Neurosurgical Outcomes After Intracerebral Hemorrhage: Results of the Factor Seven for Acute Hemorrhagic Stroke Trial (FAST)

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The value of neurosurgical interventions after spontaneous intracerebral hemorrhage (SICH) is uncertain. We evaluated clinical outcomes in patients diagnosed with SICH within 3 hours of symptom onset who underwent hematoma evacuation or external ventricular drainage (EVD) of the hematoma in the Factor Seven for Acute Hemorrhagic Stroke Trial (FAST). FAST was a randomized, multicenter, double-blind, placebo-controlled trial conducted between May 2005 and February 2007 at 122 sites in 22 countries. Neurosurgical procedures (hematoma evacuation and external ventricular drainage) performed at any point after hospital admission were prospectively recorded. Clinical outcomes evaluated were post-SICH disability, as assessed by the modified Rankin Scale; neurologic impairment, as assessed by the National Institutes of Health Stroke Scale; and mortality at 90 days after SICH onset. The impact of neurosurgical procedures on clinical outcomes was evaluated using multivariate logistic regression analysis, controlling for relevant baseline characteristics. Fifty-five of 821 patients underwent neurosurgery. Patients who underwent hematoma evacuation or EVD were on average younger, had greater baseline neurologic impairment, and lower levels of consciousness compared with patients who did not undergo neurosurgery. After adjusting for these differences and other relevant baseline characteristics, we found that neurosurgery was generally associated with unfavorable outcomes at day 90. Among the patients who underwent hematoma evacuation, those with lobar ICH had less ICH expansion than those with deep gray matter ICH, and the smaller expansion was associated with lower mortality. ICH volume was substantially decreased in patients who underwent hematoma evacuation between 24 and 72 hours after hospital admission, and this was associated with better clinical outcome. In conclusion, a small number of patients who underwent neurosurgery in FAST exhibited no overall clinical benefit from neurosurgical intervention, although outcomes varied by type of surgery, time of surgery, and hematoma location. Our findings support the need for further research into the value of neurosurgery in patients with SICH. **Key Words:** Intracerebral hemorrhage—surgical interventions—clinical outcomes—FAST—rFVIIa.

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Received July 3, 2009; revision received December 14, 2009; accepted December 21, 2009.

This study was funded by Novo Nordisk A/S. M.C. and C.V. are employees of Novo Nordisk. T.S. and S.D. were members of the FAST Trial Steering Committee and have received research support, consulting fees, and speaking honoraria from Novo Nordisk. S.M. and L.V.-T. have received consulting fees from Novo Nordisk.

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1052-3057/$ - see front matter

doi:10.1016/j.jstrokecerebrovasdis.2009.12.008

Among the various types of stroke, spontaneous intracerebral hemorrhage (SICH) is associated with the highest acute mortality and worst long-term neurologic outcomes.[1] New insights into the pathophysiology of SICH identify the volume of ICH and initial level of consciousness, as assessed using the Glasgow Coma Scale (GCS), as critical determinants of clinical prognosis. SICH has been shown to be a dynamic process rather than static phenomenon, with the hematoma developing over time in a large proportion of patients.[2,3] An early prospective study indicated that 38% of patients scanned within 3 hours of onset of SICH exhibited significant growth, defined as a >33% increase in volume over 24 hours.[3] In addition to ICH volume and initial level of consciousness, the most important predictor of mortality and clinical outcome is the presence and the quantity of intraventricular hemorrhage (IVH).[4,5]

Various treatment options have been suggested for SICH, including slowing or stopping the hemorrhage early after onset. In the Factor Seven for Acute Hemorrhagic Stroke Trial (FAST), it was confirmed that hemorrhage growth is reliably attenuated by rcombinant factor VIIa (rFVIIa); the favorable clinical effects observed in the phase 2b trial could not be confirmed, however.[6,7] Surgical removal of the clot is another option to reduce complications due to mass effect and toxic effects of blood on the surrounding brain parenchyma.[8-10] The Surgical Trial in Intracerebral Hemorrhage (STICH), a large randomized, controlled trial examining hematoma evacuation for supratentorial ICH in 1033 patients, found no overall clinical benefit of surgery compared with conservative treatment, although patients with superficial lobar hematomas (≤1 cm from the cortical surface) were more likely to have a favorable outcome than patients with deep-seated hematomas.[11] However, in that trial, the inclusion time window was 72 hours and the operation needed to be performed within the next 24 hours. Thus, STICH was not designed to examine the effect of surgery on rebleeding, which occurs mainly within the first 4 hours after onset of SICH. A retrospective study by Kaneko et al[12] identified a positive effect of surgical clot removal within 3-7 hours after onset of SICH. Similarly, a small trial conducted by Morgenstern et al[13] showed some effect of early hematoma evacuation within a 12-hour time window, with a lower mortality rate at 30 days postsurgery in the surgical group compared with the medically treated group, yet similar rates in the 2 groups at 6 months. However, in a later study using a time window for surgical intervention of only 4 hours, Morgenstern et al[14] observed an increase in mortality due to an increased rate of rebleeding.

Another neurosurgical intervention in SICH is the application of external ventricular drainage (EVD) to remove blood from the cerebrospinal fluid (CSF) space. The effect of this procedure in combination with intraventricular clot lysis is currently under investigation.[15] Thus, there is relatively limited information on the influence of neurosurgery on clinical outcome after SICH, especially when performed within 24 hours after onset of SICH.

FAST randomized 841 patients with SICH who were enrolled within 3 hours after onset of symptoms.[7] Although a foreseeable surgical procedure (with the exception of external ventricular drainage) was an exclusion criterion in the trial, some patients did undergo hematoma evacuation. In light of the limited evidence on the value of

Table 1. *Baseline patient characteristics*

	Hematoma evacuation (n = 23)	EVD (n = 32)	No surgery (n = 766)
Age, mean (SD)	56.4 (13.8)	58.7 (12.2)	65.6 (13.3)
Female, %	52	31	37
History of smoking, %	26	6	19
History of alcoholism, %	17	13	11
Comorbidity, %			
Hypertension	83	84	82
Diabetes	22	28	19
Cardiovascular disease	9	19	21
Cerebrovascular disease	26	25	21
SBP, mm Hg, mean (SD)			
At baseline	177.1 (35.8)	182.7 (38.0)	180.7 (29.5)
At 24 hours	144.6 (19.2)	157.0 (22.8)	155.3 (24.1)
At 72 hours	137.0 (22.6)	156.6 (18.6)	153.2 (23.3)
Hemorrhage location, %			
Deep gray matter	68	86	83
Lobar	32	7	13
GCS score at baseline, median (range)	13 (7-15)	14 (6-15)	15 (6-15)
NIHSS score at baseline, mean (SD)	13.5 (6.6)	13.9 (6.5)	11.6 (6.2)
mRS score pre-ICH, mean (SD)	0.04 (0.2)	0.1 (0.5)	0.2 (0.5)