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# Surgical interventions for malignant middle cerebral infarction--saving lives and functionality or increasing disabled survivors?

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## Evidence Based Medicine

### **Surgical interventions for malignant middle cerebral infarction — saving lives and functionality or increasing disabled survivors?**

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#### **Why is this study important?**

Malignant Middle Cerebral Artery infarctions are associated with 80% mortality. The patients affected are young and when cerebral oedema peaks at day three to four after stroke, herniation and death occurs. Since stroke affects Asians at a younger age, studies done on this disease are pertinent, especially if the interventions are technically possible in hospitals within Pakistan.

Before these studies were carried out, non randomized trials had shown that decompressive surgeries reduced mortality in these patients. But there was no mortality data from randomized studies and the long term outcome of the survivors was also not known.

The three trials were conducted independently in three

different European countries, DESTINY in Germany, DECIMAL in France and HAMLET in Netherlands. Before the completion of the trials it was decided that the results will be pooled since the trials had similar design and shared the same primary outcome measure. We present here the pooled results.

#### **Who were the participants?**

All three trials included patients who were 18-60 years of age and had presented with clinical deficits suggestive of large Middle cerebral artery infarction, their NIHSS score was >15 and they had radiological evidence of a large MCA infarction. The time window for inclusion in the pooled analysis was 45 hours, although for individual trials the window was 36 hours for DECIMAL and DESTINY and 96

hours for HAMLET. These patient characteristics are very similar to what we see here in our clinical practice, most of our patients are within this age range, and do manage to get to a tertiary care hospital within this time window.<sup>3</sup>

The projected sample sizes were larger but due to the opportunity of pooled analysis, all three trials were terminated early. A total of 93 patients were included in the pooled analysis. DECIMAL contributed 38 patients to the pooled analysis, DESTINY contributed 32 patients and HAMLET 23 patients. Hamlet went on to recruit a further 41 patients after the pooled analysis had been done.

### **What was the intervention?**

In all three trials the patients were randomized to either decompressive surgery or medical management and in all three trials the randomization was done centrally by a computer. Decompressive surgery consisted of a duraplasty and the creation of a large bone flap. In the conservative group, patients received best medical treatment on the basis of published guidelines for the management of acute ischaemic stroke and space-occupying brain oedema.

### **What was their outcome?**

In the pooled analysis the primary outcome measure was the score on the modified Rankin scale (mRS) at one year dichotomized between favourable (0-4) and unfavourable (5 or death). Secondary analyses included a dichotomization of the mRS, in which favourable outcome was defined as a score of 0-3 and unfavourable outcome as a score of 4 to death, and case fatality at 1 year.

For the primary outcome, fewer patients had an unfavourable outcome at 12 months (mRS 0-4), in the surgical arm, as compared to the conservative arm ( $p < 0.0001$ ). Significantly fewer patients had an mRS score greater than 3 at 12 months after surgical treatment than after conservative treatment ( $p < 0.014$ ). The survival rate at 12 months was higher after surgical treatment than after conservative treatment ( $p < 0.0001$ ).

The results of HAMLET show that surgical decompression within 4 days of symptom onset does not reduce poor outcome in patients with space-occupying hemispheric infarction, despite a substantial reduction in case fatality in these patients. Surgical decompression does, however, reduce the probability of a poor outcome in patients who were randomized within 48 hours of symptom onset. Therefore the decompressive surgery is beneficial if performed early on.

### **What were their conclusions?**

The authors conclude that after decompressive surgery

the probability of survival increases from 28% to nearly 80% and the probability of survival with an mRS of  $\geq 3$  doubles. mRS 3 means an individual with moderate disability who can still mobilize without assistance. However, the probability of surviving in a condition requiring assistance from others for walking and for bodily needs (mRS of 4) increases more than ten times. The choice of performing decompressive surgery in an individual patient with space-occupying hemispheric infarction will therefore depend on the willingness to accept survival with moderate disability. Information about quality of life of survivors is essential for guiding such decisions.

### **So is decompressive hemicraniectomy a feasible option in Pakistan?**

The three studies have clearly established that decompressive surgery has mortality benefit in large hemispheric infarctions if performed within 48 hours. They have also shown that the outcome of patients is also better with surgery. However, the risk of surviving with moderate disability increases.

These results raise several points to ponder before we adopt this as a "routine strategy in Pakistan". There are no chronic rehabilitation centers for stroke- so dealing with a larger proportion of disabled patients may be a challenge. Additionally, what the study does not address is whether patients of older age group i.e.  $>60$  years will also benefit from decompressive surgeries, so one must be restricted in offering this operation to all. Decompressive Hemicraniectomy has been carried out for brain trauma and although it may be technically feasible, its benefits are realized only in centers with aggressive and protocolized supportive medical care- the latter may be difficult to achieve.

On a more positive note, in young patients, done early, the chances of independence double, when the surgery is supported by an equally strong medical support team. Provided these conditions are met- there is now hope for a devastating condition.

### **Recommended Reading**

1. Eric Jüttler, Stefan Schwab, Peter Schmiedek, Andreas Unterberg et al. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY): A Randomized, Controlled Trial *Stroke* 2007; 38: 2518-25.
2. Jeannette Hofmeijer, L Jaap Kappelle, Ale Algra, G Johan Amelink, Jan van Gijn, H Bart van der Worp, for the HAMLET investigators. Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. *Lancet Neurol* 2009; 8: 326-33.
3. Vahedi K, Hofmeijer J, Juettler E, Vicaut E, et al for the DECIMAL, DESTINY, and HAMLET investigators. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol* 2007; 6: 215-22.
4. <http://www.strokecenter.org/trials/scales/rankin.html>. (Reference for modified Ranking Scale). Cited 4 February 2010.