic stroke patients with disability after 3 months [1–3], but this effect decreases rapidly over time [3–5]. Campaigns to increase public awareness have therefore been encouraged, together with educational programs for physicians and other health professionals involved in acute stroke care, and the use of telemedicine,

to reduce delays [6]. More patients are eligible for rt-PA when the relatives call, as recommended [7, 8], a centralised telephone number available for medical emergencies, such as number 15 in France (or 112 in all EU countries). The reason is a reduction in door-to-needle times, due to shorter delays between admission and neuroimaging [7, 9–11]. In a recent study, a preadmission notification procedure enhanced the thrombolysis rate, but the intra-hospital delays were not evaluated [12]. The influence of a notification to the neurologist by the emergency medical system (EMS) dispatcher remains, however, uncertain.

The aim of this study was to compare pre-hospital and in-hospital delays in stroke patients treated by i.v. rt-PA, between events with either: (1) a call to the emergency medical system (EMS) call centre plus notification of the neurologist, (2) a call to the EMS call centre without notification of the neurologist, or (3) no call to the EMS call centre.

Method

The study was retrospectively conducted with prospectively collected data between October 3rd 2008 and July 14th 2011, in patients admitted in the stroke unit of the Lille University Hospital. Patients with in-hospital strokes or referred from other hospitals were not eligible. The organisation of this stroke unit has been detailed elsewhere [13]. Patients were identified as possible candidates for thrombolytic therapy, either by emergency physicians working at Emergency Medical dispatcher Service ["*Service d'Aide Médicale Urgente*" (*SAMU*), also called "Centre 15"], or by physicians of the emergency department. In France, the EMS dispatching service is located in the hospital institution and an emergency physician is always on line. In the EMS dispatch centre, there are emergency physicians on line. They use both FAST and clinical assessment by phone, searching precious information such as time at onset of symptoms, delays, and possible contra-indications. We collected the information of pre-hospital notification by the registered data, and we interviewed the neurologist who did the thrombolysis to determine whether the EMS dispatching physician alerted the neurologist or not. When these kinds of information were not available, we interviewed the patient or the family to determine whether Centre 15 was called or not, and the EMS dispatching physician to understand the reason why there was no notification. We considered two levels of preadmission notification: (1) high-level, when Centre 15 was called and the neurologist was alerted by the physician of the EMS dispatching service; and (2) low-level, when Centre 15 was called, but the neurologist was not alerted by the physician of the EMS dispatching service. We prospectively recorded data on demographics, initial presentation, time of onset, and stroke characteristics. Baseline stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS) [1], and pre-stroke disability by the modified Rankin scale (mRS) [14].

We performed the statistical analysis with the SPSS 15.0 package for windows. We calculated median values, interquartile ranges (IQR), and percentages (%), and compared groups for categorical variables with the χ^2 test, and for continuous variables with the Mann–Withney *U* test or the Kruskal–Wallis *H* test. We compared baseline characteristics, and pre-hospital and in-hospital delays (onset-to-admission, admission-to-completion of imaging, imaging-to-needle, door-to-needle, and onset-to-needle times), between patients with high-level preadmission notification, low-level notification and no notification.

The stroke database was declared at the institutional data protection board. The study was considered observational and not interventional by the ethical committee of Lille.

Results

General features and main characteristics of the study population

The study population consisted of 302 patients (165 women, 54.6 %; median age 74 years, IQR 59–83; median NIHSS 11, IQR 6–16); 276 (91.4 %) had a pre-stroke mRS 0–2; 164 (54.3 %) underwent MRI as first line imaging technique; 28 patients (9.3 %) had either no lesion on a subsequent imaging or a lesion located outside the middle cerebral artery territory; the presumed cause of ischemia was athero-thrombotic in 43 (14.2 %), cardio-embolic in 118 (39.1 %), small-vessel occlusion in seven (2.3 %), other determined cause in five (1.7 %), unknown in 126 (41.7 %), and a stroke mimic in three (1.0 %); 169 (56.0 %) were treated during non-working hours.

Comparison of baseline characteristics according to the type of pre-hospital notification

The comparison of baseline characteristics found that patients with high-level, low-level and no notification differed for the severity of the clinical deficit at admission (median NIHSS scores respectively of 12, IQR 7–17; 9, IQR 6–15, and 8, IQR 6–14, $p = 0.029$), but did not significantly differ for gender, age, type of imaging (CT or MRI), hour of admission (working or nonworking hours), medical history, proportion of patients with pre-stroke mRS >2, presumed cause, territory of infarction, baseline blood pressure and serum glucose level. There was a tendency for

Table 1 Comparison of transportation modes according of the status of preadmission notification

	No notification ($n = 56$)	Any notification ($n = 246$)
Private ambulance	33 (58.9)	94 (38.2)
Fire brigade	17 (30.4)	90 (36.6)
Mobile ICU and helicopter	0 (0)	62 (25.2)
Private car	5 (8.9)	0 (0)
Unknown	1 (1.8)	0 (0)

ICU intensive care unit. Data are numbers (%). Overall p value < 0.001

a higher proportion of patients with history of myocardial infarction (11.8 % vs. 3.6 %, $p = 0.067$) in those with any type of pre-hospital notification (high-level plus low-level vs. no notification). The comparison of transportation mode between patients with and without preadmission notification is detailed in Table 1.

The reasons why relatives did not call the EMS dispatching service were not systematically searched for, but were mainly lack of knowledge about stroke being an emergency, or lack of identification of stroke. The reasons why the EMS dispatching physician did not call the neurologists could be classified in four major categories: (1) the most likely diagnosis was not a stroke in 11 patients; (2) strict interpretation of the criteria for thrombolysis (wake-up strokes, isolated aphasia, on-going oral anticoagulant therapy etc.) in 23 patients; (3) the EMS dispatching physician was involved with another emergency before calling, precluding a prompt call to the neurologist ($n = 2$) in two patients; (4) technical problem contacting the neurologist in two patients; and (5) unknown or unclear in 17 patients.

Comparison of delays according to the type of notification

The results are detailed in Table 2. The onset-to-admission time was reduced by 16 min when number 15 was called, but this reduction was not statistically significant and not influenced by a call to the neurologist. The admission-to-completion of imaging time was 9 min shorter in patients with a high level of notification, and 1 min shorter in patients with a low level of notification ($p < 0.001$). The imaging-to-needle time was not influenced by calling number 15. The door-to-needle time was reduced by 14 min in patients with a high-level notification and 6 min in patients with a low-level notification ($p = 0.003$). The onset-to-needle time was reduced by 42 min in patients with a high-level notification and by 27 min in patients with a low-level notification ($p < 0.001$).

Discussion

Our study has shown that a preadmission call to the EMS (Centre 15) reduces the door-to-needle time, mainly because of shorter delays in arriving at the hospital and completing brain imaging, but this benefit is much higher when the neurologist is notified by the EMS dispatching physician.

The limitations of our study are the small sample size, the monocenter design leading to a modest external validity, and the retrospective and observational design: each modality of notification (high-level, low-level, no notification) is potentially influenced by factors that may also influence delays, e.g. a call to EMS dispatching service is more likely in severe cases, and severe cases are more likely to be admitted earlier. We found shorter delays in patients who had a preadmission notification, but, as in all observational studies, this is not a proof of a causal relationship, because of the possibility of confounders. The strengths of our study are: (1) the baseline characteristics of the study population are similar to those reported in similar case series and registries (for age, gender, and NIHSS at baseline) [15, 16]; (2) the results are consistent with previous studies reporting shorter door-to-needle time and door-to-imaging times in case of preadmission notification [9]; (3) this is the first study that shows that the benefit of calling the EMS dispatching service is partly lost in the absence of discussion between the physician of the EMS dispatching service and the neurologist. Strbian et al. [17]

Table 2 Comparison of delays according of the status of preadmission notification

	Preadmission notification			
	No ($n = 56$)	Low-level ($n = 55$)	High-level ($n = 191$)	p values
Onset-to-admission time	97 (49–144)	81 (64–150)	81 (61–120)	0.628
Admission-to-imaging time	36 (30–58)	35 (17–54)	27 (14–35)	<0.001
Imaging-to-needle time	23 (16–35)	21 (15–29)	24 (17–33)	0.341
Door-to-needle time	63 (51–97)	57 (39–81)	49 (39–62)	0.003
Onset-to-needle time	182 (131–234)	155 (106–230)	140 (110–175)	<0.001

Values are delays in minutes (median values and interquartile range). See text for definitions of high-level and low-level notifications

suggested that a preadmission notification to the neurologist and the emergency room nurse was one of the main factors to decrease the onset to treatment time, but they did not provide quantified data and did not evaluate intra-hospital delays.

Mikulik et al. [18] recently discussed the impact of the perception of urgency by the physician in the intra-hospital delays. Therefore, the ability to reduce the delay in the decision to initiate thrombolysis and the insight of emergency may influence the reduction of physician-dependent intra-hospital delays.

Interventions aiming at increasing calls to Centre 15 need to stress the urgency of stroke symptoms. Once EMS dispatching physicians have identified a possible stroke, the prompt notification of the neurologist may allow both the radiology department and the stroke unit to be prepared and mobilise urgently resources before the patient arrives. This suggests areas for improvement in the organisation of stroke pathways, by reducing in-hospital delays.

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Conflicts of interest Barbara Casolla, Eric Wiel and Patrick Goldstein: none. Marie Bodenant and Jean-Pierre Pruvo are investigators of DIAS 3 (Lundbeck) and Thrace (French Ministry of Health). Charlotte Cordonnier, Marie Girot, and Didier Leys were investigators of ECASS 3 (Boehringer-Ingelheim), and are investigators of DIAS 3 (Lundbeck) and Thrace (French Ministry of Health).

Ethical standard All human studies must state that they have been approved by the approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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