Hemicraniectomy versus medical treatment with large MCA infarct: a review and meta-analysis

Paul Alexander,1 Diane Heels-Ansdell,2 Reed Siemieniuk,2,3 Neera Bhatnagar,4 Yaping Chang,2 Yutong Fei,2,5 Yuqing Zhang,2 Shelley McLeod,6 Kameshwar Prasad,7 Gordon Guyatt2

ABSTRACT

Objective: Large middle cerebral artery stroke (space-occupying middle-cerebral-artery (MCA) infarction (SO-MCAi)) results in a very high incidence of death and severe disability. Decompressive hemicraniectomy (DHC) for SO-MCAi results in large reductions in mortality; the level of function in the survivors, and implications, remain controversial. To address the controversy, we pooled available randomised controlled trials (RCTs) that examined the impact of DHC on survival and functional ability in patients with large SO-MCAi and cerebral oedema.

Methods: We searched MEDLINE, EMBASE and Cochrane library databases for randomised controlled trials (RCTs) enrolling patients suffering SO-MCAi comparing conservative management to DHC administered within 96 hours after stroke symptom onset. Outcomes were death and disability measured by the modified Rankin Scale (mRS). We used a random effects meta-analytical approach with subgroup analyses (time to treatment and age). We applied GRADE methods to rate quality/confidence/certainty of evidence.

Results: 7 RCTs were eligible (n=338 patients). We found DHC reduced death (69–30% in medical vs surgical groups, 39% fewer), and increased the number of patients with mRS of 2–3 (slight to moderate disability: 14–27%, increase of 13%), those with mRS 4 (severe disability: 10–32%, increase of 22%) and those with mRS 5 (very severe disability 7–11%, increase of 4%) (all differences p<0.0001). We judged quality/confidence/uncertainty of evidence high for death and severe disability, low for functional outcome mRS 0–3, and moderate for mRS 0–4 (wide CIs and problems in concealment, blinding of outcome assessors and stopping early).

Conclusions: DHC in SO-MCAi results in large reductions in mortality. Most of those who would otherwise have died are left with severe or very severe disability; for example, inability to walk and a requirement for help with bodily needs, though uncertainty about the proportion with very severe, severe and moderate disability remains (low to moderate quality/confidence/uncertainty evidence).

Strengths and limitations of this study

- Inclusion of all published randomised trial data.
- Reproducible duplicate assessment of both eligibility and risk of bias.
- Appropriate sensitivity and subgroup analyses and, rating of the quality of evidence using the GRADE approach.
- Those of the primary studies, for example, risks of bias problems included lack of concealment of randomisation, lack of blinding of outcome assessors and stopping early because of large effects.
- Small sample sizes.

BACKGROUND

Large cerebral infarction is typically associated with devastating clinical outcomes, including severe neurological disability, brain herniation and death.1–8 Massive malignant middle-cerebral-artery (MCA) infarction (space-occupying MCA infarction (SO-MCAi)) is particularly devastating; cerebral oedema that occurs in the fixed intracranial space results in increasing intracranial pressure (ICP), increasing ischaemic cell death and in many instances leading to brain herniation and death.7–13

Customary treatment for acute stroke and severe oedema is to reduce ICP using hyperosmotic agents, artificial ventilation and hyperventilation, therapeutic hypothermia, elevated head position and sedatives.14 Clinical trial evidence to support these strategies is, however, unavailable and they are at best modestly effective.14 15

Surgical decompression with hemicraniectomy and durotomy/duroplasty (external decompression involving removal of cranium overlying the oedematous brain tissue) is an aggressive approach that rapidly reduces...
ICP\textsuperscript{15} \textsuperscript{16} and thus may have a beneficial effect on neurological outcomes.\textsuperscript{8} \textsuperscript{16} \textsuperscript{17} At the same time there are risks involved with hemicraniectomy including hydrocephalus, external brain tamponade, sinking skin flap syndrome, seizures, cerebral haemorrhage and paradoxical brain herniation.\textsuperscript{17} \textsuperscript{18} \textsuperscript{19} \textsuperscript{20} More important, if hemicraniectomy reduces death but survivors suffer severe permanent disability, the value of the benefit may be questionable.

In this review we examined the effects of decompressive hemicraniectomy versus medical management (at times referred to as best management, standard care or conservative management) in patients suffering SO-MCAi with threatened brain oedema on mortality risk and disability at 6 months to 1 year. The included studies, and the essential conclusions, are similar to other recent systematic reviews of this question.\textsuperscript{21} \textsuperscript{22} \textsuperscript{23} This review is the first to use the GRADE approach to summarise the evidence, uses all available data and provides a schematic presentation (numbers and percentages at each Rankin Score cut-point) of results. The resulting perspective is likely to be particularly useful for clinicians in shared decision-making with patients’ families.

METHODS

Eligible studies: (1) were RCTs (2) included patients suffering major stroke (MCA) with threatened brain oedema or evidence of increased intracranial pressure (3) assigned patients to either conservative or usual best medical practice (the control group) or hemicraniectomy (intervention group) within 96 hours after the onset of stroke symptoms and (4) reported at least death, or disability using the modified Rankin Scale (mRS), with follow-up of at least 6 months to 1 year (12 months; table 1).

Table 1 The modified Rankin Scale\textsuperscript{24} \textsuperscript{25}

<table>
<thead>
<tr>
<th>Rankin score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No disability; no symptoms at all</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms: able to carry out all usual activities despite symptoms</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability: no assistance with one won affairs but unable to carry out all previous activities</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability: requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability: requiring assistance to walk and to attend to own bodily needs</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability: bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

Search

We accepted that a Cochrane review\textsuperscript{21} had conducted a comprehensive search up to October 2010. For our 2015 updated meta-analysis and electronic searching, we searched (1) MEDLINE (August 2010–January 2015) (2) EMBASE (August 2010–January 2015) (3) the Cochrane Database for Systematic Reviews (up to January 2015) and (4) Cochrane CENTRAL for clinical trials based on the search strategy in the prior Cochrane review.\textsuperscript{21} We enlisted the help of a medical librarian. We also searched the reference lists of all eligible articles or related reviews.

Eligibility determination, risk of bias, data abstraction and quality of evidence assessment

Following calibration exercises, reviewers, working independently in pairs, identified and retrieved the full texts of potentially eligible titles and abstracts. Subsequently, working independently and in pairs, reviewers made final adjudication of eligibility, judged risk of bias and abstracted data. For all eligibility determination, risk of bias assessment and data abstraction, reviewers resolved disagreement through discussion and, if necessary, third party adjudication. Reviewers used a modified Cochrane Risk of Bias Tool\textsuperscript{26} \textsuperscript{27} using response options of ‘yes’, ‘probably yes’, ‘probably no’ and ‘no’; the first two categories represented low risk of bias, and the latter two high risk of bias. This eliminated the often elevated ‘unclear’ response options.

We sought to collect data on a variety of trial characteristics and functional measures including the National Institutes of Health Stroke Scale, the Barthel index and the Hamilton Depression Rating Scale. The data proved, however, too incomplete to be informative. Therefore, we focused on the outcomes of death and disability measured by the modified mRS.\textsuperscript{24} \textsuperscript{25}

We used the GRADE approach\textsuperscript{28} \textsuperscript{30} to rate the quality (certainty or confidence in effect estimates) of the body of evidence for death and disability. We considered issues of risk of bias (allocation concealment, blinding, incomplete data), consistency of study estimates (heterogeneity), directness (applicability of evidence to the study question), precision (95% CIs) and publication bias, and summarised results in an evidence profile.\textsuperscript{31} We were prepared to assess the impact of loss to follow-up at the level of the entire body of evidence.\textsuperscript{32}

Analysis

For eligibility decisions and for rating risk of bias we calculated chance-corrected agreement using $\kappa$.\textsuperscript{33} Studies measured outcome at several time points; we focused on and present data/analysis at 12 months. We built forest plots and conducted meta-analyses calculating the pooled relative treatment effects (relative risks (RR)) and associated 95% CIs using random-effects inverse variance weighted modelling using thresholds of (1) dead or alive. (2) mRS of 3 or less versus $>$3 and (3) mRS of 4 or less versus $>$4.
We measured heterogeneity using Cochrane-Q and I² statistics and generated a priori hypotheses to explain heterogeneity including age of patients (<60 vs >60 years), anticipated benefit greater in those under 60 years), and timing of surgery (intervention <48 hours vs ≥48 hours from symptom onset (up to 96 hours), anticipated benefit greater in earlier intervention). We used the χ² test for subgroup differences to explore age and timing interactions for the outcome of mortality. Review Manager V.5.2.7 software was used to perform the meta-analyses.

We calculated the total number and percentage of patients in the intervention and control groups who, at 12 months, were classified as mRS 1 and 2, 3, 4, 5 and 6. The Cochran-Mantel-Haenszel χ² test for combining over multiple tables was used to test the differences in distributions. We modelled based on assumptions of ordinal and conducted a sensitivity analysis assuming non-ordinal data. We used the 6-month data which was the only data provided for one trial and conduct this (HeADDFIRST35) and conducted a sensitivity analysis omitting these data.

RESULTS
Figure 1 presents the process by which we determined that, of the 1159 citations identified, seven17 35–40 proved eligible for review inclusion (see online supplementary material file for an example of the MEDLINE search strategy). Agreement (κ) for the full title and abstract screening was 0.85, and for the full text screening 0.76. Inter-rater agreement on individual domains of the risk of bias tool ranged from 0.80 to 1.0 across the seven domains.

Effects of interventions
Table 2 presents trial characteristics. All included patients had suffered SO-MCAi and all included trials except for one40 were multicentre in design. Only seven patients were lost to follow-up17 40 and thus no adjustments for attrition32 were necessary. The seven trials that met the eligibility criteria were published from 2007 to 2014 and included 338 patients with 165 allocated to surgery group and 173 to medical management. The six trials that reported complete 12-month data involved 151 patients in the surgical group and 163 in the...
<table>
<thead>
<tr>
<th>Name, publication year and reference number, first author surname</th>
<th>Duration from symptoms onset to treatment</th>
<th>Age (years) inclusion; median age years (mean)</th>
<th>n treatment/ n control; % females</th>
<th>Rationale for timing of termination</th>
<th>Surgery vs medical management (conservative treatment/ standard care)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESTINY II 2014, Germany, Jüttler</td>
<td>Within 48 hours after the onset of symptoms</td>
<td>Over 60 years; 70</td>
<td>47/62; 50%</td>
<td>Anticipated sample size ~130 patients. Sequential analysis allowed for repeated interim analyses; trial stopped as soon as reached statistical significance for ‘success’ (proportion mRS 4 or less).</td>
<td>Hemicraniectomy and duroplasty vs basic therapy in the ICU for stroke; osmotherapy with the use of mannitol, glycerol or hypertonic hydroxyethyl starch; sedation; intubation and mechanical ventilation; hyperventilation; and administration of buffer solutions.</td>
</tr>
<tr>
<td>DESTINY I 2007, Germany, Jüttler</td>
<td>&gt;12 to &lt;36 hours</td>
<td>18–60 years; 44.5</td>
<td>17/15; 53%</td>
<td>Planned sample size of 188 patients; and after inclusion of 32 patients, the trial was interrupted according to the protocol because reached significance for the 30-day mortality end point.</td>
<td>Hemicraniectomy plus conservative vs osmotherapy; intubation and mechanical ventilation; hyperventilation; venous oxygenation; ICP monitoring; sedation; BP monitoring; head positioning; body core temperature; blood glucose level; fluid management; prophylaxis of DVT.</td>
</tr>
<tr>
<td>DECIMAL 2007, France, Vahedi</td>
<td>Within 24 hours</td>
<td>18–55 years; (43.4)</td>
<td>20/18; 53%</td>
<td>Anticipated sample size of 60 patients; sequential analysis planned, stopped after the 38th patient due to slow recruitment, a large difference in mortality between the two groups, and a planned meta-analysis with ongoing European trials.</td>
<td>Hemicraniectomy with or without duroplasty plus standard treatment vs intubation; head positioning to an angle of 30°; intravenous fluid restriction; intravenous mannitol or furosemide; intravenous antihypertensive agents; prophylactic use of anticonvulsants.</td>
</tr>
<tr>
<td>HAMLET 2009, Netherlands, Hofmeijer</td>
<td>Within 4 days (96 hours)</td>
<td>18–60 years; (48.7)</td>
<td>32/32; 41%</td>
<td>Planned sample size 112, stopped early apparently because of large significant effect.</td>
<td>Hemicraniectomy vs management in ICU consisting of osmotherapy with mannitol or glycerol; intubation and mechanical ventilation; hyperventilation; invasive monitoring of ICP; sedation; muscle relaxants; treatment of elevated BP; elevation of the head to an angle of 30°; maintenance of normothermia, normoglycaemia and normovolaemia.</td>
</tr>
<tr>
<td>HeADDFIRST 2014 pilot, USA and Canada, Frank</td>
<td>Within 4 days (96 hours)</td>
<td>18–75 years; 54</td>
<td>14/10; 38%</td>
<td>Planned sample size was 75 patients, trial stopped after 26 patients randomised because of judgement that we had achieved our aims for the pilot study without further details.</td>
<td>Hemicraniectomy and durotomy vs airway management; ventilator settings; BP control and agents; fluid and electrolyte management; gastrointestinal and nutritional management; haematological monitoring and management; ICP monitoring; sedation; use of mannitol; anticonvulsants; prophylaxis against DVT; and rehabilitation.</td>
</tr>
<tr>
<td>Decompressive Hemicraniectomy 2012, China, Zhao</td>
<td>Within 48 hours</td>
<td>18–80 years; 64</td>
<td>24/23; 28%</td>
<td>Planned sample size was 110; trial was stopped after 47 patients recruited because of large, significant effect.</td>
<td>Hemicraniectomy plus duroplasty vs head positioning; osmotherapy; administration of intravenous mannitol or glycerol; fluid management; intravenous fluid restriction; pulmonary function and airway protection; intubation and mechanical ventilation; cardiac care; BP management; blood glucose management; sedation; no seizure prophylaxis; prevention of DVT and PE.</td>
</tr>
<tr>
<td>Decompressive Hemicraniectomy 2012, Latvia, Slezins</td>
<td>Surgery within 48 hours after onset</td>
<td>Less than and greater than 60 years; (61.5)</td>
<td>11/13; 43%</td>
<td>No information provided in intended sample size of whether trial went to conclusion</td>
<td>Hemicraniectomy plus best medical treatment group or the best medical treatment (BMT) alone group. No details were provided on the BMT approach.</td>
</tr>
</tbody>
</table>

BP, blood pressure; DVT, deep-vein thrombosis; ICP, intracranial pressure; ICU, intensive care unit; PE, pulmonary embolism.
medical group (n=314). Of the 338 patients, 134 participated in three trials37–39 that enrolled only patients under 60 years of age, 95 participated in three trials35 36 40 (one of which was based on 6-month data35) that enrolled patients both over and under 60 years, and 109 in one trial17 that enrolled only patients over 60 years.

Figure 2 presents our assessment of risk of bias for the seven eligible studies. Important limitations include lack of concealment of randomisation in four studies, lack of blinding of outcome adjudicators in three studies, and stopping early because of large effects in five studies.

Figure 3A presents the observed distributions of Rankin scores in those patients who did and did not receive hemicraniectomy for all seven trials (including six trials with 12-month follow-up and one with 6-month follow-up data (p for difference in distributions <0.00001)). Based on figure 3A, the hemicraniectomy group experienced 39% fewer deaths, 4% more patients in mRS category 5, 22% more in category 4, and 13% more in categories 3 or 2. Results were similar excluding patients with only 6-month follow-up. The distribution of disability and death was also similar in the five trials that provided 6-month data (figure 3B). The one trial that followed patients to 36 months41 suggested minimal differences in groups in those with mild to moderate disability.

Hemicraniectomy increased the likelihood of being a survivor (alive; figure 4) when compared with best medical treatment (RR 2.05, 95% CI 1.54 to 2.72, p<0.00001, I² of 26%) (high-quality evidence, table 3). Considering a mRS threshold of 3 or less versus 4 or 6 (severe disability and death), surgery increased the likelihood of being alive and mRS 4 or less (RR 2.25, 95% CI 1.51 to 3.35, p<0.0001, I² 40%, figure 6, moderate quality evidence, table 3).

Subgroup/sensitivity analyses
The χ² interaction test (test for subgroup differences) suggested similar effects in mortality for age (≤60 and >60 years old) (p=0.38) and for duration between symptom onset and treatment initiation (up to 48 hours vs 96 hours) (p=0.59). Any differences could be explained by chance.

DISCUSSION
Main findings
Evidence from seven randomised trials17 35–40 in our pooled analysis demonstrates that surgical decompression for SO-MCAi with threatened oedema results in large reductions in mortality (figure 4). Our results emphasise that most of the additional survivors will be left with what many, perhaps most individuals, would consider severe disability—unable to ambulate and needing help with basic needs (potentially all bodily needs), though the proportion with severe versus very severe disability is uncertain (low-quality evidence, table 3). The increase in the proportion of patients left with mild to moderate disability is small and uncertain (low/moderate quality evidence, table 3).

Subgroup analyses failed to provide convincing evidence that the impact of mortality differs depending on the timing of surgery or the age of the patient.

Strengths and limitations
Strengths of our study include explicit eligibility criteria, a comprehensive search, inclusion of all randomised trial data,17 35–40 rigorous assessment of risk of bias and reproducible duplicate assessment of both eligibility and risk of bias. We conducted appropriate sensitivity and subgroup analyses and, in addition, rated the quality of evidence using the GRADE approach,28–31 a particular contribution of our work.

More specifically, GRADE is a system28–31 for rating not individual studies, but rather bodies of evidence addressing the impact of interventions on patient-important outcomes. In the GRADE system, evidence based on a number of randomised trials begins as high quality, but can be rated down according to any of the five categories of limitations. If individual studies have failed to conceal randomisation, to blind key personnel (in this case outcome assessors) or have stopped early for benefit (all problems in some studies in this review) the body of evidence may be rated down for risk of bias (as we have carried out for functional outcomes in this

Figure 2 Risk of bias assessment.
review). If sample sizes and number of events are small, and CIs are very wide, quality may be rated down for imprecision (as was the case for functional outcomes in these studies). Other limitations include indirectness (eg, the population enrolled differs from the population of interest), inconsistency (widely divergent results across studies) and publication bias (none of which proved concerns in this review).

An additional strength is the presentation of the numbers/frequencies and percentages by mRS cut-off point in figures 3A, B as a means to aid clinicians, surgeons, patients, caregivers and all those involved with

![Figure 3](image3.png)

(A): Functional outcome after hemicraniectomy and after medical (conservative) treatment according to the modified Rankin Scale score. (B): Functional outcome after hemicraniectomy and after medical (conservative) treatment according to the modified Rankin Scale score (6 months data, five trials).

![Figure 4](image4.png)

Figure 4 Forest Plot Alive (mRS 0-5) versus Death (mRS=6) at 12 months. mRS, modified Rankin Scale.
Table 3  GRADE evidence profile

Patients: aged 18 years and above suffering massive MCA
Intervention: decompressive hemicraniectomy surgery
Comparator: best (standard) medical management
Outcome: death and/or disability at 12 months follow-up based on mRS scores

<table>
<thead>
<tr>
<th>Quality assessment</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Absolute effect</th>
<th>Quality/certainty of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRS cut-off point; n of studies</td>
<td>Design</td>
<td>Risk of bias</td>
<td>Consistency</td>
<td>Direct-ness</td>
</tr>
<tr>
<td>mRS 0-5 vs 6 (death); n=7</td>
<td>Randomised controlled trials*</td>
<td>No Serious risk of bias</td>
<td>No serious inconsistency†</td>
<td>No serious indirect-ness‡</td>
</tr>
<tr>
<td>mRS 0-3 vs 4-6; n=7</td>
<td>Randomised controlled trials*</td>
<td>Serious¶</td>
<td>No serious inconsistency†</td>
<td>No serious indirect-ness‡</td>
</tr>
<tr>
<td>mRS 0-4 vs 5 and 6; n=7</td>
<td>Randomised controlled trials*</td>
<td>Serious¶</td>
<td>No serious inconsistency†</td>
<td>No serious indirect-ness‡</td>
</tr>
</tbody>
</table>

*Six trials that reported complete 12-month follow-up mRS data and one trial based on 6-month follow-up data from the pooled analysis; note while we judged low risk of bias, the reporting of sequence generation could be substantially improved.
†Statistical consistency (heterogeneity): χ² tests were not significant and I²s were generally low (<50%).
‡Directness: we judged that there was directness as there was clear applicability of study patients to the research question (similar patients); there were no indirect comparisons reported as part of the included trials.
§Based on our exhaustive literature search and the absence of problems of industry funding, we judged that the risk of important publication bias was low.
¶We rated down for risk of bias because in four studies allocation was not concealed, in three studies outcome assessors were not blind to allocation and all but two studies stopped early for benefit. We did not rate down for the outcome of mortality because it is not subject to bias in outcome assessment.
**Precision: we rated down particularly due to imprecision of estimates as a result of total small sample size and small number of events (particular imprecision was for mRS 0-3).

MCA, middle cerebral artery infarction; mRS, modified Rankin Scale; RR, risk ratio.

treatment and care decisions presurgery and postsurgery. Indirect evidence to support such a pictorial representation comes from studies of optimal formats for presenting information to patients and families in the setting of shared decision-making. Limitations of our review are those of the primary studies. Risks of bias problems as mentioned include lack of concealment of randomisation, lack of blinding of outcome assessors and stopping early because of large effects (figure 2 and table 3). Sample sizes were small, and the number of events in those with mild to moderate disability was particularly small (44 in surgery arm and 24 in medical intervention arm).

The use of the mRS as the sole measure of patients’ status after stroke represents another limitation. Limitations of the instrument include the subjective judgement required in making the rating without detailed guidance, and its failure to address the subjective experience (quality of life) of the stroke survivors.

Relation to prior work
Our results are largely consistent with those of other recent reviews of randomised trials of hemicraniectomy after MCA stroke. None of the prior reviews, however, have included all seven randomised controlled studies that contributed to our meta-analysis. Moreover, other reviews did not highlight the limitations associated with risk of bias and stopping early on the basis of results, nor did they apply the GRADE approach that highlights limitations in the evidence. These limitations include both risk of bias and limited sample size and number of events, particularly in the number of patients without severe disability (table 3).

One prior study is of note in that it addressed the cost implications of the trial results. Hofmeijer et al assessed clinical outcomes, costs and cost-effectiveness for the first 3 years in patients who were randomised to surgical decompression or best medical treatment using the HAMLET data. Results suggested that hemicraniectomy increases quality-adjusted life years (QALYs). The health gain comes, however, at large financial costs (€127 000 per QALY gained during the initial 3 years postsurgery with an estimated €60 000 per QALY gained during the patient’s lifetime). The Geurts et al follow-up study has also provided preliminary indications that the impact of surgery are maintained at 3 years post stroke, based on their re-examination of the HAMLET trial data.

Prior cohort studies raised the issue of optimal age limits for surgery. We however, found no evidence to suggest a different impact on mortality in those over and under 60 years.

Implications
Although hemicraniectomy reduces mortality, the majority of survivors face a life of severe disability associated...
with large caregiver burden. We have sought to highlight the latter implication of surgery given the challenges this presents to patients and caregivers.

A recent 2014 scientific statement regarding managing patients with a swollen ischaemic stroke in a cerebral or cerebellar hemisphere underscores this critical condition with potentially extensive disability, and the need for immediate, specialised neurointensive care with likely neurosurgical intervention. The American Heart Association/American Stroke Association guideline suggests that in patients with supratentorial hemispheric ischaemic stroke, decompressive craniectomy with dural expansion be the course of action in persons who exhibit continual deterioration neurologically. The guideline, while noting that some patients will benefit from the surgery (including those who are disabled but functionally independent), warns that a large proportion of patients who receive decompressive surgery will be significantly disabled with complete dependence on care.

A Statement for Healthcare Professionals from the Neurocritical Care Society and the German Society for Neuro-Intensive Care and Emergency Medicine (evidence-based guidelines for the Management of Large Hemispheric Infarction), also highlights the extensive disability that many patients undergoing decompressive craniectomy would confront. Their guideline notes the risks due to anaesthetics, surgical risks and the accompanying pain, infection, bleeding, headaches, seizures, neurological deficits and hydrocephalus. The guideline also points out the financial costs of surgery and subsequent care. Despite these warnings, the guideline, which uses GRADE methods recommends (1) decompressive hemi-craniectomy after hemispheric infarct (strong recommendation, high quality of evidence), (2) for older patients (>60 years of age), a greater reliance on patient and family input (strong recommendation, moderate quality of evidence) and (3) performing decompressive hemi-craniectomy within 24–48 hours of symptom onset and prior to any herniation symptoms (strong recommendation, moderate quality of evidence).

With the prospect for significant disability and thus extensive need for care, decisions regarding hemi-craniectomy are therefore high value and preference dependent. Thus, clinicians with access to hemi-craniectomy will need to engage in shared decision-making and counselling with families/caregivers of patients who have experienced devastating SO-MCAi and are at risk of death from herniation. The decisions are challenging and will be particularly dependent on attitudes toward living in the health state represented by mRS 4—the largest group of survivors (figure 3A)—that involves being unable to ambulate and dependent on others for at least some bodily needs. The quality of life of caregivers is also an area post-stroke and surgery that has been neglected in the published literature.

CONCLUSION

Although there is a large mortality reduction with hemi-craniectomy in patients with SO-MCAi, the disabled life that faces the survivors and the uncertain magnitude of the increase in the likelihood of surviving with small or moderate disability, will require family members/caregivers to seriously consider the values and preferences of the afflicted patient in deciding whether to proceed with surgery.

Author affiliations

1Department of Clinical Epidemiology and Biostatistics, Health Research Methods, McMaster University, Hamilton, Ontario, Canada
2Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada
3Department of Medicine, University of Toronto, Ontario, Canada
4Medical Librarian, Health Sciences Library, McMaster University, Hamilton, Ontario, Canada
5Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China
6Department of Family and Community Medicine, Schwartz/Reisman Emergency Medicine Institute, University of Toronto, Toronto, Ontario, Canada
7Department of Neurology, All India Institute of Medical Sciences, New Delhi, India

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Contributors PA took part in study concept and design, acquisition of data, analysis, writing (bulk of research work). DH-A was involved in study design, interpretation, statistical input, interpretation. RS was involved in design, editing, content analysis/interpretation. NB took part in design, search strategy, literature searching and editing. YC, YF, YZ were involved in screening, abstraction, risk of bias assessment, editing. SM was involved in initial study design and editing of various drafts. KP was involved in cosupervision, final editing/critical revisions, interpretation/important intellectual content. GG was involved in supervision, final editing/critical revisions, interpretation/important intellectual content. Rave provided initial screening of titles and abstracts and full texts but has no role in the design, analysis, writing or interpretation of this paper.

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Competing interests PA is a recent doctoral student graduate and is an assistant professor at McMaster University. He sits on no boards, receives or received no royalties, no stock options. Family members are not connected to academia and also receive no financial or non-financial payments related to this study as well as not related. He is involved in GRADE methods and a member of the GRADE methods working group. The use of GRADE in this study was to rate the certainty of the estimates of effect and not advocate for the use of GRADE. DH-A is a recent doctoral student graduate and an assistant professor at McMaster University. She sits on no boards, receives or received no royalties, no stock options. Her role is that of statistical analyst at McMaster University. She is a member of the CLARITY statistical group that provides statistical advice on analysis issues to McMaster researchers. RS is a medical student at the University of Toronto as well as student at McMaster University. He sits on no boards, receives or received no royalties, no stock options. NB is the medical librarian at McMaster University and sits on no boards, receives or received no royalties, no stock options. YC is a current doctoral student at McMaster University. She sits on no boards, receives or received no royalties, no stock options in any manner. YF is a visiting scholar from Beijing, China. She sits on no boards, receives or received no royalties, no stock options in any manner. YZ has recently graduated with a doctorate
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