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Predictors of Surgical Intervention in Patients with Spontaneous Intracerebral Hemorrhage

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Abstract

Objective: Despite no clear evidence from randomized trials, surgical intervention of spontaneous intracerebral hemorrhage (ICH) still occurs. We sought to describe the characteristics of patients undergoing surgical intervention in ICH.

Methods: Data from the Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study were analyzed, and ICH patients were categorized into surgical intervention or nonoperative management groups. Patients with primary intraventricular hemorrhage (IVH) and those without data regarding the use of surgical intervention data were excluded.

Results: The study cohort comprised 2,947 patients, and surgical intervention was performed in 289 (10%). Younger age (OR=0.967, $p<0.001$), lower baseline modified Rankin Scale (mRS; OR=0.728, $p<0.001$), higher admission Glasgow Coma Scale (GCS; OR=1.059, $p=0.007$), larger ICH volume (OR=1.037, $p<0.001$), infratentorial ICH location (OR=5.966, $p<0.001$), lobar ICH location (OR=1.906, $p=0.001$), lack of IVH (OR=0.567, $p=0.001$), ICP monitoring (OR=5.022, $p<0.001$), and mannitol use (OR=2.389, $p<0.001$) were independent predictors of surgical intervention. Younger age (OR=0.953, $p<0.001$), lower baseline mRS score (OR=0.713, $p=0.002$), larger ICH volume (OR=1.033, $p<0.001$), lobar ICH location (OR=2.467, $p<0.001$), ICP monitoring (OR=3.477, $p<0.001$), and mannitol use (OR=2.139, $p<0.001$) were independent predictors of surgical interventions in supratentorial ICHs. Larger ICH volume (OR=1.078,

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p<0.001), ICP monitoring (OR=6.099, p<0.001), and mannitol use (OR=2.952, p=0.005) were independent predictors of surgical interventions in infratentorial ICHs.

Conclusions: We identified multiple factors associated with surgical intervention for patients with ICH. Younger age, good neurological function at baseline, large ICH volume on presentation, and lobar or infratentorial hematomas were independently associated with surgical intervention in ICH patients.

Keywords

surgery; predictors; intracerebral hemorrhage; neurosurgery; evacuation

Introduction

Spontaneous intracerebral hemorrhage (ICH) is associated with the highest rates of mortality and morbidity among all stroke subtypes, and it occurs with an annual incidence of 15 to 25 per 100,000 persons.[1–5] Despite efforts to target the mechanisms of primary brain injury caused by ICH, the benefit of surgical intervention in ICH patients remains unproven.[6–8] With the exception of infratentorial ICHs, the American Heart Association (AHA)/American Stroke Association (ASA) recommendations for the role of surgery in ICH management remain weak (Class IIb).[9] Nevertheless, ICH surgery continues to be performed at medical centers in the United States. However, the selection criteria for which surgical treatment is employed in the contemporary management of ICH patients are elusive, highly variable across different institutions and individual physicians, and incompletely defined.[10] Therefore, the aim of this multicenter, retrospective cohort study is to identify predictors of surgical intervention in patients with spontaneous ICH.

Methods

Patient Cohort and Selection

The Ethnic/Racial variations of IntraCerebral Hemorrhage (ERICH) study protocol has been previously described in detail.[11] In brief, the ERICH study was a multicenter, prospective, case-control study designed to recruit 1,000 non-Hispanic whites, 1,000 nonHispanic blacks and 1,000 Hispanics with spontaneous ICH. Participants were derived from 19 United States sites comprising 42 hospitals. Institutional review board (IRB) approval and written informed consents were obtained at each site and from all patients (or legal guardians for patients who were unable to provide consent) participating in the study, respectively. All patients or legal guardians were subjected to a standardized data collection protocol, including a personal interview and medical chart abstraction. Data from each respective site were de-identified and pooled for analysis.

The present study comprised patients who were derived from the ICH case cohort of the ERICH study, and their data were retrospectively analyzed. ICH patients with available data pertaining to surgical intervention (*i.e.*, craniotomy or craniectomy for decompression or evacuation of ICH and minimally invasive surgery for ICH evacuation) were included in the study cohort. Patients with primary intraventricular hemorrhage (IVH) were excluded. Patients who underwent ICH surgery were categorized into the surgical intervention group, whereas those who did not undergo ICH surgery were categorized into the nonoperative management group.

Baseline Data and Variables

Baseline demographic and clinical data included age, sex, race/ethnicity, baseline modified Rankin Scale (mRS), and admission Glasgow Coma Scale (GCS). Serum laboratory data obtained on admission included international normalized ratio (INR), partial thromboplastin time (PTT), and platelet count. Antiplatelet and anticoagulation medication use prior to ICH were recorded. Neuroimaging and treatment data included admission ICH volume, ICH location (categorized as infratentorial vs. supratentorial and lobar vs. deep), presence of IVH, intracranial pressure (ICP) monitoring, mannitol use, and hypertonic saline use.

Statistical Analysis

All statistical analyses were performed using Stata (version 14.2, College Station, TX). Baseline, clinical, radiologic, and treatment characteristics were compared between the surgical intervention and nonoperative management groups. Student's *t* or Wilcoxon rank-sum tests were used to compare continuous variables, and Pearson's χ^2 or Fisher's exact tests were used to compare categorical variables, where appropriate. To assess for independent predictors of surgical intervention, a multivariable logistic regression model was developed using surgical intervention as the dependent variable and covariates with $p<0.10$ in univariate comparisons as the independent variables. The fit of the model was assessed using the Hosmer-Lemeshow goodness-of-fit test. To avoid listwise deletions due to missing data, a second multivariable logistic regression model was built using multiply imputed data. The multiple imputation was performed using chained equations with $m=50$. Imputed values for baseline mRS (0.4%), admission GCS (2.4%), presence of IVH (3.2%), ICH volume (3.2%), mannitol use (0.1%), and hypertonic saline use (0.2%) were generated using conditional regression models based on these auxiliary variables: age, sex, surgical intervention, lobar ICH location, infratentorial ICH location, and ICP monitoring. Parameter estimates from analyzing the imputed datasets were pooled according to Rubin's rules.[12] Subgroup analyses for supratentorial and infratentorial ICHs were performed. Statistical significance was defined as $p<0.05$, and all tests were two-tailed.

Results

Comparison of Baseline Characteristics

Of the 3,000 patients with spontaneous ICH who were enrolled in the ERICH study, 53 were excluded from the present analysis (two patients excluded for lack of documentation regarding surgical intervention and 51 patients excluded for primary IVH). The study cohort comprised the remaining 2,947 ICH patients, who were categorized into the surgical intervention (n=289) versus nonoperative management (n=2,658) groups (Figure 1).

Table 1 compares the baseline characteristics between ICH patients who underwent surgical intervention versus nonoperative management. Patients in the surgical intervention cohort were younger (mean 57 vs. 62 years old, $p<0.001$), and they had lower admission GCS (median 13 vs. 15, $p<0.001$) scores. Distributions of race/ethnicity ($p<0.001$) and baseline mRS scores (p<0.001) were different between the surgical intervention and nonoperative management groups. Patients who underwent surgical evacuation had larger ICH volumes (mean 46 vs. 18 cm^3, p<0.001), and they were more likely to have an infratentorial ICH (23% vs. 12%, p<0.001), lobar ICH (45% vs. 30%, p<0.001), and IVH (48% vs. 41%, p=0.021). ICP monitoring (52% vs. 15%, p<0.001), mannitol (49% vs. 13%, p<0.001), and hypertonic saline (10% vs. 3%, p<0.001) were more frequently used in the surgical intervention group.

Predictors of Surgical Intervention

Table 2 details the multivariable analyses for independent predictors of surgical intervention in patients with ICH. In the non-imputed multivariable model, younger age (OR=0.969 [0.957–0.980], p<0.001), lower baseline mRS (OR=0.722 [0.598–0.872], p=0.001), higher admission GCS (OR=1.059 [1.015–1.105], p=0.009), larger ICH volume (OR=1.036 [1.030–1.042], p<0.001), infratentorial ICH location (OR=5.316 [3.447–8.199], p<0.001), lobar ICH location (OR=1.922 [1.292–2.859], p=0.001), lack of IVH (OR=0.541 [0.378–0.776], p=0.001), ICP monitoring (OR=5.809 [4.035–8.361], p<0.001), and mannitol use (OR=2.135 [1.503–3.035], p<0.001) were associated with surgical intervention. These predictors remained significant in the multiply imputed model.

Subgroup analysis of Supratentorial ICH

Table 3 compares the baseline characteristics between patients with supratentorial ICH who underwent surgical intervention versus nonoperative management. Patients in the surgical intervention group were younger (mean 56 vs. 62 years old, p<0.001), and they had lower admission GCS (median 12 vs. 15, p<0.001) scores. Distributions of race/ethnicity (p<0.001) and baseline mRS scores (p<0.001) were different between the two groups. Patients who underwent surgical intervention had larger ICH volumes (mean 54 vs. 20 cm^3, p<0.001), and they were more likely to have a lobar ICH (59% vs. 34%, p<0.001). ICP monitoring (49% vs. 15%, p<0.001), mannitol (49% vs. 13%, p<0.001), and hypertonic saline (10% vs. 3%, p<0.001) were more frequently used in the surgical intervention group.

Table 4 details the multivariable analyses for independent predictors of surgical intervention in patients with supratentorial ICH. Younger age (OR=0.955 [0.942–0.969], p<0.001), lower baseline mRS (OR=0.676 [0.537–0.851], p=0.001), larger ICH volume (OR=1.032 [1.026–1.039], p<0.001), lobar ICH location (OR=2.441 [1.650–3.609], p<0.001), ICP monitoring (OR=3.806 [2.586–5.600], p<0.001), and mannitol use (OR=2.007 [1.354–2.974], p=0.001) were significantly associated with surgical intervention. These predictors remained significant in the multiply imputed model.

Subgroup analysis of Infratentorial ICH

Table 5 compares the baseline characteristics between patients with infratentorial ICH who underwent surgical intervention versus nonoperative management. Patients who underwent surgical intervention had higher INR values (mean 1.5 vs. 1.2, p=0.020) and larger ICH volumes (mean 21 vs. 8 cm^3, p<0.001), and they were more likely to have IVH (51% vs. 30%, p=0.002). ICP monitoring (61% vs. 14%, p<0.001), mannitol (51% vs. 11%, p<0.001), and hypertonic saline (9% vs. 1%, p=0.001) were more frequently used in the surgical intervention group. Specifically, the majority of patients in this subgroup who underwent surgical intervention had cerebellar ICH (n=66/67; 98.5%).

Table 6 details the multivariable analyses for independent predictors of surgical intervention in patients with infratentorial ICH. Larger ICH volume (OR=1.072 [1.038–1.107], p<0.001) and ICP monitoring (OR=7.567 [3.474–16.483], p<0.001) were associated with surgical intervention. These predictors remained significant in the multiply imputed model. Mannitol use (OR=2.952 [1.387–6.281], p=0.005) was also found to be an independent predictor of surgical intervention in the multiply imputed model.

Discussion

Given the unclear benefits of ICH surgery, it is important to understand the factors that influence the selection of ICH patients for surgical intervention in the modern era outside of clinical trial settings. The goals of ICH surgery include prevention or amelioration of cerebral herniation, relief of intracranial hypertension, reduction of locoregional mass effect and perihematomal edema, and clearance of cytotoxic and pro-inflammatory byproducts.[13] However, randomized trials that have compared surgical hematoma evacuation to medical management for ICH have failed to demonstrate a clear benefit from surgical intervention.[6–8,14–17] Other studies have suggested that decompressive craniectomy may improve outcomes in ICH patients with elevated ICP.[18–21] Despite the lack of Level A evidence to support the surgical treatment of ICH, it continues to be performed in some ICH patients outside the context of clinical trials. As such, we sought to delineate the factors that currently influence the selection of ICH patients for surgery.

The Surgical Trial in Intracerebral Haemorrhage (STICH) comprised 1,033 patients from 83 centers in 27 countries, and it randomized patients with a supratentorial hematoma ≥2 cm in size and a GCS ≥5 to early surgery or initial conservative management.[6] Subsequently, the Surgical Trial in Lobar Intracerebral Haematomas (STICH II) selected conscious patients (GCS motor component ≥5 and GCS eye component ≥2) with lobar ICHs within 1 cm from the cortical surface and 10–100 cm^3 in volume.[7] In the Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation (MISTIE) phase II trial, 96 patients aged 18–80 years with GCS ≤14 or NIHSS ≥6 and a premorbid mRS ≤1 who presented with a ICH ≥20 cm^3 in volume were randomized to image-guided minimally invasive catheter-based hematoma evacuation plus alteplase thrombolysis or conservative management.[8] The ongoing MISTIE phase III trial (ClinicalTrials.gov NCT01827046) has the same inclusion criteria, except the minimum ICH volume is 30 cm^3 and the target enrollment is 500 patients. The ongoing Early MiNimally-Invasive Removal of IntraCerebral Hemorrhage (ENRICH) trial (ClinicalTrials.gov NCT02880878) seeks to recruit 300 patients aged 18–80 years who present with a supratentorial ICH 30–80cm^3 in volume, GCS of 5–14, and premorbid mRS ≤1. The patients the ENRICH trial will be randomized to minimally invasive parafascicular surgery with the BrainPath (NICO, Indianapolis, IN) device or medical management. The Artemis in the Removal of Intracerebral Hemorrhage (MIND) trial seeks to randomized 500 patients aged 18–80 years with a supratentorial ICH 20–80 cm^3 in volume, NIHSS ≥6, GCS 5–15, and baseline mRS ≤1 to minimally invasive surgery using the Artemis Neuro Evacuation Device (Penumbra Inc., Alameda, CA) or medical management.

The most recent AHA/ASA guidelines from 2015 noted that the efficacy of surgery for supratentorial ICH remained unproven (Class IIb recommendation; Level of Evidence A).[9] In addition, the benefits from decompressive craniectomy with or without hematoma evacuation (Class IIb recommendation; Level of Evidence C) and minimally invasive ICH evacuation with or without the use of thrombolytics (Class IIb recommendation; Level of Evidence B) were deemed uncertain. In the present analysis of a large, multicenter, multiethnic cohort of ICH patients, we identified numerous independent predictors of surgical intervention. Younger age, better baseline functional status (*i.e.*, lower baseline mRS), and those with a less debilitating neurological condition (*i.e.*, higher admission GCS) were independently associated with surgical intervention, which suggests that clinicians may have deemed these patients to have a greater neurological reserve and capacity for eventual recovery and, thus, a lower likelihood of a poor outcome.[22] Interestingly, despite a lower admission GCS score found in the surgical intervention group, higher admission GCS score was associated with surgical intervention after controlling for other covariates. Lobar and infratentorial hematomas, large volume clots, and those without associated IVH were more likely to be treated surgically. Taken together, these predictors and those found in the subgroup analysis of supratentorial ICHs concur with many of the inclusion and exclusion criteria used in both previously completed and actively enrolling clinical trials investigating ICH surgery.[23] However, we acknowledge that it is not possible to determine the magnitude by which practice had been influenced or shaped by the reporting of these trials. While many of the RCTs, conducted in neurologically stable patients, have principally investigated the hypothesized benefit to surgery in mitigating the second phase of injury after ICH, the prevention of dangerous compartment shifts and cerebral herniation remains an important rationale. We also found ICP monitoring and administration of mannitol to be predictors, which may indicate that surgical intervention was more likely to be recommended for patients with clinical and/or radiologic signs of intracranial hypertension.

Due to the anatomic restrictions of the posterior fossa, cerebellar hematomas can cause rapid deterioration via obstructive hydrocephalus secondary to compression of the fourth ventricle or local mass effect on the brainstem. Several nonrandomized studies have suggested improved outcomes with surgery in patients with cerebellar hemorrhages >3 cm in diameter, brainstem compression, or hydrocephalus.[24–26] In contrast, surgical treatment of brainstem hematomas is universally avoided, due to the unacceptably high risk of neurological morbidity. Given the lack of clinical equipoise, a randomized trial comparing surgery versus conservative management for infratentorial ICHs is unlikely to ever be conducted. As such, although surgery for cerebellar ICH is Level of Evidence B, the AHA/ASA guidelines recommendation for this procedure remains Class I.[9] Furthermore, initial cerebrospinal fluid drainage, rather than surgery, in these patients is not recommended (Class III recommendation; Level of Evidence C).[9] Our subgroup analysis of infratentorial ICH identified larger ICH volume, ICP monitoring, and mannitol as predictors of surgical intervention. Since ICP monitoring and hyperosmolar therapy are often considered less effective at guiding the treatment of infratentorial mass lesions, our findings suggests that some patients with cerebellar hematomas may be improperly or inefficiently managed within contemporary algorithms for ICH management.

We acknowledge that several limitations affect the validity and generalizability of our study. Our results are contingent upon the accuracy and reliability of the collected data, which were derived from patient self-report or legal guardians of incapacitated patients and from medical chart abstraction. Therefore, this study may be subject to reporting and recall biases. Because the ERICH study was not specifically designed to assess the surgical treatment of ICH, operative details (*e.g.*, timing of surgery, reason for surgery, surgical technique or devices used, craniotomy vs. craniectomy, degree of hematoma evacuation, perioperative complications) were not captured. Although ICP monitoring and mannitol use may be surrogate indicators of elevated ICP, details regarding ICP values, waveform tracings, and presence of midline shift on neuroimaging were not available. Despite our best attempts to include variables that could govern the decision to perform ICH surgery, there may be other variables that were not captured or accounted for, including clinical deterioration days after admission that were not captured. Furthermore, the present analyses were not designed with the intent of comparing the outcomes of surgery versus conservative management for ICH. Given the observational design of the ERICH study, it is possible that some patients were enrolled in concurrent surgical ICH trials. We believe that any such juxtaposition using the available data may be difficult to rigorously perform and clearly interpret, due to the multitude of baseline differences in patient and ICH characteristics between the surgical intervention and nonoperative management cohorts that we have outlined in our findings. Nevertheless, we concede that defining the role of surgical treatment and either justifying or refuting its utilization remains one of the foremost priorities in the modern management of ICH. Lastly, it is important to note that the identified predictors represent selection bias of the treating neurosurgeon or center, and should not be taken as guidelines or selection criteria for ICH surgery.

Conclusions

Despite insufficient evidence to support the use of surgical intervention for ICH, this treatment continues to be employed in ICH patients. We clarified the selection bias for ICH surgery outside of the setting of clinical trials by identifying multiple predictors of surgical intervention. Younger ICH patients in good neurological condition at baseline and presentation with large volume, lobar or infratentorial hematomas were more likely to undergo surgery. Additional data from ongoing and future studies are necessary to ascertain the role of surgery in the management of ICH.

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Abbreviations List

ICH	intracerebral hemorrhage

OR	odds ratio
ERICH	Ethnic/Racial Variations of Intracerebral Hemorrhage
IVH	intraventricular hemorrhage
GCS	Glasgow Coma Scale
ICP	intracranial pressure
AHA	American Heart Association
ASA	American Stroke Association
IRB	Institutional review board
mRS	modified Rankin Scale
INR	international normalized ratio
STICH	Surgical Trial in Intracerebral Haemorrhage
STICH II	Surgical Trial in Lobar Intracerebral Haematomas
MISTIE	Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation
ENRICH	Early MiNimally-Invasive Removal of IntraCerebral Hemorrhage
MIND	Artemis in the Removal of Intracerebral Hemorrhage
RCT	randomized controlled trial

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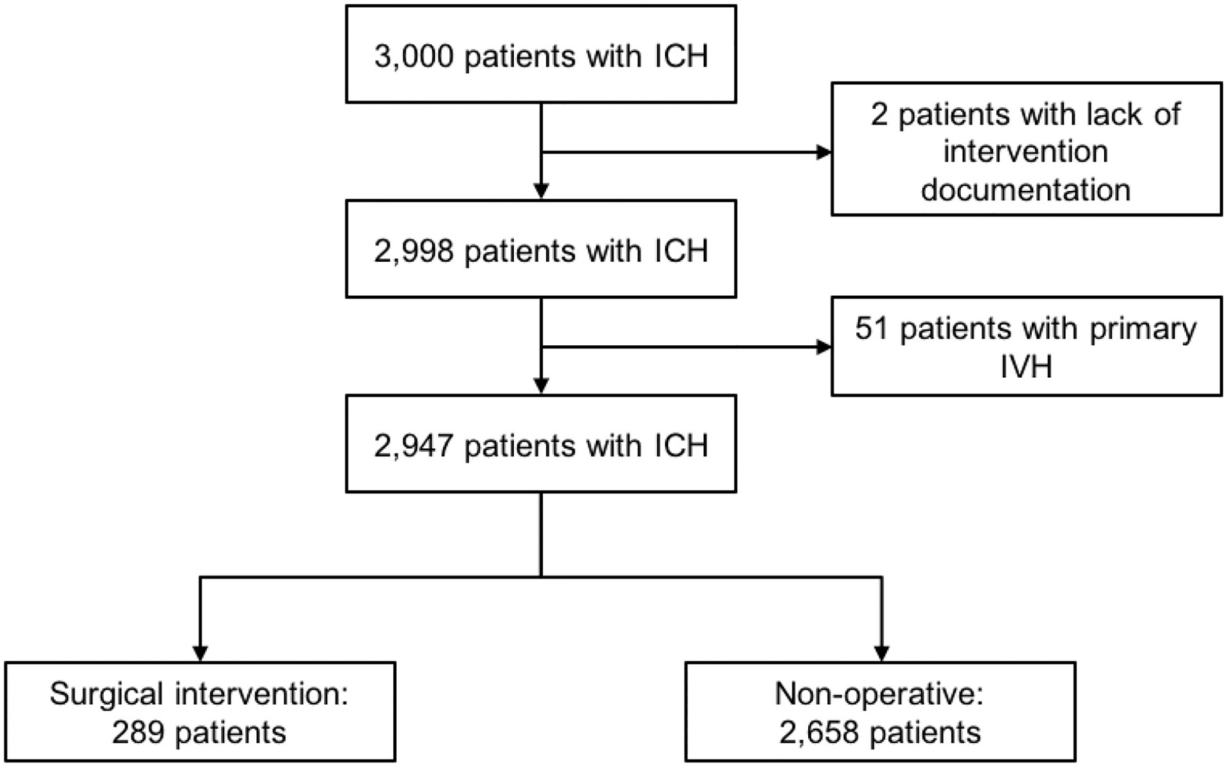

Figure 1.
Flow diagram showing the patient selection process.

Table 1.

Comparison of baseline demographic, clinical, radiologic, and treatment characteristics between ICH patients who underwent nonoperative management versus surgical intervention.

Variable	Nonoperative Management (n=2,658)	Surgical Intervention (n=289)	p-value
Age, mean yr (SD)	62.1 (14)	57.1 (13.4)	**<0.001**
Male sex, n (%)	1,550/2,658 (58.3)	183/289 (63.3)	0.100
Race/Ethnicity, n (%)			**<0.001**
White	890/2,658 (33.5)	86/289 (29.8)	
Black	920/2,658 (34.6)	69/289 (23.9)	
Hispanic	848/2,658 (31.9)	134/289 (46.4)	
Baseline mRS, n (%)			**<0.001**
0	1,837/2,648 (69.4)	238/288 (82.6)	
1	317/2,648 (12)	22/288 (7.6)	
2	267/2,648 (10.1)	16/288 (5.6)	
3	134/2,648 (5.1)	6/288 (2.1)	
4	77/2,648 (2.9)	4/288 (1.4)	
5	16/2,648 (0.6)	2/288 (0.7)	
Admission GCS, median (IQR)	15 (11–15)	13 (8–15)	**<0.001**
Antiplatelet use, n (%)	1,166/2,631 (44.3)	116/285 (40.7)	0.243
Anticoagulant use, n (%)	261/2,621 (10)	34/283 (12)	0.277
INR, mean (SD)	1.2 (0.8)	1.3 (0.8)	0.147
PTT, mean sec (SD)	29.5 (8.4)	29.5 (6.6)	0.983
Platelet count, mean k/uL (SD)	225.4 (75.9)	224.9 (82.5)	0.921
ICH volume, mean cm^3 (SD)	18.2 (23.4)	46.2 (29.3)	**<0.001**
Infratentorial ICH location, n (%)	326/2,658 (12.3)	67/289 (23.2)	**<0.001**
Lobar ICH location, n (%)	802/2,658 (30.2)	130/289 (45)	**<0.001**
Presence of IVH, n (%)	1,057/2,594 (40.8)	126/262 (48.1)	**0.021**
ICP monitoring, n (%)	398/2,658 (15)	149/289 (51.6)	**<0.001**
Mannitol use, n (%)	335/2,654 (12.6)	142/289 (49.1)	**<0.001**
Hypertonic saline use, n (%)	78/2,658 (2.9)	29/289 (10)	**<0.001**

n = number; yr = year; uL = microliter; k = ×1,000; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; GCS = Glasgow Coma Scale; IQR = interquartile range; mRS = modified Rankin Scale; ICP = intracranial pressure; INR = international normalized ratio; PTT = partial thromboplastin time.

Table 2.

Multivariable analyses for independent predictors of surgical intervention in patients with ICH.

Predictors	Odds ratio[†]	95% CI	p-value	Odds ratio[*]	95% CI[*]	p-value[*]
Age	0.969	0.957–0.980	**<0.001**	0.967	0.957–0.979	**<0.001**
Baseline mRS	0.722	0.598–0.872	**0.001**	0.728	0.610–0.868	**<0.001**
Race/Ethnicity[‡]						
White	—	—	—	—	—	—
Black	0.767	0.502–1.173	0.221	0.704	0.472–1.049	0.084
Hispanic	1.440	0.982–2.112	0.062	1.316	0.919–1.886	0.134
Admission GCS	1.059	1.015–1.105	**0.009**	1.059	1.016–1.103	**0.007**
ICH volume	1.036	1.030–1.042	**<0.001**	1.037	1.031–1.043	**<0.001**
Infratentorial ICH location	5.316	3.447–8.199	**<0.001**	5.966	3.981–8.942	**<0.001**
Lobar ICH location	1.922	1.292–2.859	**0.001**	1.906	1.308–2.780	**0.001**
Presence of IVH	0.541	0.378–0.776	**0.001**	0.567	0.401–0.803	**0.001**
ICP monitoring	5.809	4.035–8.361	**<0.001**	5.022	3.556–7.092	**<0.001**
Mannitol use	2.135	1.503–3.035	**<0.001**	2.389	1.719–3.321	**<0.001**
Hypertonic saline use	0.867	0.479–1.570	0.637	0.793	0.448–1.405	0.427

ICH = intracerebral hemorrhage; GCS = Glasgow Coma Scale; CI = confidence interval; mRS = modified Rankin Scale; IVH = intraventricular hemorrhage; ICP = intracranial pressure

[*] Values based on pooled parameter estimates from multiply imputed data using chained equations with *m*=50.

[†] Hosmer-Lemeshow goodness-of-fit test χ^2 (8)=9.27, p=0.320.

[‡] White as reference category.

Table 3.

Comparison of baseline demographic, clinical, radiologic, and treatment characteristics between patients with supratentorial ICH who underwent nonoperative management versus surgical intervention.

Variable	Nonoperative Management (n=2,332)	Surgical Intervention (n=222)	p-value
Age, mean yr (SD)	62.3 (14)	55.7 (13.5)	**<0.001**
Male sex, n (%)	1,367/2,332 (58.6)	140/222 (63.1)	0.198
Race/Ethnicity, n (%)			**<0.001**
White	797/2,332 (34.2)	68/222 (30.6)	
Black	804/2,332 (34.5)	49/222 (22.1)	
Hispanic	731/2,332 (31.4)	105/222 (47.3)	
Baseline mRS, n (%)			**<0.001**
0	1,611/2,322 (69.4)	185/222 (83.3)	
1	285/2,322 (12.3)	19/222 (8.6)	
2	231/2,322 (10)	10/222 (4.5)	
3	118/2,322 (5.1)	3/222 (1.4)	
4	64/2,322 (2.8)	3/222 (1.4)	
5	13/2,322 (0.6)	2/222 (0.9)	
Admission GCS, median (IQR)	15 (12–15)	12 (8–15)	**<0.001**
Antiplatelet use, n (%)	1,030/2,307 (44.7)	91/219 (41.6)	0.378
Anticoagulant use, n (%)	216/2,298 (9.4)	22/218 (10.1)	0.739
INR, mean (SD)	1.2 (0.8)	1.2 (0.6)	0.874
PTT, mean sec (SD)	29.5 (8.6)	29.1 (5.9)	0.535
Platelet count, mean k/uL (SD)	225.3 (76.3)	226.6 (87.5)	0.811
ICH volume, mean cm^3 (SD)	19.7 (24.4)	53.5 (29)	**<0.001**
Lobar ICH location, n (%)	802/2,332 (34.4)	130/222 (58.6)	**<0.001**
Presence of IVH, n (%)	961/2,278 (42.2)	96/203 (47.3)	0.159
ICP monitoring, n (%)	353/2,332 (15.1)	108/222 (48.7)	**<0.001**
Mannitol use, n (%)	299/2,328 (12.8)	108/222 (48.7)	**<0.001**
Hypertonic saline use, n (%)	75/2,327 (3.2)	23/222 (10.4)	**<0.001**

n = number; yr = year; uL = microliter; k = ×1,000; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; GCS = Glasgow Coma Scale; IQR = interquartile range; mRS = modified Rankin Scale; ICP = intracranial pressure; INR = international normalized ratio; PTT = partial thromboplastin time.

Table 4.

Multivariable analyses for independent predictors of surgical intervention in patients with supratentorial ICH.

Predictors	Odds ratio†	95% CI	p-value	Odds ratio*	95% CI*	p-value*
Age	0.955	0.942–0.969	**<0.001**	0.953	0.940–0.965	**<0.001**
Baseline mRS	0.676	0.537–0.851	**0.001**	0.713	0.578–0.881	**0.002**
Race/Ethnicity‡						
White	—	—	—	—	—	—
Black	0.688	0.425–1.112	0.127	0.640	0.407–1.007	0.054
Hispanic	1.404	0.919–2.145	0.116	1.336	0.895–1.995	0.157
Admission GCS	1.034	0.986–1.084	0.171	1.036	0.990–1.085	0.128
ICH volume	1.032	1.026–1.039	**<0.001**	1.033	1.027–1.039	**<0.001**
Lobar ICH location	2.441	1.650–3.609	**<0.001**	2.467	1.703–3.574	**<0.001**
ICP monitoring	3.806	2.586–5.600	**<0.001**	3.477	2.402–5.034	**<0.001**
Mannitol use	2.007	1.354–2.974	**0.001**	2.139	1.473–3.105	**<0.001**
Hypertonic saline use	0.787	0.413–1.502	0.468	0.698	0.373–1.307	0.262

ICH = intracerebral hemorrhage; GCS = Glasgow Coma Scale; CI = confidence interval; mRS = modified Rankin Scale; IVH = intraventricular hemorrhage; ICP = intracranial pressure.

*Values based on pooled parameter estimates from multiply imputed data using chained equations with m=50.

†Hosmer-Lemeshow goodness-of-fit test χ^2 (8)=6.20, p=0.624.

‡White as reference category.

Table 5.

Comparison of baseline demographic, clinical, radiologic, and treatment characteristics between patients with infratentorial ICH who underwent nonoperative management versus surgical intervention.

Variable	Nonoperative Management (n=326)	Surgical Intervention (n=67)	p-value
Age, mean yr (SD)	60.9 (14)	61.6 (11.7)	0.700
Male sex, n (%)	183/326 (56.1)	43/67 (64.2)	0.225
Race/Ethnicity, n (%)			0.497
White	93/326 (28.5)	18/67 (26.9)	
Black	116/326 (35.6)	20/67 (29.9)	
Hispanic	117/326 (35.9)	29/67 (43.3)	
Baseline mRS, n (%)			0.626
0	226/326 (69.3)	53/66 (80.3)	
1	32/326 (9.8)	3/66 (4.6)	
2	36/326 (11)	6/66 (9.1)	
3	16/326 (4.9)	3/66 (4.6)	
4	13/326 (4)	1/66 (1.5)	
5	3/326 (0.9)	0/66 (0)	
Admission GCS, median (IQR)	15 (10.5–15)	14 (9–15)	0.271
Antiplatelet use, n (%)	136/324 (42)	25/66 (37.9)	0.538
Anticoagulant use, n (%)	45/323 (13.9)	12/65 (18.5)	0.347
INR, mean (SD)	1.2 (0.7)	1.5 (1.2)	**0.020**
PTT, mean sec (SD)	29.1 (6)	30.6 (8.4)	0.098
Platelet count, mean k/uL (SD)	225.7 (72.9)	219.2 (63.8)	0.502
ICH volume, mean cm^3 (SD)	8 (9.5)	21.2 (10.3)	**<0.001**
Presence of IVH, n (%)	96/316 (30.4)	30/59 (50.9)	**0.002**
ICP monitoring, n (%)	45/326 (13.8)	41/67 (61.2)	**<0.001**
Mannitol use, n (%)	36/326 (11)	34/67 (50.8)	**<0.001**
Hypertonic saline use, n (%)	3/326 (0.9)	6/67 (9)	**0.001**

n = number; yr = year; uL = microliter; k = ×1,000; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; GCS = Glasgow Coma Scale; IQR = interquartile range; mRS = modified Rankin Scale; ICP = intracranial pressure; INR = international normalized ratio; PTT = partial thromboplastin time.

Table 6.

Multivariable analyses for independent predictors of surgical intervention in patients with infratentorial ICH.

Predictors	Odds ratio[†]	95% CI	p-value	Odds ratio[*]	95% CI[*]	p-value[*]
INR	1.311	0.801–2.147	0.281	1.360	0.855–2.162	0.194
PTT	0.996	0.939–1.056	0.888	0.997	0.943–1.054	0.926
ICH volume	1.072	1.038–1.107	**<0.001**	1.078	1.046–1.110	**<0.001**
Presence of IVH	1.086	0.488–2.419	0.840	1.058	0.504–2.220	0.882
ICP monitoring	7.567	3.474–16.483	**<0.001**	6.099	2.988–12.447	**<0.001**
Mannitol use	2.139	0.952–4.807	0.066	2.952	1.387–6.281	**0.005**
Hypertonic saline use	1.714	0.299–9.836	0.545	1.896	0.337–10.663	0.468

ICH = intracerebral hemorrhage; GCS = Glasgow Coma Scale; CI = confidence interval; mRS = modified Rankin Scale; IVH = intraventricular hemorrhage; ICP = intracranial pressure; INR = international normalized ratio; PTT = partial thromboplastin time.

[*] Values based on pooled parameter estimates from multiply imputed data using chained equations with *m*=50.

[†] Hosmer-Lemeshow goodness-of-fit test χ^2 (8)=8.30, p=0.405.