Fernando SM, Tran A, Cheng W, Rochwerg B, Taljaard M, Kyeremanteng K, English SW, Sekhon MS, Griesdale DEG, Dowlatshahi D, McCredie VA, Wijdicks EFM, Almenawer SA, Inaba K, Rajajee V, Perry JJ. Diagnosis of Elevated Intracranial Pressure in Critically Ill Adults – A Systematic Review and Meta-Analysis**.** *BMJ*.

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Supplemental Figure 1: **Electronic Search Strategies.**

Databases Searched:

- EMBASE Classic + Embase
- PubMed/Medline
- Scopus
- Web of Science
- Cochrane Central Register of Controlled Trials (CENTRAL)

EMBASE Classic + EMBASE 1947 to Week 39 2018
Date of Search: September 30, 2018

	Search Strategy	Results
1	intracranial pressure.mp.	32657
2	intracranial pressure.tw.	21394
3	intracranial pressure monitoring.mp.	3028
4	intracranial pressure monitoring.tw.	1269
5	intracranial pressure monitor.mp.	167
6	intracranial pressure monitor.tw.	146
7	intracranial hypertension.mp.	19244
8	intracranial hypertension.tw.	9234
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	43464
10	diagnos*.tw.	3077447
11	prognos*.tw.	770403
12	predict*.tw.	1775706
13	model*.tw	3060529
14	utility.tw	233183
15	scor*.tw	1237981
16	validation.tw	234880
17	risk.tw	2546031
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	9456971
19	**9 and 18**	**17744**
20	**limit 19 to (full text and human and English language)**	**2246**

PubMed/MEDLINE 1946 to Week 39 2018
Date of Search: September 30, 2018

	Search Strategy	Results
1	intracranial pressure.mp.	23800
2	intracranial pressure.tw.	16402
3	intracranial pressure monitoring.mp.	985
4	intracranial pressure monitoring.tw.	962
5	intracranial pressure monitor.mp.	122
6	intracranial pressure monitor.tw.	115
7	intracranial hypertension.mp.	9379
8	intracranial hypertension.tw.	6780

9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	28664
10	diagnos*.tw.	2164757
11	prognos*.tw.	513335
12	predict*.tw.	1342456
13	model*.tw	2458128
14	utility.tw	170633
15	scor*.tw	804682
16	validation.tw	164864
17	risk.tw	1774111
18	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	7129661
19	**9 and 18**	**10812**
20	**limit 19 to (full text and human and English language)**	**1533**

Supplemental Table 1: Standardized Data Extraction Sheet.

Data to be Extracted	Notes to Reviewer
Basic Study Information	
Study Title	
Journal/Conference	
Conference Abstract vs. Full-text	
Year of Publication	
Language	If published in language other than English - Exclude
Author	List first author only
Correspondence Email	
Study Design	
Prospective vs. Retrospective	
Number of Sites	
Country/Countries of Study	
Eligibility Assessment	
Does the study include only adult patients (i.e. ≥ 16 years of age)?	If "No" – Exclude
Does the study include patients with primary brain injury?	If "No" – Exclude
Does the study include patients from any of the following: A) Emergency Department; B) Intensive Care Unit; C) Neurological Intermediate Care Unit?	If "No" – Exclude
Does the study provide original data on accuracy of diagnostic measures for elevated ICP?	If "No" – Exclude
Was diagnosis of ICP confirmed using intracranial monitor with ICP ≥ 20 mmHg or intraoperative confirmation?	If "No" – Exclude
Does the study only include cases of confirmed elevated ICP? (i.e. without controls)	If "Yes" – Exclude
Is the data presented in the study completely included in another report?	If "Yes" – Exclude
Are the true positive, false positive, true negative and false negative counts stated, or can they be derived?	If "No" – Contact Corresponding Author, if no response after three attempts, then exclude
Index Test	
In what setting were diagnostic parameters calculated?	e.g. Emergency Department, ICU
Outcome	
How was elevated ICP confirmed?	e.g. ICP monitor ≥ 20 mmHg
Study Population	

From which setting were patients recruited?	e.g. Emergency Department, Hospital Wards, ICU
Was population was included?	
Were elderly patients included?	
Were patients with a 'Do Not Resuscitate' (or similar) order included?	
Were pregnant patients included?	
Were patients with any other co-morbidity included/excluded?	
Was the study population limited by symptom duration? If yes, indicate symptom duration	
If computed tomography was tested, what type of CT was used?	
2x2 Tables Diagnostic Parameter 1	
Diagnostic test being evaluated	e.g. Pupillary Dilation, motor posturing
Total number of patients	
Total number of ICP+ patients	
Total number of ICP- patients	
Total number of Test+ patients	
Total number of Test- patients	
True positives	
False positives	
True negatives	
False negatives	
Specificity provided	
Sensitivity provided	
2x2 Tables Diagnostic Parameter 2	
Total number of patients	e.g. Pupillary Dilation, motor posturing
Total number of ICP+ patients	
Total number of ICP- patients	
Total number of Test+ patients	
Total number of Test- patients	
True positives	
False positives	
True negatives	
False negatives	
Specificity provided	
Sensitivity provided	
Author Contact	
Contact author?	If more information needed, indicate here to contact author

Supplemental Table 2: Detailed Characteristics of the 40 Included Studies. Abbreviations: CT = computed tomography; ICH = Intracerebral hemorrhage; ICP = Intracranial pressure; SAH = Subarachnoid hemorrhage; TBI = Traumatic brain injury; TCD = Transcranial doppler

Author (Year)	Year	Journal	Type of Study	Sites	Country	Sample Size	Population	Inclusion Criteria	Exclusion Criteria	ICP Gold Standard	ICP+	ICP-	% Elevated ICP
Badri (2012)	2012	*Intensive Care Med*	Randomized trial	1	USA	365	TBI	Moderate-severe TBI (GCS < or = 12), Age >14, Cr < 177	Pregnant, prisoners, residents abroad, died within 48 hours	Intraparenchymal pressure monitor	59	306	16.16
Cardim (2012)	2012	*Neurocrit Care*	Retrospective	1	United Kingdom	27	TBI	At least one plateau wzve during ICP recording	None listed	Intraparenchymal pressure monitor	ONLY FOR TCD ANALYSIS		
Colquhoun (1989)	1989	*Clin Radiol*	Prospective	1	United Kingdom	17	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraventricular pressure monitor	14	3	82.35
Donovan (1998)	1998	*Lancet*	Retrospective	1	USA	12	Liver Disease	Patients admitted with liver cirrhosis and evidence of increased ICP	None listed	Epidural pressure monitor	7	5	58.33
Frumin (2014)	2014	*West J Emerg Med*	Prospective	1	USA	27	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraparenchymal pressure monitor	6	21	22.22
Galbraith (1981)	1981	*J Neurosurg*	Prospective	1	Scotland	26	TBI	Severe TBI with intracranial hematoma, with ICP monitoring	Patients with injury deemed to be unsurvivable	intraventricular pressure monitor	16	10	61.54
Geeraerts (2007)	2007	*Intensive Care Med*	Prospective	1	France	31	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraparenchymal pressure monitor	15	16	48.39
Hamani (2003)	2003	*Arq Neuropsiquiatr*	Prospective	1	Brazil	10	ICH	Patients with ganglionic and thalamic	None listed	intraventricular pressure monitor	3	7	30

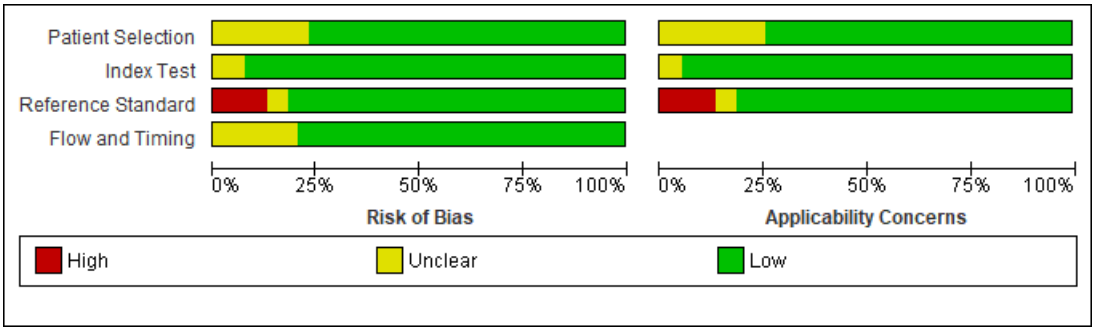
								hemorrhage; GCS 13 or less					
Hara (1998)	1998	*Neurol Res*	Retrospective	1	Japan	55	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraventricular pressure monitor	33	22	60
Hayashi (1982)	1982	*J Neurosurg*	Prospective	1	Japan	17	Mixed	ICP monitoring and plateau waves detected	None listed	intraventricular pressure monitor	12	5	70.59
Heuer (2004)	2004	*J Neurosurg*	Retrospective	1	USA	433	SAH	Aneurysmal SAH with placement of ICP monitor	None listed	Intraventricular pressure monitor	234	199	54.04
Hukkelhoven (2005)	2005	*Intensive Care Med*	Prospective	1	Netherlands	134	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraparenchymal pressure monitor	86	48	64.18
Jeon (2017)	2017	*PLoS One*	Prospective	2	South Korea	62	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	Ocular trauma; Severe mass effect; Decompression before ICP placement	Intraventricular pressure monitor	32	30	51.61
Jeon (2018)	2018	*J Intensive Care Med*	Retrospective	1	South Korea	25	Ischemic Stroke	Decompressive craniectomy for ischemic stroke	None listed	Intraparenchymal pressure monitor	5	20	20
Kamel (2012)	2012	*Neurocrit Care*	Retrospective	1	USA	57	ICH	Acute ICH with placement of ICP monitor	Transferred from a different centre; acute ICH without ICP monitor	Intraparenchymal pressure monitor	40	17	70.18
Kimberly (2007)	2007	*Acad Emerg Med*	Prospective	1	USA	38	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraventricular pressure monitor	8	30	21.05
Kramer (2016)	2016	*Neurocrit Care*	Prospective	1	Canada	644	TBI	Consecutive adult patients with moderate to severe TBI	None listed	Emergency Decompressive Craniectomy	51	593	7.92

								(GCS < or = 12), admitted to ICU					
Lee (2018)	2018	*Clin Neurol Neurosurg*	Retrospective	1	South Korea	64	Mixed	Hydrocephalus with insertion of EV drain or VP shunt	Existing EVD/VPS, no CT images 3 days before surgery	Intraventricular pressure monitor	8	56	12.5
Marshall (1983)	1983	*J Neurosurg*	Prospective	1	USA	15	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraventricular pressure monitor	6	9	40
Miller (1977)	1977	*J Neurosurg*	Prospective	1	USA	160	TBI	Adult patients with blunt head injury and decreased level of consciousness	Brain death diagnosis	Intraventricular pressure monitor	64	96	40
Moretti (2009)	2009	*Neurocrit Care*	Prospective	1	Italy	94	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraventricular pressure monitor	29	65	30.85
Nagel (2009)	2009	*J Neurosurg*	Prospective	1	Germany	182	SAH	Aneurysmal SAH with placement of ICP monitor	None listed	Intraparenchymal pressure monitor	18	164	9.89
Narayan (1982)	1982	*J Neurosurg*	Prospective	1	USA	61	TBI	Adult patients with severe TBI, inability to utter recognizable words following initial treatment	Gunshot wounds to the heads; brain death diagnosis	Intraventricular pressure monitor	8	53	13.11
Nirula (2014)	2014	*J Trauma Acute Care Surg*	Retrospective	11	USA	420	TBI	Age 16 or older; Blunt TBI; GCS of 13 or less;	None listed	Emergency Decompressive Craniectomy	210	210	50
Pace (2018)	2018	*J Trauma Acute Care Surg*	Retrospective	1	Canada	46	TBI	Age 18 or older; Blunt TBI;	CT imaging prior to transport to	Intraparenchymal or	19	27	41.30

								completion of head CT scan	peripheral hospital; died in the ED and did not undergo CT scanning	intraventricular pressure monitor			
Raffiz (2012)	2012	*Am J Emerg Med*	Prospective	1	Malaysia	41	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraparenchymal or intraventricular pressure monitor	ONLY FOR ONSD ANALYSIS		
Rajajee (2011)	2011	*Neurocrit Care*	Prospective	1	USA	65	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	Age <18; Ocular pathology;	Intraparenchymal or intraventricular pressure monitor	26	39	40
Rajajee (2018)	2018	*Neurocrit Care*	Retrospective	1	USA	23	Liver Disease	Acute Liver Failure patients with placement of ICP monitor	Poor quality of non-invasive measurements	Intraparenchymal or intraventricular pressure monitor	11	12	47.83
Rasulo (2017)	2017	*Crit Care*	Prospective	6	Italy	38	Mixed	Adult patients admitted to Neurocritical Care Unit with placement of ICP monitor	Poor ultrasound window; decompressive craniectomy; ICP treatment	Intraparenchymal or intraventricular pressure monitor			
Robba (2017)	2017	*PLoS Med*	Prospective	1	United Kingdom	445	Mixed	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	None listed	Intraparenchymal or intraventricular pressure monitor	86	359	19.33
Sadhu (1979)	1979	*Radiology*	Retrospective	1	USA	33	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraventricular pressure monitor	8	25	24.24
Selhorst (1985)	1985	*Neurosurgery*	Prospective	1	USA	21	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraparenchymal pressure monitor	18	3	85.71
Soldatos (2008)	2008	*Crit Care*	Prospective	1	Greece	32	TBI	TBI patients admitted to	Age <18; Ocular Pathology;	Intraparenchymal pressure monitor	27	5	84.38

								neurosurgical ward					
Soliman (2018)	2018	*Crit Care Res Pract*	Prospective	1	Saudi Arabia	200	TBI	TBI patients admitted to neurosurgical ward	Age <18; Ocular Pathology;	Intraparenchymal pressure monitor	177	23	88.5
Soustiel (2010)	2010	*Neurosurgery*	Prospective	1	Israel	122	TBI	Adult patients admitted to Neurosurgical Service with placement of ICP monitor	Decompressive craniectomy performed for any other reason other than ICP relief	Emergency Decompressive Craniectomy	36	86	29.51
Tabaddor (1982)	1982	*Surg Neurol*	Retrospective	1	USA	36	TBI	TBI patients admitted to neurosurgical ward	None listed	Intraventricular pressure monitor	23	13	63.89
Teasdale (1984)	1984	*J Neurol Neurosurg Psychiatry*	Retrospective	1	Scotland	37	TBI	TBI patients, comatose	None listed	Intraventricular pressure monitor	14	23	37.84
Wettervik (2018)	2018	*Acta Neurochir*	Retrospective	1	Sweden	602	TBI	TBI patients admitted to neurosurgical ward	None listed	Emergency Decompressive Craniectomy OR Thiopental for increased ICP	58	544	9.63
Zoerle (2015)	2015	*Crit Care Med*	Retrospective	1	Italy	116	SAH	Aneurysmal SAH with placement of ICP monitor	Imaging data unavailable	Intraventricular pressure monitor	42	74	36.21
Zweifel (2012)	2012	*Neurosurgery*	Prospective	1	United Kingdom	290	TBI	TBI with ICP monitor placed	None listed	Intraparenchymal pressure monitor	ONLY FOR TCD ANALYSIS		

Supplemental Figure 2: QUADAS-2 Quality Assessment for Risk of Bias and Applicability of the 40 Included Studies.


Patient Selection
Index Test
Reference Standard
Flow and Timing
0%
25%
50%
75%
100%
Risk of Bias
Applicability Concerns
High
Unclear
Low

Supplemental Table 3: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Pupillary Dilation

Question: Should pupillary dilation be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.28 (95% CI: 0.16 to 0.45)
Specificity	0.86 (95% CI: 0.75 to 0.93)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	10 studies 2126 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	85 (48 to 134)	141 (80 to 224)	197 (112 to 314)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								215 (166 to 252)	359 (276 to 420)	503 (386 to 588)	
True negatives (patients without elevated intracranial pressure)	10 studies 2126 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	601 (524 to 648)	430 (375 to 463)	258 (225 to 278)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having elevated intracranial pressure)								99 (52 to 176)	70 (37 to 125)	42 (22 to 75)	

Explanations

a. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 4: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Motor Posturing

Question: Should motor posturing be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.54 (95% CI: 0.37 to 0.71)
Specificity	0.64 (95% CI: 0.47 to 0.78)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	6 studies 830 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	163 (110 to 213)	272 (183 to 355)	380 (256 to 497)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								137 (87 to 190)	228 (145 to 317)	320 (203 to 444)	
True negatives (patients without elevated intracranial pressure)	6 studies 830 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	445 (326 to 545)	318 (233 to 389)	191 (140 to 233)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having elevated intracranial pressure)								255 (155 to 374)	182 (111 to 267)	109 (67 to 160)	

Explanations

a. Majority of included studies at high risk of bias.

b. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 5: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – GCS ≤ 8

Question: Should GCS <= 8 be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.76 (95% CI: 0.62 to 0.85)
Specificity	0.40 (95% CI: 0.27 to 0.55)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	10 studies 2234 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious [a]	serious [b]	none	227 (187 to 257)	379 (312 to 428)	531 (437 to 598)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								73 (43 to 113)	121 (72 to 188)	169 (102 to 263)	
True negatives (patients without elevated intracranial pressure)	10 studies 2234 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious [a]	serious [b]	none	279 (188 to 382)	200 (135 to 273)	120 (81 to 164)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having elevated intracranial pressure)								421 (318 to 512)	300 (227 to 365)	180 (136 to 219)	

Explanations

a. Variation in sensitivity and specificity amongst included studies.

b. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 6: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Basal Cisterns

Question: Should compression or absence of basal cisterns on CT imaging be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.86 (95% CI: 0.58 to 0.96)
Specificity	0.61 (95% CI: 0.29 to 0.86)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	5 studies 619 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	258 (174 to 289)	430 (290 to 482)	601 (406 to 675)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								42 (11 to 126)	70 (18 to 210)	99 (25 to 294)	
True negatives (patients without elevated intracranial pressure)	5 studies 619 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	427 (204 to 599)	305 (146 to 428)	183 (87 to 257)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having elevated intracranial pressure)								273 (101 to 496)	195 (72 to 354)	117 (43 to 213)	

Explanations

a. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 7: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Any Midline Shift

Question: Should midline shift >0mm be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.81 (95% CI: 0.64 to 0.91)
Specificity	0.43 (95% CI: 0.24 to 0.64)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	8 studies 627 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	243 (193 to 273)	405 (322 to 455)	566 (450 to 636)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								57 (27 to 107)	95 (45 to 178)	134 (64 to 250)	
True negatives (patients without elevated intracranial pressure)	8 studies 627 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious [a]	none	299 (168 to 446)	214 (120 to 319)	128 (72 to 191)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having elevated intracranial pressure)								401 (254 to 532)	286 (181 to 380)	172 (109 to 228)	

Explanations

a. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 8: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Midline Shift ≥ 5mm.

Question: Should midline shift >5mm be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.49 (95% CI: 0.34 to 0.64)
Specificity	0.70 (95% CI: 0.55 to 0.82)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	9 studies 832 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious [a]	not serious	none	148 (104 to 193)	247 (173 to 322)	346 (241 to 451)	⨁⨁⨁◯ MODERATE
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								152 (107 to 196)	253 (178 to 327)	354 (249 to 459)	
True negatives (patients without elevated intracranial pressure)	9 studies 832 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious [a]	not serious	none	490 (384 to 573)	350 (275 to 409)	210 (165 to 245)	⨁⨁⨁◯ MODERATE
False positives (patients incorrectly classified as having elevated intracranial pressure)								210 (127 to 316)	150 (91 to 225)	90 (55 to 135)	

Explanations

a. Variation in sensitivity and specificity amongst included studies.

Supplemental Table 9: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Midline Shift ≥ 10mm.

Question: Should midline shift >10mm be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.21 (95% CI: 0.13 to 0.31)
Specificity	0.89 (95% CI: 0.78 to 0.95)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	8 studies 651 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	62 (39 to 94)	104 (65 to 157)	145 (91 to 219)	⨁⨁⨁⨁ HIGH
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								238 (206 to 261)	396 (343 to 435)	555 (481 to 609)	
True negatives (patients without elevated intracranial pressure)	8 studies 651 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	624 (543 to 666)	446 (388 to 476)	268 (233 to 286)	⨁⨁⨁⨁ HIGH
False positives (patients incorrectly classified as having elevated intracranial pressure)								76 (34 to 157)	54 (24 to 112)	32 (14 to 67)	

Supplemental Table 10: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Marshall Score ≥ 3.

Question: Should Marshall score >= 3 be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.81 (95% CI: 0.64 to 0.91)
Specificity	0.60 (95% CI: 0.41 to 0.76)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	242 (191 to 273)	403 (318 to 455)	564 (444 to 636)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								58 (27 to 109)	97 (45 to 182)	136 (64 to 256)	
True negatives (patients without elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious </	serious [b]	none	419 (286 to 535)	300 (205 to 382)	180 (123 to 229)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having elevated intracranial pressure)								281 (165 to 414)	200 (118 to 295)	120 (71 to 177)	

Explanations

a. The majority of the included studies were at high risk of bias.

b. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 11: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Marshall Score ≥ 4.

Question: Should Marshall score >= 4 be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.54 (95% CI: 0.37 to 0.70)
Specificity	0.77 (95% CI: 0.63 to 0.87)

Prevalences	30%	50%	70%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	163 (112 to 210)	271 (187 to 351)	379 (262 to 491)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								137 (90 to 188)	229 (149 to 313)	321 (209 to 438)	
True negatives (patients without elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	538 (438 to 608)	385 (313 to 435)	231 (188 to 261)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having elevated intracranial pressure)								162 (92 to 262)	115 (65 to 187)	69 (39 to 112)	

Explanations

a. The majority of the included studies were at a high risk of bias.
b. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

Supplemental Table 12: Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Evidence Profile – Marshall Score ≥ 5.

Question: Should Marshall score >= 5 be used to diagnose elevated intracranial pressure in critically ill patients?

Sensitivity	0.45 (95% CI: 0.28 to 0.63)
Specificity	0.83 (95% CI: 0.70 to 0.92)

Prevalences	30%	50%	70%

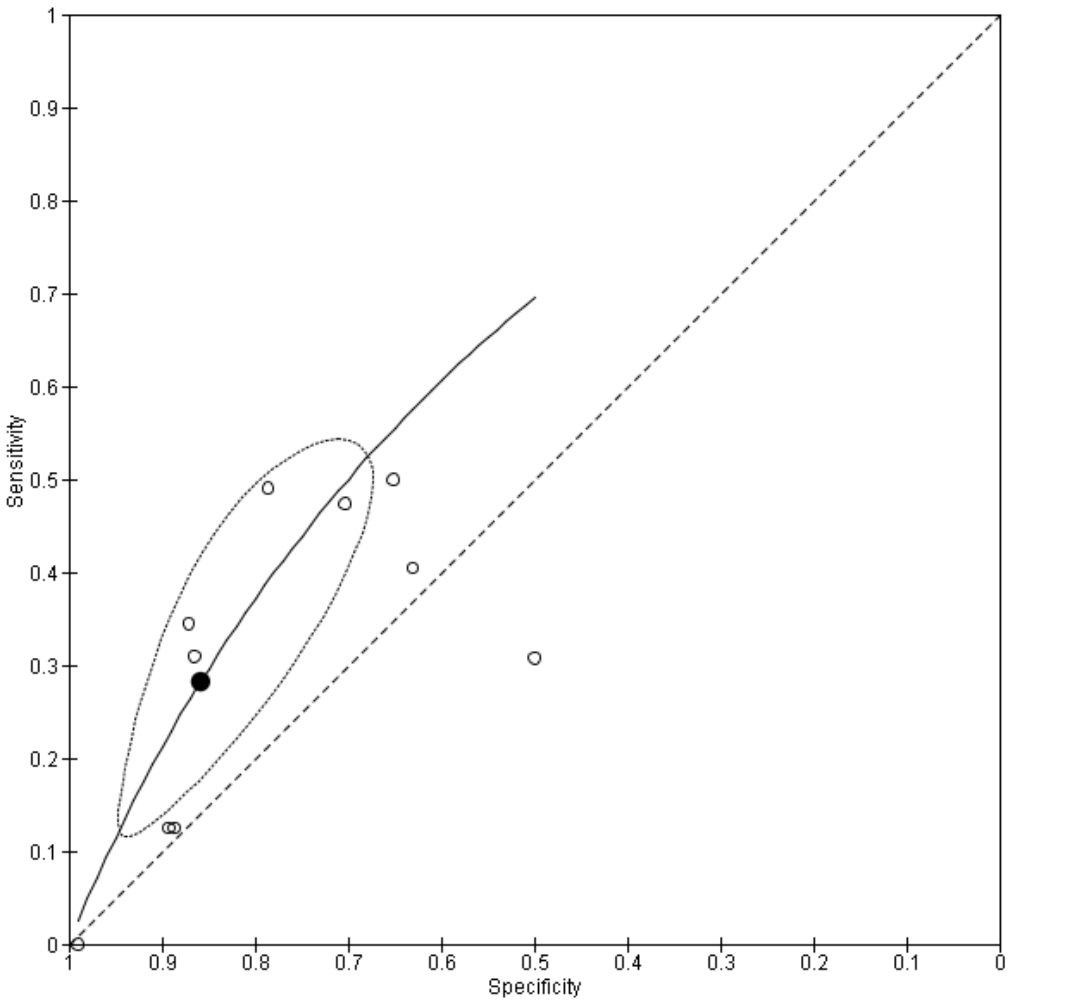
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 30%	pre-test probability of 50%	pre-test probability of 70%	
True positives (patients with elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	135 (85 to 188)	226 (143 to 314)	316 (199 to 440)	⨁⨁◯◯ LOW
False negatives (patients incorrectly classified as not having elevated intracranial pressure)								165 (112 to 215)	274 (186 to 357)	384 (260 to 501)	
True negatives (patients without elevated intracranial pressure)	4 studies 1316 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	serious [b]	none	584 (493 to 641)	418 (352 to 458)	251 (211 to 275)	⨁⨁◯◯ LOW
False positives (patients incorrectly classified as having elevated intracranial pressure)								116 (59 to 207)	82 (42 to 148)	49 (25 to 89)	

Explanations

a. The majority of the included studies were at a high risk of bias.
b. Confidence intervals for sensitivity and specificity are wide and do not exclude important differences.

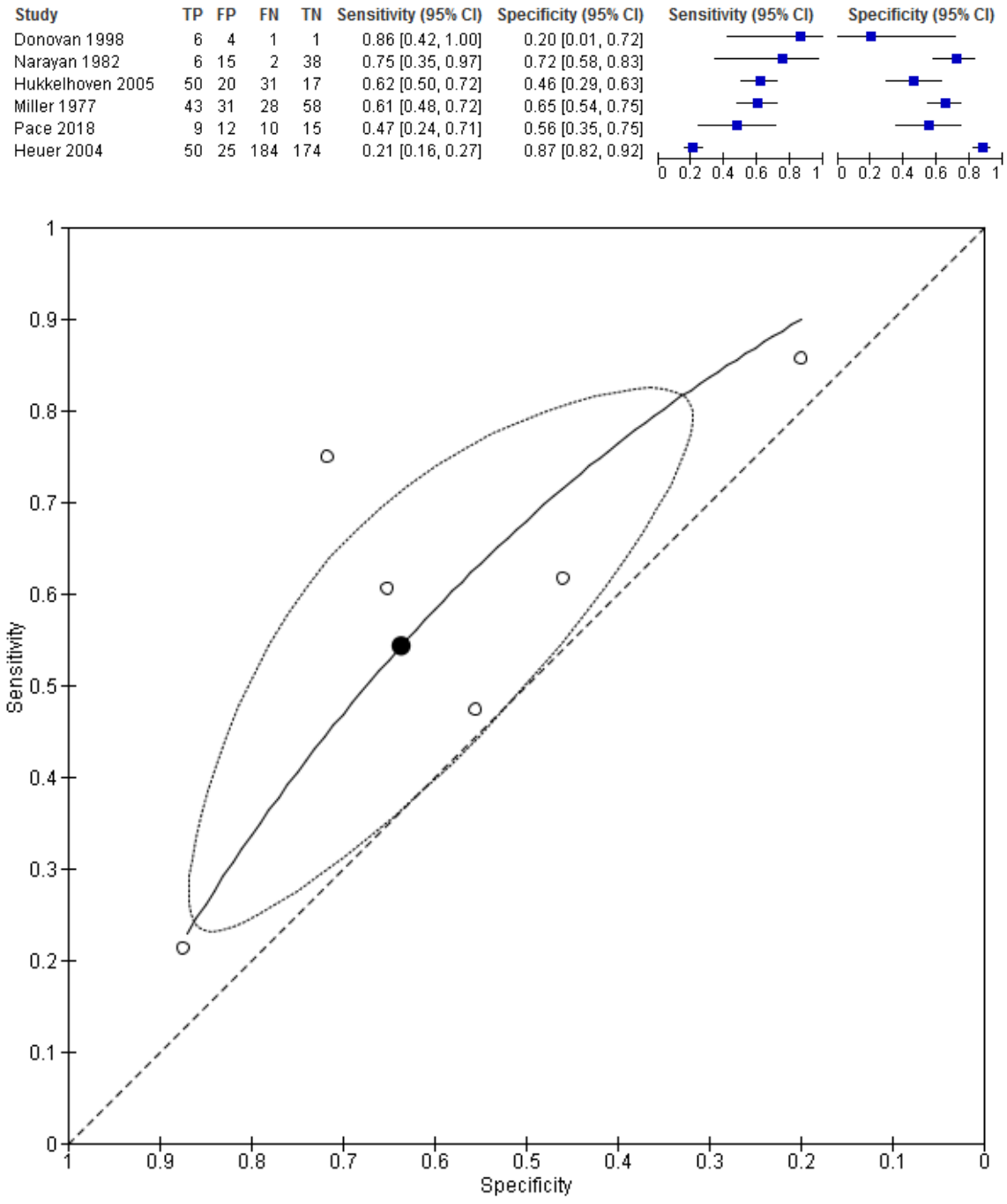
Supplemental Figure 3: HSROC Curve and Forest Plot for Pupillary Dilation. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for Pupillary Dilation to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Soustiel 2010	18	30	18	56	0.50 [0.33, 0.67]	0.65 [0.54, 0.75]
Kramer 2016	25	109	26	401	0.49 [0.35, 0.63]	0.79 [0.75, 0.82]
Pace 2018	9	8	10	19	0.47 [0.24, 0.71]	0.70 [0.50, 0.86]
Hukkelhoven 2005	34	17	50	29	0.40 [0.30, 0.52]	0.63 [0.48, 0.77]
Wettervik 2018	20	70	38	474	0.34 [0.22, 0.48]	0.87 [0.84, 0.90]
Miller 1977	22	12	49	77	0.31 [0.21, 0.43]	0.87 [0.78, 0.93]
Marshall 1983	4	1	9	1	0.31 [0.09, 0.61]	0.50 [0.01, 0.99]
Lee 2018	1	6	7	50	0.13 [0.00, 0.53]	0.89 [0.78, 0.96]
Narayan 1982	1	6	7	47	0.13 [0.00, 0.53]	0.89 [0.77, 0.96]
Badri 2012	0	3	59	303	0.00 [0.00, 0.06]	0.99 [0.97, 1.00]



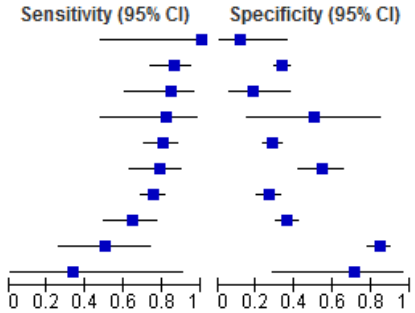
Supplemental Figure 4: HSROC Curve and Forest Plot for Motor Posturing. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for motor posturing to detect elevated intracranial pressure.
Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

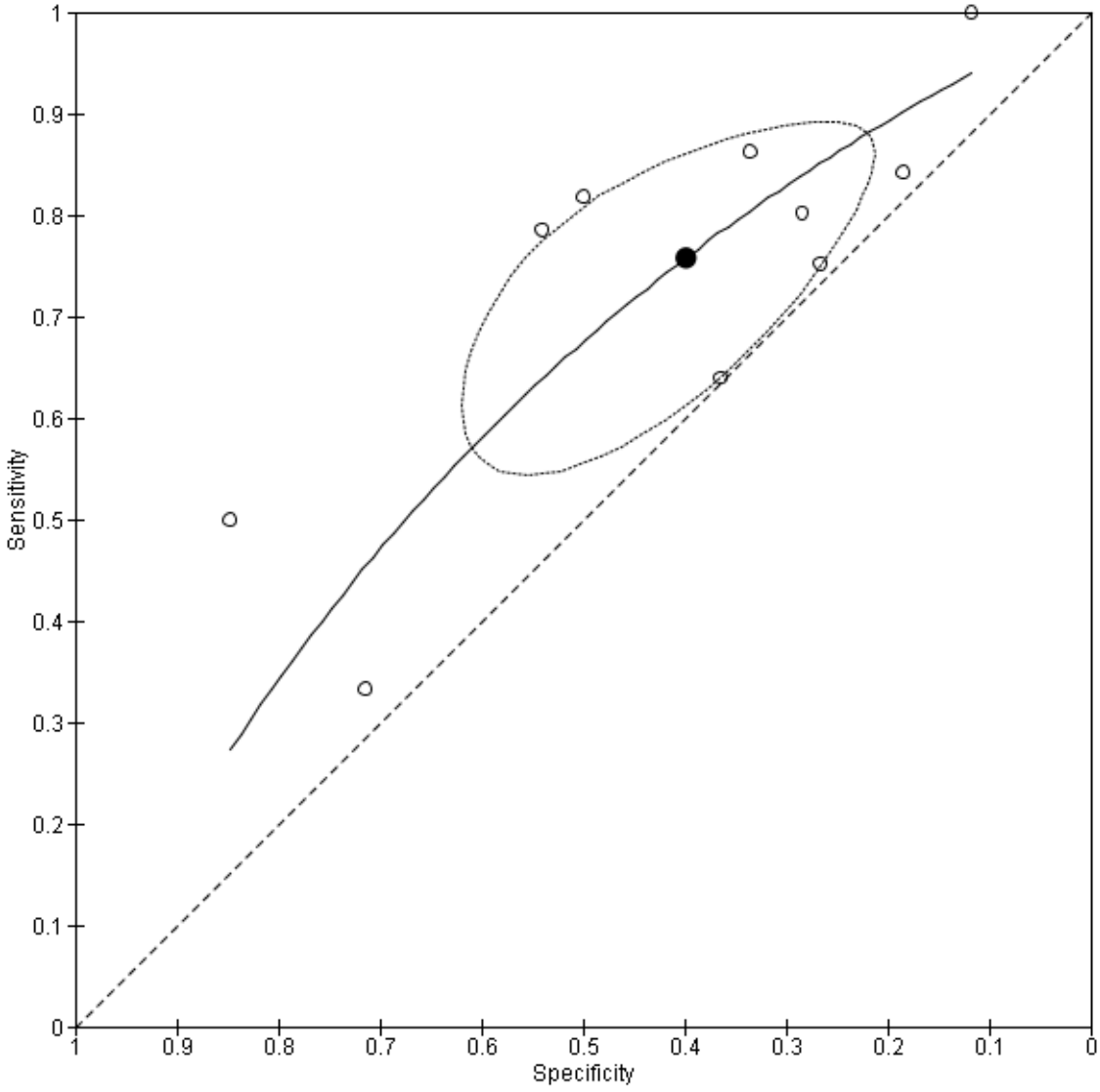
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Donovan 1998	6	4	1	1	0.86 [0.42, 1.00]	0.20 [0.01, 0.72]
Narayan 1982	6	15	2	38	0.75 [0.35, 0.97]	0.72 [0.58, 0.83]
Hukkelhoven 2005	50	20	31	17	0.62 [0.50, 0.72]	0.46 [0.29, 0.63]
Miller 1977	43	31	28	58	0.61 [0.48, 0.72]	0.65 [0.54, 0.75]
Pace 2018	9	12	10	15	0.47 [0.24, 0.71]	0.56 [0.35, 0.75]
Heuer 2004	50	25	184	174	0.21 [0.16, 0.27]	0.87 [0.82, 0.92]



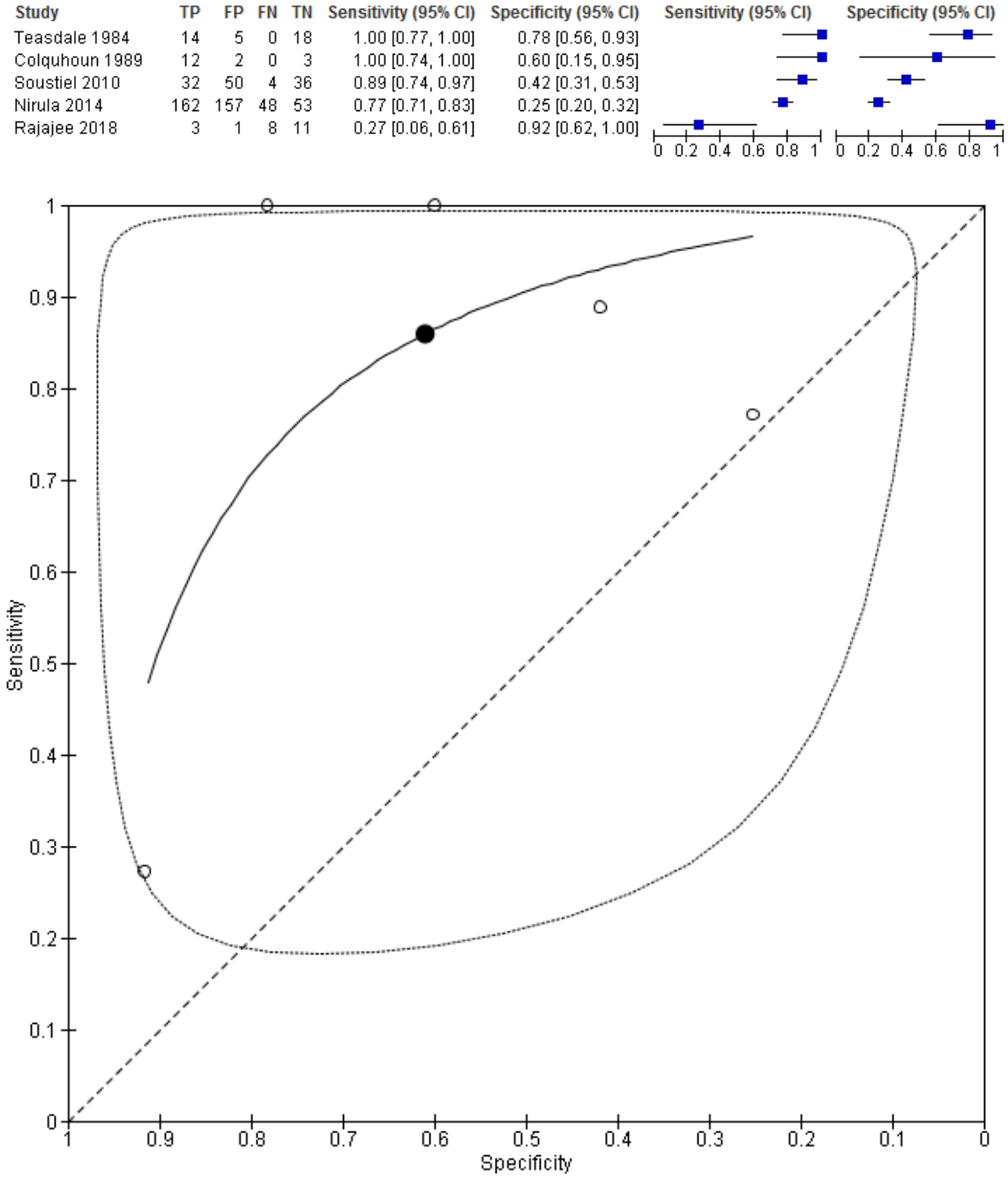
Supplemental Figure 5: HSROC Curve and Forest Plot for Decreased Level of Consciousness (GCS ≤ 8). Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for GCS ≤ 8 to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rajajee 2018	5	15	0	2	1.00 [0.48, 1.00]	0.12 [0.01, 0.36]
Kramer 2016	44	394	7	199	0.86 [0.74, 0.94]	0.34 [0.30, 0.38]
Pace 2018	16	22	3	5	0.84 [0.60, 0.97]	0.19 [0.06, 0.38]
Selhorst 1985	9	4	2	4	0.82 [0.48, 0.98]	0.50 [0.16, 0.84]
Robba 2017	69	257	17	102	0.80 [0.70, 0.88]	0.28 [0.24, 0.33]
Zoerle 2015	33	34	9	40	0.79 [0.63, 0.90]	0.54 [0.42, 0.66]
Nirula 2014	158	154	52	56	0.75 [0.69, 0.81]	0.27 [0.21, 0.33]
Badri 2012	32	178	18	102	0.64 [0.49, 0.77]	0.36 [0.31, 0.42]
Nagel 2009	9	25	9	139	0.50 [0.26, 0.74]	0.85 [0.78, 0.90]
Hamani 2003	1	2	2	5	0.33 [0.01, 0.91]	0.71 [0.29, 0.96]



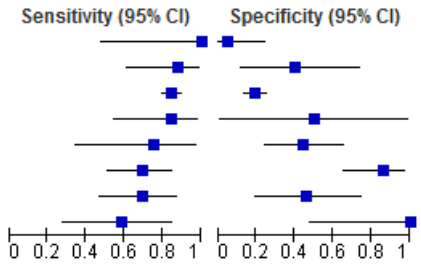


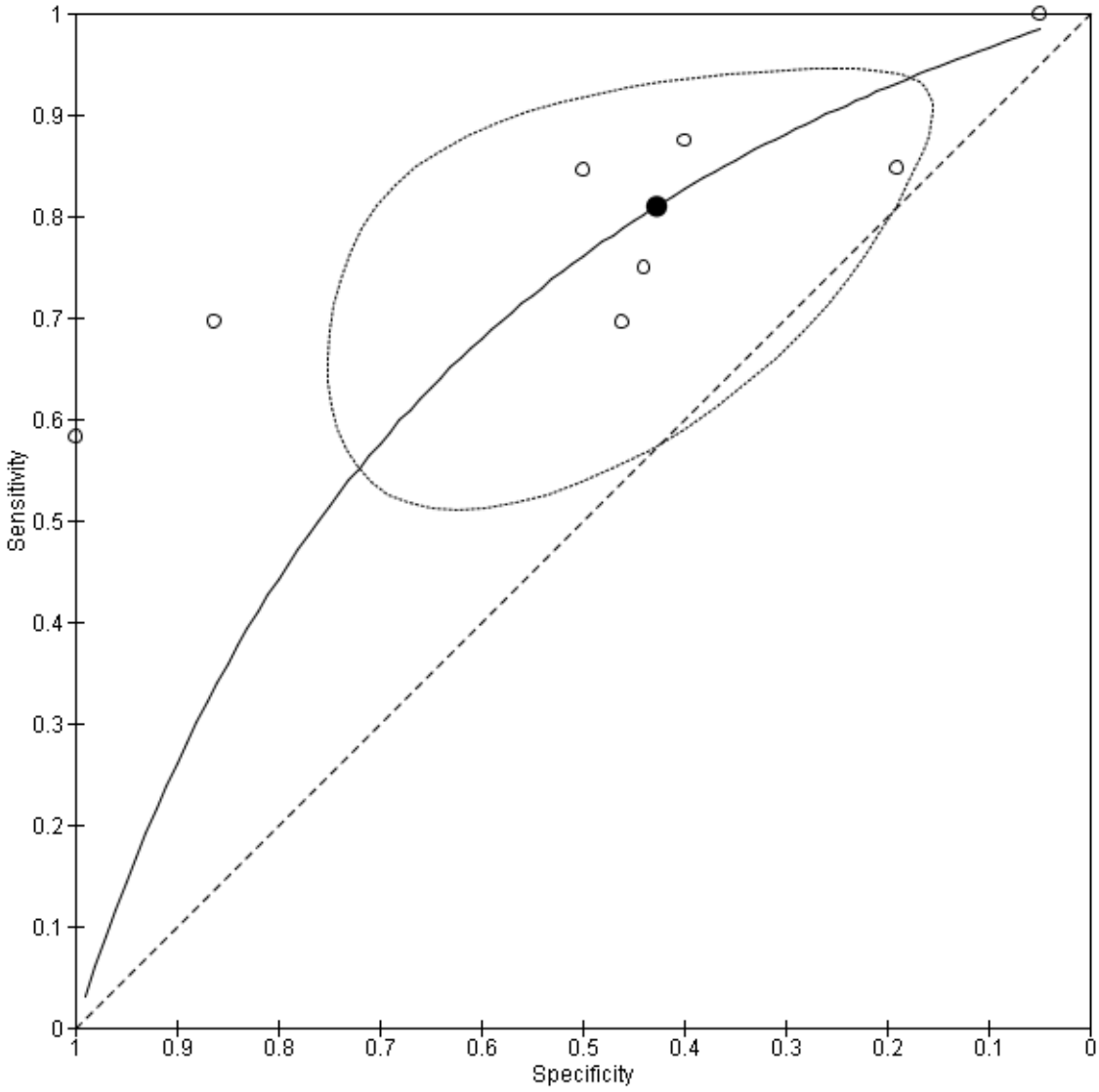
Supplemental Figure 6: HSROC Curve and Forest Plot for Compression or Absence of Basal Cisterns. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for compression/absence of basal cisterns to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.



Supplemental Figure 7: HSROC Curve and Forest Plot for Any Midline Shift. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 0mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

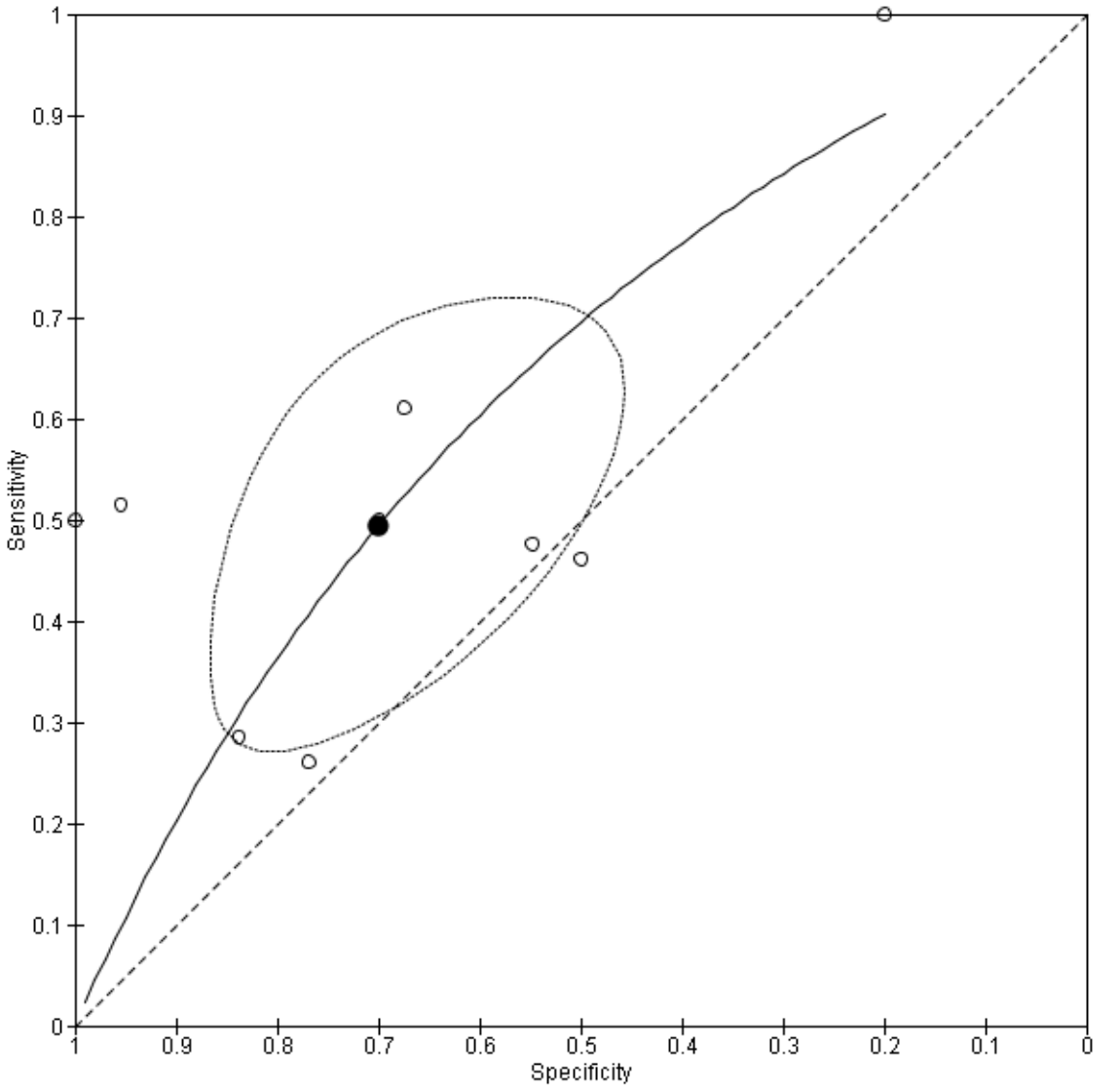
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jeon 2018	5	19	0	1	1.00 [0.48, 1.00]	0.05 [0.00, 0.25]
Galbraith 1981	14	6	2	4	0.88 [0.62, 0.98]	0.40 [0.12, 0.74]
Nirula 2014	178	170	32	40	0.85 [0.79, 0.89]	0.19 [0.14, 0.25]
Marshall 1983	11	1	2	1	0.85 [0.55, 0.98]	0.50 [0.01, 0.99]
Sadhu 1979	6	14	2	11	0.75 [0.35, 0.97]	0.44 [0.24, 0.65]
Hara 1998	23	3	10	19	0.70 [0.51, 0.84]	0.86 [0.65, 0.97]
Tabaddor 1982	16	7	7	6	0.70 [0.47, 0.87]	0.46 [0.19, 0.75]
Hayashi 1982	7	0	5	5	0.58 [0.28, 0.85]	1.00 [0.48, 1.00]





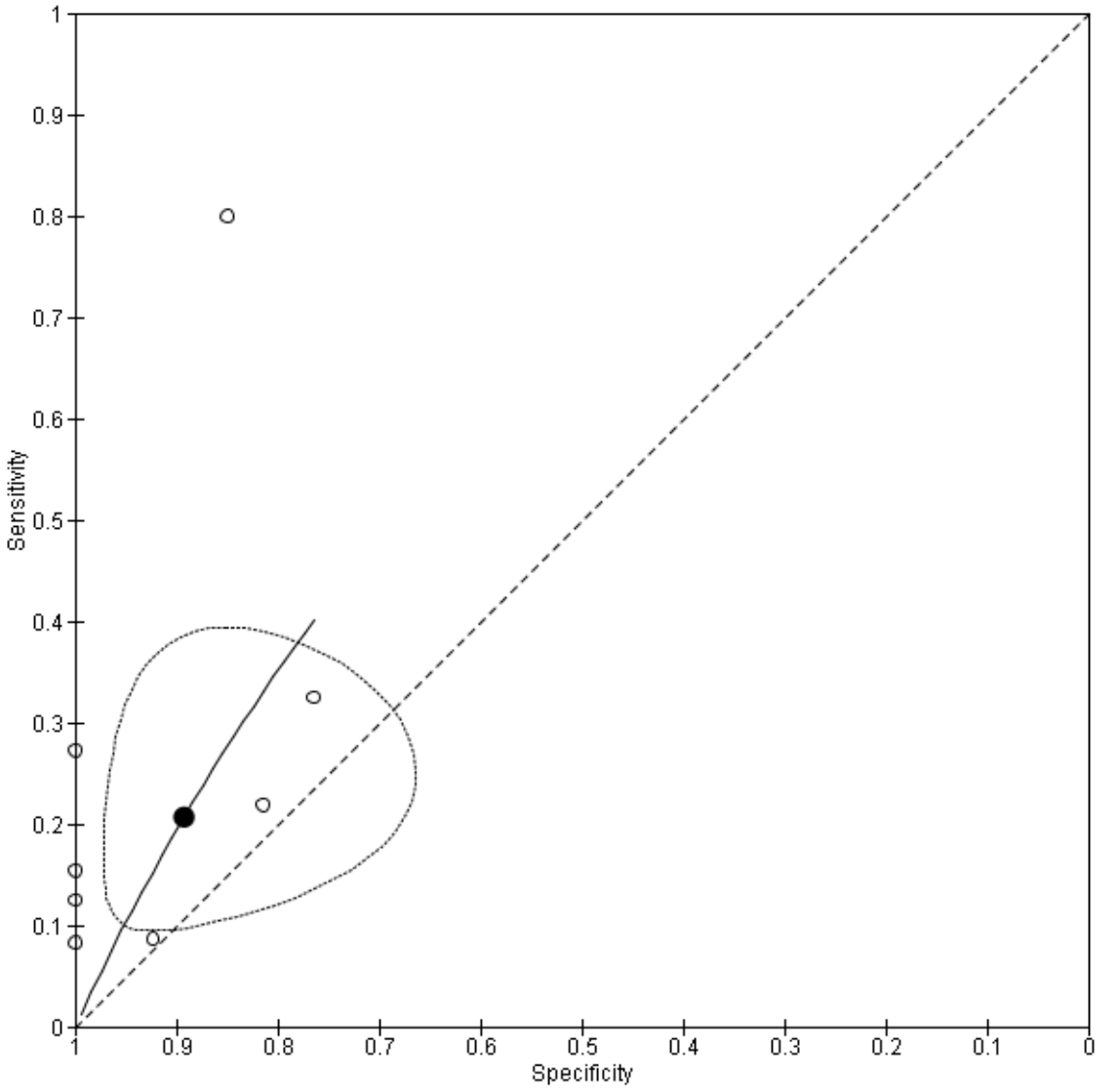
Supplemental Figure 8: HSROC Curve and Forest Plot for Midline Shift ≥ 5mm. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 5mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jeon 2018	5	16	0	4	1.00 [0.48, 1.00]	0.20 [0.06, 0.44]
Soustiel 2010	22	28	14	58	0.61 [0.43, 0.77]	0.67 [0.56, 0.77]
Hara 1998	17	1	16	21	0.52 [0.34, 0.69]	0.95 [0.77, 1.00]
Hayashi 1982	6	0	6	5	0.50 [0.21, 0.79]	1.00 [0.48, 1.00]
Galbraith 1981	8	3	8	7	0.50 [0.25, 0.75]	0.70 [0.35, 0.93]
Nirula 2014	100	95	110	115	0.48 [0.41, 0.55]	0.55 [0.48, 0.62]
Marshall 1983	6	1	7	1	0.46 [0.19, 0.75]	0.50 [0.01, 0.99]
Zoerle 2015	12	12	30	62	0.29 [0.16, 0.45]	0.84 [0.73, 0.91]
Tabaddor 1982	6	3	17	10	0.26 [0.10, 0.48]	0.77 [0.46, 0.95]



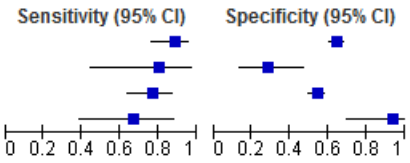
Supplemental Figure 9: HSROC Curve and Forest Plot for Midline Shift ≥ 10mm. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 10mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

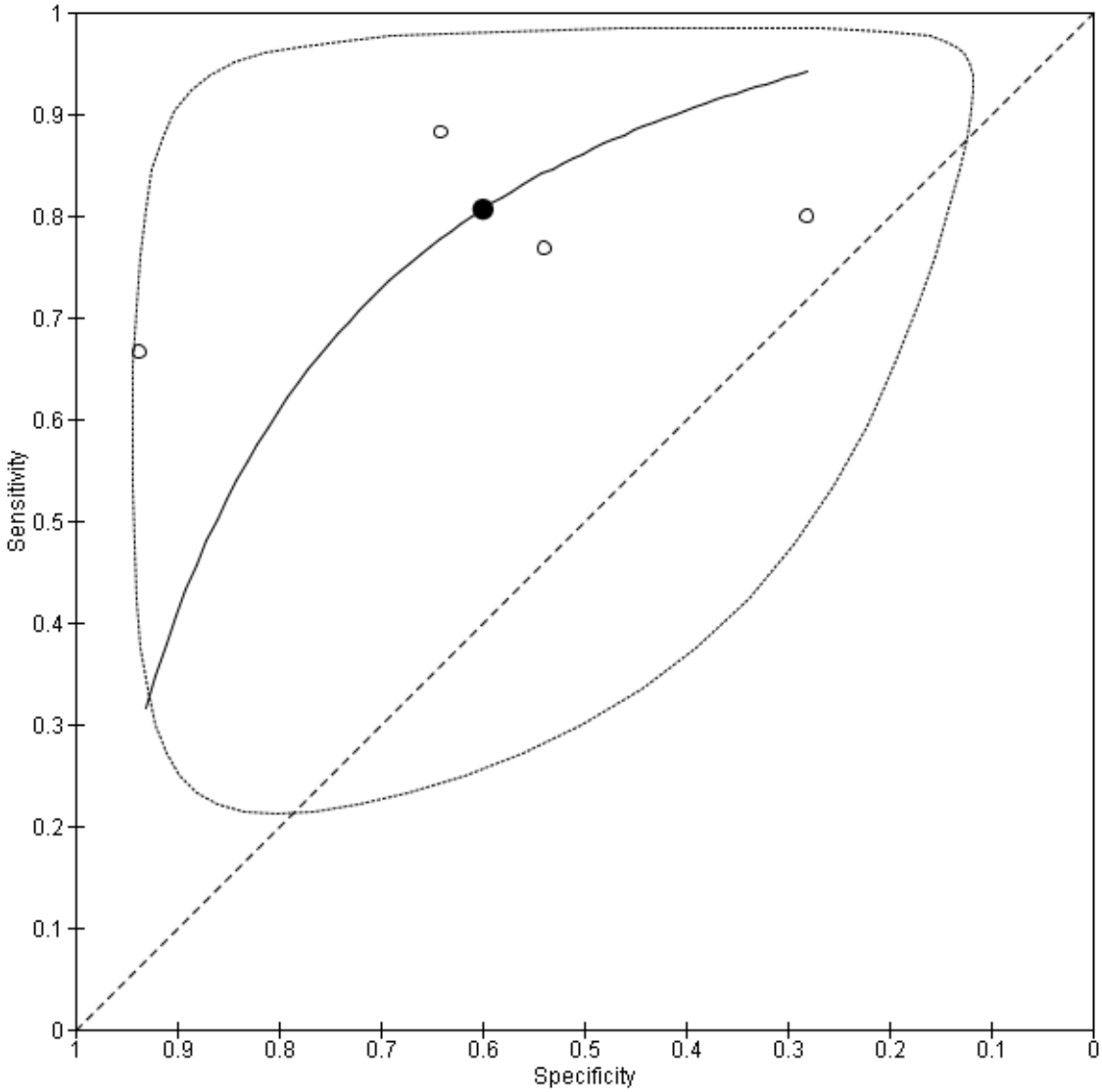
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jeon 2018	4	3	1	17	0.80 [0.28, 0.99]	0.85 [0.62, 0.97]
Kamel 2012	13	4	27	13	0.33 [0.19, 0.49]	0.76 [0.50, 0.93]
Hara 1998	9	0	24	22	0.27 [0.13, 0.46]	1.00 [0.85, 1.00]
Nirula 2014	46	39	164	171	0.22 [0.17, 0.28]	0.81 [0.75, 0.86]
Marshall 1983	2	0	11	2	0.15 [0.02, 0.45]	1.00 [0.16, 1.00]
Galbraith 1981	2	0	14	10	0.13 [0.02, 0.38]	1.00 [0.69, 1.00]
Tabaddor 1982	2	1	21	12	0.09 [0.01, 0.28]	0.92 [0.64, 1.00]
Hayashi 1982	1	0	11	5	0.08 [0.00, 0.38]	1.00 [0.48, 1.00]



Supplemental Figure 10: HSROC Curve and Forest Plot for Marshall Score ≥ 3. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for Marshall Score ≥ 3 to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

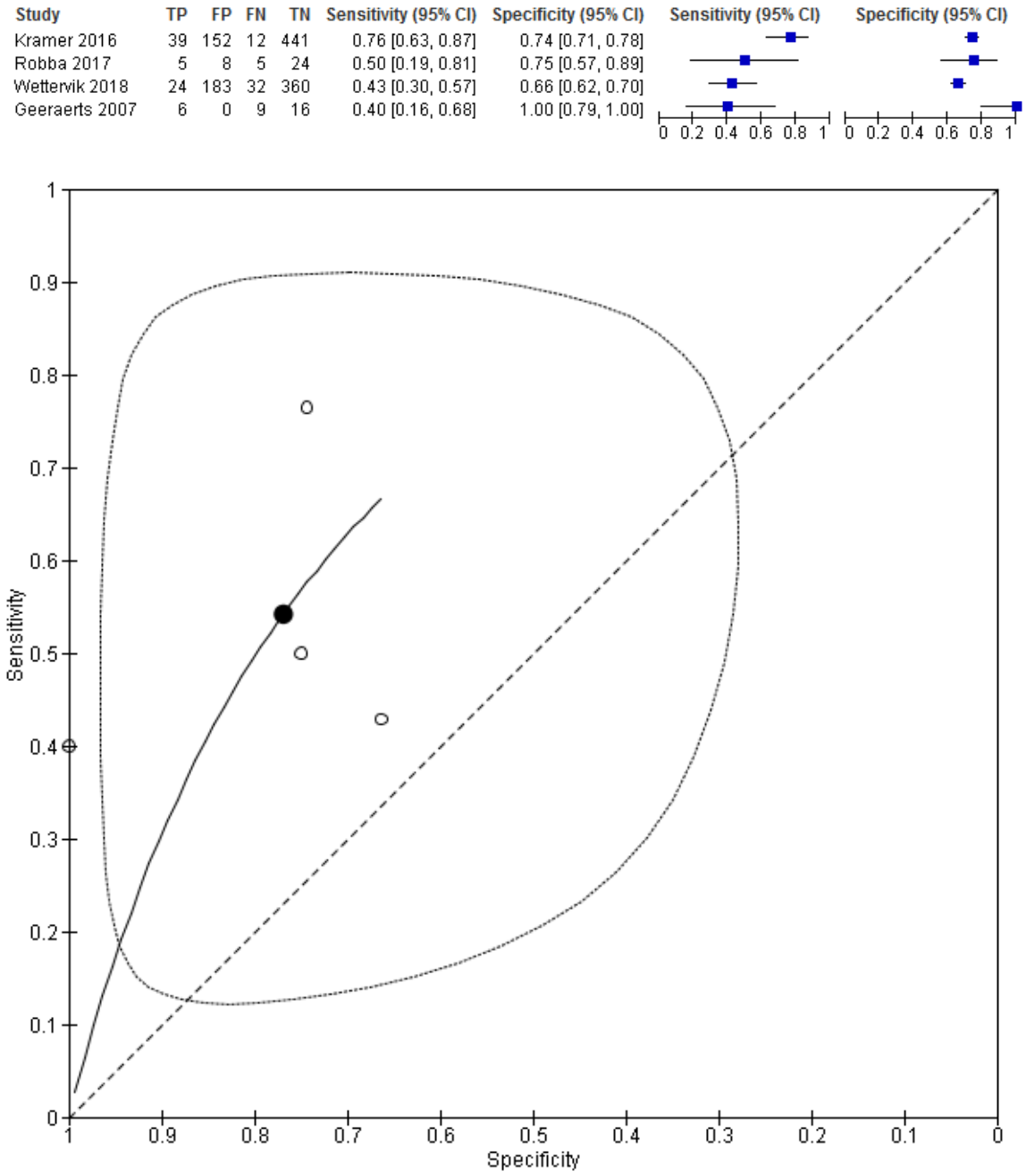
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kramer 2016	45	213	6	380	0.88 [0.76, 0.96]	0.64 [0.60, 0.68]
Robba 2017	8	23	2	9	0.80 [0.44, 0.97]	0.28 [0.14, 0.47]
Wettervik 2018	43	250	13	293	0.77 [0.64, 0.87]	0.54 [0.50, 0.58]
Geeraerts 2007	10	1	5	15	0.67 [0.38, 0.88]	0.94 [0.70, 1.00]





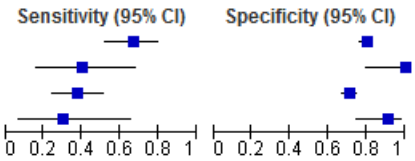
Supplemental Figure 11: HSROC Curve and Forest Plot for Marshall Score ≥ 4. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for Marshall Score ≥ 4 to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

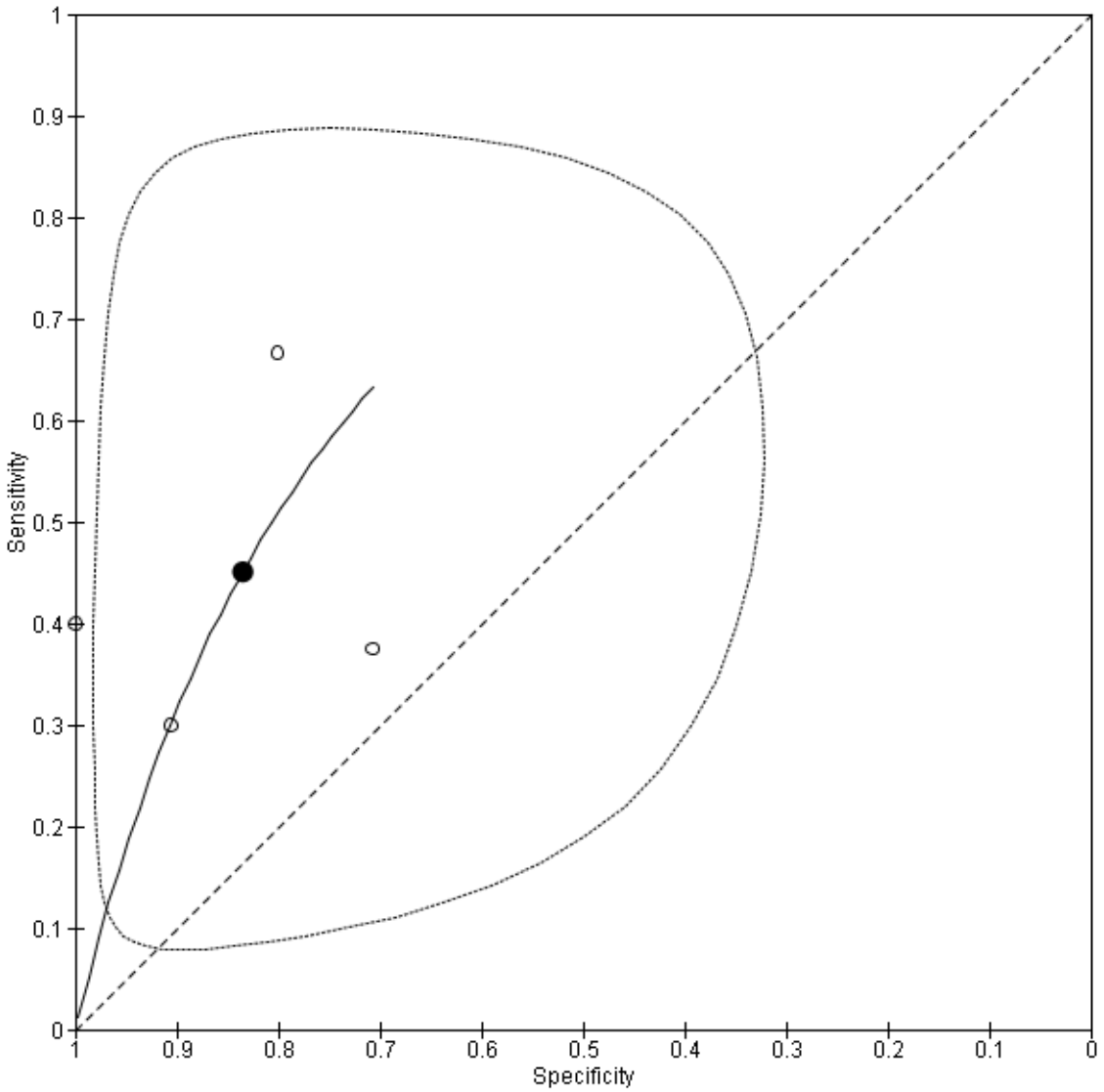
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kramer 2016	39	152	12	441	0.76 [0.63, 0.87]	0.74 [0.71, 0.78]
Robba 2017	5	8	5	24	0.50 [0.19, 0.81]	0.75 [0.57, 0.89]
Wettervik 2018	24	183	32	360	0.43 [0.30, 0.57]	0.66 [0.62, 0.70]
Geeraerts 2007	6	0	9	16	0.40 [0.16, 0.68]	1.00 [0.79, 1.00]



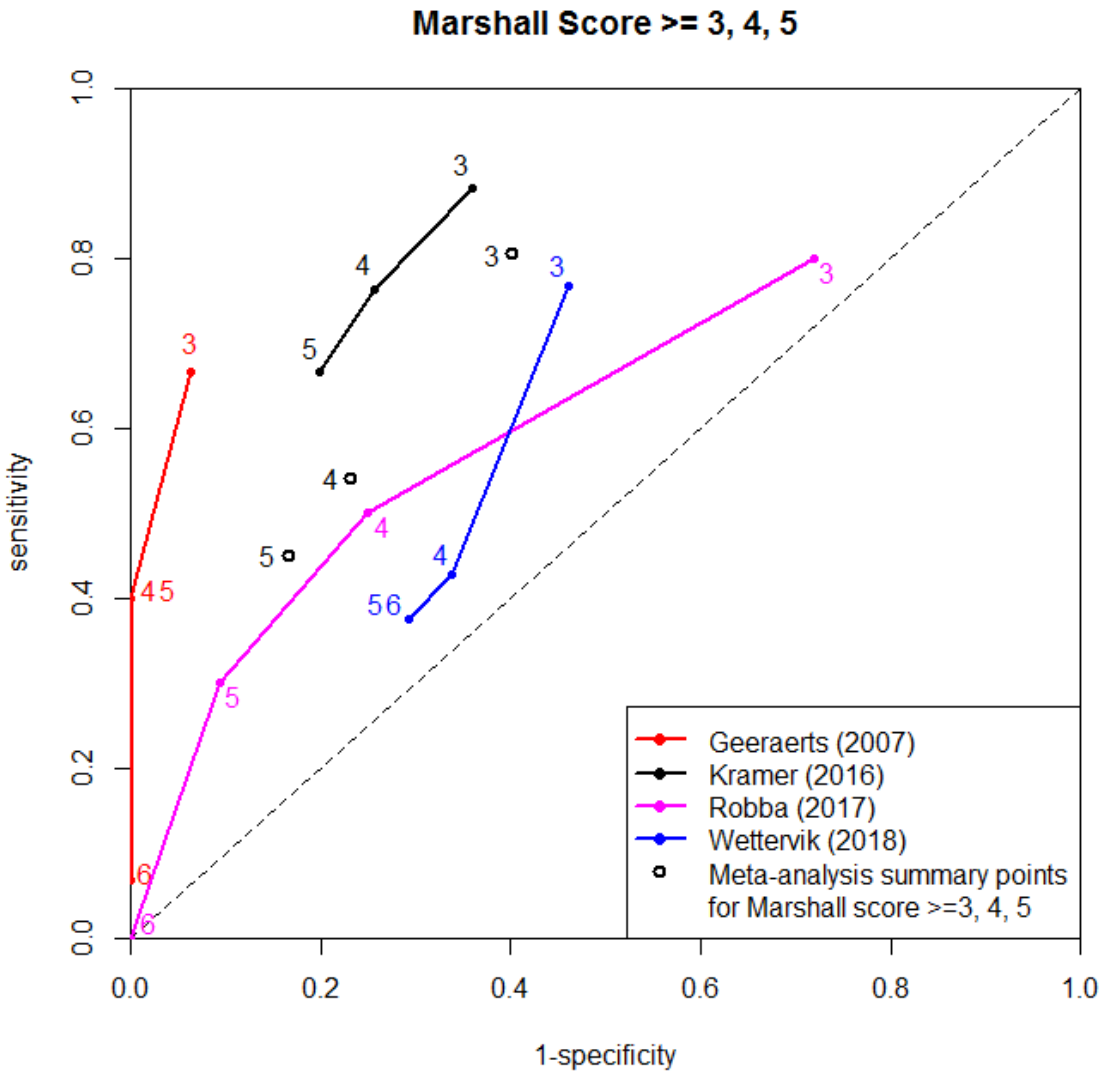
Supplemental Figure 12: HSROC Curve and Forest Plot for Marshall Score ≥ 5. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for Marshall Score ≥ 5 to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kramer 2016	34	118	17	475	0.67 [0.52, 0.79]	0.80 [0.77, 0.83]
Geeraerts 2007	6	0	9	16	0.40 [0.16, 0.68]	1.00 [0.79, 1.00]
Wettervik 2018	21	159	35	384	0.38 [0.25, 0.51]	0.71 [0.67, 0.75]
Robba 2017	3	3	7	29	0.30 [0.07, 0.65]	0.91 [0.75, 0.98]





Supplemental Figure 13: ROC Curves for Marshall Criteria By Study.

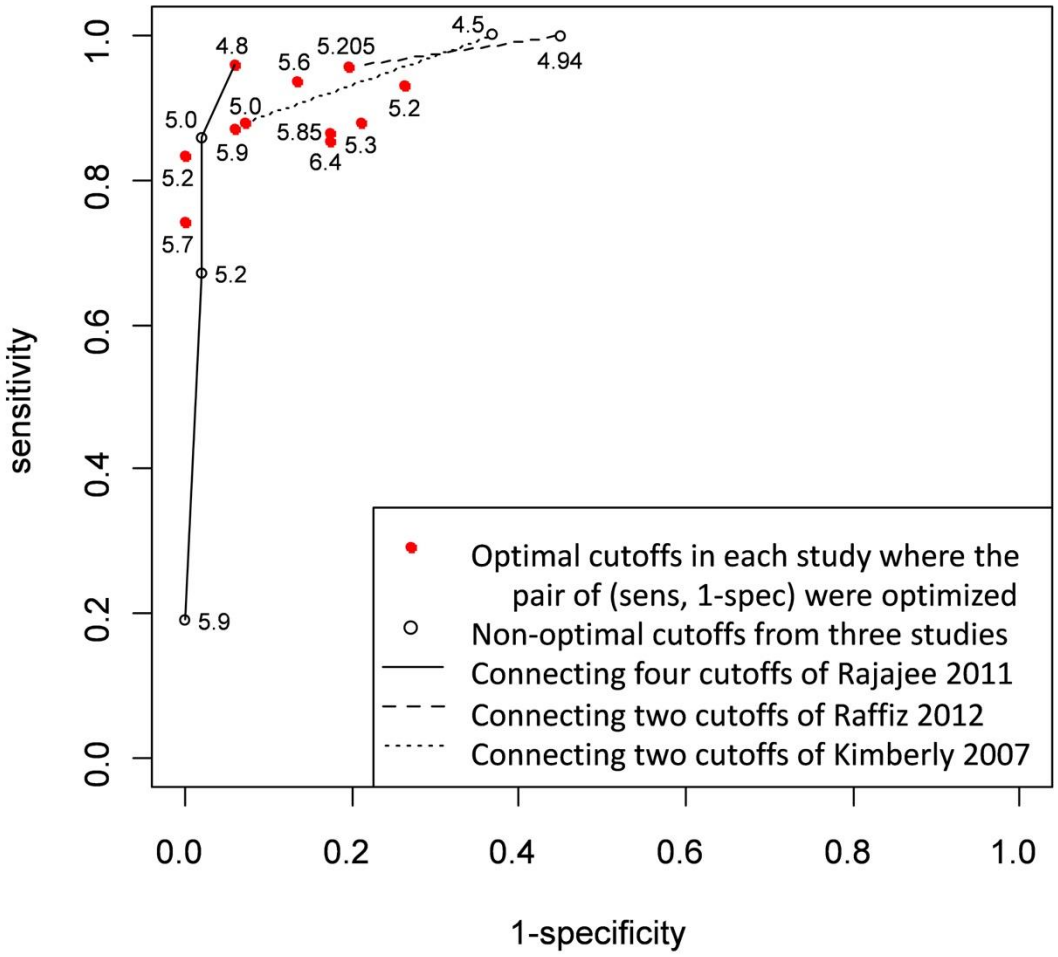


Supplemental Table 13: Diagnostic Performance of Optic Nerve Sheath Diameter. Individual studies with the AUROC of ONSD, the thresholds utilized, and associated sensitivity and specificity. Abbreviations: AUROC = Area under the receiver operating characteristics curve; CI = Confidence Interval; ICP = Intracranial pressure; ONSD = Optic Nerve Sheath Diameter; opt = reported optimal cut-off.

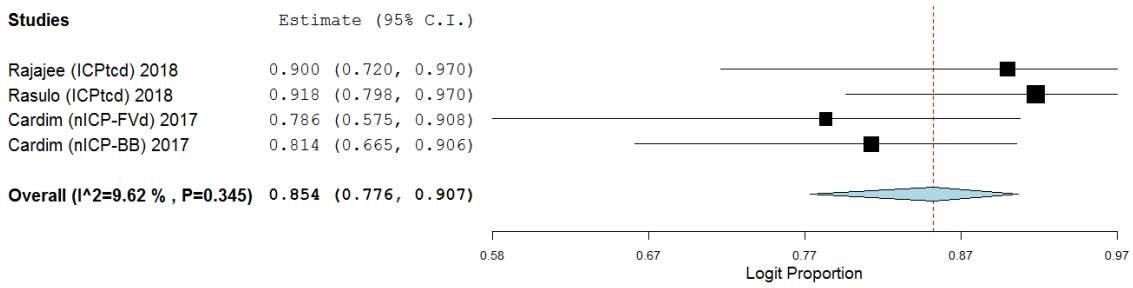
Study	Patients with ICP ≥ 20 / Total Patients	ONSD cutoff mm (optimal)	Sensitivity (95% CI)	Specificity (95% CI)	AUROC (95% CI)
Soliman (2018)	177 / 200	6.4 (opt)	85.3	82.6	0.88 (0.80-0.95)*
Jeon (2017)	32 / 62	5.6 (opt)	93.75 (79.2-99.2)	86.67 (69.3-96.2)	0.936 (0.844-0.983)*
Lee (2018)	8 / 64	5.3 (opt)	88	79	0.834
Robba (2017)	86 / 445	5.85 (opt)	86.6	82.6	0.91 (0.88-0.95)*
Frumin (2014)	6 / 26	5.2 (opt)	83.3 (35.9-99.6)	100.0 (84.6-100)	0.865 (0.66-0.96)
Raffiz (2012)	NA / 41	4.94 5.205 (opt)	100 95.8	54.9 80.4	0.964 (0.921-1.000)*
Rajajee (2011)	26 / 65	4.8 (opt) 5.0 5.2 5.9	96 (91-99) 86 (79-92) 67 (58-35) 19 (13-27)	94 (92-96) 98 (96-99) 98 (97-99) 100 (99-100)	0.98 (0.96-0.99)
Moretti (2009)	29 / 94	5.2 (opt)	93.1 (77.2-99.0)	73.85 (61.5-84.0)	0.925 (0.852-0.969)*
Soldatos (2008)	27 / 32	5.7 (opt)	74.1	100	0.93 (0.79-0.99)*
Geeraerts (2007)	15 / 31	5.9 (opt)	87	94	0.96 (0.83-0.99)
Kimberly (2007)	8 / 38	4.5 5.0 (opt)	100 88 (47-99)	63 93 (78-99)	0.93 (0.84-0.99)*

*: Reported upper limit of 95% CI not symmetric with the lower limit in the original or logit scale. Therefore, we only used the AUROCs with their lower confidence limits, and assumed symmetry in logit scale for the meta-analysis of AUROC.

Supplemental Figure 14: Diagnostic Performance of Optic Nerve Sheath Diameter with Thresholds displayed. The ONSD thresholds utilized associated with the pairs of sensitivity and specificity were displayed on the Receiver Operating Characteristics plane.



Supplemental Figure 15: TCD-ABP Methods for Detection of Elevated Intracranial Pressure. Pooled area under the ROC curve (AUROC) for transcranial doppler arterial blood pressure (TCD-ABP) methods to detect of intracranial pressure (ICP) ≥ 20 mmHg across studies.



Note: Reported upper limit of 95% CI not symmetric with the lower limit in the original or logit scale. Therefore, we only used the AUROCs with their lower confidence limits and assumed symmetry in logit scale for the meta-analysis of AUROC.

Supplemental Table 14: Descriptive Table of TCD-ABP Methods for Detection of Elevated Intracranial Pressure. Pooled area under the ROC curve (AUROC) for transcranial doppler arterial blood pressure (TCD-ABP) methods to detect of intracranial pressure (ICP) ≥ 20 mmHg across studies. Abbreviations: AUROC = Area under the Receiver Operating Characteristics curve; CI = Confidence Interval; ICP = Intracranial Pressure; NR = not reported.

Study	Patients with ICP ≥ 20 / Total Patients	cutoff (mmHg)	Sensitivity (95% CI)	Specificity (95% CI)	Reported AUROC (95% CI)
Rajajee (2018): ICPtcd	5 / 21	> 18.55	100 (48-100)	81 (58-95)	0.90 (0.72-0.98) *
Rasulo (2018): ICPtcd	18 / 38 §	NR §	NR §	NR §	0.918 (0.799-1.000) *§
Cardim (2017): nICP_FVd	28 / 37	NR	NR	NR	0.786 (0.575-0.996) *#
Cardim (2017): nICP_BB	28 / 37	NR	NR	NR	0.814 (0.665-0.962) *#

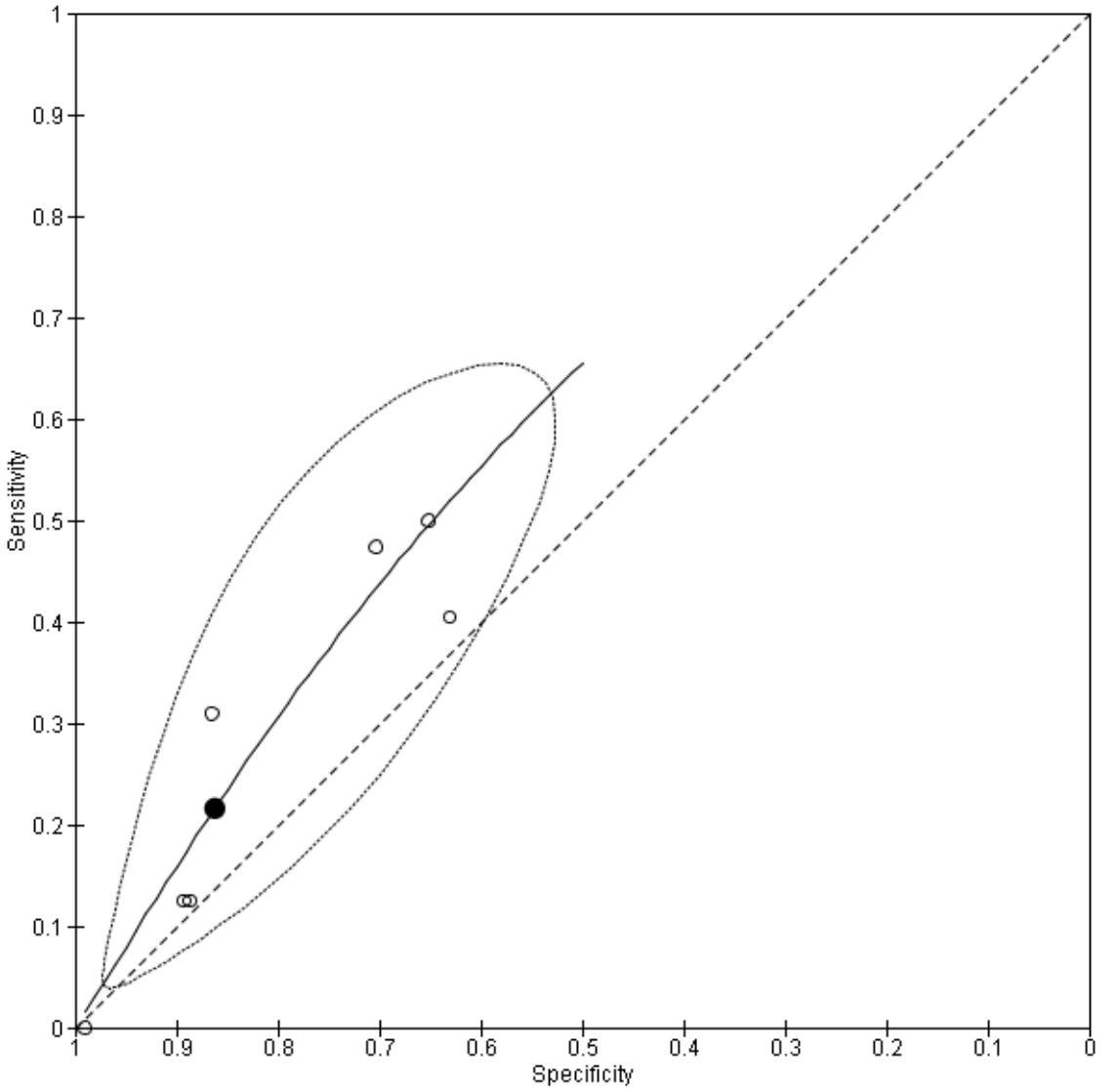
*: Reported upper limit of 95% CI not symmetric with the lower limit in the original or logit scale. Therefore, we only used the AUROCs with their lower confidence limits and assumed symmetry in logit scale for the meta-analysis of AUROC.
§: For Rasulo (2018), we only used the reported AUROC at the first ICPtcd measurement (TIME 1) performed immediately before ICPi placement.
#: Cardim (2017) reported AUROC of 0.77 (0.65-0.88) and 0.82 (0.71-0.93) for nICP_FVd and nICP_BB to detect ICP >35 mmHg. We calculated the AUROC for detection of ICP >= 20 mmHg based on individual level data.

Supplemental Table 15: Sensitivity Analyses – Summary Estimates for Physical Examination and Imaging after Removal of Studies with Potential High Risk-of-Bias. Abbreviations: GCS = Glasgow Coma Scale

	No. of Patients (No. of Cohorts)	Sensitivity	Specificity	Diagnostic Odds Ratio (DOR)	Positive Likelihood Ratio (LR+)	Negative Likelihood Ratio (LR-)
GCS ≤ 8	1170 (8)	74.9% (57.1 to 86.9%)	43.0% (26.3 to 61.5%)	2.24 (1.27 to 3.97)	1.31 (1.05 to 1.64)	0.59 (0.39 to 0.88)
Motor Posturing	830 (6)	54.3% (36.6 to 71.0%)	63.6% (46.5 to 77.8%)	2.08 (1.40 to 3.09)	1.49 (1.17 to 1.90)	0.72 (0.57 to 0.90)
Any Pupillary Dilation	948 (7)	21.6% (8.3 to 45.6%)	86.2% (69.8 to 94.4%)	1.73 (1.00 to 2.97)	1.57 (1.01 to 2.43)	0.91 (0.79 to 1.04)
Basal Cisterns Absent or Compressed	199 (4)	87.9% (53.9 to 97.8%)	72.3% (34.4 to 92.9%)	19.08 (3.04 to 119.94)	3.18 (1.08 to 9.40)	0.17 (0.04 to 0.73)
Midline Shift ≥ 0 mm	175 (5)	85.2% (62.6 to 95.2%)	42.2% (19.3 to 69.1%)	4.21 (1.65 to 10.77)	1.48 (1.02 to 2.14)	0.35 (0.16 to 0.76)
Midline Shift ≥ 5 mm	380 (6)	54.4% (30.8 to 76.2%)	71.8% (51.1 to 86.1%)	3.03 (1.77 to 5.21)	1.93 (1.35 to 2.75)	0.64 (0.45 to 0.91)
Midline Shift ≥ 10 mm	199 (5)	25.0% (12.8 to 43.1%)	92.5% (80.3 to 97.4%)	4.09 (1.34 to 12.50)	3.32 (1.23 to 8.91)	0.81 (0.67 to 0.98)

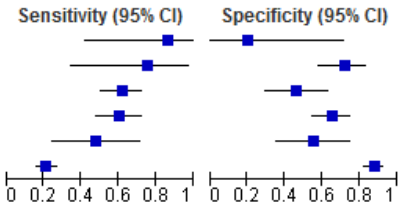
Supplemental Figure 16: Sensitivity Analysis for Pupillary Dilation after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for Pupillary Dilation to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

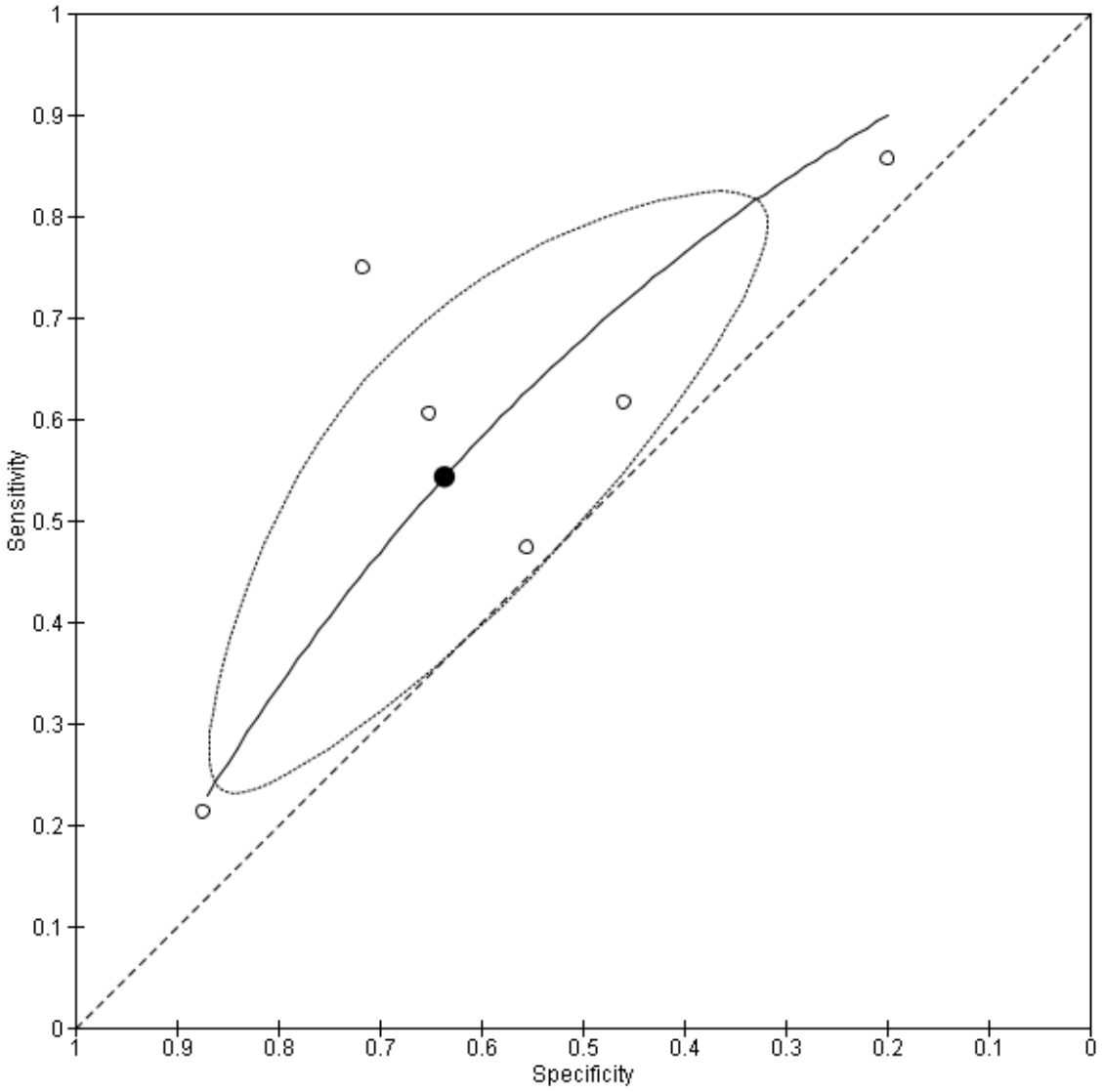
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Soustiel 2010	18	30	18	56	0.50 [0.33, 0.67]	0.65 [0.54, 0.75]
Pace 2018	9	8	10	19	0.47 [0.24, 0.71]	0.70 [0.50, 0.86]
Hukkelhoven 2005	34	17	50	29	0.40 [0.30, 0.52]	0.63 [0.48, 0.77]
Miller 1977	22	12	49	77	0.31 [0.21, 0.43]	0.87 [0.78, 0.93]
Narayan 1982	1	6	7	47	0.13 [0.00, 0.53]	0.89 [0.77, 0.96]
Lee 2018	1	6	7	50	0.13 [0.00, 0.53]	0.89 [0.78, 0.96]
Badri 2012	0	3	59	303	0.00 [0.00, 0.06]	0.99 [0.97, 1.00]



Supplemental Figure 17: Sensitivity Analysis for Motor Posturing after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for motor posturing to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

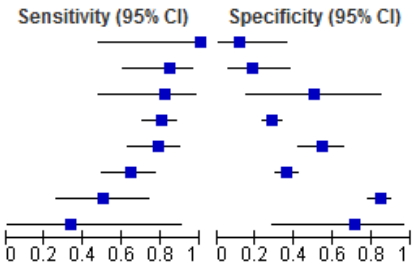
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Donovan 1998	6	4	1	1	0.86 [0.42, 1.00]	0.20 [0.01, 0.72]
Narayan 1982	6	15	2	38	0.75 [0.35, 0.97]	0.72 [0.58, 0.83]
Hukkelhoven 2005	50	20	31	17	0.62 [0.50, 0.72]	0.46 [0.29, 0.63]
Miller 1977	43	31	28	58	0.61 [0.48, 0.72]	0.65 [0.54, 0.75]
Pace 2018	9	12	10	15	0.47 [0.24, 0.71]	0.56 [0.35, 0.75]
Heuer 2004	50	25	184	174	0.21 [0.16, 0.27]	0.87 [0.82, 0.92]

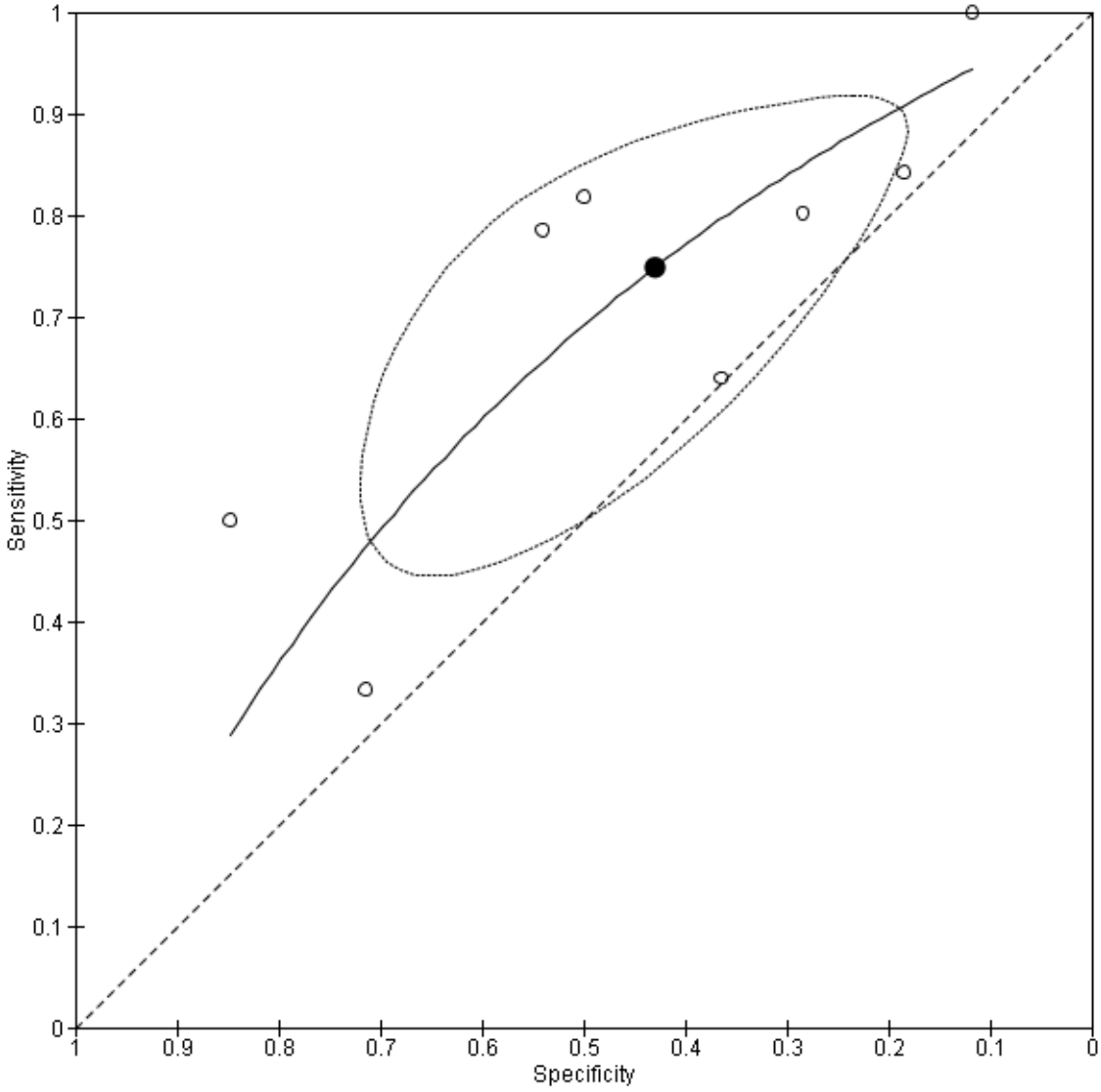




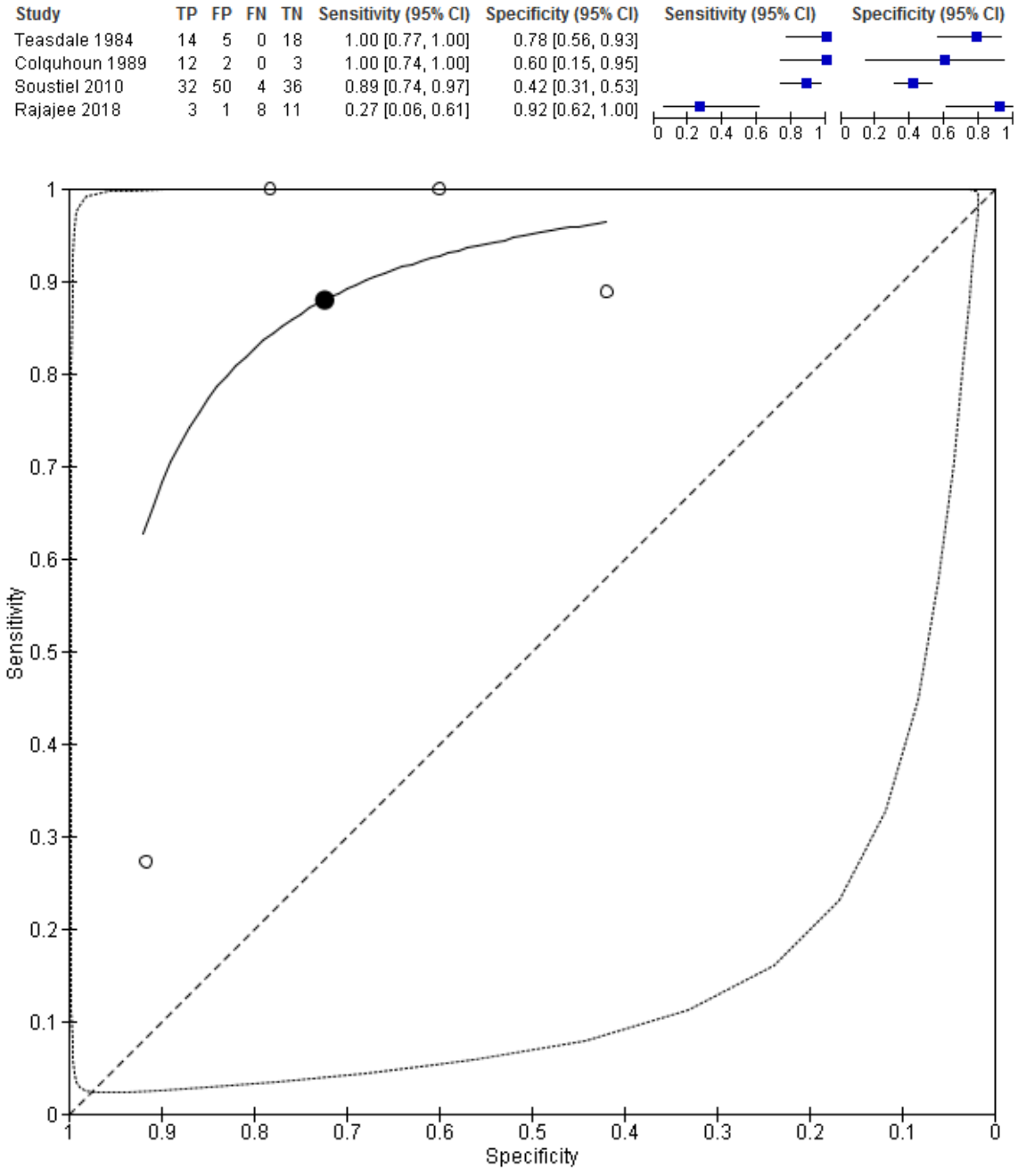
Supplemental Figure 18: Sensitivity Analysis for Decreased Level of Consciousness after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for GCS ≤ 8 to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Rajajee 2018	5	15	0	2	1.00 [0.48, 1.00]	0.12 [0.01, 0.36]
Pace 2018	16	22	3	5	0.84 [0.60, 0.97]	0.19 [0.06, 0.38]
Selhorst 1985	9	4	2	4	0.82 [0.48, 0.98]	0.50 [0.16, 0.84]
Robba 2017	69	257	17	102	0.80 [0.70, 0.88]	0.28 [0.24, 0.33]
Zoerle 2015	33	34	9	40	0.79 [0.63, 0.90]	0.54 [0.42, 0.66]
Badri 2012	32	178	18	102	0.64 [0.49, 0.77]	0.36 [0.31, 0.42]
Nagel 2009	9	25	9	139	0.50 [0.26, 0.74]	0.85 [0.78, 0.90]
Hamani 2003	1	2	2	5	0.33 [0.01, 0.91]	0.71 [0.29, 0.96]

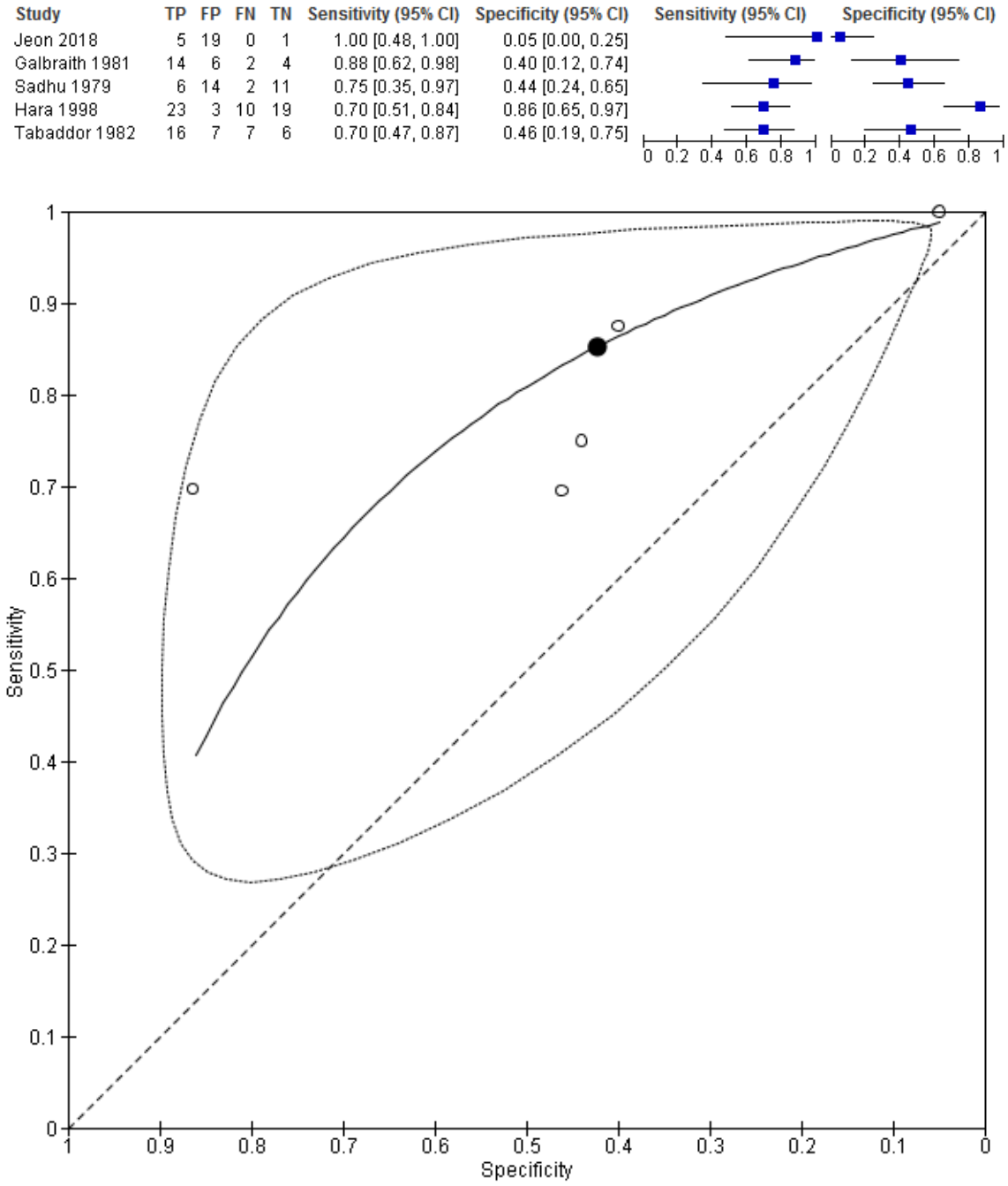




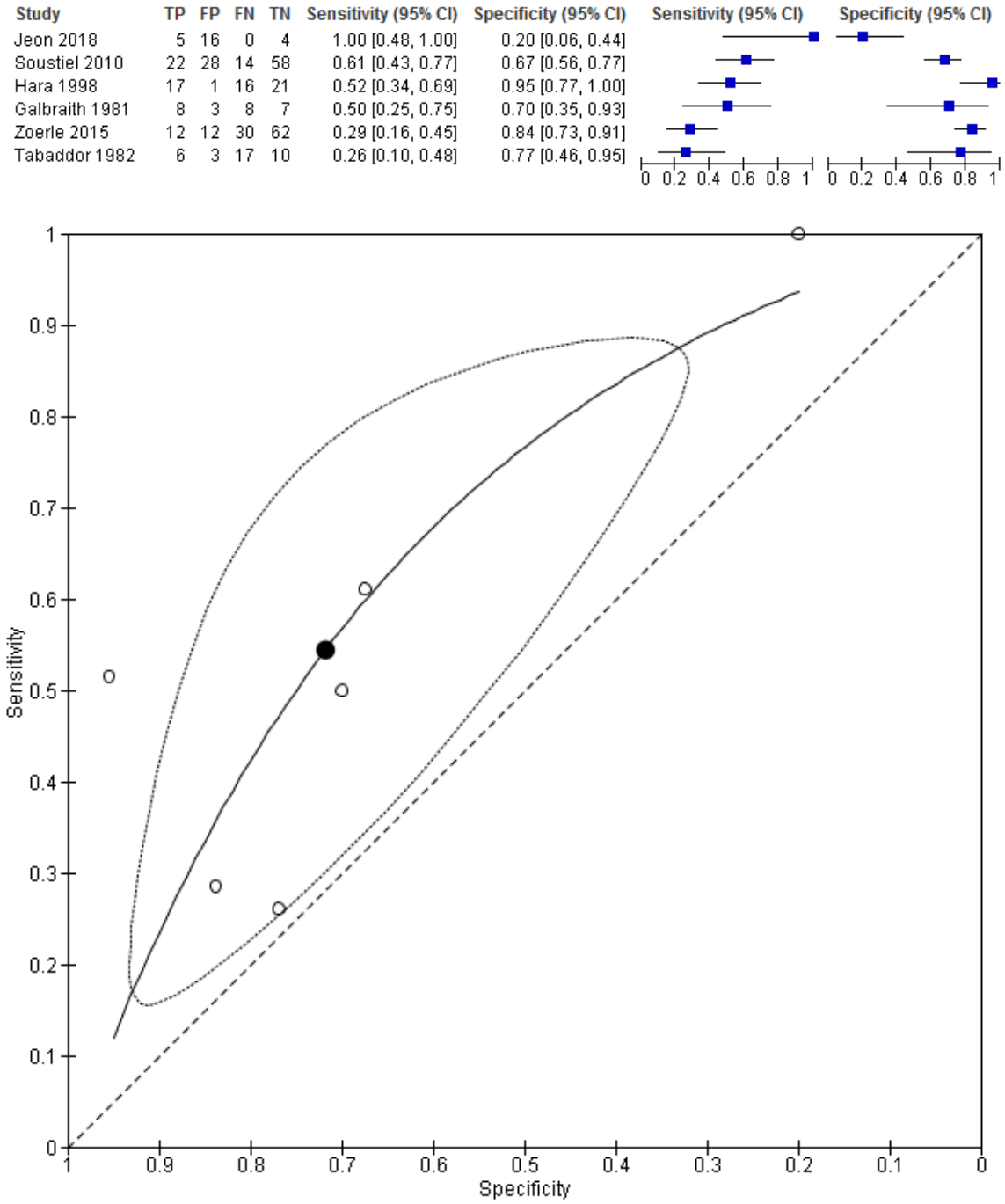
Supplemental Figure 19: Sensitivity Analysis for Compression or Absence of Basal Cisterns after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line), and 95% prediction region (dashed line) for compression/absence of basal cisterns to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.



Supplemental Figure 20: Sensitivity Analysis for Any Midline Shift after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 0mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

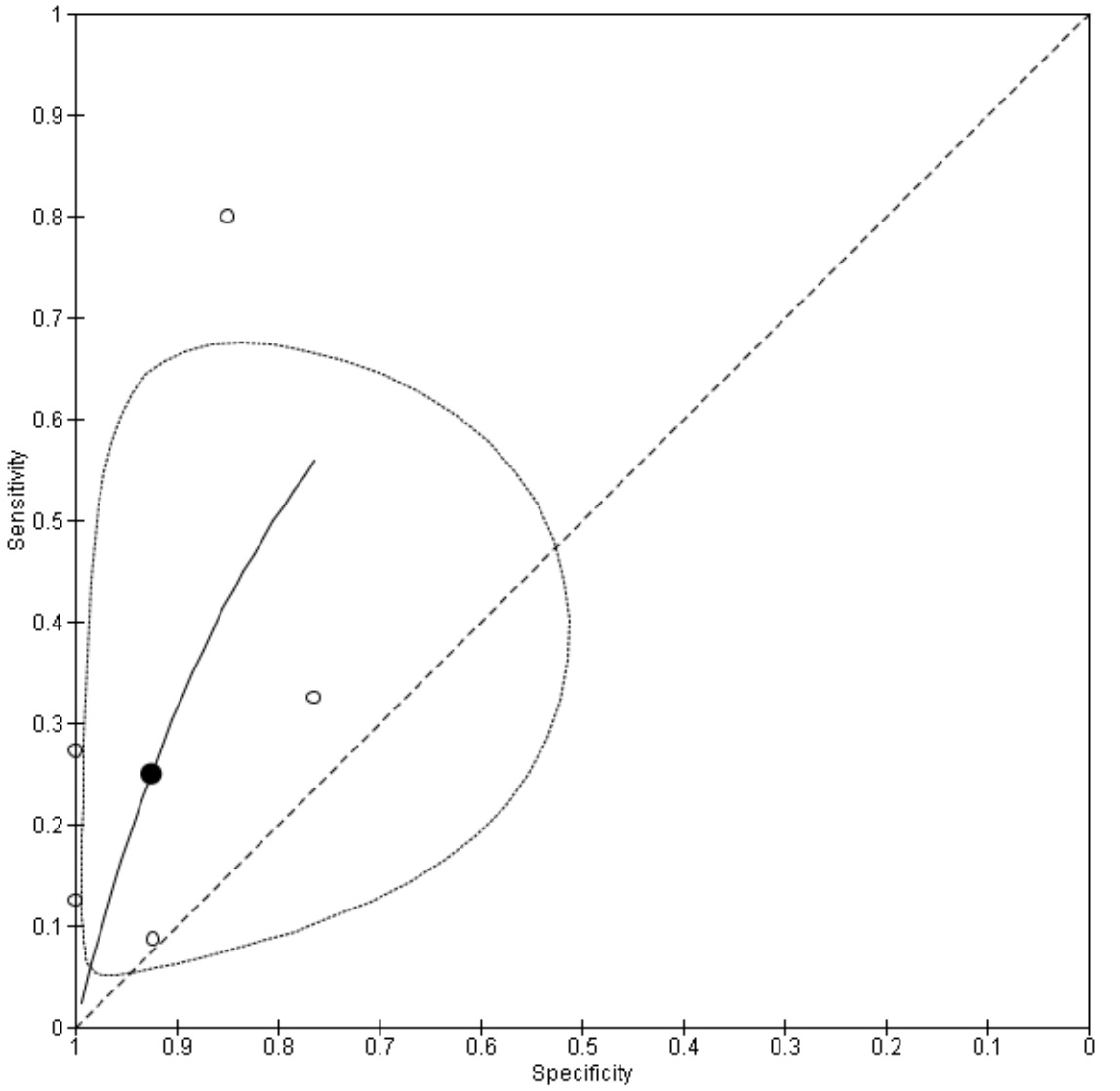


Supplemental Figure 21: Sensitivity Analysis for Midline Shift ≥ 5mm after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 5mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.



Supplemental Figure 22: Sensitivity Analysis for Midline Shift ≥ 10mm after Removal of Studies with Potential High Risk-of-Bias. Forest plot of sensitivity and specificity, the hierarchical summary receiver operating characteristic curve and bivariate summary points of (specificity, sensitivity), and their 95% confidence region (dotted line) for midline shift ≥ 10mm to detect elevated intracranial pressure. Abbreviations: TP = true positive; FP = false positive; FN = false negative; TN = true negative; CI = confidence interval.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jeon 2018	4	3	1	17	0.80 [0.28, 0.99]	0.85 [0.62, 0.97]
Kamel 2012	13	4	27	13	0.33 [0.19, 0.49]	0.76 [0.50, 0.93]
Hara 1998	9	0	24	22	0.27 [0.13, 0.46]	1.00 [0.85, 1.00]
Galbraith 1981	2	0	14	10	0.13 [0.02, 0.38]	1.00 [0.69, 1.00]
Tabaddor 1982	2	1	21	12	0.09 [0.01, 0.28]	0.92 [0.64, 1.00]



Supplemental Table 16: Pre- and Post-test Probability of Elevated ICP – Physical Examination. The post-test probabilities based upon presence or absence of physical examination signs (with sensitivity and specificity fixed at their summary estimates) given clinician-determined pre-test probability are displayed.

Pre-test probability (clinical suspicion prior to test)	Post-test probability if					
	Glasgow Comma Scale		Motor Posturing		Any Pupillary Dilation	
	<= 8	> 8	Present	Not present	Present	Not present
0.10	0.123	0.063	0.142	0.074	0.182	0.085
0.25	0.296	0.168	0.332	0.193	0.400	0.218
0.50	0.558	0.378	0.599	0.418	0.666	0.455
0.75	0.791	0.646	0.817	0.683	0.857	0.715
0.90	0.919	0.845	0.931	0.866	0.947	0.883

Supplemental Table 17: Pre- and Post-test Probability of Elevated ICP – Computed Tomography. The post-test probabilities based upon presence or absence of computed tomography signs (with sensitivity and specificity fixed at their summary estimates) given clinician-determined pre-test probability are displayed.

Pre-test probability (clinical suspicion prior to test)	Post-test probability if													
	Basal Cisterns		Marshall Score						Midline Shift (mm)					
	Absent	Present	>= 3	< 3	>= 4	< 4	>= 5	< 5	> 0	= 0	> 5	<= 5	> 10	<= 10
0.10	0.197	0.025	0.183	0.035	0.207	0.062	0.233	0.068	0.136	0.047	0.155	0.074	0.176	0.090
0.25	0.423	0.071	0.401	0.097	0.439	0.166	0.476	0.180	0.320	0.129	0.355	0.194	0.391	0.229
0.50	0.688	0.187	0.668	0.244	0.701	0.373	0.732	0.397	0.585	0.309	0.622	0.419	0.658	0.471
0.75	0.869	0.409	0.858	0.492	0.875	0.641	0.891	0.664	0.809	0.572	0.832	0.684	0.852	0.727
0.90	0.952	0.675	0.948	0.744	0.955	0.843	0.961	0.855	0.927	0.801	0.937	0.867	0.945	0.889