Predictive Value of Optic Nerve Sheath Diameter in Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis

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Abstract

Introduction : Optic nerve sheath diameter (ONSD) is a promising non-invasive marker for elevated intracranial pressure (ICP), potentially aiding in the prognostication of subarachnoid hemorrhage (SAH) outcomes. This study aimed to evaluate the predictive value of ONSD for poor outcomes in SAH patients, defined by the Glasgow Outcome Scale (GOS).

Methods : A systematic review and meta-analysis were conducted, including studies from 2010 to 2021 that examined the relationship between ONSD and outcomes in SAH patients. A total of 615 patients were analyzed, with mean ages ranging from 54.1 to 58.8 years, and a predominance of males (38.2%). SAH severity was stratified using the Hunt and Hess classification, ranging from Grade 1 to Grade 5. The QUADAS-2 tool assessed the risk of bias, and the GRADE framework evaluated evidence certainty.

Results : The pooled analysis revealed moderate predictive accuracy for ONSD in determining poor outcomes, with a pooled proportion of 0.70 (95% CI: 0.61–0.78). Significant heterogeneity (I^2 = 77.4%, p = 0.004) was observed, likely due to variability in ONSD thresholds, measurement techniques, and timing. Funnel plot analysis suggested potential publication bias, although further statistical testing is needed.

Conclusions : ONSD demonstrates potential as a non-invasive tool for predicting poor outcomes in SAH patients. However, significant heterogeneity and moderate accuracy highlight the need for standardization of ONSD thresholds and measurement protocols. Further multicenter studies are required to validate its clinical utility and integrate it into comprehensive prognostic models.

Introduction

Subarachnoid hemorrhage (SAH) is a life-threatening neurological emergency with high rates of morbidity and mortality.[1] Timely identification and management of complications, particularly elevated intracranial pressure (ICP), are essential to improving outcomes. Traditional methods of ICP monitoring, such as invasive devices, are considered the gold standard but are associated with significant risks, including infection and hemorrhage, and may not be feasible in all clinical settings.[2] This limitation highlights the need for reliable, noninvasive alternatives.

Optic nerve sheath diameter (ONSD) has emerged as a promising noninvasive surrogate marker for ICP.[3] Due to the continuity between the intracranial subarachnoid space and the optic nerve sheath, changes in ICP are reflected in the ONSD. Studies demonstrate a strong correlation between ONSD and ICP, with reported correlation coefficients ranging from 0.59 to 0.91.[4] In patients with SAH, a linear relationship between ONSD and ICP has been observed, with a correlation coefficient of $r = 0.525$ ($p = 0.036$).[5] Additionally, the mean ONSD in SAH patients is significantly higher compared to healthy controls (6.6 ± 0.8 vs. 5.1 ± 0.47 mm), reinforcing its relevance in detecting elevated ICP.

Beyond diagnostic value, ONSD also holds prognostic significance in SAH. Studies report that SAH patients with poor neurological outcomes exhibit larger ONSD measurements, and a cutoff value greater than 6.22 mm is associated with a sensitivity of 70.3% and specificity of 80.7% for predicting poor outcomes.[5] Furthermore, the predictive value of ONSD for neurological prognosis, as reflected by C-statistics ranging from 0.735 to 0.812, highlights its utility as a tool for risk stratification. Integrating ONSD with clinical grading scales, such as the Hunt and Hess scale, has further enhanced prognostic accuracy, underscoring its potential in clinical decision-making. Among a study population of 223 SAH patients, 90.6% survived until discharge, with 83.4% demonstrating favorable neurological outcomes on the Glasgow Outcome Scale (GOS).[5] However, patients with elevated ONSD were more likely to have poor outcomes, emphasizing the importance of this measure in guiding clinical management.

This systematic review and meta-analysis aim to determine the outcomes of patients with SAH in relation to ONSD measurements. By synthesizing existing data, this study seeks to clarify the diagnostic and prognostic value of ONSD in SAH and evaluate its potential role in improving patient management strategies

Material And Methods

This systematic review and meta-analysis was conducted following a predefined protocol to ensure methodological rigor and transparency. Studies were included if they evaluated ONSD in patients with SAH and reported diagnostic or prognostic outcomes, such as correlations with ICP or neurological status. Eligible study designs included randomized controlled trials, cohort studies, and case-control studies published in peer-reviewed journals. Studies without full-text availability, those not reporting ONSD measurements, or conducted in populations other than SAH patients were excluded.

The literature search was performed in PubMed, EMBASE, and Scopus databases to identify relevant studies published up to August 1, 2024. The search strategies were tailored to each database, combining Medical Subject Headings (MeSH) terms and keywords such as *"optic nerve sheath diameter," "ONSD," "subarachnoid hemorrhage," "SAH," "intracranial pressure,"* and *"prognosis."* Boolean operators (*AND*, *OR*) were used to refine results, and filters for human studies and English language articles were applied (**Table 1**). Reference lists of included articles and relevant systematic reviews were screened for additional studies.

Table 1. Comprehensive Search Strategies Employed Across Databases

Scholar Repository	Search terms
PubMed	("optic nerve"[MeSH Terms] OR ("optic"[All Fields] AND "nerve"[All Fields]) OR "optic nerve"[All Fields]) AND ("foreskin"[MeSH Terms] OR "foreskin"[All Fields] OR "sheath"[All Fields] OR "sheath s"[All Fields] OR "sheathed"[All Fields] OR "sheathes"[All Fields] OR "sheathing"[All Fields] OR "sheaths"[All Fields]) AND ("diameter"[All Fields] OR "diameters"[All Fields]) AND ("subarachnoid haemorrhage"[All Fields] OR "subarachnoid hemorrhage"[MeSH Terms] OR ("subarachnoid"[All Fields] AND "hemorrhage"[All Fields]) OR "subarachnoid hemorrhage"[All Fields])
Scopus	optic AND nerve AND sheath AND diameter AND subarachnoid AND hemorrhage OR subarachnoid AND haemorrhage
EMBASE	(((optic nerve sheath diameter and subarachnoid hemorrhage) or subarachnoid haemorrhage) and outcome).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

The population includes adult patients diagnosed with SAH, encompassing varying degrees of severity as classified by clinical grading systems such as the Hunt and Hess scale. The intervention involves the measurement of ONSD, regardless of the specific imaging modality or method used, provided that each study explicitly specifies the measurement technique. The comparison is implicit in the context of patients with differing GOS-defined outcomes, comparing those with favorable neurological recovery to those with poor outcomes. The outcome of interest is the incidence of poor neurological outcomes, specifically assessed using GOS scores, to determine the prognostic utility of ONSD in this population.

Studies were included if they evaluated the predictive value of ONSD in adult patients diagnosed with SAH, provided a clear definition of poor neurological outcomes based on the GOS, and explicitly reported the method of ONSD measurement, regardless of the imaging modality used. Both prospective and retrospective observational studies published between 2010 and 2021 were considered, provided they presented original data. Exclusion criteria included

studies involving pediatric populations, those without a clear definition of poor outcomes, studies that did not specify ONSD measurement techniques, conference abstracts without full text, case reports, reviews, and studies not published in English.

Two independent reviewers (TT and MS) screened the titles and abstracts of all identified records. Full-text articles were retrieved for studies that appeared to meet the inclusion criteria or where eligibility was uncertain. Disagreements during screening and selection were resolved by discussion. No automation tools were used in this process to ensure a thorough and unbiased review.

Data extraction was conducted independently by two reviewers (TT and MS) using a predesigned data extraction form. Extracted data included study characteristics (author, year, design, and population), ONSD measurement details, outcomes (e.g., ICP correlation, neurological prognosis), and statistical measures (e.g., c-statistics). Any discrepancies in extracted data were resolved through consensus.

The risk of bias in included studies was assessed using the QUADAS-2 tool, justified by its relevance for diagnostic accuracy studies. QUADAS-2 evaluates study quality across domains such as patient selection, index test, reference standard, and flow and timing.[6] Additionally, the GRADE approach was used to assess the certainty of evidence, as it provides a structured and transparent framework for rating the quality of evidence and strength of recommendations in systematic reviews.

Data synthesis was performed using RStudio with the *meta* package. Statistical analysis included pooling c-statistics to evaluate the diagnostic and prognostic value of ONSD in SAH patients. Heterogeneity was assessed using the I^2 statistic, and random-effects models were applied to account for variability across studies. Data were described using 95% confidence intervals (CI), and statistical significance was defined as a p-value < 0.05.

Result

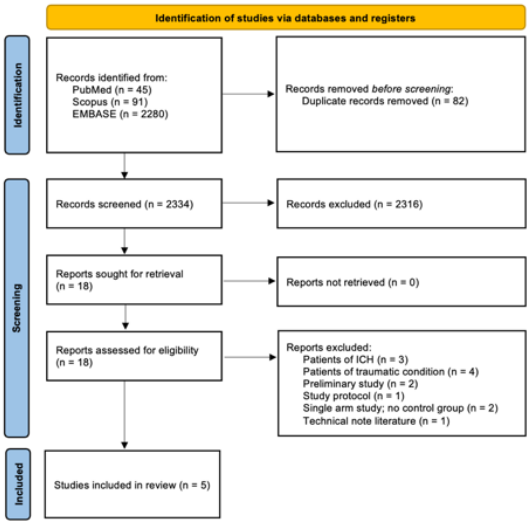

Figure 1. Screening of potential studies in adherence to the PRISMA guideline.

During the identification phase (**figure 1**), records were gathered from three databases: PubMed (45 records), Scopus (91 records), and EMBASE (2280 records), resulting in a total of 2416 records. After removing 82 duplicate entries before screening, 2334 unique records were left for further review. In the screening phase, these 2334 records underwent evaluation, and 2316 records were excluded for not meeting the inclusion criteria. Eighteen reports were sought for retrieval, all of which were successfully retrieved without any missing documents. These reports were then assessed for eligibility. Following the eligibility assessment, thirteen reports were excluded for various reasons. Specifically, three reports involved patients with ICH, four focused on patients with traumatic conditions, two were preliminary studies, one was a study protocol, two were single-arm studies without a control group, and one was technical note literature. This process left five studies that were ultimately included in the review.[5,7–10]

Table 1. Demographic characteristics of the included studies (n = 615)

Study ID, cutoff ONSD	Study duration	Total cohort, n	Age, years	Male, n	GCS	Hunt Hess Classification
Lee 2019, 6.22 mm	January 2012 and June 2017	223	58 ± 13 years	84	11.2 ± 4.4	Grade 1: 100 Grade 2: 100 Grade 3: 40 Grade 4: 36 Grade 5: 47
Yesilaras 2017, 5.76 mm	January 2010 - December 2014	61	56 (IQR = 25, min: 24, max: 90) years	24	GCS 14–15: 32 GCS 9–13: 13 GCS < 9: 15	Grade 1: 31 Grade 2: 5 Grade 3: 11 Grade 4: 7 Grade 5: 6
Cenik 2021, 4 mm	March 2019 and September 2019	56	58.8 ± 15.1 years	16	GCS 14–15: 42 GCS 9–13: 5 GCS < 9: 9	Grade 1: 20 Grade 2: 16 Grade 3: 5 Grade 4: 7 Grade 5: 8
Kim 2023, 4.78 mm	January 2015 and December 2021	171	54.1 ± 12.1 years	60	12.5 ± 3.9	Grade 1: 60 Grade 2: 40 Grade 3: 30 Grade 4: 34 Grade 5: 7
Zhu 2021, 6.4 mm	August 2015 to November 2020	104	58.8 ± 17.4 years	51	GCS 3: 27 GCS 4: 4 GCS 5: 8 GCS 6: 4 GCS 7: 4 GCS 8: 7	n/r
		615		235		

The included study period was between 2010 and 2021, encompassing a total of 615 patients diagnosed with SAH. The mean age of participants ranged from 54.1 to 58.8 years, with a predominance of males (235 patients, 38.2%) with different ONSD threshold. GCS scores varied widely across the studies, reflecting the spectrum of neurological severity at presentation. The Hunt and Hess classification, used to assess the severity of SAH, revealed the following totals across the included studies: Grade 1 (211 patients), Grade 2 (161 patients), Grade 3 (91 patients), Grade 4 (84 patients), and Grade 5 (68 patients). These distributions underscore the variability in clinical presentation, ranging from mild to severe cases, and highlight the heterogeneity in patient populations assessed across studies. According to the QUADAS-2 assessment (**figure 2**), the studies were classified as having a low risk of bias, while the GRADE evaluation indicated that the studies provided evidence of high certainty.

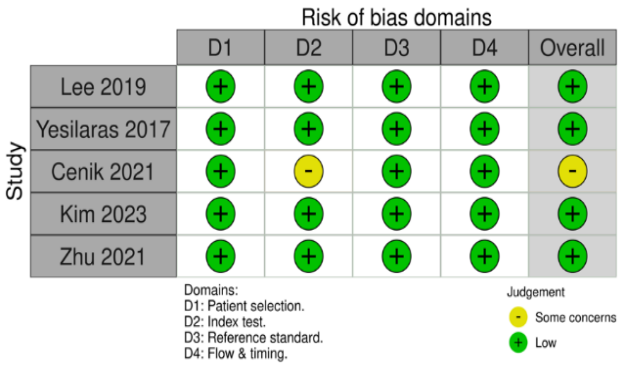

Figure 3. QUADAS-2 assessment of the included studies

The pooled analysis (**figure 2**), incorporating data from four studies, demonstrates a moderate predictive accuracy with a pooled proportion of 0.70 (95% CI: 0.61–0.78). However, significant heterogeneity (I^2=77.4, p = 0.004) highlights variability across studies, likely due to differences thresholds for ONSD. The funnel plot suggests potential publication bias, though further statistical testing is necessary for confirmation.

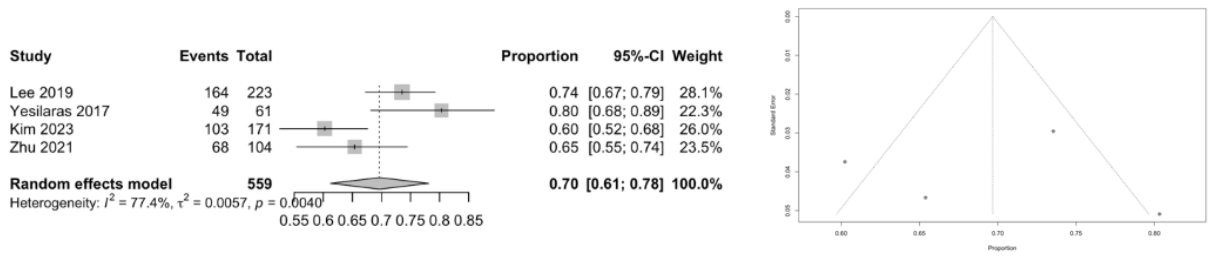

Figure 2. Pooled analysis of the concordance value of ONSD for predicting poor outcome in patients with SAH.

Discussion

The ONSD has been increasingly studied as a non-invasive marker for assessing ICP, a critical determinant of outcomes in patients with SAH. Elevated ICP is strongly associated with poor neurological outcomes, positioning ONSD as a potentially valuable prognostic tool in clinical settings.[11] This study aimed to evaluate the predictive value of ONSD for poor outcomes in SAH patients, as defined by the GOS. The variability in clinical presentations and the inherent challenges of early risk stratification in SAH underscore the importance of identifying reliable, non-invasive prognostic markers. A marker such as ONSD could contribute to improved decision-making and better patient outcomes.[12]

The analysis of four included studies, encompassing 615 SAH patients, demonstrated moderate predictive accuracy for ONSD, with a pooled proportion of 0.70 (95% CI: 0.61–0.78). These findings suggest that ONSD is capable of identifying patients at higher risk of poor outcomes. The robustness of the evidence was supported by high-certainty ratings from the GRADE assessment and a low risk of bias according to QUADAS-2.

The use of the Hunt and Hess classification in stratifying SAH severity highlighted the broad applicability of ONSD across different clinical grades.[13] The inclusion of patients with varying levels of severity, ranging from mild to severe (Grades 1 to 5), emphasized the potential utility of ONSD in diverse clinical scenarios. Additionally, the non-invasive nature of ONSD measurement presents significant advantages over invasive ICP monitoring, particularly in resource-limited healthcare settings.[14] The inclusion of studies conducted over an 11-year period, with mean participant ages ranging from 54.1 to 58.8 years, also ensured a representative sample for evaluating the clinical relevance of ONSD.

Despite the promising results, significant heterogeneity (I^2 = 77.4%, p = 0.004) was observed among the included studies, which limits the generalizability of the findings. Variations in ONSD thresholds, the timing of measurements relative to SAH onset, and differences in imaging modalities likely contributed to this inconsistency.[15,16] For instance, some studies used ultrasound for ONSD measurement, while others relied on computed tomography (CT) or magnetic resonance imaging (MRI), potentially affecting the precision and comparability of results.[17]

The funnel plot revealed a possible risk of publication bias, suggesting that studies with predominantly positive findings might have been overrepresented. Additionally, the moderate predictive accuracy of ONSD indicated that it might not account for all factors influencing patient outcomes. Confounding variables,

such as comorbidities, variations in treatment strategies, and individual patient trajectories, could also affect the reliability of ONSD as a standalone prognostic marker.[18]

Some studies have further suggested that while ONSD correlates with elevated ICP, it might lack specificity in predicting long-term outcomes. Transient increases in ICP or other pathophysiological mechanisms unrelated to ONSD could diminish its prognostic value in some cases.

Limitations and Implications of Heterogeneity

Significant heterogeneity across studies warrants further investigation to identify underlying sources. Factors such as differences in ONSD measurement techniques, timing of assessment relative to SAH onset, and variability in patient management strategies could contribute to this variability.[19] Standardizing ONSD thresholds and measurement protocols may improve consistency and enable broader clinical implementation. The potential publication bias, as suggested by the funnel plot, raises additional concerns.[20] While the implications of bias cannot be fully ascertained without further statistical testing, it underscores the need for transparency and inclusion of negative or inconclusive findings in future research.

Integration into Clinical Practice

The findings underscore the promise of ONSD as a non-invasive, rapid, and accessible tool for early risk stratification in SAH patients. When used alongside traditional clinical and radiological markers, ONSD could enhance prognostic accuracy and guide management decisions, such as the allocation of intensive monitoring or timely interventions.[21] However, given the moderate predictive accuracy observed, ONSD should not be used in isolation but as part of a comprehensive assessment.

Future Directions

Future studies should aim to standardize ONSD measurement techniques and establish evidence-based thresholds tailored to SAH severity grades. Additionally, larger multicenter studies with diverse patient populations are needed to validate these findings and explore the potential influence of demographic and clinical variables. Addressing heterogeneity through subgroup analyses and harmonized methodologies could further refine the utility of ONSD in clinical practice.

Conclusion

This study provides evidence supporting the utility of ONSD as a moderate predictor of poor outcomes in SAH patients. While promising, the heterogeneity across studies and the moderate predictive accuracy highlight the need for further standardization and validation before routine clinical implementation.

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