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Clinical Study

Is vascular imaging valuable prior to administration of intravenous tissue plasminogen activator?

Roni Eichel [a], Jose E. Cohen [b], John M. Gomori [c], Tamir Ben-Hur [a], Galina Keigler [a], Ronen R. Leker [a,*]

[a] Department of Neurology, Hadassah-Hebrew University Medical Center, P.O. Box 12000, Jerusalem 91120, Israel
[b] Department of Neurosurgery, Hadassah-Hebrew University Medical Center, Jerusalem, Israel
[c] Department of Radiology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

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ABSTRACT

Our goals were to explore whether performing computerized tomography angiography (CTA) prior to administration of tissue plasminogen activator (tPA) delays treatment and impacts outcome in patients with proximal middle cerebral artery occlusions (pMCAO). Patients with pMCAO with a National Institutes of Health Stroke scale (NIHSS) score >10 were identified from a prospective Stroke Registry. Patients underwent multi-parametric imaging studies whenever possible. Patients who underwent CTA were compared to those who only had non-contrast CT scan. Disability was measured with the modified Rankin Scale. Logistic regression was used to determine outcome modifiers. We included 73 patients (median age 73 years, 52% men) with moderate-severe stroke (median admission NIHSS 14). Of those, 44 underwent CTA and 29 did not. There were no differences between the groups in risk factor profile or baseline characteristics including stroke severity and door to needle, door to imaging or imaging to treatment times. At 90 days post-stroke there were no statistically significant differences in outcomes between the groups. On multivariate analysis, performing CTA had no impact on the chance of obtaining favorable outcome. In conclusion, CTA does not have a major impact on outcome in patients with pMCAO treated with tPA. Therefore, performing CTA should be considered on an individual basis prior to administration of tPA.

1. Introduction

Systemic thrombolysis with tissue plasminogen activator (tPA) is the gold standard of acute ischemic stroke therapy but is limited by a narrow time window [1–3]. Because many patients arrive at the Emergency Department later than 4.5 hours from stroke onset, only a fraction of stroke patients are eligible for this treatment [4]. Early target vessel recanalization with tPA in patients with proximal middle cerebral artery occlusion (pMCAO) is associated with better outcome [5] but can only be achieved in 13 to 30% of treated patients. Advanced neurovascular imaging with computerized tomography angiography (CTA) or magnetic resonance angiography is often used in patients with acute stroke to demonstrate lesion site and detailed anatomy of the cerebral vasculature as well as to assess prognosis [6–11]. However, image acquisition, processing and assessment may take a long time and delay treatment [12] and thus may reduce the chance of a favorable outcome. Therefore, our goal was to evaluate whether the use of such tests impacts outcome in patients treated with tPA.

2. Methods

We prospectively recruited consecutive patients presenting with large hemispheric stroke into our Stroke Registry and the data were retrospectively analyzed. The Institutional Review Board (Hadassah Medical Organization) authorized anonymous inclusion of patients into the consecutive database without informed consent (approval # HMO-09-0277). In the current analysis we included patients with large middle cerebral artery (MCA) infarcts treated with tPA during the period of 2005–2011.

All patients with suspected stroke underwent triage in the Emergency Department by a triage nurse and were seen exclusively by the on call neurologist. All patients with pMCAO presenting within the first 4.5 hours from symptom onset were treated with systemic tPA unless they had contraindications to treatment such as international normalized ratio (INR) over 1.7. tPA was administered in the Emergency Department or in the Stroke Unit and all patients were admitted to the Stroke Unit for the first few

* Corresponding author. Tel.: +972 2 677 6192; fax: +972 2 643 7782.
E-mail address: leker@hadassah.org.il (R.R. Leker).

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days of admission and until they were deemed to be neurologically stable. Only patients presenting later than 3–4.5 hours from symptom onset were considered for endovascular therapy. This is because tPA is considered to be the standard of care only for all patients with stroke presenting within 3–4.5 hours from stroke onset. The diagnosis of pMCAO was established according to clinical findings that included hemiparesis/hemiplegia, sensory symptoms and evidence for cortical involvement such as aphasia, neglect or gaze deviation in various combinations with an National Institutes of Health Stroke Scale (NIHSS) score of $\geqslant$10 [13]. All patients who received tPA had a baseline non-contrast CT scan to rule out hemorrhage. CTA is available at our center on a 24 hours a day, 7 days a week basis and was obtained unless patients had contraindications to contrast injections (such as known allergy to contrast or renal failure) or it was felt that data would not be available prior to 3–4.5 hours from symptom onset due to a very narrow window. CTA was specifically obtained to verify the presence of vessel occlusion and to pinpoint the exact location of the occlusion in order to help in accurate prognostication. Patients with tandem lesions involving the internal carotid artery as well as the proximal MCA were excluded and only patients with pure MCA occlusion on CTA were included. All studies were obtained on a Philips Brilliance/iCT 64/256 slice scanners (acquisition time 5 minutes; Philips Healthcare, Andover, MA, USA) and raw data were immediately available on the workstation and on the picture archiving and communication system (PACS) within an additional 5–10 minutes for remote access.

We used the Alberta Stroke Program Early CT Score (ASPECTS) on baseline non-contrast CT scans in all patients and dichotomized the score as >7 or $\leqslant$7 [14,15].

Exclusion criteria included evidence of large hemispheric infarction on admission, defined as hypodensity on CT scan covering more than one-third of the MCA territory, INR >1.7 and existing disease with limited life expectancy (for example terminal cancer). Patients with small vessel disease were excluded as were those presenting in deep coma and those with primary intracerebral or subarachnoid hemorrhage. Patients who were treated with bridging strategy in which the endovascular procedure followed intravenous tPA were not included in this analysis.

We studied demographics and cerebrovascular risk profile, and time from Emergency Department presentation to initiation of tPA. Infarct etiology was classified according to the Trial of Org 10172 in Acute Stroke (TOAST) criteria as cardioembolic, large artery atherothrombotic, other classified (for example dissection) or unclassified.

Patients had a follow up non-contrast CT scan at 24 hours from treatment to assess bleeding. The presence of symptomatic intracranial hemorrhage was determined according to the definitions used in the European Cooperative Acute Stroke Study III (ECASS III) [3] (that is, any intracranial hemorrhage leading to death or to a $\geqslant$4 point deterioration on the NIHSS).

All patients were admitted to the Intensive Care Unit for at least 24 hours post-infusion. Neurological deficits were monitored with the NIHSS and functional deficits before admission and at 90 days post-infarct were evaluated with the modified Rankin Scale (mRS). Favorable outcome was defined as a mRS score $\leqslant$2.

Statistical evaluations were performed with the Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA) version 18. Data were compared using Student's *t*-test for continuous variables or chi-squared tests for categorical variables. For assessment of shift analysis in the mRS we used the Mann–Whitney U test. Multivariate logistic regression analysis controlling for age and NIHSS at presentation (both as continuous variables), presence of symptomatic intracerebral hemorrhage and imaging modality (non-contrast CT scan *versus* neurovascular imaging) was used to determine factors association with outcome. Data are presented as mean ± standard deviation.

3. Results

The study included 73 patients with pMCAO who were treated with intravenous tPA (median NIHSS 14, median age 73 years, 52% men). Baseline characteristics of the patients are presented in Table 1. There were no significant differences between patients who were evaluated with CTA prior to tPA administration and those who only received plain non-contrast CT scan for risk factor profile or presumed stroke etiology according to TOAST criteria.

Analysis of ASPECTS scores on the admission CT scan showed that there were no statistically significant differences between the groups in the percentage of patients with large lesions already seen on CT scan (5% *versus* 7%).

Treatment related variables are presented in Table 2. Time from Emergency Department presentation to imaging (door to CT scan 27.6 ± 14.1 *versus* 36.0 ± 21.7 minutes for patients who had neurovascular imaging *versus* controls; $p = 0.12$), time from imaging to treatment (CT scan to needle 45.4 ± 21.8 *versus* 46.3 ± 28.7 minutes for patients who had neurovascular imaging *versus* controls; $p = 0.91$) and time from hospital presentation to treatment (door to needle, 76.7 ± 23.6 *versus* 70.1 ± 33.9 minutes for patients who had neurovascular imaging *versus* controls; $p = 0.46$) were similar. Time from symptom onset to treatment was also similar (133.7 ± 39.2 *versus* 130.5 ± 47.7 $p = 0.82$). Any intracranial hemorrhage and symptomatic intracranial hemorrhage rates were comparable in both groups (11% *versus* 10% and 9% *versus* 3%, for patients who had neurovascular imaging *versus* controls respectively) and did not differ statistically.

Table 1
Univariate analysis of stroke patient data according to treatment

Variable/group	With neurovascular imaging (n = 44)	Without neurovascular imaging (n = 29)	*p* value
Age	69.8 ± 15.2 (73)	74.2 ± 11.1 (75)	0.19
Sex (male %)	21 (48)	17 (58)	0.51
Hypertension	34 (77)	23 (79)	0.80
Ischemic heart disease	11 (25)	13 (45)	0.13
Atrial fibrillation	18 (41)	12 (41)	1
Diabetes mellitus	9 (20)	10 (34)	0.29
Hyperlipidemia	21 (48)	20 (69)	0.12
Smoking	17 (39)	8 (28)	0.47
Stroke etiology			0.48
Cardioembolic	30 (68)	16 (55)	
Large vessel	5 (11)	3 (10)	
Small vessel	0	0	
Other	4 (9)	2 (7)	
Unknown	5 (11)	8 (28)	
ASPECTS score			1
>7	42 (95)	27 (93)	
$\leqslant$7	2 (5)	2 (7)	
Admission NIHSS	14.7 ± 4.8 (14)	14.3. ± 4.0 (13)	0.71
Discharge NIHSS	6.9 ± 5.1 (6.5)	9.2 ± 5.0 (8)	0.06
ΔNIHSS	7.1 ± 4.5 (6.5)	5.0 ± 4.9 (4)	0.06
Hospital length of stay, days	11.1 ± 7.1 (11)	15.8 ± 9.6 (13)	0.02
Modified Rankin Score day 90			0.7
0–2	18 (41)	10 (34)	
3	13 (30)	7 (24)	
4–5	8 (18)	6 (21)	
6	5 (11)	6 (21)	

Data are presented as number (%) or mean ± standard deviation (median) unless otherwise stated.
ASPECTS = Alberta Stroke Program Early CT Score, NIHSS = National Institutes of Health Stroke Scale, ΔNIHSS – the difference between admission and discharge NIHSS score, SD = standard deviation.