

## Trends in stroke thrombolysis rate in Bosnia and Herzegovina: a hospital-based observation study

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### ABSTRACT

**Aim** To assess trends in thrombolysis rates and door-to-needle times in University Hospital Mostar.

**Methods** Data from the University Hospital Mostar Registry were used. Information on the number of ischaemic stroke patients, intravenous thrombolysis rates and „door-to-needle times“ (DNT) were collected between January 2013 and December 2021.

**Results** Out of the total of 3100 ischaemic stroke patients, alteplase was given to 130 patients giving a thrombolysis rate of 4.2%. The mean hospital thrombolysis rate increased from 2.4% in 2013 to 10.6% in 2021.

**Conclusion** Although the hospital thrombolysis rate more than quadrupled, there is still a low proportion of acute ischaemic stroke patients who received intravenous thrombolysis therapy. Education and interventions indicating the importance of recognition and treatment of acute ischemic stroke are necessary for all physicians.

**Key words:** alteplase, developing country, door-to-needle times, ischaemic stroke

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## INTRODUCTION

Intravenous thrombolytic therapy (IVT) after ischaemic stroke significantly improves functional outcomes, reduces mortality and it has been the first-line treatment worldwide since 1996 (1). Despite the revolutionary development of the treatment, stroke remains the second leading cause of death and the third leading cause of disability worldwide (2,3). During the last three decades, the burden of stroke increased substantially, with the bulk of the global stroke burden residing in low-income and middle-income countries (LMICs) (3,4). Also, a greater increase in stroke incidence, mortality and disability has been proven in LMICs comparing to high-income countries (HICs). However, stroke occurs about 15 years earlier among individuals in LMICs than in HICs (5). Additionally, quality of stroke care in developing countries is generally poor (6). Low stroke thrombolysis rates persist for years and in-hospital treatments they are delayed (7).

In Bosnia and Herzegovina (B&H) there are no studies relating to thrombolysis rate for stroke.

The aim of this study was to assess trends in thrombolysis rates and door-to-needle times, and whether there have been improvements in treatment rates and therapy delays over years.

This study should be of great significance to help further improvement of stroke care in developing countries.

## PATIENTS AND METHODS

### Patients and study design

This cross-sectional study included all patients admitted to University Hospital Mostar, B&H, with a diagnosis of acute ischemic stroke between January 2013 and December 2021. Acute ischemic stroke is defined by the International Classification of Diseases (8).

### Methods

Data for the analysis were used from the University Hospital Mostar Registry. Information on the number of ischaemic stroke patients, numbers of acute ischemic stroke (AIS) patients treated with recombinant tissue plasminogen activator (rt-PA) and „door-to-needle times“ (DNT) were collected. The rate of IVT was defined as the number of

AIS patients receiving IVT divided by the number of all patients with a diagnosis of AIS.

### Statistical analysis

The Kolmogorov-Smirnov test was used to assess the data normality of continuous variables. Categorical variables are presented as numbers and percentages. Mann-Whitney tests and chi-squared tests were performed for continuous variables and categorical variables, respectively. Statistical significance was set at  $p < 0.05$ .

## RESULTS

From January 2013 to December 2021, 3743 patients with a diagnosis of stroke were admitted to the University Hospital Mostar. Of these, there were 3100 (83%) ischemic strokes. Intravenous thrombolytic therapy was administered to 130 (4.2%) patients of all ischemic stroke (IS) patients.

The proportion of patients treated with thrombolysis substantially increased over time from 0.76% in 2015 to 10.6% in 2021 ( $p < 0.05$ ) (Figure 1).

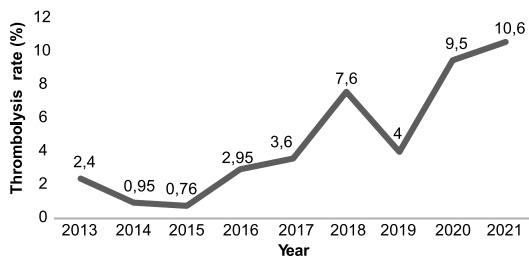


Figure 1. Thrombolysis rate during the period 2013–2021

Data on DNT were provided for all patients who received thrombolytic therapy. The initial median DNT in 2016 was 113 minutes and the final in 2021 was 81 minutes (Figure 2) ( $p < 0.05$ ). DNT  $< 20$ ,  $< 45$ , and  $< 60$  minutes were achieved in 0%, 4%, and 8.5% patients, respectively.

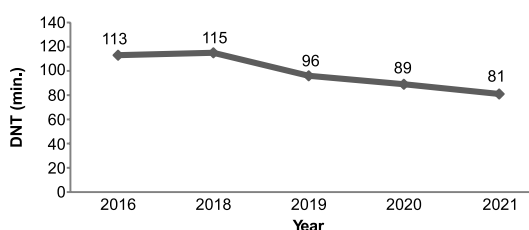


Figure 2. Door-to-needle time (DNT) during the period 2016–2021

## DISCUSSION

We have managed to achieve a thrombolysis rate of almost 11% and demonstrated a significant

increase in thrombolytic rates over the period of 9 years. To our knowledge, this is the first study that shows the thrombolysis rate for stroke in B&H. Thrombolysis rate in other studies varied from 3.8% to 24.4%. The highest thrombolysis rate was reported in the Czech Republic (23.5%), Austria (16.8%), and The Netherlands (21.7%), while the thrombolysis rate in developing countries remains low (below 4%) (9-13). However, the majority of these studies were population-based (unlike ours), which enabled comparison with our hospital-based study. Nevertheless, we showed significant improvement in thrombolytic treatment over years, and it is reasonable to expect that we will reach the thrombolytic rate of over 15% before 2030 as defined by the Stroke Action Plan for Europe (14).

Although we managed to achieve a reduction in DNT over 5 years, our results are significantly below the target set in 2018 by the American Heart Association stating that 50% of patients should achieve DNT in less than 45 minutes (15). Long DNT in our study is probably a reflection of the poor intrahospital organization and lack of prenotification system and urgent stroke protocols for patients who are candidates for reperfusion therapy. These findings are not unusual for developing countries where stroke strategies lack in general (7).

Recent studies from the Czech Republic (8) and The Netherlands (15) showed that it was possible to dramatically decrease DNT after the implementation of evidence-based guidelines in routine medical practice. These studies demonstrated

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that thrombolytic treatment can be initiated for the majority of patients within 20 or 25 minutes in the Czech Republic and The Netherlands respectively, and in this way, they established a new benchmark for DNT (9,16).

According to the Global Burden of Disease B&H belongs to the regions with the highest estimated lifetime risk of stroke, 1 of 3 people older than 25 will have stroke during their life (17). If the current trends continue, by 2050 we can expect 200 million stroke survivors and over 30 million new strokes each year, much of this burden will probably remain in developing countries if we do not take necessary actions.

The improvement in the management of stroke after the implementation of evidence-based guidelines in routine medical practice has significantly lowered the burden of stroke in HICs (18).

In conclusion, we emphasize the need for the development of national stroke strategies in Bosnia and Herzegovina, which would include, among other things, the implementation of a pre-notification system and in-hospital urgent stroke protocols for patients who are candidates for reperfusion therapy. Also, efforts should be made to raise public awareness of stroke and in this way improve stroke recognition.

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## TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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