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Retrospective Evaluation of Optic Nerve Sheath Diameters of Patients Diagnosed with Brain Death

Beyin Ölümü Tanısı Almış Hastaların Optik Sinir Kılıf Çaplarının Retrospektif Olarak İncelenmesi

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ÖZ

Amaç: Çalışmanın amacı; beyin ölümü tanısı almış hastaların optik sinir kılıf çapı (OSKÇ) ile beyin ölümü etiyolojisi arasındaki ilişkiyi ortaya koymak ve OSKÇ ile apne testi öncesi ve sonrası kan gazı parametreleri arasında korelasyon olup olmadığını araştırmaktır.
Araçlar ve Yöntem: Beyin ölümü tanısı almış 92 hastanın sağ ve sol göz için OSKÇ değerleri, parsiyel karbondioksit basıncı (pCO_2), apne testi öncesi ve sonrası kan gazı parametreleri retrospektif olarak incelendi.
Bulgular: Subaraknoid kanama ve intraserebral kanama en sık görülen beyin ölümü nedenleriydi. Sağ göz için ortalama OSKÇ değeri 6.37±1.03 mm, sol göz için 6.43±1.02 mm olarak bulundu. Sadece 8 hastanın OSKÇ çapı 5.00 mm'nin altında ölçüldü. pCO_2'nin yüzdelik değişimi ile OSKÇ arasında istatistiksel olarak anlamlı korelasyon bulunmadı ($p>0.05$).
Sonuç: Çalışmanın sonucuna göre beyin ölümü tanısı almış hastalarda OSKÇ değerleri pCO_2'den bağımsız olarak çok yüksektir. Komadaki hastaların beyin ölümü tanısı açısından değerlendirilmesinde OSKÇ'nin kendisine bir yer bulacağını düşünmekteyiz.

Anahtar Kelimeler: apne testi; beyin ölümü; kan gazı analizi; optik sinir kılıf çapı

ABSTRACT

Purpose: Purpose of this study is to reveal the relationship between optic nerve sheath diameter (ONSD) and the etiology of brain death and to investigate whether there is a correlation between ONSD and blood gas parameters before and after the apnea test in patients diagnosed with brain death.
Materıals and Methods: The data of 92 patients with brain death diagnoses were retrospectively analyzed for ONSD measurements for each eye, partial carbon dioxide pressure (pCO_2), and blood gas parameters before and after the apnea test.
Results: Subarachnoidal and intracerebral hemorrhages were the two most common brain death etiology. The mean ONSD for the right eye was 6.37±1.03 mm. The mean ONSD for the left eye was 6.43±1.02 mm. Only 8 patients had ONSD below 5.00 mm. There was no statistically significant correlation between the percent change of pCO_2 and ONSD change ($p>0.05$).
Conclusion: The present study shows that ONSD values are very high regardless of the partial pressure of carbon dioxide in patients with brain death diagnoses. We can suggest that ONSD can find a place for evaluating comatose patients for brain death diagnosis.

Keywords: apnea test; blood gas analysis; brain death; optic nerve sheath diameter

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INTRODUCTION

In the year 2021, there were approximately 25000 patients waiting for organ donation in Turkey. This number is above 100000 in the USA, but the transplantation rate is lower all over the world. Seventeen patients die each day because they cannot find a suitable organ donation in the USA. In half of 2021, the number of successful transplantations was 3703 in Turkey. Most of the organ donations are originated from cadavers or patients with brain death diagnoses. These statistics show that a quick brain death diagnosis is crucial in intensive care units (ICU) for successful transplantation and organ donation. In recent years, global healthcare policies have attached more importance to brain death diagnosis to increase the rate of organ transplantation.[1-4]

There is a direct connection between the subarachnoidal part of the optic nerve and the chiasmal cistern of the brain. Through this connection, cerebrospinal fluid (CSF) circulates freely between these two areas. CSF flow occurs in the perineural subarachnoid space, and the pressure around the optic nerve increases if a high intracranial pressure (ICP) presents, and this causes an extension of the dural sheath and an enlargement in the optic nerve sheath diameter (ONSD). The anterior portion of the dural sheath, usually 3 mm from the optic globe, is affected by this extension. Therefore, ONSD is measured at a distance of 3 mm from the optic globe on the optic nerve in brain tomography. In this area, the subarachnoid space contains a trabecular meshwork. These trabeculae are composed of leptomeningeal cells and delicate collagenous fibrils; sometimes, they contain one or two blood vessels. Through these features, it is the area with the best capacity to reflect the increased pressure.[1-4]

5 millimeter (mm) was generally accepted as an upper limit of ONSD measurement in studies, although a specific and exact cut-off value could not be determined.[5-8] Kimberly et al. have systematically confirmed that the threshold of 5 mm in ONSD reflects ICP above 20 mmHg.[9] In another study, the optimal limit of ONSD for the determination of ICP above 20 mmHg was found to be $\geq$ 5.0 mm with 94% sensitivity and 98% specificity.[8]

In our literature review, we have found that there were publications on increased ONSD values in patients followed-up with the suspicion of brain death in recent years.[10-12] However, ONSD was measured by ultrasound in these studies. Therefore, we decided to retrospectively investigate the ONSD values in brain imaging of patients with a confirmed brain death diagnosis.

The aim of the present study was to investigate whether there was a correlation between the etiology of brain death and pCO_2 change before and after the apnea test and ONSD by examining the data of patients diagnosed with brain death.

MATERIALS and METHODS

This single-center, retrospective clinical study was approved by Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee with its decision dated 16.02.2022 and numbered 2022-02/06.

The data of 92 patients who had brain death diagnoses in our hospital between the dates of 01.01.2014 and 01.01.2022 were analyzed retrospectively. Age, gender, causes of brain death, blood group type, optic nerve sheath diameter measurements for each eye, pH, pO_2, and partial carbon dioxide pressure (pCO_2) measured before and after the apnea test were recorded. Patients with no definitive diagnosis of brain death were excluded from the study.

Brain computerized tomography (CT) or magnetic resonance imaging (MRI) scans were assessed with a series of millimeter slices (one slice every 0.6 mm). ONSD was measured at a distance of 3 mm behind the eyeball, immediately below the sclera, using Sectra Uniview software (Sectra Workstation, Model 23.1, ©Sectra AB, Sweden). ONSD was measured as a cross-section from one side of the optic nerve sheath to the other side through the center of the optic nerve. The diameters were measured for the patients' both eyes separately.

Statistical Analysis

Frequency tables describing the characteristics of the patients were prepared. Normality was tested with the Shapiro-Wilk test for pH and pCO_2 values. pH and pCO_2 values before and after the apnea test were tested with the

Wilcoxon sign test. Pearson correlation analysis was used between pH, pCO_2, pO_2, and ONSD.

RESULTS

Forty-five (48.9%) of the patients were female, and 47 (51.1%) were male. Most of the brain death diagnoses (29 cases) were obtained in the year of 2019. The Rh (+) was the most frequently seen blood group type (n=37) in patients. Only one patient had blood group type AB Rh (-).

Subarachnoidal hemorrhage and intracerebral hemorrhage were the two most common brain death etiology. Other brain death etiologies are shown in Table 1.

Table 1. Etiologies of brain death.

Brain death etiology	Number (n)	Percentage (%)
Hypoxic-ischemic encephalopathy	5	5.4
Cerebral edema	1	1.1
Cerebral infarct	7	7.6
Subdural hematoma	2	2.2
Intracranial tumor	12	13
Subarachnoid hemorrhage	40	43.5
Intracerebral hemorrhage	22	23.9
Cancer in terminal phase	1	1.1
Encephalitis	1	1.1
Pulmonary thrombo-embolism	1	1.1
Total	92	100

Sixty-seven of the patients had computerized brain tomography as a cranial imaging method, and 25 of the patients had brain MRIs.

Forty patients had metabolic disorders other than brain death etiology. The mean sodium value was 150.15±12.87 mmol/L (min: 127 mmol/L, max: 178 mmol/L). Seventeen patients had cardiopulmonary resuscitation (CPR) before the brain death diagnosis, while 75 patients had not. The mean CPR duration was 6.92±2.54 minutes. Forty-eight patients had a positive result for the apnea test, while 2 patients were negative for the apnea test. Forty-two patients could not meet the appropriate clinical conditions for the apnea test. Relatives of 16 patients accepted organ donation. The mean duration between the first day of ICU hospitalization and brain death diagnosis was 13.67±21.03 days.

The mean ONSD for the right eye was 6.37±1.03 mm (min: 3 mm, max: 9 mm). The mean ONSD for the left eye was 6.43±1.02 mm (min: 3 mm. max: 8.80 mm). There was no significant difference between the left and right measurements of ONSD (p>0.05). The mean values of ONSD measurements according to apnea test positivity are shown in Table 2.

Table 2. Mean values of ONSD measurements according to apnea test positivity.

ONSD	Apnea test result	Number	Mean±SD (mm)	T	p
Right eye	Non-positive*	44	6.26±1.07		
	Positive	48	6.47±1.00	0.975	0.332
Left eye	Non-positive	44	6.47±0.97		
	Positive	48	6.39±1.07	0.387	0.700

ONSD: optic nerve sheath diameter
SD: standard deviation
*: Non-positive patient group contains 2 patients with a negative result for the apnea test and 42 patients without the apnea test.
mm: millimeter

Only 8 patients had ONSD below 5.00 mm for right eye and left eye measurements. Four patients with apnea test (+) had ONSD below 5.00 mm for both eyes and 4 patients without apnea test had ONSD below 5.00 mm for both eyes. Both 2 patients with apnea test (-) had ONSD values higher than 5.00 mm for both eyes. There was no correlation between apnea test positivity and ONSD rising above 5.00 mm (p>0.05) (Table 3).

Table 3. ONSD values according to apnea test positivity

ONSD	Apnea Test Result	Number (n)	Percentage (%)
Right ONSD ≥ 5.00 mm	Non-positive*	40	90.9
	Positive	44	91.6
Right ONSD < 5.00 mm	Non-positive	4	9.1
	Positive	4	8.4
Left ONSD ≥ 5.00 mm	Non-positive	40	90.9
	Positive	44	91.6
Left ONSD < 5.00 mm	Non-positive	4	9.1
	Positive	4	8.4

*: Non-positive patient group contains 2 patients with a negative result for the apnea test and 42 patients without the apnea test.
ONSD: optic nerve sheath diameter
mm: millimeter

In patients with a positive result for the apnea test, there was no correlation between ONSD values and the parameters of arterial blood gas analysis made for the apnea test (Table 4).

Table 4. *Correlation between ONSD values and blood gas analysis.

ONSD	pH2	pH1	$p0_2$2	$p0_2$1	$pCO_2$2	$pCO_2$1
Right ONSD	p=0.709	p=0.817	p=0.684	p=0.142	p=0.749	p=0.497
	R=0.055	R=0.034	R=0.060	r=0.215	r=0.047	r=0.101
Left ONSD	p=0.782	p=0.319	p=0.970	p=0.087	p=0.841	p=0.076
	r=0.041	r=0.147	r=0.006	r=0.249	r=0.030	r=0.259

*Spearman correlation test was used
ONSD: optic nerve sheath diameter
pH2, pO22, pCO22: pH, partial oxygen pressure, and partial carbon dioxide pressure measured in the second blood gas analysis of the apnea test.
pH1, pO21, pCO21: pH, partial oxygen pressure and partial carbon dioxide pressure measured in the first blood gas analysis of the apnea test.

When the etiology of brain death and ONSD were analyzed, the distribution of ONSD measurements according to the cut-off value of 5 mm was shown in Table 5.

Table 5. The number of patients that had ONSD values below 5.00 mm according to the etiology of brain death.

Etiology	Right ONSD		Left ONSD	
	<5.00 mm	≥5.00 mm	<5.00 mm	≥5.00 mm
Hypoxic-ischemic encephalopathy	0	5	0	5
Cerebral edema	0	1	0	1
Cerebral infarct	0	7	0	7
Subdural hematoma	1	1	1	1
Intracranial tumor	1	11	2	10
Subarachnoid hemorrhage	5	35	2	38
Intracerebral hemorrhage	1	21	3	19
Cancer in terminal phase	0	1	0	1
Encephalitis	0	1	0	1
Pulmonary thrombo-embolism	0	1	0	1

ONSD: optic nerve sheath diameter
mm: millimeter

The correlation analysis was made between the percent change of partial carbon dioxide pressure (pCO_2) and ONSD change according to the cut-off value of 5.00 mm. There was no significant correlation between the percent change of pCO_2 and ONSD change (Table 6) ($p>0.05$).

Table 6. The correlation between the percent change in pCO2 and percent change in right and left ONSD in patients with a positive result for the apnea test.

pCO2 - ONSD	Percent change for right-ONSD	Percent change for pCO2	Percent change for left-ONSD
Percent change for right-ONSD	R=1.000	p=0.636 R=-0.070	p=0.000 R=0.817
Percent change for pCO2	P= 0.636 R=-0.070	r=1.000	p=0.255 r=-0.168
Percent change for left-ONSD	p=0.000 R=0.817	p=0.255 r=-0.168	r=1.000

Pearson correlation analysis test was used
ONSD: optic nerve sheath diameter
pCO2: partial carbon dioxide pressure

DISCUSSION

This study shows that ONSD values are high in patients with brain death diagnoses. Only 8 patients had ONSD values below 5.00 mm, while 86 of 92 had ONSD values ≥5.00 mm. The cause of this rise in ONSD was researched in the study by analyzing the pCO_2 values of the apnea test, but there was no statistically significant correlation found between pCO_2 change and ONSD change above or below 5.00 mm. Although hypercapnia is blamed for increased intracranial pressure, the results showed that brain pathologies must be much more blamed for increased ICP than hypercapnia because most patients had a subarachnoid hemorrhage, intracerebral hemorrhage, intracranial tumor, and other intracranial pathologies in this study.

Usually, hemorrhagic or thrombotic intracranial events are the most common causes leading to the brain death process.[13,14] In a study by De Eira et al., the most common causes of brain death were hemorrhagic and ischemic intracranial events.[13] Subarachnoid hemorrhage, traumatic brain injury, and stroke were the most common causes of brain death in another study consisting of 1844 brain death patients.[14] According to the results of this study, the causes of brain death show parallelism with the literature.

In the study of Huzjan et al., they measured ONSD by ultrasonography in 10 patients with brain death diagnoses and 17 healthy subjects for control.[10] The mean ONSD values were found to be 7.1 mm for the left eye and 7.3 mm for the right eye in Huzjan et al.'s study, while our results were 6.26 mm for right-ONSD and 6.47 for left-ONSD. The difference in the mean ONSD results of these two studies is due to etiology and patient number. Huzjan, et al.'s study contains 10 patients with intracranial pathologies, while the present study contains non-intracranial pathologies, even the intracranial etiologies are the majority. Also, the present study contains more patients. Another difference between the two studies is the measurement method of ONSD. Huzjan et al. used ultrasonography for the measurements, while our study used cranial CT or MRI, but we think this difference cannot cause different measurements of ONSD. Even if the ultrasonography is a more subjective method than CT or MRI, repetitive ONSD measurements in comatose patients can give the same results as the ONSD measurements on CT or MRI. In awake patients, ONSD measurements can be much harder because there is a need for orientation of the patient to the process to decrease eye movements during the measurements.

In a study of Yazar[11], 45 patients were divided into 3 groups. 15 patients were in the brain death group, 15 were in the comatose group, and 15 were healthy controls. The mean ONSD values were found to be highest in the brain death group. He found mean ONSD values as 7.55 mm for brain death patients, while mean ONSD values were 6.99 mm in the comatose group. His brain death group contains a patient with drug intoxication and a patient with pneumonia, while others had intracranial pathology. This patient sample resembles our patient sample, but our study contains a higher number of patients. Again, Yazar measured ONSD with ultrasonography, while the present study measured ONSD with cranial CT or MRI. Even though the methods are different, the two studies state that ONSD values are absolutely rising in patients with brain death.

Topçuoğlu et al. measured ONSD in patients with brain death diagnoses, comatose patients, patients with neurological diseases, and healthy subjects in their study.[12] They found the mean ONSD values of patients with brain death to be 8.34 mm, which was statistically higher than other groups. All three studies about ONSD measurement with ultrasonography provided higher ONSD values than the present study. The possible cause of this result can be different methods used in these studies. While MRI shows the exact borders of the sheath of the optic nerve, some CT scans may not show the sheath well due to the capture quality of tomography. The use of both CT and MRI in this study may have affected the results.

There are some limitations of this study. Because of the retrospective nature, bias can be found. For measuring the ONSD values, a standard method was not used. Both CT and MRI were used to assess the ONSD values, and these two different choices could affect the measurements. The difference between the number of patients scanned with CT and MRI is very high; therefore, the study is not homogenized in terms of these two methods. Most of the patients had anti-edema therapy due to their cranial pathologies. ONSD measurements under anti-edema therapy were another limitation of this study.

The present study shows that ONSD values are very high regardless of the partial pressure of carbon dioxide in patients with brain death diagnoses. Even if the ONSD was measured with ultrasound or CT/MRI, it could reach absolutely high numbers in patients with brain death diagnoses. We can suggest that ONSD can find a place for evaluating comatose patients for brain death diagnosis.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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Ethics Committee Permission

This single-center, retrospective clinical study was approved by Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee with its decision dated 16.02.2022 and numbered 2022-02/06.

Authors' Contributions

Concept/Design: OG. Data Collection and/or Processing: OA. Data analysis and interpretation: OG, OA. Literature Search: OG, OA. Drafting manuscript: OG, OA. Critical revision of manuscript: OG, OA.

REFERENCES

1. Hansen HC, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surg. Radiol. Anat. 1996;18(4): 323-328.
2. Liu D, Kahn M. Measurement and relationship of subarachnoid pressure of the optic nerve to intracranial pressures in fresh cadavers. Am J Ophthalmol. 1993;116(5):548-556.
3. Killer HE, Laeng HR, Flammer J, Groscurth P. Architecture of arachnoid trabeculae, pillars, and septa in the subarachnoid space of the human optic nerve: anatomy and clinical considerations. Br J Ophthalmol. 2003;87 (6):777-781.
4. Newman WD, Hollman AS, Dutton GN, Carachi R. Measurement of optic nerve sheath diameter by ultrasound: a means of detecting acute raised intracranial pressure in hydrocephalus. Br J Ophthalmol. 2002;86 (10):1109-1113.
5. Goel RS, Goyal NK, Dharap SB, Kumar M, Gore MA. Utility of optic nerve ultrasonography in head injury. Injury. 2008;39(5):519-524.
6. Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. Ann Emerg Med. 2007;49 (4):508-514.
7. Geeraerts T, Launey Y, Martin L, et al. Ultrasonography of the optic nerve sheath may be useful for detecting raised intracranial pressure after severe brain injury. Crit. Care Med. 2007;33(10):1704-1711.
8. Maissan IM, Dirven PJ, Haitsma IK, Hoeks SE, Gommers D, Stolker RJ. Ultrasonographic measured optic

nerve sheath diameter as an accurate and quick monitor for changes in intracranial pressure. J. Neurosurg. 2015;123(3):743-747.
9. Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med. 2008;15(2):201-204.
10. Lovrencic-Huzjan A, Simicevic DS, Popovic IM, et al. Ultrasonography of the optic nerve sheath in brain death. Perspect. Biol. Med. 2012;1:414-416.
11. Yazar MA. Bedside ultrasonography of the optic nerve sheath in brain death. Transplant Proc. 2019;51(7):2180-2182.
12. Topcuoglu MA, Arsava EM, Bas DF, Kozak HH. Transorbital Ultrasonographic Measurement of Optic Nerve Sheath Diameter in Brain Death. J Neuroimaging. 2015;25(6):906-909.
13. Eira CSLD, Barros MIT, Albuquerque AMP. Organ donation: the reality of an intensive care unit in Portugal. Rev Bras Ter Intensiva. 2018;30:201-207.
14. Escudero D, Valentín MO, Escalante JL, et al. Intensive care practices in brain death diagnosis and organ donation. Anaesthesia. 2015;70:1130-1139.