Ultrasound measurement of optic nerve sheath diameter as a prognostic indicator of mortality in patients with acute intracerebral hemorrhage

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Summary

Objective: Study on ultrasound measurement of optic nerve sheath diameter (ONSD) for prognostication in acute intracerebral hemorrhage (ICH) patients. *Subject and method*: This descriptive, longitudinal study was conducted on 60 patients with acute ICH admitted to the Stroke Department of the 108 Military Central Hospital from October 2021 to August 2024. *Result*: 16/60 patients (26.67%) died within one month post-onset. Non-survivors had a higher rate of diabetes mellitus, renal failure, cirrhosis, and history of prior stroke compared to survivors. There were no statistically significant differences between the two groups in terms of Glasgow Coma Scale scores, hemorrhage location, Graeb score, Fisher score, hematoma volume, or midline shift degree. The study found that an increased ONSD correlated with a higher mortality rate and when ONSD ≥ 6mm, the mortality rate reached 40%. Predictive factors for one-month mortality included red blood cell count < 4T/l (OR: 63.64, 95% CI: 3.57 - 1132, p<0.05), ONSD ≥ 6mm (OR: 30.63, 95% CI: 2.26 - 415, p<0.05), and a history of diabetes mellitus (OR: 12.74, 95% CI: 1.26-128, p<0.05). *Conclusion*: Ultrasound measurement of ONSD is a convenient and effective method for predicting one-month mortality outcomes in patients with acute ICH.

Keywords: Ultrasound measurement of optic nerve sheath, intracerebral hemorrhage.

I. BACKGROUND

Intracerebral hemorrhage (ICH) accounts for approximately 10-15% of all stroke cases and has the highest mortality rate among stroke subtypes[1]. Elevated intracranial pressure (ICP) is a dangerous complication, contributing to early mortality[2] and the disability in ICH patients[3]. Early prediction of mortality outcomes in patients with severe ICH who exhibit increased ICP is clinically significant, impacting treatment strategies. Previous studies have demonstrated an increase in optic nerve sheath diameter (ONSD) in cases of elevated ICP[4] and this has been identified as a predictor of poor outcomes in patients with traumatic brain injury[5, 6]. Although ONSD can be measured, using ultrasound or CT imaging now, its application in non-invasive ICP monitoring has not been routinely adopted in ICH patients in Vietnam due to limited research on its prognostic value. Thus, this study was conducted to evaluate the prognostic significance of ONSD measurement by ultrasound in severe acute ICH patients.

II. SUBJECT AND METHOD

2.1. Subject

2.1.1. Inclusion criteria

Patients with ICH who met at least one of the following criteria:

Glagsow score ≤ 8.

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Glasgow score was 9-12 combined with an image of severe ICH on CT including intraventricular hemorrhage (Graeb score ≥ 8), parenchymal hemorrhage with a hematoma volume ≥ 30ml, or subarachnoid hemorrhage (Fisher 4).

Selection timeframe: within 10 days post-onset.

Patients who died within one month post-onset were included in the mortality group.

Patients who survived one month post-onset were included in the survival group.

2.1.2. Exclusion criteria

Patients or their legal representatives did not consent to participate in the study.

Patients with orbital trauma or congenital eye abnormalities that prevent orbital ultrasound.

Conditions that may affect the study results such as brain tumors, chronic hydrocephalus.

Patients who died within one month post-onset due to non-neurological causes.

2.2. Methods

Study design: Descriptive, longitudinal study.

Sample size: A convenient sample of 60 patients who met the inclusion criteria and without excluded criteria.

Study process

Patients were divided into two groups including survivors and non-survivors within one-month post-onset. The clinical and sub-clinical characteristics were collected for comparison between the two groups to evaluate prognostic factors.

General patients' characteristics: Age, gender, disease history, height, and weight.

Clinical factors: Systolic blood pressure, diastolic blood pressure, Glasgow score at admission.

Sub-clinical factors: Red blood cell count, white blood cell count, platelet count, blood glucose, sodium, and potassium levels; imaging diagnostics included brain CT scan and ultrasound measurement of ONSD. All tests were performed at the time of admission.

ONSD was measured using ultrasound by trained physicians with a linear probe in B-mode at an 8Hz frequency: Starting from the retinal margin, measure perpendicularly along the optic nerve at a distance of 3mm to mark the point for measuring the ONSD. The measurement is taken transversely at this marked point, perpendicular to the outer margin of the optic nerve sheath, including the entire hyperechoic outer layer of the sheath. The measurement was repeated three times, and the average of these three measurements is recorded as the final ONSD value for documentation in the study records.

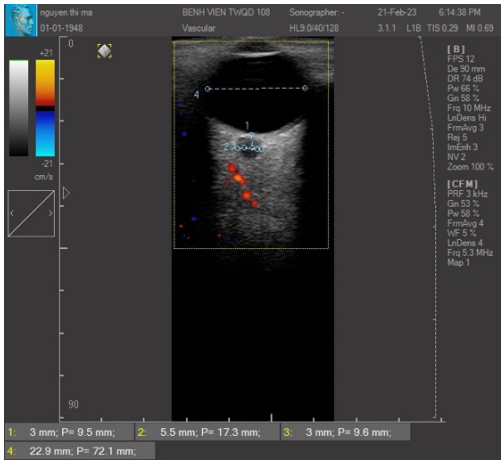

Figure 1. Ultrasound image of optic nerve sheath. 1: 3mm; 2: ONSD 5.5mm; 3: ONSD 3mm; 4: eyeball diameter 22.9mm.

Assessment of patients' outcomes: Patients were divided into two groups including the non-survival and survival group.

Patients were treated at the ICU according to the 2015 American Stroke Association treatment guidelines.

Study location and time

The study was conducted at 108 Military Central Hospital, from October 2021 to August 2024.

Data collection, processing, and analysis

Patients meeting the inclusion criteria were treated according to established protocols. The collected data were recorded into a pre-designed

questionnaire at the time of admission and follow-up after one month.

Analysis was performed using SPSS 22.0 software. Categorical variables were presented as absolute values (%), while continuous variables were presented as mean ± SD. Statistical significance between groups was assessed using Pearson's chi-square (χ2) test or Fisher's exact test for categorical variables, and Student's t-test or Mann-Whitney U test for continuous variables. Multivariate regression analysis was performed to identify independent predictors of poor outcomes at one-month mark, including variables that showed a relationship with poor outcomes in univariate analysis ($p \leq 0.1$) or risk factors reported in previous studies. A p-value < 0.05 was considered statistically significant for all tests.

2.3. Ethical consideration

The study was conducted with the agreement of both the researchers and the participants. The primary objective of the study was to protect and improve the health of patients with no other intentions.

III. RESULT

Table 1. Clinical characteristics of participants

Factors		Total (n = 60)	Groups		p
			Survival (n = 44)	Non-survival (n = 16)	
Age		59.83 ± 11.07	60.45 ± 10.85	58.13 ± 11.85	p>0.05
Gender n (%)	Male	39 (65)	26 (59.1)	13 (81.3)	p>0.05
	Female	21 (35)	18 (40.9)	3 (18.7)	
Height (cm)		162.35 ± 5.79	161.68 ± 6.95	164.19 ± 6.28	p>0.05
Weight (kg)		60.25 ± 9.04	59.3 ± 9.44	62.88 ± 7.49	p>0.05
Medical history n (%)	Hypertension	53 (88.3)	40 (90.9)	13 (81.3)	p>0.05
	Diabetes	11 (18.3)	5 (11.4)	6 (37.5)	p<0.05
	Renal failure	2 (3.3)	0 (0)	2 (12.5)	p<0.05
	Cirrhosis	3 (5)	2 (4.5)	1 (6.3)	p>0.05
	Previous stroke	5 (8.3)	3 (6.8)	2 (12.5)	p>0.05
Glasgow Coma Scale score		8.7 ± 2.83	8.8 ± 2.81	8.44 ± 2.96	p>0.05
NIHSS score		25.8 ± 10.42	24.64 ± 10.41	29 ± 10.05	p>0.05
Systolic blood pressure, (mmHg)		147.57 ± 26.99	145.57 ± 25.33	153.06 ± 31.34	p>0.05

The findings indicated that 16 out of 60 (26.67%) patients died within one month post-onset in which, the proportion of male was higher than female (81.3% vs. 18.7%). In non-survival group, the Glasgow score was lower and NIHSS was higher than those in the survival group, however the difference was not statistically significant (p>0.05). There was a higher prevalence of diabetes and renal failure in the non-survival group with statistical significance (p<0.05).

Table 2. Sub-clinical characteristics of patients

Factors		Total (n = 57)	Groups		p
			Survival (n = 43)	Non-survival (n = 14)	
RBC (T/l)	< 4, n (%)	9 (15)	10 (19.6)	6 (66.7)	p<0.05
	X ± SD	4.71 ± 0.81	4.93 ± 0.8	4.1 ± 0.47	p<0.05
WBC (G/L)		14.93 ± 5.72	14.99 ± 5.38	14.76 ± 6.75	p>0.05
PLT (G/l)		236.75 ± 78.86	240.55 ± 72.93	226.31 ± 95.14	p>0.05
PT (%)		109.48 ± 13.24	110.07 ± 11.24	107.88 ± 18.07	p>0.05
Sodium (mmol/l)		133.28 ± 17.58	133.03 ± 19.78	133.94 ± 9.63	p>0.05

Factors		Total (n = 57)	Groups		p
			Survival (n = 43)	Non-survival (n = 14)	
Potassium (mmol/l)		3.45 ± 0.45	3.4 ± 0.43	3.59 ± 0.49	p>0.05
ONSD (mm)	≥ 6, n (%)	25 (41.7)	15 (34.1)	10 (62.5)	p<0.05
	X ± SD	5.84 ± 043	5.8 ± 0.42	5.96 ± 0.48	p>0.05
Hemorrhage location n (%)	Parenchymal	40 (66.7)	29 (65.9)	11 (68.8)	p>0.05
	Intraventricular	57 (95)	42 (95.5)	15 (93.8)	p>0.05
	Subarachnoid	19 (31.7)	14 (31.8)	5 (31.3)	p>0.05
Graeb score		7 ± 2.95	7.2 ± 2.44	6.57 ± 3.81	p>0.05
Fisher score		1.27 ± 1.87	1.27 ± 1.88	1.25 ± 1.91	p>0.05
Hematoma volume		19.12 ± 28.17	15.11 ± 21.73	30.14 ± 39.89	p>0.05
Midline shift (mm)			3.44 ± 5.4	3.11 ± 4.26	p>0.05

There was no statistically significant difference in white blood cell and platelet count, serum sodium and potassium levels between the two groups. The red blood cell count at admission was lower in the non-survival group compared to the survival group with a statistical significance (p<0.05). The mean ONSD in the non-survival group was higher than in the survival group (5.96mm vs. 5.8mm), with a greater proportion of patients having ONSD ≥ 6 in the mortality group compared to the survival group (62.7% vs. 34.1%) (p<0.05).

Table 3. Treatment methods

Methods	Total (n = 57)	Groups		p
		Survival (n = 43)	Non-survival (n = 14)	
External ventricular drainage	52 (86.7%)	40 (90.9%)	12 (75%)	p>0.05
Craniotomy with hematoma evacuation	1 (1.7%)	1 (2.3%)	0 (0%)	
Hematoma drainage	4 (6.7%)	2 (4.5%)	2 (12.5%)	
External ventricular drainage and Hematoma drainage	2 (3.3%)	1 (2.3%)	1 (6.3%)	
Time of surgery from onset (day) ($\bar{X}$ ± SD)		29.91 ± 30.78	25.88 ± 31.6	p>0.05

All patients in the study underwent surgical procedures to reduce the ICP, in which 86.7% of patients underwent external ventricular drainage. There was no statistically significant difference in time of surgery from onset between the two groups.

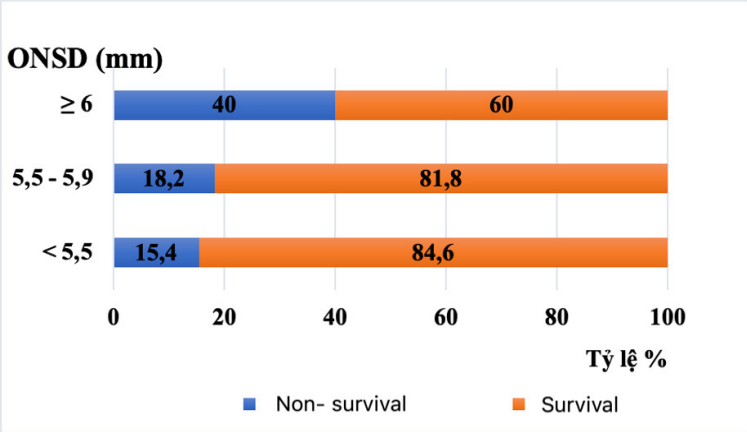

Chart 1. Percentage of treatment outcomes classified by ONSD

The larger ONSD was, the higher mortality rate was. Patients with ONSD ≥ 6mm had a mortality rate of 40%.

Table 4. Multivariate logistic regression analysis of one-month mortality outcomes in patients with severe acute ICH

	OR	B	95% CI	p value
RBC < 4 T/L	63.64	4.15	3.57-1132	0.005
ONSD ≥ 6 mm	30.63	3.42	2.26–415	0.01
Diabetes	12.74	2.54	1.26-128	0.03
Renal failure	518	22.36		0.99

History of diabetes mellitus, renal failure, ONSD ≥ 6mm, and RBC < 4T/L at admission were identified as predictive factors for increased risk of mortality after one month, based on univariate analysis (Table 1, 2, 3). In multivariate regression analysis, ONSD ≥ 6mm, RBC < 4T/L, and history of diabetes mellitus were independent prognostic factors for increased risk of mortality after one month in patients with severe ICH stroke (Table 4).

IV. DISCUSSION

This study aimed to evaluate the role of ONSD in predicting mortality in patients with severe ICH. The findings demonstrated that ONSD measured by ultrasound was a valuable prognostic factor for predicting mortality when combined with other predictive factors.

The study included 60 patients with ICH who underwent surgical intervention due to the risk of increased ICP, among whom 16 patients (26.67%) died within one month post-onset. Prognostic factors in ICH patients were evaluated, focusing on age, gender, medical and clinical history, location of hemorrhage, hematoma volume, and the presence of intraventricular hemorrhage (IVH)[7]. In this study, no statistically significant differences were observed between the two groups (survivors vs. non-survivors) in general characteristics, including age, height, weight, Glasgow score, NIHSS score, and systolic blood pressure at admission. Hypertension was the most common comorbidity, present in 88.3% of cases. However, non-survivors had higher rates of diabetes mellitus, renal failure, cirrhosis, and history of stroke compared to survivors. Notably, patients with diabetes mellitus had a mortality rate over three times higher than that of survivors, and both patients with a history of renal failure died. These differences were statistically significant, with $p<0.05$. Several studies worldwide have also shown a relationship between diabetes mellitus and stroke. A meta-analysis of 102 prospective studies involving 698.782 cases found that diabetes was a risk factor for ICH stroke, with a relative risk of 1.6[8]. Furthermore, research by Demchuk AM[9] identified elevated plasma glucose levels at admission as an independent predictor of mortality after ICH.

Following the results in Table 2, the RBC in the mortality group was lower than in the survival group, with a statistically significant difference ($p<0.05$). Previous studies have also noted that anemia or low RBC levels were associated with poor outcomes in patients with non-traumatic ICH, potentially due to reduced oxygen delivery to brain parenchyma[10]. In our study, no statistically significant differences were observed between the two groups regarding hemorrhage location, Graeb score, Fisher score, hematoma volume, and midline shift. As shown in Table 3, all patients underwent surgical intervention, with 52 out of 60 cases (86.7%) undergoing external ventricular drainage. There were no statistically significant differences were found between the mortality and survival groups regarding surgical methods and the timing of surgery after onset.

The mean ONSD measured by ultrasound in the non-survival group was higher than in the survival group. This finding aligned with previous studies where ONSD were regarded as an indirect indicator

of the ICP[11]. When the ICP increases, cerebrospinal fluid is displaced from the ventricles and cortical sulci into the space between the optic nerve and its sheath, leading to an increase in ONSD[12]. Furthermore, elevated ICP is a severe complication that can rapidly lead to mortality in patients with ICH. Chart 1 demonstrated that as ONSD increased, the mortality rate also rose, with a mortality rate of 40% observed in patients with ONSD ≥ 6mm. Among patients with ONSD < 5.5mm, 9.1% (5/57 cases) still experienced death. This could be explained by the fact that at the time of admission, the ICP may not have increased, resulting in no observable changes in ONSD. However, the progressive cerebral edema could develop, potentially leading to mortality in the following days. Therefore, in patients with severe ICH admitted early, even when ONSD measured by ultrasound remains within the normal range (< 5.5mm), close clinical monitoring is essential, and repeat ONSD measurements should be performed if clinical deterioration occurs. In the multivariate regression analysis (Table 4), RBC < 4T/l (OR: 63.64, 95% CI: 3.57-1132, p<0.05), ONSD ≥ 6mm (OR: 30.63, 95%CI: 2.26-415, p<0.05), and a history of diabetes mellitus (OR: 12.74, 95% CI: 1.26-128, p<0.05) were identified as prognostic factors for one-month mortality in patients with severe ICH. In addition to anemia and a history of diabetes, which have already been established as prognostic factors for mortality in patients with ICH in previous studies[9, 10], our study showed ONSD as a significant predictor of outcomes in these patients. This finding is consistent with the study by Haoli Xu et al. [13], which demonstrated that ONSD measured by computed tomography at the time of admission was a prognostic factor for outcomes at discharge in ICH patients. Similarly, Javad et al (2019) reported a direct association between increased ONSD and one-month mortality in patients with acute stroke [14]. Henda et al (2015) studied 86 stroke patients and found a significant difference in ONSD between survivors and non-survivors. They reported that for every 0.1cm increase in ONSD, the mortality risk increased by 4.2 and 6.2 times in ischemic and hemorrhage stroke, respectively[15].

Although our study comprehensively evaluated most variables related to the prognosis of stroke, further similar studies were necessary to identify a more precise correlation between ONSD and the prognosis of ICH patients.

V. CONCLUSION

Through the study of 60 patients with acute ICH, there were 16 out of 60 patients died within one month post-onset (26.67%). Non-survivors had higher rates of comorbidities, including diabetes mellitus, renal failure, over cirrhosis, and a history of stroke, compared to survivors. No statistically significant differences were observed between the two groups regarding Glasgow score, hemorrhage location, Graeb score, Fisher score, hematoma volume, or midline shift. Higher ONSD values at admission were associated with higher mortality rates, with a mortality rate of 40% observed in patients with ONSD ≥ 6. RBC < 4T/l (OR: 63.64, 95% CI: 3.57-1132, p<0.05), ONSD ≥ 6mm (OR: 30.63, 95% CI: 2.26-415, p<0.05), and a history of diabetes mellitus (OR: 12.74, 95% CI: 1.26-128, p<0.05) were identified as prognostic factors for one-month mortality in patients with ICH. Ultrasound measurement of ONSD was a convenient bedside method that can predict one-month mortality in patients with severe acute ICH.

REFERENCES

1. Waugh RJ (2001) *Spontaneous intracerebral hemorrhage.* N Engl J Med 345(10):770. doi:10.1056/NEJM200109063451015.
2. Cordonnier C, Demchuk A, Ziai W, Anderson CS (2018) *Intracerebral haemorrhage: Current approaches to acute management.* Lancet 392(10154): 1257-1268. doi: 10.1016/S0140-6736(18)31878-6.
3. Sykora M, Steinmacher S, Steiner T, Poli S, Diedler J (2014) *Association of intracranial pressure with outcome in comatose patients with intracerebral hemorrhage.* J Neurol Sci 342(1-2): 141-145. doi:10.1016/j.jns.2014.05.012.

4. Moretti R, Pizzi B, Cassini F, Vivaldi N (2009) *Reliability of optic nerve ultrasound for the evaluation of patients with spontaneous intracranial hemorrhage.* Neurocrit Care 11(3): 406-410. doi:10.1007/s12028-009-9250-8.
5. Legrand A, Jeanjean P, Delanghe F, Peltier J, Lecat B, Dupont H (2013) *Estimation of optic nerve sheath diameter on an initial brain computed tomography scan can contribute prognostic information in traumatic brain injury patients.* Crit Care 17(2):61. doi:10.1186/cc12589.
6. Lee S, Kim YO, Baek JS, Ryu JA (2019) *The prognostic value of optic nerve sheath diameter in patients with subarachnoid hemorrhage.* Crit Care 23(1): 65. doi:10.1186/s13054-019-2360-6.
7. Hemphill JC, Bonovich DC, Besmertis L, Manley GT, Johnston SC (2001) *The ICH score: A simple, reliable grading scale for intracerebral hemorrhage.* Stroke 32(4):891-897. doi:10.1161/01.str.32.4.891.
8. Emerging Risk Factors Collaboration; Sarwar N, Gao P et al (2010) *Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies*. Lancet 375(9733): 2215-2222. doi:10.1016/S0140-6736(10)60484-9.
9. Demchuk AM, Morgenstern LB, Krieger DW et al (1999) *Serum glucose level and diabetes predict tissue plasminogen activator-related intracerebral hemorrhage in acute ischemic stroke.* Stroke 30(1):34-39. doi:10.1161/01.str.30.1.34.
10. Kuramatsu JB, Gerner ST, Lücking H et al (2013) *Anemia is an independent prognostic factor in intracerebral hemorrhage: An observational cohort study.* Crit Care 17(4): 148. doi:10.1186/cc12827.
11. Hwan Kim Y, Ho Lee J, Kun Hong C et al (2014) *Feasibility of optic nerve sheath diameter measured on initial brain computed tomography as an early neurologic outcome predictor after cardiac arrest.* Acad Emerg Med 21(10): 1121-1128. doi: 10.1111/acem.12477.
12. Hansen HC, Helmke K (1997) *Validation of the optic nerve sheath response to changing cerebrospinal fluid pressure: Ultrasound findings during intrathecal infusion tests*. J Neurosurg 87(1): 34-40. doi:10.3171/jns.1997.87.1.0034.
13. Xu H, Li Y, Liu J et al (2022) *Dilated Optic Nerve Sheath Diameter Predicts Poor Outcome in Acute Spontaneous Intracerebral Hemorrhage.* Cerebrovasc Dis 51(2): 199-206. doi:10.1159/000518724.
14. Seyedhosseini J, Aghili M, Vahidi E, Shirani F (2019) *Association of optic nerve sheath diameter in ocular ultrasound with prognosis in patients presenting with acute stroke symptoms.* Turk J Emerg Med 19(4): 132-135. doi: 10.1016/j.tjem.2019.07.001.
15. Shushrutha Hedna V, Rastogi V, Weeks E, Patel RP (2015) *Abstract W MP83: Use of optic nerve sheath diameter in emergency department to predict stroke outcome.* Stroke 46(1):AWMP83-AWMP83. doi:10.1161/str.46.suppl_1.wmp83.