Direct Bypass Reduces the Risk of Recurrent Hemorrhage in Moyamoya Syndrome, But Effect on Functional Outcome Is Less Certain

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This important study by Miyamoto et al1 provides the strongest and best evidence to date that direct revascularization, via external carotid to internal carotid artery bypass, reduces the risk for recurrent hemorrhage in adult patients presenting with hemorrhage secondary to Moyamoya syndrome. However, surgical complication rates had to be essentially zero to achieve this benefit, and whether surgery resulted in better functional outcome is not clear from the present data.

Moyamoya syndrome is characterized by idiopathic, often bilateral, often progressive occlusion of the terminal internal carotid artery and a secondary hypertrophic and proliferative response by the lenticulostriate arteries that give the condition its name.2,3 It is commonly referred to as a disease, yet it is certain that the underlying occlusive vasculopathy is multifactorial and that the proliferative response may be variable, particularly in non-Asian populations.4–6 The syndrome has a bimodal presentation in Asia, with children generally presenting with ischemic symptoms and adults with hemorrhage.7 In North America and Europe, however, the syndrome is most common in women in their third, fourth, and fifth decades, presenting with ischemic symptoms.8–11 One explanation for the difference in presentation between Asian and North American/European populations is the timing of onset for the occlusive vasculopathy.9 Ischemic symptoms are likely an early consequence of the progressive occlusive vasculopathy. Hemorrhage is likely a late consequence of hemodynamic stress in the lenticulostriate arteries.12–14 These vessels may not have the structural integrity of normal arteries.

The role of revascularization procedures to prevent hemorrhage has been controversial. Hemodynamic studies in adult Asian populations, particularly those presenting with hemorrhage, generally show little or no evidence of hemodynamic impairment.15 The rationale for surgery in these patients has been to eliminate the stress on the potentially fragile lenticulostriate collaterals. The evidence base for surgery, until the present study, has been limited to retrospective case series, suggesting a reduction in hemorrhage risk with surgery.16–18

The Japanese Adult Moyamoya (JAM) trial was a multicenter prospective study performed at 22 high-volume centers in Japan, beginning in 2004.19 Adults presenting with intracranial hemorrhage within the preceding 12 months were randomized to bilateral superficial temporal to middle cerebral artery bypass or medical management. A total of 80 patients were randomized (42 surgical). Randomization was stratified by the location of the hemorrhage (basal ganglia versus thalamic). Surgical patients underwent bilateral external carotid to internal carotid bypass within 3 months of enrollment. Patients were followed up for 5 years after enrollment. No patient was lost to follow-up. One surgical patient was murdered and censored at the time of last follow-up. Perioperative events occurred in 8 of the 84 surgical procedures, and only 1 resulted in a neurological deficit. This was not categorized as a primary end point because it was nondisabling (more on primary end points below). Recurrent bleeding was more frequent in the medical group (12 versus 5). The risk of a primary end point, which was a combination of several events, including recurrent bleeding, disabling stroke, and any death, was more common in the medical group than in the surgical group (13 versus 6).

There are certainly some problems with this study that limit the strength of the conclusions. This is a relatively small study, and the P values are right =5%—barely under for the Kaplan–Meier survival curves and barely over using Cox proportional hazards. However, the observed difference in hemorrhage rates reported here is similar to the previous retrospective reports.16 This increases the confidence that there was a reduction in hemorrhage risk with surgery. Also, the surgical results were excellent, with no ischemic stroke or death in 84 procedures on 42 patients. If 6 of the 84 procedures had resulted in a perioperative stroke or death, the event rates between the 2 groups would be identical. As the authors acknowledge, this expertise may not be widely available.

There are also several issues related to the definition and assessment of the primary and secondary end points that raise questions on the effect of surgery on functional outcome. First, the authors did not assess or did not report the degree of disability related to recurrent hemorrhage. If the recurrent hemorrhages had little or no permanent disability, one wonders whether surgery actually improved outcome. Perhaps these data will be forthcoming. Second, perioperative events had to result in permanent and severe (modified Rankin Scale, >2) disability to qualify as an end point. This is a bias in favor of the surgical group although it seems from the reported data that only 1 patient had a permanent deficit. Third, the exact
clinical definition of recurrent hemorrhage, and how it was monitored, reported, and adjudicated in the trial is not reported. Finally, the timing of the assessment of functional outcome after hemorrhage or perioperative events was not reported.

In summary, the results of the JAM trial provide strong support for the hypothesis that hemodynamic stress on the leptomeningeal collaterals is a frequent cause of hemorrhage in Moyamoya syndrome, and that direct bypass surgery reduces the risk of hemorrhage. Whether surgery results in better functional outcome is not as clear from these data. More information from this study or others would be useful in this regard. Finally, surgical complications rates will need to be extremely low to provide a benefit.

Disclosures
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References

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