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Comparison Between Original And Modified Intracerebral hemorrhage Scores In Spontaneous Intracerebral Hematoma In Predicting Outcome In A Tertiary Care Center In Nepal

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Abstract

Introduction: Spontaneous intracranial hemorrhage is the presence of a parenchymal bleed in the absence of trauma or surgery in brain. The original Intracerebral hemorrhage score utilizes the cut-off age of 80 years, whereas the modified Intracerebral hemorrhage score used a lower cut-off age which may better prognosticate the outcome of Intracerebral hemorrhage in the populations with shorter life expectancy. The primary objective of this study was to compare the original with modified intracerebral hemorrhage scores in predicting mortality in Nepalese population with intracerebral hemorrhage.

Materials and Methods: Patients ≥16 years, with spontaneous Intracerebral hemorrhage, who were admitted in Tribhuvan University Teaching Hospital in the Department of Neurosurgery and Neurology between 15th March, 2019 and 30th November, 2019, were included in the study. Original and modified Intracerebral hemorrhage scores were recorded separately at the time of admission. The outcome was measured using the modified Rankin Scale at 6 months. To compare the predictive ability of original and modified Intracerebral hemorrhage for mortality and outcome, receiver-operating characteristics curves were compared; and areas under the curve was calculated. DeLong's test was used to compare the area under the Receiver Operating Characteristic. Sensitivity and specificity were calculated for the diagnostic accuracy; and were plotted in Receiver Operating Characteristic. Youden's index was calculated to determine the discrimination ability of both scores.

Result:A total of 89 patients were enrolled in the study. Only thirteen patients (14.6%) were ≥80 years. The 30-day and 6-month mortality was 24.7% and 33.7% respectively. Hosmer-Lemeshow test showed a good model fit for both the scores for mortality and good outcome at 6 months.

Conclusion: Prediction of 30-day mortality by modified intracerebral hemorrhage score is similar to the original intracerebral hemorrhage score. However, there was a slight trend of better prediction for good outcome at 6 months, using the modified score.

Key Words : Spontaneous intracerebral hemorrhage, Glasgow coma score, intracerebral hematoma score, modified Rankin scale, Prognosis

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INTRODUCTION

Stroke is a major global health problem with a prevalence of 32-270 per 100,000 population.[1] Spontaneous intracranial hemorrhage (ICH) is defined as the presence of parenchymal bleed in the absence of trauma or surgery seen in a brain computed tomography (CT)[2] and accounts for 10-15% of all strokes. There is a slightly higher incidence in the Asian population (18-20%) and is increasing in the low- and middle-income countries.[3,4] Spontaneous ICH increases with age (doubles each decade after 35 years of age).[5] ICH in the young is defined as spontaneous hemorrhage occurring in patient of age <50 years.6,7 One year survival is only ~30%; and the 30-day mortality is 35-52%, with half of the deaths occurring during the first 2 days after ictus.5 Management, including surgery, is still controversial since the first prospective randomized controlled trial published in 1961.8,9 Hemphill et al in 2001 proposed a clinical grading scale for spontaneous ICH, namely the original ICH score (oICH score), to prognosticate the 30-day mortality.[10] Higher scores are associated with higher mortality, (0%, 13%, 26%, 72%, 97% and 100%, corresponding to scores of 0, 1, 2, 3, 4 and 5 respectively).[10] There are several modifications of the oICH score. The modified ICH (mICH) score by Godoy et al (2006) was based on the concept that stroke occurring in younger patients needed to be evaluated from a different perspective.[11] Later papers were published explaining that the life expectancy of Asian population is less than that of developed countries; and the age of onset of spontaneous ICH is also low. As per world health organization (WHO) report in (2018), the life expectancy of the Nepalese population is reported as 70.5 years.[12] The oICH has a cut-off value of 80 years. Modified ICH score with a lower cut-off value may be more applicable in our population. The modification of oICH may have better predictive value for our population in prognosticating the outcome.[11] Hence, our study was designed to to compare the original with modified ICH scores to see the predictability of outcome including mortality, using mRS at 6 months.

MATERIALS AND METHODS

This is a prospective observational study conducted at the Department of Neurosurgery and Neurology, TUTH, Kathmandu, Nepal. The study was approved by the Institute Review Committee, Institute of Medicine (IOM) (Approval No (6-11)E2/075/76). The duration of study was 15 months. All patients with the age of ≥16 years, with CT evidence of ICH, who were admitted between 15th March, 2019 and 30th November, 2019 and were followed up till 30th May, 2020, were included in the study. Patients with post CPR status, who refused to participate, were in 'Do Not Resuscitate' status, were pregnant, left against medical advice, who were transferred to other hospitals or had secondary cause (such as aneurysm or AVM) were excluded from the study.

The statistical analyses were performed using statistics and data (STATA) package 21.0. To assess the association between categorical variables, chi-squared test or fisher exact test were used. Mann-Whitney U tests were performed. The sensitivity, specificity, positive and negative predictive values of different ICH scores were computed using the cut-off values that generated the best Youden index (J). To determine the cut-off values and its diagnostic ability, Receiver Operating Characteristic (ROC) curve was plotted and area under the curve (AUC) was calculated. DeLong’s test was used to compare the area under ROC. The cut-off values were calibrated by Hosmer and Lemeshow chi-square test through logistic regression. The outcome was measured using the modified Rankin Scale at 6 months as good (mRS 0-2) and bad outcome (mRS 3-6). To compare the predictive ability of two scoring systems (oICH and mICH) for the outcome and mortality, MEDCALC 19.2.0 was used to compare ROC curves. p-value <0.05 was considered statistically significant.

RESULTS

A total of 96 patients were enrolled in the study. Seven patients were excluded (6 were lost to follow-up and one patient was diagnosed with Glioblastoma). Hence, 89 As shown in Table 2, there is a good linear correlation between the predicted IMPACT score with GOS in 6 months. The observed values and those predicted by all these models of IMPACdiscrimination ability of the score. The overall predictive performances of IMPACT scores were good in our study which corroborates weDewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, Agrawal A, Adeleye AO, Shrime MG, Rubiano AM, Rosenfeld JV, Park KB. Estimating the global incidence of traumatic brain injury. J Neurosurg. 2018 Apr 27;130(4):1080-1097. doi: 10.3171/2017.10. JNS17352. PMID: 29701556.Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974 Jul 13;2(7872):81-4. doi: 10.1016/s0140-6736(74)91639-0. PMID: 4136544.Steyerberg EW, Mushkudiani N, Perel P, Butcher I, Lu J, McHugh GS, Murray GD, Marmarou A, Roberts I, Habbema JD, Maas AI. Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on RJ, van der Spoel JI, Z patients made the basis for final analysis.

Table: 1 Demographic charateristics of pateints, n=89

SN	Charateristics	Frequency n (%)
1	**Male**	**58 (65.2)**
2	**Female**	**31 (34.8)**
3	Mean Age	63.0±14.2 years
4	Age range	25-91 years
5	Arterial Hypertension	78 (87.6)
6	Diabetic	11 (12.4)
7	Ischemic Heart Disease.	3 (3.4)
8	Alcohol Consumers	55 (61.8)
9	Regular Smokers	52 (58.4)
10	GCS 13-15	52 (58.4)

Regarding the comorbidities, it is tabulated in Table 1. Fifty patients (56.2%) were <65 years of age. Only 13 patients (14.6%) were >80 years of age. The most common presenting symptom was sudden weakness followed by slurred speech. The median hematoma volume was 18 ml (2-151 ml) with an interquartile range of 25.25 (Q1, Q3=6.13,31.38). Hematoma volumes of <30 ml and ≥30 ml were 64 (71.9%) and 25 (28.1%) patients, respectively in oICH score. Hematoma volume of <30 ml, 30-50 ml and ≥50 ml were 64 (71.9%), 17 (19.1%) and 8 (9.0%), respectively in mICH score. Seventy eight patients (87.6%) had hematoma in the supratentorial location with most common being basal ganglia (37, 41.6%). Intraventricular extension was noted in 30 patients (33.7%). Graeb’s score was ≤3 in 11 patients (36.7%) and >3 in 19 patients (63.3%). The patients with mICH and oICH is shown in Table 2. Different variables in original and modified ICH scores are shown in Table 3. In our study, there were no patients with oICH score 5 and 6 and mICH 8 and 10.

Table 2: Original ICH score (n = 89)

I C H score	Frequency (%)	mICH score	Frequency (%)
0	24 (27)	0	6 (6.7)
1	28 (31.5)	1	18 (20.2)
2	23 (25.8)	2	23 (25.8)
3	12 (13.5)	3	15 (16.9)
4	2 (2.2)	4	11 (12.4)
5	0	5	6 (6.7)
6	0	6	6 (6.7)
		7	3 (3.4)
		8	0
		9	1 (1.1)
		10	0

TABLE: 3 Frequency in each variables (n = 89)

SN	Original ICH Score	Frequency n (%)	Modified ICH Score	Frequency n (%)
1	Age (years)		Age (years)	
	<80	76 (85.4)	<65	50 (56.2)
	≥80	13 (14.6)	≥65	39 (43.8)
2	Hematoma Volume		Hematoma Volume	
	<30 ml	64 (71.9)	<30 ml	64 (71.9)
	≥30 ml	25 (28.1)	30-50 ml	17 (19.1)
			≥50 ml	8 (9.0)
3	Location		Location	
	Supratentorial	78 (87.6)	Supratentorial	78 (87.6)
	Infratentorial	11 (12.4)	Infratentorial	11 (12.4)
4	Intraventricular Extension		Intraventricular Extension	
	Yes	30(33.7)	Yes Graeb's Score >3	19 (63.3)
			Graeb's Score ≤3	11 (36.7)
	No	59 (66.3)	No	59 (66.3)
5	GCS		GCS	
	3-4	1	3-4	1
	5-12	35	5-8	12
	13-15	53 (58.4)	9-13	26
			14-15	50

Surgery was performed in 19 patients (21.3%) among whom 6 patients (6.7%) underwent EVD placement. The majority of the patients (78.7%) underwent medical treatment alone as per the protocol of the Department of Neurology.

Outcome

Overall, a total of 30 patients with ICH died over the course of treatment, accounting for a mortality rate of 33.7%. Twenty-two patients died within the first 30 days, accounting for a mortality rate of 24.7%. In the following two months, 8 more patients died, increasing the 3-month mortality to 30 patients (33.7%). However, no patient died in the other next 3 months. While evaluating the trend of outcome at 1, 3, and 6 months, it is seen that there is an increase in good outcomes with time as shown in figure 1.

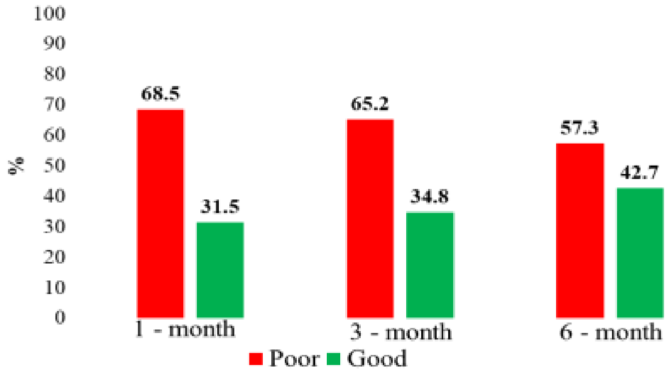

Figure 1: Bar diagram showing mRS in 1, 3, and 6 months

The different variables used were age, sex, side of hematoma, presence of IVE, GCS at the time of admission, location of hematoma, volume of hematoma, whether surgery was done or not, presence of comorbid conditions (HTN, DM and IHD), Graeb's score and systolic BP. To determine the relationship between different variables, logistic regression analysis was done. For 30-day mortality, IVE, GCS, surgery, Graeb's score, SBP, and hematoma volume were significant. Similary for 3-month mortality, IVE, GCS and surgery were significant. For 6-month mortality, IVE, GCS, surgery, Graeb's score, SBP and hematoma volume were significant. We also analyzed to see the effect of variables on the outcome at 3 and 6 months. For the 3-month outcome, IVE, GCS, surgery, Graeb's score and SBP were significant but hematoma volume was not significant. For the 6-month outcome, IVE, GCS, surgery, Graeb's score, SBP were significant. Multivariate logistic regression was done to see the composite effects of different variables. Group of variables which were significant in Univariate analysis were selected. The odds ratios was calculated at confidence interval of 95%. The 30-day mortality is 5.3 and 2.3 times more likely in patients with low GCS as compared to GCS 13-15; but the association is not significant. Hematoma volume <30 ml and 30-50 ml showed a lower likelihood for 30-day mortality; however, the association is not significant. Absence of IVE shows significantly less likelihood for 30-day mortality. The good outcome at 6 months is less likely in patients with lower GCS as compared to GCS 13-15. The association is significant for GCS 9-13. Hematoma volume <30 ml shows a higher likelihood for a good outcome at 6 months as compared to >30 ml and the association is significant.

Original and modified ICH scores both showed similar diagnostic ability as indicated by the area under ROC to diagnose mortality and outcome. Both scores showed a higher specificity than sensitivity, which indicates that the scores are better in detecting survival and good outcome than detecting mortality and poor outcome. Only in 30-day mortality, oICH score had higher sensitivity than specificity. All the cut-off values are tested for their calibration by using the logistic regression Hosmer-Lemeshow chi-squared test. The entire cut-off values showed a good model fit (p=1). MEDCALC 19.2.0 is used to compare

ROC curves. DeLong's test is used to compare the area under the ROC. Hosmer Lemeshow test for oICH and mICH showed good data fit for overall 30-day and 3-month mortality, as well as the good outcome at 1, 3 and 6 months (p=1). Stepwise analysis of significant factors using univariate analysis was done. For 30-day mortality, the presence of IVE, GCS, surgery, Graeb's score, hematoma volume, and hypertension were significant. Similarly, the factors

predicting poor outcome on multivariate analysis were GCS <8, volume >30 ml, IVE, and surgery.

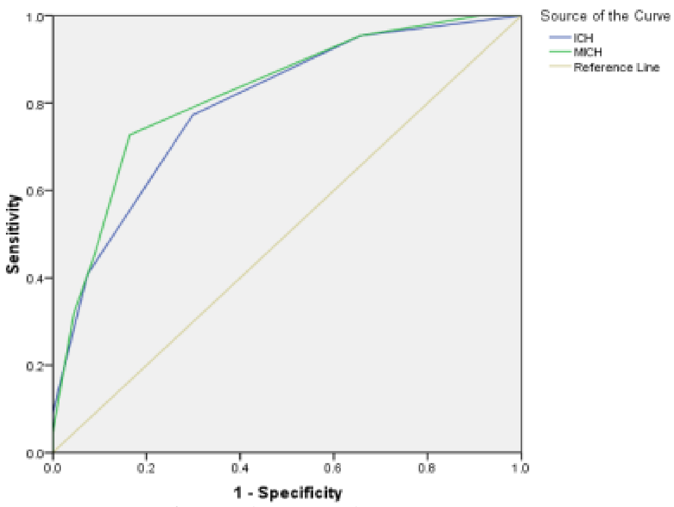

Figure 2: ROC for 30-day mortality

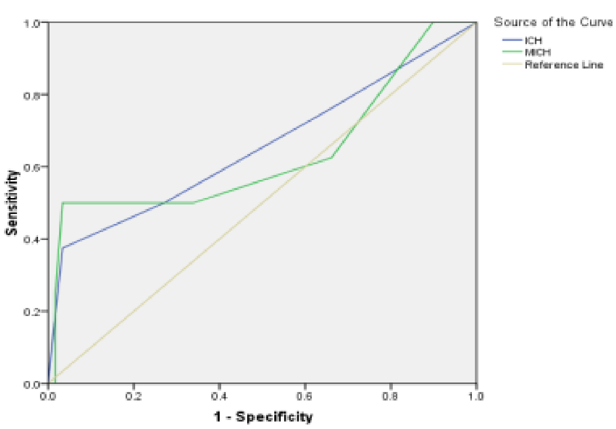

Figure 3: ROC for 6-month mortality

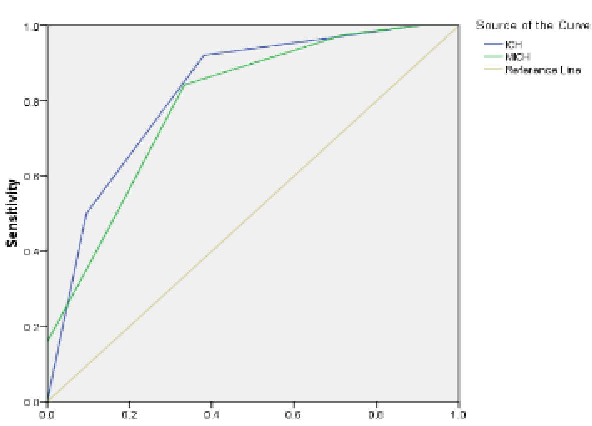

Figure 4: ROC for good outcome in 6 months

DISCUSSION

Hemorrhagic stroke has a poor prognosis despite extensive treatment modalities. There is a need to identify risk factors and customize treatment, especially in resource-limited countries like Nepal. A modified scoring system will be helpful. The modifications in our study included subgrouping of the GCS, age, and intraventricular extension. We wanted to see if this would predict the mortality and outcome equally. Male preponderance was seen, similar to other studies.[13,14] ICH is considered the disease of the elderly; however, the mean age of our patients was 63 years, similar to the paper by Hemphill et al (66 years) and reported in the STICH trial but our mean age was higher than reported by an Indian study by Hedge et al (58 years) and by Meyares et al (48 years only).[10,14–16] Only 13 patients (14.6%) were ≥80 years in our study, in contrast to Hedge et al (2.9%).[14] Our patients were predominantly young adults. Probably the Asian race has been related to the higher number of stroke in young adults and disparity in risk factor burden, with a similar study from India, which reported a mean age of 58 years and one-third being <50 years of age.[14,15,17]

Hypertension was seen in 78 patients (87.6%), which is higher than in other studies (45-60%) 14,18 but a similar percentage as in a study from India.19 Poor GCS is one of the most consistent predictors of poor outcome as documented in most of the published series.[14,19] GCS at admission was significant on univariate analysis for 30-day mortality (p<0.001), 3-month mortality (p<0.034), and 6-month outcome (p<0.001) in our study. However, using multivariate analysis, it was not significant except for the subgroup of patients with a GCS of 9-12 at 6 months. Even a patient with a good GCS died due to a large hematoma volume and other complications, such as wound infection and pneumonia, leading to sepsis.

The most common presenting symptoms were weakness, followed by slurred speech. Headache was present in only 15.7%, contrary to the study by Hedge et al.[14] Seizure was present in only 7% of patients in our study. Intraventricular extension was seen in 33.7% patients, which was lower than the study from India by Hedge et al (40-60%).[14] On univariate analysis, IVE was highly significant for 30-day mortality (p<0.001), 3-month (p<0.046) mortality, and 6-month outcome (p<0.001). On using multivariate analysis, it was only significant for 30-day mortality (p<0.039). The odds ratio for no IVE was 0.202 (CI 0.044-0.922). This implies that if there is absence of IVE, the 30-day mortality was significantly lower. The subgroup analysis of the STICH Trial data had similar results; and they concluded that the absence of IVH resulted in better outcomes (31.4% vs 15.1%; p<0.001); and the presence of hydrocephalus lowered the likelihood of favorable outcome to 11.5% (p=0.031).16 Similar results were seen in INTERACT 2 study by Moullaali TJ et al.[20]

In our study, surgical intervention was done in 21.3% patients, which is similar to the study by Hedge et al.14 Surgical evacuation through craniotomy was done in 11.2%, which is slightly less than the study by Hedge et al (16.8%), and decompressive craniectomy in 3.4%. EVD was placed in 6.7% patients similar to study from India (6.2%).[14] Placement of EVD showed poor prognosis. The role of surgery is still controversial. STICH trial concluded that there was no overall benefit from early surgery; but a recent paper by Raafat et al suggested that there is some beneficial role in early surgery.[16,21] Furthermore, the STICH-2 trial concluded that early surgery does not increase the rate of death or disability at 6 months and might have a small but clinically relevant survival advantage for the patient with spontaneous lobar ICH without IVE.[22] In our study, there was higher mortality as the majority of the patients were operated only after neurological deterioration or had intraventricular extension. The functional outcome in alive patients was better in the operated patient at 6 months (3/4th) with good mRS.

Surgery was significant for 30-day ($p<0.001$) and 3-month ($p<0.001$) mortality and for mRS at 6-months ($p<0.008$). However, it was not significant on multivariate analysis; but the odds ratio for surgery not done is 0.904, which shows that surgery is a negative predictor for 30-day mortality. The average hospital stay (17.6 days) is less than that in another study (25 days).[13]

Hegde et al attempted to validate the ICH score in an Indian setting and suggested reducing the age cut-off from 80 years to 70 years in the original ICH score.[14] This was influenced by the fact that the mean age of the affected group in other Indian studies is much younger compared to the Western population. Since the average life expectancy in Nepal is 70.5 years, we put a cut-off level of 65 years, similar to a study by Godoy et al (Argentina).11 Pinho et al stated that even though the use of prognostic scores is recommended, other factors must also be weighed when evaluating individual patients, and an early subjective clinical judgment by experienced clinicians is advised.[4]

There is almost an equal number of patients in the oICH score of 0, 1, and 2, with 27%, 31.5%, 25.8% patients, respectively. There is no patient with an ICH score of 5 and 6, as was in the original ICH paper and study by Hedge et al., as there was no patient with a score of [6. 10,14] When a patient with a high ICH score arrives at the ER, the higher mortality rate is explained. So the family members takes patient back home (left against medical advice) or do not want any surgical management. Thus, those patients who may have benefited from surgery but were denied were not included in this study. The 30-day mortality rate was higher in our study (24.7%) than that by Wang et al (15.6%), but was as high as 30.1% in other studies.[11,13,14] Our 3-month mortality was 33.7%, which was similar to the study from India (30.1%) and others.[11,14,19,23] At 6-month follow-up, a favorable outcome (mRS 0-2) was observed in 42.7% of the patients and a poor outcome (mRS 3-6) in 57.3%. Our study has a similar good outcome as compared to a study from India by Hedge et al (45.5%).14 The probable cause for the good outcome may be attributed to 1) low initial hematoma volume, 2) younger age, and 3) Asian race.24 In our study, 66.3% of the patients were alive at 6 months, with 57.3% with poor outcome and 42.7% with a good outcome. Since our study is single center-based, multi-center trials and larger sample size might be required to further support our findings.

CONCLUSION

For spontaneous ICH, the modified ICH score predicted mortality at 30 days is similar to that by the original ICH score. Both scores were comparable. However, there was a slight trend of better prediction for a good outcome at 6 months using the modified score compared to the original score. The majority of the developing countries have lower life expectancy than the developed countries. As the age cut-off used in the original score is 80 years while the modified score uses 65 years of age as cut-off, the latter may be more applicable and predictive in the developing countries like Nepal, which has a relatively lower life expectancy; however, further studies are needed.

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CONFLICT OF INTEREST
There is no conflict of interest.

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