Time to Presentation Is Associated with Clinical Outcome in Hemispheric Stroke Patients Deemed Ineligible for Recanalization Therapy

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Background: Delayed thrombolysis adversely impacts functional outcome after stroke. Therefore, great efforts are undertaken to reduce delay in patient presentation and initiate treatment as quickly as possible. However, little is known regarding the impact of time to presentation (TTP) on outcome in patients who are ineligible for acute stroke therapy. Thus, we sought to determine whether the TTP is associated with the 90-day outcome irrespective of eligibility for acute recanalization therapy. *Methods:* We retrospectively analyzed 258 consecutive acute ischemic stroke patients evaluated between January 2013 and February 2014. Multivariable logistic regression was used to determine whether a greater TTP is independently associated with a poor 90-day outcome defined as a modified Rankin scale (mRS) score of 3-6. *Results:* In the unadjusted analyses, the TTP was inversely correlated with transfer from an acute facility ($r = –.126$, $P = .043$), cardioembolic stroke etiology ($r = –.146$, $P = .019$), and acute recanalization therapy ($r = .–412$, $P < .001$). Conversely, a longer TTP was correlated with a worse 90-day mRS score ($r = .127$, $P = .045$). After adjustment, the TTP ($P = .019$), age ($P < .001$), female sex ($P = .001$), National Institutes of Health Stroke Scale score ($P < .001$), preadmission mRS score ($P = .001$), atrial fibrillation ($P < .001$), and infarct volume ($P < .001$) were independently associated with a poor 90-day outcome. Importantly, a longer TTP (odds ratio 1.016, 95% confidence interval 1.001-1.032, $P = .036$) remained independently associated with the 90-day outcome when we restricted the analyses to patients ineligible for acute intravenous and endovascular recanalization therapies. *Conclusions:* Each hour delay in the TTP decreased chances for good outcome by approximately 2% independent of patient eligibility for acute recanalization therapies. **Key Words:** Cerebral infarction—modified Rankin scale—time to presentation—tPA—endovascular intervention.

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Received April 17, 2016; revision received May 17, 2016; accepted May 24, 2016.

Grant support: Dr. Henninger is supported by K08NS091499 from the National Institute of Neurological Disorders and Stroke of the National Institutes of Health.

Authors' contributions: Yunis Mayasi: data acquisition, interpretation of data, and drafting of the article; Johanna Helenius: data acquisition and critical revision of the manuscript for important intellectual content; Richard P. Goddeau, Jr.: critical revision of the manuscript for important intellectual content; Majaz Moonis: critical revision of the manuscript for important intellectual content; Nils Henninger: study concept and design, data acquisition, statistical analysis, interpretation of data, and drafting of the article.

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.05.036

Introduction

Ischemic stroke remains one of the leading causes of morbidity and mortality worldwide[1]; 1 in 6 individuals is predicted to suffer a stroke in their lifetime.[2] The advent of intravenous (i.v.) thrombolysis with recombinant tissue-type plasminogen activator (rtPA), as well as recent breakthroughs in endovascular stroke therapy (EST), has revolutionized acute stroke care.[3-6] Nevertheless, a major prevailing issue relates to the fact that only a minority of patients are eligible to receive these treatments.[7,8]

The causes for this are multifold, but delayed presentation of patients represents the main reason why patients are ineligible for emergent i.v. thrombolysis or EST. Furthermore, later initiation of thrombolytic therapy is associated with reduced treatment efficacy.[5] Accordingly, substantial efforts have been made to improve patient presentation early to the hospital as well as to decrease in-hospital delays of patient evaluation to increase patient eligibility for acute intervention and overall increased chance for a good outcome.[4-6,9]

However, there is a paucity of data whether the time to presentation (TTP) relates to poststroke outcome irrespective of acute therapy; to our knowledge, only a single study has investigated this issue more than 2 decades ago.[10] Thus, we sought to determine whether a longer TTP in patients deemed ineligible for i.v. thrombolysis or EST is associated with the 90-day functional status after stroke in a contemporary stroke patient cohort. We hypothesized that a longer TTP is an independent risk factor for a poor 90-day outcome irrespective of patient eligibility for acute therapy.

Materials and Methods

Study Cohort

We retrospectively analyzed patients prospectively included in our local stroke registry between January 2013 and February 2014. The investigation was approved by our Institutional Review Board and a Health Insurance Portability and Accountability Act waiver of consent was granted. We adhere to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[11]

We included patients presenting to a university-affiliated emergency department with an acute hemispheric ischemic stroke. We only included patients with available brain magnetic resonance imaging (MRI) to allow for reliable quantification of the infarct volume. Furthermore, we excluded patients with an infratentorial infarct location from the present analyses because of their frequent delay to presentation[12] as well as the fact that outcome predicting variables differ from supratentorial strokes.[13-15] Included patients have been described as part of previously published studies.[16,17] All patients were evaluated by stroke-trained physicians. Patient demographics, laboratory data, comorbidities, preadmission medications, and stroke etiology (using the Trial of Org 10172 in Acute Stroke Treatment classification[16-18]), after completion of the diagnostic evaluation, were collected from all patients. In addition, we collected information on whether patients presented from home, acute, or chronic care facilities. The National Institutes of Health Stroke Scale (NIHSS) score at presentation was determined by certified members of the stroke team. All patients were treated in accordance to the American Heart Association secondary stroke prevention guidelines, which includes early implementation of statin and antithrombotic therapy as appropriate.[19]

We defined the TTP as the time from documented symptom onset or the time from last known well to the time of presentation in the emergency department. The preadmission and 90-day modified Rankin Scale (mRS) score was assessed by a certified stroke-trained physician or a stroke study nurse in a face-to-face interview or by a structured phone interview.[16,20] The 90-day outcome was dichotomized to good (mRS score of 0-2) versus poor (mRS score of 3-6).

Definition of Acute Treatment Eligibility

Ineligibility for treatment with i.v. rtPA was determined according to current guidelines.[21] Patient eligibility for EST at our institution is in general accord with the inclusion criteria of the recent positive endovascular stroke trials.[3,22,23] In brief, patients were considered for EST if they presented within 8 hours of symptom onset, had a documented large arterial occlusion (distal internal carotid artery, middle cerebral artery [M1/M2], or anterior cerebral artery [A1/A2]) and a small ischemic core as determined by either a diffusion-weighted imaging lesion less than 100 mL or an Alberta Stroke Program Early CT score higher than 6 on admission head computed tomography, and had no other documented absolute contraindication for treatment, including hypersensitivity to nickel-titanium, stenosis and/or previous stenting proximal to the thrombus, and evidence of dissection in addition to patient refusal.[3,22,23]

Risk Factor Definitions

We determined the presence of hypertension (use of antihypertensive medications, or systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg on 2 separate occasions after the first several days of hospitalization[19]), hypercholesterolemia (use of lipid-lowering agents, or fasting blood total cholesterol level of ≥200 mg/dL or low-density lipoprotein cholesterol level of ≥130 mg/dL), and diabetes mellitus (defined according to the National Diabetes Data Group and World Health Organization[24]). Cardiac studies included transthoracic echocardiography or transesophageal echocardiography, electrocardiography, in-house continuous event monitoring, and 30-day event monitoring in patients with suspected paroxysmal atrial fibrillation.