



Predictors of Mortality in Patients with Surgically Treated Spontaneous Intracranial Hemorrhage

Spontan İntraserebral Kanamalı Hastalarda Cerrahi Müdahale Sonuçlarının Belirleyicileri

İsmail Kaya¹, İlker Deniz Cingöz², İnan Uzunoğlu³, Ceren Kızmazoğlu⁴, Hasan Emre Aydın¹, Nurullah Yüceer³

¹Kutahya University of Health Sciences, Department of Neurosurgery, Kutahya, Turkey

²Alsancak State Hospital, Clinic of Neurosurgery, Izmir, Turkey

³Katip Celebi University, Atatürk Training and Research Hospital, Department of Neurosurgery, Izmir, Turkey

⁴Dokuz Eylul University Faculty of Medicine, Department of Neurosurgery, Izmir, Turkey

Abstract

Objective: To investigate mortality in patients undergoing surgical treatment for spontaneous intracranial hemorrhage (sICH) and to identify the predictive factors.

Materials and Methods: The medical records of 164 patients with sICH who underwent surgery at two institutions between 2010 and 2017 were retrospectively examined and analyzed.

Results: Among 164 patients who received surgical treatment, 83 (50.6%) were women and 81 (49.4%) were men. The mean patient age was 56±14.54 years. Of all patients, 109 (66.4%) had hypertension. Hematoma was intraparenchymal in 69 (42.1%) patients, thalamic in 33 (20.1%), intraventricular in 33 (20.1%), and cerebellar in 29 (17.7%) patients. The mortality rate among patients who underwent surgery within the first 8 h of hematoma occurrence was 55.4%; this rate was 73% among those who underwent surgery 8-24 h after diagnosis, and 72.7% among those who underwent surgery 24-48 h after diagnosis.

Conclusion: Prognosis and mortality associated with sICH are usually affected by patient age, hematoma location and volume, intraventricular hemorrhage, and patient's initial neurologic status. We found no significant relationship between surgical treatment 8 h after hemorrhage and mortality. There are still discussions about the indications of surgical treatment in intracranial hematomas.

Keywords: Surgical treatment, spontaneous intracranial hematoma, mortality, prognosis

Öz

Amaç: Bu çalışmanın amacı, spontan intrakraniyal kanama nedeniyle cerrahi tedavi uygulanan hastalarda mortaliteyi araştırmak ve prediktif faktörleri tanımlamaktır.

Gereç ve Yöntem: 2010-2017 yılları arasında iki klinikte spontan intrakraniyal hematom nedeniyle ameliyat edilen 164 hasta retrospektif olarak incelendi ve analiz edildi.

Bulgular: Cerrahi tedavi uygulanan 164 hastanın 83'ü kadın (%50,6), 81'i erkekti (%49,4), yaş ortalaması 56±14,54 idi. Hastaların 109'unda (%66,4) hipertansiyon vardı. Altmış dokuz hastada (%42,1) hematom intraparakimial, 33'ünde (%20,1) talamik, 33'ünde (%20,1) intraventriküler, 29'unda (%17,7) ise serebellar yerleşimliydi. İlk 8 saat içinde ameliyat yapılan olgularda mortalite %55,4 (56 olgu); ameliyatın tanıdan 8-24 saat sonra yapıldığı durumlarda bu oran %73 (38 olgu) idi. Cerrahi tedavinin 24-48 saat arasında yapıldığı durumlarda mortalite oranı %72,7 idi (8 olgu).

Sonuç: Spontan intrakraniyal hematomlu hastalarda cerrahi prognoz ve mortaliteyi; hastanın yaşı, hematomun yeri ve hacmi, intraventriküler kanama ve hastanın başlangıçtaki nörolojik durumu belirler. Kanamadan 8 saat sonra yapılan cerrahi tedavi ile mortalite arasında anlamlı ilişki bulunmadı. İntrakraniyal hematomlarda cerrahi tedavi endikasyonları hakkında hala tartışmalar vardır.

Anahtar Kelimeler: Cerrahi tedavi, spontan intraserebral hematom, mortalite, prognoz

Address for Correspondence/Yazışma Adresi: İlker Deniz Cingöz MD, Alsancak State Hospital, Clinic of Neurosurgery, Izmir, Turkey

Phone: +90 530 110 43 73 E-mail: i.d.cingoz@hotmail.com ORCID: orcid.org/0000-0002-0452-7006

Received/Geliş Tarihi: 12.12.2018 **Accepted/Kabul Tarihi:** 27.07.2019

©Copyright 2019 by Turkish Neurological Society

Turkish Journal of Neurology published by Galenos Publishing House.

Introduction

Spontaneous intracranial hemorrhage (sICH) causes 10-20% of all strokes and is a major cause of morbidity and mortality (1,2). Hypertension is one of the most important causes of sICH (3), and hypertension-induced sICH is associated with a high rate of morbidity and mortality despite the availability of rational and effective treatments with the development of modern imaging methods. Intracranial hemorrhage (ICH) is the third most common cause of death worldwide (4). In addition to hypertension, other causes of sICH include vascular pathologies, anticoagulant use, drug and alcohol addiction, intracranial tumors, and amyloid angiopathies, which are especially seen in the elderly.

The aim of surgical treatment in sICH is hematoma evacuation and minimization of parenchymal trauma, possibly caused by the treatment. Treatment options include stereotaxic aspiration, endoscopic aspiration, and evacuation through open craniotomy, all performed under computed tomography (CT) imaging guidance. In this study, we focused on assessing mortality in patients undergoing surgical treatment with open craniotomy and identifying its predictive factors.

Materials and Methods

Between 2010 and 2017, 164 patients underwent surgery for sICH at Izmir Katip Celebi University Atatürk Training and Research Hospital and the Dumlupınar University Evliya Celebi Training and Research Hospital. Age, sex, risk factors, arterial blood pressure, hematoma location and volume, the starting way of bleeding, neurologic status, age variances of bleeding, prognosis, and the mortality of the patients were retrospectively examined. Hematoma volume was measured using the "ABC/2 Method" as defined by Kothari et al. (5) via CT imaging. The Glasgow Coma Scale (GCS) was used to assess neurologic status; a GCS score of 7 was considered to indicate a critical level of brain damage. Scores of <7 indicated severe brain damage and scores of >7 indicated low-grade brain damage (6).

Patients who had sICH, had hypertension or were diagnosed as having hypertension after the hemorrhage, had anticoagulant use-related supratentorial and infratentorial bleeding, and had undergone surgery between the ages of 18 and 70 years were included in the study. Patients who had arteriovenous malformations/aneurysms, tumor bleeding, and postoperative bleeding were excluded.

The study was approved by the Ethics Committee of the Izmir Katip Celebi University (date: 25.04.2018, protocol number: 183). Informed consent was neither required nor obtained due to the retrospective nature of the study.

Statistical Analysis

Statistical analysis was performed using the SPSS v23 software. In addition to descriptive statistical methods (mean, median, standard deviation), the independent t-test was used to compare dichotomous groups, the McNemar chi-square test was used to compare qualitative data, and Pearson's correlation test was used to measure the linear correlation of variables. $P < 0.05$ was considered to be significant.

Results

In total, 164 patients [83 (50.6%) women and 81 (49.4%) men; mean age, 56 ± 14.54 years] were included in the study. Hematoma volume was 20-40 mL in 52.8%, 40-50 mL in 25.9%, and >50 mL in 22.2% of the patients. Hematoma was intraparenchymal in 69 (42.1%) patients, thalamic in 33 (20.1%), intraventricular in 33 (20.1%), and cerebellar in 29 (17.7%) patients (Table 1). Of all patients, 109 (66.4%) had hypertension. Twenty-five (22.9%) patients with hypertension and surgical treatment were detected as being mismatched to the treatment. Furthermore, 14 (8.5%) patients were diagnosed as having hypertension during treatment for ICH.

Anticoagulant use-related bleeding disorder was observed in 32 (20%) patients; of these, 17 (53.1%) were using warfarin and 15 (46.9%) were using low-molecular-weight heparin. The reasons for anticoagulant therapy included coronary artery disease ($n=21$), prosthetic cardiac valve ($n=8$), and venous thromboembolic prophylaxis ($n=3$). Furthermore, 24 (14.6%) patients were under antiplatelet therapy. However, all of the patients presented with hypertension-related bleeding. Mortality rates were 55.4%, 73%, and 72.7% among patients with sICH who underwent surgery within the first 8 h, 8-24 h, and 24-48 h after diagnosis, respectively (Table 2). The mortality rate was 63.1% in cases with hematoma volume $< 25 \text{ cm}^3$, 52.3% in those with hematoma volume 25-50 cm^3 , and 66.6% in those with hematoma volume $> 50 \text{ cm}^3$ (Table 3). There was no surgical mortality in 31 patients with a GCS score of 13-15; however, the mortality was 69.3% in 101 patients with GCS scores 7-12, and 100% in 32 patients with GCS scores 6-7.

On initial CT imaging studies, 113 (68.9%) patients exhibited midline shift and 74 (45.1%) had hydrocephalus; 43 (26.2%) patients underwent ventriculostomy for extraventricular drainage of cerebrospinal fluid. Mortality was found to significantly increase in patients with intraventricular hemorrhage ($p < 0.005$). Duraplasty was performed in 123 (75%) patients; there was no significant difference in mortality between patients who did and

Table 1. Hematoma location

Location	Number of cases
Thalamic	33
Intraparenchymal	69
Intraventricular	33
Cerebellar	29
Total	164

Table 2. Mortality rates by time to surgical hematoma evacuation

Surgical time	Number of cases	Number of deaths	Mortality rate
First 8 h	101	56	55.4%
8-24 h	52	38	73%
24-48 h	11	8	72.7%
Total	164	102	

did not undergo duraplasty. A significant negative correlation was detected between midline shift and GCS ($p < 0.05$, $r = 0.21$), whereas a significant positive correlation was detected between midline shift and hematoma volume ($p < 0.001$, $r = 0.425$) and between intraventricular hemorrhage and mortality ($p < 0.001$, $r = 0.245$).

Discussion

The overall incidence of intracranial hematoma is 12-13/100,000 persons. These hematomas are usually spontaneous in nature, with 80% located supratentorially, and are associated with a higher mortality rate than other causes of stroke (7). They are more common in men and occur with an increasing frequency in individuals aged 45-55 years.

The first goal of surgical treatment is to avoid mortality, and the second is to decrease residual sequelae. The largest case series to date (5255 cases) reported a 22% postoperative mortality rate (8). Lo et al. (9) studied decompressive craniectomy and hematoma evacuation and reported a 41% mortality rate; patients who underwent decompressive craniectomy alone had a 40% mortality rate. In our study, the overall mortality rate was considerably high (62.2%), even in patients undergoing surgery within the first 8 h of diagnosis. Therefore, factors other than time to surgery should be considered. The most important risk factors for sICH are old age and acute and chronic hypertension (10,11,12,13).

A history of hypertension is noted in 72-78% of all patients with ICH (7,14). In our study, 109 (66.4%) patients had hypertension, similar to previous reports. In addition, hypertension can be detected in the early stages of bleeding in patients presenting with ICH. It remains unclear as to whether this distinctive hypertension is an intracranial mass-related secondary effect or the primary reason for continued bleeding (15). Bleeding disorders account for only 2.1-13.3% of ICHs (16), and 1.6-3.1% of patients receiving anticoagulant treatment experience ICH due to other reasons (16). Overall, patients receiving oral anticoagulant treatment have an ICH risk of 7.6-11% (17,18). In our study, 32 (20%) patients had anticoagulant use-related ICH.

Hossain et al. (19) found that 71% of hematomas were located in the basal ganglia and 29% in the intraparenchymal area. Similarly, Inagawa et al. (20) observed that the most common site of ICH was the putamen (34%), followed by the thalamus (33%) and intraparenchymal areas (15%). Furthermore, they reported that the short-and long-term results after ICH were directly related with hematoma volume and bleeding severity; the overall mortality rate in their study was 54%. In our study, intracranial hematoma was intraparenchymal in 69 (42.1%) patients, thalamic in 33 (20.1%), intraventricular in 33 (20.1%), and cerebellar in 29 (17.7%) patients.

Studies have reported that the success rate of surgery performed >24 h after the onset of stroke symptoms is low (14,21). Karatay et al. (22) documented mortality rates of 41%, 61%, and 80% in patients who underwent surgery within the first 8 h, 8-24 h, and 24-48 h after symptom onset, respectively. In our study, the mortality rates for the same time intervals were 55.4%, 73%, and 72.7%, respectively. These findings indicate that surgery performed within the first 8 h yields relatively better results.

The 2005 Surgical Trial in Lobar Intracerebral Haemorrhage study included patients with a GCS score >5 and reported poor outcomes in 91% of patients with GCS scores of 5-8 (23). Yilmaz et al. (24) studied 25 comatose patients with a GCS score ≤ 8 ; the craniotomy success rate in these patients was 44% and the authors recommended that early surgical treatment be performed in patients with low GCS scores. Furthermore, hematoma volume >60 mL was found to be related to poor surgical outcomes; however, patients with low GCS scores and a low hematoma volumes exhibited better surgical outcomes (24). In contrast, Rehman and Anwar found that all patients with GCS scores ≤ 8 who underwent surgical treatment for supratentorial hematoma with a volume ≤ 50 mL died (25). In another study, Moussa and Khedr (26) observed a positive correlation between hematoma volume and mortality in patients with sICH who underwent surgery. In our study, there was no mortality after surgery in the 41 patients with GCS scores 13-15; however, mortality was 45% and 100% in those with GCS scores of 7-12 and 6-7, respectively. Furthermore, in our study, mortality rates were 63.1%, 52.3%, and 66.6% in patients with hematoma volumes <25 cm³, 25-50 cm³, and >50 cm³, respectively. The prognosis of ICH depends on GCS scores and hematoma volumes at the time of diagnosis. Early hematoma evacuation with urgent surgery should be considered because it can yield favorable outcomes. The initial neurologic examination findings, patient age, and hematoma location and volume are related to mortality in patients with sICH. Early surgical treatment can decrease mortality rates.

Study Limitations

Although the retrospective nature of our study and the limited number of patients were the main limitations of our study, we can say that our results are consistent with the literature.

Conclusion

In conclusion, it is impossible to explain the relationship between surgical treatment and mortality in patients with sICH using one parameter. The mortality rate is high in patients with poor neurologic function, hypertension, and anticoagulant use, despite early surgical treatment. In patients with sICH, the relationship between surgical treatment and mortality is multifactorial.

Table 3. Relationship between hematoma volume, location, and mortality

Hematoma volume	Lobar	Thalamic	Cerebellar	Intraventricular	Total	Exitus	Mortality rate
<25 cm ³	5	-	16	17	38	24	63.1%
25-50 cm ³	6	18	8	10	42	22	52.3%
>50 cm ³	58	15	5	6	84	56	66.6%
Total	69	33	29	33			

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of the Izmir Katip Celebi University (date: 25.04.2018, protocol number: 183).

Informed Consent: Informed consent was neither required nor obtained due to the retrospective nature of the study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: İ.K., İ.D.C., Design: İ.K., İ.D.C., İ.U., C.K., Data Collection or Processing: İ.K., İ.D.C., İ.U., Analysis or Interpretation: İ.U., H.E.A., N.Y., Literature Search: İ.K., C.K., Writing: İ.K., İ.D.C., İ.U., H.E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Cheung RT. Update on medical and surgical management of intracerebral hemorrhage. *Rev Recent Clin Trials* 2007;2:174-181.
- Rasool A, Rahman A, Choudhury S, Singh R. Blood pressure in acute intracerebral haemorrhage. *J Hum Hypertens* 2004;18:187-192.
- Ariessen MJ, Claus SP, Rinkel GJ, Algra A. Risk factors for intracerebral hemorrhage in the general population: a systematic review. *Stroke* 2003;34:2060-2065.
- Mitchell P, Gregson BA, Vindlacheruvu RR, Mendelow AD. Surgical options in ICH including decompressive craniectomy. *J NeurolSci* 2007;261:89-98.
- Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke* 1996;27:1304-1305.
- Cheung RT, Zou LY. Use of original, modified, or new intracerebral hemorrhage score to predict mortality and morbidity after intracerebral hemorrhage. *Stroke* 2003;34:1717-1722.
- Sacco RL, Benjamin EJ, Broderick JP, et al. American Heart Association Prevention Conference. IV. Prevention and rehabilitation of stroke. Risk factors. *Stroke* 1997;28:1507-1517.
- Kanaya H. Current status of surgical therapy of hypertensive cerebral hemorrhage in Japan. *Nihon Rinsho* 1982;40:2775-2782.
- Lo YT, See AAQ, King NKK. Decompressive craniectomy in spontaneous intracerebral hemorrhage: a case-control study. *World Neurosurg* 2017;103:815-820.
- Anderson CS, Chakera TMH, Stewart-Wynne EG, Jamrozik KD. Spectrum of primary intracerebral haemorrhage in Perth, Western Australia, 1989-1990: incidence and outcome. *J Neurol Neurosurg Psychiatry* 1994;57:936-940.
- Qureshi AI, Giles WH, Croft JB. Racial differences in the incidence of intracerebral hemorrhage: Effects of blood pressure and education. *Neurology* 1999;52:1617-1621.
- Drury Ivo MB, Whisnant JP, Garraway WM. Primary intracerebral hemorrhage: Impact of CT on incidence. *Neurology* 1984;34:653-657.
- Reunanon A, Aho K, Anomaa A, et al. Research institute for Social security. *Stroke* 1986;1714:675-681.
- Kaneko M, Tanaka K, Shimada T, Sato K, Uemura K. Long-term evaluation of ultra-early operation for hypertensive intracerebral hemorrhage in 100 cases. *J Neurosurg* 1983;58:838-842.
- Broderick JP, Brott TG, Tomsick T, Barsan W, Spilker J. Ultra-early evaluation of intracerebral hemorrhage. *J Neurosurg* 1990;72:195-199.
- Tatu L, Moulin T, El Mohamad R, et al. Primary intracerebral hemorrhages in the Besancon stroke registry. Initial clinical and CT findings, early course and 30-day outcome in 350 patients. *Eur Neurol* 2000;43:209-214.
- Fogelholm R, Eskola K, Kiminkinen T, Kunnamo I. Anticoagulant treatment as a risk factor for primary intracerebral haemorrhage. *J Neurol Neurosurg Psychiatry* 1992;55:1121-1124.
- Forsting M, Mattle HP, Huber P. Anticoagulation-related intracerebral hemorrhage. *Cerebrovasc Dis* 1991;1:97-102.
- Hossain M, Ahmed S, Ansary S, Islam S. Surgical outcome of spontaneous intracerebral haematoma through keyhole craniectomy. *Faridpur Med Coll J* 2010;5:60-62.
- Inagawa T, Ohbayashi N, Takechi A, Shibukawa M, Yahara K. Primary intracerebral hemorrhage in Izumo City, Japan: incidence rates and outcome in relation to the site of hemorrhage. *Neurosurgery*. 2003;53:1283-1298.
- Kaneko M, Koba T, Yokoyama T. Early surgical treatment for hypertensive intracerebral hemorrhage. *J Neurosurg* 1977;46:579-583.
- Karatay M, Mehmetoğlu R, Erdem Y, et al. The relation between surgically treated spontaneous intracerebral hematomas and mortality: retrospective evaluation of 72 cases. *Turk J Neurol* 2012;18:83-87.
- 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;365:387-397.
- Yilmaz C, Kabatas S, Gulsen S, et al. Spontaneous supratentorial intracerebral hemorrhage: Does surgery benefit comatose patients? *Ann Indian Acad Neurol* 2010;13:184-187.
- Rehman WA, Anwar MS. Surgical outcome of spontaneous supra tentorial intracerebral hemorrhage. *Pak J Med Sci* 2017;33:804-807.
- Moussa WM, Khedr W. Decompressive craniectomy and expansive duraplasty with evacuation of hypertensive intracerebral hematoma, a randomized controlled trial. *Neurosurg Rev* 2017;40:115-127.