



# In-hospital delays to stroke thrombolysis: Out of hours versus regular hours and reduction in treatment times through the creation of a 24/7 mobile thrombolysis team

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## ABSTRACT

**Background:** The main aim of this study was to evaluate the impact of the implementation of a mobile thrombolysis team (MTT) on time to thrombolysis treatment depending on patient admission time: regular hours (RH) or out of hours (OH).

**Methods:** 504 consecutive patients treated with IV tPA or with combined IV tPA and mechanical thrombectomy for acute ischemic stroke were retrospectively included between 1st January 2013 and 31st December 2017. Three sub-periods were identified: 2013–2014, 2015–2016, and 2017 during which patients were treated with the usual care (UC), by the MTT or with UC according to their time of admission, or by the MTT, in the three time periods respectively. We compared in-hospital delays according to patient admission time.

**Results:** In 2013–2014, 133 patients were included. Both median door-to-needle (DTN) and imaging to needle (ITN) times were shorter for patients admitted during RH than OH, respectively 75 min versus 85 min and 52 min versus 57 min ( $P < 0.05$ ), and the proportion of patients with DTN  $\leq 60$  min was 23% versus 9% ( $P < 0.05$ ), respectively. In 2015–2016, 223 patients were included. DTN and ITN times were shorter for patients admitted during RH and treated by the MTT than during OH with UC, respectively 54 min versus 78 min and 24 min versus 47 min ( $P < 0.001$ ), and the proportion of patients with DTN  $\leq 60$  min was 64% versus 21% ( $P < 0.001$ ), respectively. In 2017, there was no difference concerning in-hospital delays regardless of patient admission time ( $P > 0.05$ ).

**Discussion:** DTN time was significantly longer for patients admitted OH. We suggest that the implementation of an around-the-clock MTT would allow a reduction of in-hospital delays and similar times to thrombolysis treatment regardless of admission time.

## 1. Background

Intravenous (IV) thrombolysis with application of recombinant tissue plasminogen activator (tPA) is an approved treatment for acute ischemic stroke [1–3]. Nevertheless, the benefits of reperfusion are highly time-dependent with no average benefit beyond 4.5 h after symptom onset [4–6]. In-hospital delays to stroke thrombolysis represented by door-to-needle time (DTN) are the cornerstone of stroke management in the acute phase. Indeed, the delay of tPA administration is a strong determinant of clinical outcome after three months as well as one year later [4–6]. These findings have allowed the emergence of guidelines by the American Heart Association (AHA) /American

Stroke Association (ASA) which recommend starting tPA treatment within 60 min of the patient's admission to the emergency unit [1]. Despite this recommendation, fewer than 30% of patients treated with intravenous tPA receive this therapy within this timeline [7,8]. Consequently, it is essential to identify factors associated with delayed DTN in order to reduce time delays and to improve patients' clinical course.

Previous studies have demonstrated the existence of a paradoxical effect between early admission to hospital (within 3 h of symptom onset) and delayed treatment by tPA, regardless of patient admission time [9]. The impact of hospital admission time on in-hospital delays and their influence on clinical outcome have been reported with controversial results. Indeed, in some studies, neither patient admission

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during nursing shift changes, or on weekends delayed thrombolytic administration. Conversely, patient admission at night resulted in longer time to intra-arterial thrombolysis but not to IV thrombolysis [10]. However, other recent studies showed longer DTN time in patients treated during night hours and on weekends [11]. Numerous measures are known to be effective to reduce in-hospital delays such as implementation of a national quality improvement initiative (especially using specific protocols and tools) [12–15] or a mobile thrombolysis team (MTT) [16].

The main aim of this study was to evaluate the impact of the implementation of a MTT on time to thrombolysis treatment depending on patient admission time: regular hours (RH) or out of hours (OH).

## 2. Methods

This study was conducted at Rouen University Hospital between 1st January 2013 and 31st December 2017. Consecutive patients treated with IV tPA or with combined IV tPA and mechanical thrombectomy for acute ischemic stroke were retrospectively identified and included in the study. In all cases, IV tPA administration was carried out within the expanded tPA treatment window of an onset-to-treatment (OTT) time < 4.5 h, in accordance with recommendations [4–6].

Within the overall 5-year study period, three sub-periods were identified:

the 2013–2014 period, the 2015–2016 period, and the 2017 period during which patients were treated with the usual care (UC), either by the MTT or with UC according to their time of admission, or by the MTT, in the three time periods respectively.

When patients had combined IV tPA and mechanical thrombectomy, we evaluated delays until IV thrombolysis and not until arterial recanalization.

Patients were excluded from the study if they had not received tPA, if only mechanical thrombectomy had been performed or if thrombolytic therapy had been performed by telemedicine.

We compared in-hospital delays between the three time periods and compliance with AHA/ASA guidelines according to time of admission defined as RH or OH. RH were Monday to Friday from 8 am to 6 pm and OH were Monday to Friday from 6 pm to 8 am or weekends.

### 2.1. Procedures and periods

#### 2.1.1. 2013–2014 period

During the 2013–2014 period, all patients had UC and were managed by the emergency team and the vascular neurologist. IV tPA was administered exclusively in the stroke unit. These patients formed two groups: the RH group and the OH group.

#### 2.1.2. 2015–2016 period

During the 2015–2016 period, patients were treated either by the MTT or with UC according to their time of admission.

**2.1.2.1. Mobile thrombolysis team.** Patients admitted during RH were treated by the in-hospital MTT, which is composed of a specialized nurse working in the stroke unit and a vascular neurologist. The nurse and the vascular neurologist are both informed of the admission of a patient presenting stroke symptoms in the expanded tPA treatment window. As soon as the patient arrives in the emergency unit, the nurse performs an evaluation, including measuring blood pressure, pulse, temperature, capillary glycemia and a prethrombolysis blood test (complete blood count and coagulation profile). The nurse also sets up a cardiac monitoring system, an IV access and takes the patient to the radiology department. tPA is administered as soon as possible in cooperation with the vascular neurologist, regardless of the location of the patient (most of the time, in the radiology department, immediately after brain imaging). These patients formed the RH-MTT group.

**2.1.2.2. Usual care.** Patients admitted OH had UC and were managed by the emergency team and the vascular neurologist. tPA was administered exclusively in the stroke unit. These patients formed the OH-UC group.

#### 2.1.3. 2017 period

During the 2017 period, all patients were treated by the MTT regardless of their time of admission. These patients formed two groups: the RH group and the OH group.

#### 2.1.4. Imaging examinations

In most cases, brain imaging was a multimodal cerebral tomography (CT) (including non contrast CT, CT perfusion and CT angiography). More rarely, cerebral MRI (including diffusion-weighted imaging, fluid-attenuated inversion recovery, and time-of-flight MR angiography sequences) was performed.

### 2.2. Data collection

Data were collected on patient characteristics: demographics and clinical severity at admission which was assessed in the emergency unit using the National Institute of Health Stroke Scale (NIHSS) score (ranging from 0 to 42, with higher scores indicating more severe stroke).

Radiological data were collected on the type of cerebral infarct, lacunar or not, and the presence or absence of visible arterial occlusion on initial imaging.

Data were collected on time management: i) pre-hospital delays, i.e. the onset-to-admission (OTA) time defined as the time period between stroke onset and patient admission to the emergency unit; and ii) in-hospital delays, including door-to-needle (DTN) time, door-to-imaging (DTI) time and imaging-to-needle (ITN) time. The number of patients who had DTN ≤ 60 min was also recorded.

### 2.3. Statistical analysis

Statistical analysis was performed with NCSS software, version 6.0. The different scores were expressed as median values (data in parentheses are interquartile range (IQR 25th–75th)) or in absolute value (data in parentheses are the percentages). Mann and Whitney test was used to compare median differences for continuous variables and Fischer's exact test for categorical variables.  $P < 0.05$  was considered statistically significant.

## 3. Results

Overall, 504 patients were treated with IV tPA or combined IV tPA and mechanical thrombectomy for acute ischemic stroke between January 1st, 2013 and December 31st, 2017 and were included in our study.

### 3.1. 2013–2014 period

133 patients were treated with tPA for acute ischemic stroke (IS). The demographics, clinical features and radiological characteristics of the two groups (RH and OH) are summarized in [Table 1](#).

There was no statistically significant difference between the two groups with respect to age, median NIHSS score, median OTA time, stroke subtype and the proportion of arterial occlusions on initial imaging ( $P > 0.05$ ). There was a slightly larger proportion of men in the OH group than in the RH group (69%,  $P < 0.05$ ).

Delays related to time management are shown in [Table 1](#). Median DTN and ITN times were significantly shorter in the RH group than in the OH group, 75 min (IQR 63–90 min) versus 85 min (IQR 70–111 min) ( $P < 0.05$ ) and 52 min (IQR 44–63 min) versus 57 min (IQR 49–73 min) ( $P < 0.05$ ), respectively. There was no statistically

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