

Outcome Evaluation of Surgical Versus Conservative Treatment of Spontaneous Non-Traumatic Supratentorial Intracerebral Hemorrhage

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Authors' contributions

This work was carried out in collaboration between all authors. Authors Mohamed Elsherif, Mohamed Elsayed and MS designed the study and wrote the protocol. Author AE performed the statistical analysis, managed the literature search and wrote the first draft of the manuscript with assistance from all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Spontaneous supratentorial intracerebral hemorrhage (SSICH) has the greatest morbidity and fatality of all cerebral strokes, moreover the contribution of surgery stays contradictory. Early surgery to restrict the mechanical compression of the brain and the toxic impacts of blood maybe reduce damage.

Aim: To compare the outcome and efficacy of surgical evacuation of intracerebral hemorrhage (ICH) with the conservative medical treatment in cases of SSICH.

Materials and Methods: Fifty patients with SSICH was recruited to surgical or best medical treatment. Twenty-five patients experienced surgical evacuation whereas the other twenty-five were provided with conservative medical treatment. A history and neurological examination, including an assessment by Glasgow Coma Scale (GCS) and by the National Institutes of Health Stroke Scale (NIHSS), were obtained at the time of admission. Primary outcome (death or disability) using the extended Glasgow outcome scale (GOS) was 6 months after the onset.

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Secondary outcomes included mortality, the Barthel index (BI), and the modified Rankin scale (mRS).

Results: There were no statistically significant differences in GOS, GCS or NIHSS after one month of treatment. The mortality rate at 6 months for the early surgery group was 10 patients (40%) and the conservative group was 8 patients (32%) without statistically significant ($P = 0.556$). The secondary outcome by mRS and by BI was statistically significant in cases of the conservative group in comparison with cases of the surgical group ($P > 0.05$).

Conclusions: We conclude that there is no statistically significant difference in outcome between surgical and medical management of primary ICH. Patients with superficial hematomas might benefit from surgery. While, patients with GCS of ≤ 8 surgical evacuations should be avoided especially if the hematoma volume of ≥ 50 cm.

Keywords: Spontaneous intracerebral hemorrhage; surgical treatment; conservative management; GCS; GOS; NIHSS.

1. INTRODUCTION

Intracerebral hemorrhage (ICH) gives the reason for relatively 10 to 15% of all cerebral strokes. [1]. Spontaneous supratentorial intracerebral hemorrhage (SSICH) is one of the highest serious types of cerebral stroke [2]. It is calculated that this disorder influences 10-20 in 100,000 populations every year with a fatality between 23-58% [3, 4]. Intracerebral hemorrhage is identified by its site in the brain tissue, with "deep" ICH being located within the basal ganglia and internal capsule (35-70%), brainstem (5-10%), and cerebellum (5- 10%). In contrast, "lobar" ICH (15-30%) refers to hemorrhages situated in cortical-subcortical areas and follows a "lobar" pattern across one or less often multiple lobes of the brain. Deep ICH accounts for about two-third of spontaneous ICH cases, and lobar ICH accounts for the remaining one-third [5].

There is a subgroup of cerebral hemorrhages of small size of the lesion, which clinically manifests as a lacunar syndrome (hemorrhagic lacunar stroke). This subgroup accounts for 7.4% of cerebral hemorrhages and is associated with a more favorable prognosis than the remaining group of intracerebral hemorrhages, usually without in-hospital death and symptom-free at discharge in 22.8% of cases [6].

Hypertension is the most frequent accountable risk factor. While, age is a significant risk factor for ICH; the overall odds of suffering an ICH is highest at and after the age of 85 [7]. Hematologic abnormalities are linked with up to 8% of all ICH; these incorporate use of antiplatelet agents, anticoagulant-induced coagulopathy, congenital and acquired factor deficiencies [8]. The role and timing of operative

neurosurgical intervention continue contradictory and the process and timing of surgery remain to be disorganized. Operative intervention is believed to be useful in halting bleeding, avoiding rebleeding and eliminating the mass effect to prevent secondary brain injury [9].

It is an issue of debate for more than 100 years either ICH should be treated surgically. The neurosurgeons observed that the prediction for patients yet kept bad, regardless either they were surgically evacuated or not. Up to 30% of all patients experiencing from ICH die within 30 days after stroke, and a lot of patients surviving ICH continue in a serious impacted vegetative state. Therefore, the prognosis of a huge part of ICH patients is anyway disappointing. Many trials have omitted to identify target benchmarks to determine, either surgery is beneficial or not in a single case, though the surgical methods have been strengthened over the last years [10]. The International Surgical Trial in Intracerebral Hemorrhage (STICH) stated that there is no favorable prognosis with early surgery versus the conservative management [11].

Our study was designed to find out whether early surgery would improve outcomes compared with initial conservative treatment in patients with supratentorial ICH.

2. SUBJECTS AND METHODS

2.1 Study Design and Population

Patients were recruited from Mansoura Emergency Hospital, Mansoura University, Egypt. The study protocol was approved by the Local Ethical Committee at the hospital. All enrolled patients had signed written fully informed consent to participate in the study. Fifty

patients with spontaneous non traumatic ICH were studied in two groups first one was 25 patients treated by medical treatment, second group 25 patients underwent surgical evacuation of ICH. The groups were well matched during our study. Inclusion criteria were spontaneous ICH diagnosed by CT brain, ICH volume > 20 cm³ with a focal neurological deficit, age more than 18 years, presented within 24 hours from the onset of the condition. Exclusion criteria were traumatic ICH, intratentorial hemorrhage (brain stem or cerebellar hemorrhage); multiple hematomas; associated subarachnoid hemorrhage or hydrocephalus; hemorrhagic transformation into infarction; hemorrhage caused by arteriovenous malformations, aneurysms; ICH due to bleeding tendency caused by medical condition (e.g. Hepatic failure) or drug induced (e.g. Anticoagulants). Patients had severe pre-existing physical or mental disability or severe comorbidity that might interfere with the assessment of outcome.

2.2 Methods

2.2.1 Clinical evaluation

Clinical evaluation of the conscious level by Glasgow Coma Scale (GCS) [12] and neurological status by the National Institutes of Health Stroke Scale (NIHSS) [13] were performed at the time of admission and one month after treatment. Proper history taking to exclude drug induced hemorrhage. Glasgow outcome scale (GOS) was performed one month after treatment [14]. Patients with GOS of 1 or 2 were considered of good outcome and patients with GOS of 3, 4 or 5 were considered of poor outcome [15].

2.2.2 Neuroradiological assessment

The diagnosis of spontaneous ICH was performed on acute onset of neurological symptoms and signs confirmed by CT scan. The hemorrhage was classified according to site into lobar, basal ganglia and or thalamic and lastly hematoma involving both lobar, basal ganglia and thalamic sites.

The volume of ICH was measured by Broderick's formula $(Ax \times B \times C)/2$ [16], where A is the greatest hemorrhage diameter by CT, B is the diameter 90 degrees to A and C is the approximate number of 10 mm CT slices with hemorrhage.

2.2.3 Laboratory testing

Complete blood picture, Liver and renal functions, and coagulation profile were performed to exclude medical causes of bleeding tendency.

2.3 Medical Treatment

Medical therapy included control of blood pressure, osmotherapy, seizure prophylaxis, fever control, deep venous thrombosis prophylaxis, intravenous fluids, H2 blockers, maintenance of normoglycemia, and early nutritional support. Intubation was performed in patients as needed for respiratory depression, airway protection.

Patients randomized to early surgery had their hematoma evacuated within 24 h of randomization by the method of choice of the responsible neurosurgeon, combined with the appropriate and best medical treatment. Patients randomized to conservative treatment had the best medical treatment.

2.4 Surgical Treatment

Surgery was done within 24 hours of onset of the condition and patients were taken after written consent to the operating room. A decompressive craniotomy was done for all surgical cases under general anesthesia, in the supine position, and by the same surgeon. Pre and postoperative IV antibiotics, IV phenytoin and corticosteroids, intra-operative osmotherapy were administered (Mannitol and furosemide). Sterilization and scalp preparation and linear or horseshoe scalp incision was done according to the site of the hematoma. Clips were used to stop bleeding of the scalp. Periosteal incision, burr holes and the use of Gigle saw to cut the bone. Then elevation of the bone flap, stitches for the dura, cruciate incision of the dura, cricotomy incisions and using Leila spatula to open the space. Then the clots were removed and hemostasis were microscopically assisted. The closure was performed in anatomical layers by water tight dural stitches, fixation of the bone flap by stainless wire, closure of the subgaleal layer and then scalp by proline stitches with suction drain.

The primary outcome was death or disability using the extended GOS 6 months after the onset. Secondary outcomes included mortality, the Barthel index (BI), and the modified Rankin scale (mRS).

Prognosis and secondary outcomes included mortality, which was determined by a simple frequency comparison and a survival analysis. Also, the outcome was also determined by the BI and the mRS. The favorable outcome means a BI of 95/100 or higher, or an mRS of two or below, whereas poor outcome means the equivalent thresholds were 65 or higher for the BI and three or more for the mRS. For all patients, death was classified as an unfavorable outcome [17,18].

2.5 Statistical Analysis

Statistical analysis was carried out by using the SPSS (Version 15, 2006; SPSS Inc., Chicago, IL, USA) for Windows statistical package. Collected data were presented as mean \pm SD, ranges, numbers, and ratios. Pearson Qui square was used for comparisons. $P < 0.05$ was considered statistically significant. The chi-square statistic was used to compare ICH patients who died within first 30 days and the survival. P -values < 0.05 were considered to be statistically significant. Spearman's correlation was used for non-parametric correlation. The primary outcome across the subgroup analyses were compared with formal interaction tests. The variables and subgroups were: age (< 65 vs ≥ 65 years); hematoma volume (< 50 ml vs ≥ 50 ml); Glasgow coma score (≤ 8 vs 9 to 12 vs ≥ 13); lobar vs basal ganglia/thalamic hematoma, or both; severity of neurological deficit (normal or weak vs paralyzed arm, normal or weak vs paralyzed leg, normal speech vs dysphasia or aphasia). Furthermore, depth from the cortical surface was compared in both groups (< 1 cm vs ≥ 1 cm).

3. RESULTS

Fifty patients were randomized: 25 to early surgery and 25 to conservative treatment. Details of all patients' age and sex distribution were shown in Table 1. The groups were well matched at baseline. More than half the patients were men 52% of the conservative group were males and 56% of the surgical group were males. Ages ranged between 50 and 91 years, with a median of 63 ± 13 y in the conservative group. While ages ranged between 44 and 70 years, with a median of 60 ± 11 y in the surgical group.

Details of all patients' previous medical history and GCS and NIHSS at presentation are shown in Table 2. The most common risk factors for ICH in the conservative group were hypertension

(72%), smoking (36%) of patients, diabetes mellitus (DM) (24%), cardiac (20%) and hyperlipidemia (16%), and last history of the previous stroke in 12 % of cases. While, the most common risk factors for ICH in surgical group were hypertension (68%), smoking (40%) of patients, DM (20%), cardiac (16%) and hyperlipidemia (16%), and lastly history of previous stroke in 16 % of cases (no significant difference regarding to risk factors in both groups P -value = 0.994). There was no significant difference in the affected arm, leg or speech in conservative groups and P values were (0.77, 0.78 and 0.83 respectively). Also, there was no important statistical difference in both conservative and surgical groups regarding GCS ($P = 0.468$) and NIHSS ($P = 0.927$). In all cases the cause of death was cardiac arrest after failure of all life support measures.

Table 3 showing hematoma characteristics in both groups. The mean size of hematoma is slightly larger in the surgical group in comparison to the medical group but not statistically significant (45 ± 14 and 40 ± 13 respectively and $P = 0.512$). Also regarding the location of hematoma no significant difference ($P = 0.8324$): in conservative group 44% were lobar, 44% were ganglionic and/or thalamic while, 12% were in both lobar and ganglionic site. In the surgical group 52% were lobar, 36% were ganglionic and/or thalamic while, 12 % were in both lobar and ganglionic site. With no significant difference of lateralization of hemorrhage ($P = 0.3946$). The least depth from cortical surface was 1.5 cm (0.5–3.1) in conservative group and was 1.0 cm (0.0–2.0) in surgical group ($P = 0.755$).

The primary outcome for surgical group was statistically insignificant more unfavorable in (68%) of cases in comparison with conservative group it was unfavorable in (64%) of cases ($P = 0.7652$). While the mortality rate at 6 months for the early surgery group was 10 patients (40%) compared with 8 patients (32%) for the group treated by conservative medical treatment (statistically insignificant as P value = 0.556). The secondary outcome by MRS was slightly favorable but statistically insignificant in (32%) of cases of the conservative group and only (28%) of cases of the surgical group ($P = 0.5287$). Similarly, the secondary outcome by BI was slightly favorable but statistically insignificant in (28%) of cases of the conservative group and only (24%) of cases of the surgical group ($P = 0.5287$) (Table 4).

Table 5 showing the results of the subgroup analyses are shown in Fig. 1. The only subgroup to show heterogeneity of treatment response was the depth of hematoma from cortical surface. A favorable outcome from early surgery was more likely if the hematoma was 1 cm or less from the cortical surface (95% CI 1.41). A uniformly poor

outcome was seen in patients in the coma (GCS \leq 8): early surgery increased the relative risk of poor outcome (95% CI 1.95). Also, hematoma size of \geq 50 cm surgery raised the relative risk of the poor outcome for these patients (95% CI 1.07).

Table 1. Age and sex distribution in surgical and medical groups

Variables		Conservative group	Surgical group
Age mean \pm SD		63 \pm 13 y (50-91)	60 \pm 11 y (44-70)
Sex	Male number (%)	13 (52%)	14 (56%)
	Female number (%)	12 (48%)	11 (44%)
Total		25	25

Table 2. Medical history, affected limb, speech, Glasgow coma score and NIHSS at presentation

Variables		Conservative group number (%)	Surgical group Number (%)	Test of significance
Medical history	Hypertension	18 (72%)	17 (68%)	$\chi^2 = 0.235$
	DM‡	6 (24%)	5 (20%)	P = 0.994
	Cardiac	5 (20%)	4 (16%)	
	Hyperlipidemia	4 (16%)	4 (16%)	
	Smoking	9(36%)	10(40%)	
	Previous stroke	3(12%)	4(16%)	
Affected arm	Normal or weak	10 (40%)	9 (36%)	$\chi^2 = 0.0849$
	Paralysed	15 (60%)	16 (64%)	P = 0.77
Affected leg	Normal or weak	12 (48%)	11 (44%)	$\chi^2 = 0.08$
	Paralysed	13 (52%)	14 (56%)	P = 0.78
Speech	Normal	10(40%)	8 (32%)	$\chi^2 = 0.3768$
	Dysphasic-aphasic	11(44%)	12 (48%)	P = 0.828
	Cannot be assessed	4 (16%)	5 (20%)	
GCS* baseline	5–8	5(20%)	7 (28%)	Chi-square = 1.515
	9–12	10(40%)	12 (48%)	
	13-15	10(40%)	6 (24%)	
NIHSS† baseline	Mild (1-5)	3(12%)	2 (12%)	$\chi^2 = 0.4598$
	Moderate (6-15)	12(48%)	13 (42%)	P = 0.927
	Sever (16-25)	6(24%)	7 (28%)	
	Very sever >25	4(16%)	3 (12%)	

*= Glasgow coma scale, †=National institute of health stroke scale, ‡=DM

Table 3. Hematoma characteristics

Variable		Conservative group	Surgical group	Test of significance
Hemorrhage volume (cc) mean \pm SD (Range)		40 \pm 13 (21-63)	45 \pm 14 (24-70)	$\chi^2 = 1.322$ P = 0.512
Location of hemorrhage Number (%)	Lobar	11 (44%)	13 (52%)	$\chi^2 = 0.3667$
	Basal ganglia/thalamic	11 (44%)	9 (36%)	P = 0.8324
	Both	3 (12%)	3 (12%)	
Lateralization of hemorrhage	Right	15	12	$\chi^2 = 0.7246$
	Left	10	13	P = 0.3946
Least depth from cortical surface (cm)		1.5 (0.5-3.1)	1.0 (0.0-2.0)	P = 0.755
Total		25	25	

Table 4. Primary and secondary outcomes at 6 months

	Conservative group (n=25)	Surgical group (n=25)	Test of significance
Primary outcome			
Favorable	9 (36%)	8 (32%)	$\chi^2 = 0.089$
Unfavorable	16 (64%)	17 (68%)	$P = 0.7652$
Secondary outcomes			
Mortality			
Alive	17 (68%)	15 (60%)	$\chi^2 = 0.347$
Dead	8 (32%)	10 (40%)	$P = 0.5556$
MRS*			
Favorable	8 (32%)	6 (24%)	$\chi^2 = 0.396$
Unfavorable	17 (68%)	19 (76%)	$P = 0.5287$
BI†			
Favorable	7 (28%)	6 (24%)	$\chi^2 = 0.104$
Unfavorable	18 (72%)	19 (76%)	$P = 0.7471$
Total	25	25	

*=Modified Rankin scale, †=Barthel index

Table 5. The primary outcome across the subgroup analyses were compared with formal interaction tests

Subcategory		Conservative treatment n/N*	Surgery n/N*	Odds ratio (fixed) 95% CI
Age	<65	9/15	11/16	0.85 (0.64–1.27)
	65≥	7/10	6/9	0.81 (0.5–1.38)
GCS	5–8	4/5	6/7	1.95 (0.81–4.69)
	9–12	7/10	7/12	0.73 (0.46–1.14)
	13–15	5/10	4/6	0.87 (0.56–1.32)
Site of hematoma	Lobar	8/11	7/13	0.78 (0.56–1.1)
	BG†/thalamus	7/11	8/9	1.09 (0.72–1.52)
Hematoma volume	<50	11/17	9/15	0.85 (0.64–1.25)
	50≥	5/8	8/10	1.07 (0.66–1.69)
Depth from cortical surface	1≤	5/8	9/15	0.71 (0.51–1.08)
	>1	11/17	8/10	1.41 (0.97–2.27)
Side of hematoma	Right hemisphere	9/15	8/12	0.87 (0.57–1.17)
	Left hemisphere	7/10	9/13	0.91 (0.59–1.38)
Deficit of affected arm	Normal/weak	6/10	6/9	0.87 (0.52–1.2)
	Paralyzed	10/15	11/16	0.89 (0.58–1.42)
Deficit of affected leg	Normal/weak	7/12	7/11	0.90 (0.59–1.28)
	Paralyzed	9/13	10/14	0.89 (0.53–1.38)
Deficit of speech	Normal	6/10	5/8	0.72 (0.44–1.13)
	Dysphasia/aphasia	7/11	8/12	0.88 (0.73–1.39)

*=Unfavorable cases/ total number of the cases, †=Basal ganglia

4. DISCUSSION

For most patients with ICH, the value of surgery is doubtful [19]. Generally, patients with serious coma (GSC < 4) are regarded bad surgical candidates with poor outcome disregarding of management option. Nonetheless, surgical ICH evacuation is designate as soon as possible for patients with posterior fossa hemorrhages larger than 3 cm in greatest width, who are worsening clinically, or who have hydrocephalus from ventricular obstruction or brainstem compression [20].

Concerning the risk factors, in the present study the most common risk factor in both surgical and conservative groups was hypertension. Many risk factors for ICH have been designated during the previous years, particularly genetics, race, lifestyle, and pre-existing medical conditions. Lifestyle risk factors include smoking, excessive alcohol intake, drug abuse, unhealthy diet, and a lack of regular physical activity. Risk factors in a patient's past medical history include prior stroke, hypertension, diabetes mellitus, psychosocial stress, cerebral amyloid angiopathy, coagulopathy, and an underlying vascular lesion [21].

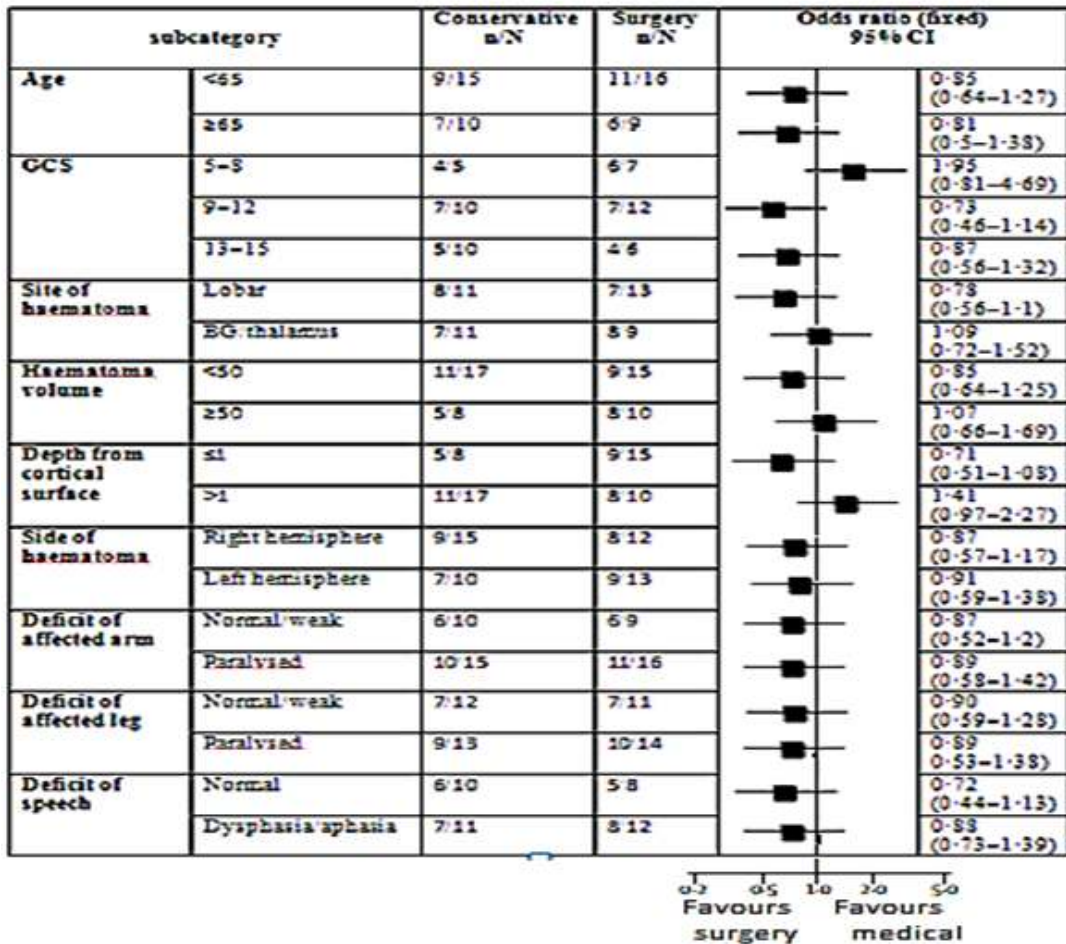


Fig. 1. The primary outcome across the subgroup analyses were compared with formal interaction tests

Regarding the GCS, the conservative group showed more GCS than surgical groups though the disparities were statistically non-significant. In our patients, there were statistically non-significant differences between surgical and conservative groups regarding NIHSS. For frequent surveillance of patients after stroke who are at the hazard for neurological deteriorating, the NIHSS offers a critical utility [22].

Evaluating the volume of the hematoma is essential as bigger hematomas have a worse outcome [23]. The surgical group in our study revealed the somewhat larger size of the hematoma but the divergences were statistically non-significant so, the disparities in hematoma size between surgical and conservative groups in our study did not influence the prognosis.

Surgical evacuation of the hematomas continues contradictory. Surgical evacuation lowers the

mass effect, and may reducing the more destruction of brain tissue and edema formation [24]. Nevertheless, this impact is counteracting by the destruction suffered during the approach via healthy brain parenchyma. Regarding primary prognosis in our study (assessed by GOS), there was about one-third of our patients with favorable prognosis and about two-thirds showed unfavorable prognosis with statistically non-significant differences between surgical and conservative groups. This was consistent with other studies as The STICH trial [25], which compared early surgery with medical treatment. Early surgery showed no benefit compared to conservative treatment; 24% versus 26% had good recovery or moderate disability. The STICH II trial particularly analyses the advantages of early surgery for lobar hematomas within 1 cm of the cortical surface without intraventricular extension. There were no statistically significant disparities between surgical and conservative

groups [26]. Mourad and his colleagues had investigated forty patients with SSICH and stated that surgical evacuation has a restricted advantage relative to conservative medical treatment [27]. Additional accessible proof consists a meta-analysis of three formerly declared trials and case series [28]. The general conclusion from these researches was that there was no characteristic in fatality or prognosis between the groups randomized to medical management of ICH compared to surgical evacuation. In comparison, a Cochrane review of ten trials clustering about 2059 ICH patients showed a statistically significant result in preferable of surgery when looking at death as an endpoint alone, and furthermore when death or dependency at ultimate follow-up were merged [29].

The secondary prognosis evaluated by the mRS and BI demonstrated no statistical disparities among the conservative and surgical groups. This is consistent with other studies. Regarding mortality, about two-thirds of either group were alive while about one-third died (statistically non-significant differences between the two groups). Auer and his colleagues declared mortality rate of 42% in the surgical group and 70% in the medical group [30]. Chen and his colleagues stated that the mortality was about 23% of surgical patients and 17% in the medical group [31]. One meta-analysis faulted to demonstrate a statistically significant decrease in death with surgical intervention relative to the classic medical therapy [32].

Patients oldest-old (aged 85 and older), as compared with younger patients, showed some peculiar clinical features and poorer outcome, including higher in-hospital mortality (50% versus 27%) and moderate or severe neurological deficit at hospital discharge (89% versus 58%) [33]. These results are in agreement with our study as patients aged 65 and older showed more unfavorable outcome when compared with younger patients (68.4% versus 64.5%).

In the present study, subgroups analysis demonstrated a few characteristic except in two groups of patients: first, in patients in whom the ICH achieved about one centimeter of the cortical surface in preferable for surgical interference (95% CI 1.41). Second, the bad prognosis in patients provided with ICH in the coma. In those with preliminary GCS of eight or below, almost all were ranked as having bad prognosis (ie, lower severe disability or worse on

the prognosis-based outcome scale). Initial surgery increased the possibility of bad prognosis for these patients (95% CI 1.95). Furthermore, hematoma size of more than or equal to 50-centimeter surgery increased the relative susceptibility of bad prognosis for these patients (95% CI 1.07). These results are in agreement with Mendelow and colleagues [25].

5. CONCLUSIONS

In our study, we found no statistically significant difference in outcome between surgical and medical management of primary intracerebral hemorrhage. Patients with superficial hematomas might benefit from surgery. But, surgical management should be avoided in patients with GCS of eight or below, especially if the hematoma volume of ≥ 50 cm.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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