CLINICAL NEUROLOGY AND NEUROSURGERY

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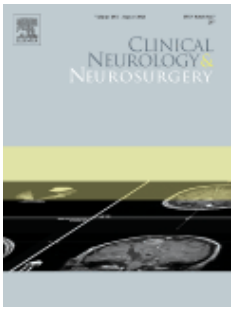

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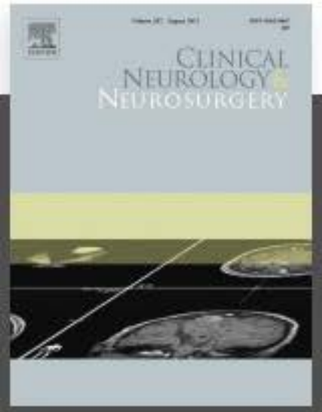

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I.Putu Eka Widyadharma [a], Angga Krishna [a], Andreas Soejitno [a], A.A.A. Putri Laksmidewi [a], Kumara Tini [b], I.B. Kusuma Putra [a], I.G.N. Budiarsa [a], I.A. Sri Indrayani [a]

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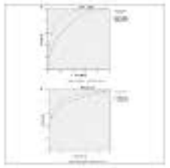
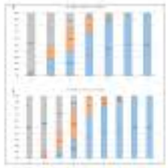

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Highlights

- ICH score had not been used to predict good outcome or significant disability for those who were alive.
- Modified ICH (mICH) score was aimed to increase prediction accuracy for mortality, significant disability, and good outcome.
- mICH score was superior to the original version for predicting 30-day mortality, significant disability, and good outcome.
- This study had been the largest that involved Asian patients.

Abstract

Introduction

Intracerebral hemorrhage (ICH) score has been widely used as a

consistent and reliable clinical grading scale for predicting mortality. However, ICH score had not been used to predict good outcome or significant disability for those who were alive. We intended to address whether any modifications would increase prediction accuracy for mortality as well as the extent of morbidity for those who survived.

Methods

We conducted a retrospective cohort study, involving all non-traumatic ICH patients admitted to our hospital between September 2018 and July 2020. All non-traumatic ICH patients who were admitted to the stroke unit and registered in our stroke database had their medical records, neuroimaging, and laboratory test results reviewed. Only patients with complete medical records and available CT imaging and laboratory test results were included in our study. Independent predictors of mortality (modified Rankin scale/mRS of 6) or good outcome vs. significant disability (mRS≤2 vs. mRS 3–5, respectively) were identified by logistic regression. A modified ICH (mICH) score was compared with the original ICH (oICH) score for its diagnostic performance (DP). Overall DPs were graded and ranked according to Youden Index (YI).

Results

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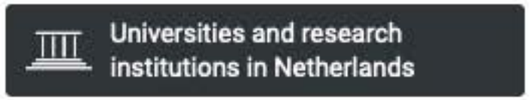

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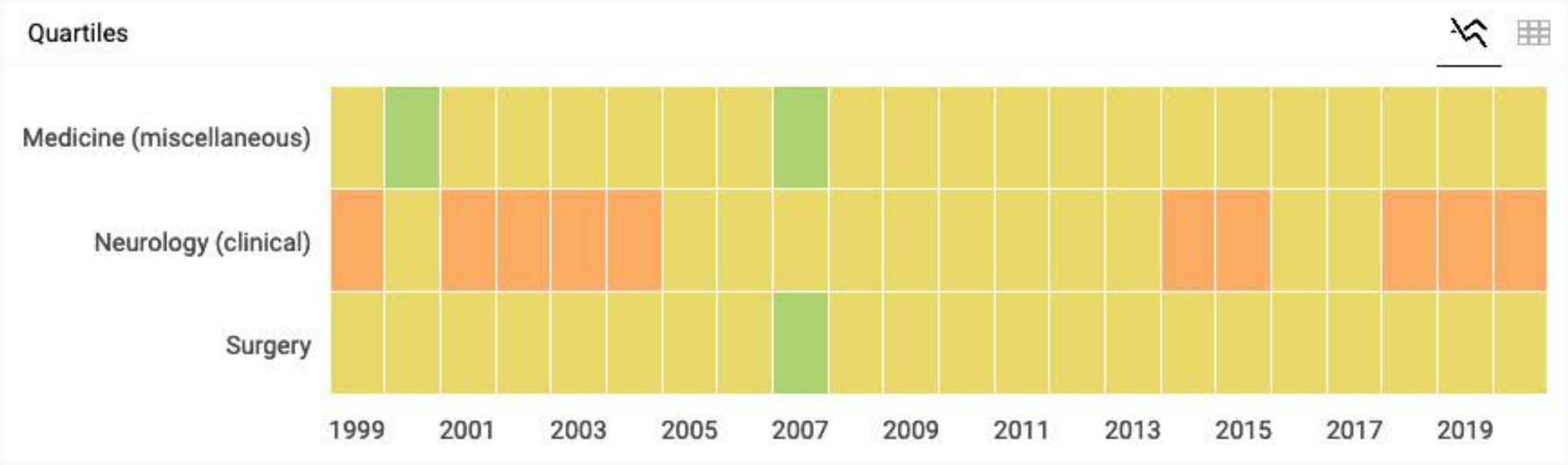

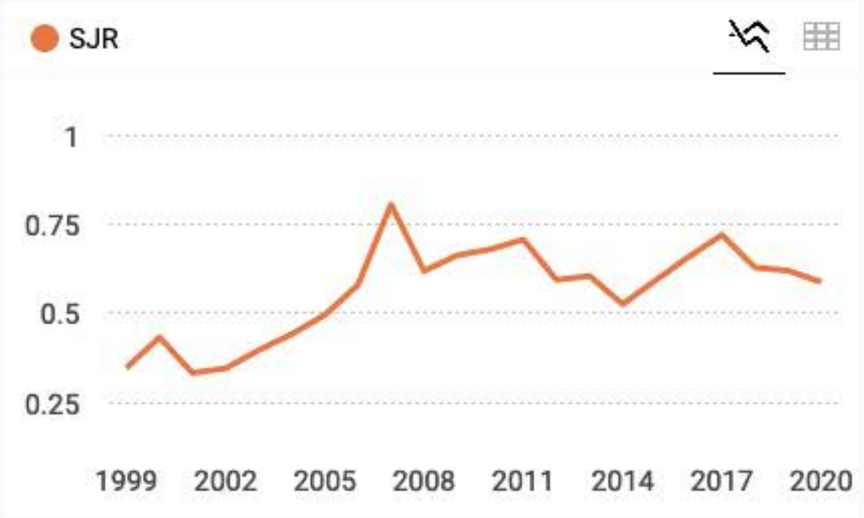
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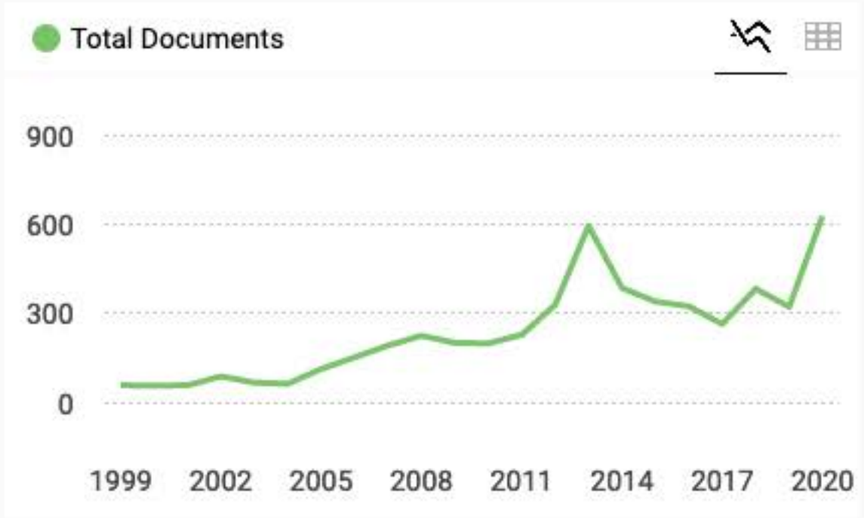
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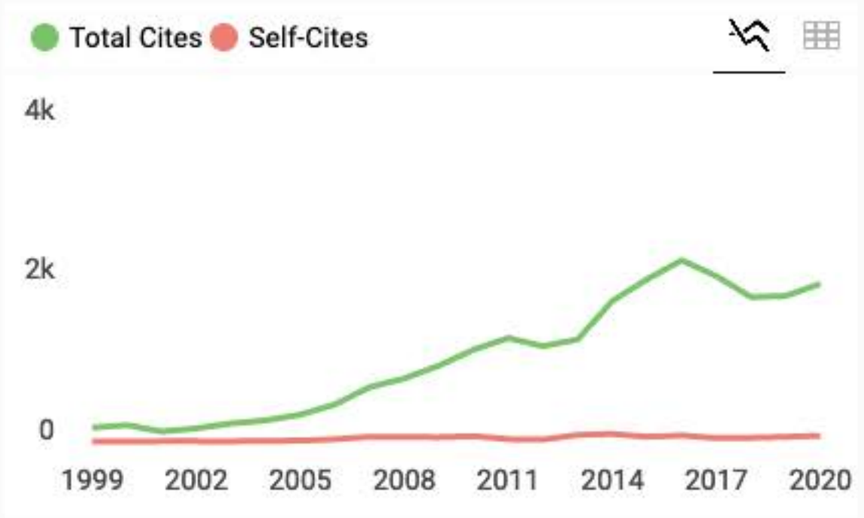
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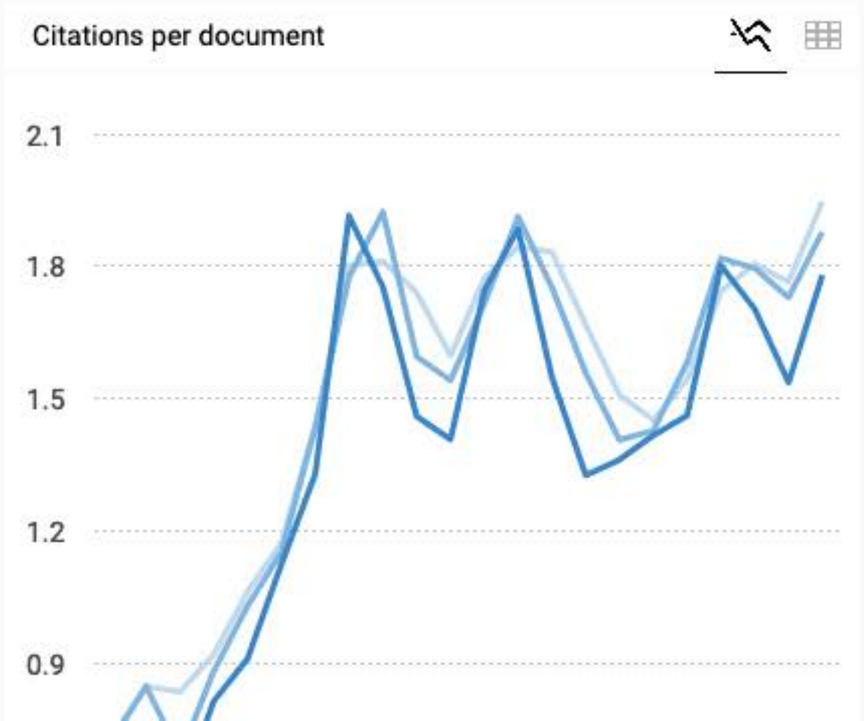
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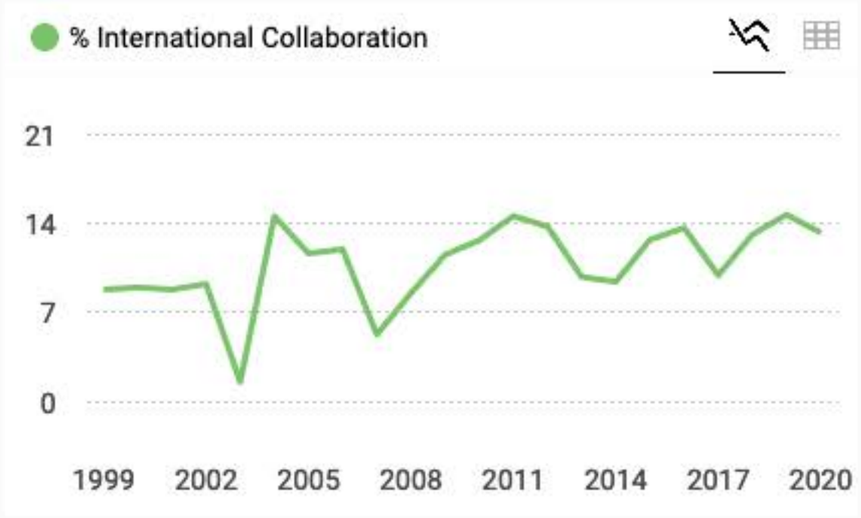

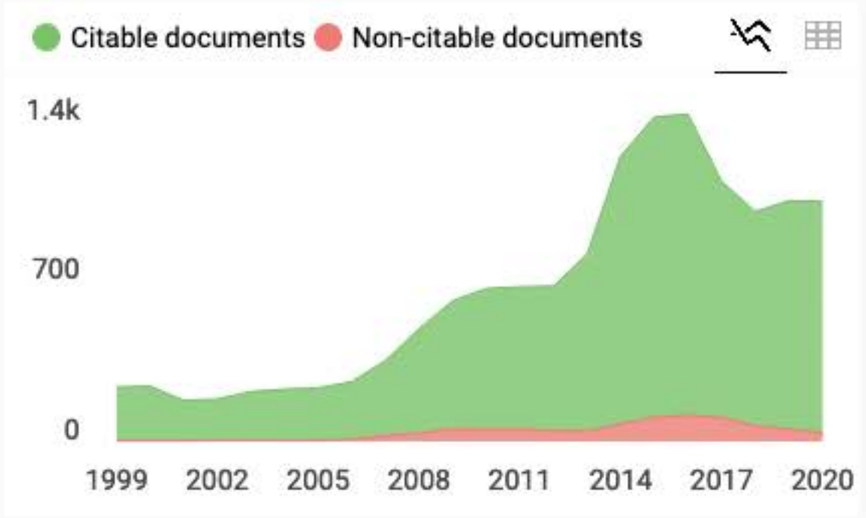

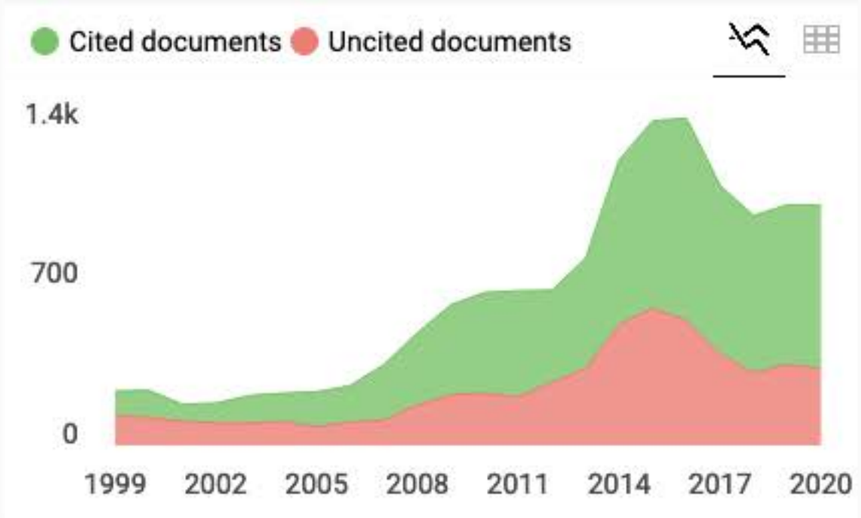

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Modified ICH score was superior to original ICH score for assessment of 30-day mortality and good outcome of non-traumatic intracerebral hemorrhage

I.Putu Eka Widyadharma [a,*], Angga Krishna [a], Andreas Soejitno [a], A.A.A. Putri Laksmidewi [a], Kumara Tini [b], I.B. Kusuma Putra [a], I.G.N. Budiarsa [a], I.A. Sri Indrayani [a]

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30-day mortality
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ABSTRACT

Introduction: Intracerebral hemorrhage (ICH) score has been widely used as a consistent and reliable clinical grading scale for predicting mortality. However, ICH score had not been used to predict good outcome or significant disability for those who were alive. We intended to address whether any modifications would increase prediction accuracy for mortality as well as the extent of morbidity for those who survived.

Methods: We conducted a retrospective cohort study, involving all non-traumatic ICH patients admitted to our hospital between September 2018 and July 2020. All non-traumatic ICH patients who were admitted to the stroke unit and registered in our stroke database had their medical records, neuroimaging, and laboratory test results reviewed. Only patients with complete medical records and available CT imaging and laboratory test results were included in our study. Independent predictors of mortality (modified Rankin scale/mRS of 6) or good outcome vs. significant disability (mRS≤2 vs. mRS 3–5, respectively) were identified by logistic regression. A modified ICH (mICH) score was compared with the original ICH (oICH) score for its diagnostic performance (DP). Overall DPs were graded and ranked according to Youden Index (YI).

Results: As many as 311 patients were eligible with both 39.9% rate of 30-day mortality and good outcome. Factors independently associated with mortality were low GCS and high NIHSS on admission ($P = 0.002$, <0.001, respectively), and presence of respiratory failure ($P < 0.001$). Independent factors for good outcome were low NIHSS on admission and mass effect (midline shift > 5 mm) [both $P < 0.001$]. A modification of ICH score from the original was made by substituting GCS with NIHSS (0 –10 = 1; 11 – 20 = 2; >20 = 3), changing age cut-off point to > 55 years old (= 1), and adding respiratory failure (= 1), and mass effect (= 1). Overall, mICH scored better over oICH score with respect to sensitivity and had comparable specificity for both 30-day mortality and good outcome (sensitivity 80.6% vs. 50.8%; specificity 88.7% vs. 89.3%; YI 0.69 vs. 0.40, respectively) and good outcome (sensitivity 86.3% vs. 77.4%; specificity 74.6% vs. 77.8%; YI of 0.61 vs. 0.55, respectively). There was only one patient with oICH and none on mICH score of 0, who died and none survived with oICH and mICH score of ≥ 5 and ≥ 7, respectively. The proportion of 30-day mortality and good outcome increased in a more linear fashion with mICH score.

Conclusions: The mICH score was proven to be reliable and consistent as a risk grading assessment for non-traumatic ICH patients. The mICH was statistically superior to oICH score in predicting 30-day mortality and good outcome.

1. Introduction

Non-traumatic intracerebral hemorrhage (ICH) accounts for approximately 10–20% of all causes of stroke [1]. Despite there have been some advances in the knowledge of the natural history, treatment approach, and thereby prognosis of ICH patients, its morbidity and mortality rate remain relatively high [2]. There have been attempts to employ several ICH prognostication models, yet some of them requires

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complex mathematical equation, ergo rendering it less practical in the clinical settings where rapid calculation is paramount to make a prompt but accurate informed-decision making [3]. Among the currently available prognostication models, ICH score devised by Hemphill et al. [4] being the simplest yet relatively accurate for wide ICH populations. However, it possesses several limitations, particularly related to Indonesian population, i.e. a recent attempt to validate oICH score among Indonesian population did not yield satisfactory prediction accuracy, with significant discrepancies in several parameters. The oICH score also lacks the ability for predicting good outcome and significant disability among those who survive, thus restricting its use for prediction of mortality per se, while seemingly omitting the well-being of the survivors.

In light of the aforementioned issues, herein we had attempted to address the significant factors associated with 30-day mortality, significant disability, and good outcome among Indonesian ICH patients, and subsequently devised a modified ICH (mICH) score followed by head-to-head comparison with oICH score thereafter.

2. Methods

2.1. Study design

This was a retrospective cohort study conducted at Sanglah Hospital, Denpasar, Bali between September 01 2018 to July 31 2020. This study had passed ethical clearance from the Ethics Committee on Human Research, Faculty of Medicine Udayana University. Written consent was obtained from patients and/or their caregivers after receiving a full explanation regarding the study. All non-traumatic ICH patients who were admitted to the stroke unit and registered in our stroke database had their medical records, neuroimaging, and laboratory test results reviewed. Only patients with complete medical records and available CT imaging and laboratory test results were included in our study.

2.2. Data extraction and operational variables

Several categories of data were abstracted from each patient, comprising demographics (age and sex), stroke comorbidities and risk factors (hypertension, diabetes mellitus, chronic cerebral infarction, hypertensive heart disease, atrial fibrillation, renal function impairment, respiratory failure [respiratory failure was defined as an impairment of gas exchange functions, marked by partial pressure of oxygen lower than 60 mmHg (hypoxemic failure or type 1) or partial carbon dioxide pressure higher than 50 mmHg (hypercapnic failure or type 2) as determined by arterial blood gas analysis within the first 5 days of stroke onset] [5], metabolic acidosis, smoking, alcohol consumption), vital signs on admission (Glasgow Coma Scale [GCS] score, National Institute of Health Stroke Scale (NIHSS), systolic and diastolic BP, mean arterial pressure/MAP [defined as $(2 \times$ diastolic BP + systolic BP)/3], pulse pressure [defined as systolic BP minus diastolic BP], pulse rate, and axillary temperature), presence of bilateral extensor plantar reflexes, aspects related to ICH (location, presumed etiology, ICH volume [measured using ABC/2 method], presence of IVH, hydrocephalus, subarachnoid extension, and mass effect [defined as midline shift>5 mm and/or any identifiable brain herniation]), whether or not any invasive surgical procedures were done (clot evacuation, EVD or VP shunt placement]), as well as relevant laboratory test results (complete blood count, CRP, PT, APTT, serum glucose, BUN, serum creatinine, serum sodium and potassium). 30-day clinical outcome was measured using modified Rankin score (mRS) with a score of 6, 3–5, and 2 being dead, having a significant disability, and good outcome, respectively.

2.3. Statistical analysis

Data comparison was divided into two steps. First step was to compare the mortality and survivor data, regardless of their disability status for the purpose of obtaining mortality risk. Second step was to compare only those who were alive with minimal and significant disability in order to obtain 30-day good outcome percentages. Baseline categorical and interval data were presented as absolute (%) and mean ± SD, respectively, and for data with many outliers, median with interquartile range (IQR) was used instead. Subjects' baseline characteristics were analyzed with Pearson's χ^2 for categorical data. Normally distributed interval data was tested with one-way ANOVA accompanied with Levene and Brown-Forsythe for equal variance assumption test, preceding post hoc (Games-Howell) test, whereas abnormally distributed data underwent Kruskal-Wallis test. All variables were screened for significant bivariate relationships and those with significant results were subsequently tested using multivariate logistic regression analyses with stepwise elimination of variables not contributing to the model ($P > 0.10$). The mICH score comprised of replacing GCS with NIHSS using identical cut-off point and weighted score to those of the oICH score version, i.e. NIHSS of 0–10 (0 point), 11–20 (1 point), 21–40 (2 points), replacing age with ≥ 55 years old (1 point), addition of respiratory failure and mass effect (1 point each if present), with the rest of it being the same with the oICH score (ICH volume ≥ 30 cm^3, infratentorial origin, and the presence of IVH equals 1 point each). Optimal cut-off points for both mICH and oICH score against 30-day mortality and good outcome were derived from receiver operator curve (ROC). The resulting mICH and oICH score were subsequently tested for its diagnostic performance parameters, comprising sensitivity, specificity, positive and negative predictive value, and the resulting Youden index (YI) thereafter. All statistical analyses were performed using SPSS version 20.0 (IBM, San Fransisco) and $P < 0.05$ was considered statistically significant.

3. Results

There were 338 patients who presented to our center within September 01 2018 to July 31 2020, 311 of whom complete medical records were available, thus eligible to be included in the study. A complete information regarding patient's baseline characteristics can be seen in Table 1. The overall rate of mortality, significant disability, and good outcome within 30 days were 39.9%, 20.3%, and 39.9%, respectively. There were several parameters with statistically significant difference between groups, comprising age (those with fatal outcome tended to be significantly older by almost a decade when compared with the rest of the groups), comorbidities (renal function impairment, respiratory failure, and metabolic acidosis), vital signs (GCS and NIHSS, pulse pressure and rate, and axillary temperature), and bilateral plantar extensor reflexes. Interestingly, all aspects related to ICH including its location, volume, presumed etiology, the presence of IVH, subarachnoid extension, hydrocephalus, mass effect, and its related surgical interventions (clot evacuation and EVD) demonstrated significant differences between groups.

Significantly different variables of 30-day mortality and good outcome obtained from baseline characteristics were, in turn, analyzed in bivariate models (Table 2). There were multiple significant parameters in the bivariate models, particularly those determining the 30-day mortality outcome. We used 55 years old as a cut-off point for age, since according to ROC, we found that the age range of 55.5–56.5 years old yielded the best compromise in terms of sensitivity and specificity (i.e. 63.3% and 54%, respectively), as opposed to the low sensitivity by using a cut-off of 80 years old (sensitivity 1.6%; specificity 98.4%).

Those significant variables derived from bivariate analyses subsequently underwent multivariate logistic regression tests and the results were displayed in Table 3. We obtained an independent association of GCS, NIHSS, and the presence of respiratory failure at admission with increased mortality risk within 30 days. Similarly, high NIHSS remained consistently significant as an independent variable to be associated with lower and increased probability of good outcome and, significant disability, respectively, within 30 days. Another significant variable in

Table 1
Univariate analyses of baseline characteristics of 311 patients in the study*.

Parameter	Fatal outcome (30-day mRS 6) [%] n = 124	Significant disability (30-day mRS 3–5) [%] n = 63	Good outcome (30-day mRS≤2) [%] n = 124	*P*
Demographics				
Age, y	60.73 ± 12.87	57.57 ± 13.34	52.29 ± 13.34	0.211
Female, sex	44 (35.5)	25 (39.7)	54 (43.5)	0.43
Comorbidities				
Hypertension	95 (76.6)	53 (84.1)	87 (70.2)	0.104
Diabetes mellitus	23 (18.5)	8 (12.7)	10 (8.1)	0.051
Chronic cerebral infarction	25 (20.2)	19 (30.2)	20 (16.1)	0.08
Hypertensive heart disease	62 (50)	35 (55.6)	54 (43.5)	0.275
Atrial fibrillation	5 (4.0)	1 (1.6)	1 (0.8)	0.213
Renal function impairment	21 (16.9)	8 (12.7)	8 (6.5)	0.032*
Respiratory failure	56 (45.2)	5 (7.9)	9 (7.3)	< 0.001*
Metabolic acidosis	23 (18.5)	5 (7.9)	5 (4.0)	< 0.001*
Smoking	30 (24.2)	13 (20.6)	23 (18.5)	0.550
Alcohol consumption	4 (3.2)	4 (6.3)	1 (0.8)	0.098
Vital and neurological signs				
GCS score on admission	7.76 ± 3.17	9.48 ± 2.54	13.25 ± 1.84	< 0.001*
NIHSS on admission	25.30 ± 6.65	16.19 ± 4.83	7.65 ± 3.67	< 0.001*
Systolic BP, mmHg	164.75 ± 33.34	161.46 ± 25.03	155.39 ± 32.69	0.282
Diastolic BP, mmHg	94.38 ± 16.80	95.73 ± 16.99	94.35 ± 17.20	0.851
MAP, mmHg	117.83 ± 21.05	117.64 ± 18.01	114.69 ± 21.45	0.436
Pulse pressure, mmHg	70.37 ± 22.84	65.73 ± 18.59	61.03 ± 20.52	0.003*
Pulse rate, bpm	93.82 ± 19.12	85.89 ± 14.03	84.11 ± 12.71	< 0.001*
Admission temperature, °C	36.79 ± 2.09	36.53 ± 0.52	36.24 ± 1.87	0.059
Bilateral extensor plantar reflexes	49 (39.5)	11 (17.5)	13 (10.5)	< 0.001*
ICH location				
Basal ganglia	37 (29.8)	37 (58.7)	64 (51.6)	0.001*
Lobar	32 (25.8)	11 (17.5)	22 (17.7)	
Thalamic	30 (24.2)	12 (19.0)	21 (16.9)	
Pontine	16 (12.9)	3 (4.8)	9 (7.3)	
Cerebellar	9 (7.3)	0 (0)	8 (6.5)	
Supratentorial ICH	99 (79.8)	61 (96.8)	107 (86.3)	0.007*
Presumed etiology				
Chronic hypertension	90 (72.6)	54 (85.7)	101 (81.5)	0.013*
Amyloid angiopathy	8 (6.5)	1 (1.6)	3 (2.4)	
Vascular malformation (incl. AVM and cerebral aneurysm)	16 (12.9)	78 (12.7)	118 (14.5)	
Bleeding diathesis	10 (8.1)	0 (0)	2 (1.6)	
ICH profiles				
ICH volume, mL†	36.5 [47.8]	30.0 [28.0]	16.4 [21.65]	< 0.001*
IVH	80 (65.4)	29 (46.0)	30 (24.2)	< 0.001*
Subarachnoid extension	48 (38.7)	14 (22.2)	13 (10.5)	< 0.001*
Mass effect	57 (46.0)	26 (41.3)	13 (10.5)	< 0.001*
Hydrocephalus	64 (51.6)	19 (30.2)	13 (10.5)	< 0.001*
Laboratory parameters				
White cell count, 10^9/L†	15.58 [9.63]	13.80 [8.53]	11.86 [5.86]	< 0.001*
Hemoglobin, g/dL	12.83 ± 3.56	13.37 ± 1.93	13.46 ± 2.96	0.237
Platelet, 10^9/L	240.45[125.10]	265.7[89.10]	262.4[107.22]	0.317
C-reactive protein	1.49 [9.50]	0.72 [6.52]	0.84 [3.30]	0.158
Prothrombin time, s	14.05 [1.9]	13.80 [1.6]	14.05 [1.5]	0.144
Activated partial thromboplastin time, s	31.18 ± 16.69	27.37 ± 10.18	27.33 ± 8.09	0.032*
Serum glucose, mg/dL	166.76 ± 80.89	139.71 ± 47.55	129.51 ± 51.52	< 0.001*
Blood urea nitrogen, mg/dL	14.8 [13.3]	14.8 [8.6]	12.5 [7.0]	0.003*
Serum creatinine, mg/dL	1.05 [1.08]	0.90 [0.45]	0.89 [0.54]	0.013*
Serum sodium, meq/L	137.29 ± 5.25	138.05 ± 4.02	136.19 ± 18.13	0.574
Serum potassium, meq/L	3.38 [0.97]	3.67 [0.87]	3.55 [0.60]	0.214
Surgical procedure				
Clot evacuation	27 (21.8)	18 (28.6)	8 (6.5)	< 0.001*
EVD	20 (16.1)	5 (7.9)	4 (3.2)	0.002*
Ventriculoperitoneal shunt	11 (8.9)	9 (14.3)	9 (7.3)	0.316

* *P* significant at < 0.05.

† Displayed as median [IQR]. BP blood pressure; MAP mean arterial pressure; IVH intraventricular hemorrhage; AVM arteriovenous malformation; EVD extraventricular drainage.

Table 2
Significant bivariate analyses of predictors for mortality and good outcome at 30 days.

Parameter	OR (95% CI)	*P**
Predictors for 30-day mortality		
Age ≥ 55 years old	2.10 (1.32 – 3.34)	0.002
Bilateral extensor plantar reflexes	3.95 (2.44 – 6.38)	< 0.001
IVH	4.33 (2.66 – 7.06)	< 0.001
Subarachnoid extension	3.74 (2.17 – 6.45)	< 0.001
Mass effect	3.23 (1.96 – 5.32)	< 0.001
Hydrocephalus	5.17 (3.08 – 8.68)	< 0.001
Respiratory failure	10.18 (5.32 – 19.48)	< 0.001
EVD	3.73 (1.64 – 8.50)	0.002
Metabolic acidosis	4.50 (2.00 – 10.11)	0.001
High risk etiologies (amyloid angiopathy and bleeding diathesis)	6.15 (2.41 – 15.73)	0.001
GCS on admission	1.46 (1.15 – 1.85)	0.002
NIHSS on admission	1.59 (1.39 – 1.81)	< 0.001
Predictors for 30-day good outcome		
IVH	0.31 (0.16 – 0.63)	0.001
Mass effect	0.19 (0.09 – 0.41)	< 0.001
Hydrocephalus	0.27 (0.12 – 0.60)	0.001
Clot evacuation	0.19 (0.08 – 0.46)	< 0.001
GCS on admission	0.74 (0.57 – 0.97)	0.026
NIHSS on admission	0.71 (0.61 – 0.84)	< 0.001
ICH volume	0.96 (0.93 – 0.99)	0.005

* *P* significant at < 0.05.

Table 3
Multivariate analyses of independent predictors for mortality and good outcome at 30 days.

Parameter	OR (95% CI)	*P**
Independent predictors for 30-day mortality		
GCS on admission	1.37 (1.10 – 1.71)	0.005
NIHSS on admission	1.51 (1.35 – 1.69)	< 0.001
Respiratory failure	7.61 (2.64 – 21.93)	< 0.001
Independent predictors for 30-day good outcome		
NIHSS on admission	0.61 (0.52 – 0.70)	< 0.001
Mass effect	0.11 (0.33 – 0.38)	< 0.001

* *P* significant at < 0.05.

the equation was the presence of mass effect which increased the probability of someone with ICH to have a good outcome within 30 days. (Table 4).

The resulting oICH and mICH score were then evaluated for its diagnostic performance. We performed ROC analyses (Fig. 1a and b) simultaneously and determined the most optimum cut-off point for each scoring system with respect to 30-day mortality and good outcome as displayed in Table 5. Overall, mICH scored better over oICH score with respect to sensitivity and had comparable specificity for both 30-day mortality and good outcome. The mICH score also covered larger AUC for both mortality and good outcome parameters. The superiority of mICH over the oICH score against 30-day mortality and good outcome were also reflected by the consistently higher YI across the two outcomes.

Finally, we back-tested both models to determine whether or not the proportion for mortality and significant disability decreased while the percentage of good outcome increased in a linear fashion with the addition of each point from both scoring systems. Complete results were displayed in Fig. 2. In general, the percentage of mortality (mRS of 6) and significant disability (mRS of 3–5) of both models increased linearly with the addition of each point in both scoring systems. For instance,

Table 4
Comparison of the original and modified CH score.

Original ICH score	Points	Modified ICH score	Points
GCS		NIHSS	
13 – 15	0	0 – 10	0
5 – 12	1	11 – 20	1
3 – 4	2	> 20	2
ICH volume, cm^3		ICH volume, cm^3	
≥ 30	1	≥ 30	1
< 30	0	< 30	0
IVH		IVH	
Yes	1	Yes	1
No	0	No	0
Infatentorial origin of ICH		Infratentorial origin of ICH	
Yes	1	Yes	1
No	0	No	0
Age, y		Age, y	
≥ 80	1	≥ 55	1
< 80	0	< 55	0
		Respiratory failure	
		Yes	1
		No	0
		Mass effect	
		Yes	1
		No	0
Total score	0 – 6	Total score	0 – 8

there were 3 out of 63 patients (4.8%) who had mRS of 6 with an oICH score of 0. On the other hand, there was none out of 40 patients who had either mRS 3–5 or 6. On the extreme right-hand side of the equations, there was only 1 out of 17 patients (5.9%) who had good outcome (mRS of 2) with an oICH score of 4, while there were no survivors (i.e. 100% mortality) with a score of 5 and 6. Similarly, there was only each 1 out of 24 patients (4.2%) who had good outcome and significant disability (mRS of 3–5) with mICH score of 6, while there we no survivors with a score of 7 and 8. Both models demonstrated linear increment and decrement with respect to the proportion mortality and good outcome with the addition of each score point.

4. Discussion

The clinical grading system such as ICH score had been proven to be very useful in clinical settings as it allows the standardization of clinical assessment and prognostication, synchronize communication among interdisciplinary healthcare providers, and useful for risk stratification and operational variable definition in the settings of clinical trials or other research purposes [6]. The grading system preceding oICH score was known to be quite complicated with certain equations involved, thus precluding its utilitarian nature under emergency clinical scenario. However, the oICH score has several weak points, which, in our opinion, still opens a room for improvement. For instance, the use NIHSS instead of GCS and the replacement of age cut-off point from 80 to 55 years old.

The use of GCS score offers a quick assessment of clinical severity and thus, patient's general prognosis. However, in our opinion, GCS score was more appropriate in the settings of traumatic ICH as what the score was intended to use initially [7]. On the other hand, NIHSS was particularly designed with stroke patients in mind. Consequently, it captures plenty of clinical variations seen in many stroke syndromes which would otherwise be omitted when graded using GCS. For example, when grading a conscious patient with severe expressive aphasia using GCS, there would be no appropriate score given for the verbal component (i.e. E4M6Vx), thus the patient gets a total GCS and ICH score of 10 and + 1 (already 13% increase of mortality), respectively. Whereas NIHSS can address the severity of aphasia (mild-to--moderate, severe, and global aphasia) and provides an incremental score

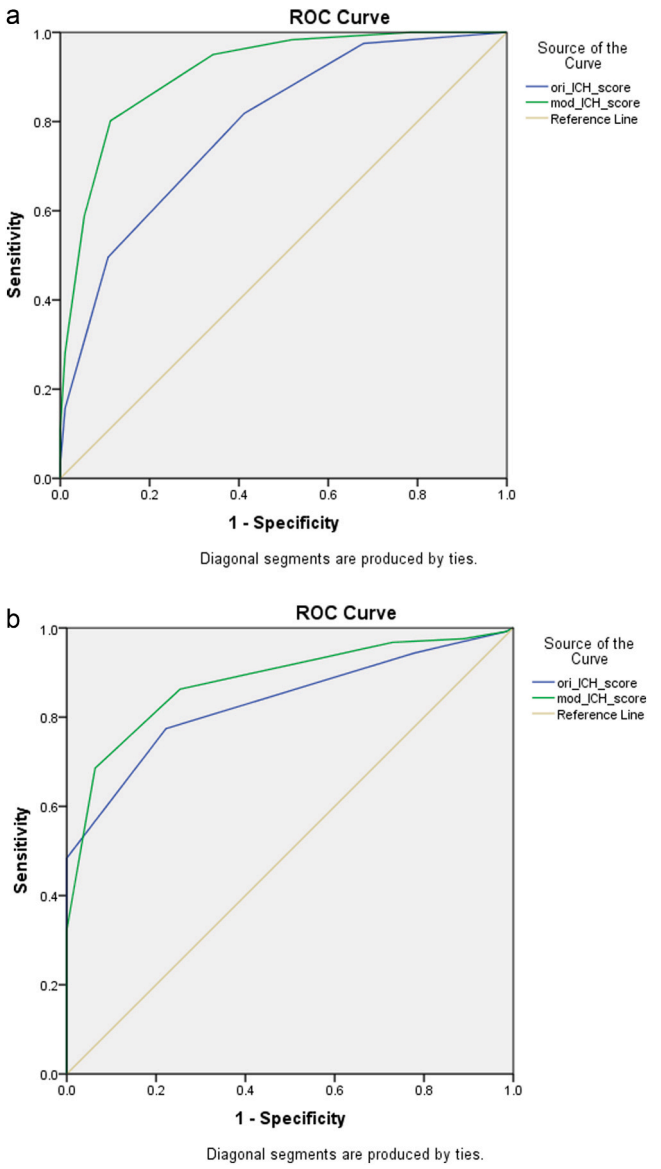

Fig. 1. Head-to-head comparison of ROC curve between oICH and mICH score for (a) 30-day mortality and (b) 30-day good outcome, respectively.

in accordance to its severity, that under the previous scenario, the patient would obtain NIHSS and mICH score of 3 and + 0, respectively. Such a clinical scenario is not uncommon, particularly among surviving patients on a recovery period. In fact, the GCS in our study displayed significantly lower Wald statistics when compared with NIHSS, thus providing further assurance of replacing GCS with NIHSS.

The second modification was made by replacing the age cut-off point of 80 with 55 years old. The use of 80 years old as a cut-off point was thought to be non-representative in our population as the original study tended to include older subjects (66 ± 15 years old) as opposed to the younger age of ICH onset among Indonesian population (48 ± 15 years old) [8]. In fact, the 80 year-old cut-off value was also deemed inappropriate in another study involving a large urban population in the U.S [9]. Consequently, our study displayed a sensitivity of only 2.9% when using 80 year-old as a cut-off, whereas the use of 55 year-old provided the best compromise for sensitivity and specificity (59.6 – 61.5% and 60.3%, respectively).

Respiratory failure at initial presentation was also shown to be an independent predictor of 30-day mortality (OR 7.61; 95% CI 2.64–21.93; $P < 0.001$). We limited the diagnosis of respiratory failure

Table 5
Diagnostic performance of the original and modified ICH score on 30-day mortality and good outcome.

Parameter	30-day mortality		30-day good outcome	
	Original ICH score (cut-off 2)	Modified ICH score (cut-off 3)	Original ICH score (cut-off 1)	Modified ICH score (cut-off 2)
ROC curve				
Area under the curve (AUC)	0.79	0.91	0.83	0.88
95% CI	0.74 – 0.84	0.88 – 0.94	0.78 – 0.89	0.83 – 0.93
P	< 0.0001*	< 0.0001*	< 0.0001*	< 0.0001*
Diagnostic performance				
Sensitivity, %	50.8	80.6	77.4	86.3
Specificity, %	89.3	88.7	77.8	74.6
Positive predictive value, %	75.9	82.6	87.3	87.0
Negative predictive value, %	73.2	87.4	63.6	73.4
Youden index	0.40	0.69	0.55	0.61

* *P* significant at < 0.05

to be within the first 5 days since stroke onset. We did this because of at least three considerations, i.e.: 1) we need to establish the scoring system for prognostication as soon as possible, as a tool to improve an informed-decision making process. Any delay in obtaining one or more of the scoring components would therefore beat the purpose of this scoring system. 2) The majority of brain edema as a result of hematoma expansion in non-ICH patients occurred during the first two days (i.e. 0.2–1.7 days) [10]. Respiratory failure that occurred at an early stage was therefore regarded due to central process, hence require immediate assessment and treatment. 3) On several occasions, we received referral of ICH patients already on mechanical ventilation. The mean duration of VAP was 3.3 days after intubation [11].

Unsurprisingly, patients with immediate onset of respiratory failure were associated with midline shift and herniation signs, thus necessitating intubation and mechanical ventilation. Consequently, the increased 30-day mortality was mostly due to subsequent complications of the procedure, including pneumonia (aspiration or ventilator associated pneumonia), ARDS, and neurogenic pulmonary edema [12,13]. According to our analysis, most of the respiratory failure were caused by pneumonia. This was relevant since our center is a tertiary and final referral hospital for stroke cases, thus many admitted patients were initially treated in the community hospital for several hours to days preceding the transfer. The causes of pneumonia were invariable with the most frequent etiology being aspiration pneumonia due to inappropriate nasogastric tube placement or feeding and ventilator-associated pneumonia due to prolonged use of ventilator in the intensive care.

Midline shift is defined as degree of displacement of septum pellucidum relative to ideal midline on axial head CT imaging. Although there is no clear consensus as to the exact cut-off point to define a significant midline shift among non-traumatic ICH patients, a value of > 5 mm has been established as an operational definition in several studies. In accordance to Brain Trauma Foundation guideline, they recommended emergency sugery for ICH causing midline shift ≥ 5 mm, as craniotomy can significantly improve the outcome. We understand that the etiology of the ICH in this study was traumatic (as opposed to stroke), but the point for prognostication is to decide whether or not to approach aggressively along with the risk of the procedure, thus should be based on a more confirming sign (i.e. significant midline shift). We understand that it is difficult to extrapolate data from TBI to non-traumatic ICH cases, because the latter tend to be older, have more comorbidities, and typically do not have multisystem injury. We therefore apply the principle of "do no harm" in the first place, and tend to be

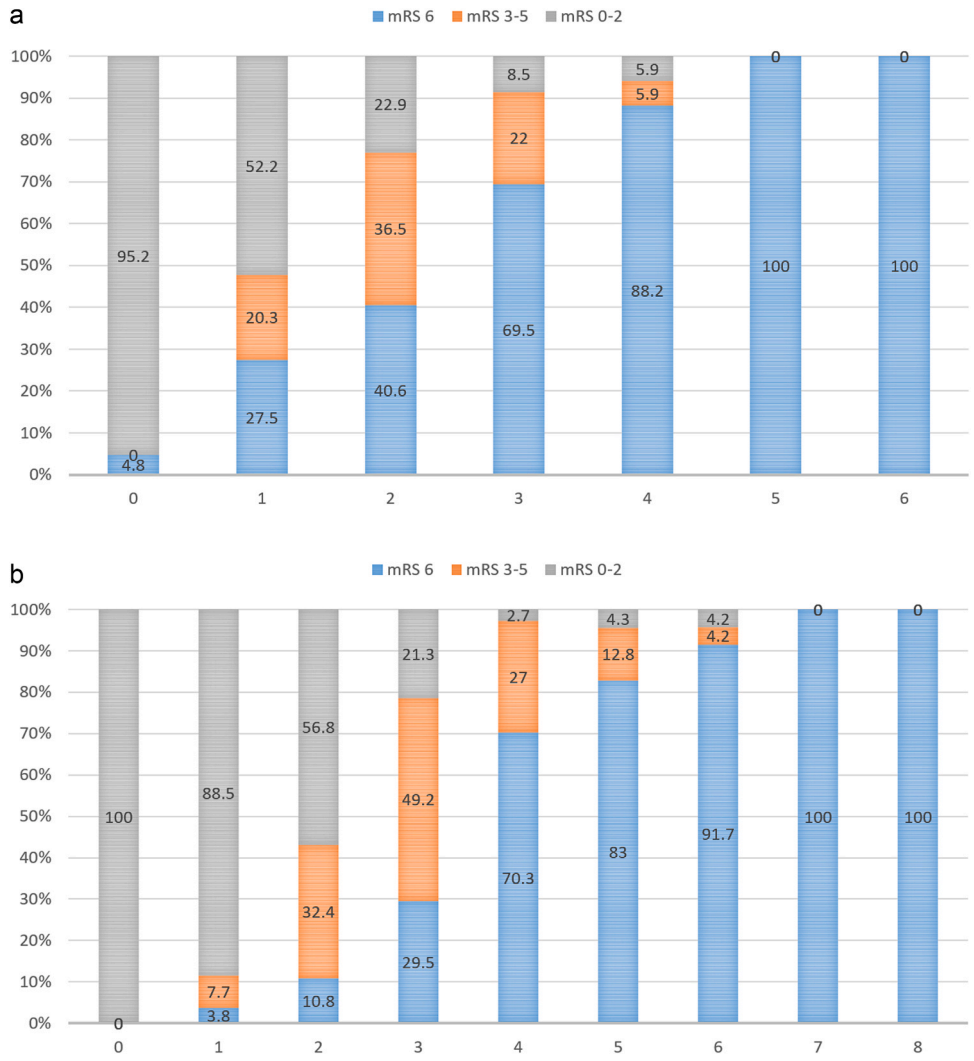

Fig. 2. The proportion of patients who died, had significant disability, or good outcome within 30 days as assessed with (A) oICH, and (B) mICH score.

more conservative (rather than aggressive) in determining the cut-off point. In addition, previous attempt to modify ICH score for non-traumatic ICH patients by Cheung and Zou [6] also define mass effect as the presence of midline shift > 5 mm.

There was one study which pointed that midline shift > 3 mm was deemed as significant in non-traumatic ICH patients [10]. We have indeed conducted ROC analysis using a cut-off of 3 and 5 mm using our data. We found that the diagnostic performance (AUROC, sensitivity, specificity, PPV, NPV) between the two cut-off points to be similar and insignificant statistically for determining 30-day good outcome.

The original scoring system had not been routinely used as a predictor for those who survived the ICH and either had good outcome or significant disability (i.e. mRS score of 2 and 3–5, respectively). Addressing patient's probability of achieving either good outcome or significant disability is as equally important as predicting the risk of mortality, as the treatment goal of ICH patients is not preventing mortality per se, but also to achieve as minimum of disability as possible, ultimately leading to accurate treatment choices and informed-decision. Herein we obtained that high NIHSS on admission and the absence of mass effect were independent predictors of significant disability over good outcome among ICH survivors. The presence of mass effect impacting the significant disability instead of mortality was explainable. First, the mass effect represents one of emergency indication for surgery, thus resulting in life-saving outcome. Secondly, mass effect occurs in a biphasic pattern, i.e. within the first 2 days due to hematoma enlargement and in the second and third week due to edema [14]. Under the first scenario, mass effect would be treated aggressively via surgery and administration of anti-edema intravenous solution, such as mannitol or hypertonic saline. Whereas the appearance of edema on the second and third week might be missed by the clinician, given that the patient was on a recovery progress and most patients had been discharged from the hospital.

The resulting mICH score was proven to be superior over oICH with respect to 30-day mortality (YI 0.69 vs. 0.40) and good outcome (YI 0.61 vs. 0.55). mICH had a decent sensitivity, specificity, PPV, and NPV, making it more reliable to be a prognosticator. In fact, mICH score accommodated a more proportional score increment, in line with the increased risk of mortality, survival rate, and significant disability (Fig. 2).

However, our study also had limitations, e.g. we did not take into account comorbidities associated with prolonged hospitalization (late-onset pneumonia, urinary tract infection, sepsis, pressure injuries, wound-related bacteremia), factors associated with risk factors for re-bleeding and clinical worsening, such as uncontrolled hypertension or the presence of late-onset hydrocephalus, as well as fundamental factors influencing long-term prognosis such as genetic predisposition, demographics, and socio-economic status [15,16]. This study also involved a relatively younger age which may not be generalizable in other countries with predominant elderly population.

5. Conclusion

The mICH score was proven to be reliable and consistent as a risk grading assessment for non-traumatic ICH patients. The mICH was statistically superior to the oICH score in predicting both 30-day mortality and good outcome.

Author's contribution

All authors contributed equally to this study.

CRediT authorship contribution statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript.

Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Clinical Neurology and Neurosurgery.

Conflict of interest disclosure

The authors have no potential conflicts of interest to disclose.

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