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Meta-Analyses of Intracerebral Hematoma Treatment

İntraserebral Hematom Tedavisi Metaanalizi

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ABSTRACT

AIM: The aim of this study is to define the position of surgery preference in the treatment choice for spontaneous intracerebral hematoma (ICH) and to compare the efficacy of surgery with the medical treatment based on data from 18 previously reported randomized prospective studies on this topic.

MATERIAL and METHODS: Literature databases and articles were searched from 1960 to 2010. Eighteen randomized studies on this topic were evaluated.

RESULTS: Among these 18 studies, 7 (38.9%) were multicenter and 11 (61.1%) were single center. Totally 204 centers were involved. 1769 patients were treated surgically and 3200 medically. Craniotomy was the most preferred method (n=14; 77.8%). Follow-up time was mostly 6 months. In general, the effect of surgical versus medical treatment on outcome (mortality/morbidity) after a supratentorial spontaneous ICH do not differ significantly. In individual analysis, the mortality was found to be significantly lower in the operated group than the non-operated group in only two studies (Kurtsoy's and Miller's studies). Meta-analysis of subgroup analysis revealed surgical treatment results were significantly better for hematoma volume >40ml, early surgery (before 24 hours), and Glasgow Coma Scale (GCS)≥6.

CONCLUSION: Surgical treatment results were found to be superior to medical treatment in cases with hematoma volume >40ml, and GCS≥6. The studies are not adequate to analyze the best type of surgery.

KEYWORDS: Intracerebral hematoma, Meta-analyses, Surgery, Glasgow coma scale

ÖZ

AMAÇ: Bu çalışmanın amacı, spontan intraserebral hematomun tedavisinde daha önceden yazılmış 18 randomize prospektif çalışmanın bulgularına dayanarak cerrahi tercih durumlarını belirlemek ve medikal ile cerrahi tedavi sonuçlarının etkinliğini karşılaştırmaktır.

YÖNTEM ve GEREÇ: 1960-2010 yılları arasında veritabanları taranarak ilgili makaleler araştırıldı. Bu konu üzerine 18 randomize çalışma değerlendirildi.

BULGULAR: On sekiz çalışmanın 7si (%38,9) çok merkezli, 11'i (%61,1) tek merkezliydi. Toplam 204 merkez dahildi. 1769 hastaya cerrahi, 3200 hastaya medikal tedavi uygulandı. Kraniotomi en çok tercih edilen yöntemdi (n=14;%77,8). Takip süresi çoğunlukla 6 aydı. Genel olarak supratentorial spontan ICH sonrası sonuçlarda (mortalite ve morbiditede) cerrahinin medikal tedaviye etkinliği anlamlı farklı bulunmadı. Bireysel analizlerde sadece iki çalışmada(biri Kurtsoy'un ve diğeri Miller'ın) mortalite opere olan grupta opere olmayanlara göre daha düşük bulundu. Alt grupların meta-analizinde cerrahi tedavi hematom hacmi 40 ml üstünde, erken cerrahide (24 saatten önce), Glasgow koma skalası 6 ve üzerinde anlamlı üstün bulundu.

SONUÇ: Hematom hacmi 40 mlden büyük, GCS 6 ve üzerinde olgularda cerrahi sonuçlar medikal tedaviden üstün bulundu. Çalışmalar en iyi cerrahi tipini belirlemek için yeterli değildir.

ANAHTAR SÖZCÜKLER: İntraserebral hematom, Metaanaliz, Cerrahi, Glasgow koma skalası

INTRODUCTION

The management and the effectiveness of the surgical treatment of spontaneous intracerebral hematoma (ICH) are still controversial. There is no clear indication of the optimal treatment choice for ICH; surgical or otherwise. Current clinical practice seems varied. Proper evaluation of the role of surgery on spontaneous ICH should be provided (8,29). In fact, 18 randomized trials (1,2,4,6,7,11,13,14,15,17,18,19,22,23,24,26,27,29) have been published on the surgical evacuation versus medical treatment of spontaneous ICH. The first, carried out in 1961 by McKissock et al (17), revealed no benefit from surgical treatment. This study had a strong influence on neurosurgical practice, even nowadays (8). Studies by Juvela et al (14) in 1989, Batjer et al (2) in 1990, Morgenstren et al (21) in 1998, Zuccarello et al (28), Kurtsoy et al (15) and Miller et al (19) were all too small in number of patients to be conclusive. Auer et al (1) in 1989 found a significant benefit from endoscopic

evacuation of ICH only in subcortical hematomas.

To investigate the feasibility of surgical treatment of ICH, we analyzed and reviewed eighteen randomized studies on surgical treatment versus current non-operative management in patients with spontaneous supratentorial ICH.

MATERIAL and METHODS

A literature search was performed using PUBMED, MEDLINE, EMBASE-Excerpta Medica databases from 1960 to 2010 on randomized studies for the treatment of spontaneous ICH. Reference lists of all the articles identified were also examined, and relevant cited references were similarly reviewed. Eighteen randomized prospective studies between the years 1960-2010 were included. All available data were then combined to be analyzed as a whole.

The summaries of the studies are given in Table I.

Statistical analysis was performed via the computer-based software SPSS 16.0 and NCSS for windows.

Simple descriptives were used for total, minimum and maximum number of centers and number of patients (surgical, medical, totally) and age while simple descriptives and frequencies were used for administration time and surgical time.

Age was divided into two groups as below and above 65 years of age.

Admission and surgical time were evaluated in two groups as before and after 24 hours.

Hematoma dimensions were given as volume and/or diameter and/or depth, and the distribution among studies was analyzed by simple descriptives.

ICH volume was grouped into four groups: group 1: <10ml, group 2:10-40ml, group 3:40-80ml and group 4:>80ml.

Glasgow Coma Scale (GCS) was evaluated in 4 groups;

Group 1 (3-5): very severe

Group 2 (6-8): severe

Group 3 (9-12): moderate

Group 4 (13-15):mild

All available data from included studies were entered and combined to be analyzed as a whole by using the well-established meta-analysis methods. Using the end points of death and dependency, the results were expressed as odds ratios with their associated 95% confidence intervals. Significance was assigned at a p value <0.05

RESULTS

An elegant description of the relevant details of the previously meta-analyzed trials is already available and will not be repeated here.

All included studies are summarized in Table I.

In this meta-analysis we analyzed all parameters of 18 studies. Among 18 studies 7 (38.9%) were multicenter, 11 (61.1%) were single center. A total of 204 centers participation was included.

A total of 5511 patients were involved in 18 studies; the minimum number of total patients in a study was 10, and the maximum was 1578. In the study by Gregson et al (11) on 542 patients, neurosurgeons were not sure of the treatment which mostly appropriate treatment and/or informed consent could not be obtained. Those patients were excluded and the final total number of patients was 4969. 1769 patients were treated surgically and 3200 medically (Table II).

The admission time was reported in 10 studies . Among these studies, admission time was the first 6 hours in 1 (10%), the first 12 hours in 2 (20%), the first 24 hours in 5 (50%) and the first 72 hours in 2 (20%) (Table III).

Age range of all studies was 15 to 80 years with a mean of 64.2±15.5 years.

Hematoma location was supratentorial in all studies. Hematoma dimensions were given as volume and/or diameter. Hematoma volume distribution among eleven studies was 10 to 100 cm3. In four studies mean hematoma volume was used; minimum 40 cm3 and maximum 96 cm3. In four studies hematoma diameter was used; minimum 2cm, maximum 5cm. Hematoma depth was given in three studies, among these the range was 1-2cm.

Surgery time was reported in 15 studies. In the study Sun DTF et al (26) surgical time was evaluated in two groups as early (before 24 hours) and late surgery (after 24 hours). Thus 16 surgical time results were present in 15 studies; surgery time was within 3 hours of submission in 1 (6.25), within 6 hours in 1 (6.25%), within 12 hours in 2 (12.5%), before 24 hours in 5 (31.25%), after 24 hours in 2 (12.5%), within 48 hours in=3 (18.75%) and within 72 hours in=2 (12.5%) (Table IV).

Surgical type was reported in 17 studies. The types of surgery are given in Table V. Craniotomy was the most preferred method (n=14; 77.8%). In three studies two types (craniotomy and stereotactic in both, stereotactic and stereotactic plus fibrinolytic in one), in two studies three types (craniotomy, stereotactic surgery, EVD) and in one study four types (craniotomy, stereotactic, endoscopic, simple aspiration with burr-hole) of surgical procedures were used.

Follow-up time was given in 14 studies, varied 1-24months and preferred, mostly at 6 months (n=9).

Meta-analysis of the effect of surgical versus medical treatment on outcome (mortality/morbidity) after a supratentorial spontaneous ICH indicate a nonsignificant increase (p=0.822) in the odds (0.92) of death and dependency at 6 months for patients treated surgically (Table VI).

Subgroup analyses were carried out for the effect of admission time, age, hematoma volume, surgical time and GCS on mortality and morbidity. Admission time, age factor did not make a significant effect on mortality or morbidity. In cases with hematoma volume >40ml, surgical treatment results were significantly better regarding mortality (p=0.04) and

Table I: Summary of Randomized Studies on Spontaneous Supratentorial ICH

Author/Year	Inclusion Criteria	Number of Cases	Surgical Technique and Timing	Outcome(S: surgical, M: medical)	Limitations	Results
Mckissock W, 1961	Any age Admission time not reported Diagnosis based on clinical symptoms, LP, angiography, ventriculography	89 surgical 91 medical	Craniotomy After 24 hours	Mortality at 6th month 80% in S, 66% in M, Morbidity at 6th month 65% in S, 51% in M.	5% diagnostic error, Before CT	No significance among the treatment groups, but a higher chance of death or dependency with surgery
Juvela S, 1989	15-65 years, Admission in 24 hours Clinic; unconscious, dysphasia, hemiparesis	26 surgical 26 medical	Craniotomy Within 48 hours	6th, 12th months results Total mortality as 42%; 46% in S , 38% in M Life with minimal or no deficit was totally 20%; 7% in S and 31% in M.	Number of patients is small	No significance among the treatment groups. Mortality rate, among cases with GCS 7-10 was significantly lower in the surgical group
Auer LM, 1989	Age 30-80 years Clinic; stable, with/without neurological deficit. Hematoma locations: subcortical, putaminal and thalamic region. ICH volume ≥10cm^3	50 surgical 50 medical	Stereotactic endoscopic removal Within 48 hours	6th month results Mortality 42% in S, 80% in M, Morbidity as 58% in S, 74% in M. Life with minimal or no deficit 40% in S, 25% in M.		No significance on mortality and recovery rates of putaminal and thalamic hematomas but surgical treatment results were better in subcortical hematomas.
Batjer AH, 1990	Age 30-75 Admission in 24 hours Putaminal hematoma, diameter>3cm HT anamnesis Neurological deficit +/-	8 surgical 9 medical 4 medical+ ICP monitori-zation	Craniotomy Within 24 hours	6th month results Total mortality 71%, 78% in S, 67% in M, Morbidity 65% in S, 51% in M. Independent life 19%	Number of patients is small	No significance among the treatment groups
Chen X, 1992	HT anamnesis Supratentorial hematoma without herniation signs	64 surgical 63 medical	Craniotomy Stereotactic surgery Ventricular drainage	Results of 1st and 3rd months were evaluated. Mortality 23% in S, 17% in M, Morbidity 63% in S, 50% in M.	Groups do not appear balanced, Differ signifi- cantly in level of consciousness, the size of the hematoma and the presence of hemiplegia.	At 1st month the medical group showed significantly higher rate of outcomes, however no differences between the groups are reported at 3 months, a trend toward a higher chance of death or dependency with surgery.
Morgenstren LB, 1998	Hematoma location: lobar or deep in location and extended outside the thalamus ICH >9 mL Clinic: with significant neurologic impairment Admission in 12 hours GCS between 5 and 15 GCS≤ 9 ICP monitori-zation is performed	17 surgical 17 medical	Craniotomy Within 12 hours	Results of 1st and 6th months were evaluated. At 6th month mortality 54% in S, 36% in M, morbidity 69% in S, 50% in M. In patients with similar hematoma volume and GCS, 1st month results; mortality 6% in S, 24% in M, and 6th month results 17% in S and 24% in M	The surgical group had larger hemorrhages (median, 96 mL) and a lower GCS (median, 10) compared with the medical group (33 mL; GCS 13).	No significance among the treatment groups. Mortality was seemed to be lower in the surgical group compared with the medical group at 1st month, but similar at 6th months.
Zuccarello M, 1999	Age >18 years ICH volume > 10 cm^3 Clinic: with a focal neurological deficit GCS score >4 at the time of enrollment; Admission in 24 hours	9 surgical 11 medical	Craniotomy Stereotactic surgery Within 3 hours of admission	3rd month results Mortality 22% in S, 27% in M Morbidity 44% in S, 64% in M Good outcome 56% in S, 36% in M	Number of patients is small Groups were not comparable with regard to location of ICH.	No significance among the treatment groups Analysis of the secondary 3-month outcome measures showed a nonsignificant trend toward a better outcome in the surgical versus medical for the median GOS, Barthel Index, and Rankin Scale and a significant difference in the National Institutes of Health Stroke score

Table I: Summary of Randomized Studies on Spontaneous Supratentorial ICH

Author/Year	Inclusion Criteria	Number of Cases	Surgical Technique and Timing	Outcome(S: surgical, M: medical)	Limitations	Results
Kurtsoy A, 2001	Admission in 6 hours Moderate and severe thalamic hematomas with brainstem reflexes GCS≥5	21 surgical 24 medical	Contralateral transcallosal microsurgical approach Within 6 hours	8th month results Mortality 14.3% in S, 50% in M Vegetative state 28.57%in S, 25% in M Severe morbidity 28.57% in S,12.5%in M Moderate morbidity 19.04%in S, 8.33%in M Life with minimal or no deficit 9.53% in S, 41.6% in M	Number of patients is small	Mortality was significantly lower in the operated group than the nonoperated group.
Teernstra OP, 2002	Age >45 years, GCS:2-10, ICH volume >10ml	36 surgical 35 medical	Stereotactic surgery with fibrinolytic treatment and aspiration. Within 72 hours	6th month results Mortality overall 57%; 56% in S, 59% in M Morbidity 79% in S, 75% in M		No significance among the treatment groups Significant ICH volume reduction was achieved by the intervention. Logistic regression analysis indicated the possibility of efficacy for surgical treatment
Gregson BA, 2003	ICH diameter >2cm, ICH depth <2cm GCS>5 Admission in 72 hours	336 surgical 700 medical 542 uncertain	Surgery within 24 hours			No significance among the treatment groups
Sun DTF, 2004	Hematoma location putaminal, subcortical and deep basal ganglia Early surgical treatment limited to age<65 years, ICH size:30-100 mL, and motor scores of normal flexion to localizing to pain. Late surgical treatment performed for patients whose GCS score was decreased 2 or more on medical treatment.	53 surgical (34 early , 19 late surgery) 71 medical	Craniotomy for putaminal and subcortical hematomas Stereotactic aspiration for deep basal ganglia hematomas. Early surgery within 24 hours Late surgery after 24 hours	6th month results Early surgery results 18% mortality, 29% independent and 53% dependent Early surgery for subcortical haematoma showed best prognosis (42%independence) In late surgical treatment recovery was encountered only in 9% Recovery of putaminal hematomas was 26% in the early surgery and 42% in M Recovery of subcortical hematomas was 42% in the early surgery and 88% in M Recovery of deep basal ganglia hematomas was 20% in the early surgery and 20% in M Overall mortality 21%, dependent recovery44% recovery 35%.		Except subcortical hematomas, both treatment approaches are not advantageous over one another. Late surgery does not affect recovery. Study support early surgery for patients with putaminal and subcortical haematomas with ICH> 50 mL. For ICH< 30 mL, conservative management is superior
Mendelow AD, 2005	Any age GCS≥5 Admission in 72 hours ICH diameter >2cm	503 surgical 530 medical	Craniotomy, Burr-hole, Endoscopy, Stereotactic surgery. Within 24 hours	6th month results Mortality 36% in S, 37% in M Morbidity 67% in S, 72% in M Satisfactory recovery 33% in S, 28% in M Favorable outcome 26% in S, 24% in M		No significance among the treatment groups

Table I: Summary of Randomized Studies on Spontaneous Supratentorial ICH

Author/Year	Inclusion Criteria	Number of Cases	Surgical Technique and Timing	Outcome(S: surgical, M: medical)	Limitations	Results
Prasad KS, 2006	Admission in 12 hours	140 surgical 390 medical	Craniotomy Within 48 hours			Surgery was to be preferred when ICH Right side, lobar superficial big shift, large volume, and early diagnosed
Hattori N, 2006	Age 35-85 years Admission in 24 hours Neurologic grades (NGs) ranging from NG1 to NG5 Only patients with spontaneous putuminal hemorrhage, whose eyes are closed but open to weak stimuli (NG2) or strong stimuli (NG3) on admission were included	121 surgical 121 medical	Stereotactic aspiration Stereotactic + fibrinolytic treatment Within 72 hours	12th month results Mortality (NG2 &NG3) in M 11.4% & 23.5% in S 4.3% & 11.8% Dependent recovery in M 48.6% & 54.9% in S 42.9% & 41.1% Independent recovery in M 40% & 21.6% in S 52.9% & 47.1%		Treatment results of both groups were insignificant, surgical treatment results seems to be better in patients with NG3 and NG2 findings.
Morioka J, 2006	Hematoma locations: putaminal, thalamic, cerebral subcortical	123 surgical 887 medical	Craniotomy Stereotactic surgery EVD			In small (<3cm) and in moderate (3-5cm) hematomas no significance was found between surgical and medical treatments. In big (>5cm) hematomas the surgical treatment results were significantly better.
Pantazis G, 2006	Clinic: neurologic impairment Hematoma locations: subcortical, putaminal ICH> 30 mL.	54 surgical 54 medical	Craniotomy Within 8 hours	12th month results Mortality 48% in S and 57% in M		Mortality rates between surgical and medical treatments did not differ significantly. Analysis of outcome revealed a significantly higher percentage of GCS scores higher than 3 for the surgical patients. Functional results were better in surgery for subcortical or putaminal hematomas. Stratifications of the initial neurologic status, hematoma volume, and location parameters and analysis showed that the positive effect of surgery on the quality of survival was statistically not valid for patients with GCS< 8 or ICH volumes ≥80 mL
Miller CM, 2008	Admission within 24 hours	6 surgical 4 medical	Stereotactic Endoscopic Evacuation within 24 hours	Mortality 20% in S, 50% in M	Number of patients is small	Image guided stereotactic endoscopic is effective in immediate hematoma evacuation
Cho Dy , 2008	Basal ganglia hemorrhage	113 surgical 113 medical	Endoscopic surgery	Early and 6th months results Early: Medical better at MICH 0 or 1 6th months Surgery better at MICH 3 or 4	Modified Intracerebral Hemorrhage (MICH) score is used for evaluation of mortality and morbidity	At MICH 5 all patients died The best cut-off for good functional outcomes GCS≥4, Barthel index≥55, MICH≥2.

Table II: Total Number of Centers & Patients, Surgically & Medically Treated Patients

	Number of centers involved	Total number of patients involved	Total number of patients finally involved	Number of surgically treated patients	Number of medically treated patients
Grand total sum	204	5511	4969	1769	3200
Minimum	1	10	10	6	4
Maximum	83	1578	1036	503	887

Table III: Admission Time

	Frequency	Percent
first 6 hours	1	10
first 12 hours	2	20
first 24 hour	5	50
first 72 hours	2	20
Total	10	100

Number of studies that had reported admission times are listed in frequency and percents.

Table IV: Surgical Time

	Frequency	Percent (%)
within 3 hours of admission	1	6,25
within 6 hours	1	6,25
within 12 hours	2	12,5
before 24 hours	5	31,25
after 24 hours	2	12,5
within 48 hours	3	18,75
within 72 hours	2	12,5
Total	16	100

Number of studies that had reported surgical times are listed in frequency and percents.

Table V: Surgical Types

	Frequency
Simple asp with burr hole	6
Craniotomy	14
Stereotactic	6
Stereotactic with fibrinolytic	2
Endoscopic	6
Stereotactic endoscopic	1
EVD	2
Contrlateral transcallosal approach	1

Number of studies that had reported surgical types are listed in frequency and percents.
Note: *More than one type of surgery were reported in some studies.*

morbidity (p=0.019). Early surgery (before 24 hours) favours the outcome regarding morbidity significantly (p=0.01) and mortality but insignificantly (p=0.075). The endoscopic approach yielded a better outcome for morbidity (p=0.048). In cases with GCS≥6, surgical results were found to be better for mortality (p=0.035) and for morbidity (p=0.044).

DISCUSSION

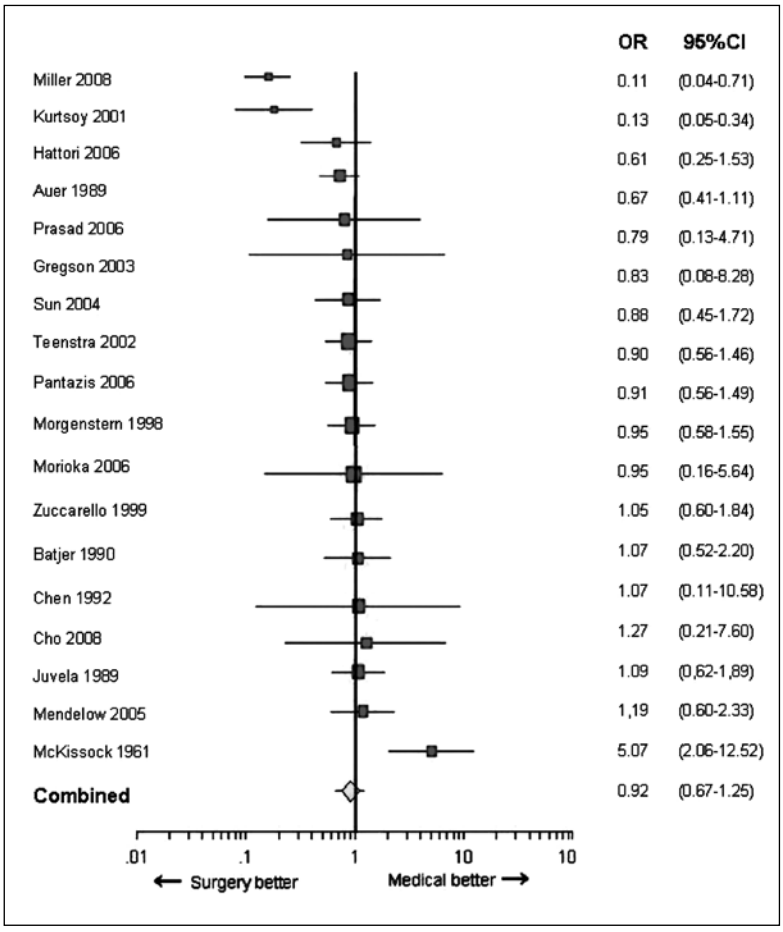
There is still debate among neurosurgeons and neurologist all over the world on the effective treatment of intracerebral hematoma (ICH) and about whether it should be surgically or medically treated. Criterias on treatment decision include; patient's age, hematoma volume, location and deepness from the surface, Glasgow coma scale (GCS), pathologies underlying hematoma (aneurysm, AVM, trauma etc.), time duration between hemorrhage and diagnosis, severe coagulopathy or presence of underlying serious medical disease, progression on neurological deficits or conscious, development of obstructive hydrocephaly, and compression of brain stem (3,8,9). However, The STICH (surgical treatment for intracerebral haemorrhage) study showed no overall benefit from early surgery when compared with initial conservative treatment (25).

The aim of surgical treatment in ICH can be summarized briefly as 'removing the most hematoma volume in the fastest way and with minimum surgical damage as possible'. If there is an underlying pathology of the hematoma, intervention should also be performed to that lesion during the surgery (3,8,9).

The percentage of preferring surgery changes in different countries. There are severe differences of surgical rates among countries and this can be attributed to the difference of patients' admission, to the difference of decision criteria among clinics, to the difference of centers' structure, to the difference of surgical expertise among countries and to the difference of people's expectations among countries. (11,26)

Surgical indication criterion of supratentorial hematomas include; progressive deterioration of consciousness, increased edema on CT, determining AVM, aneurysm or tumor on MRI and angiography, development of obstructive hydrocephalus, compression on brain stem, shift effect, patient age less than 80, GCS of 5-11, lack of severe coagulopathy or presence of systemic disease, hematoma volume greater than 30 cm3 at cerebral and diameter greater than 3 cm at cerebellar region, hematoma location on non-dominant hemisphere,

Table VI: Meta-analysis of the Effect of Surgical Versus Medical Treatment on Outcome at 6th Months (mortality/morbidity) after a Supratentorial Spontaneous ICH (p=0.822)



lobar and external capsule (1,4,6,7,11,13,14,19,22,23,26,27,29). In Broderick et al's study (3) surgical treatment was recommended for cases with low GCS, lobar hematoma, hematoma near surface and wide hematoma.

A medical approach is preferred for the patients with; hematoma volume ≤ 10 cm3 or ≥ 60 cm3 in supratentorial hemorrhage or for cases demonstrating minimal neurological deficit, in cases that would have very good or very poor prognosis, who have GCS greater than 10 or GCS less than five respectively or extravasation of contrast medium at hematoma area on CT, for cases with severe coagulopathy or presence of underlying serious medical disease, for very old (over 80) cases that would not tolerate operation and for pontine hematomas which are 60% fatal (4,7,17,26)

Surgical methods includes; simple aspiration (with Burr-hole), open craniotomy, decompression and removal of hematoma, fibrinolytic treatment, stereotactic surgery with fibrinolytic treatment, neuroendoscopic surgery with fibrinolytic treatment and stereotactic endoscopic removal (1,4,6,7,11,13,14,19,22,23,26,27,29). In contrast, the stereotactic aspiration technique can be safely performed and in a uniform manner. Despite the reduction of ICH volume, no improvement in mortality and functional result was obtained. Endoscopy is a new therapeutic option for ICH with good results for hematoma removal (7,19,25)

Timing of surgery is important. Early surgery decreases the toxic effects of blood and plasma products and this provides decrease of ischemia and edema of the neighboring glial tissues. Hematoma reaches its maximum dimensions in the first six hours (10). However very early surgery increases new hemorrhage risk. New hemorrhage risk after surgery is reported to be 40% in 4 hours and 12% in 12 hours by Morganstern et al (20), and 22% in 3-5 and 9% in 6-8 by Pantazis et al (23).

Simple aspiration by Burr-hole can be used in emergent cases. It can be performed by local anesthesia. Technically aspiration is performed after placing a catheter into hematoma but it is not preferred nowadays. Only a small volume of hematoma can be aspirated. It can cause new hemorrhage since aspiration is performed in a blind way (18).

Craniotomy is a standard approach. It can be performed with decompressive craniectomy and duraplasty. It allows intervention to underlying pathology of hematoma. Adequate amount of hematoma can be aspirated. Bleeding control is easy (2,14,17,21,23,24,29).

Fibrinolytic treatment dissolves the blood rapidly and draining or aspiration. Fibrinolytic agents that can be used are urokinase and tissue fibrinogen activator (rTPA). Urokinase is applied as 5000-10000U in 5ml saline solution 1 to 4 times a day, treatment should be continued for 7 or more days. rTPA is applied as 2mg/12hours for 2-4 days or 5mg/24hours for 2-4 days. Fibrinolytic treatment increases new hemorrhage risk (13,27)

In stereotactic surgery, a silicon catheter is placed in hematoma location by stereotactic method. Initially the technique was only used for aspiration, recently it is used with fibrinolytic treatment. It can be performed under local anesthesia. Catheter is placed in the center of the hematoma (13,27).

Neuroendoscopic surgery is used for especially putaminal and thalamic wide hematomas (5,7). Under general anesthesia burr-holes from both frontal regions are performed, hematoma is aspirated through ventricle. Endoscope also can be replaced by stereotactic frame. It can also be performed as endoscopic aspiration of the hematoma through a study canule passing the opening of single burr-hole from the ipsilateral side. (5,7). Third ventriculostomy can be performed. Both lateral ventricle atria, frontal horns and third ventricle can be aspirated. Sometimes with 30º telescopes temporal horns and forth ventricle can be seen (28).

The results of the randomized studies we included in our analysis revealed in 18 studies (1,2,4,6,7,11,13,14,15,17,18,19,22,23,24,26,27,29) overall no significance was found among surgical and medical studies. Only in two studies by Kurtsoy A et al (15) and Miller et al (19) was mortality found to be significantly lower in the operated group than the nonoperated group, although the number of included patients was limited (21 surgically, 24 medically treated in Kurtsoy's (15) and 6 surgically, 4 medically treated in Miller's studies). The most striking differences of Kurtsoy's (15) study from others are firstly the surgical technique, contralateral transcallosal microsurgical approach, in very early stage (within 6 hours), the second is the short admission time criteria (within 6 hours) and the third is they only included patients with moderate and severe thalamic hematomas with brainstem reflexes with GCS≥5. Miller et al (19) used stereotactic hematoma evacuation technique.

When we further analyze the results we found out that in two studies (4,17) in general and in one study (26) only for ICH< 30 mL, medical treatment was reported to be insignificantly superior. Surgery results seemed better overall in the early period of two studies (21,29) but later no difference was found (21). A significant ICH volume reduction was achieved by the intervention (27). Surgical treatment results were found to be superior to medical treatment results in subcortical (1,23,24,26), putaminal (22,23,26) right sided (24), lobar (24) hematomas, in large hematoma volume (>5cm diameter or >50ml volume) (22,24,26), in hematomas that caused a big shift (24) and in patients with moderate GCS (7,14,23). Early surgery improves surgical results, thus to be preferred (15,24,26).

The studies reporting medical treatment is advantageous over surgical reveal:

- No significance among the treatment groups, but a higher chance of death or dependency with surgery (17)
- At 1st month the medical group showed significantly higher rate of outcomes, however no differences between the groups are reported at 3 months, a trend toward a higher chance of death or dependency with surgery (4)
- For ICH< 30 mL, conservative management is superior (26)

The studies reporting surgical treatment is advantageous over medical reveal:

- No significance on mortality and recovery rates of putaminal and thalamic hematomas but surgical treatment results were better in subcortical hematoma. (1)
- Mortality rate, among cases with GCS 7-10 was significantly lower in the surgical treatment group than in the medical. (14)
- Mortality was seemed to be lower in the surgical group compared with the medical group at 1st month, but similar at 6th months (21)
- Analysis of the secondary 3-month outcome measures showed a nonsignificant trend toward a better outcome in the surgical versus medical for the median GOS, Barthel Index, and Rankin Scale and a significant difference in the National Institutes of Health Stroke Scale score (7,13,29)
- A significant ICH volume reduction was achieved by the intervention (7,19,27)
- Early surgery in patients with putaminal and subcortical haematomas with ICH> 50 ml is superior (6,22,23,26)
- Surgery was to be preferred when ICH had these features: Right side, lobar location, superficial, large volume, big shift, and early diagnosed and treated patients (23,24,26)
- In hematomas >5cm the surgical treatment results were significantly better (22,23)

The main question to be answered is which cases we should operate?

Fewel et al (9) suggested that surgery should be considered in patients with moderate to large lobar or basal ganglia hemorrhages and those suffering progressive neurological deterioration, Proust et al (25) suggested supratentorial craniotomy for patients with GCS>8, HC volume of 10-40ml, lobar or for hematomas located at about 1cm to cortical surface.

According to our meta-analysis results patients with the GCS score ≥ 6, and those with hematoma volume greater than 40ml benefit from surgery.

The second question is which surgical technique we should choose?

According to Zuccarello et al (29) removed hematoma volume in craniotomy group is greater than stereotactic group. According to Morioka J (22) there is no significant difference between craniotomy and stereotactic operation on patients last state. Craniotomy has the longest operation time. Blood loss is reported to be most significant in the craniotomy. The highest hematoma evacuation rate was seen in the endoscopic surgery (5,7). In Cho's study (5) the mortality rate was 0%, 6.7% and 13.3% and the complication rate was 3.3%, 10% and 16.6% in endoscopic aspiration surgery group, in stereotactic aspiration and fibrinolytic treatment group, and in craniotomy group respectively. Both endoscopic surgery and stereotactic aspiration are minimally invasive and are effective procedures with low complication and mortality rates; however, the waiting timing of stereotactic aspiration is usually longer. Endoscopic surgery may be an appropriate substitute for stereotactic aspiration. It produces good neurological outcomes and aids in rapid hematoma. (5,7,19). In 18 studies we analyzed, only in Kurtsoy A et al's (15) and Miller's et al (19) studies mortality was found significantly lower in the operated group than the nonoperated group. The surgical technique was contralateral transcallosal microsurgical approach and endoscopic evacuation respectively (15,19). However according to our meta-analysis the studies are not enough to analyze the best surgical type.

The third question is when we should operate?

Acute management of deep-seated hematomas remains controversial. Since patients with these hematoma later tend to develop severe edema and necrosis around the lesion, when surgery is indicated it should be done as early as possible (15). According to our meta-analysis results early surgery improves outcome.

CONCLUSION

We conclude that operation is to be the preferred choice of treatment for the cases GCS≥6 and for large hematomas (>40ml volume). Early surgery especially within 24 hours improves surgical results. Although craniotomy is the most preferred method, endoscopic technique seems to provide decreased morbidity and mortality rates. However the studies are not enough to analyze the best surgical type.

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