Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomized trial

The Lancet 2013 Aug 3;382(9890):397-408. doi: 10.1016/S0140-6736(13)60986-1. Epub 2013 May 29.

Intracerebral Hemorrhage (ICH) affects 4 million people worldwide each year. The median 1 month fatality in ICH is 40%, and survivors are often left with severe disability. While surgical removal of the clot in ICH is possible, the benefit to clot removal had not been shown in prior non-randomized trials. STICH I trial was the first large RTC that evaluated early surgery (<24 hrs) vs conservative management in ICH, and results were equivocal. However, based on subgroup analysis of the STICH 1 trial, the authors of STICH II hypothesized that the equivocal results of STICH I were due to 1) worse surgical outcomes in patients with deep bleeds or intraventricular extension (IVE), and 2) better surgical outcomes in patients with superficial lobar hemorrhages without IVE. However, results were not significant on metanalyses of the original data. For this reason, STICH II was designed to test the hypothesis that early surgery would improve outcomes in conscious patients with superficial lobar hemorrhages and no IVE.

Experimental Design and Statistics: STICH II was an international, multicenter, randomized controlled trial. Blinding was not feasible. Inclusion criteria were 1) spontaneous lobar (≤ 1 cm from cortical surface) ICH on CT scan, 2) ICH volume between 10 - 100 mL, 3) presentation within 48 hrs of ictus, and 4) best motor GCS score of 5 or 6 and best eye GCS score ≥2 (i.e., conscious at randomization). Exclusion criteria were ICH due to tumor, trauma, aneurysm, or angiographically-proven AVM, an ICH of the basal ganglia, thalamus, brainstem, or cerebellum, and any intraventricular blood with the ICH. Patients with severe pre-existing mental or physical co-morbidities were also excluded. Eligible patients were then randomized to early surgery (evacuation of hematoma within 12 hours of presentation, almost uniformly via craniotomy) or conservative management. Primary outcome was prognosis-based favorable or unfavorable outcome based on the Extended Glascow Outcome Scale (GOSE) at 6 months after randomization. A prognosis score was calculated at randomization based on GCS, age, and ICH volume, and a pre-defined cutoff was used to dichotomize patients into poor and good prognosis based on this score. In each prognosis group (good and poor) there were pre-defined criteria for favorable outcome. In the good prognosis group, favorable outcome was defined as good recovery or moderate disability on GOSE. In the poor prognosis group, favorable was defined as upper severe disability (patients who are completely self-caring within their homes but unable to shop or use public transport without assistance). All other patients who did not meet criteria for favorable outcome were classified as having an unfavorable outcome. Otherwise, secondary outcomes included mortality, time to death, prognosis-based dichotomized Rankin, GOSE, Rankin and quality of life metrics; all were measured at 6 months. There was also a pre-specified subgroup analysis based on age, GCS, ICH volume, time from ictus to randomization, and severity of neurologic deficit in worst limb. All groups were analyzed via an intention-to-treat analysis.

Results: A total of 601 patients from 27 countries were randomized; 305 were randomized to early surgery, and 294 to conservative management. In the end, 297 surgical and 286 conservative treatment patients were analyzed for primary outcome. Baseline characteristics between the 2 groups were very similar. Early surgery was not associated with a significant increase in the primary outcome of prognosis-based favorable outcome. 123 (41%) in the early surgery group vs 108 (38%) of the conservative

management group had a prognosis-based favorable outcome, with an absolute difference of 3.7%, (95% CI -4·3 to 11·6, p=0.367). There was a small, non-significant trend toward improved mortality at 6 months in the early surgery group (18% vs 24%, p = 0.095). There was no difference in disability at 6 months between the two treatment arms. Notably, a total of 62 (21%) of the patients assigned to conservative treatment went on to have delayed surgery. At the time of delayed surgery, the patients were in a deeper coma with worse neurological deficits than those from the early surgery group (see table 3). In the subgroup analysis, patients with poor prognosis were significantly more likely to have favorable outcome with early surgery than with conservative treatment (OR 0.49, 95% CI 0.26–0.92; p=0·02), with no significant difference between early surgery and conservative treatment in the good prognosis group. The authors also included the STICH II data in a prior meta-analyses of ICH RTCs looking at surgery vs conservative management and showed a significant advantage for surgery (OR 0.74, 95% CI 0·64–0·86; p<0·0001), but with significant heterogeneity (p=0·0002) because the studies included different patient groups and different types of surgery. When the STICH II data was included in the meta-analysis for lobar ICH without IVE there was no difference between surgery and conservative management.

Conclusions: Overall, this trial did not show an improvement in prognosis-based outcomes in conscious patients with lobar ICH without IVH with early surgery compared to conservative management. As noted, 62 (21%) of the conservative management patients did have delayed surgery due to clinical deterioration. Because of the intention-to-treat analysis, these patients were included in the conservative management arm, though the delayed surgery may have affected their outcome. Subgroup analysis showed that patients with poor prognosis (which equates to an initial GCS of 9-12) did have statistically significant benefit from early surgery, but this was not a pre-specified analysis and should be interpreted cautiously. The data from this trial in conjunction with prior trials have largely been interpreted to suggest that a select group of patients with lobar ICH without IVE (those with poor prognosis [GCS 9-12] or clinical deterioration) may benefit from surgical intervention, though the exact characteristics of such a subgroup has not been elucidated due to the high heterogeneity in the various trials. Additionally, this trial looked primarily at open craniotomy for clot evacuation, and other less invasive surgical procedures were evaluated in separate trials (MISTIE III and ENRICH).

Summary compiled by Nathan Bicher, MD