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Original Article

The Clinical Importance of Optic Nerve Sheath Diameter in Patients with Traumatic Brain Injury: Preliminary Report

Travmatik Beyin Hasarlı Hastalarda Optik Sinir Kılıf Çapının Klinik Önemi: Ön Rapor

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ABSTRACT

Objective: Traumatic brain injury (TBI) is a serious health problem that is related to an increased mortality. In cases of severe TBI, the prediction of prognosis is essential. The enlargement of the optic nerve sheath diameter (ONSD) shows an increased intracranial pressure and is associated with poor outcomes. In this study, we aimed to evaluate the prognostic value of ONSD in patients with severe TBI.

Methods: Forty-four patients with severe TBI were retrospectively enrolled in the study. The patients were divided into two groups: survivors (n=17) and non-survivors (n=27). Baseline characteristics, clinical data, Glasgow coma scale (GCS) on hospital admission, brain computed tomography (CT) results, injury severity score (ISS), and Marshall score were recorded for all patients. ONSD was calculated at 3 mm distance from the globe, immediately below the sclera.

Results: The ONSD on the initial CT was significantly higher in non-survivors compared with survivors (6.83±1.40 vs. 6.40±1.36, p<0.05). In addition, ISS and Marshall score were significantly higher, whereas GCS was significantly lower in non-survivors. ONSD was positively correlated with Marshall score (r=0.332, p<0.05). Receiver operating characteristics analysis demonstrated that ONSD ≥6.61 had a sensitivity of 70.4% and specificity of 64.7% for predicting mortality. It was shown that ONSD ≥6.61 had a 4.3-fold increased risk for in-hospital mortality (odds ratio: 4.35; 95% confidence interval: 1.195-15.865; p<0.05).

Conclusions: The enlargement of ONSD on initial CT was detected to be associated with increased in-hospital mortality in patients with severe TBI.

Keywords: Optic nerve sheath diameter, traumatic brain injury, Marshall score, injury severity score, mortality

ÖZ

Amaç: Travmatik beyin hasarı (TBH) önemli bir sağlık sorunudur ve artmış mortalite ile ilişkilidir. Ciddi TBH'de prognozun öngörülmesi esastır. Optik sinir kılıfı çapının (ONSD) genişlemesi kafa içi basıncının artmasını gösterir ve kötü prognoz ile ilişkilidir. Bu çalışmada, ciddi TBH'li hastalarda ONSD'nin prognostik önemini değerlendirmeyi amaçladık.

Yöntemler: Bu çalışmaya ciddi TBH'li toplam 44 hasta geriye dönük olarak dahil edildi. Hastalar iki gruba ayrıldı: sağ kalanlar (n=17) ve ölenler (n=27). Tüm hastalar için temel karakteristik ve klinik veriler, başvuru sırasında Glasgow koma skalası (GKS) skoru, beyin bilgisayarlı tomografi (BT) tarama sonuçları, yaralanma şiddet skoru (ISS) ve Marshall skoru kaydedildi. ONSD göz küresinin 3 mm gerisinden, skleranın hemen altından ölçüldü.

Bulgular: İlk BT'deki ONSD, ölenlerde hayatta kalanlara kıyasla anlamlı derecede daha yüksekti (6,83±1,40'a karşı 6,40±1,36, p<0,05). Ek olarak, ISS ve Marshall skoru ölenlerde anlamlı derecede daha yüksek iken, GKS ise anlamlı olarak daha düşüktü. ONSD, Marshall skoru ile pozitif korelasyon gösterdi (r=0,332, p<0,05). Alıcı işletim karakteristik analizinde, ONSD'nin ≥6,61 olması mortaliteyi öngörmede %70,4 duyarlılığa ve %64,7 özgüllüğe sahip olduğu görüldü. ONSD'nin ≥6,61 olmasının hastane içi mortalite için 4,3 kat artmış riske sahip olduğu gösterildi (risk oranı: 4,35, %95 güven aralığı: 1,195-15,865, p<0,05).

Sonuçlar: İlk BT'de ONSD genişlemesi, şiddetli TBH'li hastalarda artmış mortalite ile ilişkili bulundu.

Anahtar kelimeler: Optik sinir kılıfı çapı, travmatik beyin hasarı, Marshall skoru, yaralanma şiddet skoru, mortalite

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INTRODUCTION

Severe traumatic brain injury (TBI) is a serious health problem, which can cause mortality and disability[1,2]. Although secondary brain damage due to increased intracranial pressure (ICP) may be minimized with immediate diagnosis and treatment, the primary damage due to trauma is inevitable in head traumas. The prediction of prognosis is essential in severe TBI. Therefore, several parameters have been used to predict prognosis in patients with TBI, such as age, severity of the injury, the use of antiplatelet and anticoagulant drugs, Glasgow coma scale (GCS), injury severity score (ISS), pupil reactivity, the level of ICP, and the characteristics of the lesions detected on brain computed tomography (CT)[3-5]. To prevent patients from secondary brain injury and improve prognosis, ICP monitoring is essential. However, invasive catheter insertion is required for direct measurement of the ICP. Brain CT, a rapid and noninvasive tool in head traumas, can be used for the indirect measurement of increased ICP and therefore provides significant information about the prognosis[6,7].

The optic nerve is surrounded by dural sheath and is an extension of the central nervous system[8]. The orbital perineural subarachnoid space is dilated, and the sheath is enlarged with the hydrostatic transmission of cerebrospinal fluid in cases of increased ICP[9]. Even before the development of papilledema, the enlargement in the optic nerve sheath diameter (ONSD) caused by increased ICP is observed. As a result, the evaluation of ONSD can make significant contributions to the evaluation of patients with TBIs. It can be measured by ocular ultrasound, magnetic resonance imaging (MRI), and CT imaging. Previous studies demonstrated a strong association between ONSD and increased ICP[10,11]. There are limited studies investigating the prognostic value of ONSD on the initial CT in patients with TBI.

In this study, we aimed to investigate the prognostic importance of initial ONSD measured by CT on prognosis in patients with TBI.

MATERIALS and METHODS

The present study was conducted in the Anesthesiology and Reanimation Clinic of our hospital. Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee approved the study design (date: 31.12.2013, decision no: 2013/0118). This study retrospectively investigated 67 TBI patients who were admitted to our intensive care unit (ICU) between April 2011 and December 2012. Patients who had no cranial CT within the first 6 h of trauma, with facial trauma affecting the orbital structure and/or eyeball, with ocular disease affecting the optic nerve and/or orbital cavity, with hyperthyroidism accompanying exophthalmos, and aged below 18 years were excluded from the study. Consequently, 44 eligible patients were investigated in this study.

Baseline demographic data, the ISS, the GCS at the time of ICU admission, the presence of subarachnoid or intraventricular hemorrhage in cranial CT at the time of admission, the ONSD measurement, the frequency of emergency surgical interventions, the presence of hypotension (systolic blood pressure <90 mmHg) on at the time of admission, the requirement for inotropic drugs, biochemical and arterial blood gas parameters at the time of admission, the length of stay in the ICU, and the outcome (survival-death) were recorded for all patients. In addition, Marshall score was calculated for all patients as described previously[12]. Moreover, the following biochemical parameters and blood gas analysis were noted: glucose, sodium, hemoglobin, PaO_2/FiO_2, and $PaCO_2$.

Within the first 6 h of trauma, all CT images were taken. ONSD was calculated based on the initial brain CT. The optic nerve sheath was measured for each eye separately from one side of the optic nerve sheath to the other side from 3 mm behind the globe using the INFINITT PACS program, and the mean of the measured diameters was taken as the mean value. An illustration of the calculation of the ONSD is shown in Figure 1.

Statistical Analysis

All statistical analyses were performed with the SPSS 16.0 package program. Kolmogorov-Smirnov test was used to evaluate the distribution of data. Normally distributed data were expressed as mean ± standard deviation, whereas non-normally distributed data were expressed as median (minimum-maximum). They were compared using Student t-test and Mann-Whitney U test, respectively. The chi-square or Fisher's Exact chi-square test was used to compare categorical variables, which were expressed as number and percentage. Pearson and Spearman correlation coefficient was used for correlation analysis. Receiver operating characteristics (ROC) curve analysis was used to determine the optimal cut-off value, sensitivity, and specificity of ONSD for predicting the mortality. The results were evaluated with a significance value of $p<0.05$ with a 95% confidence interval.

RESULTS

Forty-four patients were included in this study. The mean age of the patients was 48±21, and 32 (73%) of

them were men. TBI was caused by an off-vehicle traffic accident in 21 (47.8%) patients, in-vehicle traffic accident in 7 (15.8%), a fall in 15 (34.2%), and a gunshot wound in 1 (2.2%) patient. Neurosurgical operation was conducted in 20 (45.5%), while ICP monitoring was performed in 26 (59.1%) patients.

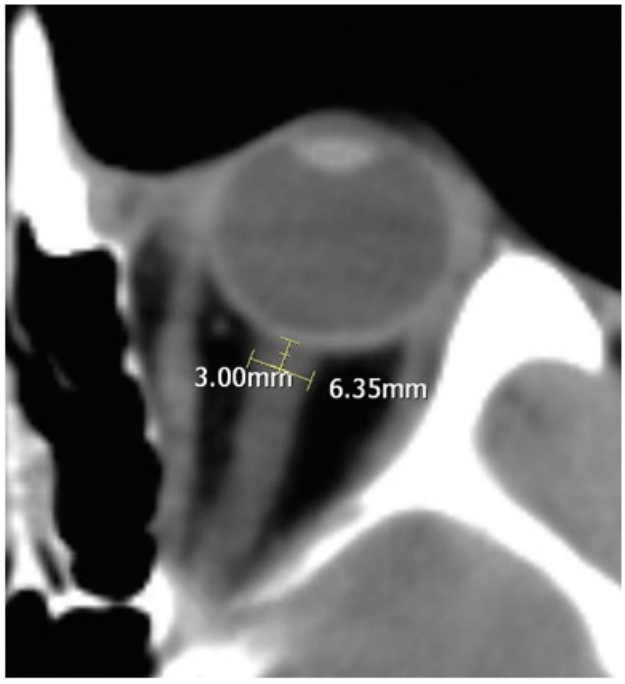


Figure 1. An illustration of the measurement of optic nerve sheath diameter (ONSD) from computed. tomography. It is measured from one side of the optic nerve sheath to the other side at 3 mm distance the globe, the measured ONSD is 6.35 mm in this patient.

Twenty-seven (61.4%) patients died during the follow-up. The comparison of baseline and clinical characteristics of survivors and non-survivors are presented in Table 1. Age and gender did not significantly differ between two groups. ISS and Marshall score were significantly higher, whereas GCS was significantly lower in non-survivors compared with survivors (Table 1).

Biochemical variables, blood gas analyses, and initial CT results are listed in Table 2. No significant difference was observed between two group regarding biochemical and blood gas analyses. However, the frequency of cistern compression, Marshall score, and ONSD were significantly higher in non-survivors compared with in survivors ($p<0.05$, for all) (Figure 2).

In a correlation analysis, ONSD was positively correlated with Marshall Score ($r=0.0032$, $p<0.05$, Figure 3). The area under the ROC curve in differentiating the non-survivor patients was found as 0.722 for ONSD, 0.703 for Marshall score, 0.700 for ISS, and 0.232 for GCS (Figure 4). The ONSD had the highest area under the curve (AUC) value for determining died patients. ONSD ≥6.61 cut-off value predicted mortality with a sensitivity of 70.4% and specificity of 64.7%. It was detected that ONSD ≥6.61 mm had a 4.35-fold increased mortality risk (odds ratio: 4.35; 95% confidence interval: 1.195-15.865; $p<0.05$).

DISCUSSION

The main finding of our study was that ONSD on the initial brain CT was significantly associated with mortality

Table 1. Comparison of baseline and clinical characteristics on admission in survivors and non-survivors.

	Non-survivor (n=27)	Survivor (n=17)	p-value
Age, years	49±23	47±19	0.81
Gender, M/F	21/6	11/6	0.48
ISS	32±16	27±17	<0.05
Initial GCS	5±3	7±2.5	<0.05
Pupil reactivity (%)	17 (38.6)	15 (34.1)	0.06
Anisocoria (%)	9 (20.5)	6 (13.6)	0.89
Hypotension on admission (%)	24 (54.5)	10 (22.7)	<0.05
Neurosurgical operation (%)	10 (22.7)	10 (22.7)	0.15
Inotrope usage (%)	24 (54.5)	14 (31.8)	0.53
Intracranial pressure monitoring (%)	18 (66.7)	8 (47.1)	0.19
Intracranial pressure (mm Hg)	20.5±17.3	5.5±15.5	<0.05
Length of the ICU stay, day	16 (1-65)	25 (3-47)	<0.05

M: Male, F: Female, ISS: Injury severity score, GCS: Glasgow coma scale, ICU: Intensive care unit

in patients with severe TBI admitted to ICU. In addition, across all clinical parameters for determining mortality, ONSD had the highest AUC value.

Patients with severe cranial damage have a significant risk for hypotension, hypoxemia, and cranial edema. If they are not prevented or treated immediately, these conditions increase the risk of mortality by worsening the cranial damage. Immediate admission to the ICU, removing the lesions causing the mass effect, monitoring ICP, and enabling adequate cerebral perfusion pressure can improve these results[13]. Hence, the chain of secondary events can be prevented.

Table 2. Comparison of the baseline biochemical variables, blood gas analyses, and initial CT results in survivors and non-survivors.

	Non-survivor (n=27)	Survivor (n=17)	p-value
Glucose, mg/dL	189±171	154±106.5	0.22
Serum Na+, mEq/L	139±6	140±3	0.15
Hemoglobin, g/L	12.2±2.9	11.4±2.7	0.27
PaO_2/FiO_2	285±196.6	325±141.5	0.30
$PaCO_2$, mmHg	43.5±14.1	41.6±14	0.51
Cistern compression (%)	15 (55.6)	5 (17.6)	<0.05
Midline shift >5 mm (%)	10 (37)	6 (35.3)	0.91
Cortical sulcus effacement (%)	23 (85.2)	14 (82.4)	0.81
Intraventricular hemorrhage (%)	4 (14.8)	1 (6)	0.36
Subarachnoid hemorrhage (%)	22 (81.5)	11 (64.7)	0.21
Marshall score	3±1	2±2	<0.05
ONSD, mm	6.8±1.4	6.4±1.4	<0.05

CT: Computed tomography, Na: Sodium, PaO_2: Partial oxygen pressure, $PaCO_2$: Partial carbon dioxide pressure, FiO_2: Fractional inspired oxygen, ONSD: Optic nerve sheath diameter

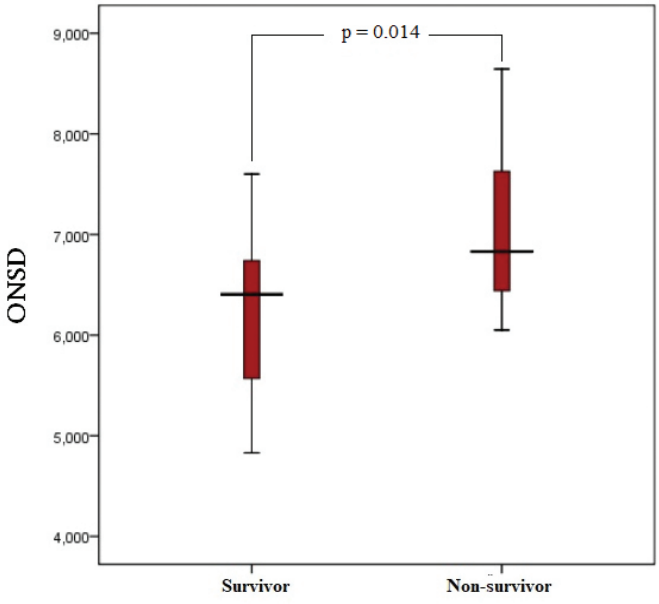


Figure 2. Comparison of optic nerve sheath diameter between survivors and non-survivors.

ONSD: Optic nerve sheath diameter

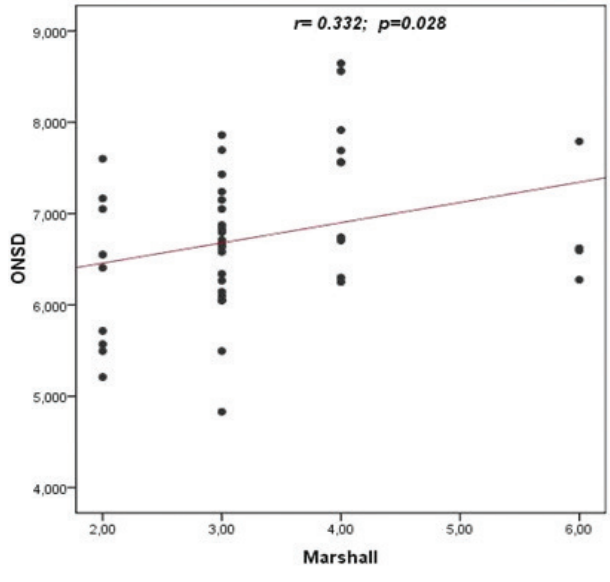
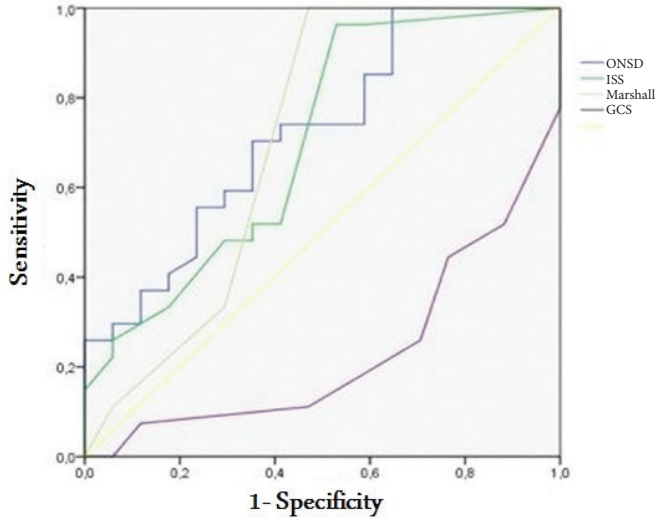


Figure 3. Correlation analysis between optic nerve sheath diameter and Marshall score.

ONSD: Optic nerve sheath diameter



	AUC	95% CI	P value
ONSD	0.722	0.568- 0.876	0.014
Marshall Score	0.703	0.520- 0.885	0.025
ISS	0.700	0.535- 0.866	0.027
GCS	0.232	0.091- 0.374	0.003

Figure 4. The area under the ROC curve values of ONSD, Marshall score, ISS, and GCS for predicting mortality.

ONSD: Optic nerve sheath diameter, ISS: Injury severity score, GCS: Glasgow coma scale, ROC: Receiver operating characteristics, AUC: Area under the curve, CI: Confidence interval

Cranial CT imaging is the most preferred imaging method in patients with head trauma. It provides rapid and accurate diagnosis rates and is noninvasive. The prognostic value of CT results including the condition of the basal cisterns, midline shift, the presence and type of the intracranial lesions, and the presence of intracranial hemorrhage has been well documented[14]. The strongest CT indicators are the association of basal cistern compression and the presence of subarachnoid hemorrhage[14,15]. They are the indicators of poor prognosis with the inclusion of other CT results used in midline shift scoring systems after hemorrhage or contusion. Marshall et al.[16] reported an association of CT scoring with prognosis in 1,030 patients with head trauma. Maas et al.[17] reported that the Marshall CT score was a strong indicator of prognosis; however, it caused a wider differentiation between diffuse injuries and mass lesions and had some limitations, such as the inability to specify the type of mass lesions (e.g., epidural hematoma, subdural hematoma). In another study, Maas et al.[18] reported that there was a strong association between CT classification and outcomes, and the association was worse for patients with diffuse damage Class III (swelling) and Class IV (shift). We also found that the frequency of the cistern compression and Marshall score were significantly higher in non-survivors compared with survivors. These results suggest that initial CT provides important clinical information regarding the prognosis in patients with head trauma. Nevertheless, an appropriate parameter with prognostic value is still required for patients with TBI at the stage of presentation.

Increased ICP is the main cause of secondary brain damage in head traumas[1,2]; hence, monitoring of ICP is important to improve outcomes. The noninvasive evaluation of the increase of ICP is performed with clinical symptoms. In addition, some radiological imaging modalities may be used for monitoring the complications of increased ICP. Detecting the increased ICP in early period of head traumas may enable rapid triage in the emergency room[19].

The optic nerve sheath is the most accessible component of the cranial meninges[8]. Cerebrospinal fluid is present in the subarachnoid compartment surrounding the optic nerve, which communicates with the cranial subarachnoid space. It was demonstrated that increased ICP caused to the enlargement in optic nerve sheath, especially in the subarachnoid compartment of the nerve[20]. Within minutes of acute changes in ICP, this phenomenon occurs. Therefore, in patients with TBI, measurement of optic nerve sheath may provide very significant information. Previous studies reported a strong association between ONSD and increased ICP[10,11]. Therefore, ONSD has been frequently used for the evaluation of patients with TBI. Using bedside ultrasonography (USG), Cammarata et al.[21] demonstrated a significant relationship between intracranial hypertension and ONSD. In addition, it was demonstrated that an increased ONSD was a good indicator for the detection of an increased ICP[22-24]. Furthermore, it was proposed that ONSD measurement might be used for therapeutic intervention planning when invasive ICP monitoring cannot be performed or is contraindicated[25]. However, the specificity and positive predictive value of ONSD is significantly reduced when ICP is >20 mmHg. As a result, the measurement of ONSD in early term may be a better indicator for prediction of increased ICP and evaluation of the prognosis. We also used the early term ONSD in our study and excluded patients who had no cranial CT taken within the first 6 h of trauma.

Measurement of ONSD with CT in the early term (initial measurement) may be beneficial in the early diagnosis and initiate the treatment faster by detecting increased ICP because it is well known that increased ICP

and poor prognosis in patients with TBI are related[26]. There are limited studies investigating the prognostic value of ONSD on the initial CT in patients with TBI. According to Legrand et al.[4], ONSD measured on the initial brain, CT scan is independently associated with ICU mortality rate in severe TBI patients. In addition, Waheed et al.[27] found that a significant positive correlation between the ONSD and Marshall score. Moreover, Sekhon et al.[20] found that ONSD measured on CT scanning was independently associated with ICP and mortality. In line with previous studies, we also observed that ONSD on the initial CT was positively correlated with Marshall score and that it was significantly higher in non-survivors compared with survivors. However, we evaluated the AUC value of ONSD and compared it with the AUC of other clinical scores (ISS, GCS, and Marshall) for predicting mortality, which is different to these mentioned studies. We found that ONSD had the highest AUC value for predicting mortality among the AUC of all these clinical scores. We detected that ONSD ≥6.61 value predicted mortality with a sensitivity of 70.4% and specificity of 64.7%, and patients with ONSD ≥6.61 had a 4.35-fold increased risk for mortality. All these results suggest that ONSD on initial CT is a good prognostic indicator in patients with TBI. Our findings should be supported with future prospective studies.

Different imaging modalities may be used for the measurement of ONSD including USG, CT and MRI. Although previous studies demonstrated that the ONSD values measured by CT imaging differs slightly according to the USG and MRI measurements, it has been detected that these three measurements show good correlation with each other[28-30]. On the other hand, USG is a physician dependent imaging modality and ONSD may not be fully visible at different angles because two-dimensional images are used. In addition, some studies reported interobserver disagreement for the measurement of ONSD with USG[31,32]. CT provides a faster triage than USG and MRI in the emergency room for detecting increased ICP in patients with TBI. Moreover, a CT measurement of the ONSD is easier and has more reproducibility[29]. Therefore, in our study, we measured ONSD with CT scans.

Our study has some limitations. The retrospective design and small sample size are its most significant limitations. Second, the frequency of ICP monitoring in our study was low (59%). Third, we evaluated 44 patients in this study. Although we presented many features including laboratory and CT data, evaluating detailed information about ICU features, laboratory parameters, and patient admission characteristics could provide additional contribution to the study. Further prospective studies with larger participant are required to better elucidate the relationship between ONSD and TBI.

CONCLUSION

ONSD measurement may serve the opportunity to identify patients requiring immediate therapeutic intervention and/or patients with increased ICP that requires invasive pressure monitoring to guide treatment. In this study, we discovered that ONSD enlargement in initial CT was associated with increased mortality in patients who were followed up ICU due to TBI.

Ethics

Ethics Committee Approval: Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee approved the study design (date: 31.12.2013, decision no: 2013/0118).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: B.A.O., M.G.C., H.G.O., T.B.T., Concept: B.A.O., M.G.C., Design: B.A.O., M.G.C., Data Collection and/or Processing: B.A.O., T.B.T., H.G.O., M.G.C., Analysis and/or Interpretation: B.A.O., T.B.T., H.G.O., M.G.C., Literature Search: B.A.O., T.B.T., H.G.O., M.G.C., Writing: B.A.O., T.B.T., H.G.O., M.G.C.

Conflict of Interest: The authors have no conflict of interest to declare.

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