ASSESSMENT OF ACUTE SPONTANEOUS INTRACEREBRAL HEMATOMA BY CT PERFUSION IMAGING

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SUMMARY
A single-section deconvolution-derived computerized tomographic perfusion imaging was performed in 45 patients (22 male and 23 female; mean age=69.89±10.07 years) with acute supratentorial spontaneous intracerebral hemorrhage. Mean rCBF and rCBV were lower in the hemorrhagic core than in the perihematomal low density area (p<0.001), and in the perihematomal low density area than in normal appearing brain parenchyma (p<0.001). Mean rMTT values were higher in perihematomal low density area than in normal appearing area (p<0.01) and in both hemorrhagic and perihematomal area than in controlateral ROI (p<0.001). There were no differences in rMTT mean values between hemorrhagic core and perihematomal area, as well as between normal appearing and controlateral areas. We found a concentric distribution of all CT perfusion parameters characterized by an improvement from the core to the periphery, with low perihematomal rCBF and rCBV values suggesting edema formation.

Key words: CT-perfusion, intracerebral hematoma.

INTRODUCTION
A better understanding of the pathophysiological mechanisms underlying secondary neuronal damage that can affect the perihematomal tissue early after spontaneous intracerebral hemorrhage (SICH) is crucial for the choice of appropriate strategies of therapy [19]. Several efforts have previously been made to verify whether in the region peripheral to hematoma there exists a zone of ischemic penumbra, defined as severely hypoperfused tissue at risk for infarction which is functionally compromised but structurally intact and, therefore, still viable and salvageable if blood flow is rapidly restored [6]. However, the presence of ischemic penumbral tissue surrounding the hematoma remains controversial in both animal [1, 18] and human studies [7, 12, 15, 20, 21, 27]. Among the different techniques currently available to investigate perfusion abnormalities, dynamic computed tomography (CT) perfusion scanning has recently proven to be a promising tool for the detection of cerebral blood flow (CBF) disorders related to penumbral tissue [4, 25]. In this setting, it has been proposed that ischemic but hypothetically salvageable brain tissue could be identified by CT perfusion parameters [8, 13]. Based on these considerations and in an attempt to provide further insight into the assessment and the distribution of lesional and perilesional perfusion alterations, we sought to quantify CBF changes within and around acute SICH by using deconvolution-derived CT perfusion hemodynamic imaging.

MATERIALS AND METHODS

Patients
We recruited in the study 45 patients with acute supratentorial SICH on unenhanced admission CT scans carried out within 24 hours of symptomatic onset. Time of onset was considered as the last time the patient was known to be neurologically normal. Patients with infratentorial hemorrhage, hematoma related to tumor, trauma, coagulopathy, aneurysms,
vascular malformations, hemorrhagic transformation of brain infarction, intraventricular extension of hemorrhage and patients who had undergone surgical hematoma evacuation were excluded. Disease severity was scored in all patients at entry using Glasgow Coma Scale (GCS) [22]. Hematoma location was classified as basal ganglia or lobar. Hematoma volume was calculated using the formula A×B×C/2 [9]. Informed consent was obtained from each patient or from close relatives before the perfusion CT was performed.

CT perfusion studies

CT perfusion examinations were performed by using a single-section CT scanner (CT HiSpeed ZXi; GE Healthcare, Milwaukee, Wis) equipped for CT perfusion imaging (CT Perfusion; GE Healthcare, Milwaukee, Wis). After hematoma localization on unenhanced CT scanning, the imaging protocol for CT perfusion consisted of a series of 45 CT scans acquired in a single slice (10-mm slice thickness, 80kVp; 200mAs; matrix 512×512; FOV 25-cm; total scan time 50sec) located at the hematoma level during the automatic injection of 50ml of non-ionic contrast agent at the rate of 3.5ml/sec, starting 5 seconds before the initial image. The reference image on non-enhanced CT scans was selected on the basis of the level containing the largest volume of blood. All CT perfusion scans were assessed with a deconvolution-based algorithm by using an imaging workstation (Advantage Windows; GE Medical System, Milwaukee, Wis) supplied with a commercial dedicated software (CT Perfusion 2, GE Healthcare, Milwaukee, Wis). CBF, CBV and MTT perfusion maps were generated for each patient. As illustrated in figure 1,

![CT perfusion image of spontaneous intracerebral hemorrhage located in the left thalamus. Image A shows hematoma location on admission unenhanced CT scan. Image B and C show regions of interest placed around and around the hematoma and in the contralateral hemisphere on the baseline single slice CT scan. Image D, E and F depict maps of cerebral blood flow, cerebral blood volume and mean transit time.](image)

FIG. 1. – CT perfusion image of spontaneous intracerebral hemorrhage located in the left thalamus. Image A shows hematoma location on admission unenhanced CT scan. Image B and C show regions of interest placed around and around the hematoma and in the contralateral hemisphere on the baseline single slice CT scan. Image D, E and F depict maps of cerebral blood flow, cerebral blood volume and mean transit time.

![Image de perfusion CT d’un hématome intracérébral spontané au niveau du thalamus gauche. L’Image A montre la localisation de l’hématome au scanner sans injection à son admission. Les images B et C montrent les régions d’intérêt placées dans l’hématome, à sa périphérie et en contralatéral sur une coupe de scanner de base. Les images D, E, F illustrent la cartographie du débit sanguin cérébral, du volume sanguin cérébral et le temps de transit moyen.](image)


Regional CBF (rCBF), CBV (rCBV) and MTT (rMTT) levels were measured in three different regions of interest (ROIs) larger than 1cm² and manually outlined on the baseline single slice CT scan and including: 1) hemorrhagic core; 2) perihematomal low density area; 3) 1cm rim of normal appearing brain tissue surrounding the perilesional low density area. An additional ROI that mirrored the region including the clot and perihematomal low density area was placed in the contralateral hemisphere. CBF, CBV and MTT values were expressed in ml/100g/min, ml/100g and seconds, respectively. rCBF values lower than 10 ml/100g/min, ranging from 10 to 20ml/100g/min, and included between 20 and 40ml/100g/min were considered as ischemic, penumbral and oligemic, respectively [5]. In addition, rCBF levels greater than 55ml/100g/min were regarded as hyperperfusional [17]. rCBV levels lower than 1.5ml/100g, and rMTT levels higher than 6 seconds were considered as abnormal [4].

Data analysis

Mann-Whitney U test was used to compare mean values among the various groups. The Spearman rank correlation coefficient test was used to identify possible relationships among the different variables. Statistical significance was set at p<0.05.

RESULTS

Patients characteristics

Demographic and clinical features of the 45 patients included in the study are listed in the table I. Overall, mean hematoma volume was 18.38±25.32 (range=0.72-129.25), whereas the mean time from symptom onset and CT perfusion scanning was 10.10±4.90 hours (range=2.44-21.24 hours; median=9.42 hours).

CT perfusion measurements

Mean rCBF and rCBV levels were significantly lower in hemorrhagic core (10.30±6.85ml/100g/min and 0.82±0.456ml/100g, respectively) than in perihematomal low density area (34.50±15.78ml/100g/min and 2.25±0.927ml/100g, respectively) (p<0.001), and in perihematomal area than in normal appearing area

<table>
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<tr>
<th>TABLE I. – Demographic and clinical characteristics in 27 patients with acute spontaneous intracerebral hemorrhage (SICH).</th>
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<tr>
<td>TABLEAU I. – Caractéristiques cliniques et démographiques de 27 patients avec hématome intracérébral spontané.</td>
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<td>Sex (male/female)</td>
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<td>Mean age, years</td>
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<td>Mean admission Glasgow Coma Scale (range)</td>
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**Note:**

- Table I data are presented as mean ± standard deviation (SD) where appropriate.
- All analyses were performed using the statistical software package SPSS (version 11.0; SPSS Inc., Chicago, IL).
(68.779±52.393ml/100g/min and 3.692±2.349ml/100g, respectively) and contralateral ROI (68.158±35.021ml/100g/min and 3.675±1.651ml/100g, respectively) (p<0.001). rCBF and rCBV mean levels were similar in normal appearing and contralateral area. Mean rMTT values were significantly higher in both hemorrhagic core and perihematomal area (5.507±1.832 and 5.74±1.245 seconds, respectively) than in normal appearing area (4.542±0.973 seconds) (p<0.01) and contralateral ROI (4.53±0.796 seconds) (p<0.001).

There were no differences in rMTT mean values between hemorrhagic core and perihematomal area, as well as between normal appearing and contralateral areas. Interestingly, when we evaluated absolute mean values of each perfusion parameter, rCBF levels approached irreversible ischemic levels in hemorrhagic core, while they were oligemic in perihematomal low density area and hyperperfusion in both normal appearing and contralateral areas. rCBV levels were decreased only in hemorrhagic core, whereas none of the ROI examined showed rMTT abnormal levels.

Correlations between perfusion parameters and hematoma volume

In acute SICH patients, rCBF and rCBV mean levels and hematoma volume were inversely and significantly correlated (r=–0.500 and r=–0.589, respectively; p<0.001) in hemorrhagic core. A negative significant correlation was also seen between rCBF and rCBV mean levels and hematoma volume (r=–0.453 and r=–0.423, respectively; p<0.01) in perihematomal area.

DISCUSSION

By employing an accurate topographic approach, we explored perfusion changes occurring within 24 hours after the onset of symptoms in a group of patients with SICH using, for the first time, single-section deconvolution-derived CT hemodynamic imaging. As expected from previous studies [7, 12, 15, 20, 21, 27], we found that perfusional parameters were concentrically distributed and gradually improved from the core to the periphery but we did not observe zero-flow values within the hemorrhagic core having rCBV at severe ischemic levels, but rCBF and rMTT values which were only close to the threshold of irreversible tissue damage. This apparent paradox may be due to the presence of a thin peripheral border with residual flow and relatively preserved CBV and MTT surrounding the central part of the hemorrhagic core with no flow. This outer band, probably reflecting penumbral tissue evolving into infarction [6], is easily visible in figure 1. On the other hand, as opposed to some studies [12, 21], but in agreement with others [7, 15, 20, 27], no evidence of ischemic penumbra was identified in perihematomal low density area where CBF levels were largely indicative of oligemic tissue not at risk for infarction. More precisely, the concomitant decrease of rCBF and rCBV detected in this area seems to suggest the development of brain edema [16]. These findings appear to be concordant with data coming from animal investigations reporting that perihematomal edema formation is mediated by the clotting of intrahemoma blood with liberation of the remaining serum proteins, especially thrombin, into the surrounding brain parenchyma [11, 23] and by the toxic effect of hemoglobin degradation products derived from erythrocyte lysis [26]. In addition, recent MRI studies with diffusion-weighted imaging [2] seem to confirm the existence of perilesional vasogenic edema associated to hematoma, even if other reports have failed to demonstrate any sign of edema development around intracerebral hemorrhage [7, 20]. Therefore, as more recently proposed [20], the possibility that perihematomal perfusion disturbances due to regional hypometabolism cannot be completely excluded. In this regard, the strong inverse correlation emerging between perihematomal hemodynamic alterations and hematoma size apparently supports the hypothesis that the amount of bleeding may contribute to injury of brain tissue surrounding the hematoma by mechanical compression of small perilesional blood vessels [1]. Nevertheless, more recent data suggest that perihematomal damage is mainly mediated by the release of coagulation factors and red blood cell lysis components [11, 23, 26] rather than by hematoma-related mass effect [18, 23]. The findings obtained from normal appearing and normal contralateral brain in which, in agreement with others [12, 15] we found hyperperfusional levels that were not associated to a decrease in rCBV and rMTT values are of particular relevance as they most likely indicate luxury perfusion or abnormal vasodilatation [14]. The occurrence of this hyperperfusional pattern in brain regions remote to SICH currently remains a poorly understood phenomenon and could be ascribed to compensatory vasodilatation or, alternatively, to impaired autoregulation or inflammatory response [12]. The main limitations of the study were the inclusion of large blood vessels in CBF calculation that could lead to an overestimation of CBF values [10] and the restriction of the brain coverage to a single section. However, the first-pass bolus-tracking CT perfusion methodology and the accuracy of the deconvolution process have been validated [3, 24], and the advent of multislice CT scanners could overcome the limited extension of the perfusion analysis. Collectively taken, our findings suggest that dynamic CT perfusion scanning with deconvolution analysis is a powerful method for the evaluation of perfusion deficits associated with acute SICH. They further indicate that perfusion parameters are concentrically distributed and gradually improve from the core to the periphery. In addition, no evidence of ischemic penumbra was found in perihematomal area with rCBF and rCBV levels arguing for oligemia and edema formation. Finally, hyperperfusion values were observed in normal appearing brain tissue located both ipsilaterally and contralaterally to hematoma.

REFERENCES


