Original Article

# Ultrasound Measurement of Optic Nerve Sheath Diameter in Acute Hypertensive States For Detection of Intracranial Involvement: A Meta-Analysis

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## Abstract

**Background:** **Detection of intracranial involvement in acute hypertension traditionally relies on fundoscopy, a method with limited applicability at the bedside. Ultrasonographic measurement of the optic nerve sheath diameter (ONSD) has emerged as a rapid, non-invasive alternative.**

**Objective:** **To synthesize evidence on ONSD in adults and pregnant women with acute hypertensive states, assessing the difference in measurements between groups and its diagnostic performance for elevated intracranial pressure (ICP).**

**Methods:** **Systematic review and meta-analysis following PRISMA guidelines. Three databases were searched through July 2026, including observational studies. The primary outcome was the standardized mean difference (Hedges' g) in ONSD between hypertensive and control groups, using a random-effects model.**

**Results:** **Fourteen studies (995 participants) were included. Nine studies (426 hypertensive and 283 control participants) provided combinable continuous data: ONSD was significantly higher in hypertensive patients ($g = 1.55$; 95% CI 1.06 to 2.04; $p < 0.001$; $I^2 = 87.0\%$). Excluding a single discordant study reduced heterogeneity and strengthened the effect ($g = 1.77$; 95% CI 1.50 to 2.04; $I^2 = 51.8\%$). In five studies with observed counts, the odds of ONSD above the threshold were higher in hypertensive patients (OR 11.58; 95% CI 1.45 to 92.85; $I^2 = 73.7\%$). No study included ONSD with invasive ICP measurement.**

**Conclusion:** **ONSD is consistently higher in acute hypertensive patients, with a robust effect. However, substantial heterogeneity, reliance on statistical conversions, the presence of a discordant study, and the absence of validation against the invasive gold standard warrant caution, underscoring the need for methodological standardization and dedicated validation.**

**Keywords:** **Optic Nerve; Ultrasonography; Intracranial Pressure; Pre-Eclampsia; Hypertensive Crisis.**

## Introduction

Arterial hypertension is one of the leading causes of cardiovascular morbidity and mortality worldwide, and its acute presentations – hypertensive emergencies and urgencies, hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES), spontaneous intracerebral hemorrhage, and the hypertensive disorders of pregnancy, including pre-eclampsia and eclampsia – may course with acute elevation of intracranial pressure (ICP) and potentially severe neurological repercussions. Early bedside recognition of this repercussion traditionally relies on fundoscopic examination for papilledema. However, this assessment is difficult to perform outside the ophthalmologic setting: it requires mydriasis and patient cooperation, shows limited interobserver agreement when performed by non-specialists, and, importantly, papilledema may appear only hours to days after ICP elevation, delaying decision-making in urgent scenarios. These limitations justify the search for a rapid, objective, and reproducible marker.

The optic nerve sheath diameter (ONSD) measured by transorbital ultrasonography has been proposed for this purpose. The subarachnoid space surrounding the optic nerve is contiguous with the intracranial subarachnoid space; thus, elevations in ICP are transmitted through the distensible nerve sheath, increasing its diameter. Studies comparing ONSD with direct invasive ICP measurement have confirmed this correlation, and meta-analyses in neurocritical populations have demonstrated good diagnostic accuracy of the method for intracranial hypertension.[1,2] Because it is non-invasive, low-cost, and can be performed within minutes, the technique is particularly attractive when fundoscopic examination is impractical.

It is important to note that papilledema itself is an indirect sign of intracranial hypertension, not the target condition. The perineural subarachnoid space is contiguous with the

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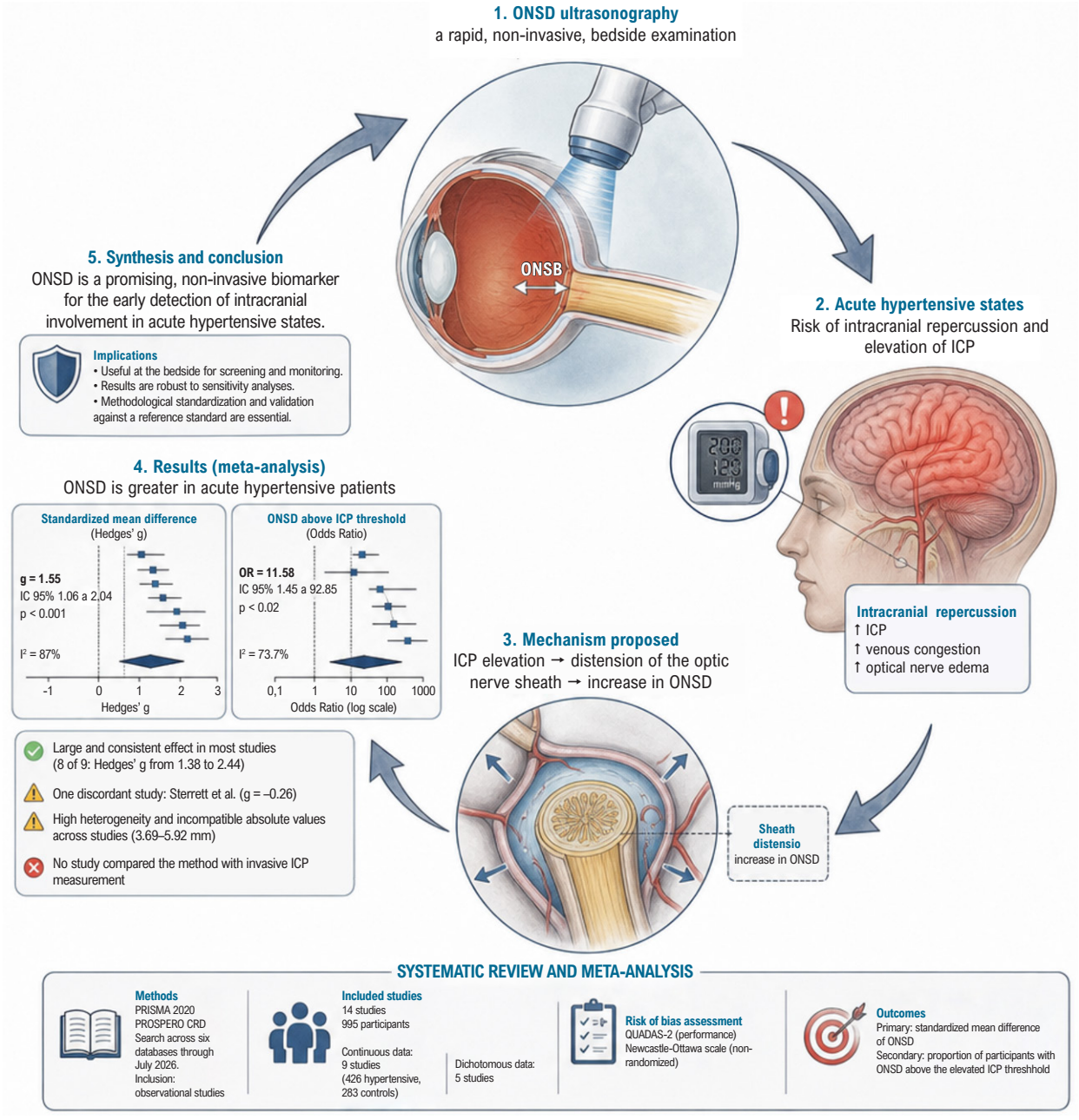
**Central Illustration: Ultrasound Measurement of Optic Nerve Sheath Diameter in Acute Hypertensive States For Detection of Intracranial Involvement: A Meta-Analysis**

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*ONSD: optic nerve sheath diameter; ICP: intracranial pressure.*

intracranial compartment, and ICP elevation affects the optic nerve through two distinct pathways: mechanical distension of the sheath, which increases ONSD, and stasis of axoplasmic flow at the optic nerve head, which produces disc edema. These two findings are therefore parallel – both downstream manifestations of the same process – and not sequential. The second pathway depends on progressive accumulation of axoplasmic material and appears later, helping explain why papilledema may be absent in the first hours of ICP elevation and why the sensitivity of fundoscopic examination

is described as limited in the acute setting.[3] This leads to the central question of this review: the goal is not to determine whether ONSD reproduces the fundoscopic finding, but whether it provides information about the underlying condition reflected by both signs.

In acute hypertensive states, failure of cerebral autoregulation and endothelial dysfunction promote cerebral edema and increased ICP – a pathophysiological substrate common to hypertensive encephalopathy and PRES. In hypertensive patients, ONSD increases and subsequently decreases after blood pressure control,[4] and among pregnant women, pre-eclampsia and eclampsia are associated with higher ONSD values compared with normotensive women.[5-7] The relevance of this topic to cardiovascular imaging is reinforced by the recognition that hypertensive disorders of pregnancy are predictors of future cardiovascular disease.

Despite this growing body of evidence, studies evaluating ONSD in acute hypertensive states are heterogeneous in terms of population, reference standard, and diagnostic threshold, and are dispersed across small samples. Available systematic reviews focus on other populations, such as traumatic brain injury and non-traumatic neurocritical patients, without a synthesis dedicated to the hypertensive scenario.[1] This study aimed to systematically review this evidence, quantifying the difference in ONSD compared with controls and its performance in detecting elevated ICP.

## Methods

### Protocol and registration

This systematic review was conducted and reported in accordance with the PRISMA 2020 guidelines.[8] The protocol was prospectively registered in PROSPERO (No. CRD420261459770) before the initiation of data extraction.

### Eligibility criteria

Eligible studies included observational designs, namely case-control, cross-sectional, and prospective cohort studies, that evaluated ultrasound measurement of the ONSD in adults (≥18 years), as well as in pregnant or postpartum women presenting with acute hypertensive disorders. These conditions were defined as preeclampsia with or without severe features, eclampsia, hypertensive encephalopathy, PRES, spontaneous hypertensive intracerebral hemorrhage, hypertensive emergency or urgency, and severe acute hypertension.

The index test was ONSD measured by transorbital B-mode ultrasonography using a high-frequency linear probe, with measurements obtained approximately 3 mm posterior to the globe. Accepted comparators or reference standards included normotensive controls (the basis for the primary outcome), ICP monitoring, lumbar puncture opening pressure, neuroimaging findings consistent with elevated ICP, and the clinical diagnosis of eclampsia.

Case reports, case series, reviews, editorials, letters, and conference abstracts without extractable data were excluded. Studies conducted exclusively in healthy volunteers or animal models, as well as studies involving non-hypertensive neurocritical populations when results could not be separated, were also excluded.

### Information sources and search strategy

The following databases were searched from inception to July 2026, without language restrictions: MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy combined three groups of terms using the Boolean operator AND: (1) the condition of interest (preeclampsia, eclampsia, acute hypertension, hypertensive emergency and urgency, hypertensive encephalopathy, and PRES); (2) the imaging modality (ultrasonography, ultrasound, sonography); and (3) the index test (ONSD). The search was supplemented by manual screening of the reference lists of included studies and relevant previous reviews. The complete search strategy for each database is provided in the Supplementary Material.

### Study selection and data extraction

Two reviewers independently screened titles and abstracts, followed by full-text assessment of potentially eligible studies. Disagreements were resolved by consensus or, when necessary, by consultation with a third reviewer. Data extraction was performed independently in duplicate using a standardized, pilot-tested form. Extracted variables included study identification, country, study design, hypertensive etiology, number of participants per group, ONSD measurement technique and threshold, reference standard, and, depending on the analysis, mean and standard deviation of ONSD for each group and/or event counts by group. All extracted values were verified against the tables reported in the original articles before analysis.

### Risk of bias assessment

Risk of bias was assessed independently by two reviewers using the tool appropriate for each study design: QUADAS-2[9] for diagnostic accuracy studies and ROBINS-I[10] for comparative observational studies. Disagreements were resolved by consensus or by a third reviewer.

### Data synthesis

The primary outcome was the standardized mean difference (Hedges' g)[11] in ONSD between patients with acute hypertensive conditions and controls, estimated using a random-effects meta-analysis with the DerSimonian-Laird estimator.[12] The pooled standard deviation was calculated as the weighted average of the sample variances according to their respective degrees of freedom. Heterogeneity was quantified using Cochran's Q test and the $I^2$ and $\tau^2$ statistics.[13]

As a secondary outcome, the proportion of participants with ONSD above the threshold for intracranial hypertension was synthesized as an odds ratio, restricting the analysis to studies reporting observed event counts. For contingency tables with zero events, a continuity correction of 0.5 was applied. Studies with paired within-subject designs or lacking an independent control group were not included in the independent-group meta-analytic models and were instead summarized through

a structured narrative synthesis. Publication bias was assessed using funnel plot inspection and Egger's test,[14] with the explicit acknowledgment that these methods have low statistical power when fewer than ten studies are available. All analyses were performed in Python 3 (NumPy and SciPy libraries) using direct implementation of the statistical formulas, with a two-sided significance level of 5%.

### Diagnostic threshold analysis

No statistical pooling of the reported cutoff values was performed for two prespecified reasons. First, the thresholds derived from receiver operating characteristic (ROC) curve analyses in the primary studies were intended to distinguish preeclampsia from normotension, rather than to diagnose intracranial hypertension. Second, the fixed thresholds used in other studies had been adopted from neurocritical care populations without local validation. Pooling sensitivities and specificities obtained against different diagnostic targets would therefore produce an estimate without a clearly defined clinical reference.

To assess whether a single threshold might be transferable across studies, an exploratory analysis was conducted in which each proposed cutoff was applied to all studies. Expected sensitivity and specificity were calculated from the mean and standard deviation of each group under a normal distribution assumption. Using the same approach, the threshold that maximized the Youden index was estimated for each study. These estimates represent modeled projections rather than observed event counts and are identified as such in the Results section. In addition, under the assumptions of normality and homoscedasticity, the area under the ROC curve (AUC) is related to the standardized mean difference through the identity $AUC = \Phi(g/\sqrt{2})$, which was used to estimate overall discriminative performance independently of any specific cutoff definition.

### Harmonization of reported data

The included studies reported ONSD in different formats, requiring standardization before data synthesis. Values reported in centimeters were converted to millimeters; because the standardized mean difference is dimensionless, it is unaffected by the unit of measurement. When ONSD was reported as a median with interquartile range, the mean and standard deviation were estimated using the method of Wan et al.[6,15] When reported as a median with a confidence interval, the standard deviation was estimated from the confidence interval width and sample size.[5]

In one study,[7] the dispersion values reported in the outcome table (±0.02 and ±0.03 cm) were, by magnitude, incompatible with standard deviations. These values were therefore interpreted as standard errors and converted using the relationship standard deviation = standard error × $\sqrt{n}$. However, another table in the same study reported eye-specific standard deviations (±0.05 cm in the eclampsia group and ±0.03 cm in the control group) that were internally consistent with the corresponding standard error column, but did not match either interpretation of the main outcome table. This ambiguity was addressed through sensitivity analyses. For studies with multiple hypertensive groups compared against a common control group (Dikmetaş 2020, Singh 2018, and Sterrett 2022),[4,16,17] the hypertensive arms were combined into a single group to avoid double-counting the shared control group.

### Sensitivity and Subgroup Analyses

Sensitivity analyses were conducted by successively excluding the discordant study, the study with ambiguous dispersion, and all studies requiring dispersion conversion, in addition to a leave-one-out influence analysis. Subgroups were prespecified according to gestational condition and etiology.

## Results

### Study selection and characteristics

The process of identification, screening, and selection is summarized in the PRISMA 2020 flowchart (Figure 1). Fourteen studies[4-7,16-25] with 995 participants were included in the systematic review (Central Illustration). Of these, nine provided means and standard deviations of ONSD per group – either directly or after conversion – and were included in the meta-analysis of the primary outcome, totaling 426 patients with acute hypertensive states and 283 controls (Table 1).

Five studies could not be incorporated into the independent-groups model: Assu et al.[24] (n = 30) and Rani et al.[25] (n = 47) are single-arm studies with paired measurements before and after magnesium sulfate; Mowafy & Elsayed[21] (n = 54) compared paired measurements before and after delivery; Ortner et al.[20] (n = 95) is a single-cohort study of preeclampsia without a control group, reporting a mean ONSD of 5.4 ± 0.5 mm and 27 participants (28%) above 5.8 mm; and Brzan Simenc et al.[18] presented ONSD only in a box plot, with no numerical values in the text. The latter, however, reported observed counts and was included in the binary secondary outcome.

Most studies evaluated preeclampsia and eclampsia; only one study[4] included non-pregnant hypertensive individuals. Control groups were heterogeneous – normotensive pregnant women, asymptomatic normotensive adults, and postpartum women admitted to intensive care for other causes – which represents a relevant source of variability.

### Primary outcome: difference in ONSD

The pooled standardized mean difference in ONSD between patients with acute hypertensive states and controls was g = 1.55 (95% CI 1.06 to 2.04; $p < 0.001$), indicating higher ONSD in the hypertensive group, with substantial heterogeneity ($Q = 61.4$; $df = 8$; $p < 0.001$; $I^2 = 87.0\%$; $\tau^2 = 0.485$; Figure 2).

Study-level effects were consistent and large in eight of the nine studies, ranging from g = 1.38[5] to g = 2.44,[17] and discordant in a single study,[16] g = -0.26 (95% CI −0.80 to 0.28) – the only one not showing a difference between groups. In that study, the mean ONSD of controls (5.92 ± 0.84 mm) was numerically higher than that of patients with preeclampsia (5.67 ± 0.98 mm), an inverse pattern compared with all other

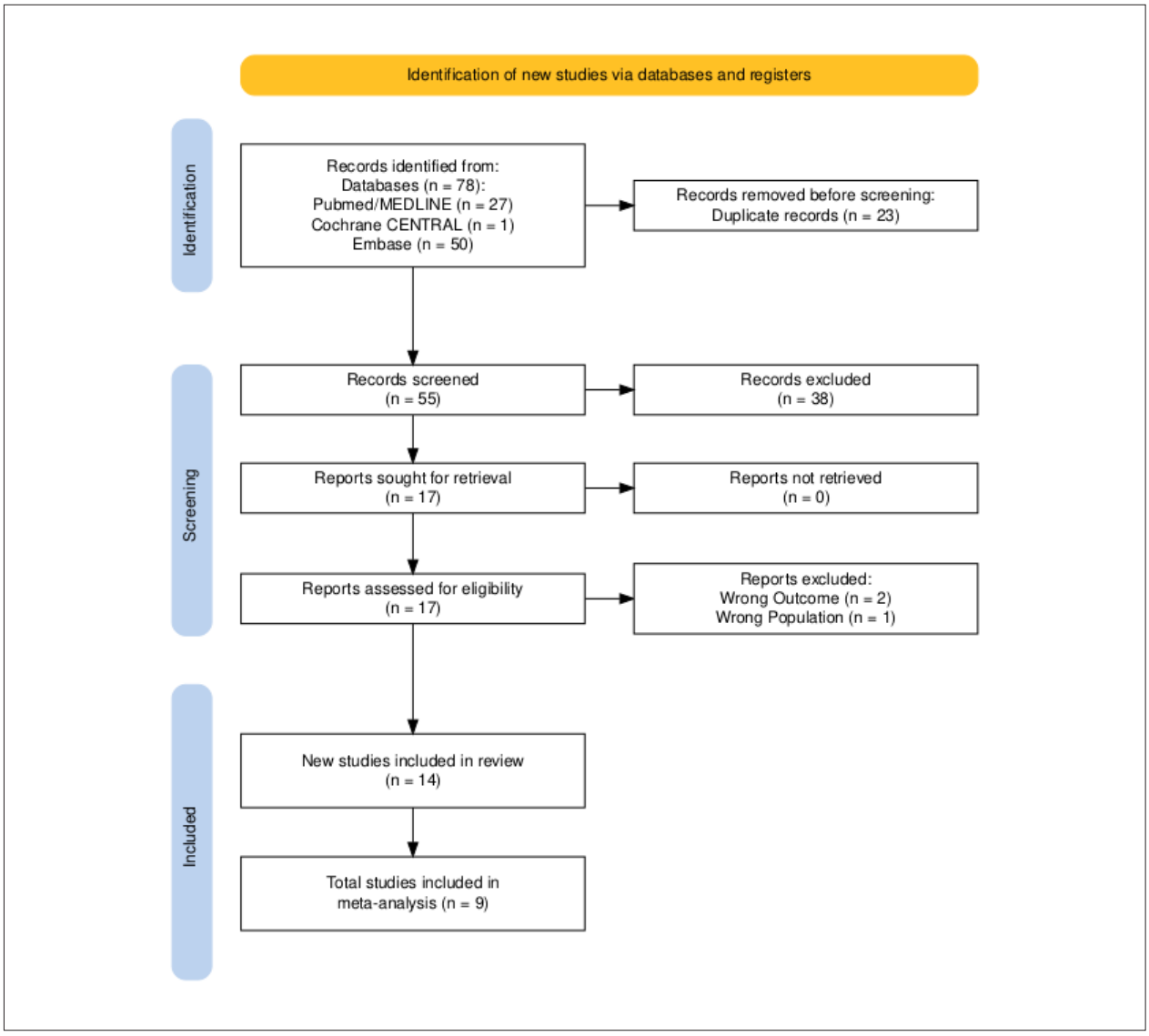


**Figure 1 –** *Study selection flowchart (PRISMA 2020).*

studies, and confirmed upon checking the original table, which reports adjusted differences that are likewise null or negative across all arms.

Influence analysis showed that heterogeneity was concentrated almost entirely in this study: its exclusion increased the pooled effect to g = 1.77 (95% CI 1.50 to 2.04) and reduced heterogeneity from $I^2$ = 87.0% to 51.8%. Excluding any other study individually changed the pooled effect by less than 0.11 and did not substantially modify $I^2$ (Table 2).

The effect remained stable and of large magnitude across all sensitivity analyses, including restriction to the six studies that did not require any dispersion conversion (g = 1.55; 95% CI 0.82 to 2.27) and the alternative interpretation of dispersion in Bala et al.[7] (g = 1.82; 95% CI 1.21 to 2.43). In the gestational subgroup (eight studies), the effect was g = 1.56 (95% CI 0.98 to 2.15); the non-gestational subgroup included a single study and could not be meta-analyzed, preventing formal subgroup comparison.

### Secondary outcome: proportion above the threshold

Five studies reported observed counts of participants with ONSD above the intracranial hypertension threshold (Figure 3). The odds of elevated ONSD were higher in the hypertensive group (OR 11.58; 95% CI 1.45 to 92.85; p = 0.021; $I^2$ = 73.7%). Excluding Sterrett et al.[16] the estimate was OR 29.54 (95% CI 6.98 to 124.99) with $I^2$ = 0%. Four of the five studies recorded no events in the control group, requiring continuity correction and resulting in very wide confidence intervals; these results should therefore be interpreted as evidence of the *direction* of the effect, not its precise magnitude.

**Tabela 1 – Características dos estudos incluídos na meta-análise do desfecho primário**

| Study (year) | Population / etiology | n (hip./ctrl) | ONSD (mm) hypertensive | ONSD control (mm) | Reporting form | Hedges' g (95%CI) |
|---|---|---|---|---|---|---|
| Arzpeyma et al.[19] | Preeclampsia | 38 / 38 | 5.37 ± 0.96 | 4.26 ± 0.55 | mean ± SD | 1.40 (0.91; 1.90) |
| Kumar et al.[7] | Eclampsia (ICU) | 24 / 22 | 6.40 ± 0.98 [a] | 4.50 ± 1.41 [a] | SE → SD | 1.55 (0.90; 2.20) |
| Biswas et al.[6] | Preeclampsia | 60 / 30 | 5.17 ± 0.84 [b] | 3.69 ± 0.80 [b] | median+ IQR | 1.78 (1.27; 2.28) |
| Dikmetaş et al.[4] | Acute hypertension (non-pregnant) | 99 / 50 | 5.25 ± 0.61 | 4.42 ± 0.39 | mean ± SD | 1.51 (1.13; 1.89) |
| Dubost et al.[5] | Preeclampsia | 26 / 25 | 5.40 ± 0.65 [c] | 4.50 ± 0.64 [c] | median + 95%CI | 1.38 (0.77; 1.98) |
| Nagpal et al.[23] | Preeclampsia | 35 / 35 | 5.06 ± 0.46 | 4.24 ± 0.38 | mean ± SD | 1.92 (1.36; 2.48) |
| Singh et al.[17] | Severe preeclampsia + eclampsia | 49 / 25 | 5.70 ± 0.38 | 4.70 ± 0.46 | mean ± SD | 2.44 (1.82; 3.05) |
| Sterrett et al.[16] | Preeclampsia | 44 / 18 | 5.67 ± 0.98 | 5.92 ± 0.84 | mean ± SD | □0.26 (□0.80; 0.28) |
| Su et al.[22] | Preeclampsia | 51 / 40 | 4.34 ± 0.18 | 3.96 ± 0.14 | mean ± SD | 2.30 (1.77; 2.83) |

*ONSD: optic nerve sheath diameter; SD: standard deviation; SE: standard error; IQR: interquartile range; [a] Standard deviation obtained from the reported standard error (SD = SE × √n); [b] Mean and SD estimated from median and IQR using the method of Wan et al.[15] [c] SD estimated from the width of the confidence interval; Values converted from centimeters to millimeters in Kumar et al.,[7] and Dikmetaş et al.[4] Multiple arms combined in Dikmetaş et al.,[4] Singh et al.,[17] and Sterrett et al.[16]*

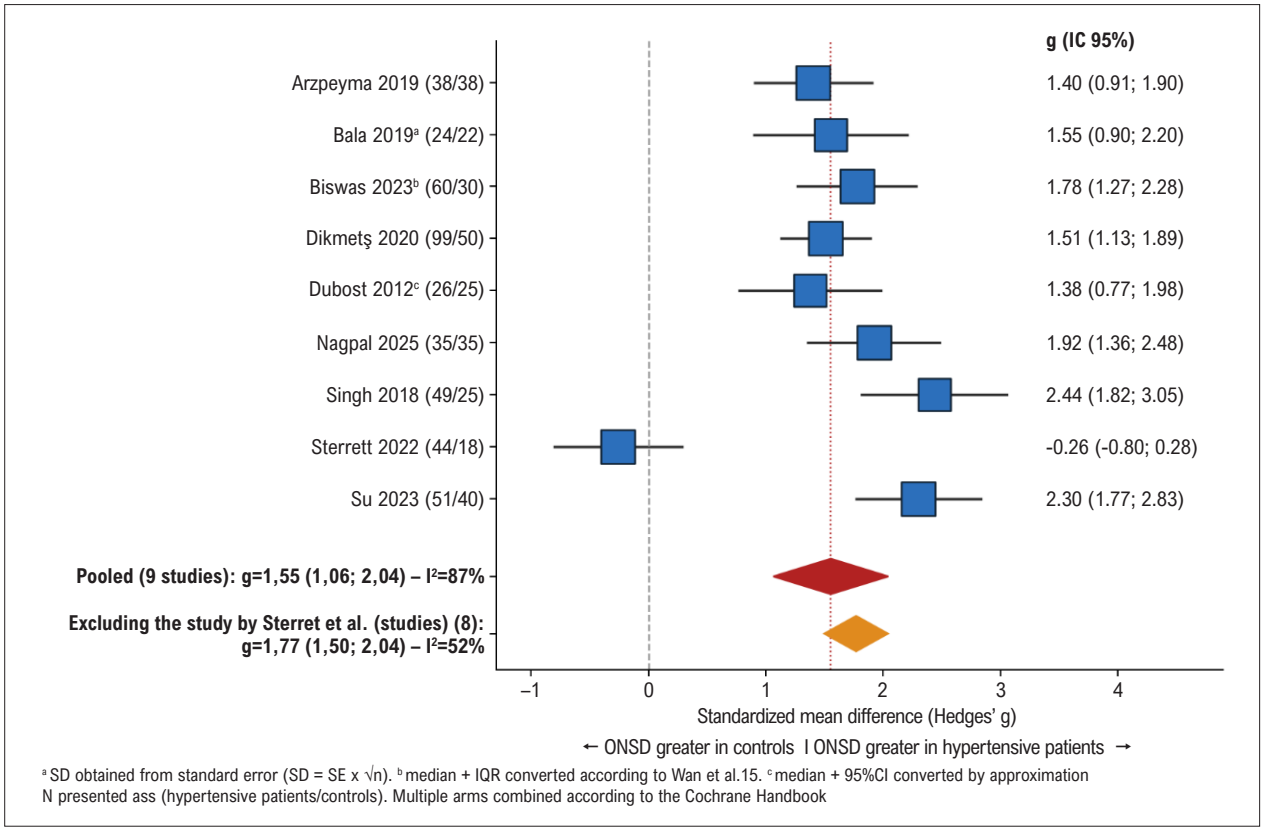


**Figure 2 –** *Meta-analysis of the standardized mean difference (Hedges' g) in ONSD between patients with acute hypertensive states and controls, using a random-effects model (DerSimonian–Laird). Squares: study-specific estimates, with area proportional to weight; horizontal lines: 95% CI; diamonds: pooled effect of the main model (nine studies) and of the sensitivity analysis excluding the discordant study (eight studies).*

**Table 2 – Sensitivity and subgroup analyses of the primary outcome**

| Analysis | k | Pooled g (95%CI) | $I^2$ (%) | $\tau^2$ |
|---|---|---|---|---|
| Main model (all combinable studies) | 9 | 1.55 (1.06; 2.04) | 87.0 | 0.485 |
| Sterrett et al.[16] excluded (discordant) | 8 | 1.77 (1.50; 2.04) | 51.8 | 0.078 |
| Bala et al.[7] excluded (ambiguous dispersion) | 8 | 1.55 (1.01; 2.10) | 88.6 | 0.541 |
| Only studies without dispersion conversion | 6 | 1.55 (0.82; 2.27) | 91.7 | 0.745 |
| Bala et al.[7] with the reported per-eye SD | 9 | 1.82 (1.21; 2.43) | 91.0 | 0.760 |
| Subgroup: gestational | 8 | 1.56 (0.98; 2.15) | 88.6 | 0.630 |
| Subgroup: non-gestational | 1 | 1.51 (1.13; 1.89) [d] | — | — |

*k: number of studies; g: standardized mean difference (Hedges' g); $I^2$: proportion of variability attributable to heterogeneity; $\tau^2$: between-study variance.* [d] *Single study;4 estimate from the study itself, without pooling.*

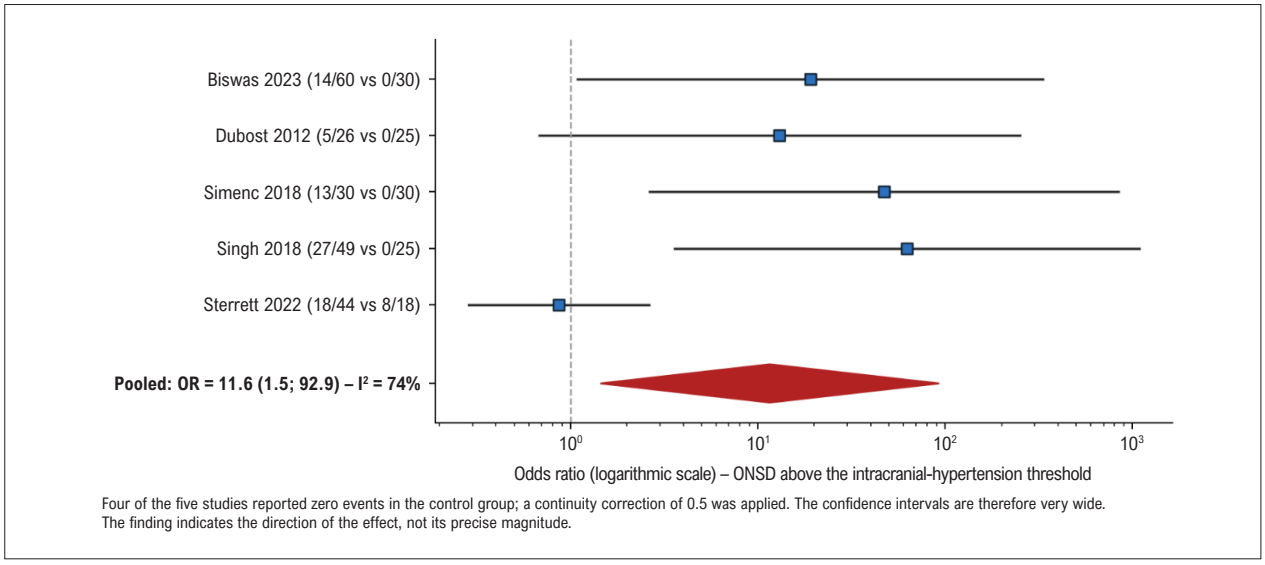


**Figure 3 –** *Proportion of participants with ONSD above the intracranial hypertension threshold, expressed as odds ratios (logarithmic scale), restricted to studies with observed counts; a continuity correction of 0.5 was applied to tables with zero events.*

Counts derived from sensitivity and specificity reported in three studies[19,22,23] were not included in this synthesis because they do not represent observed counts; using them would amount to introducing reconstructed events into the model.

### Diagnostic accuracy and reference standard

It was not possible to fit a bivariate model or estimate a summary ROC curve. None of the fourteen included studies compared ONSD with invasive ICP measurement or CSF opening pressure. The available ROC curves discriminated preeclampsia from controls – a diagnostic target distinct from intracranial hypertension – with areas under the curve of 0.82 (Arzpeyma et al.,[19] cutoff 4.55 mm), 0.958 (Su et al.,[22] cutoff 4.10 mm), and 0.907 (Nagpal et al.,[23] cutoff 4.65 mm). Because they involve a different diagnostic target and highly heterogeneous thresholds, these values are presented descriptively and were not pooled.

### Risk of bias assessment

All fourteen observational studies were evaluated using the ROBINS-I tool. In this instrument, most studies show critical or serious risk in the initial domains – especially D1 (confounding) and D2 (selection of participants) – which severely compromises the overall quality of the evidence. Domains D3 (classification of interventions), D4 (deviations from intended interventions), and D5 (missing data) were frequently rated as low or moderate risk.

The QUADAS-2 tool was applied to six diagnostic accuracy studies, revealing high risk of bias, particularly in D1 (patient selection) and D2 (index test). As a result, the overall classification of most included studies was rated as critical or serious, indicating a high risk of bias that limits confidence in the conclusions (Figures 4A and 4B).

### Diagnostic thresholds

The thresholds used in the included studies fell into two distinct ranges: values from 4.10 to 4.65 mm, derived from

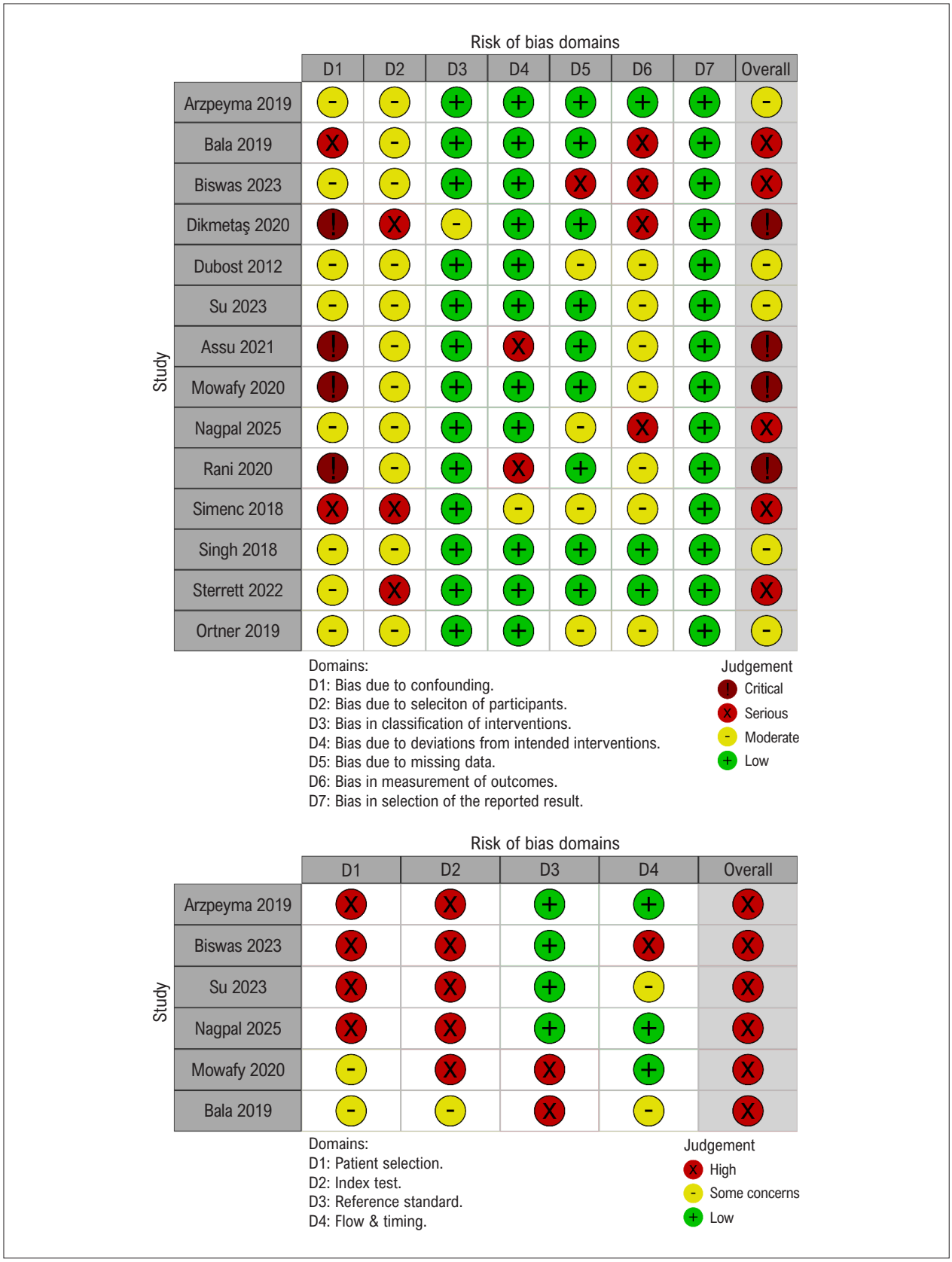


**Figure 4 –** *Assessment of the risk of bias in the included studies (ROBINS-I for comparative observational studies and QUADAS-2 for studies with accuracy data).*

ROC curves designed to discriminate preeclampsia from normotension, and values from 5.7 to 5.8 mm, imported from neurocritical populations and applied as presumed markers of intracranial hypertension.

Absolute ONSD values were incompatible across studies, preventing the transferability of any single threshold. Control-group means ranged from 3.69 $mm^4$ to 5.92 $mm^3$), a span of 2.23 mm, which exceeds the mean difference between hypertensive and control groups in most studies. The mean ONSD of controls in Sterrett et al.[16] (5.92 mm) was higher than the hypertensive-group means in Su et al.[22] (4.34 mm), Nagpal et al.[23] (5.06 mm), and Fallah Arzpeyma et al.[19] (5.37 mm), meaning that participants classified as normal in one study would be classified as abnormal in another (Supplementary Material S2).

Cross-application of thresholds confirmed this incompatibility. The 4.10 mm cutoff – optimal in Su et al.[22] – would yield 84% specificity in that study but only 2% in Sterrett et al.[16] Conversely, the 5.80 mm cutoff would produce zero sensitivity in Su 2023[22] and 22% in Biswas et al.[6] When applied to control groups using observed counts, the 5.80 mm threshold was not reached by any participant in four studies (0/30 in Biswas et al.,[6] 0/25 in Dubost et al.,[5] 0/30 in Brzan Simenc et al.,[18] and 0/25 in Singh et al.[17] – the latter using a 5.7 mm cutoff), but was reached by 8 of 18 controls (44%) in Sterrett et al.[16]

The thresholds that would maximize the Youden index in each study ranged from 4.14 mm to 7.79 mm – a span of 3.64 mm (Table 3) – with no central value approaching optimal performance in more than a handful of studies. For this reason, no pooled cutoff was estimated.

As an estimate of the global discriminative ability independent of any threshold, the identity AUC = $\Phi(g/\sqrt{2})$ applied to the pooled standardized mean difference corresponds to an AUC of 0.863 (95% CI 0.773 to 0.925), or 0.895 when the discordant study is excluded (Figure 5). It should be reiterated that this estimate refers to the distinction between acute hypertensive state and normotensive control, not to the detection of elevated ICP.

Exploration of heterogeneity through meta-regression was not informative: the models were dominated by a single influential study, and the apparent associations disappeared once that study was excluded. In addition, mathematical coupling occurred when the covariate was the control-group mean, such that the results are presented solely as a diagnostic indication of non-interpretability given the number of studies available (Supplementary Material S3).

### Narrative synthesis of non-poolable studies

The four paired-design studies converge in showing a reduction in ONSD after intervention or delivery. In Rani et al.[25] (n = 47), ONSD decreased from 5.56 ± 0.30 mm at baseline to 4.79 ± 0.13 mm four hours after magnesium sulfate (p = 0.01), remaining at 4.76 ± 0.11 mm at 24 hours. In Assu et al.[24] (n = 30), the reduction was more gradual, from 6.02 ± 0.77 mm to 5.64 ± 0.81 mm at 24 hours postpartum. In Mowafy et al.[21] (n = 54), ONSD decreased from 5.84 ± 0.82 mm before delivery to 5.24 ± 0.73 mm 24 hours later, with a strong correlation between ONSD and the lung comet score ($r^2$ = 0.96 before delivery). In Brzan Simenc et al.,[18] 13 of 30 patients with severe preeclampsia (43%) had ONSD above 5.8 mm before delivery, compared with none of the 30 controls, with normalization within four days in most cases. This pattern of reversibility is consistent with the hypothesis that ONSD reflects a dynamic phenomenon of ICP elevation, but none of these studies allows estimation of the difference relative to independent normotensive controls.

### Publication bias

With nine studies in the primary outcome – below the recommended threshold of ten – the methods for assessing asymmetry have low power. Egger's test did not indicate asymmetry (intercept 1.33; SE 6.19; p = 0.836), a result that, given the number of studies, should not be interpreted as evidence of absence of bias. The funnel plot is provided solely for transparency (Supplementary Material S1).

## Discussion

This systematic review compiled the available evidence on ONSD ultrasonography in acute hypertensive states and showed that ONSD was, on average, higher in hypertensive patients than in controls, with a large effect size.

The pooled standardized mean difference was g = 1.55 (95% CI 1.06 to 2.04) and, excluding the single discordant study, g = 1.77 (95% CI 1.50 to 2.04), with a substantial reduction in heterogeneity. The finding proved robust: no sensitivity analysis — including restriction to studies that did not require dispersion conversion — shifted the effect below g = 1.5, and the influence analysis did not identify dependence on any individual study other than Sterrett et al.[16] However, diagnostic performance against an objective ICP reference standard could not be established.

Contrary to what might be assumed from the neurocritical-care literature, none of the studies identified in the hypertensive setting compared ONSD with invasive ICP measurement. In our view, this is the most consequential finding of the review: the current body of evidence consistently demonstrates that ONSD differs between hypertensive and normotensive individuals, but does not establish that this difference reflects objectively measured intracranial hypertension. This distinction is important because the thresholds currently used in practice – particularly the 5.8 mm cutoff – are derived from neurocritical populations and have not been validated in the hypertensive context.

From a cardiovascular imaging standpoint, ONSD expands the bedside ultrasound arsenal beyond the heart and great vessels, offering a non-invasive window into the intracranial repercussions of hypertensive crises. This positioning is particularly relevant in hypertensive disorders of pregnancy, whose association with future cardiovascular risk reinforces the relevance of the topic for cardiologists and imaging specialists.

**Table 3 – Thresholds that would maximize the Youden index in each study (modeled projection)**

| Study (year) | Optimal threshold (mm) | Sensitivity (%) | Specificity (%) | Youden index |
|---|---|---|---|---|
| Su et al.[22] | 4.14 | 86.3 | 90.4 | 0.77 |
| Biswas et al.[6] | 4.43 | 81.0 | 82.4 | 0.63 |
| Nagpal et al.[23] | 4.65 | 81.3 | 86.0 | 0.67 |
| Dikmetaş et al.[4] | 4.86 | 73.6 | 87.5 | 0.61 |
| Arzpeyma et al.[19] | 4.90 | 68.8 | 87.8 | 0.57 |
| Dubost et al.[5] | 4.95 | 75.3 | 76.2 | 0.52 |
| Singh et al.[17] | 5.21 | 90.1 | 86.8 | 0.77 |
| Kumar et al.[7] | 5.37 | 85.4 | 73.2 | 0.59 |
| Sterrett et al.[16] | 7.79 | 1.6 | 98.7 | 0.00 |

*Estimated values derived from the means and standard deviations of each group under a normal-distribution approximation; they do not represent observed counts nor thresholds reported by the original authors. The diagnostic target is the distinction between acute hypertensive state and control, not intracranial hypertension. In Sterrett et al.,[16] the absence of separation between groups renders the Youden index null and the threshold practically indeterminate.*

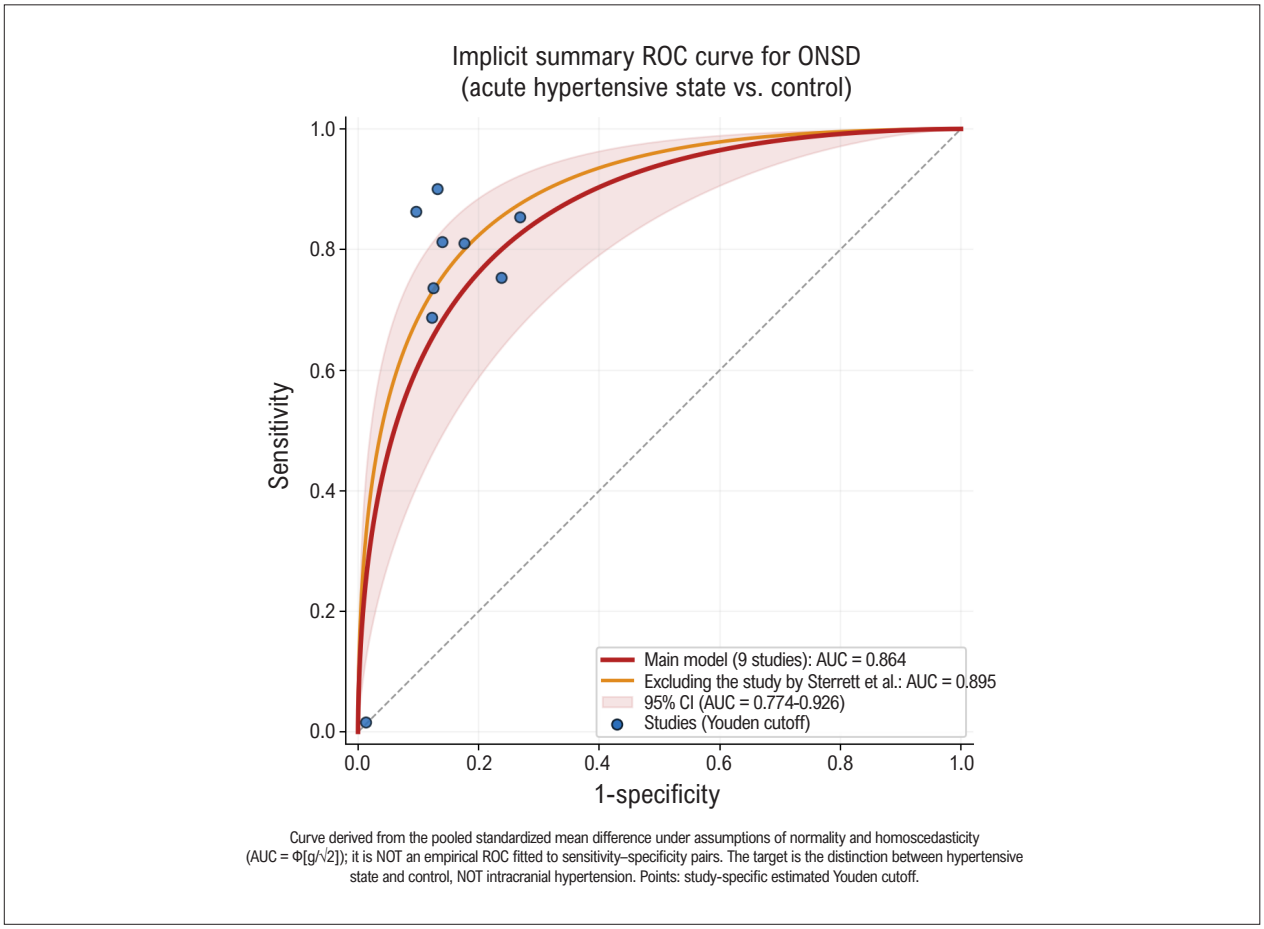


**Figura 5 –** *Implicit summary ROC curve for ONSD in distinguishing acute hypertensive state from control, derived from the pooled standardized mean difference under assumptions of normality and homoscedasticity [AUC = Φ(g/√2)]. Red line: main model (nine studies; AUC 0.864); orange line: sensitivity analysis excluding the discordant study (AUC 0.895); band: 95% confidence interval; points: operating point of each study at the estimated Youden cutoff. The curve is not an empirical ROC fitted to sensitivity–specificity pairs; the target is the hypertensive-versus-control distinction, not intracranial hypertension.*

The discordant study warrants specific consideration. In Sterrett et al.,[16] the control group exhibited a higher mean ONSD than patients with preeclampsia, and the absolute values across all groups (5.5 to 5.9 mm) were substantially higher than those in the other studies, where control values ranged from 3.7 to 4.7 mm. This systematic shift suggests differences in acquisition technique or in the definition of the measurement point rather than a true absence of effect, and illustrates why methodological standardization is essential for comparability across studies.[16] Technical differences described in the literature – internal versus external dural measurement, chosen axis, interocular asymmetry, and the ratio between ONSD and globe diameter – influence absolute values and thresholds and help interpret the observed heterogeneity.

The issue of a diagnostic cutoff deserves separate treatment, because the clinical question actually contains two distinct questions with opposite answers. A threshold intended to detect intracranial hypertension is, within this body of evidence, structurally underivable: a cutoff only exists in relation to a measured target, and none of the studies measured ICP. A threshold intended to distinguish hypertensive from normotensive patients is derivable – as three of the included studies attempted – but has limited clinical utility, since the hypertensive condition is already known from blood pressure measurement at the time of the exam.

Even if this more modest target were accepted, the data do not support a single unified threshold. The 2.23-mm span between control-group means and the 4.14- to 7.79-mm range of study-specific optimal cutoffs indicate that the same numerical ONSD value carries different meanings depending on the study. The most plausible explanation is technical: whether the measurement is referenced to the inner or outer dural border, the acquisition axis, and the imaging plane all produce systematic differences in the literature on the order of 0.5 to 1 mm – a magnitude comparable to the very effect one seeks to detect. Pooling thresholds obtained under non-standardized techniques and against different diagnostic targets would amount to combining quantities known to differ from one another, a practice against which the methodological literature on metanalysis explicitly warns.

A direct practical implication follows from this: the 5.8-mm threshold, currently the most widely used in obstetric studies, was transposed from neurocritical populations without validation in the hypertensive setting, and its performance here ranged from perfect to useless depending on the study – from no control participant reaching the value in four studies to 44% of controls reaching it in another.

Until technical standardization and validation against an objective reference standard are available, thresholds should be derived and reported by technique and by population, rather than transferred across contexts. Obtaining a defensible pooled cutoff would require individual participant data or multi-threshold modeling, approaches that the available aggregated data do not permit.

### Reference standard: why fundoscopic examination is not an appropriate comparator

None of the fourteen studies performed fundoscopic examination or documented papilledema, which prevents any direct comparison between the two techniques. This absence, however, is not the main gap in the body of evidence. Because papilledema is itself an indirect sign of intracranial hypertension, fundoscopy does not qualify as a reference standard: estimates of sensitivity and specificity require that each individual be classified according to a standard considered definitive, and validating a test against an imperfect reference penalizes it precisely in situations where it would be earlier or more sensitive than that reference.

It follows that agreement with fundoscopic findings is not the appropriate criterion for judging ONSD, and that the relevant reference standard remains measured ICP – which, as already noted, none of the included studies assessed. An indirect piece of evidence from the dataset itself illustrates the issue. Brzan Simenc et al.[18] measured, in the same 30 patients with severe preeclampsia and during the same examination session, two ultrasonographic markers: optic disc height, which reflects papilledema, and ONSD.[18] Optic disc height was abnormal in 23 participants (76.7%; 95% CI 59.1 to 88.2), whereas ONSD exceeded 5.8 mm in 13 participants (43.3%; 95% CI 27.4 to 60.8), with no positive cases among the 30 controls for either marker. The 33-percentage-point difference between markers obtained at the same moment and in the same individuals is consistent with the hypothesis that the 5.8-mm threshold, imported from neurocritical populations, is insensitive in this setting – an interpretation that aligns with the threshold analysis presented in the results.

This observation should be interpreted with caution. It comes from a single study with thirty participants; the proportions are paired, but the article does not publish the cross-tabulation, meaning that a formal paired-data test cannot be calculated and only marginal distributions can be compared. Both markers are ultrasonographic, and optic disc height measured by ultrasound is not equivalent to papilledema identified on fundoscopy; moreover, the 1-mm threshold for disc height has likewise not been validated against objective ICP measurement. The finding therefore raises a hypothesis regarding the adequacy of the ONSD threshold, but does not allow one to conclude that ONSD is superior, equivalent, or inferior to fundoscopy – a comparison that the available data simply do not permit.

The convergence of the paired-design studies adds an independent argument. ONSD decreased after magnesium sulfate administration and after delivery in four distinct studies, with magnitudes consistent across them. This temporal reversibility, although not poolable with the primary outcome, is difficult to explain by selection bias and supports the interpretation that ONSD tracks a dynamic pathophysiological phenomenon.

### Limitations

This work has several important limitations. The first is the complete absence of comparison with an objective

ICP reference standard among the included studies, which restricts inference to mean differences and prevents any statement about true diagnostic accuracy. The second arises from how the primary data were reported: three studies required dispersion conversion – two from medians and one from standard error – and in the latter, the main table of the article was internally inconsistent with another table from the same study, an ambiguity that could only be addressed through sensitivity analysis. Although these conversions follow established methods and the effect remained stable when converted studies were excluded, they introduce uncertainty and rely on assumptions of symmetry.

The third limitation is the high heterogeneity, only partially explained by the discordant study and by variability in control groups. The fourth is the impossibility of deriving or validating a diagnostic threshold, both because of the absence of a reference standard and because of the variability in absolute values across studies, which restricts the immediate bedside applicability of the method. The fifth is the predominance of studies on preeclampsia, with only one study involving non-pregnant hypertensive patients, which prevented formal subgroup comparison and limits generalization to other hypertensive etiologies. Additional limitations include the risk of bias in the source studies, the small sample size in most of them, and the inability to formally assess publication bias with fewer than ten studies.

It is therefore reinforced that future studies should report the mean and standard deviation of ONSD for each group – clearly distinguishing them from the standard error – so as to allow direct and reproducible pooling.

### Implications

For clinical practice, the findings support that ONSD is a bedside-measurable marker, reproducible and sensitive to clinical variation, whose behavior is consistent with the pathophysiology of intracranial involvement in acute hypertensive states. They do not, however, support its adoption as a substitute for fundoscopy or as a diagnostic test for intracranial hypertension: the reference standard needed to quantify its performance is lacking, and no threshold is transferable across populations and techniques. As long as these two gaps persist, the method may inform clinical decision-making alongside neurological assessment and neuroimaging, but cannot replace them.

For research, the findings allow precise specification of the study that is missing. It consists of a design in which the same participants undergo ONSD measurement and an objective ICP reference standard – either invasive measurement or opening pressure on lumbar puncture – preferably conducted in a population with non-obstetric hypertensive emergencies, currently represented by only one study among the nine poolable ones. Fundoscopy may be incorporated into this design as a clinically relevant comparator, but not as a reference standard, for the reasons discussed. Prior standardization of the acquisition technique – definition of the measurement border, axis, and plane – and availability of individual participant data are prerequisites for population-specific thresholds to be finally estimated and validated.

## Conclusion

In acute hypertensive states, the ONSD measured by transorbital ultrasonography was consistently greater than in controls, with a large effect size (g = 1.55; 95% CI 1.06 to 2.04) and robustness to sensitivity analyses, supporting its potential as a non-invasive bedside marker of intracranial involvement when fundoscopy is impractical. However, heterogeneity was high; one study yielded a discordant result; part of the data depended on dispersion conversions; no study compared the method with an objective ICP reference standard; and the data do not support adoption of a single cutoff value, given the incompatibility of absolute measurements across studies. These findings should be interpreted with caution and reinforce the need for standardization of both technique and threshold, for reporting of group-specific means and standard deviations, and for studies pairing ONSD with objective reference standards in the hypertensive setting.

## Author Contributions

Conception and design of the research, acquisition of data, analysis and interpretation of the data, statistical analysis, writing of the manuscript and critical revision of the manuscript for intellectual content: Ramos JVO, Melo MDT.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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### Study Association

This study is not associated with any thesis or dissertation work.

### Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

### Use of Artificial Intelligence

During the preparation of this work, the authors used **Claude (Anthropic)** to assist in the preparation of the text and in performing and verifying the resulting calculations. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

### Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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### *Supplemental Materials

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