When You Are Old

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When You Are Old,” has been variously interpreted, but to the literary rube, it could reflect a fundamental value that it is better to be alive than dead. A recent study on craniectomy for stroke investigates this.1

Prehistoric skulls have holes or trepanations/trephinations in them that are believed to have been made antemortem.2

Why these procedures were performed is unknown, but most are thought to have been for head injuries. As early as 1956, Scarcella operated on 6 patients with presumed cerebral infarctions, 2 of them in the acute stage, and recommended removing the infarcted tissue because the patients who did not have this done were more likely to die.3

Surgery to reduce mortality in patients with large cerebral infarctions was controversial until publication of randomized clinical trials in 2007.4,5

Some patients with ischemic stroke develop brain swelling and will die from this, particularly those with large hemispheric and cerebellar infarctions. The pathophysiology begins with edema formation that leads to brain swelling, increased local pressure in adjacent tissue, expansion of ischemia, hemorrhagic conversion, and a vicious cycle of further edema and swelling.6 Brain shifts develop that are associated with altered consciousness even before increased intracranial pressure develops.7,8

Edema and brain swelling, with or without hemorrhagic conversion, eventually leads to herniation, increased intracranial pressure, and death in ≥80% of patients with large cerebral infarctions.9 A review of published case series of craniectomy suggested it improved survival, with mortality being 24%, but that the effect on functional outcome was uncertain.10

These data in part stimulated the conduct of randomized clinical trials (Table I in the online-only Data Supplement). There are at least 6 randomized clinical trials of craniectomy for middle cerebral artery (MCA) territory infarction.1,4,5,11–13 Pooled analysis of the Hemicraniectomy of Stroke Trial (HAMLET), Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarcts (DECIMAL), and Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY) trials that included 93 patients between 18 and 60 years of age undergoing decompressive craniectomy for MCA territory infarction <48 hours reduced mortality from 71% to 22% (odds ratio [OR], 0.10; 95% confidence interval [CI], 0.04–0.27; Table II in the online-only Data Supplement).4 Poor outcome, defined as modified Rankin Scale (mRS) score ≥3, was also reduced (OR, 0.33; 95% CI, 0.13–0.86). When HAMLET concluded, additional patients were included in a second meta-analysis (109 patients), and the results were the same with a reduction in mortality with craniectomy from 71% to 21% and increased survival with a mRS of 0 to 3 from 24% to 40%.11

Vahedi et al4 noted that 1 person is saved for every 2 treated, and 1 in 4 survives to walk without assistance. When the patients in HAMLET who were operated on between 48 and 96 hours were included in a meta-analysis (n=134), death was still significantly reduced (63% to 22%; OR, 0.19; 95% CI, 0.09–0.37) and survival with mRS 0 to 4 improved (34% to 68%; OR, 0.26; 95% CI, 0.13–0.51), whereas there was no difference in survival with mRS 0 to 3 (25% to 38%; OR, 0.56; 95% CI, 0.27–1.15).14

American Heart Association guidelines are that craniectomy in such cases is effective and life-saving (class 1, level of evidence B) but that the age of the patient and patient and family opinions about the possibility of survival in a severely disabled condition need to be considered.13,16 Thus, questions remain about the effect of craniectomy on functional survival, the time after stroke during which it is effective, and the effect in patients aged >60 years.

Two more trials are published, Hemicraniectomy and Durotomy Upon Deterioration From Infarction-Related Swelling Trial (HeADDFIRST) and DESTINY 2.1,12

HeADDFIRST adds important information about selection of patients and medical management, but DESTINY 2...
addresses a key question about the effect of age on outcome in patients undergoing craniectomy. DESTINY 2 randomized 112 patients with MCA infarctions involving over two third of its territory who had National Institutes of Health Stroke Scale scores >14 (nondominant) or 19 (dominant hemisphere) and reduced level of consciousness <48 hours of onset. The key difference from prior studies was the patients were aged >60 years. Patients were randomized to the standard, large, craniectomy or to medical management only. Craniectomy increased survival with a mRS of 0 to 4 from 18% in the control group to 38% in the craniectomy group (OR, 2.9; 95% CI, 1.06–7.49). This was because of reduction in mortality; there was no difference in survival with mRS 0 to 3 (6% versus 5%). Almost two thirds of the survivors of craniectomy were severely disabled (mRS 5) or required assistance with most bodily needs (mRS 4), and these numbers were similar between the groups. The authors conclude that craniectomy improves survival but does not increase the chances of living with disability in patients aged >60 years.

The findings provide solid evidence that is consistent with case series reporting that age >60 years is associated with worse outcome in this disease, whether or not craniectomy is performed. Interestingly, mortality in the craniectomy group (43%) is similar to that reported (44% of 1099 patients) in the US National Inpatient Sample that underwent craniectomy between 1999 and 2008. And equally of note is that in this US database, a third of craniectomies were done in patients aged >60 years, even before publication of DESTINY 2. In addition, although mortality is higher in this population, craniectomy still significantly improved survival. But the question regarding quality of survival that has been raised in the prior studies is even more important. In DESTINY 2, the most likely outcome if the patient survived was substantial disability (mRS 4 or 5) or 24 of 27 (89%) survivors of craniectomy and 12 of 15 (80%) survivors in the medical group. Because there are more survivors, craniectomy increases the absolute numbers of severely disabled survivors. In contrast, in the meta-analysis of patients aged <60 years operated <48 hours, there was a significant increase in more functional survival (mRS 0–3). Despite these outcomes, most patients gave restrospective consent, which means they would undergo craniectomy again knowing now they are surviving most likely with severe disability. Fewer caregivers were as positive. The numbers are the same for both groups, suggesting that people will generally be fundamentally pleased to be alive. This is consistent with prior studies addressing this question. A review of decompressive craniectomy listed remaining questions, with, after the question of age, the next being what disability is an acceptable substitute for almost certain or ≤70% chance of dying? Reviews of this suggest that patients want to be alive, even if they are disabled.

What is next? One question is whether the selection criteria for craniectomy can be refined to those who ultimately will go on to die without it. Decompressive craniectomy and subsequent replacement of the bone carries up to a 20% overall risk of complications, including intracranial hemorrhage, infection, hydrocephalus, and seizures. Some studies as well as the randomized trials have used infarct volumes as 1 factor.

Analysis of 140 patients found that diffusion-weighted imaging lesion volume >82 mL, combined with MCA/internal carotid artery occlusion and lower National Institutes of Health Stroke Scale, could be used to develop models predicting malignant swelling. Further insight was provided by HeADDFIRST in which development of brain shift <96 hours of symptom onset differentiated patients who were at risk of death. These models need to be revisited including data from other studies such as HeADDFIRST and DESTINY 2 to determine if age now can be modeled better.

A second fundamentally important question is can a medical or pharmacological treatment be developed to prevent brain swelling and the need for craniectomy. HeADDFIRST had a lower mortality in the medical group compared with other studies, which suggests that a careful analysis of medical management in craniectomy studies might lead to insights into maneuvers that can minimize brain swelling. Neuroprotection and prevention of secondary brain swelling remain elusive. Gliburide may reduce brain edema, swelling, and hemorrhagic conversion after stroke and is a potential therapy. Finally, timing of craniectomy still remains uncertain.

When faced with a 65-year-old drowsy patient with a large MCA infarction a day after onset, what do we do? Although optimism for a potential functional outcome can be maintained in younger patients, a realistic discussion with the patient and their significant others can be undertaken now with some data in hand. When families ask me what I recommend, it is generally to let nature take its course and to not intervene surgically.

Disclosures

None.

References

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