A Pilot Study: The Effect of COVID-19 on Sonographic Optic Nerve Sheath Diameter Measured for Critical Patient Management

Seval Komut[1], Nurdan Fidan[2]

[1] Department of Emergency Medicine, Faculty of Medicine, Hitit University, Corum, Türkiye
[2] Department of Radiology, Faculty of Medicine, Hitit University, Corum, Türkiye

Address for Correspondence: Department of Emergency Medicine, Faculty of Medicine, Hitit University, 19040, Corum, Türkiye
e-posta: drsevalkomut@hotmail.com

Orcid ID: KS: 0000-0002-9558-4832
FN: 0000-0002-2995-6220

Cite As: Komut S, Fidan N. A Pilot Study: The Effect of COVID-19 on Sonographic Optic Nerve Sheath Diameter Measured for Critical Patient Management. Hitit Med J 2023;5(3):202-208 https://doi.org/10.52827/hititmedj.1344000

Abstract

Objective: The aim of this study is to evaluate the effects of the Coronavirus disease 2019 on sonographic optic nerve sheath diameter measurement and thus avoid possible misleading results in clinical practice.

Material and Method: Each volunteer was first evaluated using carotid system color Doppler ultrasonography. Patients with a history of PCR-confirmed Coronavirus disease 2019 infection were classified as group 1 and patients without a history of Coronavirus disease 2019 infection were classified as group 2, and sonographic optic nerve sheath diameter values of both groups were analyzed.

Results: Of the 123 patients included in the study, 70 (56.9%) were female and 58 (43.1%) were male. 83 (67.5%) of the patients included in the study were in group 1 and 40 (32.5%) were in group 2. The mean sonographic optic nerve sheath diameter values for the groups were 3.53 mm and 3.46 mm, respectively. The sonographic optic nerve sheath diameter differences between the two eyes for the groups were determined to be 0.203±0.139 mm and 0.282±0.2 mm.

Conclusion: Due to the variable effects of Severe Acute Respiratory Syndrome Coronavirus-2, the use of sonographic optic nerve sheath diameter measurement in current standards for critical patient management may lead to false-positive or false-negative results.

Keywords: COVID-19, Critical patient, Optic nerve, Pandemic, Ultrasonography

Özet

Amaç: Bu çalışmanın amacı, Coronavirüs hastalığı 2019'un merkezi sinir sistemi üzerindeki etkileri ile ilişkili olarak; sonografik optik sinir kılıf çapı ölçümünün güvenilirliğini değerlendirmek ve böylece klinik pratikte olası yanıltıcı sonuçları önlemektir.

Gereç ve Yöntem: Her gönüllü öncelikle karotis sistemi renkli Doppler ultrasonografi kullanılarak değerlendirildi. PCR ile doğrulanmış Coronavirüs hastalığı 2019 enfeksiyonu öyküsü olan hastalar grup 1, Coronavirüs hastalığı 2019 enfeksiyonu öyküsü olmayan hastalar ise grup 2 olarak sınıflandırılarak her iki grubun sonografik optik sinir kılıfı çapı değerleri analiz edildi.

Bulgular: Çalışmaya dahil edilen 123 hastanın 70'i (%56,9) kadın, 58'i (%43,1) erkekti. Çalışmaya dahil edilen hastaların 83'ü (%67,5) grup 1'de, 40'ı (%32,5) grup 2'de yer aldı. Grupların ortalama sonografik optik sinir kılıfı çapı değerleri sırasıyla 3,53 mm ve 3,46 mm idi. Gruplar için iki göz arasındaki sonografik optik sinir kılıf çapı farkları 0,203±0,139 mm ve 0,282±0,2 mm olarak belirlendi.

Sonuç: Severe Acute Respiratory Syndrome Coronavirus-2'nin değişken etkileri nedeniyle, kritik hasta yönetimi için mevcut standartlarda sonografik optik sinir kılıf çapı ölçümünün kullanılması yanlış pozitif veya yanlış negatif sonuçlara yol açabilir.

Anahtar Sözcükler: COVID-19, Kritik hasta, Optik sinir, Pandemi, Ultrasonografi

Date of Submission: 15.08.2023
Date of Acceptance: 23.09.2023
Date of Publication: 10.10.2023

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: Ethical approval for the study was granted by the Non-Interventional Research Ethics Committee of Hitit University (decision no: 13, dated: 31.05.2022)
Plagiarism Checks: Yes - iThenticate
Conflict of Interest: No conflict of interest has been declared by the authors.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: SK Design: SK Data Collection/Data Processing: SK, NF Data Analysis: SK, NF Article Preparation: SK, NF
Informed Consent: Consent was obtained from the patients.
Financial Disclosure: No financial support has been received.

Introduction

The optic nerve, showing continuity with the central nervous system (CNS), protrudes from the diencephalon towards the orbita during embryogenesis and is in the form of three layers, the pia, dura, and arachnoid mater, enclosed in a meningeal sheath (1, 2). The cerebral spinal fluid (CSF) in the subarachnoid space circulates freely in the intraorbital and intracranial compartments. Therefore, changes in intracranial pressure (ICP) are observed with variability in the subarachnoid space around the optic nerve in the orbital compartment (3). When ICP increases, an increase in optic nerve sheath diameter (ONSD) is expected. This measurement of transorbital sONSD is used as a preferred marker for non-invasive monitoring of ICP (4-8). However, it has been emphasized in many studies that for this method to be used safely, the patient should have no history of glaucoma, trauma, or tumor affecting ophthalmic anatomy, endocrinopathy, electrolyte imbalance, or the use of drugs that can affect ICP (1, 9-11). It has also been reported that atherosclerotic or micro embolic processes that can affect the internal carotid artery (ICA)-origin vascularity of the optic nerve, affect sONSD measurements (12). The efficacy of the method will increase with the elimination of these factors or the use of corrected values, thereby preventing misdiagnosis in the critical patient group who need ICP monitoring.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the agent of coronavirus disease 2019 (COVID-19), first emerged in Wuhan, China in December 2019, and has had profound effects throughout the world (13). A broad range of symptoms are caused by COVID-19, and no specific pathophysiology has yet been revealed. However, it has been reported that the penetration of the CNS by the virus leads to neurological symptoms and complications (14-16). Thromboembolism and microthromboembolic events as well as neural and neurovascular hyperinflammation, are evaluated as the basic neurological effects of COVID-19. Therefore, it is probable that just as all CNS elements are affected, the optic nerve is also affected in patients who have contracted COVID-19 (17, 18). The aim of this study was to evaluate the reliability of the sONSD measurement, which has become more widely used and valuable in recent years, associated with the effects of COVID-19 on the CNS, and to thereby prevent possible misleading results in clinical practice.

Material and Method

Ethical approval for the study was granted by the Non-Interventional Research Ethics Committee of Hitit University (decision no: 13, dated: 31.05.2022). This study was conducted in the Emergency Medicine and Radiology Clinics of Erol Olçok Training and Research Hospital between June 2022 and January 2022. The study sample comprised healthy hospital employees who volunteered to participate in the study. Volunteers who had undergone cranial Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) imaging for at least 2 months for any reason and no intracranial pathology that can affect ICP, were included in the study. Patients with a history of PCR-confirmed Coronavirus disease 2019 infection were classified as group 1 and patients without a history of Coronavirus disease 2019 infection were classified as group 2, and sonographic optic nerve sheath diameter values of both groups were analyzed.

Exclusion criteria were defined as a history of glaucoma, any surgery affecting the orbital anatomy, electrolyte imbalance, or the use of any medical agent that could cause a change in ICP (19). A record was made for each participant of age, sex, smoking status, COVID-19 positivity confirmed with a polymerized chain reaction (PCR) test, current or pre-COVID-19 use of antiaggregant or anticoagulant drugs, the presence of neurological symptoms at the time of the last PCR positivity, and the pattern of symptoms (visual impairment, loss of sense of smell, vertigo, confusion- dizziness, cephalgia, etc). Hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), and other diseases were defined as comorbidities.

Carotid System Color Doppler Ultrasonography (CD) Technique

Each volunteer was first evaluated using carotid system color Doppler ultrasonography (CD) to exclude significant stenosis and occlusion of the common carotid artery (CCA) and internal carotid artery (ICA). The right and left carotid CD examinations were performed with the subject positioned supine, the head in extension, and the neck turned 30°-45° towards the side being evaluated. Narrowings and occlusions were discounted using B-mode US examination, CD examination, and Doppler spectral analysis with a 40-60 Doppler spectrum angle. After the carotid system CD examination, transorbital sONSD measurements were performed on subjects with no significant carotid artery narrowing.

sONSD measurement Technique

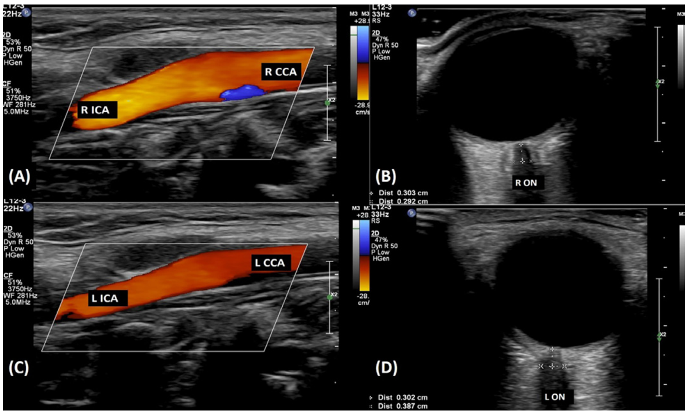
For the sONSD measurement, the subjects were positioned supine with the head and neck elevated 20°-30°, so as not to make any pressure change in the eyes. Before starting the examination, the subjects were instructed to hold this position for at least 1 minute and then close their eyes. Ultrasonic contact gel was applied to the eyelids. The probe was placed on the eyelids and the subjects were instructed to look straight ahead in this position. When the lens, globe, and optic nerve became visible, the brightness and contrast settings were optimized to obtain accurate sONSD measurements. As reported in the literature, the ONSD was measured transversely, perpendicular to the optic nerve, and 3 mm proximal to the optic disc to include hypoechoic lines (Figure I) (1, 20, 21).

Carotid system CD examination and transorbital sONSD measurements were performed by a radiology specialist with 15 years of neuroradiology experience using an Affiniti 70 US device (Philips Healthcare, Amsterdam, Netherlands) with L12-3 and L18-5 high-frequency linear probes.

Statistical Analysis

The data obtained in this study were statistically analyzed using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA). The conformity of numerical data to a normal distribution was examined using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Descriptive statistics were reported using mean ± standard deviation values for numerical data when normally distributed, and median (min-max) values when the distribution was not normal. Descriptive statistics of categorical variables are reported using numbers (n) and

Figure I. A, The right CD image in the sagittal plane of a 35-year-old female patient; with a history of COVID-19 positivity confirmed by PCR testing, without significant stenosis in the right CCA and ICA. B, Right ONSD is measured 2.9 mm. C, The CD image in the sagittal plane shows that the same patient has no significant stenosis in the left CCA and ICA. D, Left ONSD is measured 3.8 mm. (CCA, common carotid artery; ICA, internal carotid artery; L, left; ON, optic nerve; R, right)



percentages (%). Relationship studies and ratio comparisons between categorical variables were performed using either the chi-square test or Fisher's exact test, depending on the sample sizes in the crosstab cells. The Homogeneity of variances was evaluated using Levene's test. Comparisons of numerical data between two independent groups were performed with the Student's t-test for independent groups when parametric test assumptions were met, and with the Mann-Whitney U test when parametric test assumptions were not met. A value of $p<0.05$ was accepted as statistically significant. Differences were considered statistically significant at $p <0.05$.

Results

The Evaluation was made of the data of a total of 123 subjects, comprising 70 (56.9%) females and 53 (43.1%) males with a mean age of 35.1±8.25 years (range, 22-60 years). No additional disease was present in 111 (90.2%) subjects, DM was determined in 5 (4.1%), CAD in 5 (4.1%), and HT in 2 (1.6%). Of the total group, 59 were smokers (48%). 83 (67.5%) of the patients included in the study were in group 1 and 40 (32.5%) were in group 2.

The clinical characteristics of the subjects with and without a history of COVID-19 and the statistical findings of the comparisons of the right- and left-eye sONSD values are presented in Table I. No statistically significant difference was found between the groups with and without a history of COVID-19 with respect to age, sex, comorbidities, and smoking status (*p=0.246, p=0.064, p=0.749, and p=0.943*, respectively) (Table I).

The differences in the right-left eye sONSD values were determined to be statistically significantly higher in the group with a history of COVID-19 than in the group without COVID-19 (*p=0.026*) (Table I). The distribution of sONSD differences between the groups is shown as a boxplot in Figure II. No significant difference was found between the groups with respect to the right eye sONSD measurements, left eye sONSD measurements, and the mean sONSD value for the right and left eyes (*p=0.226, p=0.628, p=0.360*, respectively) (Table I).

Subjects who had experienced COVID-19 infection at least once were separated into subgroups of those with and without neurological symptoms. The statistical results of comparisons of the absolute values of the sONSD differences between these two subgroups are shown in Table II. No statistically significant difference was found between the sONSD differences of subjects who had and had not lost a sense of smell, and between those who had and did not have confusion (*p=0.236* and *p=0.099*, respectively).

Table I. Statistical findings regarding the comparison of socio-demographic characteristics and Optic Nerve Sheath Diameter (ONSD) differences of patients between groups

		COVID-19 negative (n=40)	COVID-19 positive (n=83)	*P values*
Gender	**Male** **Female**	22 (55%) 18 (45%)	31 (37.3%) 52 (62.7%)	0.064*
Additional disease	**No** **Yes**	37 (92.5%) 3 (7.5%)	74 (89.2%) 9 (10.8%)	0.749†
Smoking	**No** **Yes**	21 (52.5%) 19 (47.5%)	43 (51.8%) 40 (48.2%)	0.943*
Age		33.85±8.09	35.70±8.3	0.246‡
ONSD difference (mm)		0.203±0.139	0.282±0.2	0.026‡
ONSD right (mm)		3.43±0.41	3.54±0.48	0.226‡
ONSD left (mm)		3.49±0.44	3.53±0.43	0.628‡
ONSD mean (mm)		3.46±0.41	3.53±0.42	0.360‡

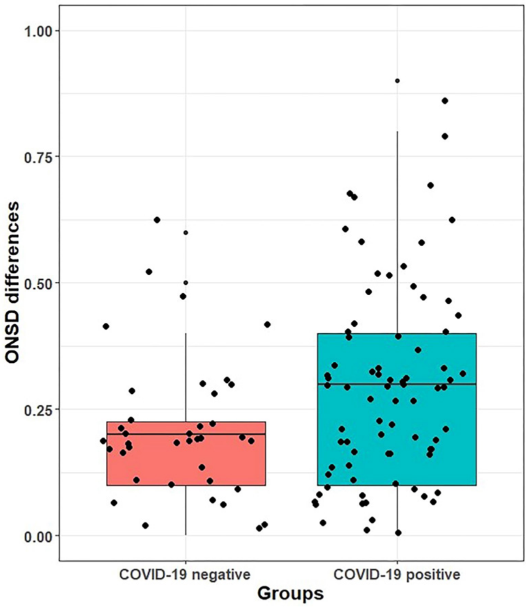
*Chi-square test
†Fisher exact test
‡Student's t-test with mean±standard deviation
ONSD: Optic Nerve Sheath Diameter

Table II. Statistical findings for the comparison of Optic Nerve Sheath Diameter (ONSD) differences between groups formed according to neurological symptoms

		ONSD difference	*P values*
Loss of smell	**No (n=53)**	0.262 ± 0.199	*0.236‡*
	Yes (n=30)	0.316 ± 0.2	
Defect of vision	**No (n=79)**	0.269 ± 0.193 0.3 (0 - 0.9)	***0.012§***
	Yes (n=4)	0.525 ± 0.189 0.45 (0.4 - 0.8)	
Vertigo	**No (n=78)**	0.262 ± 0.186 0.25 (0 - 0.9)	***0.001§***
	Yes (n=5)	0.58 ± 0.178 0.6 (0.4 - 0.8)	
Confusion	**No (n=73)**	0.268 ± 0.193	*0.099‡*
	Yes (n=10)	0.38 ± 0.229	
Headache	**No (n=61)**	0.255 ± 0.16	***0.046‡***
	Yes (n=22)	0.354 ± 0.273	
At least one neurological symptom	**No (n=37)**	0.218 ± 0.144	***0.009‡***
	Yes (n=46)	0.332 ± 0.224	

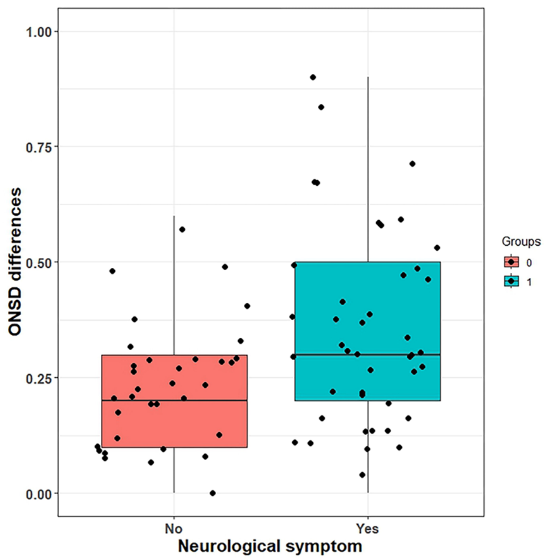
‡Student's t-test with mean±standard deviation
§Mann Whitney U test with mean±standard deviation and median (min-max)
ONSD: Optic Nerve Sheath Diameter

Figure II. Boxplot showing the distribution of ONSD differences between COVID-19 positive and negative patient groups



The sONSD differences of the subjects with visual impairment were determined to be statistically significantly higher than those of the subjects without visual impairment (*p=0.012*). The sONSD differences of the subjects with vertigo were determined to be statistically significantly higher than those of the subjects with no vertigo (*p=0.001*). The sONSD differences in the subjects with headaches were determined to be statistically significantly higher than those in the subjects without headaches (*p=0.046*). The sONSD differences of the subjects with at least one neurological symptom were determined to be statistically significantly higher than those of the subjects with no neurological symptoms (*p=0.009*). The distribution of the right-left eye sONSD differences between the subjects with at least one neurological symptom and those with no neurological symptoms is shown as a boxplot in Figure III.

Figure III. Boxplot showing the distribution of ONSD differences among COVID-19 positive patients with at least one neurological symptom and those without any neurological symptoms



Discussion

Since the onset of the destructive effects of COVID-19 worldwide, neurological symptoms throughout the course of the disease indicate that SARS-CoV-2 creates potential CNS involvement in patients (14, 15). The SARS-CoV-2 virus binds to cells on angiotensin-converting enzyme (ACE)-2 receptors (22). Therefore, it can be said that cells with ACE-2 receptors are more sensitive to the virus and a priority target. In addition to neuronal and glial cells, ACE-2 receptors are also located in Müller, ganglion, retinovascular endothelial, and photoreceptor cells (15, 23). The widespread presence of ACE-2 receptors in both neural and non-neural tissues in the CNS has been shown to be a basic cause of the neuroinvasive behavior of the SARS-CoV-2 virus (14). This reveals that the retina and optic nerve are extremely likely to be affected in patients with COVID-19. However, it has also been reported that in addition to endothelial cell dysfunction, SARS-CoV-2 infection creates hypercoagulability due to intense thrombin production (24, 25). Associated with this, cerebrovascular events (CVE) and various neurological symptoms have been reported to be caused by hypercoagulability status, hypoxemia, ischemia, and severe inflammation (26-28). This strengthens the hypothesis that COVID-19 triggers non-arteritic anterior optic neuropathy (29). Blood flow to the optic nerve is provided by the ophthalmic artery, which includes common arterial variations (30). Therefore, when it is considered that the optic nerve is directly affected by significant stenoses or occlusions in the CCA or ICA, there is a high probability that this sensitive structure fed by the terminal branches of the ICA is exposed to microembolic ischemia caused by SARS-CoV-2 (12).

Spectral-domain (SD)-Optical Coherence Tomography (OCT) is a non-invasive, high-resolution imaging method, that provides cross-sectional evaluation of the retina and optic disc. It plays an important role in the quantitative evaluation of the optic nerve head (ONH) and the thickness of the peripapillary retinal nerve fiber layer (pRNFL) (31, 32). The retina and optic nerve are accepted as intraorbital extensions of the CNS. Therefore, quantitative changes determined with OCT in the retina, ONH, and RNFL can be evaluated as being associated with CNS pathologies. It has been shown in the literature that when ICA narrowing occurs, morphological changes can occur in the retina depending on the severity of the narrowing, and data obtained with OCT have shown that the macula and RNFL thicknesses are reduced in these cases (33-35).

In studies that have examined OCT data of patients who have contracted COVID-19, changes in RNFL thickness have drawn attention, and ONH involvement has been indicated in COVID-19 (14, 18, 36, 37). SARS-CoV-2 causes hypercoagulability and micro embolic processes, which show neurotropic and neuroinvasive behavior and can undoubtedly show similar morphological effects created in the RNFL on the optic nerve. This can give rise to misleading results in sonographic transorbital ONSD measurements, which have become more important in recent years in emergency departments and in the monitoring of critical patients in intensive care units. Therefore, as false positive or false negative results in this method can lead to irreversible clinical errors, its reliability must be investigated to be able to continue effective use after the COVID-19 pandemic.

In the current study, no significant difference was found between ONSD values measured by transorbital sonography in cases with a history of PCR-confirmed COVID-19 infection and those with no history of COVID-19 infection. There is no clear consensus on the subject of normal sONSD values in healthy adults. In the current study, the mean sONSD values for the groups who had or had not experienced COVID-19 were 3.53 mm and 3.46 mm, respectively. Although these values were consistent with the normal sONSD range in healthy volunteers and studies conducted in a European population, they were lower than the results of some studies in different populations (20, 38-42). There are no studies in the literature that have examined sONSD values in COVID-19 patients or those who have recovered. Studies conducted with OCT have reported different results, such as thickening, thinning, or no significant change in the RNFL in COVID-19 patients compared to those with PCR-negativity (36, 37, 43). In the current study, although not statistically significant, the fact that the sONSD values were higher in the group with a history of COVID-19 compared to the other group, supports the variable effects of SARS-CoV-2 on the optic nerve, similar to the results of OCT-based studies.

The basis for the use of transorbital sONSD measurement in the early diagnosis of unilateral intracranial pathologies is the difference that emerges between the right-left eye sONSD measurements associated with ICP increase on the side of the pathology, creating expansion on the ipsilateral optic nerve sheath. Studies in the literature have revealed the reliability of this method and although differences are seen in the studies, it has been attempted to determine cut-off values in healthy individuals taking sONSD asymmetry into consideration (1). In a study of 129 patients that examined the relationship between carotid system narrowing and sONSD thickness, the sONSD difference was reported to be 0.05±0.05 mm for both eyes in the group with no difference in respect to carotid pathology (12). Another study examined sONSD differences in ischemic stroke patients and reported the mean sONSD difference in healthy individuals to be 0.07±0.06 mm (10). The sONSD thickness was determined in elderly volunteers in another study, and the sONSD difference between both eyes was determined to be 0.15±0.17 mm in females and 0.18±0.19 mm in males, and it was emphasized that the sONSD difference was independent of age (11, 20). Other studies that have performed sONSD measurements in healthy volunteers of different ethnic populations have reported no significant differences between the right and left eye sONSD values (39, 44, 45).

In the current study, the sONSD difference between the two eyes was determined to be 0.203±0.139 mm in the group with a history of PCR-confirmed COVID-19 infection and 0.282±0.2 mm in the group with no history of COVID-19. These differences were larger than the sONSD differences reported in the literature for healthy individuals, and this can cause false-positive results in ICP monitoring related to sONSD measurement in patients with COVID-19.

Cut-off values for a unilateral ICP increase show a difference in the literature, and in one of these studies, a cutoff value of 0.45 mm was reported to have 80% sensitivity and 60% specificity (1). Another study that investigated the diagnostic efficacy of sONSD in patients with acute ischemic stroke reported a cutoff value of 0.29±0.06 mm (10). Although the right-left eye sONSD difference determined in the current study subjects with a history of COVID-19 exceeded these cutoff values, it is highly likely that it could cause false-positive or false-negative results even in critical patient management. Therefore, this value could be used to determine the corrected sONSD. However, in cases of suspected unilateral intracranial pathology, the question of which side-corrected sONSD should be used must be answered.

Symptoms such as dizziness, headache, loss of taste or smell, vertigo, and visual loss or impairment have been reported in COVID-19 patients (13). There are studies in the literature that have used OCT to examine the relationship between the presence and frequency of neurological symptoms in the course of COVID-19 with the optic nerve (13). However, no study has investigated the relationship between sONSD and neurological symptoms after disease onset. In the current study, the right-left eye sONSD differences in cases with at least one neurological symptom during COVID-19 infection were found to be significantly higher than those in cases with no neurological symptoms. The sONSD differences in the cases with visual impairment, vertigo, and/or headache during COVID-19 infection were higher than those in the cases with other symptoms. Studies have reported that the frequency of neurological symptoms in COVID-19 patients with have is 40% (46). From this result, it is clear that the right-left eye sONSD difference determined in cases with a history of COVID-19 will make ICP monitoring more difficult in cases with visual impairment, vertigo, and headache symptoms during the disease.

The relationship between the range of COVID-19 symptoms and the neurotropic behavior characteristics of SARS-CoV-2 is not yet clearly understood. However, the data obtained in this study demonstrated the effect of COVID-19 on sONSD measurements. To continue to safely use transorbital sONSD measurements in critical patient care units and emergency departments, there is a need for further studies with larger cohorts to present quantitative data and standardize this effect.

The statements of the current study participants that they had not had COVID-19 were confirmed by checking their health records, the hospital information system, and the healthcare network. Although the other demographic variables were similar in both groups, it is possible that there were some cases of asymptomatic disease or that SARS-CoV-2 positivity was not proven by PCR, which constitutes the most important limitation of this study.

Although the data obtained in this study opens up a discussion of the utility of sONSD in ICP monitoring and the best use of this method which has been standardized in many recent studies, there remains a need for further studies with larger patient groups. Histopathological studies that reveal the neuroinvasive character of SARS-CoV-2 will undoubtedly make a great contribution in this respect.

Limitations

Optic nerve diameter can be affected by age, gender, and previous chronic diseases. Studying in homogeneous groups may be beneficial in eliminating these effects. However, Coronavirus disease 2019 patients admitted to the emergency department do not consist of a certain age and gender. In order to create an accurate sample, patients of all age groups presenting with Coronavirus disease 2019 were included in the study (47).

Conclusion

Transorbital sONSD measurement has become the preferred method for non-invasive ICP monitoring. However, this study was the first to examine the effect of COVID-19 on the reliability of this method. The data obtained in this study support the findings of previous OCT-based studies and have revealed varying effects of SARS-CoV-2 infection on sONSD. Certainly; future studies in which US and OCT will be used simultaneously will provide more effective results. This demonstrates that the existing standards for the use of this method, which has proven efficacy in critical patient management, could lead to false-positive or false-negative results. As this study has made the reliability of this method debatable, further studies with larger patient groups and different populations are needed to test the reliability of this method after COVID-19.

Acknowledgements: We thank Dr. Erdal KOMUT for editing of the manuscript.

References

1. Komut E, Kozacı N, Sönmez BM, et al. Bedside sonographic measurement of optic nerve sheath diameter as a predictor of intracranial pressure in ED. The American journal of emergency medicine 2016;34:963-967.

2. Hirzallah MI, Lochner P, Hafeez MU, et al. Quality assessment of optic nerve sheath diameter ultrasonography: Scoping literature review and Delphi protocol. Journal of Neuroimaging 2022;32:808-824.

3. Hansen H, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surgical and radiologic anatomy: SRA 1996;18:323-328.

4. Maissan IM, Dirven PJ, Haitsma IK, et al. Ultrasonographic measured optic nerve sheath diameter as an accurate and quick monitor for changes in intracranial pressure. Journal of neurosurgery 2015;123:743-747.

5. 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. Intensive care medicine 2007;33:1704-1711.

6. Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive care medicine 2018;44:1284-1294.

7. Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive care medicine 2011;37:1059-1068.

8. Yılmaz F, Sonmez BM, Kavalci C, Arslan ED, Caliskan G, Beydilli I. Efficacy of bedside optic nerve sheath diameter measurement in differentiating provoked seizure from unprovoked seizure in the emergency department. Annals of Saudi Medicine 2023;43:42-49.

9. Bekerman I, Sigal T, Kimiagar I, Almer ZE, Vaiman M. Diagnostic value of the optic nerve sheath diameter in pseudotumor cerebri. Journal of Clinical Neuroscience 2016;30:106-109.

10. Kozaci N, Avci M, Caliskan G, Yuksel S. Variability of optic nerve sheath diameter in acute ischemic stroke. Hong Kong Journal of Emergency Medicine 2020;27:223-228.

11. Yagar A, Kozaci N, Avci M, Yildiz S, Karaman, Y. Determination of optic nerve sheath diameter variability with age in pediatric groups and comparison of increased intracranial pressure and optic nerve sheath diameter in pediatric patients with head trauma. Ann Med Res 2018;25:460.

12. Komut E, Murat M, Büyükşireci M, Komut S, Kozaci N. Relationship between internal carotid artery stenosis grade and optic nerve sheath diameter measured by transorbital ultrasonography. Journal of Clinical Ultrasound 2021;49:724-730.

13. Burgos-Blasco B, Güemes-Villahoz N, Vidal-Villegas B, et al. Optic nerve and macular optical coherence tomography in recovered COVID-19 patients. European Journal of Ophthalmology 2022;32:628-636.

14. Abrishami M, Daneshvar R, Emamverdian Z, Tohidinezhad F, Eslami S. Optic nerve head parameters and peripapillary retinal nerve fiber layer thickness in patients with coronavirus disease 2019. Ocular Immunology and Inflammation 2022;30:1035-1038.

15. Zhou Z, Kang H, Li S, Zhao X. Understanding the neurotropic characteristics of SARS-CoV-2: from neurological manifestations of COVID-19 to potential neurotropic mechanisms. Journal of neurology 2020;267:2179-2184.

16. Jossy A, Jacob N, Sarkar S, Gokhale T, Kaliaperumal S, Deb AK. COVID-19-associated optic neuritis–A case series and review of literature. Indian Journal of Ophthalmology 2022;70:310.

17. Pansell J, Rudberg PC, Bell M, Friman O, Cooray C. Optic nerve sheath diameter is associated with outcome in severe Covid-19. Scientific Reports 2022;12:17255.

18. Burgos-Blasco B, Güemes-Villahoz N, Donate-Lopez J, Vidal-Villegas B, García-Feijóo J. Optic nerve analysis in COVID-19 patients. Journal of Medical Virology 2021;93:190.

19. Demir TA, Yılmaz F, Sönmez BM, Karadaş MA, Okudan RN, Keskin O. Association of optic nerve sheath diameter measurement with hyponatremia in emergency department. The American Journal of Emergency Medicine 2019;37:1876-1879.

20. Avci M, Kozaci N, Komut E, Komut S, Caliskan G, Tulubas G. The measurement of elderly volunteers' optic nerve sheath diameters by ocular ultrasonography. Medicina.2019;55:413.

21. Akça E, Yılmaz F, Baltacıoğlu B, Tiftikçi İ, Arslan ED, Kavalcı C, et al. Bedside Ultrasonographic Assessment of the Optic Nerve Sheath Diameter to Assess Intracranial Pressure in Patients Given Ketamine in Emergency Department. Albanian Journal of Trauma and Emergency Surgery 2023;7:1273-1278.

22. Liu M-Y, Zheng B, Zhang Y, Li J-P. Role and mechanism of angiotensin-converting enzyme 2 in acute lung injury in coronavirus disease 2019. Chronic Diseases and Translational Medicine 2020;6:98-105.

23. Choudhary R, Kapoor MS, Singh A, Bodakhe SH. Therapeutic targets of renin-angiotensin system in ocular disorders. Journal of current ophthalmology 2017;29:7-16.

24. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased

mortality in severe coronavirus disease 2019 patients with coagulopathy. Journal of thrombosis and haemostasis 2020;18:1094-1099.

25. Schmitt FCF, Manolov V, Morgenstern J, et al. Acute fibrinolysis shutdown occurs early in septic shock and is associated with increased morbidity and mortality: results of an observational pilot study. Annals of intensive care 2019;9:1-15.

26. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet 2020;395:507-513.

27. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics in 7 patients with critical COVID-2019 pneumonia and acro-ischemia. Zhonghua xue ye xue za zhi 2020:302-307.

28. Nunes NDSM, Nascimento JSFD, Nascimento JKFD, et al. Brain and Covid-19: an integrative review. E-CRONICON NEUROLOGY 2020;12.

29. Catharino A, Neves M, Nunes N, Nascimento, JS, Nascimento JK. COVID-19 related optic neuritis: Case report. J Clin Neurol Neurosci 2020;1.

30. Prasad S, Galetta SL. Anatomy and physiology of the afferent visual system. Handbook of clinical neurology 2011;102:3-19.

31. Holló G, Zhou Q. Evaluation of retinal nerve fiber layer thickness and ganglion cell complex progression rates in healthy, ocular hypertensive, and glaucoma eyes with the Avanti RTVue-XR optical coherence tomography based on 5-year follow-up. Journal of Glaucoma 2016;25:e905-e909.

32. Cabrera DeBuc D, Gaca-Wysocka M, Grzybowski A, Kanclerz P. Identification of retinal biomarkers in Alzheimer's disease using optical coherence tomography: recent insights, challenges, and opportunities. Journal of clinical medicine 2019;8:996.

33. Çakır A, Düzgün E, Demir S, Çakır Y., Ünal MH. Spectral-domain optical coherence tomography findings in carotid artery disease. Turkish Journal of Ophthalmology 2017;47:326.

34. Sayin N, Kara N, Uzun F, Akturk IF. A quantitative evaluation of the posterior segment of the eye using spectral-domain optical coherence tomography in carotid artery stenosis: a pilot study. Ophthalmic Surgery, Lasers and Imaging Retina 2015;46:180-185.

35. Utsugi N, Takahashi K, Kishi S. Choroidal vascular occlusion in internal carotid artery obstruction. Retina 2004;24:915-919.

36. Dag Seker E, Erbahceci Timur IE. COVID-19: more than a respiratory virus, an optical coherence tomography study. International Ophthalmology 2021;41:3815-3824.

37. Örnek K, Temel E, Aşıkgarip N, Kocamış Ö. Localized retinal nerve fiber layer defect in patients with COVID-19. Arquivos Brasileiros de Oftalmologia 2021;83:562-563.

38. Chan P, Mok K. Transorbital sonographic evaluation of optic nerve sheath diameter in normal Hong Kong Chinese adults. Hong Kong Journal of Emergency Medicine 2008;15:197-204.

39. Asghar A, Hashmi M, Hussain A. Optic nerve sheath diameter evaluated by transorbital sonography in healthy volunteers from Pakistan. Anesthesia, Pain & Intensive Care 2019:282-286.

40. Bäuerle J, Lochner P, Kaps M, Nedelmann M. Intra- and interobsever reliability of sonographic assessment of the optic nerve sheath diameter in healthy adults. Journal of Neuroimaging 2012;22:42-45.

41. Goeres P, Zeiler FA, Unger B, Karakitsos D, Gillman LM. Ultrasound assessment of optic nerve sheath diameter in healthy volunteers. Journal of critical care 2016;31:168-171.

42. Ballantyne S, O'neill G, Hamilton R, Hollman AS. Observer variation in the sonographic measurement of optic nerve sheath diameter in normal adults. European journal of ultrasound 2002;15:145-149.

43. Aydin N, Çapraz M. Optic Nerve and Retinal Layer Measurements with Optical Coherence Tomography in PCR Positive and Negative COVID-19 Patients. Journal of Contemporary Medicine 2022;12:1-.

44. Kim DH, Jun J-S, Kim R. Ultrasonographic measurement of the optic nerve sheath diameter and its association with eyeball transverse diameter in 585 healthy volunteers. Scientific reports 2017;7:15906.

45. Maude RR, Amir Hossain M, Hassan MU, et al. Transorbital sonographic evaluation of normal optic nerve sheath diameter in healthy volunteers in Bangladesh. PloS one 2013;8:e81013.

46. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA neurology 2020;77:683-690.

47. Biondino D, Costigliola R, Mottola F, Graziano M, Yılmaz F. Comment on: Optic nerve sheath diameter measurement by ultrasound and age group. Annals of Saudi Medicine 2023;43:196-197.