Validation of ICH and ICH-GS Scores in an Indian Cohort: Impact of Medical and Surgical Management

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Objective: Prognostic scores help in predicting mortality and functional outcome post intracerebral hemorrhage (ICH). We aimed to validate the ICH and ICH-GS scores in a cohort of Indian patients with ICH and observe the impact of any surgical intervention on prognostication. *Methods:* This was an ambispective observational study of primary ICH cases enrolled between January 2014 and April 2018. Observed mortality on ICH and ICH GS scores for the entire cohort and individually for the medically and surgically managed patients was compared to the published mortality in the original derivation cohorts. *Results:* 617 patients, (464 retrospective and 153 prospective) of ICH were included. In hospital mortality and 30-day mortality was 28.7% and 28.5% respectively. There was a significant association of increasing mortality with increasing ICH and ICH-GS scores. Area under receiver operating characteristic curve for 30-day mortality was 75.9% and 74.1% for ICH and ICH-GS scores respectively. However, mortality observed at individual scores was significantly less than previously reported. Among the surgically intervened patients (n = 265), both the expected mortality at baseline and discriminative ability of ICH and ICH-GS scores for 30-day mortality was significantly reduced following surgical intervention (ROC in surgically intervened groups: 59.9 (52.6-67.2) and 63(56-70) for ICH and ICH-GS scores respectively). *Conclusions:* Although ICH and ICH-GS scores are valid in Indian population, mortality at individual scores is lower than previously reported. Mortality prediction using ICH and ICH GS scores is significantly modified by surgical interventions. Thus, newer prognostic tools which incorporate surgical intervention need to be developed and validated in future.

Key Words: ICH score—ICH GS score—intracerebral hemorrhage—prognostic scores.

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Introduction

Stroke is the second leading cause of death and disability in India.[1] Intracerebral hemorrhage (ICH) accounts for 10%-27% of strokes all over the world and incidence of ICH is found to be higher among Asian population. The overall 30-day mortality in ICH is 40.4% and functional independence at 12 months ranges from 12% and 39%, which reflects severity of this stroke subtype.[2] There has been a significant increase in the incidence of ICH in lower-middle-income countries with a mean age of 63.8 ± 0.13 years. Incidence of ICH is highest in Central and East

Asia region while highest mortality is seen in South East Asia (90.12%, 95% CI: 80.42-98.70).[3]

Despite recent advances, ICH remains without a proven beneficial treatment. There is heterogeneity in the application of various medical and surgical measures for ICH treatment, even though guidelines for management of ICH have been published from various continents.[4]

Numerous prediction models have been developed for assessment of post-ICH mortality and functional outcome. These prognostic scales are useful in improving prediction of prognosis, for informed decision making in ICH management and reducing variability in clinical trials of interventions in ICH. ICH score[5] and ICH GS score[6] are most commonly used models to date and have been validated in different populations.[7] Our aim was to explore the ability of two most commonly used intracerebral hemorrhage prognostic scores, i.e., ICH and ICH-GS scores in predicting mortality and functional outcome in Indian patients with ICH and to observe if surgical intervention (s) modifies the prognostication of these scores.

Methods

This study was conducted in Department of Neurology, All India Institute of Medical Sciences, New Delhi. It was an ambispective observational study of primary ICH cases admitted in our department from January 2014 till April 2018. The study was approved by the Institutional Ethics Committee. All admitted cases of spontaneous ICH (SICH) presenting within 72 hours of onset, greater than or equal to 18 years of age and giving informed consent were included. Cases with one or more of following were excluded: primary intraventricular hemorrhage, ICH secondary to tumor, trauma, coagulopathies, vascular malformations, and prior modified Rankin score (mRS) of greater than 2. Anonymized data will be shared by request from any qualified investigator depending upon the academic need and as per local sharing guidelines.

Retrospective cases were enrolled from January 2014 till February 2017. Data was retrieved from inpatient records from medical records department and discharges were obtained from Computerized Patient Record System. SICH cases admitted from March 2017 till April 2018 were enrolled prospectively.

Demographic data and history of risk factors were noted. Vitals, Glasgow coma scale (GCS) score, clinical findings on initial evaluation, and baseline biochemical parameters including blood glucose levels were recorded. All cases underwent computed tomography (CT) imaging of brain at presentation, at 24 hours, and later as per requirement. Imaging details like location (supra or infratentorial), site (basal ganglia, thalamic, lobar, brainstem, and cerebellar), volume of hematoma calculated by ABC/2 method[8] and presence of intraventricular extension were noted. The ICH and ICH GS scores for each patient were computed as described in their derivation cohort by Hemphill et al[7] and Ruiz-Sandoval et al[8] respectively. Details of any neurosurgical intervention including external ventricular drainage (EVD), hematoma evacuation and decompressive hemicraniectomy, and need for mechanical ventilation during hospitalization was recorded. Modified Rankin score (mRS) at discharge was noted for both prospective and retrospective cases. Prospective cases were followed up for mRS at 30 days and 3 months (either on follow-up visit or telephonically). Primary outcomes assessed were 30-day mortality and 3-month functional outcome (categorized poor when mRS > 3).

Statistical Analysis

The ICH and ICH-GS scores were considered as quantitative variables along with other continuous variables such as age, vitals, and biochemical parameters and were summarized as mean ± SD or median values with 25th and 75th percentiles. The mortality associated with each score was expressed in percentage. The linear trend in the outcome (mortality, poor functional outcome) with increasing scores was assessed by trend Chi square test. The discriminating ability of the scores between dead and survived cases was assessed using the ROC curve analysis. The validity of the ICH and ICH-GS scores in predicting the mortality was assessed by applying goodness-of-fit Chi square test on our observed mortality at each score and was compared to predicted mortality from the respective original derivation cohorts. Similar analysis was also done separately for cases with and without any surgical intervention. The entire analysis was carried out using Stata (version14.2). A *P* value of <.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 617 patients of SICH were included in the study, of which 464 and 153 patients were enrolled retrospectively and prospectively respectively.

The mean age of the entire cohort was 56.4 ± 13.4 years with 422 (68.4%) males and 195 (31.6%) females. Among the risk factors recorded, 85.9% of patients had hypertension, 17% has diabetes, 11.9% had previous history of stroke, 26.6% were smokers, 20.6% had history of alcohol intake, and 10.2% were tobacco chewers. Mean systolic and diastolic blood pressures were 180 ± 32.5 and 103.4 ± 18.6, respectively. Median GCS was 9 (interquartile range 7). Among the biochemical parameters, mean values of random blood glucose was 161.2 ± 69 mg/dL, blood urea was 41 ± 28 mg/dL, and creatinine were 1.2 ± 1.2 mg/dL (Table 1).

Radiological imaging revealed mean ICH volume of 34 ± 28.6 cm^3 with 10.9% of cases having an infratentorial bleed. Intraventricular extension was seen in 57.7%. Most

Table 1. *Baseline characteristics of the ICH cohort*

Demographic characteristics	
Age in years, mean (SD)	56.4 (13.4)
Sex; Male/Female, n (%)	422 (68.4)/195 (31.6)
Time delay in presentation, mean (SD)	15.9 (16.9)
Duration of stay in days, median (IQR), range	12 (19), 1-118
Risk factors	
Hypertension	530 (85.9)
Diabetes	105 (17)
Coronary artery disease (CAD)	21 (3.4)
Previous stroke	38 (11.9)
Smoking	164 (20.6)
Alcohol	127 (26.6)
Oral tobacco intake	63 (10.2)
Vitals	
SBP, mean (SD)	180.3 (32.5)
DBP, mean (SD)	103.4 (18.6)
GCS, median (IQR)	9 (7)
Biochemical parameters	
RBS, mean (SD)	161.2 (69)
Urea, mean (SD)	41 (28)
Creatinine, mean (SD)	1.2 (1.2)
Sodium, mean (SD)	142.7 (5.4)
Potassium, mean (SD)	4.1 (0.6)
Total cholesterol, mean (SD)	165.4 (41.8)
LDL, mean (SD)	103.4 (34.5)
HDL, mean (SD)	43.7 (10.5)
VLDL, mean (SD)	19.9 (9.5)
Triglycerides, mean (SD)	128 (58.7)
Imaging characteristics	
Supratentorial/ Infratentorial, n (%)	550 (89.1)/67 (10.9)
Putamen	223 (66)
Thalamus	73 (18)
Brainstem	16 (6)
Cerebellum	32 (5)
Lobar	8 (5)
Hematoma Volume, mean (SD)	34 (28.6)
IVH, n (%)	356 (57.7)
In-hospital management	
Intervention (Yes), n (%)	265 (42.9)
Evacuation, n (%)	171 (27.7)
Evacuation with decompression, n (%)	22 (3.6)
EVD, n (%)	76 (12.3)
EVD + Evacuation, n (%)	18 (2.9)
Ventilator, n (%)	420 (68.5)

common location of ICH was putamen (65.8%) followed by thalamus (18.7%), brainstem (5.5%), cerebellum (5.5%), and lobar (4.5%) (Table 1).

A total of 265 (42.95%) patients underwent neurosurgical intervention. Hematoma evacuation was done in 171 (27.7%), evacuation with decompression was done in 22 (3.6%), EVD in 76 (12.3%) and EVD followed by evacuation done in 18 (2.9%) patients. Ventilator assistance was required in 68.5% of patients (Table 1). Total duration of hospital stay varied from a range of 1-118 days with a median stay of 12 days. In hospital mortality and 30-day mortality were 28.7% and 28.5% respectively.

Performance of the Scores in the Overall Cohort

30-Day Mortality

Overall 30-day mortality was 28.5%. Both ICH and ICH-GS scores showed increase in mortality with increasing scores which was significant for both scores using Chi square test for linear trend ($P < .001$) (Fig 1, A, B). Mortality associated with ICH scores of 0, 1, 2, 3, 4, and 5 was 1.5%, 14.4%, 22.5%, 35.4%, 79.1%, and 100% respectively. Only 1 patient with score 0 died and there was no patient with a score of 6. For ICH-GS scores of 6, 7, 8, 9, 10, 11, and 12, the observed mortality was 7.1%, 10.4%, 20.4%, 39.8%, 41.5%, 54.4%, and 57.7% respectively. No patient died with a score of 5 and there was no patient with a score of 13. The results indicate that both prognostic scores are valid for mortality prediction in the present cohort.

However, the validity of the ICH and ICH-GS scores in predicting mortality at each score was compared with predicted mortality at each score as per the original derivation cohort. Substantial differences were noted in the magnitude of mortality between observed and expected number of deaths, at each value of the ICH and ICH-GS score (Figs. 1, A, B, 3, 4). The goodness of fit Chi square showed that the overall differences in the mortality at each score value are statistically significant ($P < .0001$) (Tables 2 and 3). The discordance between our observed and the predicted mortality in the original ICH and ICH-GS cohort indicates that though the increasing ICH and ICH-GS scores are associated with increasing death, prediction of mortality at individual ICH and ICH-GS score values may not be valid.

Area under Curve Analysis

Area under receiver operating characteristic (AUROC) for 30-day mortality was 75.9% (95% CI: 71.8-79.9) for ICH and 74.1% (95% CI, 70.0%-78.1%) for ICH-GS score respectively (Fig 2, A). In contrast, AUROC for 3 month poor functional outcome was better for ICH-GS score [87.8% (95% CI: 82.4%-93.3%)] than AUROC for ICH score [86.9% (95% CI: 80.9%-92.8%)] (Fig I). The best cutoff values with sensitivity, specificity, PPV and NPV for each outcome were derived (Supplemental Table I).

3-Month Functional Outcome

Poor functional outcome was defined by mRS score of greater than 3. Out of 153 prospective cases, 144 cases were analyzed (9 patients were lost to follow up at 3rd month). There was increase in poor functional outcome with increasing ICH and ICH-GS score values, which was

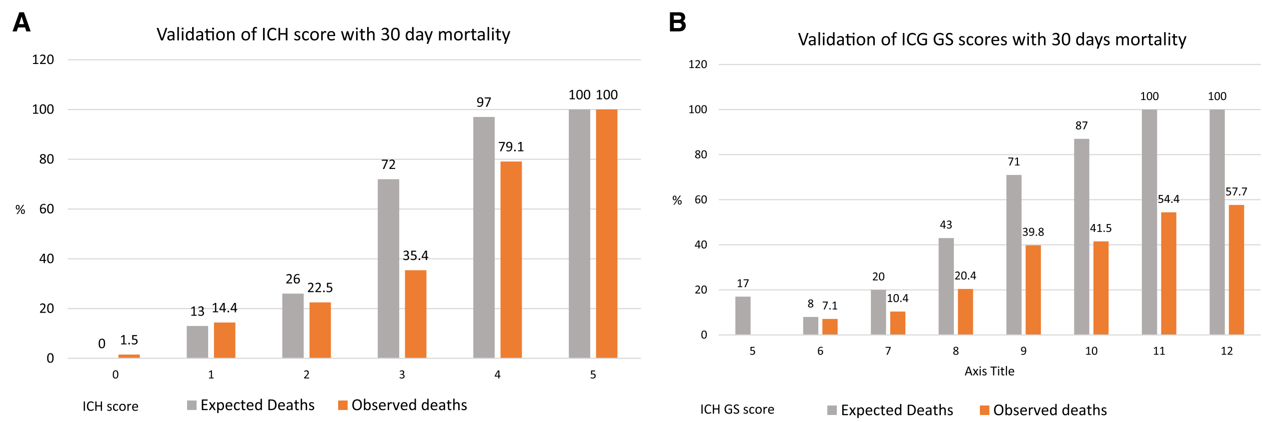

Figure 1. *(A) Individual ICH scores and 30-day mortality. (B) Individual ICH-GS scores and 30-day mortality.*

statistically significant ($P < .001$) as per chi square test for linear trend (Supplemental Fig I, A). This indicates that the overall ICH and ICH-GS score criteria are validating the pattern of poor functional outcome in our cohort.

Performance of Scores in Surgically and Conservatively Managed Groups

265 cases out of 671 of the total study population received surgical intervention. We examined effect of intervention on prediction abilities of both prognostic scores.

30-Day Mortality

Mortality prediction by ICH and ICH-GS scores in both conservative and surgically managed group correlated with increasing mortality with increasing scores. This linear trend of increasing mortality with increasing score was statistically significant ($P < .0001$) in both the groups (Supplemental Tables II and III). Observed mortality among patients who underwent any surgical intervention was compared to mortality published in the original derivation cohort at each ICH and ICH GS score. Although the mortality was proportionately higher with increasing score, ($P < .05$) the proportionate mortality at each score was lesser in patients with both prognostic scores when compared to the original cohort (Figs. 3 and 4).

AUC Analysis

AUROC curve in conservative management group for 30-day mortality was 85.3(81-89.6) and 82.9 (78.3-87.5) for ICH and ICH-GS scores respectively (Fig 2, B). In surgically managed group AUROC curves were 59.9 (52.6-67.2) and 63 (56-70) for ICH and ICH-GS scores respectively (Fig 2, C). These findings suggest significantly better outcome prediction of mortality in conservatively managed group than the surgically managed group. Hence, we observe that surgical intervention affects outcome predictability by ICH and ICH-GS scores in view of much lower mortality at individual scores. The best cutoff values with sensitivity, specificity, PPV, and NPV with respect to each outcome are summarized in the Supplement (Supplemental Table IV).

Table 2. *Validation of ICH score according to the management of patients*

ICH score	Conservatively managed		Surgically managed		Total	
	Observed deaths (%)	Expected deaths* (%)	Observed deaths (%)	Expected deaths* (%)	Observed deaths (%)	Expected deaths* (%)
0	1/66 (1.5)	0.00 (0)	0	0 (0)	1/68 (1.5)	0.00 (0)
1	14/101 (13.9)	13.13 (13)	5/31 (16.1)	4.03 (13)	19/132 (14.4)	17.16 (13)
2	16/81 (19.8)	21.06 (26)	23/92 (25)	23.92 (26)	39/173 (22.5)	44.98 (26)
3	32/60 (53.3)	43.20 (72)	30/115 (26.1)	82.8 (72)	62/175 (35.4)	126.00 (72)
4	39/42 (92.9)	40.74 (97)	14/25 (56)	24.25 (97)	53/67 (79.1)	64.99 (97)
5	2/2 (100.0)	2.00 (100)	0	0 (100)	2/2 (100.0)	2.00 (100)
Total	104/352 (29.5)	120.13	72/265 (27.2)	135	176/617 (28.5)	255.13
Goodness of Fit χ^2	4.3 $P = 0.51$		38.3 $P < 0.0001$		35.7 $P < 0.0001$	

*expected deaths as per the original derivation cohort.

Table 3. *Validation of ICH-GS score according to the management of patients*

ICH GS score	Conservatively managed		Surgically managed		Total	
	Observed deaths (%)	Expected deaths* (%)	Observed deaths (%)	Expected deaths* (%)	Observed deaths (%)	Expected deaths* (%)
5	0/16 (0.0)	2.72 (17)	0/2 (0)	0.34 (17)	0/18 (0.0)	3.06 (17)
6	4/59 (6.8)	4.72 (8)	1/11 (9.1)	0.88 (8)	5/70 (7.1)	5.60 (8)
7	9/89 (10.1)	17.80 (20)	3/26 (11.5)	5.2 (20)	12/115 (10.4)	23.00 (20)
8	14/60 (23.3)	25.80 (43)	9/53 (17)	22.79 (43)	23/113 (20.4)	48.59 (43)
9	26/53 (49.1)	37.63 (71)	19/60 (31.7)	42.6 (71)	45/113 (39.8)	80.23 (71)
10	19/37 (51.4)	32.19 (87)	20/57 (35.1)	49.59 (87)	39/94 (41.5)	81.78 (87)
11	23/29 (79.3)	29.00 (100)	14/39 (35.9)	39 (100)	37/68 (54.4)	68.00 (100)
12	9/9 (100)	9.00 (100)	6/17 (35.3)	17 (100)	15/26 (57.7)	26.00 (100)
Total	104/352 (29.55)	158.86	72/265 (27.2)	177.4	176/617 (28.5)	336.26
Goodness of Fit χ^2	22.8		63.2		78.5	
	$P < 0.01$		$P < 0.0001$		$P < 0.0001$	

*expected deaths as per the original derivation cohort.

AUC for 90-day poor functional outcome in conservatively managed groups were 86.8(79.1-94.5) and 85.2(77-93.3) for ICH and ICH-GS scores respectively; in surgically intervened groups AUC were 79(65.5-92.5) and 85.2 (74.5-95.9) for ICH and ICH-GS scores respectively (Supplemental Figs I, B and C). This analysis suggests better 90-day functional outcome prediction by ICH-GS score in both groups, similar to the observation in overall study population (Supplemental Table V).

Discussion

SICH has highest mortality and morbidity amongst all stroke subtypes. Despite advanced clinical knowledge, most patients are managed conservatively as there is limited evidence available on benefit of surgical intervention in ICH. Clinical grading scales are important tools for prognostication, risk stratification, and improving the communication amongst healthcare providers. Clinical scores not only predict mortality but also help to prognosticate functional outcome of the patient. They also help in standardizing the guidelines and ensuring consistency for research protocols; thereby decreasing the wide heterogeneity in clinical care and clinical research.

ICH score is the most widely accepted clinical grading scale to predict 30-day mortality, short term and long-term outcomes in patients with ICH. Amongst the various revisions available of this score, ICH-GS score is the most robust refinement with equivalent performance.[9-11]

External validation of a score in various subpopulations ensures its wide acceptability beyond the cohort from which it was derived. There is no published data on the predictive ability of both these scores in Indian population and no data exists about the impact of surgical interventions on prediction of these scores and prognostication implications. In this study, we have attempted to validate ICH and ICH-GS scores in Indian population and tried to test its ability to predict mortality and poor functional outcome in both surgical and conservatively managed patients with ICH. We included 617 patients with primary ICH. Our study cohort was different at baseline from the original derivation cohort in view of higher male patients, significantly younger age of presentation and higher proportion patients with hypertension.

A statistically significant correlation was found between the ICH and ICH-GS score and 30-day mortality, i.e. higher score rates correlated with higher mortality. There was a linear trend between increase of ICH and ICH-GS score values and 30-day mortality. However, the predicted mortality rate at each score in the original derivation cohorts did not correlate with the observed mortality rates in the present study. This observation was especially true for patients who presented with ICH scores of 4 and 5. This could be due to considerably younger population, intensive management of the ICH, and surgical interventions at our tertiary care center. Also, these patients are sicker, have larger ICH volumes, and are therefore more likely to undergo surgical intervention, which in turn has modified outcome in this cohort. In contrast, patients who present with ICH score of 2-3 are relatively stable, have lesser ICH volumes, and are less likely to undergo surgical intervention. This makes them more similar to patients in the original cohort and explains similar proportionate mortality in this subgroup.

The ROC analysis revealed a higher AUC of ICH score than ICH-GS suggesting better predictability of 30-day mortality by the former in our cohort. This was in agreement with previously done studies of ICH score derivation by Hemphill and colleagues[12] as well as other ICH score validation studies.[13-15] However, previously done validation studies comparing performance of ICH and ICH-GS scores suggested ICH-GS as better predictor than ICH score for mortality outcome at 30 days.[8,14-16]

We also tried to study the effect of surgical intervention on prediction of mortality and poor functional outcome by ICH and ICH-GS scores by analyzing these 2 groups

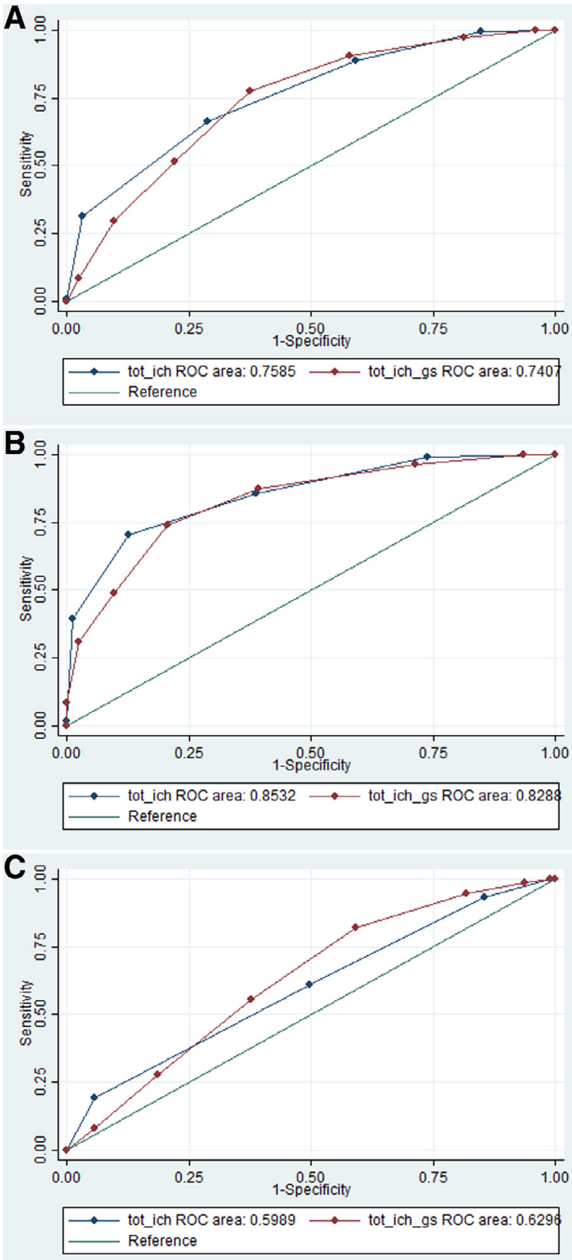

Figure 2. *ROC curves of ICH and ICH-GS for 30-day mortality, (A) total cohort, (B) conservatively managed group and (C) surgically managed group.*

separately. There is no data analyzing the effect of surgical intervention in the original cohort. The evidence for benefit of surgery in ICH has evolved over time. Rational reasoning suggests that removal of clot should reduce the intracranial pressure, reduce ischemia, and prove to be beneficial. However, earlier trials like ISTICH and STITCH II[17,18] did not show benefit of early hematoma evacuation in supratentorial ICH. This may be due to several reasons including patient selection, delay in surgery, and lesser elective surgeries. The last 2 decades has also seen emerging evidence on use of minimally invasive techniques for clot removal. MISTIE II trial[19,20] showed a trend toward better outcome in patients who underwent clot catheterization with intermittent rtPA and results of MISTIE III[21] using CT-guided endoscopic surgery enrolled 499 patients with supratentorial intracerebral hemorrhage. The results showed 6%-8% difference in estimated allcause mortality at 1 year, which was significantly lower in the minimal invasive group ($P = .037$). Also, the mean reduction in hematoma size and the end of treatment volume was significantly lower in the minimally invasive group. In our cohort, the AUC analysis revealed that outcome discrimination of ICH and ICH-GS scores was negatively affected by surgical intervention and better correlation was found in conservatively managed group. This observation indicates that surgical intervention reduces the mortality irrespective of baseline ICH and ICH-GS scores. It encourages us to insist on intensive management of ICH to reduce mortality. Thus compiling the available literature, it may be logical to suggest that surgery reduces overall mortality in ICH. At the same time, there is a concern that surgery may not change the morbidity, but it will definitely help in reducing the days in intensive care, total hospital stay and it will aid to reach the final mRS faster. It gives an opportunity for patients with poor grade to survive; an ethical dilemma between mortality and morbidity will always remain in these patients. But, if the aim is to predict mortality alone, then it is imperative to consider surgical intervention as an effect modifier in patients with ICH. The same dilemma exists when performing decompressive craniectomy for large infarcts where mortality benefits are high but morbidity is heterogeneous across all Rankin scores. We do not recommend that a decision for surgical intervention be based on ICH and ICH-GS scores alone. However, a general nihilism about surgical intervention in ICH needs to be changed, as many factors like age, hematoma volume, delay in intervention, type of intervention, and duration of follow up influence the outcome of patients with ICH.

ROC analysis for ICH and ICH-GS scores in predicting poor outcome at 90 days revealed marginally better prediction by ICH-GS score which was similar to findings observed in previous validation studies.[8,16,22] The ICH-GS model uses more detailed criteria with better stratification of various variables contributing to its better outcome predictability.

To the best of our knowledge, our study is one of the largest single-center series of ICH from our country. However, certain limitations deserve a mention. Due to the observational and ambispective nature of the study, some selection and referral bias are likely. The analysis is not stratified on the basis of type of intervention. Patients may not have been referred to our hospital or they may have died before arrival to the hospital. This may apply especially to patients in the oldest age groups. Many

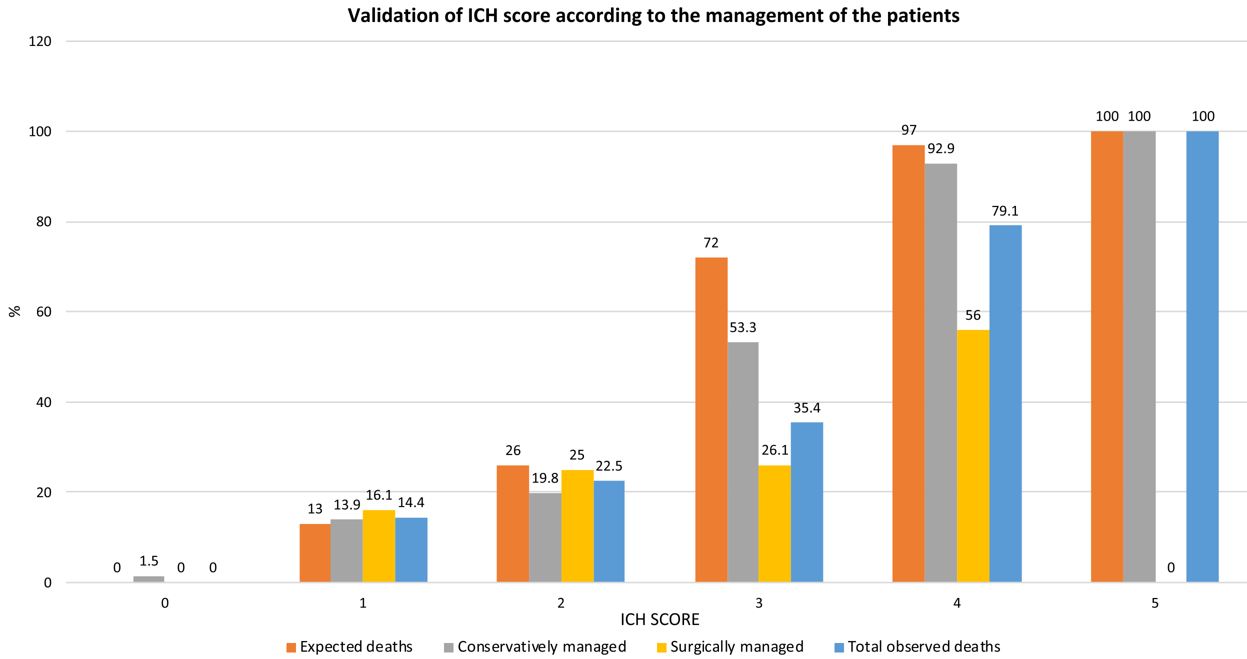

Figure 3. *Validation of ICH score as per patient management.*

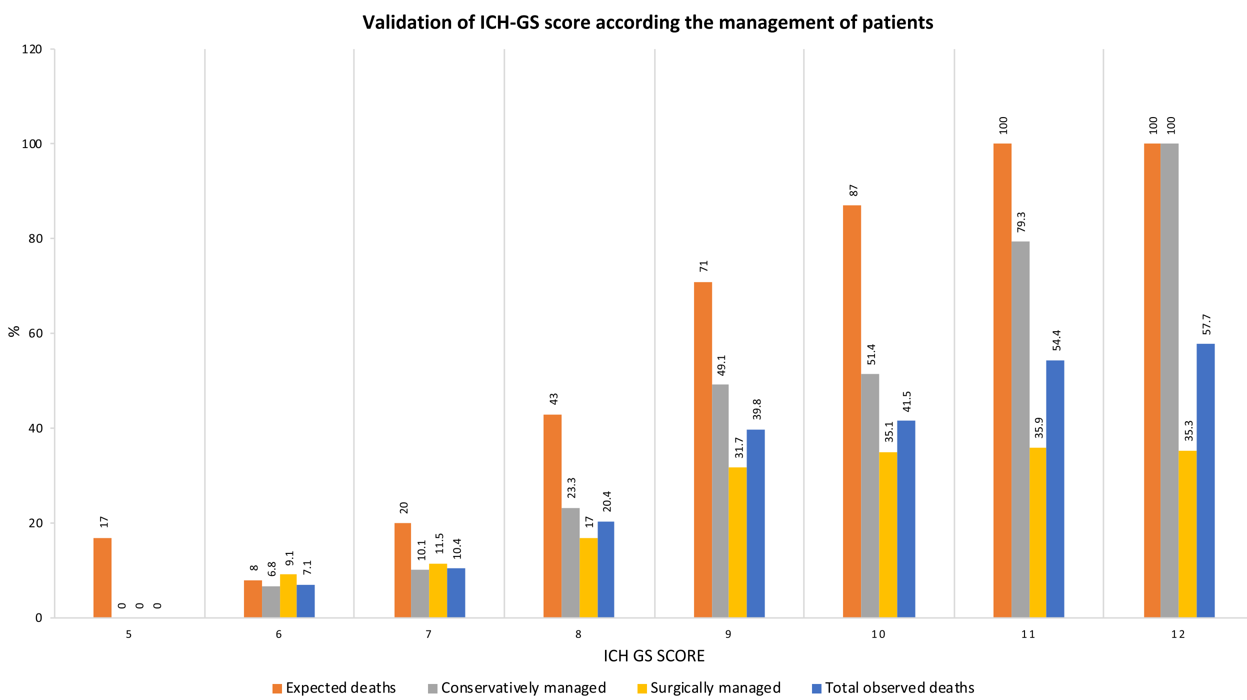

Figure 4. *Validation of ICH-GS score as per patient management.*

unmeasured confounders predictive of mortality and functional outcome after ICH might have been missed.

Conclusions

We conclude that both ICH and ICH-GS scores can be effectively used for prognostication in ICH patients in Indian population, although mortality at individual scores is lower than reported. Mortality prediction using ICH and ICH GS scores is modified by surgical interventions. Thus, newer prognostic tools which incorporate surgical intervention need to be developed and validated in future.

Conflicts of Interest

We have no conflicts of interest to disclose.

Supplementary materials

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2019.05.003.

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