

## Outcomes of Nonagenarians with Acute Ischemic Stroke Treated with Intravenous Thrombolytics

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*Background:* Nonagenarians are under-represented in thrombolytic trials for acute ischemic stroke (AIS). The effectiveness of intravenous thrombolytics in nonagenarians in terms of safety and outcome is not well established. *Materials and Methods:* We used a multinational registry to identify patients aged 90 years or older with good baseline functional status who presented with AIS. Differences in outcomes—disability level at 90 days, frequency of symptomatic intracerebral hemorrhage (sICH), and mortality—between patients who did and did not receive thrombolytics were assessed using multivariable logistic regression, adjusted for prespecified prognostic factors. Coarsened exact matching (CEM) was utilized before evaluating outcome by balancing both groups in the sensitivity analysis. *Results:* We identified 227 previously independent nonagenarians with AIS; 122 received intravenous thrombolytics and 105 did not. In the unmatched cohort, ordinal analysis showed

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a significant treatment effect (adjusted common odds ratio [OR]: .61, 95% confidence interval [CI]: .39-.96). There was an absolute difference of 8.1% in the rate of excellent outcome in favor of thrombolysis (17.4% versus 9.3%; adjusted ratio: .30, 95% CI: .12-.77). Rates of sICH and in-hospital mortality were not different. Similarly, in the matched cohort, CEM analysis showed a shift in the primary outcome distribution in favor of thrombolysis (adjusted common OR: .45, 95% CI: .26-.76). **Conclusions:** Nonagenarians treated with thrombolytics showed lower stroke-related disability at 90 days than those not treated, without significant difference in sICH and in-hospital mortality rates. These observations cannot exclude a residual confounding effect, but provide evidence that thrombolytics should not be withheld from nonagenarians because of age alone. **Key Words:** Acute stroke treatment—acute stroke—nonagenarian—thrombolysis—elderly.

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## Introduction

The world's population is aging and the number of older people is increasing. The oldest-old are the fastest-growing segment of the global population.<sup>1</sup> In 2011, nonagenarians comprised 4.7% of Americans over the age of 65, compared with 2.8% in 1980.<sup>2</sup> By 2050, this figure is likely to reach 10%.<sup>2</sup> This demographic shift is expected to increase the public health burden of stroke. Currently, about 8%-11% of acute ischemic stroke (AIS) cases occur in people aged 90 years or older.<sup>3,4</sup> Compared with younger patients, those of advanced age have worse outcomes after AIS, regardless of treatment with intravenous recombinant tissue-type plasminogen activator (rtPA).<sup>5-7</sup> The current guidelines do not specify a maximum age limit for thrombolytic treatment of AIS within the 3-hour window. Some neurologists, however, are reluctant to treat the very old with intravenous rtPA possibly due to the presumed higher risk of thrombolytic-associated symptomatic intracerebral hemorrhage (sICH) or due to existing baseline disability.<sup>8,9</sup> Small case series have shown that nonagenarians do not have higher rates of sICH and have similar benefits with rtPA, compared with their younger counterparts.<sup>4,10-14</sup> However, the efficacy and safety of intravenous rtPA in nonagenarians remain inadequately understood due to their underrepresentation in thrombolytic trials and the small sample sizes of previous studies.<sup>5-18</sup> Further, it is unclear whether the findings from randomized controlled trials for this age group would translate into clinical practice.

The objective of the present study was to characterize clinical outcomes and neurological treatment complications of nonagenarians with AIS treated with intravenous rtPA within 4.5 hours from symptom onset in the Intravenous Thrombolysis in Acute Stroke in Patients 90 Years and Older (ITAS-90+) collaborative.

## Materials and Methods

### *The ITAS-90+ Collaborative*

The ITAS-90+ collaborative was designed as a quality improvement data repository focused on the very elderly

with AIS and based on the voluntary contribution of participating centers ([Supplemental Table S1](#)). Center participation in this data repository was based on previous collaborations between group members, in addition to integration of international centers with high experience in the treatment of the oldest-old patients with AIS (identified via literature search). Twenty-one centers were identified as suitable; after formal contacts, 14 centers decided to participate, 4 centers declined invitation, and 3 centers did not respond. The Neurological Service of San Camillo de' Lellis General Hospital (Rieti, Italy) served as the data management and analysis center. All participating centers received institutional review board approval to participate in the present study.

### *Study Cohort*

The present analysis of the ITAS-90+ registry includes patient data from 8 centers across Europe (n = 4), North America (n = 3), and South America (n = 1), with patients treated between January 1, 2007, and December 31, 2015. The definition for AIS was based on the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease project.<sup>19</sup> All patients aged 90 years or older who were hospitalized for AIS were included irrespective of the time frame within which they presented. We excluded from the analysis patients with AIS with onset after hospital admission, patients with medical conditions that were expected to shorten life expectancy to 1 year or less, patients with moderate to severe baseline disability (modified Rankin Scale [mRS] score of >2) before presentation, patients presenting in critical condition (such as respiratory failure, pulmonary edema, acute congestive heart failure, severe myocardial infarction, aortic dissection, and pulmonary embolism), and those with mild (National Institutes of Health Stroke Scale [NIHSS] score of <4) or rapidly improving symptoms. Patients with a confirmed diagnosis of stroke mimic were also excluded.

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