Sequential MR Imaging of Early Reperfusion in acute ischemic stroke patients

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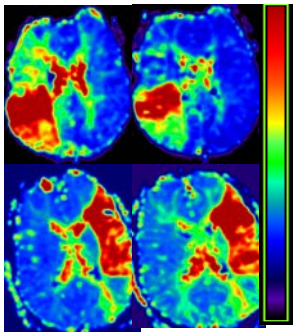
Introduction

tPA is a proven therapy for acute stroke patients which aims to dissolve blood clots and restore blood flow to ischemic areas, to minimize permanent neurological dysfunction. While many studies have reported results on the clinical outcomes of tPA, little is known about the extent to which early reperfusion may occur and the factors influencing early reperfusion in stroke patients receiving intravenous tPA. In addition, prior studies have utilized recanalization of major vessels (TCD, DSA or MRA) as a marker of reperfusion which does not represent the true perfusion status of brain tissue. In this study, we performed sequential MR perfusion imaging to examine the temporal characteristics of reperfusion status in relation to baseline clinical variables, including the onset-to-tPA treatment time and NIHSS.

Method

Ten acute ischemic stroke patients were prospectively studied with two sequential MR scans. The time intervals between stroke symptom onset and imaging were 160±41 and 377±14 minutes for the first (tp1) and second (tp2) scans, respectively. Eight patients received intravenous tPA (102±25 minutes from symptom onset) while the remaining two patients did not receive tPA due to contraindications. Dynamic susceptibility contrast method was used to obtain perfusion weighted images (PWI) for both tps. Mean transit time (MTT) maps were computed and a rigid image registration was performed to align MTT maps at tp1 and tp2 for each patient. A voxel with an MTT > 4 seconds of the mean contralateral MTT was defined as "hypoperfused". A "reperfused" voxel was defined as a voxel which was hypoperfused at tp1 but not at tp2. A voxel without hypoperfusion at tp1 but with hypoperfusion at tp2 was termed "new" hypoperfusion. After computing the volume of reperfusion (V_reperf) and new hypoperfusion (V_newhypo), the net change of hypoperfused volume (ΔV_hypo) was calculated as the subtraction of V_reperf from V_newhypo. A negative ΔV_hypo indicates an overall improvement of tissue perfusion from tp1 to tp2. Linear regression analysis was performed in patients receiving tPA to examine the relationship of onset-to-treatment time, reperfusion status, and clinical improvement as measured by the NIHSS.

Results



tp1 tp2

Figure 1. Representative MTT maps from patient 3 (upper row) and 5 (lower row) at tp1 and tp2. The full range of the colorbar is from from 0 to 20 seconds for MTT.

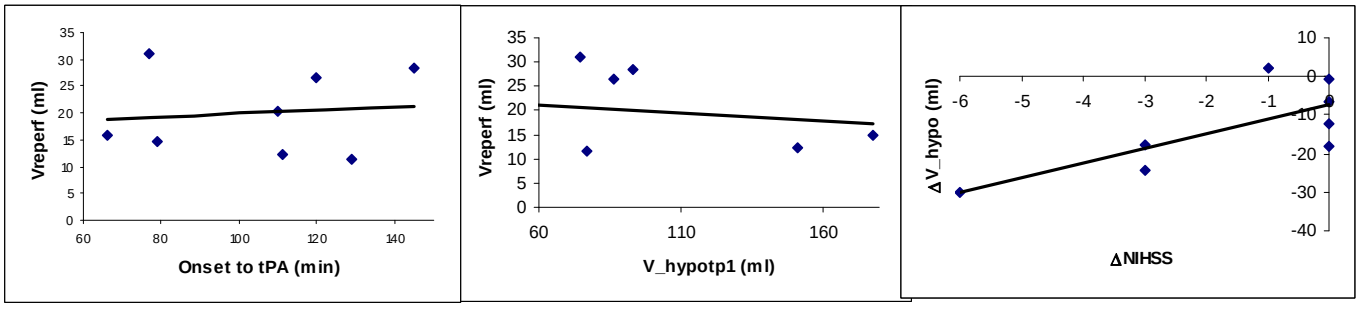
Patient	1	2	3	4	5	6	7	8	9	10
tPA	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ΔNIHSS	-4	0	-6	0	-1	-3	0	0	-3	0
V_hypotp1	80.4	102.7	74.7	86.3	151	27.2	17	177.8	93.3	76.7
Vreperf	53.7	15.3	31.2	26.5	12.3	20.4	15.8	14.7	28.3	11.5
V_newhypo	8.7	39.1	1	8.5	14.6	2.7	3.4	8.2	4.2	10.7
ΔV_hypo	-46.7	23.8	-30.2	-18	2.3	-17.7	-12.4	-6.5	-24.1	-0.8

Table 1. Summary of Patient information. The unit of volume is ml.

Clinical characteristics (tPA treatment and ΔNIHSS) and reperfusion/ hypoperfusion volumes are summarized for each patient in Table 1. Representative MTT maps in two patients at tp1 and tp2 are shown in Figure 1. Patient #3 (Fig 1, upper row) shows an area of reperfusion at tp2 relative to tp1, while in Patient #5 (Fig. 1, lower row), a newly hypoperfused region developed after tPA treatment. One of the two patients who did not receive tPA (Patient #1) showed a large spontaneous reperfusion with a small new hypoperfused volume whereas Patient #2 exhibited limited spontaneous reperfusion, accompanied by a substantial increase in new hypoperfused regions. For patients receiving tPA, no correlation was found between onset-to-tPA treatment (T_tPA) and V_reperf (r=0.113, P=0.79, Figure 2a). At tp2, the reperfused volumes (V_reperf) ranged from 11.5 ml to 28.3 ml (Table 1) regardless of the initial size of the hypoperfused volume at tp1 (r=-0.24, P=0.5684, Figure 2b). All patients demonstrated some degree of "new" hypoperfusion at tp2 (Table 1). A net decrease of total hypoperfused volume (ΔV_hypo) from tp1 to tp2 significantly correlated with improvement in the NIHSS (ΔNIHSS) (r=0.75, P<0.05, Figure 2c).

Discussion and Conclusions

Our results demonstrate the dynamic nature of cerebral perfusion during acute ischemia with the development of reperfusion and new hypoperfusion volumes concurrently. As expected, improvement of NIHSS correlated with net decrease in hypoperfused tissue from tp1 to tp2. Unexpectedly, there was no correlation between the volume of reperfused tissue and the onset-to-tPA treatment time within the three-hour therapeutic window. In addition, larger hypoperfused volumes on tp1 were not accompanied by larger volumes of reperfusion on tp2, suggesting that larger strokes may be less receptive to the benefits of tPA. Future studies with sequential imaging in greater numbers of patients (both tPA-treated and untreated) are required to understand the mechanisms by which tPA leads to improved outcomes in some individuals, while offering little benefit in others.



(a) (b) (c)

Figure 2. Correlation between Onset-to-tPA time and Vreperf (a), V_hypotp1 and Vreperf (b), ΔNIHSS and ΔV_hypo (c).