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Transcranial Doppler Ultrasonography for Noninvasive Intracranial Pressure Monitoring: A Systematic Review and Meta-Analysis

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Abstract

Background and objectives:

Elevated intracranial pressure (ICP) is a critical secondary insult in acute brain injury. Invasive monitoring remains the reference standard but carries hemorrhagic and infectious risks. This systematic review and meta-analysis evaluates the diagnostic accuracy of transcranial Doppler (TCD)-derived indices for detecting intracranial hypertension compared with invasive ICP monitoring.

Methods

We searched PubMed, Embase, and Scopus to June 2026 for studies comparing TCD-derived indices (e.g., pulsatility index, estimated ICP [eICP]) with invasive intracranial monitoring in adults with acute brain injury. Methodological quality was assessed using QUADAS-2. Sensitivity and specificity were pooled using univariate random-effects models on the logit scale for studies providing sufficient 2×2 data.

Results

Nineteen studies evaluating heterogeneous acute brain injury populations met the inclusion criteria. Considerable methodological heterogeneity was observed across index tests and ICP thresholds. Four studies (925 paired observations) provided sufficient data to pool the performance of Czosnyka-derived eICP. Pooled specificity was relatively consistent at 74.1% (95% confidence interval [CI], 70.8–77.3%; I^2=24.9%), whereas pooled sensitivity was highly variable and imprecise at 50.3% (95% CI, 1.5–98.5%; I^2=81.7%). Other TCD parameters, including pulsatility index and venous flow velocity, demonstrated promising but inconsistent threshold-dependent diagnostic discrimination. Although several cohorts reported high negative predictive values, agreement between TCD-derived and invasive absolute ICP measurements was inconsistent, frequently exhibiting wide limits of agreement.

Conclusions

TCD-derived measures provide informative serial physiological assessments of cerebral hemodynamics but cannot interchangeably replace invasive ICP monitoring. Given its moderate specificity but heterogeneous sensitivity, TCD is most appropriately utilized as a complementary tool for noninvasive screening and multimodal monitoring rather than as a standalone absolute ICP estimator.

Introduction

Acute brain injury, including traumatic brain injury (TBI), aneurysmal subarachnoid hemorrhage, intracerebral hemorrhage, and large-vessel ischemic stroke, is a leading cause of death and disability worldwide, with more than 20 million incident cases annually[1]. Elevated intracranial pressure (ICP) is a common secondary insult across these conditions and a key determinant of cerebral perfusion, herniation risk, and functional outcome[2]. Invasive intraventricular and intraparenchymal monitoring remains the reference standard[3]. However, it requires neurosurgical placement and is relatively contraindicated in coagulopathy. It also carries hemorrhagic and infectious risks that increase with monitoring duration[4,5]. These constraints limit its use in resource-limited settings and in patients who cannot safely undergo placement.

These limitations have sustained interest in noninvasive alternatives, among which transcranial Doppler (TCD) ultrasonography is uniquely suited to bedside, repeatable assessment of cerebrovascular hemodynamics[6]. TCD-derived indices, including the pulsatility index (PI) and diastolic flow velocity–based estimators of cerebral perfusion pressure (CPP), have been compared with invasive ICP in single-center cohorts for more than two decades[6,7], with methodological refinements summarized in technical reviews[8]. More recently, scoping reviews and multicenter diagnostic accuracy studies have expanded this evidence base[9,10], while multimodal comparisons combining TCD with optic nerve sheath diameter (ONSD) and pupillometry suggest that combined approaches may outperform single indices[11]. However, prior meta-analyses have either been restricted to TBI in lower-middle-income settings[12] or evaluated TCD, largely through PI, as one of several noninvasive modalities[13], and reported diagnostic accuracy varies considerably with injury etiology, ICP threshold, and insonation timing[14].

No prior synthesis has examined TCD-derived indices, stratified by estimation method, across the full spectrum of adult acute brain injury with formal risk-of-bias appraisal using QUADAS-2[15]. We therefore conducted a systematic review and meta-analysis to evaluate the diagnostic accuracy of TCD-derived indices for detecting intracranial hypertension compared with invasive ICP monitoring and to characterize sources of heterogeneity relevant to future validation and clinical adoption.

Methods

Protocol and Registration

This systematic review and meta-analysis was conducted and reported in accordance with the PRISMA 2020 statement[16] and its extension for diagnostic test accuracy studies (PRISMA-DTA)[17]. The review protocol was prospectively registered with PROSPERO (CRD420261459625) before data extraction.

Artificial Intelligence

ChatGPT (Open AI) was used for editorial work (writing and editing). The authors confirm that they have reviewed all AI output, verify its accuracy and take full responsibility for accuracy of the content. We ensured there is appropriate attribution of all quoted material, including full citations.

Eligibility Criteria

Studies were eligible if they enrolled adult patients (≥ 18 years) with acute brain injury (TBI, aneurysmal subarachnoid hemorrhage, intracerebral hemorrhage, or acute ischemic stroke) who underwent paired or simultaneous assessment of a TCD-derived index test (PI, TCD-estimated ICP, TCD-estimated CPP, venous TCD, or TCD combined with ONSD) against invasive ICP monitoring (intraparenchymal, intraventricular, or lumbar cerebrospinal fluid opening pressure) as the reference standard. Eligible studies reported diagnostic accuracy metrics (sensitivity, specificity, predictive values, likelihood ratios, or area under the receiver-operating-characteristic curve [AUC]), sufficient data to calculate them, or correlation and agreement statistics (Pearson/Spearman coefficients, Bland–Altman bias and limits of agreement). Case reports, case series with fewer than 10 patients, animal studies, pediatric-only cohorts, conference abstracts without a peer-reviewed full text, and studies lacking a clearly defined ICP threshold or timing relative to invasive monitoring were excluded.

Information Sources and Search Strategy

PubMed/MEDLINE, Embase, and Scopus were searched from database inception to June 2026, supplemented by manual screening of the reference lists of included studies and relevant reviews. The search strategy combined Medical Subject Headings (MeSH) and free-text terms for “transcranial Doppler,” “pulsatility index,” “intracranial pressure,” “intracranial hypertension,” “noninvasive,” and “brain injury,” joined with Boolean operators. No language restriction was applied, and non-English reports were translated where necessary.

Study Selection

Two reviewers independently screened titles and abstracts and then assessed full texts of potentially eligible articles using Rayyan. Disagreements were resolved by discussion or, where necessary, adjudication by a third reviewer. The selection process is summarized in the PRISMA 2020 flow diagram (Fig. 1).

Data Extraction

Two reviewers independently extracted data using a standardized, piloted form, capturing study-level characteristics (author, year, country, design, sample size), population characteristics (age, sex, injury etiology, baseline severity), index-test characteristics (TCD modality, insonated vessel, cut-off value), reference-standard characteristics (monitor type, ICP threshold, timing relative to the index test), and outcome data (sensitivity, specificity, predictive values, likelihood ratios, AUC, correlation coefficients, and Bland–Altman bias and limits of agreement) at each reported threshold and timepoint. The unit of analysis (patient or measurement) and the handling of repeated measurements were recorded for each study

Risk of Bias and Applicability Assessment

The methodological quality of all included studies was assessed using the QUADAS-2 tool[15] across four domains: patient selection, index test, reference standard, and flow and timing. Concerns regarding applicability to the review question were also rated for the first three domains[15].

Signaling questions were specifically tailored to our review question, establishing invasive intracranial monitoring (intraparenchymal or ventricular) as the reference standard. Patient selection was rated as high risk if sampling was conducted by convenience, if groups were formed based on ICP status, or if selection depended on outcome or reference-test availability. The index test was judged as high risk when operators were unblinded to invasive ICP during operator-dependent readings, or when an estimation formula was both derived and tested within the same dataset. Furthermore, post hoc threshold selection was explicitly noted as a source of optimistic bias. The overall risk of bias was judged as High if any single domain was rated High, Unclear if any domain was Unclear, and Low otherwise.

All risk of bias judgments were made independently by two reviewers, with any discrepancies resolved through discussion and consensus. The final assessment results were visualized using the *robvis* package in R (McGuinness & Higgins, 2021).

Statistical Analysis

A univariate random-effects model was prespecified for pooling sensitivity and specificity[18]. Only four studies reported extractable 2×2 data for Czosnyka-derived estimated ICP (eICP); therefore, sensitivity and specificity were pooled separately using univariate random-effects models on the logit scale, with 95% confidence intervals. Correlation and agreement outcomes were summarized narratively because index tests, thresholds, and reporting formats were too heterogeneous for pooling. Heterogeneity was quantified using the I^2 statistic and Cochran Q test. Prespecified subgroup analyses by injury etiology (TBI vs. subarachnoid hemorrhage vs. intracerebral hemorrhage vs. ischemic stroke), index-test modality, ICP threshold, and timing of measurement relative to invasive monitoring, together with meta-regression, were not feasible given the number of pooled studies. Deeks’ funnel plot asymmetry test[19] was planned but not performed because fewer than 10 studies contributed to pooling. All analyses were performed using R version 4.4.5 (R Foundation for Statistical Computing, Vienna, Austria) with the meta and mada packages, with a two-sided $p < 0.05$ considered statistically significant[20].

Results

Search and Study Selection

The initial literature search across three databases (PubMed, Embase, and Scopus) identified a total of 1,682 records. Prior to screening, 453 duplicate records were removed, leaving 1,229 unique articles for evaluation. Title and abstract screening resulted in the exclusion of 1,197 records, leaving 32 reports that were all successfully retrieved for full-text eligibility assessment. Upon full-text review, 13 reports were excluded for the following reasons: wrong population (n = 6), wrong intervention and comparator (n = 5), and being review articles (n = 2). Ultimately, 19 studies met all inclusion criteria and were included in the final review, as detailed in Fig. 1[6,7,9,11,21–35].

Study Characteristics

Nineteen studies (Table 1) evaluated TCD-derived measures for noninvasive assessment of ICP, encompassing heterogeneous acute brain injury populations and a range of TCD approaches. Sixteen studies were prospective (two multicenter) and three were retrospective; sample sizes ranged from 14 to 280 patients. Six studies enrolled TBI-only cohorts, and 13 enrolled mixed or non-traumatic acute brain injury populations.

Table 1
Baseline characteristics of included studies

Study (Author, Year)	Country	Study Design	Setting; Recruitment Period	Patient Population	Sample Size (N)	Age (Years)†	Male (%)	GCS at Admission	TCD Parame Evaluate
Bellner et al. (2004)[7]	Sweden	Prospective observational	Single centre (University Hospital of Lund); period NR*****	Neurosurgical ICU patients with various intracranial disorders (SAH 57%, severe head injury 26%, ICH 9%, other 9%)	81 (658 PI measurements)	52 (2–79)**	46%	NR*****	Pulsatili Index (F Mean Fl Velocity (mFV)
Cardim et al. (2016)[28]	United Kingdom	Prospective observational	Single centre (Addenbrooke's Hospital, Cambridge); 2013–2015	Traumatic brain injury (TBI) patients in neurocritical care	40 (66 recordings)	35 ± 15	80%	6 (3–14) (median [range], pre-intubation)	Black-B Model (nICP_B Diastoli Flow Ve (nICP_F Critical Closing Pressur (nICP_C Pulsatili Index (nICP_P
Chang et al. (2021)[30]	China	Retrospective observational	Single centre (Second Affiliated Hospital of Air Force Medical University, Xi'an); Jan 2018–Apr 2019	Traumatic brain injury (TBI) patients post-surgery (age ≥ 16 years)	68 (115 valid TCD measurements)	46.17 ± 16.87	67.60%	6.59 ± 2.45 (mean ± SD)	Pulsatili Index (F Optic Ne Sheath Diamete (ONSD)'
Czosnyka et al. (1998)[6]	United Kingdom	Prospective observational	Single centre (Addenbrooke's Hospital, Cambridge); period NR*****	Head-injured ICU patients (GCS < 13)	96 (421 daily examinations)	35 (6–75)**	67.70%	6 (3–12) (mean [range])	Flow Ve Ratio (FVd/FV Gosling Pulsatili Index (G Spectra Pulsatili Index (S Estimat CPP (eC
Edouard et al. (2005)[21]	France	Prospective observational	Single centre (Bicêtre Hospital, Le Kremlin-Bicêtre); period NR*****	Severe traumatic brain injury (GCS ≤ 8) with diffuse brain injuries	20 (two groups of 10)[a]	33 (21–57)[a]	80%	Group A: 6 (3–8); Group B: 5 (3–8) (median [range])[a]	Estimat CPP (CP Critical Closing Pressur (CrCP), Cerebra Flow Ind (CFI), M Flow Velocitie
Hamzah et al. (2020)[29].	Indonesia	Prospective observational	Single centre (Dr. Soetomo General Hospital, Surabaya); Apr–May 2019	Brain injury patients (TBI 37%, stroke 50%, CNS infection 13%)	30 (87 examinations)	46.4 ± 17.11	53.30%	7.47 ± 1.76 (mean ± SD)	Middle Cerebra Artery Pulsatili Index (M PI), Opti Nerve Sheath Diamete (ONSD)'
Klavansky et al. (2025)[34]	United States	Retrospective observational	Single centre (Mount Sinai Hospital, New York); Mar 2019–Jun 2022	Acute brain injury patients requiring EVD placement	40 (56 measurements)	54.5[c]	39.00%[c]	NR*****	Middle Cerebra Artery Pulsatili Index (M PI)***
Moraes et al. (2023)[32]	Brazil	Prospective observational	Single centre (Federal University of São Paulo); Mar 2019–Mar 2020	Neuro-ICU stroke patients (SAH, IPH, IS) requiring ICP monitoring	18 (60 measurements)	53.6 ± 14.3[d]	NR*****	NR*****	Middle Cerebra Artery Pulsatili Index (M PI)***

Study (Author, Year)	Country	Study Design	Setting; Recruitment Period	Patient Population	Sample Size (N)	Age (Years)†	Male (%)	GCS at Admission	TCD Parame Evaluat
Prunet et al. (2012)[22]	France	Prospective observational (blinded; convenience sample)	Single centre (Sainte Anne Military Teaching Hospital, Toulon); Jan–Dec 2008	Neurocritical care patients (TBI, stroke, SAH); 20 with high ICP and 20 with normal ICP[e]	40	49.5 ± 17.5[e]	77.50%[e]	NR*****	Middle Cerebra Artery Pulsatili Index (M PI; TCD TCCS)
Qu et al. (2026)[35]	China	Prospective observational	Single centre (tertiary hospital, Qinghai-Tibet Plateau; median residential altitude 2520 m); Apr–Jul 2025	Neurocritically ill patients at moderate-to-high altitude (intracerebral haemorrhage, cerebral contusion/laceration, space-occupying lesions)	54 (158 measurements)	54 (48–62)*[f]	81.50%[f]	NR*****	TCCD-derived Middle Cerebra Artery Pulsatili Index (M PI)
Rajajee et al. (2023)[33]	United States	Prospective observational	Single centre (University of Michigan); Jan 2018–Nov 2021 (enrolment suspended Mar–Oct 2020)	Adult neurocritical care patients with acute brain injury (SAH, brain tumour, TBI, ICH, VP shunt)	55	54 (40–62)*[g]	49%[g]	NR*****	Middle Cerebra Artery F Velocitie Estimat ICP (ICF Pulsatili Index (F (with & without angle correcti
Rasulo et al. (2017)[26]	Italy	Prospective multicentre observational	Six neurocritical care units; Nov 2013–Aug 2014	Acute severe brain injury patients (TBI 53%, aSAH 29%, ICH 18%)	38 (114 measurements)	57.8 ± 15.7	NR*****	NR*****	Estimat ICP (ICF derived MCA diastolic mean velocitie
Rasulo et al. (2022)[9]	International (7 Countries)	Prospective multicentre observational	Sixteen centres in seven countries; Jul 2017–Apr 2020	Acute brain injury patients (TBI 53%, SAH 30%, ICH 14%, IS 3%)	262 (687 measurements)	65 ± 24.8[h]	70.40%[h]	TBI: 6 (4–7); ICH: 7 (4–8)*[h]	Estimat ICP (ICF derived MCA flo velocitie and MA
Robba et al. (2017)[27]	United Kingdom	Prospective observational	Single centre (Addenbrooke's Hospital, Cambridge); Jan–Nov 2016	Neurocritical care brain injury patients (TBI 70%, aneurysmal SAH 23%, ICH 6%)	64 (445 measurements)	53 (37–64)*	76.60%	7 (3–14) (median [range])	MCA Pulsatili Index (F MCA Diastolic Flow Ve (FVd), Straight Sinus Systolic Velocity (FVsv)**
Robba et al. (2020)[11]	Belgium	Prospective observational	Single centre (Erasme Hospital, Brussels); Jan 2017–Sep 2018	Acute brain injury patients (TBI 30%, SAH 47%, ICH 23%)	100	52 (44–62)*	55%	8 (5–12)*	Pulsatili Index (F Estimat ICP (eIC using Czosnyk formula
Shrestha et al. (2021)[31]	Nepal	Prospective observational	Single centre; May 2017–Feb 2020	Adult patients with severe traumatic brain injury (GCS < 8)	26 (≈ 4 readings per patient)[i]	43.57 ± 19.95	84.60%	< 8 (inclusion criterion; mean NR*****)	Peak Systolic Velocity Middle Cerebra Artery (I PSV)

Study (Author, Year)	Country	Study Design	Setting; Recruitment Period	Patient Population	Sample Size (N)	Age (Years)†	Male (%)	GCS at Admission	TCD Parame Evaluat
Varsos et al. (2015)[24]	United Kingdom	Retrospective observational	Single centre (Addenbrooke's Hospital, Cambridge); 2002–2011	Sedated and ventilated traumatic brain injury (TBI) patients	280 (780 recordings)	29 (20–43)*	78.20%	6 (4–8)* (pre-intubation)	MCA Flo Velocity Critical Closing Pressur (CrCP)-derived Estimat CPP/ICI
Cardim et al. (2019)[28]	United Kingdom	Prospective observational (consecutive patients)	Single centre (Addenbrooke's Hospital, Cambridge); Jan 2016–Aug 2017b	Traumatic brain injury (TBI) patients requiring invasive ICP monitoring	100 (single TCD measurement per patient)	43 (26.7–59.5)*	74%	7 (3–9)*	Estimat ICP (ICI diastolic velocity-derived estimat using FV FVm an MAP)
Zweifel et al. (2012)[23]	United Kingdom	Retrospective analysis of prospectively collected data	Single centre (Addenbrooke's Hospital, Cambridge); 1992–2009	Head-injured patients in the neurosciences critical care unit	290 (762 recorded daily sessions)	32.8 ± 15.9	NR**	6 ± 3 (mean ± SD)	Gosling Pulsatili Index (F

Notes and definitions

† Age is mean ± SD unless otherwise indicated by a footnote symbol. Values are as reported in each source article; percentages are shown as reported or ca

* Median (interquartile range, IQR); for GCS, "median [range]" is stated where the source reports a range.

** Mean (range); standard deviation (SD) not reported in the source article.

*** Multimodal study: the TCD parameter was assessed together with other non-invasive modalities in the same patients (e.g., optic nerve sheath diameter [(waveform morphology, venous TCD). Only the TCD-derived findings are relevant to this review.

**** Age reported only as a range/category band (40–49, 50–59, 60–69, 70–79 years); mean or median not reported.

***** NR = not reported in the source article.

[a] Edouard et al. enrolled 20 patients in two groups of 10 (group A: repeated CPP estimation during the clinical course; group B: CPP estimation during a CO_2 the value reported for group A (group B: 33 [23–50]); the article does not state whether the central value is a mean or median, and parentheses give the rang from the individual patient listing (16/20).

[b] Diagnoses as listed in the source Table 1 (SAH 6, ICH 6, acute subdural haematoma 1, malignant MCA infarction 1 of 14 patients); the Methods text descri is based on acoustic signal propagation and is not a Doppler technique.

[c] Klavansky et al. report age only as group means by ICP category (ICP < 15 mmHg: 59.6 years, n = 30; ICP ≥ 15 mmHg: 40.7 years, n = 11); the value shown i age range are not reported. Male (39%) is calculated from the reported female counts (25 of the 41 records with sex data).

[d] Mean age from the source Table 2 (mean 53.6, median 54, SD 14.3, range 31–84; N = 60 measurements in 18 patients); the abstract reports 52 ± 14.3 year

[e] Prunet et al. studied two groups of 20 patients (high ICP: age 49 ± 17 years, 80% male; normal ICP: age 50 ± 18 years, 75% male). Age and sex shown are th mean of the two group SDs, not a pooled SD). High-ICP and normal-ICP groups were selected to be equal in size (convenience sample), so the cohort is not

[f] Qu et al.: age (median [IQR]) is calculated across the 158 measurements; male sex (81.5%) is 44 of 54 patients. ICP was measured by lumbar puncture ma

[g] Rajajee et al.: 60 patients were enrolled and 55 underwent TCCS; age and sex are as reported in the source Table 1, which is labelled n = 63 (sex: 32 women

[h] Rasulo et al. (2022): 266 patients were enrolled and 262 analysed (687 paired measurements). Age is mean ± SD as reported; sex percentage (178 men, 70 reported by injury type (TBI, ICH); SAH patients were graded by WFNS (median 4 [2–5]) and ischaemic stroke patients by NIHSS (median 21 [20–23]). Intraci min in TBI.

[i] Shrestha et al. recorded ICP in cm H_2O (1 cm H_2O = 0.7356 mmHg); readings were taken on day 1 and day 3 on both sides, about 4 readings per patient on

Abbreviations: aSAH, aneurysmal subarachnoid haemorrhage; CFI, cerebral flow index (CPPe/RI); CNS, central nervous system; CPP, cerebral perfusion pres pressure; EVD, external ventricular drain; FVd, diastolic flow velocity; FVm/mFV, mean flow velocity; FVsv, straight sinus systolic flow velocity; GCS, Glasgow Gosling pulsatility index; ICH, intracerebral haemorrhage; ICP, intracranial pressure; ICPe/eICP, estimated ICP; ICPtcd, ICP estimated from TCD (MAP – CPPe, haemorrhage; IQR, interquartile range; IS, ischaemic stroke; LP, lumbar puncture; MAP, mean arterial pressure; MCA, middle cerebral artery; NA, not applicabl of Health Stroke Scale; NR, not reported; ONSD, optic nerve sheath diameter; PI, pulsatility index; PIa, MCA pulsatility index from arterial TCD; PSV, peak syst haemorrhage; SD, standard deviation; SDH, subdural haematoma; SPI, spectral pulsatility index (F1/FVm); TBI, traumatic brain injury; TCCD/TCCS, transcrani VP, ventriculoperitoneal; WFNS, World Federation of Neurosurgical Societies.

Considerable methodological heterogeneity was observed in both index tests and reference standards. TCD measures included raw arterial PI, diastolic and systolic flow velocities, venous flow velocity, eICP, estimated CPP (eCPP), and critical-closing-pressure-based approaches. Several studies used the Czosnyka-derived relationship between mean arterial pressure and the ratio of diastolic to mean flow velocity to estimate CPP and subsequently ICP,

whereas others used PI-based regression equations or alternative hemodynamic models. Most studies used intraparenchymal probes or external ventricular drains as the invasive reference standard, although ICP thresholds varied, most commonly between 15 and 22 mmHg.

TCD-Estimated ICP Using the Czosnyka Method

The largest prospective multicenter evaluation was IMPRESSIT-2 [9], which included 262 patients and 687 paired TCD/invasive ICP measurements across 16 intensive care units in seven countries. At an invasive ICP threshold > 22 mmHg, averaged measurements yielded a sensitivity of 70.4% (95% CI, 40.7–92.6), specificity of 71.9% (51.9–94.0), and AUC of 0.756 (0.656–0.855). Diagnostic performance varied with timing and ICP threshold; sensitivity and specificity were 65.1% and 74.4%, respectively, for ICP > 20 mmHg and 81.2% and 84.1% for ICP > 25 mmHg. At the > 22-mmHg threshold, the negative predictive value (NPV) was high (95.6%), whereas the positive predictive value (PPV) was low (23.0%). Agreement with invasive ICP was modest (concordance correlation coefficient, 0.333), with a mean bias of − 3.3 mmHg and wide limits of agreement (− 26.1 to + 19.5 mmHg).

The earlier IMPRESSIT-1 pilot [26] included 38 patients and 114 paired measurements and reported 100% sensitivity for detecting ICP > 20 mmHg, with an AUC of 0.960 (95% CI, 0.898–1.000); however, only 12 patients experienced at least one intracranial-hypertension episode. In Robba et al. (2020) [11], Czosnyka-derived eICP demonstrated a sensitivity of 73%, specificity of 84%, and AUC of 0.86 (95% CI, 0.77–0.93) for ICP > 20 mmHg. eICP correlated moderately with invasive ICP (Spearman r = 0.61, p < 0.001), although Bland–Altman analysis again showed wide limits of agreement (− 20.70 to + 17.44 mmHg). Conversely, Cardim et al. (2020) found poor performance of the same diastolic-flow-velocity-derived approach in 100 patients with TBI, with 0% sensitivity, 74.4% specificity, an AUC of 0.345 (95% CI, 0.231–0.459), and no significant correlation with invasive ICP (r = − 0.17, p = 0.097).

Pulsatility Index and Other TCD Parameters

Performance of raw MCA PI also varied substantially across studies. Robba et al. (2020) reported a sensitivity of 81%, specificity of 78%, and AUC of 0.85 (95% CI, 0.77–0.93) using PI > 0.97 for ICP > 20 mmHg, with a moderate correlation between PI and invasive ICP (r = 0.50, p < 0.001). In a non-TBI cohort, Moraes et al. reported 78.6% sensitivity, 77.3% specificity, and an AUC of 0.75 for PI > 1.28, with a repeated-measures correlation of r = 0.62 (p < 0.001). Prunet et al. reported sensitivity and specificity of 80% and 90%, respectively, for TCD PI > 1.35, with an AUC of 0.901; comparable performance was observed using portable transcranial color-coded sonography.

Other cohorts showed similarly variable results. Hamzah et al. reported 92.3% sensitivity, 75.0% specificity, and an AUC of 0.884 for MCA-PI > 1.11 at an ICP threshold > 15 mmHg, and Qu et al. reported 85% sensitivity, 93.6% specificity, and an AUC of 0.916 for PI > 1.21 against an ICP threshold > 15 mmHg measured by lumbar manometry. In contrast, Klavansky et al. reported sensitivity and specificity of 58% and 59%, respectively, for PI > 1.2[34]. Zweifel et al., using 762 recording sessions, demonstrated threshold-dependent discrimination of PI for elevated ICP, with AUCs increasing from 0.62 at ICP > 15 mmHg to 0.74 at ICP > 35 mmHg[23].

Alternative TCD-Derived ICP and CPP Approaches

Alternative TCD-based models showed variable diagnostic and agreement characteristics. Cardim et al. (2016) compared several noninvasive ICP estimators in TBI. The averaged estimator achieved the highest AUC (0.73), followed by the diastolic-flow-velocity estimator (0.70), black-box model (0.66), critical-closing-pressure estimator (0.64), and PI-based estimator (0.43). Correlations with invasive ICP were modest (r = 0.15–0.47), and limits of agreement remained relatively wide. Venous TCD showed promising discrimination in Robba et al. (2017), in which straight-sinus systolic flow velocity correlated with ICP (r = 0.72, p < 0.001) and yielded an AUC of 0.81 (95% CI, 0.74–0.87), whereas arterial PI and a diastolic-flow-based estimator were not significantly associated with ICP.

TCD-derived CPP estimation was also evaluated. The original Czosnyka study [6] demonstrated a correlation of r = 0.73 (p < 0.001) between estimated and measured CPP, with estimation errors < 10 mmHg in 71% and < 15 mmHg in 84% of examinations. The critical-closing-pressure-based method developed by Varsos et al. showed stronger correlation with measured CPP (r = 0.851, p < 0.001) and an AUC of 0.913 (95% CI, 0.883–0.944) for detecting CPP < 70 mmHg. In contrast, Edouard et al. observed worsening agreement between estimated and measured CPP during changing cerebrovascular conditions, with mean error increasing from approximately 2.8 mmHg under stable conditions to 8.1 mmHg during CO_2 reactivity testing.

Overall, diagnostic performance differed substantially according to the TCD parameter, estimation equation, ICP threshold, patient population, and measurement protocol. While several individual studies reported high AUCs and NPVs, agreement between TCD-derived and invasive absolute ICP measurements was inconsistent, with particularly wide limits of agreement for Czosnyka-derived eICP in larger validation cohorts.

Pooled Diagnostic Accuracy of Czosnyka-Derived eICP

Four studies provided sufficient 2×2 data to evaluate the diagnostic accuracy of eICP using the Czosnyka method for detecting intracranial hypertension (Table 2; Fig. 2). These studies included 925 paired observations, with individual study sizes ranging from 38 to 687 observations. The included cohorts represented patients with acute brain injury and used invasive ICP monitoring as the reference standard.

Table 2
Pooled diagnostic accuracy of Czosnyka-derived estimated ICP for detecting intracranial hypertension

Outcome	Studies (observations)	Pooled Estimate, % (95% CI)	I^2, %	P (Cochran Q)
Sensitivity for intracranial hypertension (Czosnyka-derived eICP)	4 (925)	50.3 (1.5–98.5)	81.7	0.0009
Specificity for intracranial hypertension (Czosnyka-derived eICP)	4 (925)	74.1 (70.8–77.3)	24.9	0.262

Abbreviations: CI, confidence interval; eICP, estimated intracranial pressure (Czosnyka method); ICP, intracranial pressure; I^2, I-squared statistic; τ^2, tau-squared statistic. P values are from the Cochran Q test for heterogeneity. Univariate random-effects models on the logit scale.

Sensitivity varied markedly across studies, ranging from 0% to 100%. Individual estimates were 37.8% (95% CI, 29.8–46.2) in Rasulo et al. (2022), 72.9% (58.2–84.7) in Robba et al. (2020), 100% (73.5–100) in Rasulo et al. (2017), and 0% (0–15.4) in Cardim et al. (2020). The pooled sensitivity was 50.3% (95% CI, 1.5–98.5%), with substantial between-study heterogeneity (I^2=81.7%; p = 0.0009); this estimate is too imprecise to be clinically informative.

Specificity was more consistent, ranging from 65.4% to 84.6%. Study-specific estimates were 73.5% (95% CI, 69.6–77.2), 84.6% (71.9–93.1), 65.4% (44.3–82.8), and 74.4% (63.2–83.6) in Rasulo et al. (2022), Robba et al. (2020), Rasulo et al. (2017), and Cardim et al. (2020), respectively. The pooled specificity was 74.1% (95% CI, 70.8–77.3%), with low between-study heterogeneity (I^2=24.9%; p = 0.262). Overall, these findings indicate considerable variability and imprecision in sensitivity, contrasted with relatively consistent moderate specificity across studies.

Summary of findings:

Overall, diagnostic performance differed substantially according to the TCD parameter, estimation equation, ICP threshold, patient population, and measurement protocol. While several individual studies reported high AUCs and NPVs, agreement between TCD-derived and invasive absolute ICP measurements was inconsistent, with particularly wide limits of agreement for Czosnyka-derived eICP in larger validation cohorts. A comprehensive summary of the diagnostic accuracy metrics across all 19 included studies is provided in Table 3.

Table 3
Summary of Findings: Diagnostic Accuracy of TCD-Derived Indices

Study (Author, Year)	Population Studied	Sample Size (N)	Sensitivity	Specificity	PPV	NPV
Cardim et al. (2019)[28]	Traumatic brain injury patients requiring invasive ICP monitoring	100	0%	74.4%	NR	NR
Bellner et al. (2004)[7]	Neurosurgical ICU patients with various intracranial disorders	81	88.0–91.0%	69.0–92.0%	NR	NR
Cardim et al. (2016)[25]	Traumatic brain injury (TBI) patients in neurocritical care	40	0.0%	74.4%	NR	NR
Chang et al. (2021)[30]	Traumatic brain injury (TBI) patients post-surgery	68	NR	NR	NR	NR
Czosnyka et al. (1998)[6]	Head-injured ICU patients (GCS < 13)	96	High*	High*	94.0%	NR
Edouard et al. (2005)[21]	Severe traumatic brain injury (GCS ≤ 8) with diffuse brain injuries	20	NR	NR	NR	NR
Zweifel et al. (2012)[23]	Head-injured patients	290	NR	NR	NR	NR
Hamzah et al. (2020)[29]	Brain injury patients (TBI, stroke, central nervous system infection)	30	92.3%	75.0%	NR	NR
Klavansky et al. (2025)[34]	Acute brain injury patients requiring EVD placement	40	58.0%	59.0%	21.0%	84.0%
Moraes et al. (2023)[32]	Neuro-ICU stroke patients (SAH, IPH, IS) requiring ICP monitoring	18	78.6%	77.3%	50.0%	91.7%
Prunet et al. (2012)[22]	Neurocritical care patients (TBI, stroke, SAH)	40	80.0%	90.0%	NR	NR
Qu et al. (2026)[35]	Neurocritically ill patients at moderate-to-high altitude	54	85.0%	93.6%	NR	NR
Rajajee et al. (2023)[33]	Adult neurocritical care patients with acute brain injury	55	100%	30.0%	17.0%	100%
Rasulo et al. (2017)[26]	Acute severe brain injury patients (TBI, aSAH, ICH)	38	100%	65.4%	NR	98.0%
Rasulo et al. (2022)[9]	Acute brain injury patients (TBI, SAH, ICH, IS)	262	70.4%	71.9%	23.0%	95.6%
Robba et al. (2017)[27]	Neurocritical care brain injury patients (TBI, SAH, ICH, stroke)	64	NR	NR	NR	NR
Robba et al. (2020)[11]	Acute brain injury patients (TBI, SAH, ICH)	100	73.0%	84.0%	NR	NR
Shrestha et al. (2021)[31]	Adult patients with severe traumatic brain injury (GCS < 8)	26	82.1%	84.4%	NR	NR
Varsos et al. (2015)[24]	Sedated and ventilated traumatic brain injury (TBI) patients	280	NR	NR	NR	NR

NR = Not Reported (or insufficient diagnostic threshold data extracted).

* Values for Czosnyka (1998) were qualitatively reported as highly sensitive/specific in extraction.

Risk of bias

A total of 19 studies were assessed for methodological quality using QUADAS-2. Overall, 1 study was at low risk of bias, 9 were unclear, and 9 were at high risk.

In the patient selection domain, 6 studies were high risk, 4 were low risk, and 9 were unclear. The high-risk ratings were primarily driven by retrospective designs, convenience sampling, or case-control-type selection. In the index test domain, 5 studies were high risk, 3 were low risk, and 11 were unclear. The main methodological issues identified were operators remaining unblinded to invasive ICP and estimation formulas being derived and tested within the same cohort.

The reference standard domain carried the lowest risk of bias, with 18 studies rated as low risk due to the use of invasive intracranial monitors. A single exception, which utilized lumbar puncture pressure, was rated unclear. For flow and timing, 1 study was high risk, 8 were low, and 10 were unclear. The lack of clarity in this domain was mostly due to unreported time intervals between the index and reference tests. Additionally, optimal PI thresholds were frequently chosen post hoc, which may overestimate diagnostic accuracy.

Discussion

This systematic review and meta-analysis shows that TCD provides clinically relevant information on intracranial hemodynamics in acute brain injury, but its diagnostic performance for intracranial hypertension varies substantially with parameter, estimation method, ICP threshold, and clinical setting. Across the

included studies, TCD-derived approaches ranged from simple arterial PI and flow-velocity measurements to mathematical estimation of ICP or CPP and venous or critical-closing-pressure-based methods. The principal quantitative finding was that Czosnyka-derived eICP had moderate and consistent specificity (74.1%; 95% CI, 70.8–77.3%; I^2=24.9%), whereas sensitivity was highly heterogeneous and could not be estimated with useful precision (50.3%; 95% CI, 1.5–98.5%; I^2=81.7%). These findings suggest that TCD-derived ICP should not be considered an interchangeable surrogate for invasive ICP measurement; rather, its potential value may lie in noninvasive screening, serial physiological assessment, and integration with other bedside information.

The marked heterogeneity in sensitivity is an important finding. Even among studies evaluating the same Czosnyka-derived approach, sensitivity ranged from 0% to 100%, while specificity was comparatively consistent. This indicates that performance cannot be attributed to the estimation equation alone and is likely influenced by differences in patient spectrum, cerebrovascular physiology, measurement timing, ICP threshold, and study methodology. The Czosnyka approach derives CPP from arterial pressure and the relationship between diastolic and mean cerebral blood-flow velocities, with ICP subsequently calculated from mean arterial pressure and estimated CPP [36]. Consequently, its performance depends not only on ICP but also on cerebrovascular resistance, autoregulatory state, arterial pressure, vascular compliance, and cerebral blood-flow dynamics[37]. Thus, similar ICP values may produce substantially different Doppler waveforms across patients and disease states[38,39].

The contrast between early studies and larger validation cohorts is particularly informative. IMPRESSIT-1 reported excellent discrimination, including 100% sensitivity and an AUC of 0.96, whereas the larger international IMPRESSIT-2 study demonstrated more modest performance[26]. In IMPRESSIT-2, sensitivity and specificity at the > 22-mmHg threshold were approximately 70%, while concordance with invasive ICP was limited and Bland–Altman limits of agreement were wide[9]. Robba et al. similarly found moderate-to-good discrimination but wide limits of agreement, whereas Cardim et al. reported essentially no sensitivity and an AUC below 0.50 in a TBI cohort[8,11]. Promising diagnostic performance in small or single-center cohorts should not be interpreted as evidence of interchangeability with invasive monitoring[40]. This contrast highlights an important distinction between discrimination and measurement agreement. A noninvasive method may distinguish patients with relatively higher versus lower ICP with reasonable accuracy without providing an absolute ICP estimate sufficiently close to the invasive value for direct substitution[41]. The wide limits of agreement observed in several studies are therefore clinically important, particularly when therapeutic decisions depend on relatively narrow ICP thresholds.

The findings for PI further support the concept that TCD reflects cerebrovascular physiology rather than ICP in isolation[14]. PI demonstrated moderate-to-high discrimination in several cohorts, with reported AUCs of 0.85–0.92 in some studies, but substantially poorer performance in others. Zweifel et al.[23] observed increasing discrimination as the ICP threshold increased, with AUC rising from 0.62 at ICP > 15 mmHg to 0.74 at > 35 mmHg. This threshold-dependent behavior is physiologically plausible: pronounced intracranial hypertension may produce sufficiently large changes in diastolic flow and waveform pulsatility to become detectable, whereas modest ICP elevations may be difficult to distinguish from alterations caused by vascular resistance, arterial pressure, $PaCO_2$, autoregulation, or other systemic and cerebral factors[42]. Accordingly, a single universal PI threshold is unlikely to provide equivalent diagnostic performance across heterogeneous neurocritical-care populations[43]. An isolated elevated PI should therefore not be read as a surrogate for a specific ICP value; rather, PI may be more appropriately regarded as a marker of altered cerebrovascular impedance whose clinical meaning depends on the surrounding physiological context[44].

TCD may also be more informative for characterizing CPP and cerebral hemodynamics than for generating an absolute ICP value[45]. The original Czosnyka eCPP method correlated with invasively measured CPP, while the critical-closing-pressure-based approach of Varsos et al. achieved a correlation of 0.851 and an AUC of 0.913 for detecting CPP < 70 mmHg[46]. Similarly, venous TCD demonstrated promising discrimination in Robba et al. (2017), whereas several arterial ICP estimators performed less consistently[47]. These findings are conceptually important because the primary physiological effect of rising ICP is mediated through its interaction with arterial pressure, cerebral perfusion, vascular resistance, and intracranial compliance[2]. TCD measures the consequences of these interactions on cerebral blood-flow velocity, not pressure itself[48]. Future applications may therefore benefit from treating TCD as a multidimensional cerebral hemodynamic monitor rather than reducing its information to a single estimated ICP value. This interpretation may also explain why approaches incorporating multiple hemodynamic variables, rather than PI or a single velocity measurement alone, have shown potential in selected cohorts. However, such approaches require prospective external validation before their clinical utility can be established.

The high NPVs reported in several studies also suggest a possible role for TCD in screening or ruling out clinically important intracranial hypertension, particularly where invasive monitoring is unavailable, delayed, or contraindicated[41]. For example, IMPRESSIT-2 reported an NPV of 95.6% at an ICP threshold > 22 mmHg despite a PPV of only 23%[9]. However, predictive values are strongly dependent on disease prevalence, and the prevalence of intracranial hypertension varied substantially across the included populations[49]. Moreover, the low and imprecise pooled sensitivity argues against using a negative TCD result alone to exclude elevated ICP[26]. The high NPV observed in individual cohorts should therefore not be generalized across populations with different prevalences of intracranial hypertension, and TCD should be interpreted alongside neurological examination, neuroimaging, systemic physiology, and other noninvasive measures rather than as a standalone gatekeeper for invasive monitoring[50].

The heterogeneity observed across studies also identifies priorities for future research. Standardization is needed in insonated vessel and depth, side of insonation, averaging of bilateral measurements, angle correction, timing relative to invasive ICP, ICP thresholds, and handling of repeated measurements[51]. Studies should report complete 2×2 diagnostic data at prespecified clinically relevant thresholds rather than only correlations or optimized ROC-derived cut-offs. The available literature frequently mixed patient-level and measurement-level observations, and several studies obtained multiple measurements from individual patients. Treating repeated measurements from the same patient as statistically independent observations may artificially narrow confidence intervals and overstate precision if within-patient correlation is not appropriately modeled. Future diagnostic studies should account explicitly for within-patient clustering and evaluate temporal changes, because the capacity of TCD to detect a change in ICP within an individual may ultimately prove more useful than its ability to estimate a single absolute ICP value.

Multimodal approaches represent another important direction. Because individual noninvasive markers interrogate different components of intracranial physiology, combining TCD with ONSD, pupillometry, imaging findings, or other waveform-based measures may improve diagnostic performance beyond any individual parameter [11]. Future models should therefore focus not only on maximizing AUC in derivation cohorts but also on prospective external validation, calibration, clinically meaningful rule-out and rule-in thresholds, and demonstration that incorporation of TCD changes management or patient outcomes.

Limitations

Several limitations should be considered when interpreting this review. First, substantial clinical and methodological heterogeneity existed across studies, including differences in brain-injury etiology, ICP thresholds, TCD techniques, estimation equations, reference standards, and measurement timing. Second, many studies were small and single-center, while only a limited number provided complete diagnostic contingency data suitable for quantitative synthesis. Consequently, the pooled sensitivity estimate for the Czosnyka method was highly imprecise and accompanied by substantial heterogeneity. Third, repeated measurements were common and were not uniformly handled across studies, potentially introducing unit-of-analysis effects; our pooled analysis also used measurement-level data and may therefore overstate precision. Fourth, differences in the prevalence and severity of intracranial hypertension may have influenced PPV and NPV and contributed to spectrum effects. Fifth, the small number of pooled studies precluded formal assessment of publication bias and the prespecified subgroup analyses. Finally, the diversity of TCD-derived indices prevented meaningful pooling of several promising approaches, including PI, venous TCD, and CPP-based estimators; therefore, their comparative performance should be interpreted primarily from individual studies rather than as evidence of superiority of one technique.

These findings warrant cautious clinical interpretation. TCD appears most defensible as a complementary physiological assessment rather than as a replacement for invasive ICP monitoring. In settings where invasive monitoring is unavailable or contraindicated, TCD may provide useful additional information, but its results should be interpreted within the broader clinical context. Importantly, the evidence does not establish a single TCD parameter or threshold that can reliably identify or exclude intracranial hypertension across heterogeneous adult acute brain-injury populations.

Conclusions

TCD provides a rapid, repeatable, and physiologically informative bedside assessment of cerebral hemodynamics, but current evidence does not support replacing invasive ICP monitoring with TCD-derived absolute ICP estimates. Czosnyka-derived eICP showed moderate and relatively consistent specificity but highly variable sensitivity, while PI and alternative TCD-derived approaches demonstrated promising yet heterogeneous diagnostic performance. The most compelling future role for TCD may therefore be as a complementary monitoring tool—supporting serial assessment of intracranial hemodynamic changes, identifying patients who warrant further evaluation, and contributing to multimodal noninvasive assessment—rather than as a standalone substitute for invasive ICP measurement.

Abbreviations

aSAH
Aneurysmal subarachnoid hemorrhage
AUC
Area under the receiver-operating-characteristic curve
CFI
Cerebral flow index
CI
Confidence interval
CPP
Cerebral perfusion pressure
CrCP
Critical closing pressure
eCPP
Estimated cerebral perfusion pressure
eICP
Estimated intracranial pressure
EVD
External ventricular drain
GCS
Glasgow Coma Scale
ICH
Intracerebral hemorrhage
ICP
Intracranial pressure
MAP
Mean arterial pressure
MCA

Middle cerebral artery
NPV
Negative predictive value
ONSD
Optic nerve sheath diameter
PI
Pulsatility index
PPV
Positive predictive value
SAH
Subarachnoid hemorrhage
TCD
Transcranial Doppler

Declarations

The authors confirm that manuscript complies with all instructions to authors

We confirm that authorship requirements have been met and the final manuscript was approved by all authors

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal

We Confirm adherence to ethical guidelines. IRB approval and Consent were not applicable due to review nature of the draft and lack of any identifiable patient data.

Contributions: AA and SBJ collected data and wrote the manuscript. YP wrote the manuscript. BCM and DMM oversaw data and statistical analyses. RBS supervised the work and revised the manuscript. All authors reviewed, edited and approved the final manuscript.

Artificial Intelligence: ChatGPT (Open AI) was used for editorial work (writing and editing). The authors confirm that they have reviewed all AI output, verify its accuracy and take full responsibility for accuracy of the content. We ensured there is appropriate attribution of all quoted material, including full citations.

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Figures

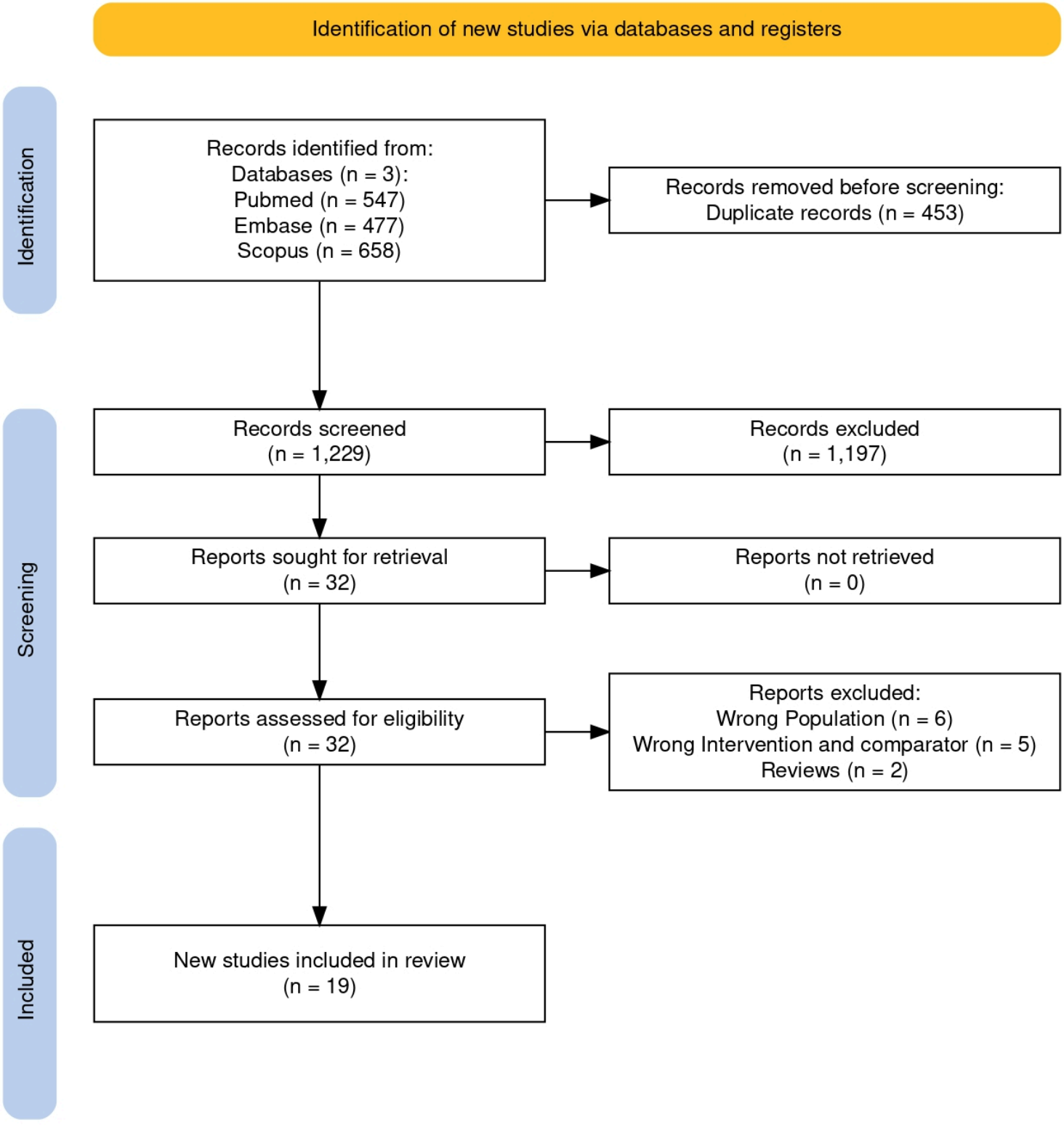


Figure 1

Prisma flow diagram

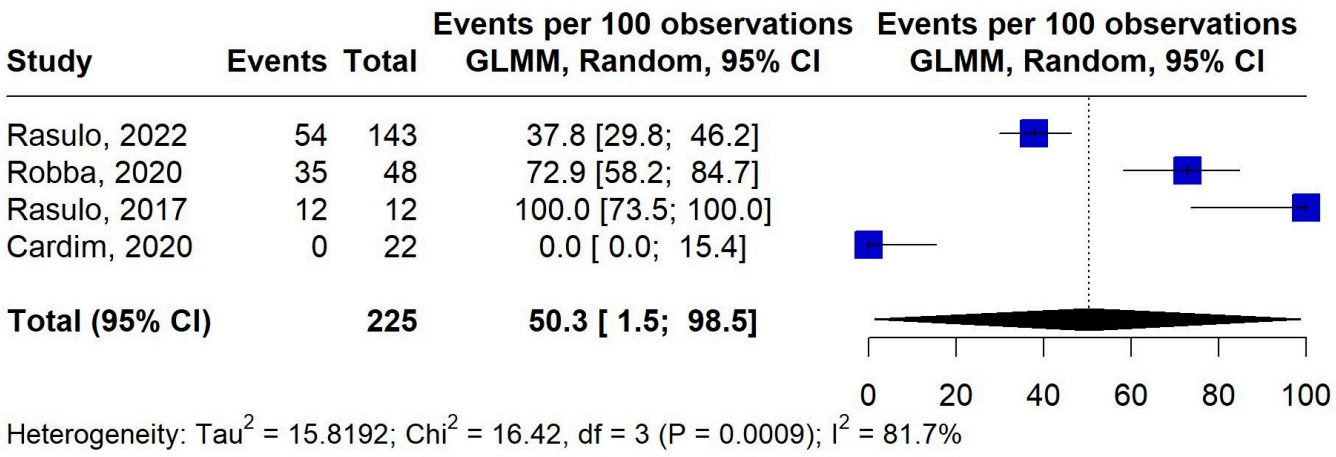


Figure 2

Forest plot representing the pooled sensitivity of studies using Czosnyka-derived estimated Intracranial pressure. 'Events' represent true positive cases (TP) and 'Total' represents TP and false negative (FN) cases.

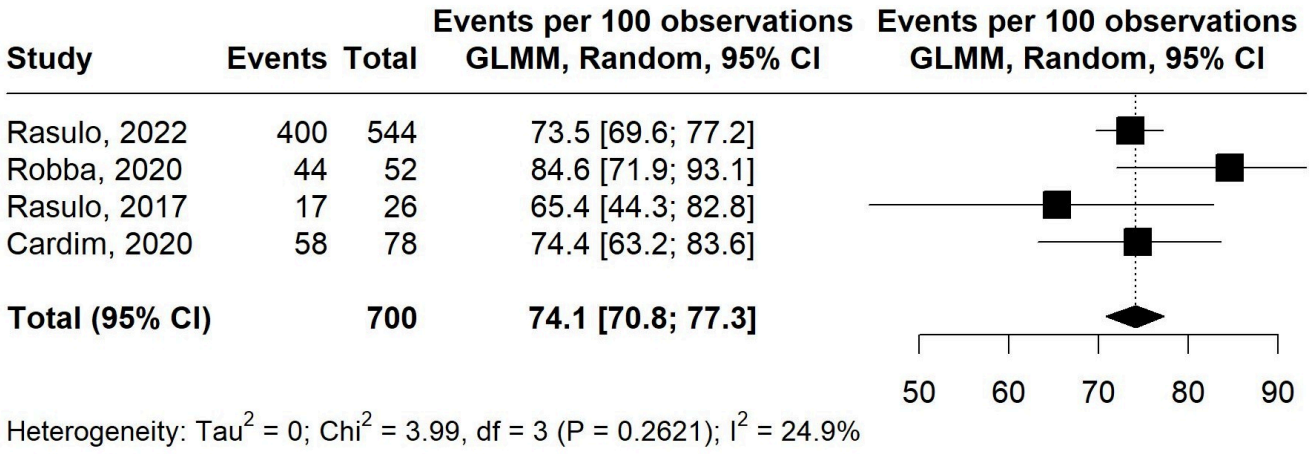


Figure 3

Forest plot representing the pooled specificity of studies using Czosnyka-derived estimated Intracranial pressure. 'Events' represent true negative cases (TN) and 'Total' represents TN and false positive (FP) cases.

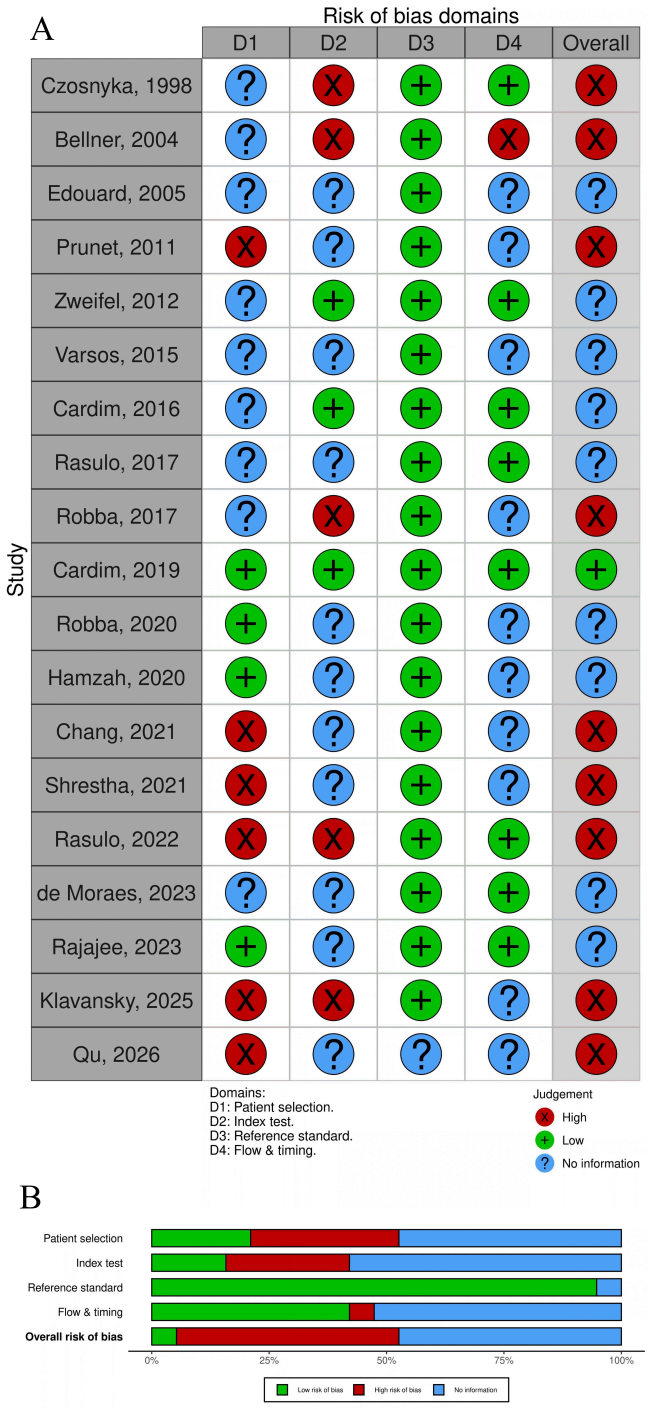


Figure 4

Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) risk of bias evaluation. (A) Traffic light plot displaying the specific risk of bias judgments for each domain across all individual included studies. **(B)**Weighted bar plot summarizing the proportion of studies with low, high, or unclear risk of bias (no information) within each domain. Green indicates low risk of bias, red indicates high risk of bias, and blue indicates unclear risk. Abbreviations: D1, Patient selection; D2, Index test; D3, Reference standard; D4, Flow and timing.