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Short-Term Prognostic Model for Non-Traumatic Intracerebral Hemorrhage Patients: A Combination of Four Score, FUNC Score, and ICH Score

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ABSTRACT

Introduction: Currently, the Functional Outcome in Patients With Primary Intracerebral Hemorrhage (FUNC) score, Full Outline of UnResponsiveness (FOUR) score, and Intracerebral Hemorrhage (ICH) score are utilized to predict outcomes in non-traumatic intracerebral hemorrhage (ICH) patients. The high mortality rate in non-traumatic ICH patients emphasizes the importance of scoring systems as predictive models for mortality prognosis. The aim of this study was to determine a short-term prognostic model for non-traumatic ICH patients by combining FUNC score, FOUR score, and ICH score.
Method: This observational cohort study took place at the neurology ward and Intensive Care Unit of RSUP H. Adam Malik – Medan, from March to September 2023. Subjects meeting the study criteria were observed for 30 days to assess short-term outcomes (mortality). Multivariate logistic regression analysis was then conducted for the combined scores.
Results: Significant effects were found between FUNC score, FOUR score, and ICH score on short-term mortality in non-traumatic ICH patients, each with a p-value < 0.001. However, the multivariate logistic regression analysis yielded statistically non-significant results ($p > 0.05$).
Conclusion: While FUNC, FOUR, and ICH scores individually show a significant correlation with short-term mortality in non-traumatic ICH patients, their combination is ineffective for predicting mortality in this group.

Keywords

FUNC score, FOUR score, ICH score, short-term mortality, non-traumatic intracerebral hemorrhage

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INTRODUCTION

Non-traumatic intracerebral hemorrhage (ICH) is defined as the spontaneous acute bleeding into the brain parenchyma.[1-6] Non-traumatic intracerebral hemorrhage can be classified into primary and secondary, with primary hemorrhage accounting for up to 85% of all ICH cases and being associated with chronic hypertension or amyloid angiopathy.[2] Secondary hemorrhage can result from coagulopathy, vascular malformations, intracranial tumors, hemorrhagic conversion of ischemic stroke, and drug-related bleeding.[1,2,7-13]

Non-traumatic intracerebral hemorrhage contributes to 10 to 15% of all strokes and is associated with a higher mortality rate compared to ischemic stroke.[2,8,13,14] Data indicates that both short-term and long-term mortality rates due to ICH have significantly decreased in the past decade. However, some previous studies suggest that short-term mortality rates have largely remained constant over time.[15] Intracerebral hemorrhage has a mortality rate of up to 40%-50%, typically occurring within the first few days.[2,8] Only 12%-39% of patients achieve functional independence within 6 months, and most of them will experience some degree of disability for the remainder of their lives.[16]

The high non-traumatic ICH mortality underscores the crucial need for a prognostic model to predict mortality in non-traumatic ICH patients. Several prognostic models have been introduced and modified to predict outcomes in non-traumatic ICH patients, with three scores that have been well-validated and widely accepted for clinical use. The ICH score was developed to estimate 30-day mortality,[17] the Functional Outcome in Patients With Primary Intracerebral Hemorrhage (FUNC) score to predict functional independence at 90 days,[11] and the Full Outline of Unresponsiveness (FOUR) score to assist clinicians in clinical assessment and lesion localization in the brains of patients with altered consciousness.[18]

The high morbidity and mortality rates in non-traumatic ICH patients emphasize the necessity for a prognostic model in predicting mortality for these individuals. It is noteworthy that, to date, there is no research predicting mortality in non-traumatic ICH patients based on the combination of FUNC Score, FOUR Score, and ICH Score.

METHOD

This research is an observational study with a prospective cohort approach. The study was conducted in the neurology ward and Intensive Care Unit (ICU) of RSUP. H. Adam Malik Medan from March 2023 to September 2023. Inclusion criteria include patients aged ≥ 18 years with non-traumatic ICH treated in the neurology ward and ICU of RSUP. H. Adam Malik Medan, diagnosed based on history, physical examination, and supporting examinations. Patients with a history of ischemic and hemorrhagic stroke, as well as traumatic and non-traumatic ICH, were excluded from this study. If patients choose to leave on their own request during treatment or do not agree to continue participating in the study during the treatment period, they are considered dropouts from the study. The sample size in this study was determined using the G-Power Statistical application with an effect size of 0.5, alpha error probability of 0.05, and power of 0.8 with the chi-square option. This resulted in a minimum sample size of 32 people, with an additional 25% added to the minimum sample size, resulting in a total sample size of 40 people.

The research population was selected using consecutive sampling, wherein individuals meeting the inclusion and exclusion criteria were chosen as the study sample. Selected participants were then requested to provide consent or complete an informed consent form to participate in the research. The FOUR score, FUNC score, and ICH score were calculated once the diagnosis of non-traumatic ICH was established. Patients were observed for 30 days to determine the outcomes. After the follow-up period, data on the FOUR score, FUNC score, ICH score, and outcomes were collected.

Research data were analyzed using the SPSS Statistics program for Windows, version 21. Univariate, bivariate, and multivariate analyses were conducted. Univariate analysis aimed to obtain the characteristics of the study subjects. Categorical data were assessed in the form of percentages (%), while numeric data were described using mean and standard deviation (SD) for normally distributed data. Median and interquartile range were used for non-normally distributed data. Normality was assessed using the Shapiro-Wilk test, with data considered normally distributed if $p > 0.05$.

Bivariate analysis was performed to assess the relationship between each score and outcomes using the chi-square test. Fisher's test was employed when the expected count was < 5. The cut-off determination in this study utilized the Receiver Operating Characteristic (ROC) Curve, and the Area Under the Curve (AUC) was used to determine predictive values. Multivariate analysis, conducted after bivariate testing, involved logistic regression with $p < 0.05$ considered significant for evaluating combined scores.

RESULTS

The total number of research subjects obtained was 40 individuals. In this study, a total of 40 research subjects were recruited, resulting in two outcomes: patients with a favorable outcome and patients with a fatal outcome. The number of patients who survived at the end of the follow-up period was 18 individuals (45.0%), while the number of patients who succumbed was 22 individuals (55.0%). Complete data on the demographic characteristics of the research subjects can be found in Table 1.

Table 1. Demographic Characteristics of Non-Traumatic ICH Patients at HAM Medan General Hospital

Demographics	Total (n = 40)	Survived (n = 18)	Deceased (n = 22)
Age (years)	54.52 ± 14.47	55.61 ± 13.07	53.64 ± 15.78
Gender			
Male	26 (65.0%)	10 (55.6%)	16 (72.7%)
Female	14 (35.0%)	8 (44.4%)	6 (27.3%)
Ethnicity			
Batak	25 (62.5%)	12 (66.7%)	13 (59.1%)
Javanese	9 (22.5%)	4 (22.2%)	5 (22.7%)
Malay	6 (15.0%)	2 (11.1%)	4 (18.2%)
Educatiom			
Elementary	11 (27.5%)	5 (27.8%)	6 (27.3%)
Junior High school	9 (22.5%)	6 (33.3%)	3 (13.6%)
Senior High school	18 (45.0%)	6 (33.3%)	12 (54.5%)
Bachelor's	1 (2.5%)	0 (0.0%)	1 (4.5%)
Master's	1 (2.5%)	1 (5.6%)	0 (0.0%)
Surgery			
Yes	8 (20.0%)	2 (11.1%)	6 (27.3%)
No	32 (80.0%)	16 (88.9%)	16 (72.7%)
Room			
Ward	24 (60.0%)	15 (83.3%)	9 (40.9%)
ICU	16 (40.0%)	3 (16.7%)	13 (59.1%)
Length of Stay (days)	8.5 [3.25 – 14.5]	10.5 [8.0 – 13.0]	5.50 [2.0 – 15.0]
Scoring			
FOUR *Score*	11.0 [7.25 – 16.0]	15.0 [14.0 – 16.0]	8.0 [5.0 – 10.0]
FUNC *Score*	8.5 [7.00 – 9.75]	9.5 [9.0 – 10.0]	7.0 [5.0 – 9.0]
ICH *Score*	2.0 [1.0 – 3.0]	1.00 [0.0 – 1.0]	3.0 [2.0 – 4.0]

*Numeric data normally distributed = mean ± SD; Numeric data not normally distributed = median [Q25 – Q75]; Categorical data = n (%)

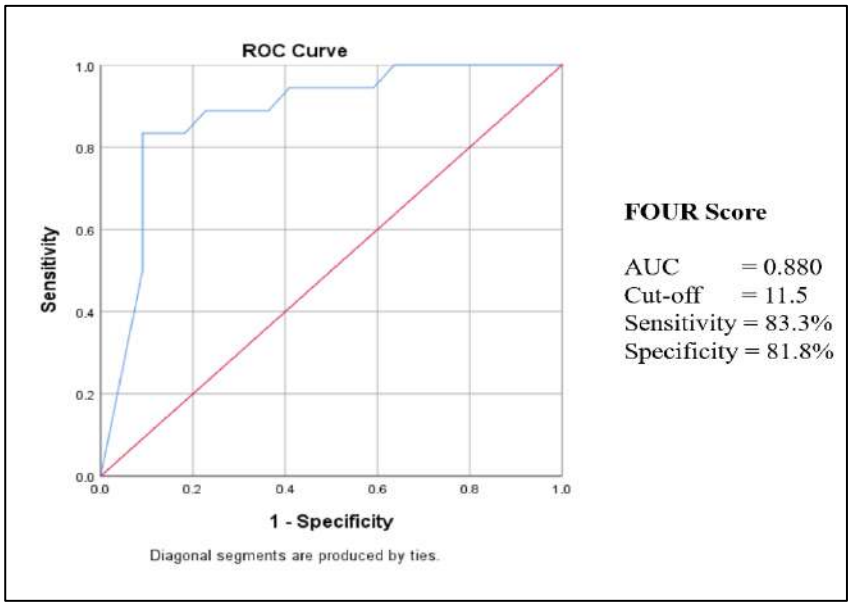

Figure 1. ROC curve for the FOUR score

In Figure 1, the ROC curve of the FOUR score is depicted. The obtained AUC value is 0.880 (indicating good accuracy). The respective cut-off, sensitivity, and specificity values for the FOUR score are 11.5, 83.3%, and 81.8%. In Figure 2, the ROC curve of the FUNC score is displayed. The AUC value obtained is 0.826 (indicating good accuracy). The corresponding cut-off, sensitivity, and specificity values for the FUNC score are 8.5, 77.8%, and 72.7%.

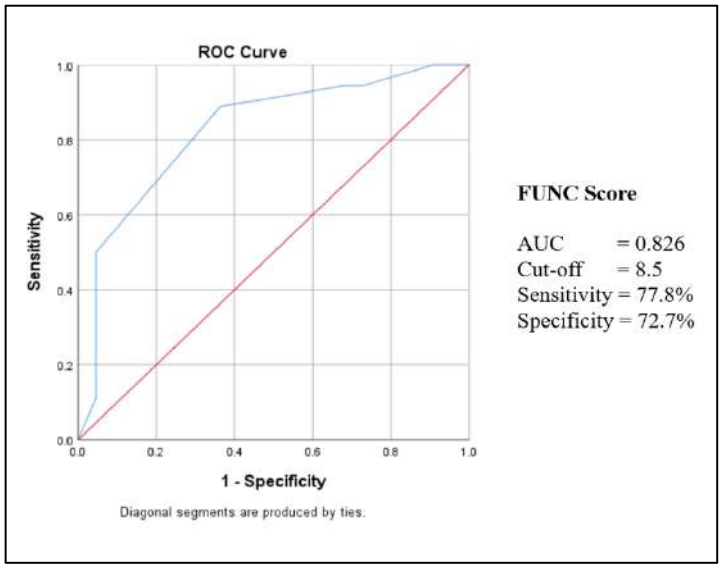

Figure 2. ROC curve for the FUNC score

Based on Figure 3, the ROC curve of the ICH score in predicting 30-day mortality in non-traumatic ICH patients is shown. The AUC value obtained is 0.903 (indicating excellent accuracy). The cut-off for the ICH score is 2.5, with sensitivity and specificity values of 63.6% and 94.4%, respectively.

Figure 3. ROC curve for the ICH score

Referring to Table 2, a total of 18 patients (81.8%) with a FOUR score of ≤ 11.5 died, while only 4 patients (18.2%) with a FOUR score > 11.5 died. The number of surviving patients was found to be 3 (16.7%) with a FOUR score of ≤ 11.5, whereas 15 patients (83.3%) with a FOUR score > 11.5 survived. Bivariate analysis using chi-square indicates a significant relationship between the FOUR score and the outcome in non-traumatic ICH patients.

Table 2. Relationship between FOUR Score and patient mortality

Outcome	FOUR *Score*		Total	p *value*
	≤ 11.5	> 11.5		
Deceased	18 (81.8%)	4 (18.2%)	22 (100.0%)	<0.001*
Survived	3 (16.7%)	15 (83.3%)	18 (100.0%)	

*Chi-square

Based on Table 3, a total of 16 patients (72.7%) died with FUNC scores ≤ 8.5, while only 6 patients (27.3%) died with FUNC scores > 8.5. The number of surviving patients was found to be only 4 (22.2%) with FUNC scores ≤ 8.5, whereas 14 patients (77.8%) were found to be alive with FUNC scores > 8.5. Bivariate analysis using the chi-square test indicates a significant relationship between FUNC scores and outcomes in non-traumatic ICH patients.

Table 3. Relationship between FUNC Score and patient mortality.

Outcome	FUNC *Score*		Total	p *value*
	≤ 8.5	> 8.5		
Deceased	16 (72.7%)	6 (27.3%)	22 (100.0%)	<0.001*
Survived	4 (22.2%)	14 (77.8%)	18 (100.0%)	

*Chi-square

Based on Table 4, 8 patients (36.4%) died with an ICH score of <2.5, while 14 patients (63.6%) died with an ICH score ≥2.5. The number of surviving patients was 17 (94.4%) with an ICH score <2.5, and only 1 patient (5.6%) survived with an ICH score ≥2.5. Bivariate analysis using chi-square indicates a significant association between ICH score and outcomes in non-traumatic ICH patients.

Table 4. Relationship between ICH Score and Patient Mortality

Outcome	ICH *Score*		Total	p *value*
	< 2.5	≥ 2.5		
Deceased	8 (36.4%)	14 (63.6%)	22 (100.0%)	<0.001*
Survived	17 (94.4%)	1 (5.6%)	18 (100.0%)	

*Chi-square

The results of logistic regression analysis can be seen in Table 5. It has been found that the odds ratios (OR) for FOUR, FUNC, and ICH Score regarding the mortality of non-traumatic ICH patients are 0.116 (0.009-1.443), 1.280 (0.101-16.153), and 7.471 (0.488-114.289), respectively. The results of multivariate analysis using logistic regression yield a p-value > 0.05, indicating that the statistical analysis of these three scores is not significant. Therefore, it cannot be continued to formulate an equation. This indicates that FOUR score, FUNC score, and ICH score cannot be combined to predict mortality in non-traumatic ICH patients.

Table 5 Multivariate analysis of the influence of FOUR, FUNC, and ICH Score

Scoring	*Odds Ratio* (OR)	95% Cl	*p value*
FOUR *Score*	0.116	0.009-1.443	0.094
FUNC *Score*	1.280	0.101-16.153	0.849
ICH *Score*	7.471	0.488-114.289	0.148

*logistic regression

DISCUSSION

Non-traumatic ICH remains an emergency case that requires appropriate management. The reported 30-day mortality rate for these cases ranges from 25 to 52%.[13] To date, several scoring systems have been mentioned for risk stratification and prognosis assessment in patients with non-traumatic ICH. The first scoring system mentioned is the ICH score. Subsequently, new scoring systems have emerged, such as Modified ICH, FUNC, and FOUR score, which are also used to assess patient mortality.[19] In this study, we utilized FOUR, FUNC, and ICH Score to evaluate patient mortality within the next 30 days.

The foundation of this research is to assess short-term outcomes, with short-term death as the primary outcome of interest. Therefore, we defined the main endpoint of this study as death or a maximum follow-up of 30 days, in line with the research conducted by Dian A. Safatli. In their analysis using Pearson correlation, a strong correlation of 0.986 was found between ICH score and 30-day mortality (P < 0.001), and 0.853

between FUNC score and 30-day mortality (P = 0.001).[13] Based on the final results of this study, we found that in the group experiencing mortality, the ICH score was higher, while the FOUR and FUNC scores were lower.

The use of the ICH score has been reported for predicting 30-day mortality in non-traumatic ICH patients. The ICH scoring includes five variables: Glasgow Coma Scale (GCS) score, hemorrhage volume, intraventricular hemorrhage, infratentorial origin, and patient age. Each variable in the ICH score has been found to be associated with mortality in non-traumatic ICH patients.[20] Based on the results of this analysis, we found that the AUC for the ICH score was 0.903 (indicating excellent accuracy). The cutoff for the ICH score as a predictor of short-term mortality was determined to be 2.5, with sensitivity and specificity of 63.6% and 94.4%, respectively. Similar results were reported by Rahmani et al., where 107 non-traumatic ICH patients diagnosed between October 2015 and 2016 were included in the study. The AUC for the ICH score in that study was 0.855, with a cutoff value of $\geqslant 2$ and corresponding sensitivity and specificity of 63.0% and 87.0%. The study also reported that 61 patients (57%) experienced mortality within 30 days of inpatient treatment, while only 46 patients (43%) survived. [21]

In a single-center study conducted at Shariati Hospital, Tehran, Iran, from April 2015 to August 2019, 100 patients were included. The results showed that 32 out of 100 patients died during hospitalization. Statistical analysis revealed that a high ICH score was a risk factor for inpatient mortality. The ICH score in the mortality group was 2.62 ± 0.78, whereas in the survival group, it was 0.85 ± 0.72 ($p < 0.001$). [22]

The FUNC score is another scoring system that can be utilized to guide clinicians in determining appropriate actions for patients with non-traumatic ICH. Components of the FUNC score include age, GCS, ICH location, ICH volume, and pre-ICH cognitive impairment. The score values help estimate the likelihood of patients achieving functional independence.[6,11] However, more recently, this scoring system has also been reported as useful in predicting patient mortality.

A study by Safatli et al. demonstrated a strong correlation between FUNC score and 30-day mortality in patients with non-traumatic ICH ($r = 0.853$; $p = 0.001$).[23] Early neurological deterioration (END) is a crucial factor influencing the mortality of patients with non-traumatic ICH. According to a study by Masotti et al., FUNC score has been reported to have good capability in assessing END events.[23] Therefore, FUNC score is considered a reliable scoring system for assessing the prognosis of patients. In the present study, the AUC value obtained from FUNC score was 0.826, indicating its strong accuracy in assessing short-term mortality in patients with non-traumatic ICH. The identified FUNC score cutoff value was 8.5, with corresponding sensitivity and specificity of 77.8% and 72.7%, respectively. Similar results were reported by Lim et al., where the AUC of FUNC score was 0.851, with cutoff, sensitivity, and specificity values of 7, 75.0%, and 85.3%, respectively.[19]

The FOUR score is a scoring system designed to assist clinicians in assessing clinical status and lesion location in patients with altered consciousness. This scoring system is considered more relevant compared to the GCS in the neurological evaluation of patients with ICH.[18] However, the use of the FOUR score in assessing mortality in non-traumatic ICH patients is still limited.

One study conducted by Mittal and Lele in 2011 reported the use of the FOUR score as a predictor of mortality. The study included 92 patients from January 2008 to May 2010. The analysis revealed that a FOUR score $\leqslant 10$ was a predictor of mortality (relative risk for mortality = 4.10 [2.43-6.91]) and poor functional outcome (relative risk for poor functional outcome = 1.60 [1.27-2.02]) in non-traumatic ICH patients. Additionally, a FUNC score $\leqslant 5$ was also reported as a predictor of mortality.[12] In our study, we found that the AUC for the FOUR score was 0.880, with sensitivity and specificity of 83.3% and 81.8%, respectively, and a cutoff value of 11.5.

We also conducted bivariate analysis to assess the impact of FOUR, FUNC, and ICH scores on patient outcomes. The results showed that both FOUR, FUNC, and ICH scores had a significant impact on outcomes in non-traumatic ICH patients ($p < 0.05$). With the analyzed cutoff values, mortality was found in 63.6% of subjects with ICH score $\geqslant 2.5$, 81.8% with FOUR score $\leqslant 11.5$, and 72.7% with FUNC score $\leqslant 8.5$.

Furthermore, we conducted multivariate analysis to assess the odds ratios (OR) of the three scoring systems for patient mortality. The results showed that the OR for FOUR, FUNC, and ICH scores in relation to non-traumatic ICH patient mortality were 0.116 (0.009-1.443), 1.280 (0.101-16.153), and 7.471 (0.488-114.289) respectively. Unfortunately, the multivariate analysis did not show a significant influence of these scoring systems on non-traumatic ICH patient mortality ($p > 0.05$). Due to the results of the multivariate analysis using logistic regression, these three scores were found to be not significant. Therefore, these scores cannot be integrated into a formula to predict 30-day mortality in non-traumatic ICH patients. Previous studies have attempted to compare the use of these scores, with Braksick et al.'s study comparing ICH and FOUR scores stating that FOUR score provides additional information about the patient's status and has accuracy similar to ICH score in predicting 30-day mortality.[18] On the other hand, another study investigating the use of FUNC and FOUR scores suggests the combination of these two scoring systems in predicting the prognosis of ICH patients. However, in that study, multivariate analysis was not performed to determine the relationship between the combination of scores and patient mortality.[12]

This research is the first to combine these three scores to predict non-traumatic ICH mortality over 30 days. The basis for the lack of significance in this study has not been fully explained but may be due to the small sample size. The study involved only 40 samples collected over a period of 6 months. Another limitation is that it only examined non-traumatic ICH patients at one hospital, RSUP Haji Adam Malik Medan, which may limit the generalizability of the findings to non-traumatic ICH patients overall.

CONCLUSION

There is a significant influence between the FUNC score, FOUR score, and ICH score in predicting short-term mortality in non-traumatic ICH patients. However, the combination of FOUR score, FUNC score, and ICH score is not effective in predicting mortality in non-traumatic ICH patients.

DECLARATIONS

None

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting and revising. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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