The influence of decompressive craniectomy for major stroke on early cerebral perfusion

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OBJECT Multiple trials have shown improved survival and functional outcome in patients treated with decompressive craniectomy (DC) for brain swelling following major stroke. It has been assumed that decompression induces an improvement in cerebral perfusion. This observational study directly measured cerebral perfusion before and after decompression.

METHODS Sixteen patients were prospectively examined with perfusion CT within 6 hours prior to surgery and 12 hours after surgery. Preoperative and postoperative perfusion measurements were compared and correlated.

RESULTS Following DC there was a significant increase in cerebral blood flow in all measured territories and additionally an increase in cerebral blood volume in the penumbra (p = 0.03). These changes spread as far as the contralateral hemisphere. No significant changes in mean transit time or Tmax (time-to-peak residue function) were observed.

CONCLUSIONS The presurgical perfusion abnormalities likely reflected local pressure-induced hypoperfusion with impaired autoregulation. The improvement in perfusion after decompression implied an increase in perfusion pressure, likely linked to partial restoration of autoregulation. The increase in perfusion that was observed might partially be responsible for improved clinical outcome following decompressive surgery for major stroke. The predictive value of perfusion CT on outcome needs to be evaluated in larger trials.


KEY WORDS stroke; decompressive craniectomy; cerebral perfusion; traumatic brain injury
ing the following inclusion criteria: 1) acute supratentorial unilateral middle cerebral artery (MCA) territory infarction, 2) selected for DC, 3) preoperative PCT scanning within 6 hours before surgery, 4) postoperative PCT scanning within 12 hours after DC, 5) patient age greater than 18 years, and 6) informed consent for study participation obtained from the patient or a legal representative.

The present study was reviewed and approved by the local institutional ethics review board of the medical faculty of the Heinrich Heine University, Düsseldorf, Germany.

Exclusion criteria were 1) hemorrhagic infarction, 2) multi-territorial stroke, 3) admission more than 12 hours after onset, 4) pregnancy, 5) clotting disorders, and 6) surgical complications.

**Study Design**

For patients allocated to the present analysis, a standardized PCT screening protocol was performed immediately after admission. The management of these patients, their selection for DC, and the surgical procedure itself were in accordance with current international guidelines. After the decompressive surgery, the patients enrolled in this study underwent a second PCT study in addition to the routine postoperative CT scan. Preoperative and postoperative perfusion measurements were compared and correlated.

**PCT Methods and Definitions**

As previously described, 360° cortical banding analysis and singular value decomposition were used for calculation of PCT data such as mean transit time (MTT), time to peak of the residue function (Tmax), cerebral blood flow (CBF), and cerebral blood volume (CBV). The PCT acquisition time was 50 seconds. After generation of perfusion maps using the software stroketool-CT (Version 2.0, www.digitalimagesolutions.de), the ischemic tissue was determined by the steep decrease in CBF as described in previous publications. The penumbra was defined as the area adjacent to the ischemic tissue, where the CBF showed an increase before reaching the plateau of perfusion in the non-ischemic brain; this area extended for approximately 10°–15° in both the anterior and posterior directions (Fig. 1). The rest of the hemisphere ipsilateral to the stroke, excluding the ischemic core, was defined as ipsilateral residual hemisphere. The contralateral hemisphere was also analyzed. Volumetric calculations were conducted using 3DSlicer (freeware, www.slicer.org) segmentation and quantification routines.

**Statistical Analysis**

Statistical analyses were performed using SPPS Version 19 (IBM Corp.) and GraphPad prism (GraphPad Software Inc.). Paired t-tests were performed for pre- and post-DC comparisons following verification of normal distribution by Kolmogorov-Smirnov test. Results given are arithmetic means for continuous variables unless otherwise stated. The level of significance was stipulated as 0.05.

MTT and Tmax are given in deciseconds (dsec); CBV and CBF are relative parameters and are therefore given in arbitrary units (AU).

**Results**

**General**

Twenty-nine patients underwent DC for the treatment of major stroke at a German university tertiary care center from November 2011 to January 2013.

Ten patients were excluded because of missing or out-of-time-frame imaging and 3 patients were excluded due to hemorrhages. Overall, 32 PCT maps obtained in 16 patients treated by DC for major stroke between 2011 and 2013 were included in this analysis. The study group included 6 women and 10 men, and the patients’ mean age was 50.2 years (SD 9.2 years). Eight patients suffered a right MCA stroke and 8 a left MCA stroke; 1 patient had a partial MCA infarction plus a posterior cerebral artery infarction.

The mean volume of infarction determined by clearly demarcated tissue in pre-DC CT imaging was 213.2 cm³ (SD 77.4 cm³). The mean time between onset of symptoms and surgery was 33.7 hours, and the median Glasgow Coma Scale score at initiation of surgery was 9 (range 3–15). The median time between DC and postsurgery PCT was 8.3 hours (SD 2.4 hours).

**Perfusion Changes in the Penumbra**

Reflecting close-range effects of DC, the penumbra was defined as the area of perfusion changes between ischemic tissue and brain not affected or only remotely af-
fected by the ischemic event, as indicated by stable CBF values. This technique resulted in the identification of regions adjacent to the ischemic tissue extending 10°–15° in the anterior and posterior directions (Fig. 1). A mean decrease in MTT of 2.41 dsec in the penumbra was observed, although this difference did not reach statistical significance (p = 0.454). Similar findings were evident for Tmax, with a mean decrease of 7.86 dsec (p = 0.274).

CBF and CBV both showed a significant increase following DC (15.02 AU for CBF, p = 0.014; 3.86 AU for CBV, p = 0.030; Table 1, Fig. 2).

**Perfusion Changes in the Ipsilateral Residual Hemisphere**

To determine medium-range effects of DC, the ipsilateral residual hemisphere—excluding the ischemic area but including the penumbra—was also analyzed.

Similar effects as for the penumbra were observed. Decreases in MTT (5.95 dsec, p = 0.067) and Tmax (8.19 dsec, p = 0.068) were observed, although neither of these changes were statistically significant. CBF was significantly increased (9.62 AU, p = 0.037); CBV was slightly increased, although the increase did not reach statistical significance (0.81 AU, p = 0.653) following DC (Table 2, Fig. 2).

**Perfusion Changes in the Contralateral Hemisphere**

Remote effects of space-occupying infarction on cerebral perfusion are a likely explanation of clinical deterioration not explained by local ischemia. In the contralateral hemisphere a marked increase in CBF was observed (20.96 AU, p = 0.006). A decrease in MTT and Tmax and a slight increase in CBV were observed, although the difference did not reach statistical significance (Table 3, Fig. 2).

**Clinical Outcome**

The median follow-up was 20.8 months (SD 7.6 months), and the median modified Rankin Scale score at most recent follow-up was 4 with a Barthel Index score of 27 (SD 26). Two patients died during the follow-up period, and in both cases death was due to coronary events. Eleven patients underwent cranioplasty following rehabilitation; 9 patients received an autologous implant and 2 an artificial implant. Three patients required permanent CSF shunting.

**Discussion**

Our findings showed that distinct and consistent short-term effects of DC on cerebral perfusion can be measured by PCT: 1) an increase in CBF was observed in all regions investigated, 2) an increase in CBV was observed in the vicinity of the infarction, and 3) MTT and Tmax were not significantly influenced by DC.

The changes in CBF and CBV were concentrated in, but not limited to, the penumbra and the ipsilateral residual hemisphere and spread as far as the contralateral hemisphere.

Our present observations are only partially in line with the findings of a recently published study of 29 patients treated by DC for malignant stroke, in which Amorim et al. found that DC significantly improved MTT in the contralateral hemisphere and penumbra and CBF in the whole brain, but not MTT or CBV in the ipsilateral hemisphere. In contrast, MTT and Tmax were not significantly influenced in our series, but CBF was changed in all regions investigated, and CBV was changed in the vicinity of the infarction. A decrease in MTT and also Tmax was observed in the ipsilateral residual hemisphere and a decrease in MTT was observed in the contralateral hemisphere, although these decreases did not reach significance. A larger patient population would likely lead to significant results. Reduced cerebrovascular reserve capacity and reduced overall CBF and CBV in older patients are a likely explanation for the observed worse clinical outcome in the elderly. Interestingly, hemodynamic benefit was barely evident after DC for patients older than 55 years in the publication by Amorim et al., and the differences observed in the hemodynamic PCT parameters might be explained by an older patient population in our series. Timing of surgery is another factor known to significantly influence the outcome of DC for stroke and will most likely impact PCT results.

Our results are in line with the first description of PCT measurement before and after DC for stroke published by Bendzsus et al. in 2003. In their case report they observed an increase in CBF and CBV in the penumbra and a decrease in Tmax following DC, but they did not offer a pathophysiological explanation for their observations.

Relative MTT as a tissue-specific marker was considered as a surrogate for final infarct size after ischemic stroke and for prediction of perfusion impairment during delayed cerebral ischemia after subarachnoid hemorrhage. MTT—in combination with other perfusion parameters—is believed to be an accurate marker for prediction of cerebral ischemia. However, cerebral perfusion changes after DC for malignant stroke should be pathophysiologically comparable to perfusion changes during cerebral hematoma evacuation. In the study by Etminan et al., MTT was globally elevated in both hemispheres initially and did not improve in either hemisphere after surgical hematoma removal. In contrast, Tmax, CBF, and CBV were impaired in the perihematomal zone and resolved after hematoma evacuation.

Similar results were observed in the current series but likely for different reasons: as in the perihematomal zone of intracerebral hemorrhage, pre-DC perfusion in the penumbra and the ipsilateral residual hemisphere might not only be affected by cerebral hypoperfusion due to low cerebral perfusion pressure but also by pressure effects hindering autoregulation.

Clinically these assumptions are supported by the commonly observed rapid improvement in neurological state following DC and reports on neurological improvement by anti-edema therapy with mannitol.
Reduction of CBF and CBV prior to DC is thought to be a surrogate for local pressure on the microvasculature, reduced cerebral perfusion pressure, and impaired autoregulation. Increase in both parameters after DC might represent an increase in cerebral perfusion pressure, likely accompanied by the restoration of autoregulation. The distinct rise in CBV in the penumbra might resemble early vasoparalysis following surgery or reactive hyperperfusion in the penumbra. This post-ischemic hyperperfusion has long been thought to be of detrimental effect, although this assumption is still under discussion. Therefore the effect of CBF and CBV increase on functional outcome cannot be conclusively assessed.

Venous outflow obstruction due to increased local or global intracranial pressure resulting in venous congestion can be discussed as an additional pathomechanism. Venous pooling or stasis effects cannot be measured directly by PCT, therefore no evaluation of this mechanism can be given. But low pre-DC CBV values and the post-DC increase in CBF and CBV suggest reduced arterial inflow with reduced overall blood volume in the penumbra prior to decompression.

Table 2. Perfusion parameter statistics before and after DC: ipsilateral residual hemisphere

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean Difference</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTT (dsec)</td>
<td>-5.95</td>
<td>-0.47 to 12.38</td>
<td>0.067</td>
</tr>
<tr>
<td>Tmax (dsec)</td>
<td>-8.19</td>
<td>-0.68 to 17.06</td>
<td>0.068</td>
</tr>
<tr>
<td>CBF (AU)</td>
<td>9.62</td>
<td>-18.60 to -0.65</td>
<td>0.037</td>
</tr>
<tr>
<td>CBV (AU)</td>
<td>0.81</td>
<td>-4.61 to 2.97</td>
<td>0.653</td>
</tr>
</tbody>
</table>

Table 3. Perfusion parameter statistics before and after DC: contralateral hemisphere

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean Difference</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTT (dsec)</td>
<td>-3.92</td>
<td>-0.82 to 8.67</td>
<td>0.098</td>
</tr>
<tr>
<td>Tmax (dsec)</td>
<td>-0.67</td>
<td>-3.87 to 5.22</td>
<td>0.756</td>
</tr>
<tr>
<td>CBF (AU)</td>
<td>20.96</td>
<td>-34.87 to -7.05</td>
<td>0.006</td>
</tr>
<tr>
<td>CBV (AU)</td>
<td>3.03</td>
<td>-6.30 to 0.23</td>
<td>0.067</td>
</tr>
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Reduced mortality and reduced morbidity might be triggered by two different effects of DC in major stroke. Mortality reduction is most likely induced by prevention of herniation, while morbidity reduction might at least be in some part induced by improvement of penumbra and overall brain perfusion resulting in a reduction of additional tissue damage beyond the immediate ischemic zone. This assumption might help to interpret results from past and future clinical trials in DC for major stroke, especially regarding the observed significant differences in populations of different ages.

Fig. 2. Time course of measured perfusion parameters before and after DC in the contralateral hemisphere (A), penumbra (B), and ipsilateral residual hemisphere (C). Time is given in deciseconds on the y-axis for MTT and Tmax; CBV and CBF are relative values given in arbitrary units.
sion for traumatic brain injury. Additionally, this finding provides a possible explanation for neurological deficits involving functions other than those located in the ischemic area and loss of consciousness in patients without signs of herniation. Protection of the hemisphere contralateral to the stroke is a strong argument for early decompression.

The parameter thought to best reflect increased ICP is Tmax. Tmax is known to be mainly influenced by blood inflow—e.g., decreased carotid artery inflow due to decreased cerebral perfusion pressure. The slight decrease in Tmax observed throughout the areas investigated likely results from decompression-induced general ICP reduction. This can only be assumed, as no data on pre-DC ICP are available.

Besides missing data on ICP we acknowledge some further limitations to our study. 1) The study included a relatively small number of patients. 2) PCT only provides relative values on the most interesting parameters, CBF and CBV. Absolute CBF and CBV values, which it is possible to measure (e.g., by using xenon-enhanced perfusion imaging), would reveal additional information and might provide decision guidance for surgery. 3) No additional PCT measurements were performed during the later course of the disease, and such measurements might have allowed deeper insight into the intermediate and long-term effects of DC in this patient group. 4) No perfusion data from patients not undergoing DC were available for comparison.

A correlation of clinical outcome and perfusion parameter changes was not performed in our study, as a meaningful analysis would require much higher patient numbers. Based on the findings presented in this study we expect a clinical relation to exist and adding PCT to further studies on DC in cerebral infarction might provide deeper insight into this intriguing subject.

Conclusions
Distinct perfusion changes can be observed in PCT imaging immediately before and after decompressive craniectomy (DC) for major stroke.

Perfusion improvement is not limited to the penumbra. Similar effects can be observed in the residual ipsilateral and contralateral hemispheres. The pre-DC changes observed most likely reflect pressure-induced hypoperfusion. Post-DC perfusion improvement implies increased cerebral perfusion pressure, likely accompanied by incipient restoration of autoregulation. The increase in perfusion observed might be partially responsible for improved clinical outcome. The predictive value of PCT still has to be evaluated in larger trials.

References

Perfusion after DC for major stroke
of perfusion-related parameters derived from perfusion CT. *Stroke* 32:431–437, 2001


**Authors Contributions**

Conception and design: Slotty, Hänggi. Acquisition of data: Slotty, Beez, Beenen, Turowski. Analysis and interpretation of data: Slotty, Beez, Beenen, Turowski, Hänggi. Drafting the article: Slotty. Critically revising the article: Slotty, Kamp, Beez, Steiger, Hänggi. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Slotty. Statistical analysis: Slotty.

**Administrative/technical/material support:** Beenen, Steiger, Turowski. Study supervision: Slotty, Hänggi.

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