

## Supplementary Material

**Table S1.** Comprehensive list presenting the search strategy.

### Embase.

No.	Searches	Results
1	(return of spontaneous circulation or ROSC).ti,ab. or exp heart arrest/ or cardiac arrest*.ti,ab. or cardiovascular arrest*.ti,ab. or heart arrest*.ti,ab. or cardiopulmonary arrest*.ti,ab. or asystol*.ti,ab. or pulseless electrical activity.ti,ab. or exp ventricular fibrillation/ or exp advanced cardiac life support/ or (advanced cardiac life support or ACLS).ti,ab. or exp cardiopulmonary resuscitation/ or CPR.mp. or cardiopulmonary resuscitation.ti,ab.	224,915
2	optic nerve sheath diameter.mp. or exp optic nerve/ or exp optic nerve sheath diameter/ or nerve sheath/	27,533
3	ONSD.ti,ab.	37
4	2 or 3	27,533
5	1 and 4	87

### Medline.

No.	Searches	Results
1	(return of spontaneous circulation or ROSC).ti,ab. or exp heart arrest/ or cardiac arrest*.ti,ab. or cardiovascular arrest*.ti,ab. or heart arrest*.ti,ab. or cardiopulmonary arrest*.ti,ab. or asystol*.ti,ab. or pulseless electrical activity.ti,ab. or exp ventricular fibrillation/ or exp advanced cardiac life support/ or (advanced cardiac life support or ACLS).ti,ab. or exp cardiopulmonary resuscitation/ or CPR.mp. or cardiopulmonary resuscitation.ti,ab.	98,122
2	exp Optic Nerve/ or optic nerve sheath diameter.mp.	31,556
3	ONSD.ti,ab.	11
4	2 or 3	31,556
5	1 and 4	41

### Cochrane library.

No.	Searches	Results
1	MeSH descriptor: (Return of Spontaneous Circulation) explode all trees	1
2	MeSH descriptor: (Heart Arrest) explode all trees	1998
3	MeSH descriptor: (Resuscitation) explode all trees	5177
4	MeSH descriptor: (Advanced Cardiac Life Support) explode all trees	60
5	1 or 2 or 3 or 4	6463
6	MeSH descriptor: (Optic Nerve) explode all trees	332
7	(ONSD):ti,ab,kw (Word variations have been searched)	83
8	6 or 7	399
9	5 and 8	0

**Table S2.** Patients' characteristics.

CPR														After ROSC	
	Outcome	N	Age	Male, %	Cardiac origin, %	Witness, %	Bystander CPR, %	Shockable, %	No flow time, min	Low flow time, min	ROSC, min	Time of image modality, min	TTM %		
Chae 2016	GNO	45	48.8 (16.3)	71.1	88.9	-	53.3	55.6	4 (5.8)	20.6 (17.9)	24.6 (18.6)	55.5 (35.5–121.5)	100		
	PNO	74	56.4 (17.4)	55.4	36.5	-	35.1	20.3	12.7 (13.2)	26.4 (15.0)	39.0 (20.7)	63 (39–125)	100		
	Total	119	53.53 (17.32)	61.3	-	-	-	33.6	-	-	-	-	100		
Chelly 2016	Survival	19	53 (40–65)	68	53	90	79	63	1 (1–2)	10 (3-16)	-	-	-		
	Death	17	58 (55–73)	71	18	65	41	18	9 (2–10)	20 (10-32)	-	-	-		
	Total	36	58 (45–69)	69	36	78	64	42	2 (1–9)	15 (7-30)	-	-	-		
Ertl 2018	Survival	23	59 (20–90)	74	-	-	-	74	-	-	-	-	77		
	Death	26	69 (35–96)	69	-	-	-	46	-	-	-	-	46		
	Total	49	65 (20–96)	71	-	-	-	59	-	-	-	-	60		
Kim 2014	GNO	23	50 (44–59)	74	61	91	61	52	-	-	11 (5–25)	60 (21–149)	56		
	PNO	68	61 (48–71)	59	31	34	29	15	-	-	31.5 (20.5–48)	55 (30–120)	40		
	Total	91	57.73 (16.60)	62.6	-	-	-	24.2	-	-	-	-	-		
Lee 2018	GNO	99	52.03 (14.41)	71.72	84.85	79.80	72.73	60.61	2.42 (4.35)	21.28 (13.68)	-	-	100		
	PNO	230	61.47 (15.92)	69.13	51.74	62.61	59.13	14.35	4.58 (7.56)	29.07 (14.93)	-	-	100		
	Survival	162	54.61 (15.69)	65.42	71.60	73.46	66.67	43.83	2.79 (4.43)	22.14 (13.07)	-	-	100		
	Death	167	62.64 (15.44)	71.86	52.10	62.28	59.88	13.17	5.04 (8.39)	31.19 (15.40)	-	-	100		
	Total	329	58.63 (16.06)	69.9	-	-	-	28.3	-	-	-	-	100		
Park 2019	GNO	18	50.67 (15.49)	83.33	50.00	72.22	88.89	61.11	0.5 (0–5.0)	12.67 (9.05)	-	-	100		
	PNO	18	53.00 (15.93)	61.11	11.12	50.00	61.11	11.12	3.5 (0.75–16.25)	27.50 (13.68)	-	-	100		
	Total	36	51.83 (15.53)	72.22	30.56	61.11	75.00	14.11	2.0 (0-12.75)	20.08 (13.68)	-	-	100		
Rush 2017	GNO	18	57.7 (15.3)	83.3	-	94.4	88.9	38.9	-	-	9.3 (7.8)	9.3 (10.0)	-		
	PNO	54	64.1 (15.1)	83.3	-	76.0	79.6	27.8	-	-	27.7 915.0)	10.2 (11.2)	-		
	Total	72	62.5 (15.3)	83.3	-	-	-	30.6	-	-	-	-	-		
Ryu 2017	GNO	19	41.0 (32.0–70.5)	73.7	-	100	100	42.1	-	-	-	-	36.8		
	PNO	23	52.0 (43.0–60.5)	65.2	-	100	100	39.1	-	-	-	-	39.1		
	Total	42	51.0 (34.0–65.0)	69.0	-	100	100	40.5	-	-	-	-	38.1		
Ueda 2015	Total	17	74.8 (55–92)	53	-	-	71	29	-	-	-	-	24		

Data are presented as mean (SD) or median (interquartile range).

**Table S3.** Detailed analysis of prognostic accuracy of the optic nerve sheath diameter for poor neurologic outcomes in each study.

Study	ONSD cut-off point (mm)	N	TP (n)	FP (n)	FN (n)	TN (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Chae	7.0	119	4	0	70	45	5.5	100	100	38.4
Kim	6.21	91	38	0	30	23	55.9	100	100	43.4
Park	4.9	36	15	1	3	17	83.3	94.4	93.8	85.0
Ryu	6.69	42	5	0	18	19	21.7	100	100	51.4
Ueda	5.4	17	8	1	3	5	72.7	83.3	88.9	62.5

ONSD = optic nerve sheath diameter; TP = true positive; FP = false positive; FN = false negative; TN = true negative; PPV = positive predictive value; NPV = negative predictive value.

**Supplementary Table S4.** Subgroup analysis of included studies to identify the association of optic nerve sheath diameter with poor neurologic outcome.

<b>Covariate</b>	<b>N</b>	<b>ONSD, SMD (95% CI)</b>	<b>p-value</b>	<b>I<sup>2</sup>, %</b>	<b>p-value for heterogeneity</b>
All	7	0.74 (0.22, 1.27)	0.006	87	<0.001
Country					
South Korea	5	0.93 (0.27, 1.60)	0.006	91	<0.001
Other countries	2	0.15 (−0.5, 0.80)	0.65	33	0.22
PNO, %					
> 65	3	0.56 (−0.4, 1.51)	0.25	93	<0.001
< 65	4	0.91 (0.21, 1.62)	0.01	78	0.004
Modality					
CT	5	0.55 (0.01, 1.09)	0.05	88	<0.001
US	2	1.37 (0.03, 2.71)	0.04	76	0.04
TTM					
100%	3	0.7 (−0.04, 1.44)	0.06	90	<0.001
<100%	3	1.11 (0.43, 1.79)	0.001	65	0.06

N = the number of studies; ONSD = optic nerve sheath diameter; SMD = standardized mean differences; CI = confidence interval; PNO = poor neurologic outcome; CT = computed tomography; MRI = magnetic resonance imaging; US = ultrasound; TTM = targeted temperature management.

**Table S5.** Sensitivity analysis of included studies to identify the association of optic nerve sheath diameter with neurologic outcome.

<b>Study</b>	<b>ONSD, SMD (95% CI)</b>	<b>p-value</b>	<b>I<sup>2</sup>, %</b>	<b>p-value for heterogeneity</b>
All	0.74 (0.22, 1.27)	0.006	87	< 0.001
Omitting Chae 2016	0.83 (0.15, 1.51)	0.02	89	<0.001
Omitting Kim 2014	0.55 (0.09, 1.00)	0.02	79	0.0002
Omitting Lee 2018	0.88 (0.24, 1.52)	0.007	85	< 0.001
Omitting Park 2019	0.56 (0.07, 1.05)	0.03	85	< 0.001
Omitting Rush 2017	0.89 (0.29, 1.49)	0.004	89	< 0.001
Omitting Ryu 2017	0.74 (0.14, 1.34)	0.02	89	< 0.001
Omitting Ueda 2015	0.76 (0.18, 1.33)	0.01	89	< 0.001

ONSD = optic nerve sheath diameter; SMD = standardized mean differences; CI = confidence interval.

**Table S6.** Meta-regression analyses for potential causes of heterogeneity.

Covariates	N	p-value	Regression coefficient (B)
Sample size	7	0.2510	-0.0031
Time from ROSC to ONSD measurement	7	0.9824	0.0003
Age	7	0.4006	-0.0336
Male, %	7	0.5100	-0.0212
Shockable rhythm, %	7	0.0805	-0.0624

N = the number of studies; ROSC = return of spontaneous circulation; ONSD = optic nerve sheath diameter.

**Table S7.** Analysis of prognostic accuracy for poor neurologic outcome of this updated meta-analysis comparing with previous meta-analyses.

This updated meta-analysis (total N)							Previous meta-analyses (total N)			
	3 CT + 2 US (5)	I <sup>2</sup> (%)	3 CT (4)	I <sup>2</sup> (%)	2 US (2)	I <sup>2</sup> (%)	5 CT + 3 US (8) (Lee 2019)	I <sup>2</sup> (%)	3 CT + 5 US (8) (Zhang 2020)	I <sup>2</sup> (%)
<b>Pooled SEN</b>	0.361 (0.293–0.433)	94.7	0.285 (0.217–0.360)	95.9	0.793 (0.603–0.920)	0	0.41 (0.20–0.67)	95.7	0.60 (0.45–0.73)	-
<b>Pooled SPE</b>	0.982 (0.936–0.998)	42.0	1.000 (0.958–1.000)	0	0.917 (0.730–0.990)	0	0.99 (0.82–1.0)	94.6	0.94 (0.83–0.98)	-
<b>Pooled PLR</b>	9.097 (3.258–25.402)	0	11.382 (2.227–58.175)	0	7.852 (2.094–29.442)	0	49.0 (2.4–958.9)	-	-	-
<b>Pooled NLR</b>	0.504 (0.254–1.002)	96.9	0.703 (0.397–1.245)	96.5	0.241 (0.116–0.501)	0	0.59 (0.39–0.90)	-	-	-
<b>DOR</b>	23.971 (7.182–80.008)	0	16.408 (3.048–88.322)	0	35.527 (5.799–217.64)	9.2	83 (4–1525)	-	15.62 (5.50–44.34)	-
<b>SROC (AUC)</b>	0.8668	-	0.7395	-	0.5000	-	0.86 (0.83–0.89)*	-	0.87 (0.84–0.90)	-
<b>SE (AUC)</b>	0.0776	-	0.0882	-	0	-	-	-	-	-
<b>Q</b>	0.7973	-	0.6848	-	0.5	-	-	-	-	-
<b>SE (Q)</b>	0.0760	-	0.0723	-	0	-	-	-	-	-

N = the number of studies; ROSC = return of spontaneous circulation; ONSD = optic nerve sheath diameter; CT = computed tomography; US = ultrasonography; SEN = sensitivity; SPE = specificity; PLR = positive likelihood ratio; NLR = negative likelihood ratio; DOR = diagnostic odds ratio; SROC = summary receiver operating characteristic; SE = standard error; AUC = area under the curve; CI = confidence interval; ONSD = optic nerve sheath diameter; LR = likelihood. \* hierarchical summary receiver operating characteristic (HSROC).

**Table S8.** GRADE profile for assessing quality of evidence for the included studies for outcomes

**Author(s):**  
**Question:** Optic nerve sheath diameter for predicting outcomes in post-cardiac arrest syndrome  
**Setting:**  
**Bibliography:**

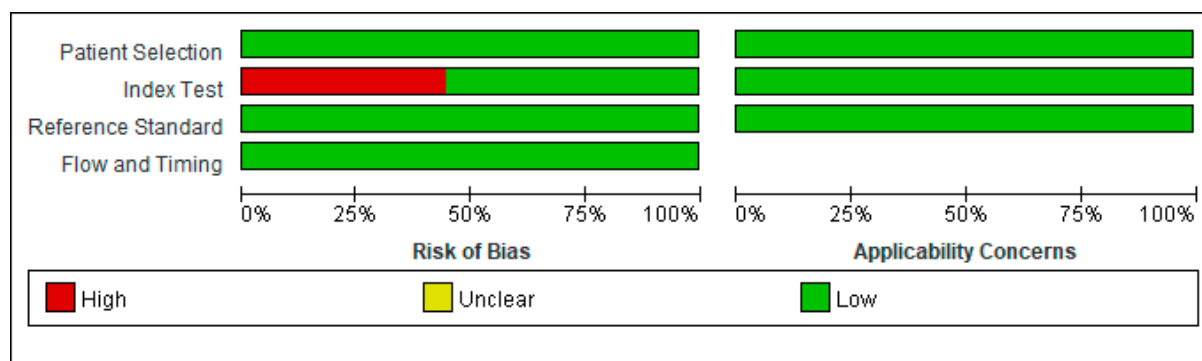
ibliography:

Certainty assessment							N <sub>2</sub> of patients		Effect		Certainty	Importance
N <sub>2</sub> of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ONSD of PNO or death	ONSD of GNO or survival	Relative (95% CI)	Absolute (95% CI)		
Poor neurological outcome at hospital discharge												
3	observational studies	not serious	serious <sup>a</sup>	not serious	serious <sup>b</sup>	none	145	60	-	SMD <b>0.8 SD higher</b> (0.25 lower to 1.85 higher)	⊕⊕○○ Low	CRITICAL
Poor neurological outcome at 1 month												
2	observational studies	not serious	serious <sup>c</sup>	not serious	serious <sup>b</sup>	none	85	51	-	SMD <b>0.39 SD higher</b> (0.04 higher to 0.74 higher)	⊕⊕○○ Low	CRITICAL
Poor neurological outcome at 3 months												
1	observational studies	serious <sup>d</sup>	serious	not serious	serious <sup>b</sup>	none	18	18	-	SMD <b>2.02 SD higher</b> (1.2 higher to 2.84 higher)	⊕○○○ Very low	CRITICAL
Poor neurological outcome at 6 months												
1	observational studies	serious <sup>e</sup>	not serious	not serious	serious <sup>f</sup>	none	230	99	-	SMD <b>0.11 SD higher</b> (0.13 lower to 0.34 higher)	⊕⊕○○ Low	CRITICAL
Death at hospital discharge												
2	observational studies	serious <sup>e</sup>	not serious	serious <sup>g</sup>	serious <sup>b</sup>	none	42	43	-	SMD <b>1.28 SD higher</b> (0.81 higher to 1.75 higher)	⊕○○○ Very low	CRITICAL
Death at 6 months												
1	observational studies	not serious	not serious	not serious	serious <sup>f</sup>	none	167	162	-	SMD <b>0.12 SD higher</b> (0.09 lower to 0.34 higher)	⊕○○○ Very low	CRITICAL

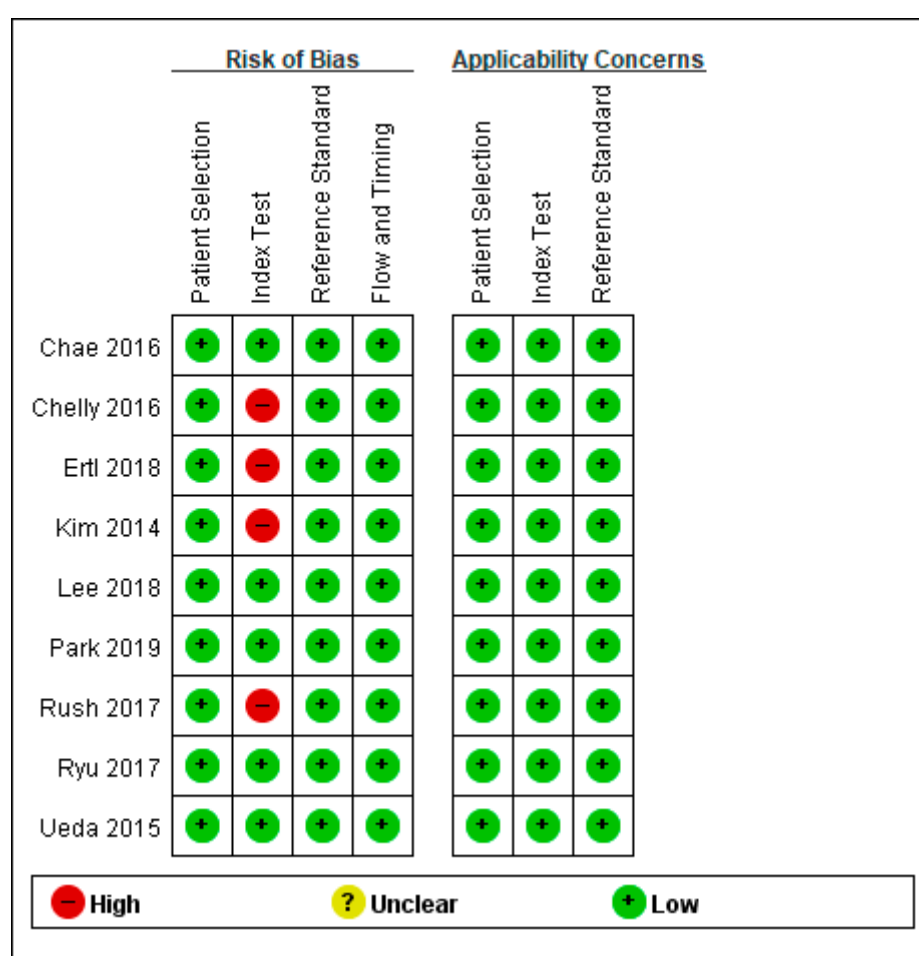
**CI:** confidence interval; **SMD:** standardised mean difference

#### Explanations

- a. Neither the same direction nor similar magnitude of the effect
- b. Total sample size limited
- c. The studies had a wide confidence interval spanning.
- d. High flow and timing
- e. High index test
- f. The total included studies are too small
- g. the only short-term outcome was measured.

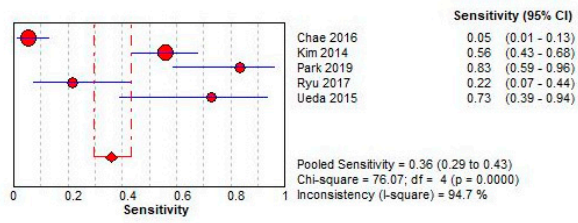


(a)

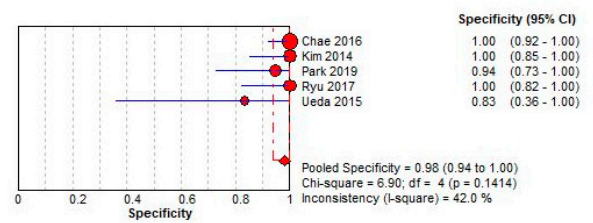


(b)

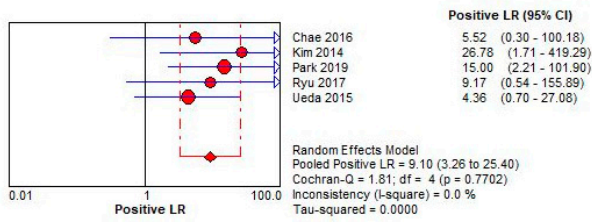
Figure S1. Assessment of study quality.



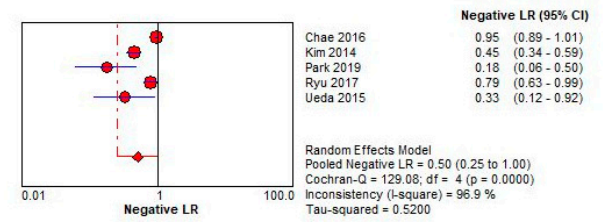
A



B



C



D

**Figure S2.** Pooled prognostic accuracy of the optic nerve sheath diameter for poor neurological outcome. **A:** Pooled sensitivity, **B:** pooled specificity, **C:** pooled positive likelihood ratio, **D:** pooled negative likelihood ratio. Abbreviations: CI = confidence interval; LR = likelihood.