Prospective Study

The Value of the Optic Nerve Sheath Diameter (ONSD) in Predicting Postdural Puncture Headache (PDPH): A Prospective Observational Study

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Background: Postdural puncture headache (PDPH) is one of the serious complications after lumbar puncture, but there is no effective tool to predict it.

Objectives: To explore whether ultrasound measurement of optic nerve sheath diameter (ONSD) as a predictor of PDPH can be a reliable tool supported by reliable protocols and data.

Study Design: A prospective observational study.

Setting: Department of Anesthesiology.

Methods: This prospective observational study was performed in 156 patients undergoing cesarean section (CS). The patient's ONSD was recorded before anesthesia (T0), 10 minutes after anesthesia (T1), at the end of the operation (T2), at the first postoperative day (T24), at the second postoperative day (T48), and the third postoperative day (T72). During the 3-day follow-up, the patients were evaluated, identified, and divided into a PDPH group and a non-PDPH group. Age, weight, height, ASA, lumbar puncture location, and the number of lumbar puncture attempts were also recorded. We mainly analyzed the changes and differences between the 2 groups of ONSD.

Results: Twenty-four patients (15%) developed PDPH. The ONSD was significantly lower in the PDPH group than in the non-PDPH group at T2, T24, T48, and T72. All patients showed a significant reduction in ONSD at T1 compared to T0. Women whose ONSD continued to fall without recovery from T0 to T2 were more likely to experience PDPH (RR 5. 022; 95 CI 3.343 to 7.508). The ONSD at T24 was the best predictor of PDPH (ACU 0. 9787, 95 CI 0.9578 to 0.9996), with a cutoff value of 0.40 cm (sensitivity 92%, specificity 94%).

Limitations: This is a single-center study, and ONSD may vary in different regions or ethnic groups.

Conclusions: We believe that continuous measurements of ONSD may be a useful tool for predicting PDPH.

Key words: Postdural puncture headache (PDPH), Optic nerve sheath diameter (ONSD), Combined spinal-epidural anesthesia (CSEA), cesarean section

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Postdural puncture headache (PDPH) is one of the serious complications occurring after spinal anesthesia, with an incidence ranging from approximately 1% to 36%(1). Ninety percent of headaches occur within 72 hours after lumbar puncture (2). Most scholars agree that PDPH occurrence is highly correlated with needle size and type, gender, and BMI(1,2). Notably, PDPH is more likely to occur in patients undergoing cesarean section (3,4), which not only prolongs the maternal hospital stay and increases the financial burden but can also negatively affect the quality of life and the bonding of mother and baby (5). PDPH caused by spinal anesthesia usually resolves spontaneously within one week, but this cannot be considered entirely benign and self-limiting (6,7). Any delay in the diagnosis or treatment of PDPH can lead to serious complications: postpartum major depression, visual impairment, cranial nerve palsy, and subdural hematoma (5,8). For a minority of people, PDPH may develop into a long-term chronic condition with chronic headache, back pain, and neck pain (9).

The accepted mechanisms for PDPH development are mainly the loss-pull theory and the Monro-Kellie theory, in which cerebrospinal fluid (CSF) loss leads to a reduction in volume, thereby pulling on pain-sensitive brain tissue (e.g., blood vessels and nerves). The rate of CSF loss is greater than the rate of production, and the intracranial arteries increase the cerebral blood flow by expanding their diameter in order to speed up CSF production, resulting in PDPH (2).

All of these hypotheses are essentially the result of excessive CSF loss. Changes in the volume of CSF are likely to cause changes in the ONSD, which is a sheath-like structure encased in meninges (arachnoid, dura), and the CSF in the subarachnoid space is freely accessible. An increase or decrease in fluid in the subarachnoid space can cause the ONSD to widen or narrow (10-12). The validity of using ultrasound measurements of the ONSD to assess intracranial pressure has been demonstrated, and this noninvasive and safe method has been used to assist in clinical diagnosis (13-16).

It is hypothesized that the occurrence of PDPH can be predicted by ONSD. This will be beneficial to patients undergoing spinal anesthesia, especially those with high-risk factors for PDPH (thicker needle is used, low body mass index, suffering headache before lumbar puncture, PDPH has occurred before) (1,17,18).So that timely intervention can be carried out in advance, which greatly reduces the occurrence of this short- to long-term complication and improves the patient's hospital experience. In the present study, we aimed to analyze the potential correlation between ONSD and PDPH after combined spinal-epidural anesthesia in women undergoing cesarean section. We also attempted to explore the threshold of ONSD for the occurrence of PDPH.

Methods

Study Population

This prospective observational clinical study was conducted at Chaohu Hospital, Anhui Medical University, from October 18, 2021, to April 28, 2022, in 163 pregnant women, ASA I or ASA II, aged 18-40 years, who underwent cesarean section under combined spinal-epidural anesthesia. Approval was obtained from the local ethics committee, and written informed consent was obtained from the patients. These explorations were declared on ClinicalTrials.gov (ChiCTR2100051934) prior to starting this study.

All pregnant women aged 18-40 years undergoing cesarean delivery under combined spinal-epidural anesthesia met the inclusion criteria. Exclusion criteria included patient refusal, ASA class III and IV patients, hypertensive disorders during pregnancy, any contraindications to local anesthesia (e.g., local infection at the injection site), coagulation disorders, history of allergy to the local anesthetics used, eye disease or optic nerve damage, and conditions that could lead to changes in intracranial pressure (cerebrovascular disease, hemorrhage, intracranial tumors, etc.).

Preoperative Assessment

Preoperative visits to all participating patients before surgery can help reduce preoperative anxiety and establish a good doctor-patient relationship. Explain to the patient the anesthesia plan and the advantages and possible side effects of combined spinal-epidural anesthesia. Inform the patient of the purpose and importance of the study and the operations that need to be performed on the patient, and obtain the patient's consent.

Procedure

Inform all patients to lie in a supine position with their eyes closed. Place a film over their eyes to isolate the gel, as it may cause discomfort to the patient. After covering the film with the gel directly above the eye, the ultrasound probe is placed on the pre-applied gel. The optic nerve sheath is measured 3 mm behind the eye (19). Two measurements are taken on the lateral

(probe horizontal) and sagittal (probe vertical) planes of each eye 4 times in total, and the average is recorded as the final value (20).

Intraoperative Protocol

The anesthetist enters the operating room in advance, tests the anesthesia machine, checks the monitoring instruments, and prepares the emergency drugs. Once the patient is in the operating room, ECG monitoring, noninvasive blood pressure monitoring, and oxygen saturation monitoring are performed.

Administer oxygen (5 L/min) by face mask to the patient, continuing this treatment until the end of the operation. Wait until the patient is stable and assess the ONSD as a basal value (T0) by following the above standard procedure. After the nurse establishes peripheral venous access, all patients are preloaded intravenously with 15 mL/kg sodium lactated Ringer's solution. Patients are placed in a supine position with the left knee flexed so that the lumbar intervertebral space is fully opened. Combined spinal-epidural anesthesia is performed in the L2-3 or L3-4 spinal space through the bypass approach. An 18-gauge epidural puncture needle and a 25-gauge lumbar puncture needle are used. After the free flow of CSF is seen, the drug (2 mL 0.75% ropivacaine hydrochloride + 1 mL 10% glucose injection) is injected at a rate of 5 s/mL. Immediately after the injection, an epidural tube is quickly placed and inserted into the epidural space to a length of 3-4 cm. Sensory block is achieved with T4-6 sensory skin planes and Bromage motor scores with adequate motor block before the surgical incision. ONSD is measured 10 minutes after injection (T1) and at the end of surgery (T2). The heart rate (HR), mean arterial pressure (MAP), ECG, and oxygen saturation are monitored continuously intraoperatively, and maintenance fluids are given at a rate of 10 mL/kg/hour throughout the operation.

Postoperative Protocol

In this study, patients were followed up at 24 hours (T24), 48 hours (T48), and 72 hours (T72) postoperatively to evaluate ONSD. All assessments were performed in a comfortable and quiet environment and when the patient was emotionally stable. At the same time, all patients were asked about the occurrence of headache and then were evaluated and diagnosed. PDPH is diagnosed according to the International Classification of Headache Disorders (ICH-III) guidelines. There are 4 criteria for diagnosing PDPH, including a headache that occurs within 5 days of dural puncture, worsens within 15 minutes of sitting or standing, improves within 15 minutes of lying down, and is accompanied by at least one of the following: neck stiffness, nausea, photophobia, and tinnitus that resolves spontaneously within one week or 48 hours after effective treatment of spinal fluid leak.

All measurements were performed by the same anesthetist with at least 3 years of experience in the use of ultrasound. ONSD measurements were performed using an ultrasound machine with a 13-6 MHz ultrasound frequency probe. All diagnoses and evaluations of PDPH were performed by another anesthesiologist in a blinded manner so that subjective factors affecting the study results were avoided. Patients were divided into a PDPH group and a non-PDPH group according to follow-up results.

Age, weight, height, ASA, lumbar puncture location, and number of lumbar puncture attempts were also recorded for all patients.

Statistical Analysis

Based on the pre-experimental results, a sample size of 156 was calculated using G*Power 3.1.9.7 software with a 95% confidence interval and 80% test power. Statistical analysis of the data was carried out using GraphPad Prism 9.3.1 (GraphPad Software, La Jolla, CA). According to the type of data, qualitative data were represented as number and percentage; quantitative data were represented by mean ± SD. The following tests were used to test differences for significance: we used a t-test (all quantitative data meet normality, independence, and homogeneity of variance) to compare means between the 2 groups for normally distributed, continuous data (e.g., age, height, and weight), and a chi-squared test to compare proportions (e.g., ASA classification, lumbar puncture location, number of puncture attempts, whether ONSD recover at T2); a continuity correction chi-squared test to analyze the number of puncture attempts and whether ONSD recovers at T2; a Pearson's chi-squared test to analyze ASA classification and lumbar puncture location; ONSD to predict PDPH was studied using receiver operator characteristic (ROC) curves. Statistical significance was accepted as $P < 0.05$. For each ROC curve, the optimal cutoff point of ONSD with maximal sensitivity and specificity for predicting PDPH was calculated.

Results

A total of 163 patients were recruited for this study. Seven patients were excluded: 5 refused to par-

ticipate in the study, and 2 met the exclusion criteria. No patient was excluded from follow-up due to missing data. One hundred fifty-six of whom completed the full study and follow-up. The clinical course of these 156 women during the study period is shown in Fig. 1.

The ages of patients ranged from 21 to 40 years, with a mean of 30.54 ± 4.00 years. All patients completed the 3-day follow-up. Twenty-four patients (15%) developed PDPH, and statistical analysis showed no significant differences between the PDPH and non-PDPH groups in terms of age, height, weight, ASA, lumbar puncture space, or number of lumbar puncture attempts (Table 1).

There was no statistically significant difference in ONSD between the PDPH group and the non-PDPH group at T0 ($P = 0.346$) and T1 ($P = 0.181$). There was a statistically significant difference in ONSD between the 2 groups at T2 ($P < 0.0001$), T3 ($P < 0.0001$), T4 ($P < 0.0001$), T5 ($P < 0.01$), with patients in the PDPH group having a significantly smaller ONSD. Compared with T0, the ONSD of T1 decreased significantly in the PDPH group ($P < 0.0001$) and the non-PDPH group ($P < 0.0001$) (Fig. 2).

We found that the risk of PDPH was significantly higher in women who did not show an upward trend in ONSD at T2. Exposure factors (with no recovery in ONSD at T2) were strongly associated with PDPH (Relative Risk [RR] 5.022; 95 confidence interval [CI] 3.343 to 7.508, $P < 0.0001$) (Fig. 3).

The results of the ROC analysis of the ONSD at different time points for predicting PDPH are presented in Fig. 4 and Table 2; in summary, ONSD at T24 was the most accurate parameter for predicting PDPH (Area Under Curve [ACU] 0. 9787, $P < 0.0001$, cutoff value 0.40 cm, sensitivity 92%, specificity 94%) (Fig. 4, Table 2).

Discussion

In this study, we observed a significantly lower

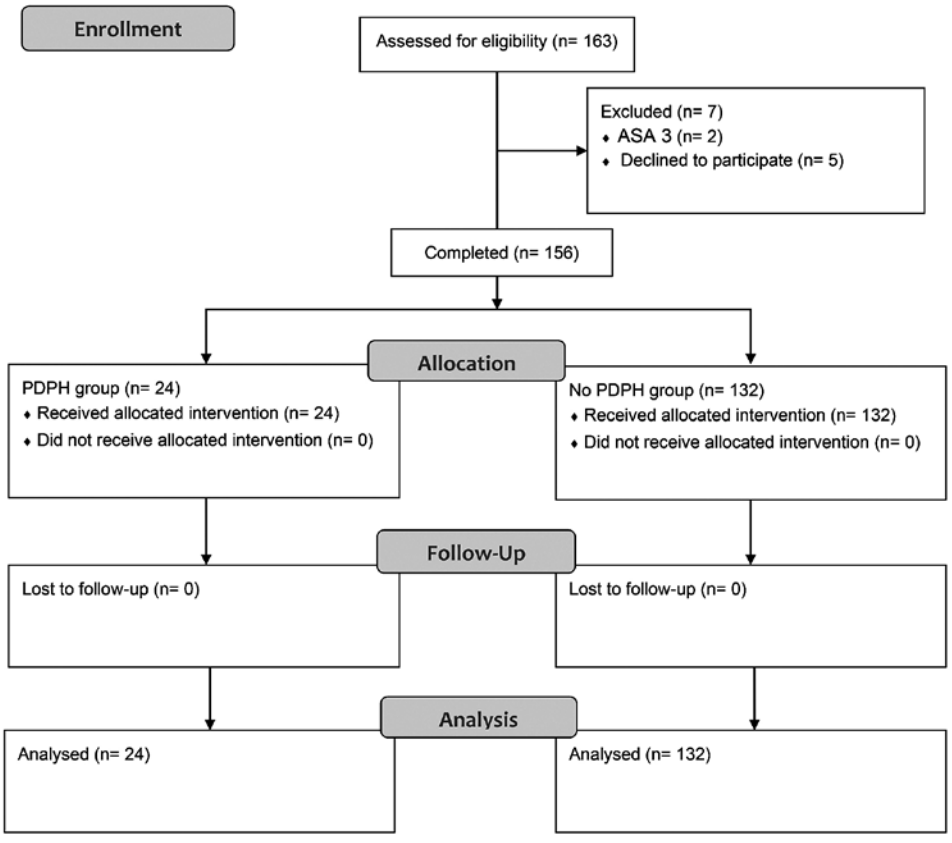

Fig. 1. *Clinical course of study patients.*

Table 1. *Patient characteristics.*

		Patients without PDPH (n 132)	Patients with PDPH (n 24)	*P* value
Age (years)	Mean ± SD Median (Min-Max)	30.31 3.98 31 (21-40)	31.83 3.91 33(26-39)	[a]0.09
Weight (kg)	Mean ± SD Median (Min-Max)	73.31 10.50 72 (50-107)	72.81 13.81 72.75 (40-110)	[a]0.84
Height (cm)	Mean ± SD Median (Min-Max)	161.0 4.79 160 (149-175)	159.4 3.55 160 (152164)	[a]0.13
ASA classification, n (%)				[b]0.41
	I	108 (81.82)	18 (75.00)	
	II	24 (18.18)	6 (25.00)	
Lumbar puncture location, n (%)				[b]> 0.99
	L2-3	93 (70.45)	17 (70.83)	
	L3-4	39 (29.55)	7 (29.17)	
Number of puncture attempts, n (%)				[c]0.25
	One	121 (91.67)	20 (83.33)	
	Two	11 (8.33)	4 (16.67)	

[a]: Student t test; [b]: Pearson's chi-squared test; [c]: Continuity correction chi-squared test
Abbreviations: SD, standard deviation; ASA, American Society of Anesthesiologists; PDPH, postdural puncture headache; L, lumbar; N, total number of patients in each group

ONSD in women who developed PDPH than in women without PDPH (0.44 ± 0.03 cm vs 0.36 ± 0.02 cm) (Fig. 2). The ONSD value at 24 hours after spinal anesthesia (T 24) was the best predictor of PDPH, with a cutoff value of < 0.40 cm, a sensitivity of 92% and a specificity of 94%. We also observed that women whose ONSD decreased consistently between T0 and T2 and did not recover after the decrease were more likely to experience PDPH, with a strong association (RR 5.022). Therefore, this assessment could be a new way to predict PDPH. This discovered pattern greatly facilitates the use of ultrasound measurement of ONSD as an aid in the diagnosis and differential diagnosis of PDPH, allows early screening of patients at risk of developing PDPH before it occurs as well as timely interventions to prevent its occurrence for the benefit of these women.

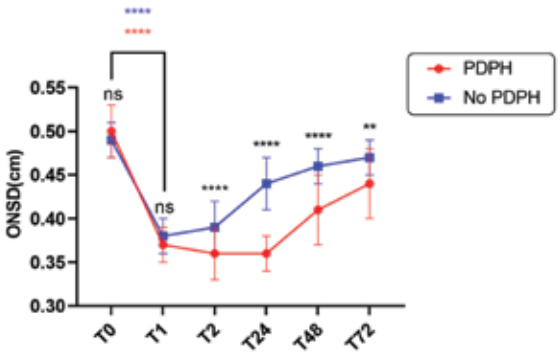

Fig. 2. *The ONSD measurement values of the two groups of puerperae at different times. Ns no significance, **P < 0.01, ****P < 0.0001.*

Since Karl August Bier reported on PDPH in the late 1890s, this serious complication has become more widely recognized. ICHD III classifies PDPH as a headache caused by a nonvascular intracranial disease (21). The attacks may be accompanied by neck pain or stiffness, photophobia, tinnitus, hearing loss, and nausea (22). The best way to prevent PDPH is to use a small-bore needle. Once PDPH occurs, in addition to epidural blood patching (EBP), both pterygopalatine and occipital nerve blocks have been shown to be effective in relieving neck stiffness and nausea without side effects (23,24).

In 1997, Hansen, H C (25) infused Ringer's solution into the patient's subarachnoid space while monitoring the optic nerve using ultrasound instruments and confirmed a strong correlation between CSF pressure and ONSD (r = 0.78). PDPH occurs mainly when CSF leaks cause a decrease in intracranial pressure (ICP), resulting in an upright headache. We hypothesized that monitoring changes in ICP in patients with multiple risk factors for PDPH using ONSD parameters might help predict the occurrence of PDPH.

The mean ± SD of the ONSD in the 156 Chinese adult women in this study was 0.51 ± 0.02 cm. Han Chen et al (26) used B-scan ultrasound to determine ONSD reference values in a cohort of 519 healthy Chinese adults. They found an ONSD of 0.51 0.05 cm in women. This is similar to the results of this study. In contrast, Lijuan Wang et al(19) measured an ONSD of 0.32 ± 0.01 cm in underweight women, 0.33 ± 0.02 cm in normal-weight women, 0.34 ± 0.02 cm in overweight women and 0.37 ± 0.01 cm in obese women in a study of 230 healthy Chinese adults. These findings are different from the results of this study. We believe that this difference may be due to differences in different regions.

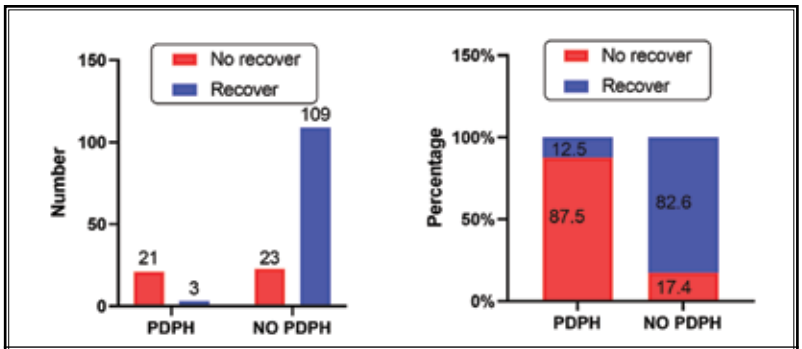

Fig. 3. *Comparison of the PDPH group and the non-PDPH group between recovery and nonrecovery of the T2 ONSD.*

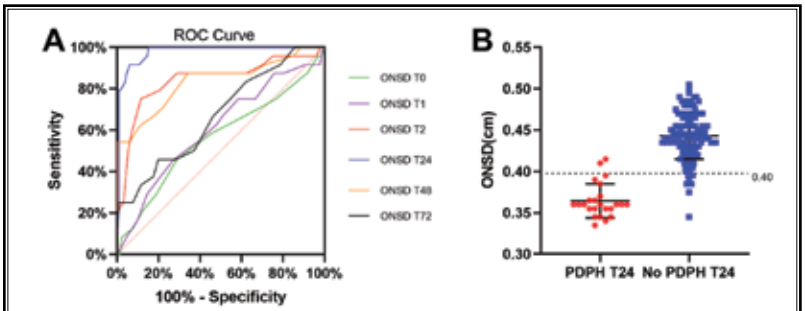

Fig. 4. *A: ROC curve of the ONSD cutoff for PDPH prediction. B: T24 ONSD predicted PDPH cutoff.*

In subjects with PDPH, the ONSD, while headache was present, was significantly smaller than the ONSD in the absence of headache (Fig. 2). This is consistent with the results of Ahmet Besir et al (20). In their study, the ONSD in the PDPH group (n = 20) vs the non-PDPH group (n = 20) was 3.8 ± 0.2 mm vs 3.2 ± 0.3 mm; *P* 0.001. Ahmet Besir et al also assessed the degree of headache in patients using the Numeric Rating Scale (NRS) and observed that in patients with low cranial pressure-induced headache, headache severity was inversely correlated with ONSD, with higher NRS scores being associated with a greater reduction in ONSD. However, they did not give a threshold value for ONSD in the event of PDPH.

The best time to predict PDPH using ONSD is 24 hours after the puncture. Sherif MS Mowafy et al (27) also confirmed that 24 hours after puncture is the best time to predict PDPH using the Gosling pulsatility index (PI) measured by Doppler ultrasound. Although different from the variables measured by Sherif MS Mowafy et al, there was agreement in the timing of the prediction of PDPH. This may be due to some potential association between PI and ONSD.

We have tried to explain this observation by saying that combined spinal-epidural anesthesia leads to a continuous leakage of CSF due to a perforation in the arachnoid. The size of the puncture hole is the most important risk factor for the rate of loss, and the amount

Table 2. *Accuracy of ONSD parameters at different times of measurement in predicting PDPH.*

Variable	Cutoff	AUC	*P*	Sensitivity (%)	Specificity (%)
ONSD T0	< 0.50	0.5632	< 0.332	46	71
ONSD T1	< 0.36	0.6061	< 0.100	46	73
ONSD T2	< 0.37	0.8433	0.000	55	82
ONSD T24	< 0.40	0.9787	0.000	92	94
ONSD T48	< 0.40	0.8351	0.000	54	100
ONSDT72	< 0.45	0.6695	< 0.008	46	80

ONSD, optic nerve sheath diameter; PDPH, postdural puncture headache; ONSD T0, ONSD measured before spinal anesthesia; ONSD T1, ONSD measured 10 min after spinal; ONSD T2, ONSD measured at the end of surgery; ONSD T24, ONSD measured 24 h after spinal anesthesia; ONSD T48, ONSD measured 48 h after spinal anesthesia; ONSD T72, ONSD measured 72 h after spinal anesthesia; AUC, Area under the curve; CI, confidence interval.

of CSF lost (28). Women in the high-risk group are less able to heal themselves and are more likely to develop PDPH if the rate of loss is greater than the rate of production, and CSF is not replenished in a timely manner.

Interestingly, a study by Pamela Angle et al(29) found that the obstetrician instructed 23 women to actively push in the second stage of labor, and 74% of them developed headaches; only 10% of the 10 women who did not actively push developed headaches. The researchers explained that this was because active downward pressure during the second stage of labor leads to a significant increase in CSF pressure, increasing the risk of CSF leakage. Similarly, obstetrician compressions on the abdomen during cesarean section assist in labor, which increases intra-abdominal pressure, leading to increased CSF pressure and accelerating the rate of CSF loss even more. This may be one of the reasons for the higher incidence of maternal PDPH and supports our interpretation.

Limitations

There are certain limitations in this study that need to be addressed, this was a single-center study with a relatively small sample size of patients, and a large amount of data is still needed to confirm the results of this study. Another limitation is that 90% of patients will experience low blood pressure after spinal anesthesia, causing dizziness, nausea, vomiting, etc. (30). At this time, the patient's emotion is unstable and leads to non-cooperation, resulting in errors in the ONSD T1 measurement.

Conclusions

In conclusion, our findings demonstrate a potential correlation between ultrasound measurements of ONSD and PDPH that has not been reported before. This may later become a useful predictor of PDPH and deserves further study. We also predicted a cutoff value for ONSD, which is not present in the current knowledge base. Of course, this will require a large number of clinical studies to validate our findings and further improve them.

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