Turkish Journal of Cerebrovascular Diseases 2022; 28(2): 80-86 Türk Beyin Damar Hastalıkları Dergisi 2022; 28(2): 80-86
Turk J Cereb Vasc Dis
doi: 10.5505/tbdhd.2022.09216

RESEARCH ARTICLE **ÖZGÜN ARAŞTIRMA**

PROGNOSTIC VALUE OF OPTIC NERVE SHEATH DIAMETER IN COMA

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ABSTRACT

INTRODUCTION: The aim of this study was to evaluate the relationship between optic nerve sheath diameter and prognosis in comatose patients admitted to the intensive care unit with acute structural brain injury and low Glasgow coma score (GCS≤8).
METHODS: Our study was designed as a prospective, observational clinical study. In this study, comatose patients over 18 years of age, with GCS ≤8, diagnosed with acute structural brain injury, and the decision to measure optic nerve sheath diameter by ultrasonography in the first 24 hours after admission to the intensive care unit were included. According to the modified Rankin scale on the 28th day, the patients were divided into two groups as good prognosis and poor prognosis. In the modified Rankin scale, scores of 0, 1, 2 and, 3 were considered good neurological prognosis, while scores of 4, 5, and 6 were considered poor neurological prognosis.
RESULTS: Optic nerve sheath diameter in patients with poor neurological prognosis was significantly greater than that in patients with good neurological prognosis (7.04±0.75 vs. 6.02±0.62 mm, p<0.01). In logistic regression analysis, there was a significant correlation between optic nerve sheath diameter and modified Rankin scale at 28th day [OR 1.224 (1.087-1.595), p=0.005]. A similarly significant relationship was also found between optic nerve sheath diameter and intensive care unit mortality and in-hospital mortality [OR 1.124 (1.006-1.256), p=0.039 and OR 1.131 (1.012-1.264), p=0.031, respectively].
DISCUSSION AND CONCLUSION: The significant relationship between optic nerve sheath diameter and prognostic parameters shows that optic nerve sheath diameter can be used to predict prognosis in patients followed up in the intensive care unit for coma due to acute structural brain injury.
Keywords: Stroke, coma, optic nerve sheath diameter, prognosis, intensive care.

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Please cite this article as following: Mengi T, Kaçmaz M, Yakar H. Prognostic value of optic nerve sheath diameter in coma. Turkish Journal of Cerebrovascular Diseases 2022; 28(2): 80-86. doi: 10.5505/tbdhd.2022.09216

KOMADA OPTİK SİNİR KILIF ÇAPININ PROGNOSTİK DEĞERİ

ÖZ

GİRİŞ ve AMAÇ: Bu çalışmanın amacı, akut yapısal beyin hasarı ve düşük Glasgow koma skoru (GKS≤8) ile yoğun bakım ünitesine yatırılan komatöz hastalarda optik sinir kılıf çapı ile prognoz arasındaki ilişkiyi değerlendirmektir.
YÖNTEM ve GEREÇLER: Çalışmamız prospektif, gözlemsel bir klinik çalışma olarak tasarlandı. Bu çalışmaya 18 yaş üzerinde, GKS≤8 olan, akut yapısal beyin hasarı tanısı koyulan, yoğun bakım ünitesine kabul sonrası sonrası ilk 24 saatte ultrasonografi ile optik sinir kılıf çapı ölçümü kararı verilen komatöz hastalar dahil edildi. 28. gündeki modifiye Rankin skalasına göre hastalar iyi prognoz ve kötü prognoz olmak üzere iki gruba ayrıldı. Modifiye Rankin skalasında, skor 0, 1, 2 ve 3 iyi nörolojik prognoz olarak kabul edilirken; 4, 5 ve 6 kötü nörolojik prognoz olarak kabul edildi.
BULGULAR: Kötü nörolojik prognozu olan hastalarda optik sinir kılıfı çapı, iyi nörolojik prognozu olan hastalardan anlamlı olarak daha genişti (7,04±0,75'e karşı 6,02±0,62 mm, p<0,01). Lojistik regresyon analizinde optik sinir kılıf çapı ile 28. gündeki modifiye Rankin skalası arasında anlamlı ilişki mevcuttu [OR 1,224 (1,087-1,595), p=0,005]. Benzer anlamlı ilişki optik sinir kılıf çapı ile yoğun bakım mortalitesi ve hastane içi mortalite arasında da mevcuttu [sırasıyla OR 1,124 (1,006-1,256), p=0,039 ve OR 1,131 (1,012-1,264), p=0,031].
TARTIŞMA ve SONUÇ: Optik sinir kılıf çapı ile prognostik parametreler arasındaki anlamlı ilişki, yoğun bakım ünitesinde akut yapısal beyin hasarına bağlı koma nedeniyle takip edilen hastalarda optik sinir kılıf çapının prognozu öngörmede kullanılabileceğini göstermektedir.

Anahtar Sözcükler: İnme, koma, optik sinir kılıf çapı, prognoz, yoğun bakım.

INTRODUCTION

One of the main symptoms of severe brain injury leading to coma is intracranial hypertension. An important component of critical care in these patients is the recognition and treatment of high intracranial pressure (1). The way to diagnose increased intracranial pressure is to measure it directly or indirectly. The gold standard is invasive intracranial pressure monitoring. Intraventricular catheterization and intraparenchymal monitors are the most commonly used methods. Nevertheless, it has many risks such as hemorrhage and infection since it is an invasive measurement. In addition, it has contraindications such as coagulopathy and thrombocytopenia. These complications and contraindications have increased interest in non-invasive methods. One of the non-invasive diagnostic methods is the measurement of the optic nerve sheath diameter by ultrasonography. The optic nerve is the continuation of the brain, and the optic nerve sheath is the continuation of the dura mater, and the subarachnoid space containing the cerebrospinal fluid continues between the optic nerve and the sheath. It was found that there was an increase in pressure in the subarachnoid space due to the increase in intracranial pressure and therefore, an enlargement in the optic nerve sheath diameter (2,3). In addition to its diagnostic purpose, a limited number of studies have demonstrated that the optic nerve sheath diameter could be used in predicting the prognosis (4-11).

The purpose of this study is to evaluate the relationship between optic nerve sheath diameter and prognosis in comatose patients admitted to the intensive care unit with acute structural brain injury and low Glasgow coma score (GCS≤8).

METHODS

Our study was designed as a prospective, observational clinical study. This study included comatose patients over 18 years of age, with GCS≤8, who were diagnosed with acute structural brain injury, hospitalized in the intensive care unit, and underwent ultrasonography and optic nerve sheath diameter measurement in the first 24 hours after admission to the intensive care unit. The exclusion criteria were pregnancy, anatomical eye defect that prevented examination, history of glaucoma, major maxillofacial trauma, orbital hematoma large enough to prevent ultrasonography or laceration, and not agreeing to participate in the study.

Demographic data, health history variables, physical examination and laboratory variables, treatment variables, and outcome variables of the patients were recorded in the data collection form. The results of the cranial computed tomography (CT) performed before the optic nerve sheath diameter measurement were evaluated. In addition, if a follow-up cranial CT was performed, progression in the results of the cranial CT was also noted. Progression findings were accepted as worsening of pathological changes detected in cranial computed tomography performed before optic nerve sheath diameter measurement or newly added pathological changes. The neurological prognosis was determined by the modified Rankin scale (mRS). The patients were classified into two groups as good neurological prognosis and poor neurological prognosis according to the mRS on Day 28. Scores of 0, 1, 2, and 3 in the modified Rankin scale were considered a good neurological prognosis, while scores of 4, 5, and 6 were considered a bad neurological prognosis.

Examination of Optical Nerve Sheath Diameter: A water-soluble ultrasonography gel was applied to the patient in the supine position, eyes closed, head in the neutral position, and the head elevated at an angle of 20-30 degrees to prevent any pressure. The examination was performed using a linear probe with a frequency width of 10 MHz on the "Mindray" ultrasonography device. External optic nerve sheath diameter was measured sagittally and transversely in both eyes. The image was frozen at the location where the optic nerve was best viewed at the globe entry point. Measurement was performed 3 mm below the point of entry to the globe. The mean of the four measurements (right eye transverse, right eye sagittal, left eye transverse, left eye sagittal) was calculated and used as a single value.

Statistical Analysis: Statistical analyses were performed in the "SPSS for Windows version 22.0" package software. Numerical variables were summarized with mean ± standard deviation. The normality of numerical variables was examined using the Kolmogorov-Smirnov test. The t-test was used in independent groups to compare the variables with normal distribution between the groups. Mann-Whitney U-test was used for the variables where normality was not achieved. Pearson $\chi 2$ test or Fisher's exact test were used for evaluating the statistical significance between categorical variables. The level of significance was taken as $p < 0.05$. The cause and effect relationship between the dependent variable and the independent variables was examined by logistic regression analysis. A reference variable was defined for each group and the rate was considered significant if it was reported in the relevant tables with a 95% confidence interval, did not contain OR 1.00, and p was <0.05.

The study was carried out in accordance with the ethical rules specified in the Helsinki Declaration. Ethics committee approval of the study was obtained from Niğde Ömer Halisdemir University Clinical Research Ethics Committee (Number: 38497978-645-E.1727, Date: 10/03/2020). The patients or the relatives of the patients included in the study were informed and their signed consents were obtained.

RESULTS

A total of 30 comatose patients, who were admitted to the intensive care unit between May 2020 and September 2020 due to acute structural brain injury and low GCS and whose optic nerve sheath diameter was measured, were evaluated. The mean age ± SD was 53.3±23.5 years. According to the evaluation of the comorbidities, 3 patients had diabetes mellitus (10%), 15 patients had hypertension (50%), 4 patients had atrial fibrillation (13.3%), 1 patient had chronic obstructive pulmonary disease (3.3%), 1 patient had liver cirrhosis (3.3%), 1 patient had malignancy (3.3%), and 6 patients had neuropsychiatric comorbidity (20%). None of the patients had heart failure or chronic renal failure. The demographic characteristics and comorbidities of the groups were evaluated in Table 1.

Table 1. Demographic characteristics and comorbidities of the groups.

	Good Neurological Prognosis (n:10)	Poor Neurological Prognosis (n:20)	P
Age, years mean (SD)	41.3 (19)	59.3 (23.6)	**0.048**
Female, n (%)	1 (10%)	8 (40%)	0.204
Diabetes mellitus, n (%)	0	3 (15%)	0.532
Hypertension, n (%)	3 (30%)	12 (60%)	0.121
Atrial fibrillation, n (%)	0	4 (20%)	0.272
Chronic obstructive pulmonary disease, n (%)	1 (10%)	0	0.333
Liver cirrhosis, n (%)	0	1 (5%)	0.472
Malignancy, n (%)	1 (10%)	0	0.333
Neurological comorbidity, n (%)	1 (10%)	5 (25%)	0.633

The causes of coma were traumatic brain injury (53.3%), intracerebral hemorrhage (23.3%), ischemic stroke (10%), and other causes (13.3%). It was determined that all patients had undergone cranial CT in the first 24 hours before the optic nerve sheath diameter measurement. It was found that 28 patients had undergone a follow-up cranial CT. According to the CT results, progression was detected in 10 of the patients (35.7%). The mean optic nerve sheath diameter values measured in the first 24 hours after admission to the intensive care unit was 6.7±0.85 mm. Vital signs (systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, body temperature) and GCS were evaluated during the measurement of the optic nerve sheath diameter. It was found that the measurement of the optic nerve sheath diameter was vasopressor/inotropic (23.3%) in 7 patients and intravenous antihypertensive (13.3%) in 4 patients. The clinical and laboratory data of the groups were summarized in Table 2. Data concerning the treatment of the groups were compared in Table 3.

Intensive care mortality, in-hospital mortality, and mRS on Day 28 were evaluated as outcome variables. The mortality rate of the 28-day intensive care was 40%, in-hospital mortality was 50%, mean mRS on Day 28 was 4.3±1.9. When grouped according to the modified Rankin scale, the mean optic nerve sheath diameter was 6.02±0.62 mm in the good neurological prognosis group and 7.04±0.75 mm in the poor neurological prognosis group. The optic nerve sheath diameter was significantly greater in the poor neurological prognosis group (p<0.01).

According to the logistic regression analysis, there was a significant relationship between the optic nerve sheath diameter and the poor neurological prognosis group according to mRS on Day 28 (p=0.005). A similar significant relationship was found between optic nerve sheath diameter and 28-day intensive care mortality (p=0.039). In addition, there was a significant relationship between optic nerve sheath diameter and in-hospital mortality (p=0.031) (Table 4).

Table 2. Clinical and laboratory data of the groups.

	Good Neurological Prognosis (n:10)	Poor Neurological Prognosis (n:20)	P
Causes of coma			
Traumatic brain injury, n (%)	7 (70%)	9 (45%)	0.260
Intracerebral hemorrhage, n (%)	1 (10%)	6 (30%)	0.682
Ischemic stroke, n (%)	0	3 (15%)	1.000
Other, n (%)	2 (20%)	2 (10%)	1.000
Optic nerve sheath diameter, mm mean (SD)	6.02 (0.62)	7.04 (0.75)	**0.001**
Vital signs			
Systolic blood pressure, mmHg mean (SD)	124.6 (21.6)	131 (41.2)	0.648
Diastolic blood pressure, mmHg mean (SD)	69.3 (15.7)	68.6 (19.1)	0.826
Heart rate, heart rate/min mean (SD)	108.5 (24.6)	102.4 (33.4)	0.617
Respiratory rate, respiration/min mean (SD)	18.9 (5.8)	18.3 (5.5)	0.773
Body temperature, °C mean (SD)	36.5 (2.3)	36.6 (4.3)	0.974
Scores			
Glasgow coma score, mean (SD)	7.3 (0.8)	5.65 (2.1)	**0.025**
APACHE II*, mean (SD)	21.8 (5.6)	27.4 (6)	**0.010**
Results of computed tomography			
Pressure on the 3rd ventricle, n (%)	0	8 (40%)	**0.029**
Pressure on the 4th ventricle, n (%)	0	3 (15%)	0.532
Hydrocephalus, n (%)	0	3 (15%)	0.532
Subdural pressure, n (%)	0	2 (40%)	0.540
SAH† and/or and/or intraventricular hemorrhage, n (%)	4 (40%)	12 (60%)	0.442
Midline shift greater than 5 mm, n (%)	0	7 (35%)	0.064
Deletion in basal cisterns, n (%)	2 (20%)	12 (60%)	0.058
Deletion in cortical sulcus, n (%)	8 (80%)	20 (100%)	0.103
Progression in the follow-up CT‡ results, n (%)	1 (10%)	9 (50%)	**0.034**

APACHE II*: Acute physiological and chronic health evaluation II, SAH†: Subarachnoid hemorrhage, CT‡: Computed tomography.

Table 3. Treatment data of the groups.

	Good Neurological Prognosis (n:10)	Poor Neurological Prognosis (n:20)	P
Antiedema, n (%)	9 (90%)	20 (100%)	0.333
Craniotomy, n (%)	1 (10%)	5 (25%)	0.633
Craniectomy, n (%)	1 (10%)	5 (25%)	0.633
Vasopressor/inotrope, n (%)	1 (10%)	6 (30%)	0.372
Intravenous antihypertensive, n (%)	0	4 (20%)	0.272
Mechanical ventilation, n (%)	9 (90%)	17 (85%)	1.000

Table 4. Outcome variables and mean optic nerve diameter in logistic regression analysis.

	Univariate Analysis OR (95% CI)	P
Poor prognosis according to mRS* on day 28	1.224 (1.087-1.595)	**0.005**
28-day intensive care mortality	1.124 (1.006-1.256)	**0.039**
In-Hospital Mortality	1.131 (1.012-1.264)	**0.031**

mRS*: Modified Rankin scale.

DISCUSSION AND CONCLUSION

In our study, the prognostic value of the optic nerve sheath diameter was evaluated with mRS on Day 28, intensive care mortality, and in-hospital mortality. A significant relationship was found between the optic nerve sheath diameter measured in the first 24 hours after admission to the intensive care unit and these prognostic parameters. In neurological intensive care units, prediction of prognosis is very valuable in terms of neurocritical patient management. Therefore, various studies have been conducted to predict the prognosis in neurocritical patients. Age, type, and severity of the disease, results of the neurological examination, and various scoring systems have been used to predict the prognosis in patients with acute cerebral lesions admitted to the intensive care unit (12-15). In our study, age and GCS were lower while acute physiological and chronic health evaluation II (Apache II) score was higher in the poor neurological prognosis group. In a study conducted with 555 patients in the neurological intensive care unit, the APACHE II score was found to be associated with poor neurological prognosis (13). In another study conducted with neurocritical patients, the effect of diagnoses at the time of admission, age, gender, length of stay in the intensive care unit, and the effect of the TISS-28 score on mortality and functional outcome were evaluated in 1155 patients. Age and TISS-28 were found to be associated with a negative outcome. In this study, mortality was highest in intracerebral hemorrhage (28%), while mortality was found to be 8% in traumatic brain injury (14). In addition, the rate of traumatic brain injury was low and the rate of intracerebral hemorrhage and ischemic stroke was higher in the poor neurological prognosis group; however, there was no statistically significant difference.

The main cardinal finding in severe brain injury including ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, traumatic brain injury, infections, and neoplasms is an increase in intracranial pressure and it contributes to a poor neurological outcome (1). Suspected high intracranial pressure is usually based on clinical and CT results. Indirect radiological indicators of increased intracranial pressure include midline shift, pressure on the 3rd ventricle, hydrocephalus, deletion in the sulcus due to diffuse edema, and deletion in the basal cisterns (3,5). In our study, no significant difference was found between the good neurological prognosis and poor neurological prognosis groups in terms of markers indirectly indicating intracranial hypertension on cranial CT except for the pressure on the 3rd ventricle. Pressure on the 3rd ventricle was significantly higher in the poor neurological prognosis group. One of the diagnostic methods for increased intracranial pressure is the measurement of the optic nerve sheath diameter (2). The prognostic value of the optic nerve sheath diameter was examined in ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and traumatic brain injury (4-11,16). In most of these studies, CT was used to measure the optic nerve sheath diameter (4-6,8,9,11). When compared with computed tomography, ultrasonography has certain advantages as the measurements do not contain ionizing radiation and no patient transport is required for imaging (17). These advantages show that the optic nerve sheath diameter has the potential for widespread use in predicting prognosis in neurocritical patients followed up in the intensive care unit. Current studies on prognosis have had a greater focus on traumatic brain injury (4,5,9,16,18). A total of 54 comatose patients with supratentorial lesions due to acute ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and traumatic brain injury were examined in a recent study with similar features to our study (11). Optic nerve sheath diameter was evaluated by CT, and the neurological prognosis was evaluated by Glasgow outcome score. In this study, the optic nerve sheath diameter was significantly greater in the poor prognosis group compared to the good prognosis group (6.03±0.61 mm compared to 6.40±0.56), (11). In our study, the optic nerve sheath diameter was found to be wider in the poor prognosis group compared to the good prognosis group according to the mRS (7.04±0.75 vs 6.02±0.62 mm). In addition, a significant relationship was found between optic nerve sheath diameter and mRS on Day 28, intensive care mortality, and in-hospital mortality in the logistic regression analysis. When the groups were compared in terms of treatment variables such as anti-edema, craniotomy, craniectomy, vasopressor/inotrope, intravenous antihypertensive, and mechanical ventilation, no statistically interesting difference was found. Based on these data, we concluded that although similar and effective treatments were administered to both groups, the prognosis was worse in patients with optic nerve sheath diameter in the first 24 hours after admission to the intensive care unit. The result we obtained from logistic regression analysis is that the width of the optic nerve sheath diameter could predict poor prognosis in comatose patients with acute structural brain injury.

Our study had various limitations. The most significant limitations were the inclusion of experiences in a single center and the small sample size. Intraventricular measurement, which was the gold standard method for intracranial pressure monitoring, had not been performed on the patients. Therefore, we did not compare the optic nerve sheath diameter and intracranial pressure values. The distance between the inner and outer edges of the echolucent lines around the hyperechoic area surrounding the optic nerve is determined as the external and internal optic nerve sheath diameter (19). In our study, we only measured the external optic nerve sheath diameter. Another limitation was that we did not evaluate the internal sheath diameter. The terminology of the optic nerve sheath diameter in the literature is not clear. In a limited number of studies, both external and internal measurements of the optic nerve sheath diameter were performed (19). In most of the studies in the literature, the width of the optic nerve sheath diameter varied because the distinctions between the optic nerve, optic nerve internal and external diameter were not made clearly (19).

In conclusion, we examined the prognostic value of the optic nerve sheath diameter in comatose patients due to acute structural brain injury in this study. In the poor prognosis group, age and GCS were lower while the pressure on the 3rd ventricle in the cranial CT, APACHE II score, and the rate of progression in CT results were greater. There was no significant difference between the good neurological prognosis and poor neurological prognosis groups in demographic, clinical, radiological, and treatment data. On the other hand, the optic nerve sheath diameter was wider in the poor neurological prognosis group according to the mRS. In addition, we found a significant relationship between optic nerve sheath diameter and poor neurological prognosis, intensive care mortality, and in-hospital mortality according to the mRS on day 28. This information suggests that the optic nerve sheath diameter can be used to predict prognosis in comatose patients with acute structural brain injury. This method has the potential to be widely used in predicting prognosis in the intensive care unit with its advantages such as the ability to repeat measurements, the non-invasive nature of the technique, the readiness of the equipment, the mobility of the equipment, its rapid performance, the absence of ionizing radiation, and no requirement of patient transport for imaging. In future studies, an early risk classification can be made by measuring the optic nerve sheath diameter. A decrease in mortality and hospital and intensive care stay can be achieved as a result of risk classification and appropriate measures to be taken in patient groups.

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Ethics

Ethics Committee Approval: The study was approved by Clinical Research Ethics Committee of Niğde Ömer Halisdemir University (Date: 10/03/2020, Number: 38497978-645-E.1727).

Informed Consent: The authors declared that informed consent was obtained from the patients.

Copyright Transfer Form: Copyright Transfer Form was signed by all authors.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices: TM, MK, HY. Concept: TM. Design: TM. Data Collection or Processing: TM, MK, HY. Analysis or Interpretation: TM, MK. Literature Search: TM. Writing: TM.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

*This study was presented as an oral presentation at the 5th Stroke Academy of Turkey with the title "Prognostic Value of Optic Nerve Sheath Diameter in Coma Due to Stroke and Other Causes of Acute Structural Brain Injury: Preliminary Report".