Predictors of early in-hospital death after decompressive craniectomy in swollen middle cerebral artery infarction

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Abstract

Background Swollen middle cerebral artery infarction is a life-threatening disease and decompressive craniectomy is improving survival significantly. Despite decompressive surgery, however, many patients are not discharged from the hospital alive. We therefore wanted to search for predictors of early in-hospital death after craniectomy in swollen middle cerebral artery infarction.

Methods All patients operated with decompressive craniectomy due to swollen middle cerebral artery infarction at the Department of Neurosurgery, Oslo University Hospital Rikshospitalet, Oslo, Norway, between May 1998 and October 2010, were included. Binary logistic regression analyses were performed and candidate variables were age, sex, time from stroke onset to decompressive craniectomy, NIHSS on admission, infarction territory, pineal gland displacement, reduction of pineal gland displacement after surgery, and craniectomy size.

Results Fourteen out of 45 patients (31%) died during the primary hospitalization (range, 3–44 days). In the multivariate logistic regression model, middle cerebral artery infarction with additional anterior and/or posterior cerebral artery territory involvement was found as the only significant predictor of early in-hospital death (OR, 12.7; 95% CI, 0.01–0.77; p = 0.029).

Conclusions The present study identified additional territory infarction as a significant predictor of early in-hospital death. The relatively small sample size precludes firm conclusions.

Keywords Decompressive craniectomy · Swollen · Middle cerebral artery infarction · Predictors · Outcome

Introduction

Swollen middle cerebral artery infarction (SMCAI) is a life-threatening condition due to space-occupying cerebral edema that usually peaks within 2 to 5 days after stroke onset [6, 21, 24]. The mortality is approximately 80% despite optimal intensive care treatment [1, 9, 19]. Surgical intervention with decompressive craniectomy was introduced already in 1956 [22], and three recent European randomized controlled trials have demonstrated that surgery improves survival [11, 13, 30]. However, the pooled analysis from these trials showed that even with surgery, 22% of the patients do not survive [29]. Predictors of short-term mortality after decompressive craniectomy are therefore important to identify in order to facilitate the decision-making regarding surgical or conservative treatment of the individual patient. High levels of malondialdehyde, a biomarker of lipid oxidation, higher age, additional anterior and/or posterior cerebral artery involvement, and midline shift are possible predictors of early mortality [3, 16, 18]. Time from stroke onset to decompressive craniectomy and the degree of preoperative neurological impairment assessed by the National Institutes of Health Stroke
Scale (NIHSS) [2] have also been shown to be prognostic factors [3, 15, 33]. However, other studies have not been able to confirm these results [8, 32], and found only concurrent anterior cerebral artery (ACA) involvement to be associated with early mortality [32].

The aim of the present study was to identify predictors of early in-hospital death in a cohort of patients with SMCAI operated with decompressive craniectomy during a 12-year time period.

Methods

Study design and participants

All patients operated with decompressive craniectomy for SMCAI at the Department of Neurosurgery, Oslo University Hospital Rikshospitalet, Oslo, Norway, between May 1998 and October 2010, were included. Our department served a population of 2.7 million people in a well-defined catchment area in southeast Norway. Patients were transferred from local neurological departments when they were considered possible candidates for decompressive craniectomy. Surgery was performed when the patient’s level of consciousness was declining, consistent with space-occupying cerebral swelling, visualized on computed tomography (CT). The study methods are described in detail in a previous publication [26].

Surgical procedure

A standard frontotemporoparietal craniectomy was performed whereupon the dura mater was opened in astellate fashion. The craniectomy was made as large as possible in the anteroposterior direction, and basally, at the level of the pineal gland, to prevent brain stem compression. A dura substitute (Neuro-Patch® Aesculap AG, Tuttingen, Germany) was then placed over the cerebral cortex, and the opened dura repositioned over the substitute. No patients underwent resection of brain tissue. During later years, a second dura substitute was positioned between the dura and the temporal muscle in order to facilitate surgical dissection of the temporal muscle during replacement of the patients’ cryopreserved bone. The subcutis and cutis were closed separately. A drainage (Abdovac™ Wellspect HealthCare, Mölndal, Sweden) was placed subcutaneously, and an intracranial pressure sensor (Johnson & Johnson, New Brunswick, NJ, USA) were placed for postoperative monitoring.

Data collection

We identified eligible patients through a search of all patients admitted with the diagnosis of stroke, and by reviewing all relevant medical records and surgical reports. Data recorded were age, sex, comorbidities (cancer, hypertension, heart disease, previous stroke or transient ischemic attack, and diabetes mellitus), NIHSS score on admission with a higher score representing increased functional impairment, time from stroke onset to decompressive craniectomy, dominant side, and time of death. Time of stroke onset was obtained from the emergency medical services records.

Pre- and postoperative cerebral CT was carried out with a multidetector scanner using bone algorithm, display field of view (dFOV) 15–18 cm, between 80 and 100 mA and 120 KV, 1-mm increment with coronal and sagittal reconstructions. The images were assessed to identify infarction territory (middle cerebral artery [MCA], ACA, posterior cerebral artery [PCA]), pineal gland displacement, reduction of pineal gland displacement after surgery, and craniectomy size. All scans were evaluated by a senior neuroradiologist (EAJ) who was blinded to the clinical outcome.

Follow-up of the patients discharged from hospital alive was conducted as home visits (n = 18) (JS, AS), or outpatient assessments (n = 12) (JS, BT, MA).

Ethical considerations

The study was approved by the Regional Committee for Medical and Health Research Ethics, and the data protection official for research. Surviving patients, their care takers, or closest relatives were contacted by the first author (JS) by phone and informed about the study. All agreed to receive an informational letter about the trial, and all but one accepted participation. Written consent was given by the patients, close relatives, or legal guardians.

Statistical analysis

Categorical variables are presented as frequencies and percentages. Between-group differences were determined by χ² statistics or Fisher’s exact test, as appropriate. Continuous normally distributed data are presented as means and standard deviations (SD), and non-parametric data as medians and interquartile ranges (IQR). Between-group differences were determined by independent two-sample t test or Mann–Whitney U test depending on assumptions on statistical distribution.

To identify predictors of early in-hospital death after decompressive craniectomy, logistic regression analyses were performed. Candidate variables (age, sex, time from stroke onset to decompressive craniectomy, NIHSS on admission, infarction territory, pineal gland displacement, reduction of pineal gland displacement after surgery, and craniectomy size) were chosen because of their predictive value as described in the literature, or because we considered them to be of importance. Variables were eliminated stepwise from the multivariate logistic regression model, removing those with a significance level p ≥ 0.2. The limit of 0.2 was chosen since even
higher $p$ values ($p < 0.2$ or $p < 0.5$) have been found to provide more power for the selection of predictors with relatively weak effects, and to provide better predictions in small data sets with a set of established candidate predictors [25]. Results are presented as odds ratios (ORs) with 95% confidence intervals (CI). Nagelkerke $R^2$ was used as goodness-of-fit measure, with values ranging from 0 to 1, where higher values indicate better model fit.

$p < 0.05$ was used as a level of significance. IBM SPSS Statistics 22 (IBM Corporation, Armonk, NY, USA) was used for all analyses.

## Results

From May 1998 to October 2010, a total of 45 patients (58% male) with SMCAI underwent decompressive craniectomy. Their mean age (SD) was 48.1 (11.6) years (range, 19–74 years). The mean age of females was 48.8 (11.4) years (range, 21–74 years), and of males 47.5 (12.0) years (range, 19–66 years). The median time from stroke onset to decompressive craniectomy was 46.7 h (IQR, 30.7–72.7 h). The speech-dominant hemisphere was affected in 20 patients (44%), of which 19 have been previously presented [26]. The MCA territory was affected in 33 patients (73%), MCA and ACA territory in ten patients (22%), and MCA and PCA territory in two patients (4%).

Fourteen patients (31%) died during primary hospitalization at a median of 7 days after decompressive craniectomy (range, 3–44 days). All died due to herniation secondary to the ischemic edema. The surviving patients were followed for a median of 66 months (IQR, 32–93 months). Two patients (4%) died during follow-up, a 74-year-old woman after 510 days from unknown causes, and a 47-year-old woman after 1921 days from burn injuries at a nursing home. One patient refused to participate in the study.

The patients’ characteristics are presented in Table 1. In the early mortality group, 42.9% of the patients had MCA infarction with additional ACA and/or PCA territory involvement, compared to 19.4% of the survivors. The preoperative mean pineal gland displacement was 6.3 mm in the early mortality group, and 5.5 mm among the survivors. The differences between the groups did not reach statistical significance.

In the univariate regression model, the variables age, NIHSS on admission, and infarction territory reached $p < 0.20$ (Table 2), and were subjected to the multivariate analysis. After stepwise elimination, only middle cerebral artery infarction with additional anterior and/or posterior cerebral artery territory involvement was associated with early inhospital death (OR, 12.7; 95% CI, 0.01–0.77; $p = 0.029$). The model had a Nagelkerke $R^2$ of 0.40.

## Discussion

SMCAI is a life-threatening condition, and decompressive craniectomy has been shown to reduce mortality significantly. However, even with decompressive surgery, many patients do not survive the initial postoperative phase. In the present study, MCA infarction with additional ACA and/or PCA territory involvement was identified as a predictor of early inhospital death after decompressive craniectomy.

Our findings, that additional ACA involvement was identified as a predictor of early mortality in SMCAI, are in accordance with the results of previous studies [3, 15, 16, 18, 32, 33], but there is no consensus among physicians regarding factors which may have an impact on the decision-making in relation to surgical treatment.

Age is described as a predictor of early mortality after decompressive craniectomy for SMCAI in several studies [3, 8, 16, 18], but others have failed to find such an association [27]. The pooled analysis of the three European randomized controlled trials, including patients < 60 years, showed a 30-day mortality of 22% [29]. This is comparable to a 21-day mortality of 20% in a North American trial, including patients up to 75 years of age [7]. In the present study, the patients who died during primary hospitalization were somewhat older, but age did not predict early in-hospital death.

Preoperative neurological impairment, assessed by the NIHSS score, has been shown to be a predictor of mortality [15, 33]. Kim and colleagues identified a NIHSS score >18 on admission as an independent predictor of life-threatening brain swelling [14]. In our study, the NIHSS score on admission did not predict early in-hospital death, which is consistent with the results of Walcott and colleagues [32].

A prolonged time from stroke onset to decompressive surgery is another factor previously shown to predict early mortality or worse clinical outcome [3, 5]. This is not consistent with the present results, where patients who died during primary hospitalization were operated on almost 10 h earlier than those who were discharged alive (39.8 vs. 49.1 h). The most likely explanation for this difference is, however, that the patients who were operated on earlier, where those who suffered from the most rapid development of life-threatening brain swelling and thus, a swifter deterioration in clinical condition. This also complies with the fact that more patients in this group had additional infarction territory involvement compared to those who survived (42.9 vs. 19.4%).

The degree of midline shift at the time of decompressive craniectomy has been associated with early mortality [18], and a postoperative midline shift of <5 mm is associated with favorable outcome [28]. The impact of lateral displacement
of the pineal gland on the level of consciousness in patients with acute hemispheric mass was assessed by Ropper, and a displacement of > 6 was associated with stupor or coma [20]. To our knowledge, no previous study has assessed the degree of pineal gland displacement at the horizontal level of the brainstem as a predictor of early mortality in SMCAI. We chose to use the pineal gland instead of septum pellucidum midline shift to assess the degree of hemisphere swelling due to (1) the calcification of the pineal gland being a specific measuring point, equal from patient to patient, (2) the level of the maximal midline shift varying between patients, and (3) the largest midline shift depending on how the CT scans are

Table 1  Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Early mortality n = 14</th>
<th>Survival n = 31</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>49.6 (11.8)</td>
<td>47.4 (11.7)</td>
<td>0.55</td>
</tr>
<tr>
<td>Male</td>
<td>7 (50.0)</td>
<td>19 (61.3)</td>
<td>0.48</td>
</tr>
<tr>
<td>Comorbiditya</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancerb</td>
<td>0</td>
<td>3 (9.7)</td>
<td>0.54</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (21.4)</td>
<td>7 (22.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Heart diseasec</td>
<td>4 (28.6)</td>
<td>7 (22.6)</td>
<td>0.72</td>
</tr>
<tr>
<td>Previous stroke or TIAd</td>
<td>2 (14.3)</td>
<td>2 (6.5)</td>
<td>0.58</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (14.3)</td>
<td>4 (12.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>NIHSS on admission, mean (SD)</td>
<td>14.4 (6.1)</td>
<td>15.1 (4.8)</td>
<td>0.65</td>
</tr>
<tr>
<td>Timee in hours, median (IQR)</td>
<td>39.8 (25.1–56.4)</td>
<td>49.1 (33.0–76.8)</td>
<td>0.15</td>
</tr>
<tr>
<td>Dominant side</td>
<td>5 (35.7)</td>
<td>15 (48.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>Additional territoryf</td>
<td>6 (42.9)</td>
<td>6 (19.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>Pineal gland displacement in mm, mean (SD)</td>
<td>6.3 (1.5)</td>
<td>5.5 (2.6)</td>
<td>0.40</td>
</tr>
<tr>
<td>Reduction of pineal gland displacement in mm, mean (SD)</td>
<td>1.4 (2.6)</td>
<td>2.2 (2.3)</td>
<td>0.45</td>
</tr>
<tr>
<td>Cranietectomy size in cm, mean (SD)</td>
<td>13.1 (0.9)</td>
<td>12.5 (1.0)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

SD standard deviation, TIA transient ischemic attack, IQR interquartile range, NIHSS National Institutes of Health Stroke Scale

Results are n and (%), unless indicated otherwise

a Prior to stroke
b Known prior to craniectomy and considered stable disease
c Coronary heart disease and/or atrial fibrillation
d Without sequelae
e Time from stroke onset to decompressive craniectomy
f Middle cerebral artery and anterior and/or posterior cerebral artery territory

Table 2  Logistic regression of predictors of early mortality after decompressive craniectomy for swollen middle cerebral artery infarction

<table>
<thead>
<tr>
<th></th>
<th>Univariate regression</th>
<th>Multivariate regression after stepwise elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>0.96–1.08</td>
</tr>
<tr>
<td>Male</td>
<td>0.63</td>
<td>0.18–2.26</td>
</tr>
<tr>
<td>Time</td>
<td>1.00</td>
<td>0.99–1.00</td>
</tr>
<tr>
<td>NIHSS on admission</td>
<td>0.97</td>
<td>0.86–1.10</td>
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<td>Territory</td>
<td>3.57</td>
<td>0.87–14.60</td>
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<tr>
<td>Pineal gland displacement</td>
<td>1.16</td>
<td>0.83–1.63</td>
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<tr>
<td>Reduction of pineal gland displacement</td>
<td>0.87</td>
<td>0.62–1.23</td>
</tr>
<tr>
<td>Cranietectomy size</td>
<td>1.81</td>
<td>0.81–4.07</td>
</tr>
</tbody>
</table>

OR odds ratio, CI confidence interval, NIHSS National Institutes of Health Stroke Scale

a Time from stroke onset to decompressive craniectomy
b Middle cerebral artery and anterior and/or posterior cerebral artery territory
reconstructed, and possibly varying between patients. We found a larger pineal gland shift before decompressive surgery, and less reduction of shift after surgery in the early mortality group. However, the difference did not reach statistical significance, and pineal gland displacement did not predict early in-hospital death.

The size of the craniectomy in decompressive surgery for SMCAI may vary, depending on the surgeon, and several studies postulate that the craniectomy size should be at least 12 cm in the largest anteroposterior diameter [10, 12, 17, 23]. Accordingly, Wagener and colleagues found that a craniectomy size of less than 12 cm in diameter could cause more cortical damage, and decreased survival [31]. In the present study, however, we could not reveal any association between craniectomy size and early in-hospital death.

The finding that additional ACA and/or PCA territory involvement was a significant predictor of early in-hospital death after decompressive craniectomy was somewhat expected, because larger infarcts are assumed to be associated with higher mortality. The fact, however, that none of the other variables predicted early death is perhaps as important, and shows that the decision-making regarding surgical or non-surgical treatment is still difficult.

Limitations of our study

The study is a retrospective observational cohort study, and statistical analyses may thus have suffered from anticipated deficiencies related to loss of patient information. Further, the radiological analyses were conducted by one senior neuroradiologist and not by two independent radiologists by consensus or as interobserver variation with kappa statistics. The relatively small sample size also precludes firm conclusions.

Conclusions

MCA infarction with additional ACA and/or PCA territory involvement was identified as a significant predictor of early in-hospital death after decompressive craniectomy in SMCAI. However, the study’s small sample size precludes reliable conclusions.

Acknowledgements We thank all patients and their close relatives for their benevolent participation.

Compliance with ethical standards

Funding Gidske and Peder Jacob Sørensens’ research foundation provided financial support for the study to be completed. The sponsor had no role in the design or conduct of this research.

Conflict of interest None.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study, their close relatives or legal guardians.

References


