Clinical Deterioration and Early Imaging Changes after Intravenous Tissue Plasminogen Activator Administration in Acute Ischemic Stroke Patients

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Background and Purpose: Clinical worsening is a known complication following acute ischemic stroke. This study attempted to determine the mechanism of deterioration by correlating clinical findings with changes on computed tomography or magnetic resonance. *Methods:* From a single university medical center, 30 consecutive acute ischemic stroke patients who received intravenous tissue plasminogen activator within 3 hours of symptom onset during a 3-year period were identified from a quality database that included all hospitalized patients either admitted with strokes or with in-hospital strokes. Images were reviewed by a single neuroradiologist for changes including edema, extension of infarct, hemorrhage, herniation, and midline shift and were correlated to National Institutes of Health Stroke Scale (NIHSS) scores obtained from data in the medical chart. *Results:* Ten patients had documented clinical deterioration with a corresponding increase in the NIHSS score. Of these, 4 patients had follow-up scans that showed worsening changes concurrent with deterioration. In the 20 patients who remained clinically stable, 3 patients had worsening changes on follow-up scans. Patients who deteriorated were no more likely to have imaging changes than those who had a stable clinical course. Appearance of herniation, both subfalcine and uncal, was the only specific imaging change associated with clinical deterioration. *Conclusions:* This study demonstrates that processes besides hemorrhage, including edema, midline shift, herniation, extension of infarct, and new infarct, are neither frequent nor specific for predicting clinical course. Other factors associated with these processes that may or may not be quantifiable on imaging are likely involved. Furthermore, in over half of the cases of worsening, deterioration occurs without associated imaging, metabolic, or infectious etiologies. **Key Words:** Acute ischemic stroke—computerized tomography—neurological deterioration—magnetic resonance imaging.

Introduction

Clinical worsening following ischemic stroke has been reported to occur in 10%-43% of patients, depending on the measure and time from the onset of symptoms.[1] In intravenous tissue plasminogen activator (IV-tPA)-treated patients, clinical worsening has been reported to occur in 12%-30% within 24 hours and in 3%-20% from 7 to 10 days, and has been associated with inability to achieve or sustain vessel patency, baseline computed tomography (CT) findings, and baseline clinical and laboratory parameters.[2-4]

While hemorrhagic conversion is an emphasized mechanism for deterioration in IV-tPA-treated patients, rates

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of both early and late deterioration are similar in tPA- and non–tPA-treated populations and are associated with hemorrhagic conversion, cerebral edema, infarct extension, or systemic factors.[2,3]

The purpose of the present study is to describe the incidence and timing of deterioration in patients receiving IV-tPA and to determine mechanisms of worsening by correlating the clinical course to findings on follow-up CT or magnetic resonance imaging (MRI).

Methods

Consecutive acute ischemic stroke patients treated with IV-tPA at the Ohio State University Wexner Medical Center within 3 hours of symptom onset between January 1, 2006, and December 31, 2009, were obtained from a quality database that included all hospitalized patients either admitted with strokes or with in-hospital strokes. Patients who were treated with IV-tPA at an outside hospital and then transferred to Ohio State University Wexner Medical Center, patients who received interventional treatment, and patients who had a diagnosis other than stroke were not included. The present study was approved by the Ohio State University Institutional Review Board.

Charts were reviewed for demographics, admission National Institutes of Health Stroke Scale (NIHSS) score, and discharge modified Rankin Scale (mRS) score. Stroke etiology was defined using Trial of Org 10172 in Acute Stroke Treatment criteria.[5] For most patients, the NIHSS and mRS scores were recorded in the chart. Where they were not, admission NIHSS scores were determined by reviewing the admission exam and discharge mRS scores by examining progress notes and physical therapy and occupational therapy notes prior to discharge. Good outcomes were defined as a discharge mRS score of 2 or lower. Instances of secondary deterioration were first identified by reviewing resident progress notes for mentions of deterioration or worsening. NIHSS scores in alertness, motor, or language subsets for these patients were determined and compared to scores from admission or the previous day. Resident progress notes were used because they consistently included both subjective and objective evaluations. These NIHSS subsets were selected because changes in these parameters are more likely than others to influence functional outcome and are readily scored based on the exam recorded in the progress notes. Only patients with changes in these subscale scores were considered to have deteriorated, because otherwise subjective reports of worsening could not be quantified. Progress notes were also reviewed to determine if metabolic or infectious processes were present in association with clinical worsening. CT scans and magnetic resonance (MR) images read by a single neuroradiologist (E.B.) were used to characterize imaging changes including edema or mass effect, appearance of new infarct, extension of existing infarct, midline shift, herniation, hemorrhage, and location of infarct, either cortical or subcortical. The timing of follow-up scans was recorded, specifically in relation to whether or not imaging changes were seen in association with clinical deterioration. For the initial follow-up imaging after treatment, the appearance of an infarct corresponding to the clinical presentation was not classified as a new infarct. If such a scan had no other changes, it was classified in the "no change" category. If other changes were identified along with the infarct, these changes were classified accordingly. New infarcts or extension of infarct were only recorded in follow-up scans after an acute infarct associated with the clinical presentation was observed. In patients with multiple follow-up studies, "no change" was defined as either no change or improvement in findings from the prior study. Six patients who did not deteriorate during their hospital courses had MRI instead of CT as the only follow-up study. Rather than excluding these patients, 20% of the total study population, they were included in the analysis while recognizing that the sensitivity to detect changes may be different for CT and MR. Student's *t*-test, Wilcoxon test, or Fisher's exact test was used in comparing variables in statistical analysis.

Results

During the study period, 30 patients met eligibility criteria. One patient was treated for 2 separate strokes. The second occurred 5 months after the first, at which time the patient had improved to the point of independent living but had not returned to work. The admission NIHSS score for the second stroke was 11 and the discharge mRS score was 4. Analysis did not include the second stroke, although this patient did not experience clinical worsening during that hospitalization.

Thirteen patients (43%) were noted to have deteriorated according to the progress notes. However, only 10 of these patients had a corresponding increase in the NIHSS subscore. The 3 patients with documented clinical deterioration without increase in the NIHSS score had changes in the level of alertness. Two of the three were later diagnosed with urinary tract infections. All three were included in the nondeterioration group for analysis.

Demographic characteristics of the patient population are outlined in Table 1. None of the 10 patients who deteriorated had infections or metabolic abnormalities associated with worsening. Deterioration in 8 of the 10 patients (80%) occurred within 24 hours of IV-tPA treatment. Another patient worsened within 48 hours. For the final patient, worsening occurred twice, at 5 and 13 days. The mean time to worsening was 3.1 days in patients with changes in alertness with or without motor changes and 1 day in patients with only motor changes. Cortical infarcts were seen in all 5 patients with changes in only alertness, 2 patients with worsening alertness and motor signs, and 1 of the 3 patients with only motor changes.