The influence of decompressive craniection 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

A LTHOUGH numerous aspects of decompressive craniectomy (DC) for major stroke are still under discussion, its beneficial effect on overall survival and clinical outcome is widely accepted nowadays. Multiple randomized clinical trials have shown improved survival and functional outcome in patients treated with DC compared with conservative or best medical treatment.10,11,15,21,24,31 Despite these findings patient selection and timing of surgery remain controversial.14,29

The pathophysiological background of DC in major stroke has been only sparsely investigated.2,6,23 An increase in cerebral perfusion pressure was shown following DC for traumatic brain injury.4 Perfusion improvement following DC for major stroke has been described, and whole-brain and penumbral perfusion improvement has been stated as a therapeutic target in DC in multiple publications.5,14,24,31 An animal study investigating the effect of DC in a rat model of stroke showed a significant reduction in final infarct size and an improvement in perfusion via leptomeningeal collateral vessels, as measured by MRI.5

Perfusion CT (PCT) is widely used in stroke imaging.18 It can be used to monitor penumbral perfusion, to detect additional infarction, and to monitor treatment success in revascularization.3,16,25

It can be postulated that DC is followed by an improvement in cerebral perfusion due to reduced general and local pressure. We therefore designed a study to investigate cerebral perfusion changes before and early after DC for major stroke by PCT.

Methods

Patient Population

The present study analyzed data from patients meet-
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 SPSS 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 re-
gions 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 ob-
served, 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 fol-
lowing 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 ipsilat-
eral residual hemisphere—including the ischemic area but
including the penumbra—was also analyzed.

Similar effects as for the penumbra were observed. De-
creases 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 signifi-
cantly 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 ce-
rebral perfusion are a likely explanation of clinical dete-
rioration not explained by local ischemia. In the contralat-
eral 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 dif-
ference 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 pe-
riod, and in both cases death was due to coronary events.
Eleven patients underwent cranioplasty following reha-
libilitation; 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 re-
sidual 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 con-
tralateral hemisphere and penumbra and CBF in the whole
brain, but not MTT or CBV in the ipsilateral hemisphere.1
In contrast, MTT and Tmax were not significantly influ-
enced in our series, but CBF was changed in all regions in-
vestigated, 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, al-
though 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 ex-
planation for the observed worse clinical outcome in the
elderly.12,18,19,21,33 Interestingly, hemodynamic benefit was
barely evident after DC for patients older than 55 years
in the publication by Amorim et al.,1 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 like-
ly impact PCT results.17

Our results are in line with the first description of PCT
measurement before and after DC for stroke published
by Bendzsus et al. in 2003.2 In their case report they ob-
served 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 consid-
ered as a surrogate for final infarct size after ischemic
stroke and for prediction of perfusion impairment dur-
ing delayed cerebral ischemia after subarachnoid hem-
orrhage.27,32 MTT—in combination with other perfusion
parameters—is believed to be an accurate marker for pre-
diction of cerebral ischemia.2 However, cerebral perfusion
changes after DC for malignant stroke should be patho-
physiologically comparable to perfusion changes during
cerebral hematoma evacuation. In the study by Etminan
et al., MTT was globally elevated in both hemispheres ini-
itially and did not improve in either hemisphere after surgi-
cal hematoma removal.4 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 pen-
umbra and the ipsilateral residual hemisphere might not
only be affected by cerebral hypoperfusion due to low ce-
rebral perfusion pressure but also by pressure effects hin-
dering autoregulation.

Clinically these assumptions are supported by the com-
monly observed rapid improvement in neurological state
following DC and reports on neurological improvement
by anti-edema therapy with mannitol.2

**TABLE 1. Perfusion parameter statistics before and after DC: penumbra**

<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>−2.41</td>
<td>−4.28 to 9.11</td>
<td>0.454</td>
</tr>
<tr>
<td>Tmax (dsec)</td>
<td>−7.86</td>
<td>−6.90 to 22.63</td>
<td>0.274</td>
</tr>
<tr>
<td>CBF (AU)</td>
<td>15.02</td>
<td>−26.54 to −3.49</td>
<td>0.014</td>
</tr>
<tr>
<td>CBV (AU)</td>
<td>3.86</td>
<td>−7.29 to −0.43</td>
<td>0.030</td>
</tr>
</tbody>
</table>

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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>
</tbody>
</table>

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.

Neurological deficits exceeding functions located in the ischemic area are commonly observed in patients suffering from major stroke. Models of explanation include but are not limited to accumulation of toxic metabolites, hydrocephalus, and global hypoperfusion. We observed remote perfusion changes in the contralateral hemisphere including a high MTT prior to DC and a significant increase in CBF following DC. These remote changes are most likely a response to intracranial pressure (ICP) decrease followed by an increase in cerebral perfusion pressure. This effect has been shown to occur in decompressions...
Perfusion after DC for major stroke

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


Authors Contributions
Conception and design: Slotty, Hänggi. Acquisition of data: Slotty, Beez, Beenen, Turowski. Analysis and interpretation of data: Slotty, Beez, Beenen, Turowski, Hänggi. Writing 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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