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REVIEW ARTICLE

Optic Nerve Sheath Diameter in Predicting the Neurological Outcomes of Cardiac Arrest Survivors: A Systematic Review and Meta-analysis

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Abstract: **Introduction:** Previous studies have investigated different methods for estimating neurological outcomes after cardiac arrest. However, there is still much uncertainty about using optic nerve sheath diameter (ONSD) measurement as an indirect method for predicting neurological outcomes following cardiac arrest. In this meta-analysis, we aimed to investigate the value of ONSD for predicting the neurological outcomes of cardiac arrest survivors. **Methods:** We comprehensively performed a systematic search in three main electronic databases, including Scopus, Medline, and Web of Science Cochrane, from inception to August 2024. Based on the heterogeneity evaluation results, fixed or random effects models were used to estimate the pooled diagnostic parameters. Meta-regressions were performed for subgroup analysis. **Results:** The pooled sensitivity and specificity of ONSD for predicting the neurological outcomes were 0.56 (95% CI, 0.35–0.74) and 0.92 (95% CI, 0.85–0.96), respectively. Meta-regression revealed that as the cutoff level of ONSD increases, the sensitivity significantly decreases ($P < 0.01$), while the specificity significantly increases ($P = 0.01$). Furthermore, meta-regression analysis revealed that ONSD measurement using CT scans is significantly associated with lower sensitivity and higher specificity compared to ultrasound ($P = 0.009$ and $P = 0.01$). **Conclusion:** Our meta-analysis showed that ONSD has low sensitivity and high specificity for predicting neurological outcomes in survivors of cardiac arrest. However, since the cut-off values and methods of ONSD measurement affect its predictive performance, further studies will be required to standardize these factors to achieve optimal predictive parameters.

Keywords: Diagnostic Techniques, Neurological; Heart Arrest; Meta-analysis; Optic Nerve; Prognosis

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1. Introduction

During recent years, developments in cardiopulmonary resuscitation, education regarding the use of automated external defibrillators, and treatment of post-cardiac arrest syndrome have improved the survival of patients following cardiac arrest. However, many cases show poor post-cardiac arrest outcomes, including severe sequelae, disability, being bedridden, and brain death (1). Targeted temperature management (TTM) and post-cardiac arrest management are used as neuroprotective care. Estimation of the neurologic prognosis of patients with cardiac arrest is required to use appropriate interventions and allocate resources according to the predicted severity of outcomes (2, 3). Previous studies have investigated different methods as estimators of neurological outcomes after cardiac arrest, including blood biomarkers, imaging, electroencephalography, and physical examinations (4-7). However, there is no definite prognostic method for estimating neurological outcomes, and the results of the majority of these methods are conflicting, need to be repeated to provide consistent findings, and are predictive only after 72 hours of cardiac arrest (8). Increased intracranial pressure and brain edema can be estimated by the optic nerve sheath diameter (ONSD), which also predicts neurological outcomes. While most studies on the prognostic application of ONSD for neurological outcomes have been conducted in brain trauma patients, investigations on the predictive performance of ONSD after cardiac arrest are limited (9, 10). Recent studies have investigated the predictive role of ONSD measurement using computed tomography (CT) or ultrasound for predicting neurological outcomes after cardiac arrest, but their findings have been inconsistent. Therefore, there is still great uncertainty about the usage of ONSD measurement as an indirect method for the prediction of neurological outcomes following cardiac arrest. In this systematic review and meta-analysis, we aimed to investigate the predictive value of ONSD measurement for neurological outcomes in cardiac arrest survivors.

2. Methods

2.1. Literature Search

We performed this meta-analysis according to the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA). We comprehensively performed a systematic search in three main electronic databases including Scopus, Medline, and Web of Science Cochrane spanning the period from inception to August 2024. We incorporated the following keywords and MeSH terms “resuscitation” OR “arrest” OR “cardiopulmonary resuscitation” OR "heart arrest" OR “cardiac arrest” OR “cardiac life support” AND “optic nerve sheath diameter” in our search. Systematic search was carried out by two independent authors and disagreements were resolved by the third author.

2.2. Study Selection

Our systematic review focused on cardiac arrest survivors who were evaluated using ONSD measurement by ultrasound or CT scan to predict neurological outcomes. Studies reporting the sensitivity and specificity of ONSD for predicting neurological outcomes were included. Studies that did not report these diagnostic parameters or where sensitivity and specificity could not be calculated based on the provided data were excluded. Letters to editors, editorials, commentary, expert opinions, reviews, conference abstracts, case reports, and case series with fewer than 10 cases were excluded from our study.

2.3. Data Extraction

The data of the following variables were collected from included studies: first author, year of publication, country, design of the study, methods of ONSD measurement, sample size, cut-off for ONSD, sensitivity, and specificity. Data extraction was conducted by two independent authors and inconsistencies were resolved by the third author.

2.4. Quality Assessment

Seven domains of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool were evaluated for each study to assess the risk of bias. The results for each item were categorized as unclear, low, or high risk.

2.5. Statistical Analysis

Pooled results of diagnostic parameters were estimated using Comprehensive Meta-Analysis (CMA) version 3. Heterogeneity between studies regarding the results of each diagnostic parameter was assessed using the I^2 statistic and the Q test. Based on the heterogeneity evaluation results, fixed or random effects models were used to estimate the pooled diagnostic parameters. Meta-regressions were performed for subgroup analysis. Publication bias was assessed using Begg’s test and funnel plot analysis.

3. Results

3.1. Study Selection

A total of 305 eligible published studies were identified through our systematic search of electronic databases. After removing duplicates, 261 articles remained for the title and abstract review stage. After the title and abstract review, 50 studies were selected for full-text review. Two studies that did not report the exact values of sensitivity and specificity were excluded from our analysis (4, 11). Finally, 14 studies

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were included in our meta-analysis. The PRISMA flowchart depicting the process of study selection is shown in Figure 1.

3.2. Characteristics of the Included Studies

In our meta-analysis, 14 published articles involving 871 patients were included to estimate the predictive value of ONSD for neurological outcomes. Ten studies were conducted in South Korea, two in Germany, one in France, and one in Japan. The included studies were published between 2013 to 2024. Ten studies were retrospective and the remaining four studies were prospective. Other characteristics of the included studies are summarized in Table 1.

3.3. Quality Assessment and Publication Bias

Quality assessment of the 14 included studies using QUADAS-2 showed that the majority of the studies had a low risk of bias. Some studies did not report the details of their patient selection, which was categorized as unclear for this item. Egger's test for sensitivity showed no significant bias (P = 0.45), while the test for specificity was statistically significant (P = 0.001). The funnel plot used to evaluate publication bias showed similar findings (Figures 2 and 3).

3.4. Meta-analysis and Meta-regression

The pooled sensitivity and specificity for predicting neurological outcomes using ONSD measurement were 0.56 (95% CI, 0.35–0.74) and 0.92 (95% CI, 0.85–0.96), respectively (Figures 4 and 5). The results of the I^2 and Cochrane Q statistic tests showed significant heterogeneity between the included studies with respect to sensitivity (I^2 = 95% and P < 0.01) and specificity (I^2 = 77% and P < 0.01). Meta-regression revealed that as the cutoff level of ONSD increases, the sensitivity significantly decreases (P < 0.01), while the specificity significantly increases (P = 0.01) (Figures 6 and 7). Furthermore, meta-regression analysis revealed that ONSD measurement using CT scans is significantly associated with lower sensitivity and higher specificity compared to ultrasound (P = 0.009 and P = 0.01, respectively).

4. Discussion

This meta-analysis aimed to investigate the predictive value of ONSD measurement for neurological outcomes after cardiac arrest. It showed low sensitivity (0.56) and high specificity (0.92). We also found that using a higher cut-off for ONSD is associated with lower sensitivity and higher specificity. Interestingly, assessment of ONSD using CT scans instead of ultrasound is correlated with lower sensitivity and higher specificity. The majority of our included studies had a low risk of bias. Publication bias was found for specificity, while this was not significant for sensitivity.

In a similar study, Lee et al. (12) performed a meta-analysis using a systematic search in PubMed and Embase from inception to 2018 to identify articles investigating ONSD for predicting neurological outcomes in survivors of cardiac arrest. They used a simple search query, which yielded eight studies involving 766 patients. They found that ONSD had a sensitivity of 0.41 and a specificity of 0.99 for predicting neurological outcomes. Their reported sensitivity was lower than what we found, while their specificity was higher than ours. After publishing their meta-analysis, a letter to the editor was published regarding this meta-analysis (13). The letter stated that the meta-analysis by Lee et al. included a study incorrectly. In the incorrectly included study, predictive parameters, and cut-off values were not reported, so this study could not be used for the meta-analysis. This study accounted for 43% of the assessed cases in the meta-analysis by Lee et al., which could considerably affect the pooled estimations. We did not include this study in our meta-analysis, which may partly explain the differences in the values of sensitivity and specificity between our study and those reported by Lee et al. Another explanation for the difference between our findings and those reported by Lee et al. is that they performed a systematic search with a lower number of keywords in PubMed and Embase, which yielded eight studies. In contrast, we used a comprehensive search query in Medline, Scopus, and Web of Science, which identified 14 eligible studies. Moreover, it should be noted that they used a Bayesian method to construct 2×2 tables. In contrast, since the majority of our included studies did not report sufficient data to construct 2×2 tables, we pooled the sensitivities and specificities directly.

Another systematic review and meta-analysis was conducted by Zhang et al. (14) on the predictive performance of ONSD for neurological outcomes after cardiac arrest. They performed a systematic search in electronic databases, including Web of Science, Cochrane, PubMed, and ScienceDirect, from their inception to 2020. Similar to the meta-analysis by Lee et al., they included eight studies but did not include the study that was incorrectly included in that meta-analysis. However, the number of patients included in the meta-analysis by Zhang et al. was 473, which was considerably lower than in our study and the study by Lee et al. They reported a sensitivity of 0.6 and a specificity of 0.94 for ONSD. Their sensitivity and specificity were slightly higher than those we calculated in our study. These differences can be explained by the variations in the number of studies and patients included in the meta-analyses. Their subgroup analysis indicated that the cut-off of ONSD and the method of ONSD measurement do not affect the predictive performance of ONSD for neurological outcomes, which is inconsistent with our subgroup analysis.

In a meta-analysis by Kim et al. (15), a systematic search was conducted in Medline, Cochrane, and Embase to find studies that investigated the predictive performance of ONSD. They included nine studies in their systematic review, but for the estimation of the sensitivity and specificity of ONSD, they only included five studies. They reported a sensitivity of 0.36 and a specificity of 0.98 for predicting neurological outcomes using ONSD measurement. Similar to the meta-analysis by Lee et al., they included a study that was indicated as incorrect in a letter to the editor in this meta-analysis.

5. Limitations

Our study had three main limitations. First, the included studies used different methods of ONSD measurement, study designs, and cut-off values for ONSD, which resulted in significant heterogeneity in the results and made extrapolation of our findings complicated. Second, the majority of the included studies had a small number of cases. Third, most studies did not report exact data for true positives, true negatives, false positives, and false negatives, or data that could be used to calculate these values, leading to limitations in estimating other diagnostic parameters.

6. Conclusions

Our meta-analysis showed that ONSD has low sensitivity and high specificity for predicting neurological outcomes in survivors of cardiac arrest. However, since the cut-off values and methods of ONSD measurement affect its predictive performance, further studies will be required to standardize these factors to achieve optimal predictive parameters.

7. Declarations

7.1. Acknowledgments

The authors thank all those who contributed to this study.

7.2. Author Contribution

All authors contributed to study design, data collection, and writing the draft of the study. All authors read and approved the final version of manuscript.

7.3. Funding/Support

None.

7.4. Conflict of interest

None.

7.5. Data Availability

Not applicable.

7.6. Using Artificial Intelligence Chatbots

None.

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Table 1: The characteristics of the included studies

Authors	Year	Country	Design	Method	Sample Size	Cutoff	Sensitivity	Specificity
Ueda et al. (16)	2015	Japan	Retrospective	Ultrasound	17	5.4	0.83	0.73
Chae et al. (17)	2016	Korea	Retrospective	CT scan	119	7	0.055	1
Chelly et al. (18)	2016	France	Prospective	Ultrasound	36	6.7	0.88	0.79
Eartl et al. (19)	2019	Germany	Prospective	Ultrasound	49	5.75	0.6	1
Hwan Kim et al. (20)	2014	Korea	Retrospective	CT scan	91	6.21	0.56	1
Park et al. (21)	2019	Korea	Prospective	Ultrasound	36	4.9	0.833	0.944
Ryu et al. (22)	2017	Korea	Retrospective	CT scan	42	6.69	0.217	1
You et al. (23)	2018	Korea	Retrospective	Ultrasound	83	5.11	0.592	0.765
Hohmann et al. (24)	2024	Germany	Prospective	Ultrasound	30	4.2	0.88	0.72
Kwon et al. (25)	2022	Korea	Retrospective	CT scan	159	7.4	0.071	0.957
Kim et al. (26)	2019	Korea	Retrospective	CT scan	52	5.79	0.718	0.923
Kang et al. (27)	2019	Korea	Retrospective	MRI	37	5.99	0.9	0.98
Dong Kim et al. (28)	2013	Korea	Retrospective	CT scan	24	5.57	0.867	0.778
Lee et al. (29)	2021	Korea	Retrospective	CT scan	96	27.20%*	0.085	1

*: this study was used Rate of Change. CT: computed tomography scan; MRI: magnetic resonance imaging.

Table 2: Quality assessment of the include studies using QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow & timing	Patient selection	Index test	Reference standard
Ueda et al.	☺	☺	☺	☺	☺	☺	☺
Chae et al.	?	☺	☺	☺	☺	☺	☺
Chelly et al.	☺	☺	☺	☺	☺	☺	☺
Eartl et al.	?	☺	☺	☺	☺	☺	☺
Hwan Kim et al.	☺	☺	☺	☺	☺	☺	☺
Park et al.	☺	☺	☺	☺	☺	☺	☺
Ryu et al.	☺	☺	☺	☺	☺	☺	☺
You et al.	☺	☺	☺	☺	☺	☺	☺
Hohmann et al.	☺	☺	☺	☺	☺	☺	☺
Kwon et al.	☺	☺	☹	☺	☺	☺	☺
Kim et al.	☺	☺	☺	☺	☺	☺	☺
Kang et al.	☺	☺	☺	☺	☺	☺	☺
Dong Kim et al.	?	?	?	?	?	☺	☺
Lee et al.	☺	☺	☺	☺	☺	☺	☺

☹: High risk; ☺: Low risk; ?: unclear.

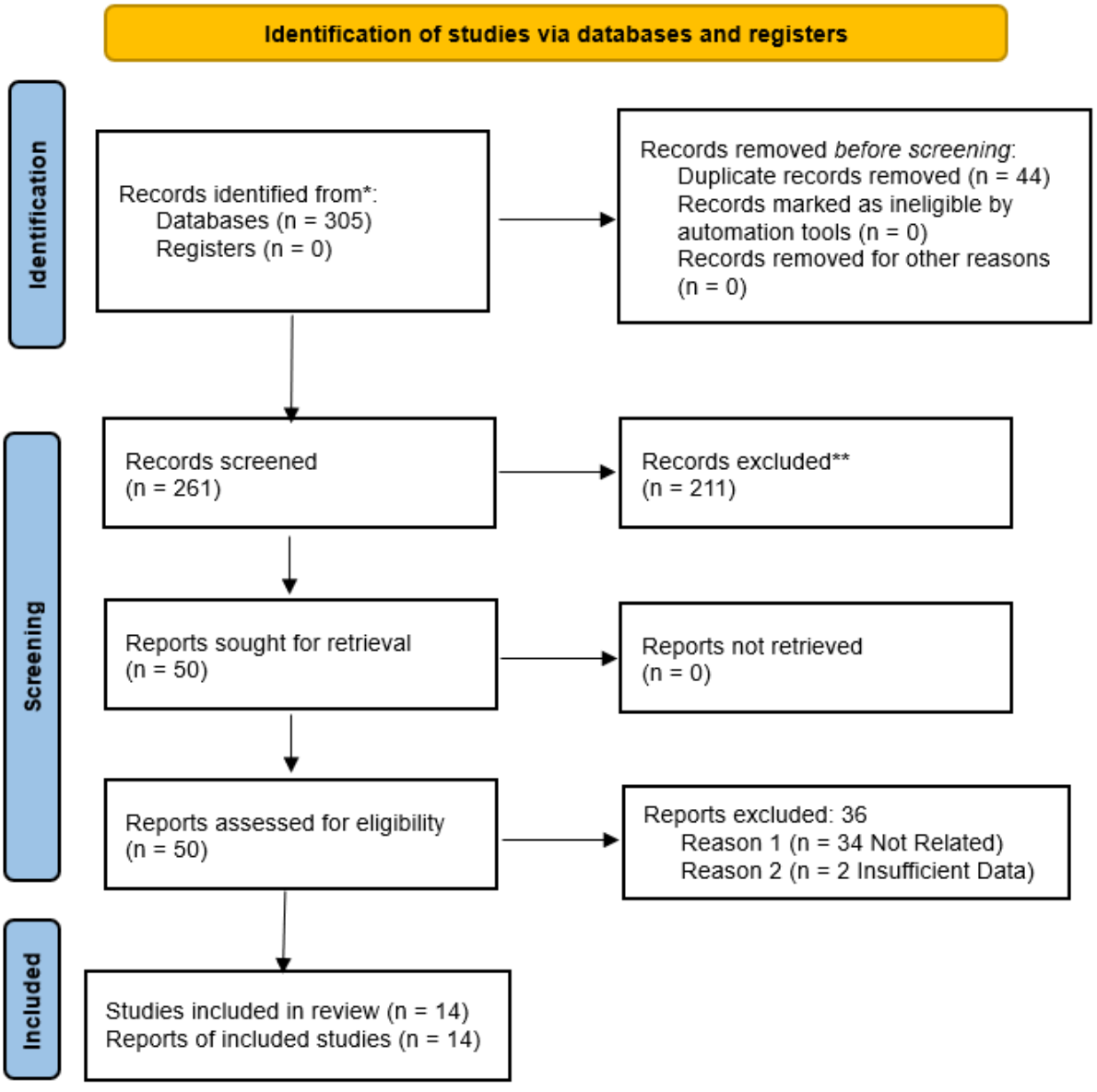

Figure 1: PRISMA flowchart of the literature search and selection of articles that measured ONSD for prediction of neurological outcomes in cardiac arrest survivors.

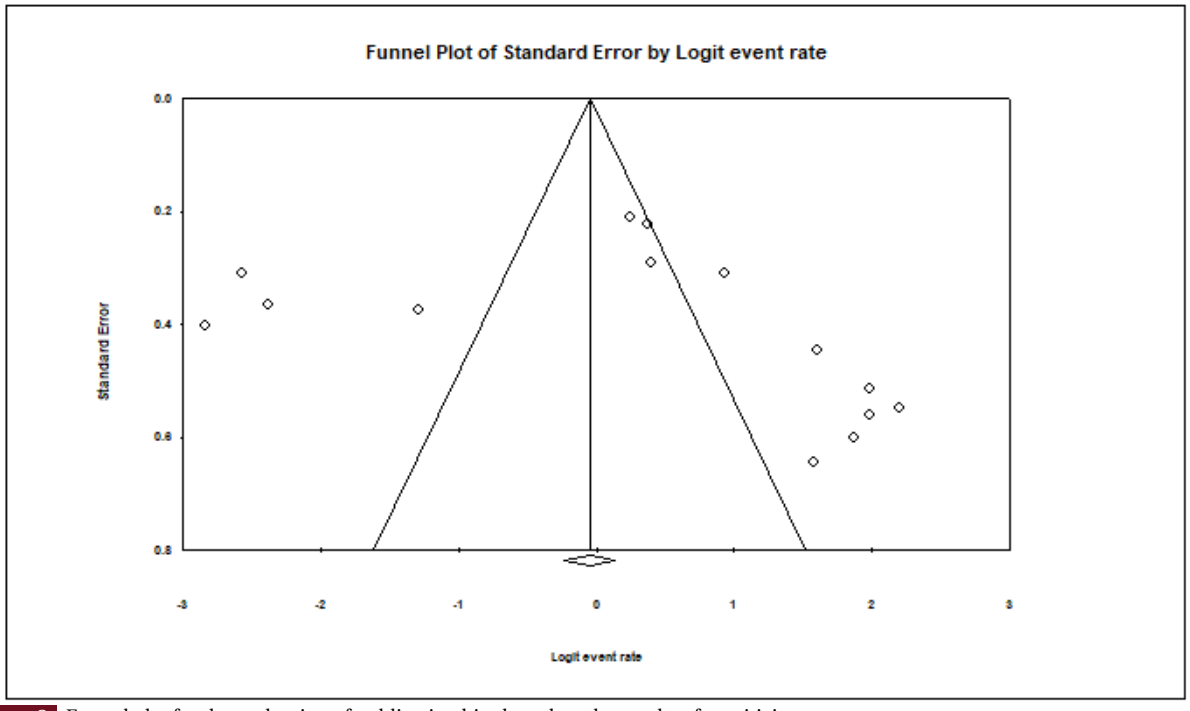

Figure 2: Funnel plot for the evaluation of publication bias based on the results of sensitivity.

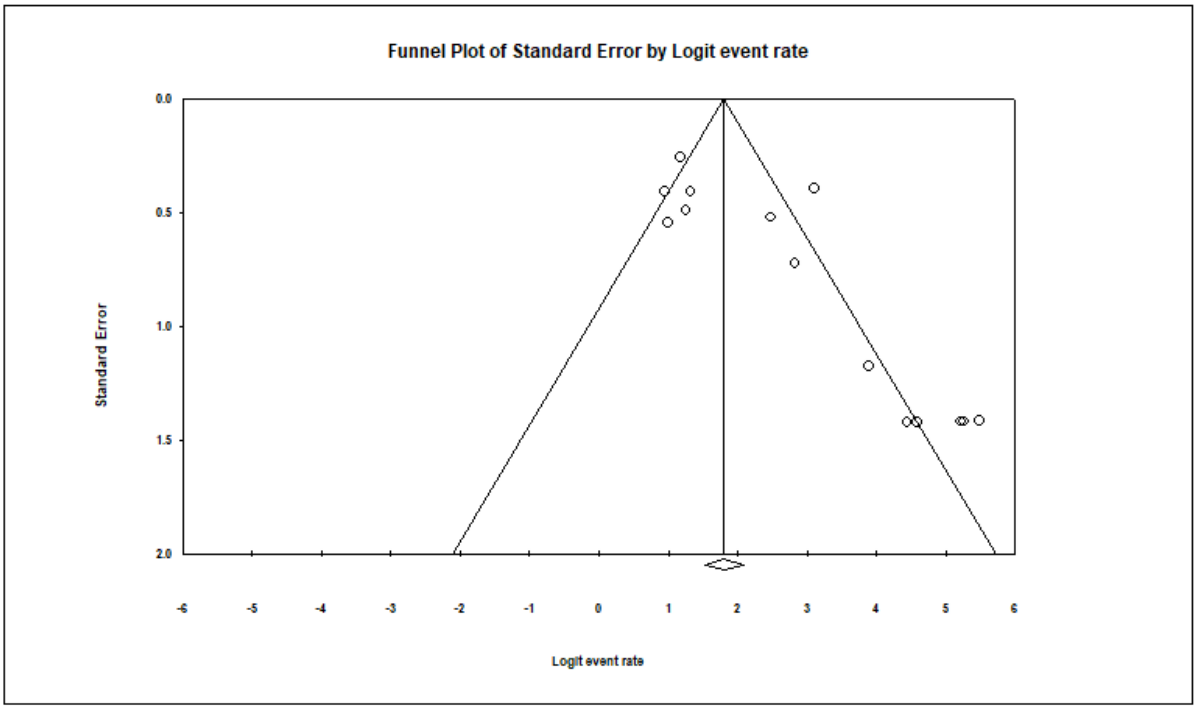

Figure 3: Funnel plot for the evaluation of publication bias based on the results of specificity.

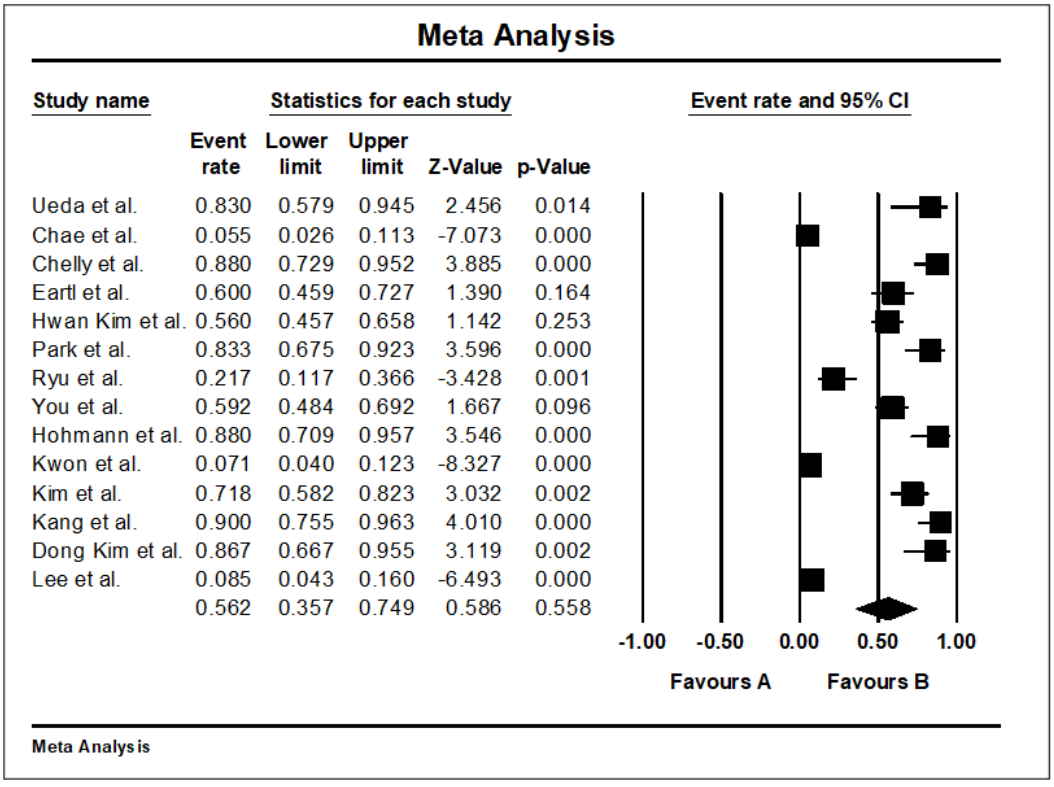

Figure 4: Forest plot of pooled sensitivity.

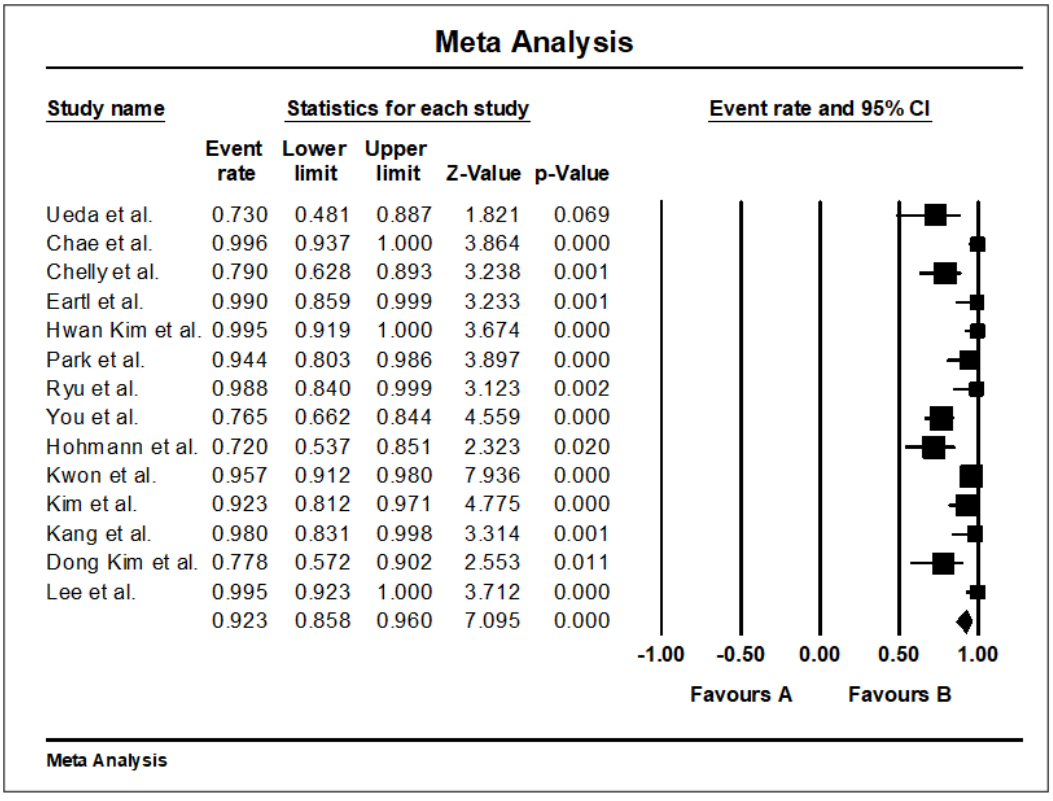

Figure 5: Forest plot of pooled specificity.

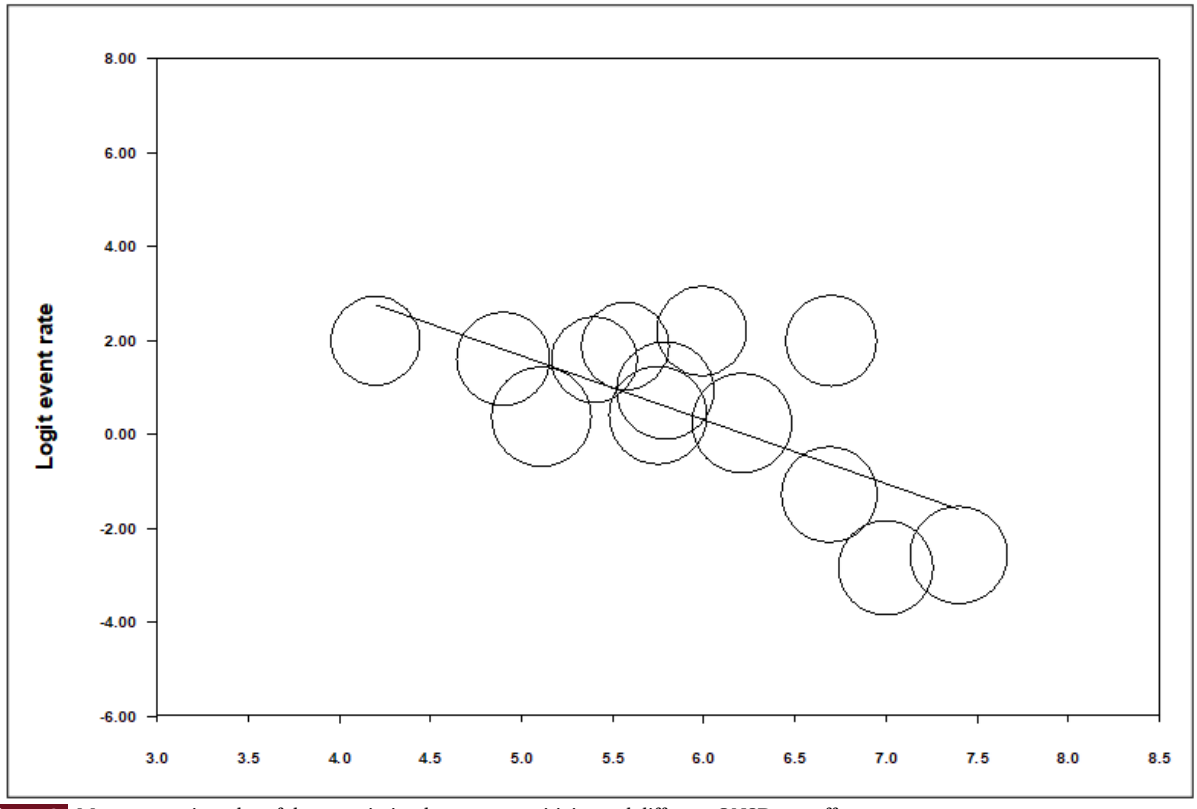

Figure 6: Meta-regression plot of the association between sensitivity and different ONSD cut-offs.

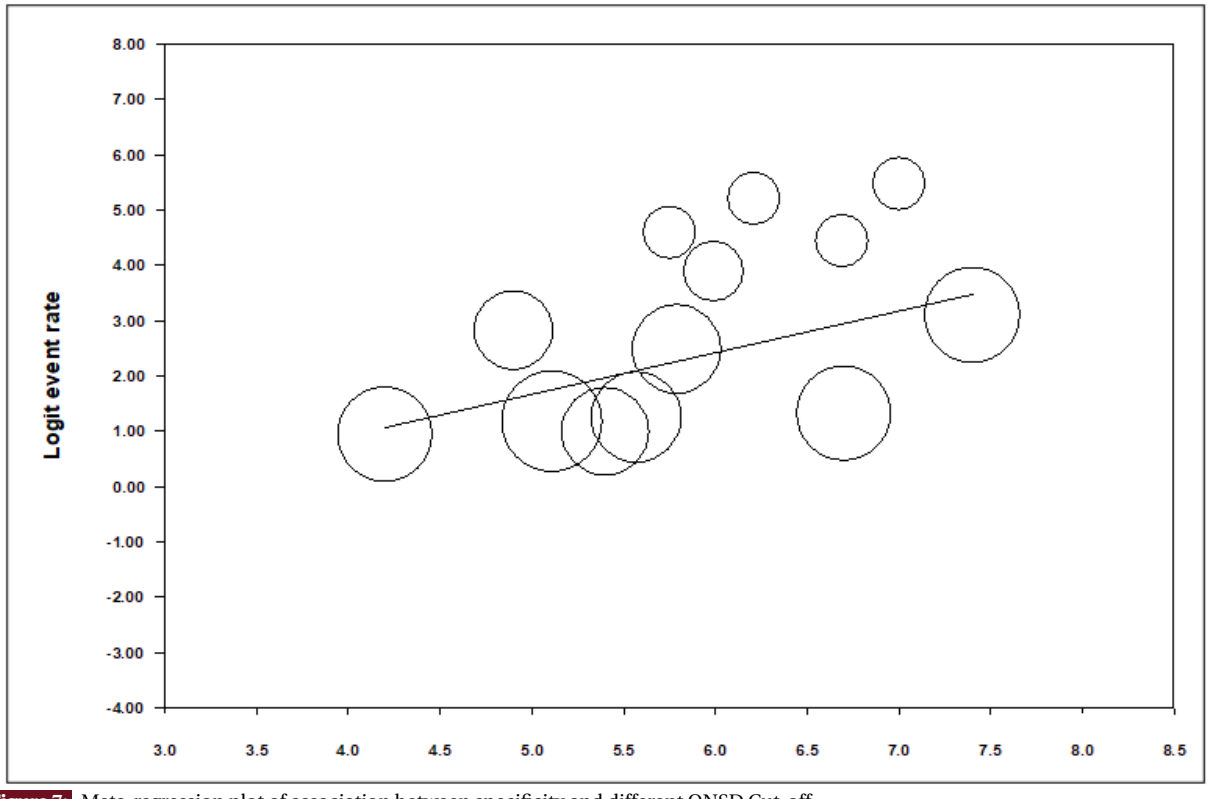

Figure 7: Meta-regression plot of association between specificity and different ONSD Cut-off.