Perfusion CT in Patients With Spontaneous Lobar Intracerebral Hemorrhage
Effect of Surgery on Perihemorrhagic Perfusion

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Background and Purpose—The aim of the present study was to investigate cerebral hemodynamics in patients requiring surgical treatment for lobar intracerebral hemorrhage.

Methods—Twenty patients who underwent surgery to remove a lobar spontaneous intracerebral hemorrhage were scanned before and after surgery using perfusion CT mapping. Mean transit time, time to peak of the residue function, cerebral blood volume, and cerebral blood flow were measured in 4 defined regions of interest.

Results—Preoperatively, time to peak of the residue function, cerebral blood volume, and cerebral blood flow were significantly impaired in the perihemorrhagic zone as compared with the ipsilateral and contralateral hemisphere. Perihematoma perfusion improved significantly after clot evacuation and there was no difference in time to peak of the residue function, cerebral blood flow, and cerebral blood volume values between the perihemorrhagic zone and ipsilateral as well as contralateral hemisphere after surgical treatment.

Conclusions—Our findings illustrate distinct perihemorrhagic perfusion impairments in a selected patient population with lobar intracerebral hemorrhage as evident by impaired time to peak of the residue function, cerebral blood flow, and cerebral blood volume and their improvement after early surgical treatment. Whether these early improvements in hemodynamic measurements may influence secondary neuronal injury and ultimately clinical outcome, as opposed to the natural course of spontaneous intracerebral hemorrhage remains unclear. (Stroke. 2012;43:759-763.)

Key Words: intracerebral hemorrhage ■ perfusion CT ■ surgical treatment

Spontaneous intracerebral hemorrhage (SICH) accounts for 10% to 20% of all strokes and is characterized by high morbidity and mortality.1 To date, the optimal management of SICH remains uncertain and therefore additional pathophysiological knowledge is needed.2–4

In this respect, cerebral perfusion imaging studies, either based on MRI or CT technology, have gained importance over the last decade for patients with SICH.5–7 The main use of such studies is to identify tissue at risk of secondary neuronal injury, especially in brain tissue surrounding the hematoma.8 The identification of critical perihematomal hypoperfusion might facilitate decision-making in the treatment of these patients. The majority of recent perfusion studies demonstrate perihemorrhage hypoperfusion for deep SICH, but there are still conflicting interpretations of these findings.6,9,10 Additionally, little is known about the impact of early surgical treatment on perihemorrhagic perfusion in patients with space-occupying lobar SICH.

Therefore, we investigated the time course of cerebral hemodynamics in patients who underwent surgical treatment for lobar SICH. Hemodynamics were measured using perfusion CT (PCT) both before and early after surgical hematoma removal.

Subjects and Methods

Data Acquisition
All patients admitted to the Heinrich-Heine University Medical Centre with ischemic or hemorrhagic (intracerebral or subarachnoid hemorrhage) stroke undergo standard CT and PCT imaging. This retrospective analysis includes data from 20 patients, who underwent surgical treatment for space-occupying, lobar SICH and had received PCT scanning according to the stroke imaging protocol. The decision for surgical treatment was made independently of, and before, inclusion in the present analysis. Criteria for inclusion were: (1) patients >18 years; (2) medical and neurological state amenable to follow-up imaging; (3) intracerebral hematoma present on initial nonenhanced CT; (4) symptom onset <12 hours at the time of admittance to our department; and (5) informed consent obtained for scientific data analysis from the patient or a legal representative. Criteria for exclusion from the study were: (1) renal insufficiency or history of contrast agent allergy; (2) pregnancy; (3) clinical instability or radiological signs of herniation; (4) deep thalamic/putaminal or
infratentorial hematomas; and (5) hematomata due to previous infarction, aneurysm, vascular malformation, or tumor.

Study Design
For patients allocated to the present analysis, an early preoperative PCT was performed at the level of the hematoma equator. Additionally, hematoma volume was calculated in accordance to the A×B×C/2 method based on the initial CT and PCT scan (Volume Zoom; Siemens, Erlangen, Germany).11 Within 6 hours after surgical removal of the hematoma, patients underwent follow-up CT and PCT. In accordance with the initial scan, the scanning plane was again aligned with the equator of the previous hematoma cavity and the same perfusion parameters were calculated. Pre- and postoperative perfusion measurements were then compared and correlated with hematoma volume.

PCT Methods
As previously described, 360° cortical banding analysis and singular value decomposition were used for calculation of PCT data such as mean transit time, time to peak of the residue function (Tmax), cerebral blood flow (CBF), and cerebral blood volume (CBV).12–15 PCT acquisition time was 50 seconds. After generation of perfusion maps using the software STROKETOOL-CT (Version 2.0; www.digitalimagesolutions.de), 4 regions of interest (ROIs), derived from Tmax maps, were defined: (1) the perihemorrhagic zone (PHZ); (2) a zone exactly mirrored to the PHZ on the contralateral hemisphere; (3) the ipsilateral hemisphere, excluding the hematoma, and PHZ; and (4) the hemisphere contralateral to the hematoma (Figure 1). These ROIs were also applied for mean transit time, CBF, and CBV maps. Finally, PCT data from all included patients were pooled and expressed as mean and 95% CI values. Uncalibrated CBF and CBV values were expressed in mL/min/100 g and mL/min, respectively.

Definition of PHZ
The outer margin of the PHZ (ROI A) was defined based on overlap between the CT and Tmax maps and the following characteristics: (1) the perihematomal area on CT; and (2) a Tmax deviation of more than twice the SD of mean Tmax values in the healthy contralateral mirrored zone (ROI B). The inner margin of the PHZ (ROI A) was defined in correspondence to intracerebral hemorrhage location on CT and after exclusion of 0 perfusion values within the hematoma (Figure 1).

All PCT values within the medial and lateral margin in ROI A were then expressed as mean values. Identical ROIs were applied for postoperative PCT measurements.

Statistical Analysis
Statistical analyses were performed using SPSS Version 15.0.1 (SPSS Inc, Chicago, IL). For each test, P<0.05 was used as the level of significance. For independent samples with metric variables, the t-test was used to determine the difference between the mean values. If sample variances differed significantly, Welch adaptation of the t-test was used. For related samples such as when comparing pre- and postoperative values, the paired t-test was used. Finally, Pearson product-moment correlation was used to investigate the relation of PCT impairment to hematoma volume.

Results
A total of 40 PCT studies from 20 patients (8 females and 12 males), before and after the surgical removal of the hematoma, were included and pooled in the final analysis. The mean age within the cohort was 59.5±11.2 years (mean±SD). Hematoma volume was 68.5±35.9 mL (mean±SD). The intracerebral hemorrhage location was: frontal (n=7), temporal (n=6), parietal (n=5), and occipital (n=2). The intracerebral hemorrhage side was the left hemisphere in 12 patients and the right hemisphere in 8. There were no imaging- or contrast-agent-related complications. Furthermore, the PCT imaging process did not slow the treatment sequence: median time span and interquartile range from admission until initial PCT scan (PCT 1) was 0:35 hours (interquartile range, 18.25 minutes), 2:10 hours from PCT 1 (interquartile range, 50.75 minutes) until surgery, and 4:58 hours (interquartile range, 195.5 minutes) after surgery until PCT 2. Median length of surgery was 3:24 hours.

Focal PCT Analysis in ROI A (PHZ) Compared With ROI B (Contralateral Zone)
The initial Tmax measurements were significantly (P<0.0001) prolonged in ROI A (4.1 seconds; 95% CI, 3.64–4.55) as compared with ROI B (2.41 seconds; 95% CI, 2.07–2.75), and they improved significantly postoperatively in ROI A (P<0.0001). Postoperatively, there was no difference (P=0.2025) between the 2 ROIs (A: 2.36 seconds; 95% CI, 1.72–2.99; B: 1.90 seconds; 95% CI, 1.72–2.99). CBF and CBV values were significantly decreased in ROI A (59.18 mL/min/100 g; 95% CI, 46.16–72.21; P=0.0057 and 21.10 mL/min; 95% CI, 17.08–25.11; P=0.0148, respectively) as compared with ROI B (88.2 mL/min/100 g; 95% CI, 72.1–104.2 and 28.63 mL/min; 95% CI, 23.95–33.3, respectively). After hematoma removal, CBF and CBV values increased (P=0.01 and P=0.039, respectively) in ROI A as compared
with preoperative measurements, and CBV and CBF values adjusted between the 2 ROIs (P/H11005 0.6083 and P/H11005 0.7179, respectively). Mean transit time values were elevated in both ROIs and did not differ between ROI A and ROI B (3.92 seconds; 95% CI, 3.41–4.44 and 3.69 seconds; 95% CI, 3.35–4.03, respectively; P/H11005 0.4307) initially or after surgical hematoma removal (P/H11005 0.7972; Figures 2 and 3). Preoperative impairment of T max in ROI A was correlated with hematoma volume (P/H11005 0.048, R/H11005 0.448). This correlation was no longer evident after hematoma evacuation (P/H11005 0.551, R/H11005/H11002 0.142).

Hemispheric PCT Analysis in ROI C (Ipsilateral Hemisphere Excluding the Hematoma and PHZ) and ROI D (Contralateral Hemisphere) Before and After Hematoma Removal

Hemispheric T max values were increased in the hemisphere bearing the hematoma (ROI C: 2.97 seconds; 95% CI, 2.31–3.63) before surgery as compared with the contralateral hemisphere (ROI E 2.16 seconds; 95% CI, 1.57–2.74). This difference approached statistical significance (P=0.061). After hematoma removal, T max values nearly matched in both hemispheres (P=0.88). CBF in ROI C and in ROI D (99.6 mL/min/100 g; 95% CI, 73.11–126.1 and 96.25 mL/min/100 g; 95% CI, 72.67–119.9) did not differ before or after hematoma removal (P=0.435 and P=0.7363, respectively). CBV was 32.58 mL/min (95% CI, 26.08–39.08) in ROI C and 36.74 mL/min (95% CI, 26.67–46.81) in ROI D initially and, after surgery, adapted between the ipsilateral and contralateral hemisphere (ROI C: 30.16 mL/min; 95% CI, 24.53–35.8; ROI D: 32.05 mL/min; 95% CI, 23.37–40.83).

Intrahemispheric Analysis of ROI A (PHZ) and ROI C (Ipsilateral Hemisphere Excluding the Hematoma and PHZ)

T max was primarily impaired in the PHZ (ROI A: 4.10 seconds; 95% CI, 3.41–4.44 versus ROI C: 2.97 seconds; 95% CI, 2.31–3.63; P=0.0056). After hematoma removal, T max improved significantly in ROI A and there was no difference between the ROIs (P=0.6321). Before treatment, CBF values in ROI A were significantly (P=0.008) decreased compared with ROI C (59.18 mL/min/100 g; 95% CI, 46.16–72.21 and 99.60 mL/min/100 g; 95% CI, 73.11–126.1, respectively). After hematoma evacuation, there was significant improvement of CBF in the PHZ and no difference compared with the remaining hemisphere (ROI A versus C: P=0.9). CBV values followed the same trend (CBV before surgery: ROI A: 21.10 mL/min; 95% CI, 17.08–25.11 versus ROI C: 32.58 mL/min; 95% CI, 26.08–39.08; P=0.004). After surgical hematoma removal, there were no significant differences between the CBV values in ROI A and C (P=0.715). Mean transit time values did not differ significantly within the affected hemisphere before (P=0.696) and after hematoma removal (P=0.813; Figure 4).
mental animal studies.18,19 

Early reduction of $T_{\text{max}}$ values in the PHZ after clot removal and there was no postoperative difference in $T_{\text{max}}$, CBF, or CBV between the ROIs. The correlation between preoperative perihematomal $T_{\text{max}}$ impairment and hematoma volume was no longer evident after surgery.

PCT is increasingly used to investigate perihematomal perfusion in patients with SICH. Previous studies illustrated a gradient of decreasing cerebral perfusion toward intracerebral hematoma and consecutively decreased oxygen demand.22–24 However, the simultaneous increase of CBV after evacuation of the hematoma implies reduced compression of the microvasculature or even active autoregulatory compensation for previous substrate deficits.5 Perfusion impairments in the PHZ of patients with deep or lobar SICH have been described to resolve within the subacute course after SICH.9 Nevertheless, the impact of acute versus subacute perfusion improvement in the PHZ on prevention of secondary neuronal tissue damage and, ultimately, on clinical outcome remains to be elucidated. The preoperative association of hematoma volume and perfusion disturbances found in our study has also been shown by others, albeit for smaller mean hematoma volumes.6,7,25 Importantly, the reversal of this association after clot removal has not yet been reported.

Our study has some limitations. PCT uses a mathematical model to measure tissue perfusion and the numeric values remain to be validated in the context of SICH. Additionally, we proposed a combined mathematical and radiological definition of the PHZ. The advantage of this method is that interindividual (ie, variation in the extent of PHZ due to hematoma features) and intraindividual (ie, variation in the extent of the PHZ over time) differences in PHZ extension are accounted for. Furthermore, the PHZ in the acute phase of SICH can be difficult to outline on CT, increasing the risk of inclusion of artificially depressed PCT values, especially in the vicinity of the hematoma. Hence, the assumption of a size-steady PHZ (ie, 1 cm) in PCT, without confirmation by MRI T2 or fluid-attenuated inversion recovery images, might be false for larger intracerebral hematomas. The interpretation of our results mainly relies on knowledge derived from animal models or stroke studies, because the literature on hemodynamic assessment of surgically treated patients is scarce. The data from our study may not define a threshold for surgical treatment based on PCT measurements because a much larger patient collective with lobar SICH would be necessary to correlate patient outcome data with hemodynamic parameters.

In summary, our findings demonstrate early improvement of CT-based perihematomal perfusion parameters after acute surgical treatment. Our data are consistent with the previous assumption that lobar intracerebral hematomas can lead to increased local pressure with subsequent compression of the microvasculature, translating in initial $T_{\text{max}}$, CBF, and CBV impairment. Whether the early improvement of perfusion parameters after surgical hematoma removal may prevent secondary mechanic, ischemic, or toxic damage in the perihemorrhagic zone remains unclear. Future prospective studies on lobar SICH should investigate PCT measurements with a
focus on $T_{\text{max}}$ throughout the course of treatment in correlation with clinical characteristics.

**Conclusions**

Our findings illustrate distinct perihemorrhagic perfusion impairments in a selected patient population with lobar intracerebral hemorrhage as evident by impaired $T_{\text{max}}$, CBF, and CBV and their improvement after early surgical treatment. Whether these early improvements of hemodynamic measurements may influence secondary neuronal injury and, ultimately, poor clinical outcome, as opposed to the natural course of SICH, remains unclear.

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**Disclosures**

None.

**References**


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