

Spontaneous Intracerebral Hemorrhage: To Operate or Not To Operate, That's the Question

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Abstract

Background The occurrence of a spontaneous intracerebral hemorrhage in Israel's Prime Minister attracted the scrutiny of local and international media on neurosurgeons as they made therapeutic decisions. In the ensuing public debate, it was suggested that extraordinary measures (surgical treatment) were undertaken only because of the celebrity of the patient.

Objectives: To evaluate the criteria used to select surgical versus medical management for SICH.

Methods: We retrospectively reviewed the files of 149 consecutive patients with SICH admitted to our medical center from January 2004 through January 2006. Their mean age was 66 (range 3–92 years), and 62% were male. SICH localization was lobar in 50% of patients, thalamus in 23%, basal ganglia in 15%, cerebellum in 13%, intraventricular in 6%, and pontine in 1%. Mean admission Glasgow Coma Score was 9 (range 3–15). Risk factors included hypertension (74%), diabetes mellitus (34%), smoking (14%) and amyloid angiopathy (4%). Fifty percent of patients were on anticoagulant/antiplatelet therapy, including enoxaparin (3%), warfarin (7%), warfarin and aspirin (9%), or aspirin alone (34%).

Results: Craniotomy was performed in 30% of patients, and ventriculostomy alone in 3%. Rebleed occurred in 9% of patients. Six months after treatment 36% of operated patients were independent, 42% dependent, and 13% had died. At 6 months, 37% of non-operated patients were independent, 15% dependent, and 47% had died.

Conclusions: One-third of the SICH patients, notably those who were experiencing ongoing neurologic deterioration and had accessible hemorrhage, underwent craniotomy. The results are good, considering the inherent mortality and morbidity of SICH.

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The syndrome of dominant hemisphere stroke is described in the Old Testament, in the *Lament over the Destruction of Jerusalem*, in Psalms 137: "If I forget you O Jerusalem, let my right hand wither! Let my tongue cling to the roof of my mouth, if I do not remember you" [1]. Although it is not possible to date the *Lament*, there is linguistic evidence that it may have been written during the Judean exile in Babylonia (586–538 BC) [2]. A description of unilateral head injuries associated with neurologic defects on the opposite side of the body, and of aphasia correlated with right hemiplegia is found in the *Corpus Hippocraticum* (5th century BC) [3]. Apoplexy (from the Greek *apo* meaning *after* and *plexy* signifying *blow*) was used in the Hippocratic Corpus to describe a sudden loss of consciousness, including loss of consciousness due to seizure. Opinions regarding the primary

role of the brain versus the heart/vessels in apoplexy differed. Soranus (98–138 AD), a physician who was born in Ephesus in Greece and practiced in Rome, described the sudden onset of coma, including early signs (headache, etc.), and differentiated coma from paralysis, seizures, etc. [4]. Isidore, Bishop of Seville, writing in 600 AD, attributed apoplexy to a "sudden effusion of blood" [4]. It was only in 1658 that Johannes Jakob Wepfer demonstrated that apoplexy is due to cerebral hemorrhage, in his autopsy of Marcello Malpighi, the famous anatomist and physician to Pope Innocent XII [5].

In recent history, strokes have resulted in the sudden incapacitation of world leaders at critical historical crossroads, including American Presidents Woodrow Wilson (1919) and Delano Roosevelt (1945), and Soviet Premiers Vladimir Lenin (1924) and Joseph Stalin (1953) [6]. Recently there was concern about the election of Pope Benedict XVI because of his history of hemorrhagic stroke [7].

Physicians treating such powerful public figures must make therapeutic decisions under enormous pressure. In 1559 Ambroise Paré treated French King Henry IV after he was badly injured in a jousting tournament when a splintered lance penetrated his right orbit. Paré experimented with the stump of the lance, making thrusts at the severed heads of four criminals who were executed by Catherine de Medici to provide dissecting material. His consultant, Andreas Vesalius, repeated the experiment on the head of a murdered man. Still they hesitated to operate, and the king died 9 days after his injury [8,9].

Is there an accepted algorithm defining the indications and optimal timing for surgical management of SICH? Since McKissock et al. [10] demonstrated that non-operated patients fared better in a 1961 randomized study (first of its kind), it has been accepted that there are no indications for elective surgery for SICH. Most neurosurgeons would operate on such patients only if their condition was deteriorating. Neither the findings of Luessenhop and co-workers [11] in 1967 showing better outcome with elective early (less than 24 hours) surgery, nor the series of early microsurgical surgery by Kaneko [12] in 1977 changed this trend. The advent of modern imaging (computed tomography) and the availability of fibrinolytic agents (urokinase) facilitated experimental minimally invasive procedures to remove the clot [13,14]. However, clinical studies [15] have not shown advantages of this approach. The results of image-guided mechanical aspiration are also controversial [16].

Guidelines for management of SICH, published in 1999,

SICH = spontaneous intracerebral hemorrhage

established that patients with small hemorrhage and minimal neurologic deficit do well with medical treatment, and that patients with Glasgow Coma Score ≤ 4 will die or remain extremely disabled regardless of treatment (levels of evidence II through V, grade B recommendation) [17]. Deteriorating patients with cerebellar hemorrhage > 3 cm diameter should undergo clot removal (level of evidence II through V, grade C recommendation). The usefulness of removing large lobar clots in deteriorating young patients, and the efficacy of ultra-early clot removal remains to be demonstrated in large randomized studies [17]. The outcome of supratentorial SICH, whether treated surgically or medically, was dismal in this report. In a summary of trials until 1999, Broderick et al. [17] reported that 74–100% of patients were dependent, vegetative, or dead at 6 months.

In 2005, Mendelow and colleagues [18] completed the international trial randomizing early surgery versus initial conservative treatment. No overall benefit from early surgery was found but further studies are necessary to rule benefits in “superficial” hemorrhages.

Despite these reports, the controversy regarding whether to perform surgery in patients presenting with SICH who are rapidly deteriorating but who have a potentially salvageable hemorrhage will continue.

During the public debate as to whether it was appropriate or indicated to operate on the Israeli Prime Minister, serious confusion resulted from the wrong assumption of some non-surgical specialists that there is latitude of choice between surgical vs. medical management in a patient developing signs of herniation on admission due to lobar SICH of the non-dominant hemisphere. When a patient is deteriorating rapidly, failure to remove the clot could even lead to charges of negligence. However, if a similar patient arrives at the Emergency Department with a stable deficit, there is indication for initial medical treatment. Only further deterioration may require surgical treatment. Likewise, a similar patient arriving at the Emergency Department an hour after herniation would no longer be a surgical candidate.

In summary, surgical treatment of SICH is not elective but obligatory in a patient who is deteriorating and who has reasonable outcome potential (non-dominant hemisphere). We sought to determine whether this algorithm has been used regularly in our hospital without discrimination, and whether this more aggressive treatment is not reserved only for more influential patients. For this purpose we decided to analyze the characteristics of operated and non-operated patients with SICH during the last 2 years.

Patients and Methods

We retrospectively reviewed the medical charts of all patients admitted to our medical center from January 2004 through January 2006 with the diagnosis of SICH. Descriptive statistics and graphics were used to describe patient characteristics. Patient outcome at 6 months was determined according to discharge notes from rehabilitation and/or from an EQ-5D questionnaire administered to the patient or a family member by telephone.

Results

During the 2 year study period, 149 consecutive patients were admitted with SICH to our medical center. Their mean age was 66 (range 3–92 years) [Figure 1], and 62% were male. Mean admission Glasgow Coma Score was 9 (3–15) [Figure 2]. SICH localization was lobar in 50% of patients, thalamic in 23%, basal ganglia in 15%, cerebellar in 13%, intraventricular in 6%, and pontine in 1% [Figure 3]. Risk factors included hypertension in

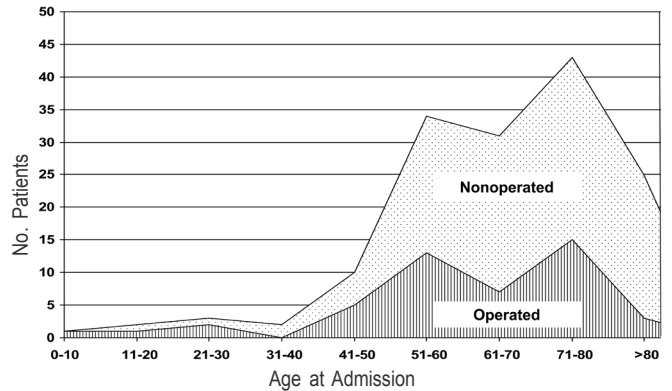


Figure 1. Age distribution of operated and non-operated patients.

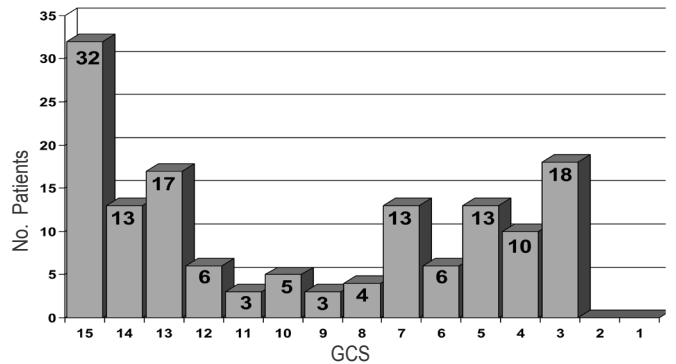


Figure 2. Glasgow Coma Score at admission.

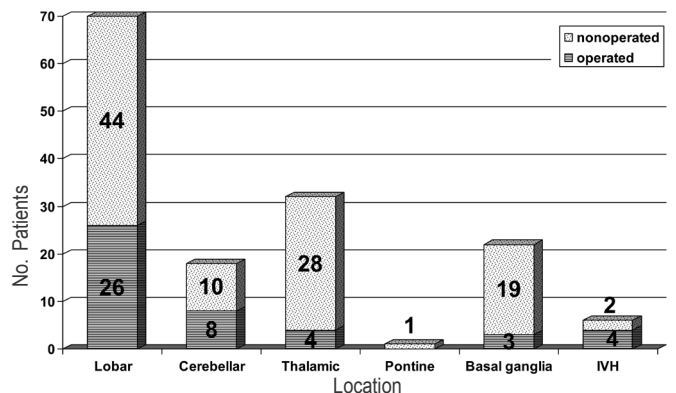


Figure 3. Location of hemorrhage.

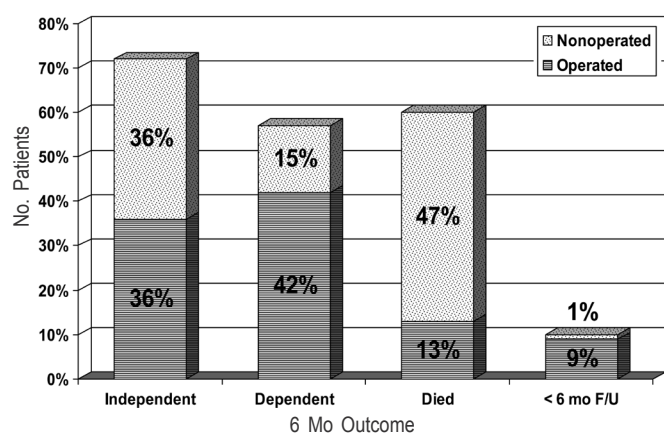


Figure 4. Outcomes for operated and non-operated patients

74% of patients, diabetes mellitus in 34%, smoking in 14%, and amyloid angiopathy in 4%. A full 50% were on anticoagulant/antiplatelet therapy, including enoxaparin (3%), warfarin (7%), warfarin and aspirin (9%), and aspirin alone (34%).

Craniotomy was performed in 30% of SICH patients, and ventriculostomy alone was performed in 3%. Rebleed occurred in 9% of the total group. At 6 months, 36% of operated patients were independent, 42% were dependent, and 13% had died. Of the non-operated patients, 37% were independent, 15% dependent, and 47% had died [Figure 4].

Discussion

According to our data the incidence of SICH in Jerusalem (12.3 per 100,000/year) closely resembles that of the United States [19]. Anticoagulation/anti-aggregation (50% of patients) was second only to hypertension (74%) as a risk factor in our series. Enoxaparine is a risk factor in only 3% of cases, however the low incidence may be misleading because this medication has been commonly prescribed in Israel only since 2003. We observed a high association (34%) between prophylactic doses of aspirin alone and SICH, which may be attributed to its widespread use among the general population. Clearly, many unresolved questions remain regarding the use of oral anticoagulation agents [20].

We found that a significant percentage of the SICH patients admitted to our medical center underwent craniotomy (30%), thus the choice of surgical treatment is not exceptional. The 6 month survival rate among operated patients is remarkable at 87%. This may be explained in part by preoperative selection. We operated on patients with low GCS (< 5) only when they deteriorated acutely from higher scores upon hospital arrival, as was the case with the Prime Minister. Most evacuated hemorrhages were easily accessible. We also did not exclude cerebellar hemorrhages from this series. Many series on SICH exclude patients with cerebellar hemorrhage, since there seems to be a disproportionate benefit from surgery in the cerebellum compared to benefits from surgery

following supratentorial hemorrhage. This benefit is strongest for lesions > 3 cm. Note that studies showing this result were non-randomized [17]. Still, cerebellar hemorrhages represent not more than 13% of our operated patients.

The large number of surviving patients after surgery resulted in a higher ratio of dependent (42%) compared with independent (36%) patients. Among patients in our series who were not operated, the same proportion was independent 6 months after admission (37%), but mortality was very high (47%) and there was a smaller proportion of dependent patients (13%).

It is clear that we cannot compare the operated and non-operated groups because, by definition, there are biases of selection. Still, the debate of surgical versus medical management is likely to persist. Some might suggest that surgery tends to preserve life but results in a very poor quality of life for many survivors, as occurred in other series describing patient outcomes with aggressive management of severe head injury [21].

The use of recombinant activated factor VII for acute intracerebral hemorrhage has been reported recently [22]; however, the majority of intracranial hemorrhage in the study resulted from trauma. The single SICH patient in our series who was treated with recombinant factor did in fact rebleed after surgery, in spite of this treatment. This was not surprising since there is a high incidence of rebleed following ultra-early craniotomy [23].

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References

- Segal R, Shalit M. Biblical and Talmudic texts of neurosurgical interest [Abstract]. Presented at the International Congress of Neurological Surgery, Sydney, Australia, 2001.
- Rendsburg GA, Rendsburg SL. Physiological and philological notes to Psalm 137. *Jewish Quarterly Review* 1993;Lxxx III:385-99.
- Lokhorst GJ. The first theory about hemispheric specialization: fresh light on an old codex. *J Hist Med Allied Sci* 1996;51:293-312.
- Karenberg A, Hort I. Medieval descriptions and doctrines of stroke: preliminary analysis of select sources. Part I: The struggle for terms and theories – late antiquity and early Middle Ages. *J Hist Neurosci* 1998;7:162-73.
- Wepfer JJ. *Historia apoplepticorum* 1658. In: Pearce JMS, ed. Wepfer's Description of the Apoplexy of Malpighi. *Neurol Neurol Psychol* 1997;62:394.
- Thompson JE. The evolution of surgery for the treatment and prevention of stroke. The Willis Lecture. *Stroke* 1996;27:1427-34.
- The Times*. Pope has had second stroke. 2005. Access via the World Wide Web at: <http://www.timesonline.co.uk/article/0,2089-1592856,00.html> on Jul 23 2006. In. London UK: Times Online
- Faria, MA Jr. The death of Henry II of France. *J Neurosurg* 1992;77:964-9.
- Martin G. The death of Henry II of France: a sporting death and post-mortem. *Aust NZ J Surg* 2001;71:318-20.
- McKissock W, Richardson A, Taylor J. Primary intracerebral hemorrhage: a controlled trial of surgical and conservative treatment in 180 unselected cases. *Lancet* 1961;ii:222-6.

GCS = Glasgow Coma Score

11. Luessenhop AJ, Shevlin WA, Ferrero AA, McCullough DC, Barone BML. Surgical management of primary intracerebral hemorrhage. *J Neurosurg* 1967;27:419–27.
12. Kaneko M, Koba T, Yokoyama T. Early surgical treatment for hypertensive intracerebral hemorrhage. *J Neurosurg* 1977;46:579–83.
13. Matsumoto K, Hondo H. CT-guided stereotaxic evacuation of hypertensive intracerebral hematomas. *J Neurosurg* 1984;61:440–8.
14. Segal R, Dujovny M, Nelson D, et al. Local urokinase treatment for spontaneous intracerebral hematoma [Abstract]. *Clin Res* 1982;30:412A.
15. Teernstra OP, Evers SM, Lodder J, et al. Stereotactic treatment of intracerebral hematoma by means of a plasminogen activator: a multicenter randomized controlled trial (SICHPA). *Stroke* 2003;34:968–74.
16. Hoseini H, Leguerinel C, Hariz M, et al. Stereotactic aspiration of deep intracerebral hematomas under computed tomographic control: a multicentric prospective randomized trial [Abstract]. Presented at the European Stroke Conference, Valencia, Spain, 2003.
17. Broderick JP, Adams HP Jr, Barsan W, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke* 1999;30:905–15.
18. Mendelow AD, Gregson BA, Fernandes HM, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. *Lancet* 2005;365:387–97.
19. Fang J, Alderman MH. Trend of stroke hospitalization, United States, 1988-1997. *Stroke* 2001;32:2221–6.
20. Steiner T, Rosand J, Diringer M. Intracerebral hemorrhage associated with oral anticoagulant therapy: current practices and unresolved questions. *Stroke* 2006;37:256–62.
21. Ransohoff J, Benjamin MV, Gage EL Jr, Epstein F. Hemispherectomy in the management of acute subdural hematoma. *J Neurosurg* 1971;34:70–6.
22. Mayer SA, Brun NC, Begtrup K, et al. Recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med* 2005;352:777–85.
23. Morgenstern LB, Demchuk AM, Kim DH, Frankowski RF, Grotta JC. Rebleeding leads to poor outcome in ultra-early craniotomy for intracerebral hemorrhage. *Neurology* 2001;56:1294–9.

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