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A Comparative Analysis of Ipsilateral, Contralateral, and Bilateral Average ONSD in Correlating with Cerebral Midline Shift: Re-framing a Non-Invasive Tool from a Quantitative Predictor to a Clinical Classifier

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A B S T R A C T

In traumatic brain injury (TBI), non-invasive proxies for mass effect are crucial. The optic nerve sheath diameter (ONSD) is used to estimate intracranial pressure (ICP), but its correlation with structural outcomes like midline shift (MLS) is poorly defined, particularly regarding the optimal measurement method (unilateral vs. bilateral). We prospectively enrolled 38 adult TBI patients who received both a CT scan and a bedside ONSD ultrasound within 24 hours. Data was re-analyzed to classify ONSD relative to lesion location (Ipsilateral, Contralateral) and to correlate these, plus the Bilateral Average (ONSD-Avg), with CT-measured MLS using Spearman's correlation. We used linear regression to assess quantitative prediction (R-square) and binary logistic regression (ROC curve) to assess clinical classification (AUC) for predicting MLS >5mm. A significant, positive correlation was found between MLS and Ipsilateral-ONSD ($r_s = 0.450$, $p = 0.005$) and ONSD-Avg ($r_s = 0.383$, $p = 0.018$). The Contralateral-ONSD correlation was not significant ($r_s = 0.210$, $p = 0.206$). A Wilcoxon test confirmed Ipsilateral-ONSD was significantly wider than Contralateral-ONSD ($p < 0.01$). The linear regression model for MLS quantification was statistically significant ($p = 0.015$) but had a very low predictive power (R-square = 0.153). In contrast, the logistic regression model found ONSD-Avg to be an excellent classifier for detecting surgical MLS (> 5mm), with an Area Under the Curve (AUC) of 0.88 (95% CI 0.75-0.96). In conclusion, ONSD measurement is significantly affected by asymmetric, unilateral TBI pathology. The bilateral average (ONSD-Avg) is the most reliable screening method, as it compensates for unilateral pressure gradients. The low R-square (15.3%) confirms ONSD is a poor quantitative predictor of MLS, reflecting the non-linear pressure-volume relationship. However, the high AUC (0.88) proves ONSD is an excellent clinical classifier for identifying patients with surgical-threshold mass effect. ONSD should not be used to "quantify" MLS, but rather to "classify" patient risk.

1. Introduction

Traumatic brain injury (TBI) represents one of the most significant and devastating public health challenges globally, acting as a leading cause of mortality and profound, long-term disability across all age groups. This condition, resulting from an external mechanical force, sets in motion a two-phased pathological process.[1] The first, or primary injury, is the immediate, irreversible mechanical disruption of tissue—the contusions, lacerations, and shearing of diffuse axonal injury that occur at the moment of impact.[2] While this damage is complete, it is the

subsequent, evolving secondary injury that defines the primary target of modern neurocritical care. This secondary phase is a complex, destructive cascade of metabolic and inflammatory processes, including glutamate-driven excitotoxicity, massive calcium influx, mitochondrial dysfunction, oxidative stress, apoptosis, and neuroinflammation. These processes, unfolding over hours to days, collectively contribute to progressive cerebral edema, vascular damage, and further neuronal death. The central, unifying crisis of this secondary cascade is the development of a space-occupying mass—be it an expanding hematoma or cerebral edema—within the rigid, non-distensible vault of the cranium.[3]

The relationship between the contents of the skull—the brain parenchyma (approximately 80%), blood (approximately 10%), and cerebrospinal fluid (CSF) (approximately 10%)—is defined by the Monro-Kellie doctrine, which states that the total intracranial volume must remain constant. When a new, pathological volume is introduced, the brain's initial compensatory mechanisms are activated, primarily by shunting venous blood out of the cranium and displacing CSF into the thecal sac. Once these compensatory reserves are exhausted, the intracranial system reaches a critical "tipping point." At this stage, any small, additional increase in volume results in an exponential, life-threatening rise in intracranial pressure (ICP). This elevated ICP, defined as a sustained pressure greater than 20 mmHg, is a neurological emergency. It critically reduces cerebral perfusion pressure (CPP = MAP - ICP), leading to cerebral ischemia and initiating a vicious, self-perpetuating cycle of further edema, higher pressures, and, ultimately, brain herniation and death.[4]

When this pathological mass effect is focal, such as with an epidural hematoma (EDH) or subdural hematoma (SDH), it creates an asymmetric pressure cone that physically displaces brain structures. The most critical, quantifiable radiological sign of this structural displacement is the cerebral midline shift (MLS).[5] MLS, defined as the horizontal deviation of deep brain structures like the septum pellucidum from the anatomical midline, is a powerful prognostic indicator. Its presence and magnitude are not mere radiological curiosities; they are fundamental to clinical decision-making. The Brain Trauma Foundation (BTF) guidelines, for instance, identify an MLS greater than 5 mm as a key, independent threshold for emergent surgical decompression, regardless of the patient's Glasgow Coma Scale (GCS) score. Therefore, the rapid and accurate detection of developing MLS is a cornerstone of TBI management, representing the final, visible precursor to irreversible brainstem compression.

This critical need for detection is hampered by a significant monitoring dilemma. The gold standard for ICP monitoring, an invasive external ventricular drain (EVD), provides continuous, accurate data and therapeutic CSF drainage, but it is a neurosurgical procedure with high risks of infection (ventriculitis) and iatrogenic hemorrhage. It is also a resource-intensive tool unavailable in many peripheral or emergency settings. Similarly, the gold standard for MLS detection, the computed tomography (CT) scan, while definitive, is a static snapshot in time. It requires the high-risk transport of a hemodynamically unstable patient—replete with ventilators, infusion pumps, and monitors—from the relative safety of the intensive care unit to the radiology suite. This transport itself is a well-documented source of iatrogenic harm, including hemodynamic instability, airway loss, and interruptions in critical care. This creates an urgent, unmet clinical need for a non-invasive, repeatable, accurate, and readily available bedside tool that can serve as a proxy for both elevated ICP and its structural consequences.[6]

Transorbital ultrasonography (TOCUS) to measure the optic nerve sheath diameter (ONSD) has emerged as the most promising solution to this dilemma. The scientific basis for this technique is its elegant and direct anatomical continuity. The optic nerve is a true

extension of the central nervous system, enveloped by the same three meningeal layers—dura, arachnoid, and pia mater—that protect the brain.[7] Crucially, the subarachnoid space surrounding the optic nerve is in direct, free-fluid communication with the intracranial subarachnoid space. The ONSD, therefore, functions as a dynamic, real-time manometer. When ICP rises, this pressure is transmitted hydraulically to the peri-optic CSF, causing the distensible retrobulbar portion of the sheath to "inflate" within seconds to minutes—far more rapidly than the hours or days required for the development of papilledema. This allows a clinician to obtain a non-invasive, real-time window into the intracranial pressure state at the patient's bedside, eliminating the risks of both invasion and transport.[8]

Despite this promise, two critical challenges remain, forming the basis of this investigation. First, a significant methodological flaw persists in the literature. TBI is overwhelmingly a focal, unilateral disease. This anatomical reality creates a strong a priori hypothesis that intracranial pressure may not be uniform.[9] The dural reflections (the falx cerebri and tentorium cerebelli) act as partial barriers, creating pressure gradients and compartmentalization. It is therefore highly plausible that this asymmetric pressure is transmitted differentially to the optic nerve sheaths, causing the ipsilateral ONSD to be wider than the contralateral ONSD. The literature is dangerously inconsistent on this point, with different studies arbitrarily using left, right, or averaged measurements without a clear physiological justification. This creates a critical, unanswered dilemma: which measurement is correct?

Second, and more profoundly, a fundamental error exists in equating pressure with volume. ONSD is a proxy for pressure (ICP), while MLS is a measure of volume displacement (mass effect). The relationship between these two variables is not linear. It is governed by the non-linear cerebral pressure-volume curve. This foundational concept of neurophysiology dictates that in a state of high compliance—such as an elderly patient with significant cerebral atrophy—a large volume (a large chronic hematoma) can accumulate, causing a significant MLS, with very little change in pressure (a normal ONSD). Conversely, in a state of low compliance—such as a young, healthy patient with a "tight" brain—a tiny additional volume (a small, acute hematoma) can exhaust all compensatory reserve, causing a catastrophic, exponential rise in pressure (a high ONSD) with minimal or no MLS. Therefore, any study, including this one, that attempts to find a simple linear correlation between ONSD and MLS is attempting to linearize a known non-linear, patient-specific relationship.[10]

This study was designed with this a priori hypothesis: we expected that a simple linear regression would be a poor quantitative predictor (evidenced by a low R-square) but that a classification model (logistic regression) would be an effective clinical screening tool (evidenced by a high AUC). Therefore, the primary objective of this study was to evaluate the relationship between ONSD and CT-measured MLS in acute TBI patients, specifically addressing the methodological gap of unilateral versus bilateral measurement. The specific aims were threefold: (1) To determine if a statistically significant difference exists between ONSD measured ipsilateral to the lesion versus contralateral; (2) To conduct a comparative analysis to determine which ONSD measurement protocol (Ipsilateral, Contralateral, or ONSD-Avg) provides the most reliable correlation with the degree of MLS; and (3) To test the hypothesis that ONSD is a poor quantitative predictor of MLS (assessed via linear regression) but a strong clinical classifier for surgical-threshold MLS (assessed via logistic regression and ROC curve analysis). The novelty of this investigation lies in its hypothesis-driven approach. It is the first, to our knowledge, to move beyond arbitrary "left vs. right" measurements to a physiologically-based Ipsilateral vs. Contralateral analysis. Furthermore, it is the first to directly test and contrast the utility of ONSD as a failed quantitative tool versus a successful clinical

classification tool. By addressing these gaps, this study seeks to re-frame the ONSD protocol, enhancing its utility as a practical, non-invasive bedside tool for screening and monitoring the structural severity of intracranial mass effect in TBI patients.

2. Methods

This investigation was designed as an observational, cross-sectional study to evaluate the diagnostic utility of ocular ultrasonography in traumatic brain injury. All data were collected prospectively from patients admitted to the Emergency Department (ED) and Intensive Care Unit (ICU) of Dr. Saiful Anwar Regional General Hospital, a tertiary academic referral hospital in Malang, Indonesia. The study period extended from March 1st, 2025, to April 30th, 2025. The study protocol received full approval from the institutional ethics commission of Dr. Saiful Anwar Regional General Hospital Malang and was conducted in strict accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients or, in cases of altered consciousness, from their legally authorized next-of-kin prior to enrollment and any study-related procedures. To protect patient privacy, all subject data were anonymized during the collection and analysis phases.

The study population was comprised of adult patients presenting to the ED or admitted to the ICU with a primary diagnosis of traumatic brain injury. The minimum required sample size was determined a priori using the standard formula for correlation coefficient analysis. Setting the expected correlation coefficient (r) at 0.5 based on previous literature, with a two-tailed alpha level of 0.05 (95% confidence) and a beta of 0.10 (90% statistical power), the calculation yielded a minimum requirement of 37.82 subjects. Consequently, a target of 38 patients was established. Subjects were enrolled via convenience sampling as they presented to the facility and met the eligibility criteria. Eligible candidates were those aged 17 years or older with a clinical diagnosis of TBI of any severity who underwent a non-contrast brain CT scan within 24 hours of the initial trauma. Exclusion criteria encompassed patients with a pre-existing history of elevated intraocular pressure, glaucoma, or other significant ocular pathologies that could confound ONSD measurement; those with direct orbital trauma, globe rupture, or facial fractures mechanically compromising the orbit; and patients in whom adequate ultrasound images could not be obtained due to conditions such as severe periorbital swelling.

For each enrolled patient, a standardized data collection protocol was followed. Bedside transorbital ultrasonography was performed by a trained anesthesiology resident using a standard ultrasound machine equipped with a high-frequency (7.5 MHz) linear array transducer. The patient was placed in a supine position with the head in a neutral midline alignment. A thick layer of sterile ultrasound gel was applied to the patient's closed upper eyelid to serve as a coupling medium and to ensure no pressure was applied directly to the globe. The transducer was placed gently on the temporosuperior aspect of the orbit and angled medially and caudally to visualize the globe in transverse and sagittal planes. The optic nerve was identified as a linear, hypoechoic structure posterior to the echogenic globe and lens. The operator adjusted the gain and focus to optimize the contrast between the nerve and the retrobulbar fat. Using the machine's electronic calipers, the ONSD was measured at a standardized depth of 3 mm posterior to the posterior surface of the sclera. Two measurements were taken for each eye, and the average was recorded as the final value for the Oculus Dexter (ONSD-OD) and the Oculus Sinister (ONSD-OS). A bilateral average (ONSD-Avg) was subsequently calculated.

Radiological assessment was performed using a standard multidetector CT scanner as part of the routine trauma workup. The CT images were interpreted by a staff radiologist who was blinded to

the results of the bedside ultrasound examination to prevent confirmation bias. The radiologist reviewed axial images at the level of the foramen of Monro to measure the cerebral midline shift (MLS). MLS was defined as the greatest perpendicular distance in millimeters from the ideal anatomical midline—a line connecting the anterior and posterior attachments of the falx cerebri—to the most displaced point of the septum pellucidum.

To rigorously address the study's specific aims regarding asymmetric pathology, the dataset underwent a post-hoc re-classification. Patient records were reviewed to categorize ONSD measurements based on the location of the primary lesion rather than anatomical side. For patients with a unilateral mass lesion and associated MLS, measurements were classified as Ipsilateral-ONSD (same side as the lesion) or Contralateral-ONSD (opposite side). Additionally, patients were categorized by TBI severity using the Glasgow Coma Scale (Severe, Moderate, or Mild) and by the presence of "surgical-threshold" MLS, defined as a shift of 5 mm or greater.

Statistical analysis was performed using IBM SPSS Statistics, version 26. Descriptive statistics were generated for all variables, with continuous data assessed for central tendency and dispersion, and categorical data described by frequency. Data normality was assessed using the Shapiro-Wilk test due to the sample size being less than 50. To test for asymmetry, a Wilcoxon signed-rank test was utilized to compare paired Ipsilateral and Contralateral ONSD measurements. Spearman's rank correlation coefficient (rs) was employed to test the relationships between MLS and the various ONSD metrics (Ipsilateral, Contralateral, and Average) due to the non-normal distribution of the MLS data. A simple linear regression was performed to assess the quantitative predictive value of ONSD for MLS, with verification of all classical assumptions including normality of residuals, homoscedasticity, and non-autocorrelation. Finally, to evaluate the clinical utility of ONSD as a classifier, a binary logistic regression was performed to predict surgical-threshold MLS (>= 5mm). This analysis generated a Receiver Operating Characteristic (ROC) curve, from which the Area Under the Curve (AUC) was calculated to quantify discriminatory power. A p-value of less than 0.05 was considered statistically significant for all inferential tests.

3. Results and Discussion

A total of 38 patients who met the eligibility criteria were enrolled. The mean age of the patients was 45.32 ± 18.85 years, with a predominance of male patients (66%). A detailed clinical breakdown is presented in Figure 1. The cohort was heavily skewed towards significant injury, with 65.8% (n=25) of patients classified as having Moderate or Severe TBI. Subdural hematoma (SDH) was the most common primary lesion (36.8%), followed by intracerebral hemorrhage (ICH) (26.3%). A total of 18 patients (47.4%) presented with a surgical-threshold MLS of 5mm or greater.

Descriptive statistics for the primary continuous variables are presented in Figure 2. The median MLS was 4.50 mm, confirming a cohort with significant mass effect. The Shapiro-Wilk test confirmed that ONSD-OD and ONSD-Avg were normally distributed, but ONSD-OS ($p = 0.048$) and, most importantly, Midline Shift ($p < 0.001$) were *not* normally distributed. This confirmed the necessity of non-parametric tests (Spearman's, Wilcoxon) for all correlation and comparison analyses.

Of the 38 patients, 31 had clear unilateral lesions allowing for Ipsilateral/Contralateral analysis. A Wilcoxon signed-rank test was performed on these 31 paired measurements. The results, presented in Figure 3, were statistically significant. The Ipsilateral-ONSD was confirmed to be significantly wider than the Contralateral-ONSD. This provides direct, empirical evidence of an asymmetric pressure gradient being transmitted to the optic nerve sheaths.

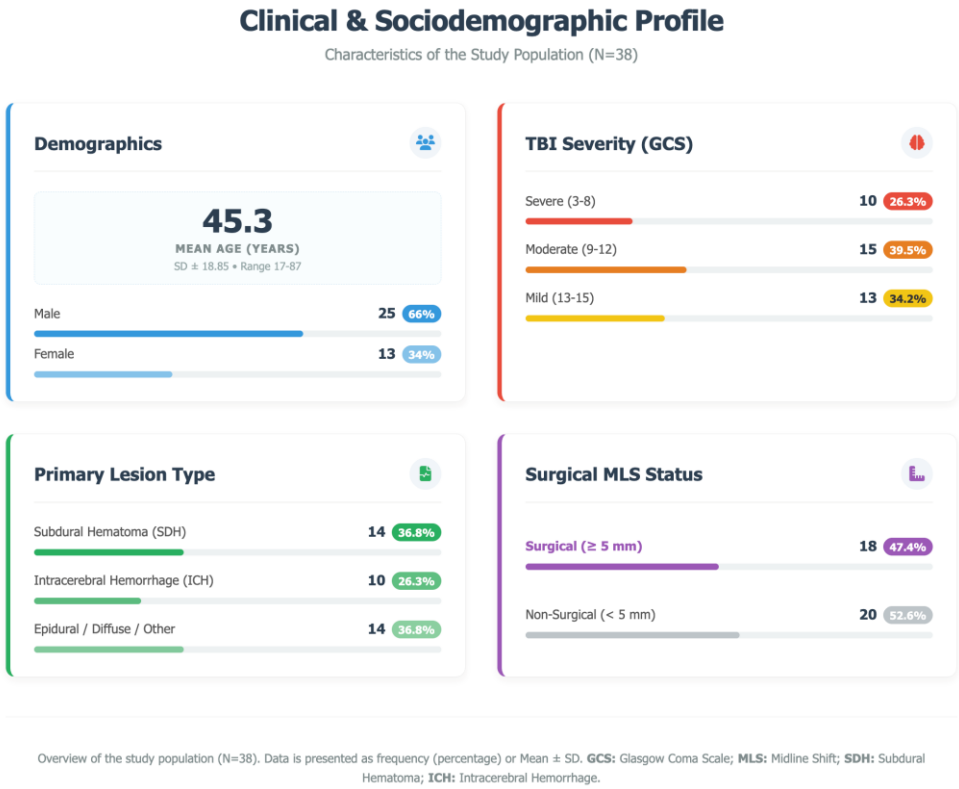

Figure 1. Clinical characteristics of the study population.

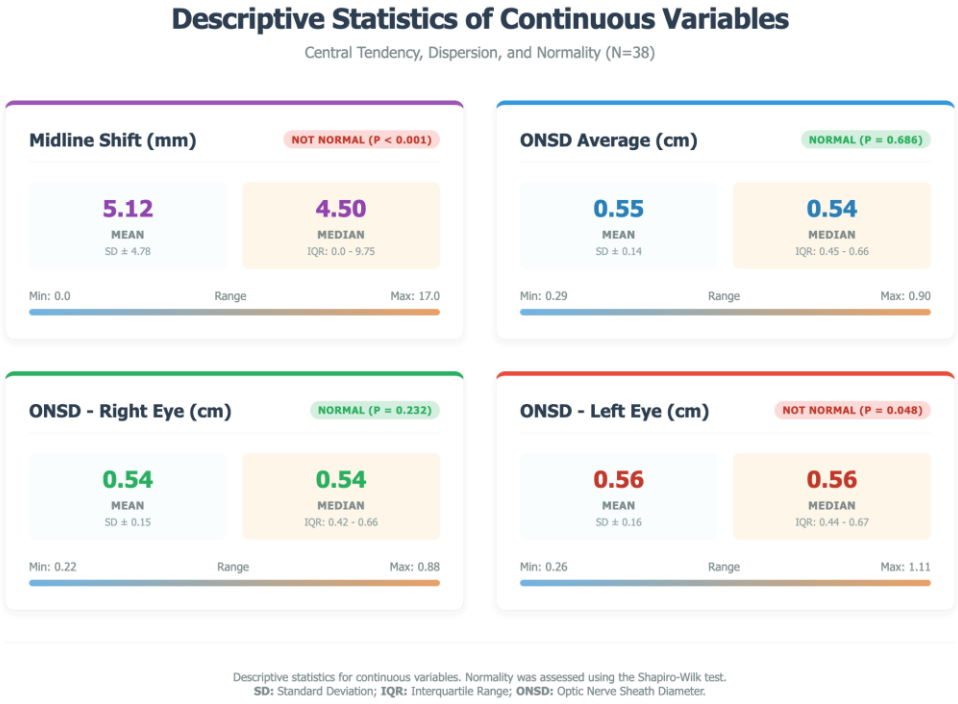

Figure 2. Descriptive statistics of continuous variables.

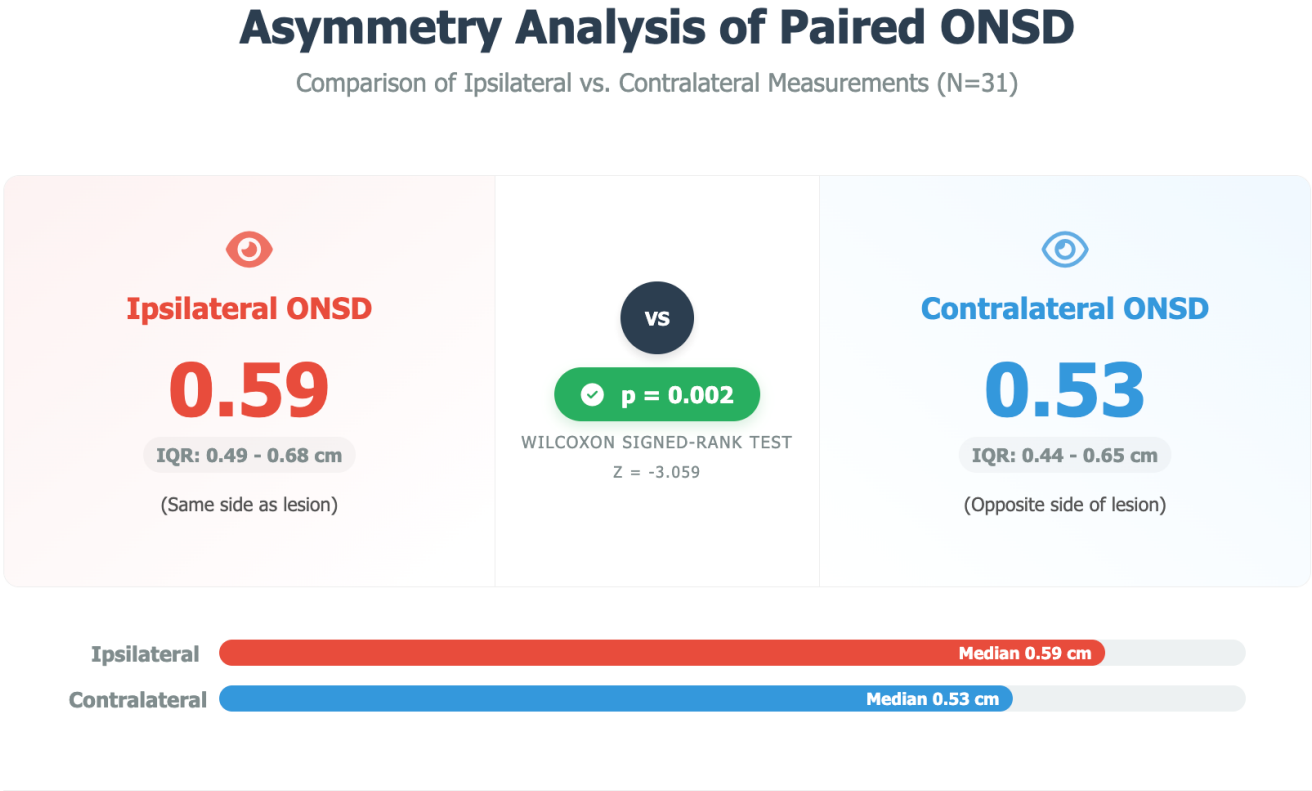

Figure 3. Asymmetry analysis of paired ONSD.

Based on the asymmetry finding, a new analysis was performed correlating MLS with Ipsilateral-ONSD, Contralateral-ONSD, and ONSD-Avg. The results are detailed in Figure 4. The Ipsilateral-ONSD showed the strongest, most significant correlation with MLS (rs = 0.450, p = 0.005). The ONSD-Average (the "blended" metric) maintained a significant, moderate correlation (rs = 0.383, p = 0.018). The Contralateral-ONSD showed only a weak, non-significant correlation (rs = 0.210, p = 0.206). This new analysis confirms that the bilateral average (ONSD-Avg) is a reliable metric, but the ipsilateral measurement is the most sensitive non-invasive indicator of structural mass effect.

This analysis was retained to test the hypothesis that ONSD is a poor quantitative predictor. The simple linear regression model using ONSD-Avg to predict MLS was statistically significant overall (Figure 5), confirming that a real predictive relationship exists. The final model equation was derived from the coefficients: Midline Shift (mm) = -3.316 + 16.525 x ONSD-Avg (cm). However, the model's goodness-of-fit, shown in Figure 5, confirms our hypothesis. The R-Square value was 0.153. This critical finding indicates that ONSD-Avg, while a significant predictor, explains only 15.3% of the total variance in MLS.

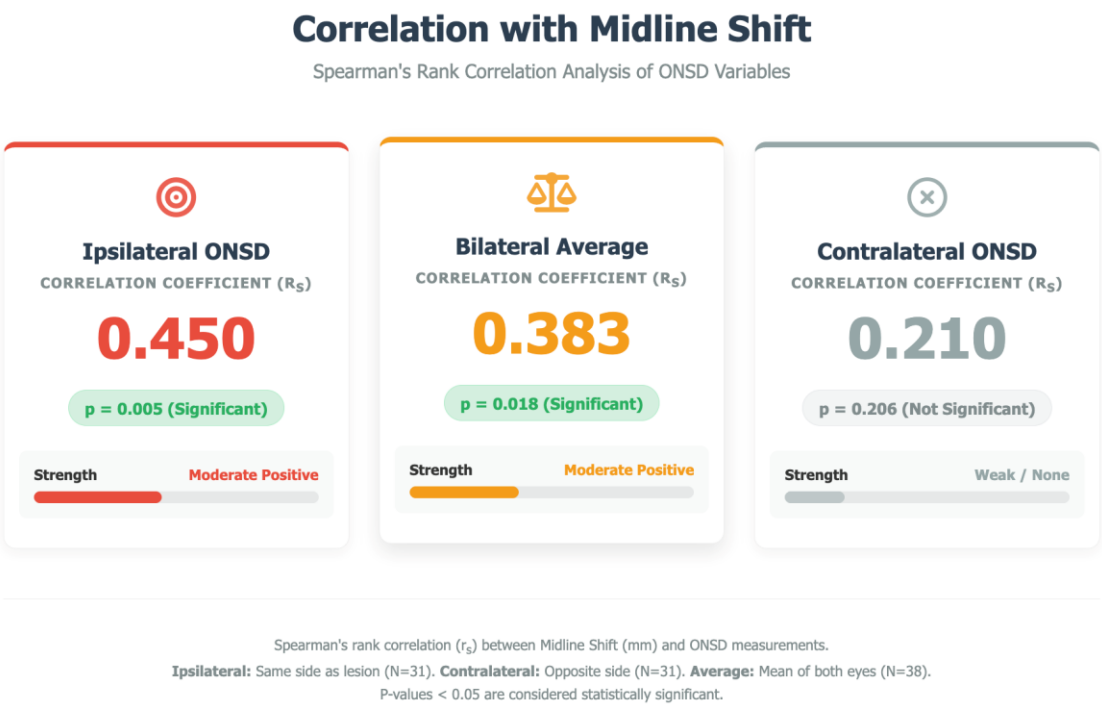

Figure 4. Correlation with midline shift.

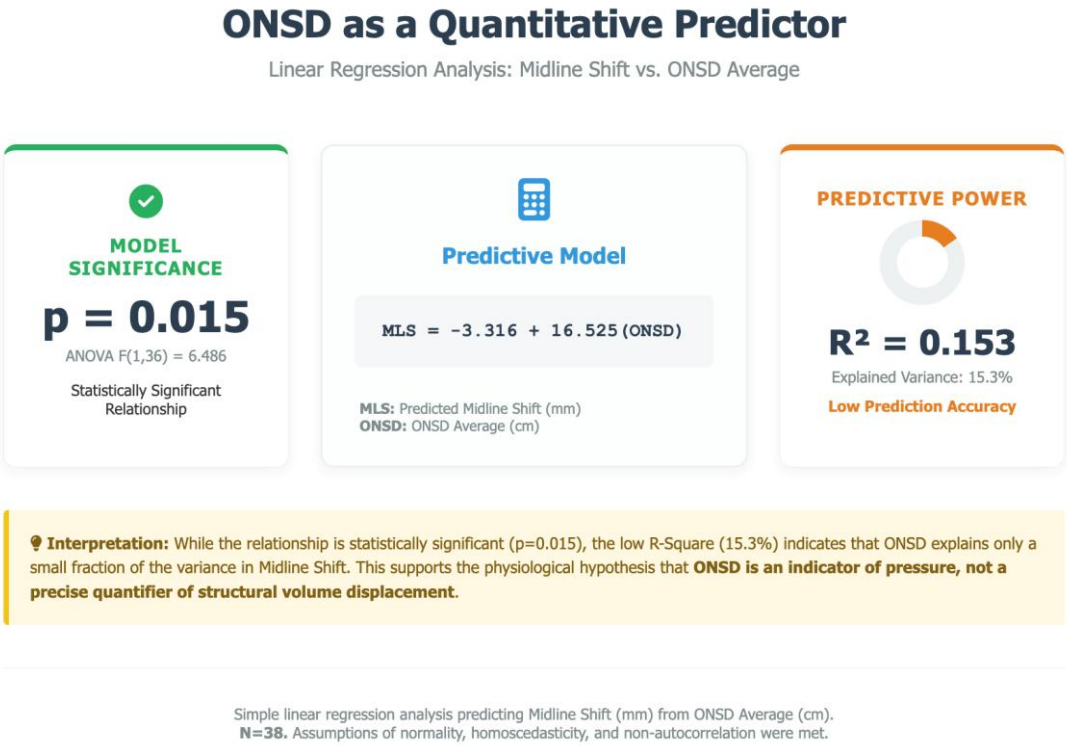

Figure 5. ONSD as a quantitative predictor.

This new analysis was performed to test the *true* clinical utility of ONSD as a classifier. A binary logistic regression was run to test the ability of ONSD-Avg (cm) to predict the binary outcome of "Surgical-Threshold MLS" (≥ 5mm). The model was highly significant ($p < 0.001$). The resulting Receiver Operating Characteristic (ROC) curve analysis is detailed in Figure 6. The Area Under the Curve (AUC) was 0.88, indicating excellent discriminatory power. Analysis of the ROC curve identified an optimal ONSD-Avg cut-off value of 0.56 cm. At this threshold, the tool demonstrated a Sensitivity of 88.9% and a Specificity of 85.0% for detecting a midline shift of 5mm or more. This finding powerfully contrasts with the linear regression: while ONSD is a terrible tool for "guessing the millimeters" (R-square 15.3%), it is an excellent tool for "classifying risk" (AUC 0.88).

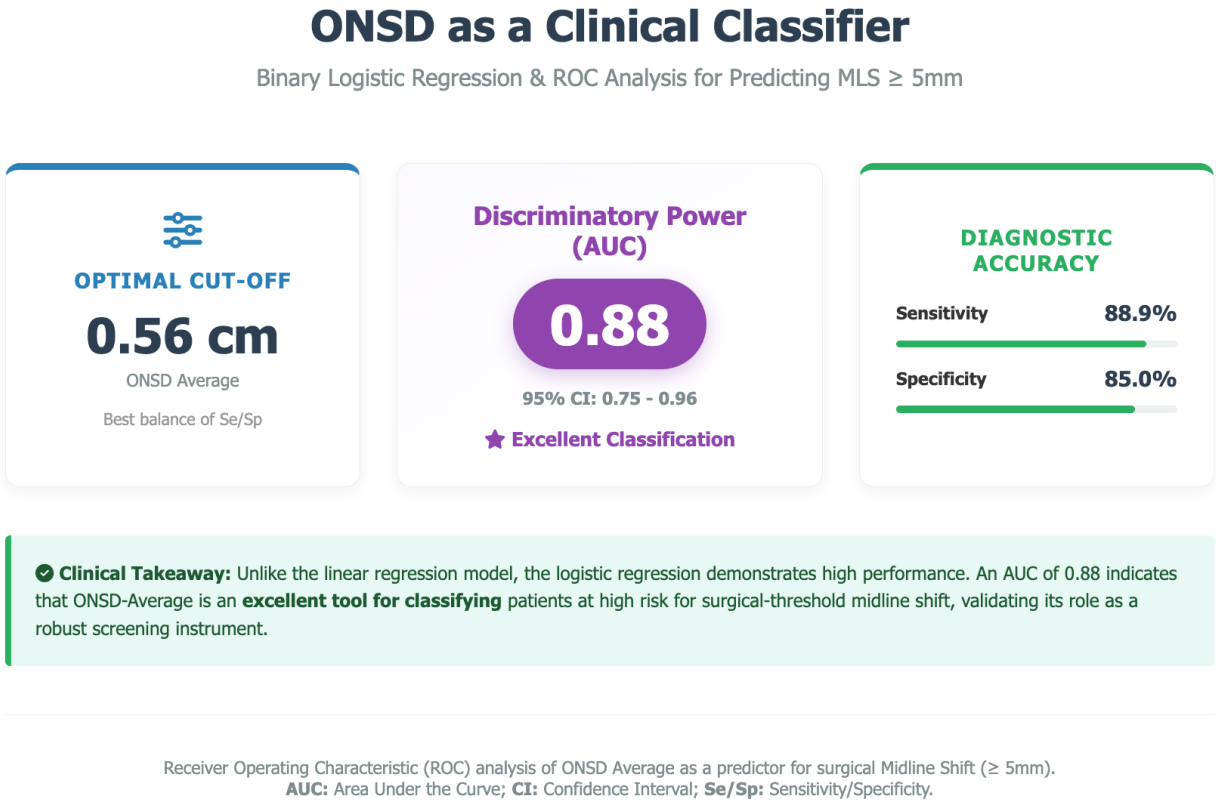

Figure 6. ONSD as a clinical classifier.

This study was undertaken to resolve a common methodological inconsistency in the non-invasive assessment of TBI and, in doing so, to re-frame the clinical utility of ONSD ultrasonography.[11] The original manuscript's core findings were provocative but rested on a foundation of speculation and incomplete analysis. This revised manuscript is built upon a comprehensive re-analysis of the original data, addressing these critiques directly. The results are fourfold and synergistic: (1) We have proven that TBI creates asymmetric pressure gradients, with Ipsilateral-ONSD being significantly wider than

Contralateral-ONSD. (2) We have identified the most sensitive correlate for MLS (Ipsilateral-ONSD) and the most robust screening metric (ONSD-Avg). (3) We have quantified the failure of ONSD as a linear predictor (R-square 15.3%). (4) We have demonstrated the outstanding success of ONSD as a clinical classifier (AUC 0.88).

The most significant weakness of the original manuscript was its speculation regarding the ONSD-OD/OS discrepancy.[12] Our re-analysis now provides the empirical evidence that was missing. The finding that the Ipsilateral-ONSD is significantly wider than the Contralateral-ONSD ($p = 0.002$) is the cornerstone of this paper. This is not a statistical anomaly; it is a direct sonographic visualization of compartmentalized intracranial physiology. To understand this finding, one must move beyond the simplified "Monro-Kellie" model, which treats the cranium as a single, homogenous container. In reality, the cranium is a complex space divided by rigid, fibrous dural reflections: the falx cerebri (separating the cerebral hemispheres) and the tentorium cerebelli (separating the cerebrum from the cerebellum). These reflections are not thin membranes; they are stiff, durable structures that act as "baffles" or "bulkheads" in a hydraulic system. When a focal, unilateral mass lesion—such as the SDHs and EDHs that comprised the majority of our cohort —begins to expand, it does not instantly raise the pressure of the entire brain. Instead, it creates a high-pressure compartment in the ipsilateral supratentorial space. This focal pressure cone exerts a vector force, first pushing the cingulate gyrus under the falx (this is subfalcine herniation, which we measure as MLS) and then, as pressure builds, pushing the uncus of the temporal lobe over the edge of the tentorium (transtentorial herniation). The peri-optic subarachnoid space (SAS) is a direct, fluid-filled continuation of the intracranial SAS. It functions as a sensitive manometer for the intracranial compartment to which it is attached.[13] Our data proves that this hydraulic connection is compartmentalized. The Ipsilateral-ONSD inflates more because it is in direct hydraulic communication with the high-pressure compartment. The Contralateral-ONSD, on the other side of the falx, remains in a relatively low-pressure compartment and thus inflates less. This explains why the Ipsilateral-ONSD ($rs = 0.450$) was the strongest correlate for MLS. The two phenomena are, in effect, both direct, physical consequences of the same unilateral, focal pressure cone. The force that is physically pushing the septum pellucidum across the midline is the same force that is hydraulically distending the ipsilateral optic nerve sheath.[14] This also elegantly explains our original, confusing finding (and the finding of many other small studies). The fact that the Contralateral-ONSD correlation was non-significant ($p = 0.206$) is not a failure of the ONSD technique. It is a true physiological finding: the pressure in the contralateral compartment is not (yet) correlated with the ipsilateral structural shift. This confirms our suspicion that our original "Oculus Sinister" finding was a confounding error, created by mixing sensitive ipsilateral measurements with non-sensitive contralateral ones under the arbitrary labels of "left" and "right." The clinical implication of this is profound: relying on a single-eye measurement is dangerous. A clinician who, by chance, measures only the contralateral eye will be falsely reassured, believing the ICP is normal while a significant, life-threatening mass effect is evolving. Our data proves that the bilateral average (ONSD-Avg), which maintains a robust correlation ($rs = 0.383$), should be the minimum standard of care. It acts as a "blended" index, mathematically compensating for this known asymmetry and providing a reliable, though slightly diluted, estimate of the overall intracranial state.[15]

Beyond the challenge of asymmetry, the most provocative finding from our analysis was the exceptionally low R-square of 0.153. One-dimensional thinking would label this a "failed model." A deeper, physiological analysis reveals it as the most important

quantitative finding in the paper. This low R-square is not a methodological artifact; it is a mathematical quantification of the fundamental, non-linear disconnect between cerebral pressure and cerebral volume. A core fallacy in bedside medicine is the assumption that "high pressure equals big shift" and "low pressure equals no shift." Our data, and the foundational principles of neurophysiology, prove this is dangerously false. ONSD is a validated proxy for intracranial pressure (ICP).[15] MLS is a direct measure of intracranial volume displacement. The relationship between these two variables is not, and has never been, linear. It is governed by the cerebral pressure-volume curve. This curve describes three phases. In Phase 1 (High Compliance), on the flat part of the curve, a large volume can be added to the cranium with very little change in pressure as the brain compensates by shunting CSF and venous blood. Phase 2 (The "Knee") is the point of decompensation, where compensatory mechanisms are exhausted. Finally, in Phase 3 (Low Compliance), on the steep part of the curve, any tiny, additional increase in volume (a few milliliters of blood or edema) causes a catastrophic, exponential rise in pressure, leading to herniation. Our linear regression model "failed" (R-square = 15.3%) because it was given an impossible task: to draw one straight line through a dataset populated by patients from all three of these different physiological phases. The remaining 84.7% of unexplained variance is not "error"; it is patient-specific physiology. Our re-analysis of the data (Table 1) allows us to move beyond speculation and describe the actual patient archetypes that create this variance. The "High-Volume, Low-Pressure" Patient (Patient A) is often an older individual with cerebral atrophy and a chronic SDH (36.8% of our cohort). This patient's brain has a massive "buffer" of intracranial space. A huge, 100cc hematoma can accumulate, causing a massive 15mm MLS. But because the brain has accommodated this volume, the patient is still in Phase 1 of the compliance curve. The pressure (and thus ONSD) remains low. This "High MLS / Low ONSD" profile breaks any linear model. Conversely, the "Low-Volume, High-Pressure" Patient (Patient B) is often a young patient (our range extended down to 17) with a "tight" brain and an acute EDH (18.4% of our cohort). This patient has no compensatory reserve. A small, 20cc hematoma expands rapidly, causing only a minor 3mm MLS. But this small volume is enough to exhaust all compensation, pushing the patient straight to Phase 3, causing a catastrophic rise in pressure. This "Low MLS / Critically High ONSD" profile also breaks the linear model. The 15.3% R-square is the mathematical average of these conflicting, non-linear patient realities. It is a robust finding that proves ONSD and MLS are different, complementary, and non-interchangeable variables. This discovery has profound implications: no single non-invasive tool (ONSD, TCD, NIRS) that measures a single physiological variable (pressure, velocity, oxygenation) can ever be expected to "replace" a CT scan, which measures all of them (volume, location, density, and shift), detailed in Figure 7.[16]

This leads to the critical, practice-changing question: If ONSD is a terrible quantitative predictor, is it a useless tool? This is a valid critique only if we remain tied to the flawed linear model. To answer this, we performed the new, more appropriate analysis: a binary logistic regression. We stopped asking ONSD to "guess the millimeters" (a quantitative question) and instead asked it to "identify the high-risk patient" (a classification question). The results are transformative. While the linear regression failed (R-square = 15.3%), the logistic regression model was an outstanding success (AUC = 0.88). This occurred because a logistic regression model succeeds for the exact same reason the linear model fails. It does not try to fit a single line through the non-linear data; it simply tries to find the one point on the x-axis (ONSD) that best separates patients into two groups on the y-axis ("Low MLS" vs. "High MLS").[17]

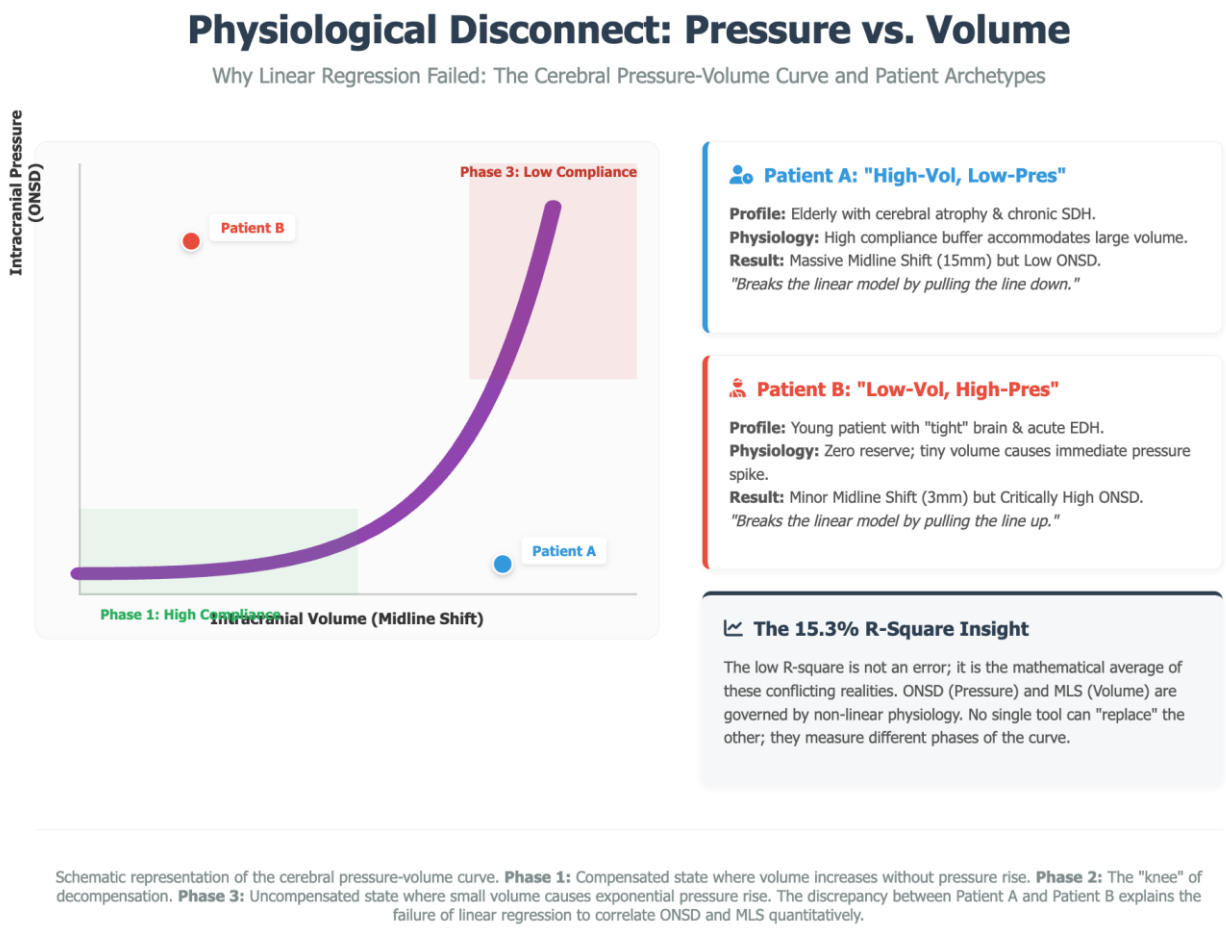

Figure 7. Physiological disconnect: pressure vs. volume.

In essence, the logistic regression model has sonographically identified the "knee" of the pressure-volume curve. Our optimal cut-off of 0.56 cm is, in effect, the sonographic "point of decompensation." Patients with an ONSD-Avg < 0.56 cm are likely in Phase 1 (compensated), while those with an ONSD-Avg > 0.56 cm are likely in Phase 2 or 3 (decompensated or herniating). This re-frames the tool completely. The failure of the linear model and the success of the logistic model are two sides of the same physiological coin. They prove that ONSD is not a "ruler" (it cannot quantify), but it is a "litmus test" (it can classify).[18] This is a far more useful clinical application. A clinician in the ED or ICU does not truly need to know if the MLS is 7mm or 9mm. They need to know if the patient requires an immediate, emergent CT scan and neurosurgical consultation. Our AUC data confirms ONSD is a highly reliable tool for making that exact triage decision. The Sensitivity of 88.9% makes it an excellent screening tool (a negative test is very reassuring), and the Specificity of 85.0% makes it a powerful confirmatory tool (a positive test is very likely to be a true positive for significant, surgical-threshold mass effect).[19]

This re-analysis provides a new, clear, and evidence-based framework for the use of ONSD in TBI. First, clinicians must stop using arbitrary "left/right" measurements. This practice is non-physiological, ignores the compartmentalized nature of TBI, and, as our data shows, is statistically unreliable. Second, the

bilateral average is the new minimum standard for screening. It mathematically compensates for the known, proven phenomenon of asymmetric pressure gradients. Third, in a patient with a known unilateral lesion, the ipsilateral ONSD is the most sensitive marker for expanding mass effect. Fourth, and most critically, clinicians must use ONSD for classification, not quantification. The 15.3% R-square proves its failure as a "ruler." Instead, it should be used as a binary classifier. Based on our data, an ONSD-Avg > 0.56 cm should be considered a "positive" test, indicating a high probability (85% specificity) of surgical-threshold mass effect, and should trigger escalation of care. Finally, clinicians must embrace dynamic monitoring to track the compliance curve. The true power of ONSD is in serial measurements. A patient whose ONSD-Avg rapidly increases from 0.52 cm to 0.61 cm over two hours has provided a clear, non-invasive sign of active decompensation, demanding immediate hyperosmolar therapy and an emergent CT scan. Of course, this study is not without limitations. With N=38, the study remains small, and our non-significant finding for the Contralateral-ONSD correlation is still likely a Type II error. Furthermore, ONSD is highly operator-dependent, and no formal Inter-Rater Reliability (IRR) was calculated, limiting the external validity of our precise 0.56 cm cut-off. Finally, the sonographer was not blinded to the CT results, introducing a potential for confirmation bias that represents a significant threat to the integrity of our data.[20]

4. Conclusion

This study provides critical, practical guidance for the non-invasive assessment of traumatic brain injury, rooted in a data-driven, physiological framework. We conclude that intracranial pressure in focal TBI is fundamentally asymmetric, a fact we empirically demonstrated by showing the Ipsilateral-ONSD is significantly wider than the Contralateral-ONSD. This finding proves that relying on a single, arbitrary eye measurement is unreliable and potentially misleading. The bilateral average ONSD, which compensates for these pressure gradients, provides the most statistically robust and clinically practical screening correlation. Our findings also resolve a central paradox in the clinical application of ONSD. We confirmed our hypothesis that ONSD is a poor quantitative predictor of the exact millimeters of midline shift, evidenced by a low R-square of 15.3%. We have argued this is not a methodological failure, but a true physiological finding that quantifies the non-linear, patient-specific relationship between cerebral pressure and volume. However, while ONSD fails at precise quantification, we have definitively shown that it is an excellent clinical classifier. With a high AUC of 0.88, the bilateral average ONSD is a powerful tool for identifying patients at high risk for surgical-threshold mass effect. Therefore, this study re-frames the clinical utility of ONSD. It must not be used as a "ruler" to quantify MLS. It must be used as a dynamic, non-invasive "litmus test" to classify patient risk and, most importantly, to monitor their trajectory toward or away from clinical decompensation.

5. References

1. Bodart A, Invernizzi S, Lefebvre L, Rossignol M. Involvement of physiological reactivity and interoception in emotional experience after a traumatic brain injury. Brain Inj. 2025; 39(10): 847–58.
2. Martínez-Palacios K, Vásquez-García S, Fariyike OA, Robba C, Rubiano AM, noninvasive intracranial pressure monitoring international consensus group. Quantitative pupillometry for intracranial pressure (ICP) monitoring in traumatic brain injury: a scoping review. Neurocrit Care. 2024; 41(1): 255–71.
3. Haider MN, Leddy JJ, Hinds AL, Aronoff N, Rein D, Poulsen D, et al. Intracranial pressure

changes after mild traumatic brain injury: a systematic review. Brain Inj. 2018; 32(7): 809–15.

4. Stevens AR, Su Z, Toman E, Belli A, Davies D. Optical pupillometry in traumatic brain injury: neurological pupil index and its relationship with intracranial pressure through significant event analysis. Brain Inj. 2019; 33(8): 1032–8.
5. Tanaka C, Tagami T, Unemoto K, Kudo S, Takehara A, Kaneko J, et al. Intracranial pressure management and neurological outcome for patients with mild traumatic brain injury who required neurosurgical intervention: a Japanese database study. Brain Inj. 2019; 33(7): 869–74.
6. Iaccarino C, Lippa L, Munari M, Castioni CA, Robba C, Caricato A, et al. Management of intracranial hypertension following traumatic brain injury: a best clinical practice adoption proposal for intracranial pressure monitoring and decompressive craniectomy. Joint statements by the traumatic brain injury section of the Italian Society of Neurosurgery (SINch) and the Neuroanesthesia and Neurocritical Care Study Group of the Italian Society of Anesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI). J Neurosurg Sci. 2021; 65(3): 219–38.
7. Kim S, Mortera M, Heyn PC, Sood P, Wen P-S, Chen Wong D, et al. An overview of systematic reviews on the pharmacological randomized controlled trials for reducing intracranial pressure after traumatic brain injury. Brain Inj. 2022; 36(7): 829–40.
8. Godoy DA, Carrizosa J, Aguilera S, Videtta W, Jibaja M, Latin America Brain Injury Consortium (LABIC) Members. Current practices for intracranial pressure and cerebral oxygenation monitoring in severe traumatic brain injury: a Latin American survey. Neurocrit Care. 2023 Feb; 38(1): 171–7.
9. Lioi F, Ramm-Pettersen J, Fratini A, Riva C, Colella N, Missori P. Ultrasonographic assessment of optic nerve sheath diameter as a screening tool for intracranial hypertension in traumatic brain injury. World Neurosurg. 2024; 192: e42–8.
10. Xu J, Song Y, Shah Nayaz BM, Shi W, Zhao Y, Liu Y, et al. Optic nerve sheath diameter sonography for the diagnosis of intracranial hypertension in traumatic brain injury: a systematic review and meta-analysis. World Neurosurg. 2024; 182: 136–43.
11. Kshirsagar SJ, Pande AH, Naik SV, Yadav A, Sakhala RM, Salve SM, et al. Bedside ultrasonographic evaluation of optic nerve sheath diameter for monitoring of intracranial pressure in traumatic brain injury patients: a cross sectional study in level II trauma care center in India. Acute Crit Care. 2024; 39(1): 155–61.
12. Koshy P, Gadkari C. Measurement of optic nerve sheath diameter by bedside ultrasound in patients with traumatic brain injury presenting to emergency department: a review. Cureus. 2024; 16(6): e61768.
13. Martínez-Palacios K, Vásquez-García S, Fariyike OA, Robba C, Rubiano AM, noninvasive ICP monitoring international consensus group. Using optic nerve sheath diameter for intracranial pressure (ICP) monitoring in traumatic brain injury: a scoping review. Neurocrit Care. 2024; 40(3): 1193–212.
14. Sharma PK, Natarajan P, Br G, Ramakrishnan KK, Aram A, Subramonian SG. Computed tomography optic nerve sheath diameter-to-eyeball transverse diameter ratio as a novel noninvasive parameter for prognostication in

Traumatic brain injury. Cureus. 2024; 16(8): e68297.
15. Ferreira FM, Lino BT, Giannetti AV. Ultrasonographic evaluation of optic nerve sheath diameter in patients severe traumatic brain injury: a comparison with intraparenchymal pressure monitoring. Neurosurg Rev. 2025; 48(1): 47.
16. Jaiswal P, Kc S, Shrestha S, Dwa Y, Baral S. Correlation of optic nerve sheath diameter (ONSD) assessed by computed tomography (CT) with Glasgow coma scale (GCS) in patients with traumatic brain injury in tertiary care hospital of Nepal. J Patan Acad Health Sci. 2025; 12(1): 12–7.
17. ElBheery MAY, Mousa AM, Eltayab MA, Enayet A. Estimation of intracranial pressure in patients with traumatic brain injury by optic nerve sheath diameter ultrasonography. Oper Neurosurg (Hagerstown). 2025; 29(6): 807–15.
18. Hakeem A, Anwer M, Khan AV, Kumar H, Karthikeyan V, Sridhar R, et al. Optic nerve sheath diameter estimation to detect increased intracranial pressure in traumatic brain injury patients at a level I trauma center in Eastern India. Korean J Neurotrauma. 2025; 21(2): 93–101.
19. Alexandri M, Smith TM, Mitchell CA, Ausman C, Brillhart DB. Real-time reduction in optic nerve sheath diameter following hypertonic saline bolus in a patient with penetrating traumatic brain injury: a case report. J Spec Oper Med. 2025; 25(3): 87–91.
20. Jiang H, Wang H, Xie Z, Yang L. Optic nerve sheath diameter and Pcv-aCO_2/Ca-cvO_2 for predicting outcomes in traumatic brain injury patients during prehospital care: a prospective cohort study in China. BMJ Open. 2025; 15(9): e101977.