

# Ultrasonographic Measurement of Optic Nerve Sheath Diameter in Patients undergoing Open Heart Surgery: A Prospective Cross-sectional Study

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## ABSTRACT

**Introduction:** Adverse neurologic outcomes following cardiac surgery can be catastrophic to the patient, next of kin, healthcare facility and community at large. Ultrasonographic measurement of Optic Nerve Sheath Diameter (ONSD) has emerged as a promising modality to reflect Intracranial Pressure (ICP) and neurological status in various neurological settings.

**Aim:** To explore ONSD as a tool to reflect ICP changes and predict neurologic outcomes in a cardiac surgical perioperative setting during Cardiopulmonary Bypass (CPB).

**Materials and Methods:** This was an open-label, prospective cross-sectional study conducted in Department of Anaesthesia, Command Hospital, Karnataka, India, from June 2016 to July 2018. Total 50 patients aged between 15 and 80 years who underwent open heart surgeries irrespective of gender, primary diagnosis and preoperative American society of Anaesthesiologist's Physical Status (ASA PS) grade were enrolled in the study. Serial ultrasonographic ONSD of both eyes in two planes (viz. sagittal and transverse) were acquired by a single observer at the following time intervals: baseline (prior to general anaesthesia induction, immediately postintubation, and every 15 minutes interval during CPB (until 150 minutes or end of the CPB whichever was earlier). Postoperative neurologic reassessment was done at 6 hours/postextubation (whichever earlier), at 24 hours and after 7 days, postoperatively. Continuous variables were

compared using the student t-tests, while Chi-square or Fisher's-exact test was used to compare categorical variables. To assess inter-rater reliability for categorical variables, the Cohen's Kappa statistic was used.

**Results:** The mean age of the study cohort was 56.30±11.42 years. A slight male preponderance (56%) was observed. With regards to mean of total CPB time, it was insignificantly higher in patients with adverse neurologic outcomes as compared to those without adverse neurological outcomes (165.83±53.61 minutes vs. 121.36±21.41 minutes; p-value=0.098). Patients with adverse neurologic outcomes had significantly higher ONSD (average of both planes) on CPB from 60 minutes through 150 minutes/end of CPB timeline for right eye (p-value <0.001), left eye (p-value <0.001), and both eyes (p-value <0.001). For patients with ONSD value (average of both eyes in both planes of each eye) ≥5.5 mm had more likelihood to develop adverse neurologic outcomes, postoperatively. With respect to maximum ONSD anytime during CPB (average of both eyes in both planes of each eye), an arbitrary cut-off of ≥5.5 mm showed a sensitivity of 100%, specificity of 95%, diagnostic accuracy of 100%, and predictive value of 100% with significant p-value of <0.001.

**Conclusion:** Serial ultrasonographic ONSD measurement is assuredly a promising tool to monitor elevated level of ICP as well as a good predictor for the assessment of major adverse neurologic outcomes secondary to open heart cardiac surgeries.

**Keywords:** Adverse neurological outcomes, Cardiopulmonary bypass, Intracranial pressure, Ultrasonography

## INTRODUCTION

There are presently over 500 centres where approximately 60,000 open heart surgeries performed annually in India and the majority of surgeries are carried out for coronary artery disease and valvular heart disease [1]. Over the last four decades, major technical breakthroughs in cardiac surgeries have resulted in a continuous decline in mortality and morbidity. Notwithstanding, neurological injury continues to be the leading source of postoperative morbidity and disability secondary to cardiac surgeries and also accounts for a growing percentage of perioperative mortality [2].

Since the advent of Cardiopulmonary Bypass (CPB) in the early 1950s, the neurological consequences of cardiac surgeries have been a prominent concern. As a matter of fact, a considerable proportion of patients experience a perioperative complication including complication of central nervous system. Adverse neurological outcomes following cardiac surgery may occur because of damage to the brain, spinal cord and/or peripheral nerves. These neurological injuries have a very wide range of manifestations from subtle changes in personality, behaviour and cognitive function to fatal brain injury, called the 'Cerebral Catastrophe'. Cardiac surgeries have a formidable impact on the quality of social life and economic growth [3]. Optic Nerve Sheath Diameter

(ONSD) is being used as a non invasive method of measuring Intracranial Pressure (ICP) in an emergency setting in cases of severe head injury, cerebrovascular accident, meningococcal meningitis and metabolic encephalopathy [4].

Quantification of ONSD is a promising and versatile method for detecting alterations in Intracranial Pressure (ICP). In fact, many recent studies have discovered a strong relationship between ONSD enlargement and elevated ICP [5-7]. The parallel increase in the ONSD with ICP occurs owing to the fact that the optic nerve is in the direct continuity of brain (extension of white matter). Like the brain, the optic nerve is also surrounded by subarachnoid space and filled with cerebrospinal fluid. Whenever there is variation in ICP, there seems to be a transfer of pressure through the subarachnoid space [8]. As far as we know, diverse methods have been used to measure ONSD comprising Magnetic Resonance Imaging (MRI), computed tomography and ultrasonography. However, due to the fact that retrobulbar optic space is full of soft tissues, values obtained from MRI are presumed as a gold standard [9].

It has been reported that the measurements taken by the transorbital ultrasonography have good agreement with the measurements acquired by 3 Tesla MRI. Moreover, ONSD measured by transbulbar

ultrasonography appears to have high agreement with MRI along with ready availability, reproducibility, cost-effectiveness and a method that has low slope of learning [7].

What makes the present study novel is the fact that despite the best endeavours, no study could be found that investigated the role of serial ultrasonographic ONSD measurement, as a non invasive tool to monitor ICP in patients undergoing open heart surgery and predict adverse neurological outcomes postoperatively. This study aimed at making a humble attempt at evaluating the possibility of serial ultrasonographic ONSD measurements as a surrogate monitor of elevated ICP, and to correlate the same with adverse neurologic outcomes (if any), in the setting of open heart surgeries done under CPB.

## MATERIALS AND METHODS

This was an open-label, prospective, cross-sectional study conducted in Department of Anaesthesia, Command Hospital, Karnataka, India, from June 2016 to July 2018. The study protocol was approved by the Institutional Ethics Committee (Reference no: CHAFB/1911/2/PG). Informed consent was obtained from each of the participants prior to enrolling.

**Inclusion criteria:** All consecutively patients aged between 15 and 80 years who underwent open heart cardiac surgeries irrespective of gender, primary diagnosis and preoperative American society of Anaesthesiologist's Physical Status (ASA PS) grade were enrolled.

**Exclusion criteria:** All off-pump cardiac surgery, minimally invasive cardiac surgery irrespective of cardiopulmonary bypass, recent history of cerebrovascular accident or intracranial hypertension due to any cause, active ocular ailments confounding ONSD measurements, debilitating psychiatric illness precluding valid consent and/or assessment of neurologic status, and known allergy to ultrasound conductive gels were excluded from the study.

### Study Procedure

All enrolled patients were explained in detail about anaesthetic procedure on the day of the surgery. Preanaesthetic evaluation, appropriate laboratory, and radiological investigations were carried out.

Baseline neurological examinations such as higher mental functions, cranial, sensory and motor nerves examination, reflex-stone power, localising signs, and any focal neurologic deficits were performed in each patient and duly recorded. All patients were kept Nil per Os (NPO) from 12 midnight to before surgery and had received ranitidine 150 mg tablet as pre medication unless contraindicated.

Importantly, peripheral oxygen saturation, blood pressure (systolic and diastolic mean arterial pressure), heart rate, core and peripheral temperature, end-tidal carbon dioxide concentration, central venous pressure, pulmonary artery wedge pressure (whenever applicable), 12 channel electrocardiogram were monitored throughout the cardiac surgery. Both eyelids closed with sterile transparent film and liberal use of ultrasound transmission jelly.

Surgical procedures were performed with the aid of a portable point of care ultrasound device (serial no: LW-62002685 z6 model by Mindray Medical International Ltd., Shenzhen, China) along with a 5-10 MHz (probe code 7L4P) linear ultrasound probe throughout the surgery. All observations were recorded by a single observer. After completion of the cardiac surgery, as a routine institutional cardiothoracic and vascular surgery (CTVS)/Intensive Coronary Care Unit (ICCU) protocol, all patients were shifted to the ICCU for elective postoperative mechanical ventilation. The first assessment of readiness for extubation (i.e the first postoperative neurological assessment) was made at six hours, and then further recorded at 24 hours and after 7 days postoperatively.

After the surgery, the patients were stratified into the following two groups:

- Patients with adverse neurological outcomes
- Patients without adverse neurological outcomes

## Optic Nerve Sheath Diameter (ONSD) Measurement

After surgery, ONSD measurement was carried out in each patient. Ultrasonographically, ONSD was identified at a point 3 mm behind the point of entry of optic nerve into the globe, in both eyes, for each measurement. For each optic nerve, the four measurements were made in each instance: two in the sagittal plane and two in the transversal plane. The ultrasound probe was rotated clockwise while switching between measurements in the planes in order to maintain uniformity. The ONSD reading prior to induction (baseline) and immediately following endotracheal intubation were noted for both eyes in each patient. Then, serial ONSD measurements were made at 15 min intervals after the institution of CPB until the end of bypass. However, after 150 minutes of bypass time, only the last 15 minutes reading was recorded. Complete postoperative monitoring and management in each case were done as per institutional protocols by a multi-disciplinary team comprising various consultants, residents, nursing staff and paramedical staff of the hospital.

## STATISTICAL ANALYSIS

Statistical analyses were done using the Statistical Package for Social Sciences (SPSS) version 18.0 software (SPSS Inc., Chicago, IL, USA) and R Environment version 3.2.2. Continuous variables were expressed as mean and standard deviation and were compared using the student t-tests. Chi-square or Fisher's-exact test (depending on sample size) was used to compare categorical variables that were presented as numbers and percentages. To assess inter-rater reliability for categorical variables, the Cohen's Kappa statistic was used. The Kappa result was interpreted as follows:

- $\leq 0$ : no agreement
- 0.01-0.20: slight
- 0.21-0.40: fair
- 0.41-0.60 moderate
- 0.61-0.80 substantial
- 0.81-1.00 perfect agreement

The p-value of  $<0.05$  was deemed as statistically significant.

## RESULTS

A total of 50 patients, who underwent open heart surgery, were assessed. The mean age of the study cohort was  $56.30 \pm 11.42$  years. A slight male preponderance (56%) was noted. As demonstrated in [Table/Fig-1], a variety of primary diagnosis was associated with cardiac surgery, among them; triple vessel coronary artery disease (56%) was the most frequent primary diagnosis.

Distribution of surgical procedures among patients with and without adverse neurological outcome is demonstrated in [Table/Fig-2]. Out of the total 50 patients, 6 patients (12) had adverse neurological outcome postoperatively, of which, 4 patients (66.7) had undergone Coronary Artery Bypass Graft Surgery (CABG), 1 (2) had undergone double valve replacement and one patient (16.7%) had undergone mitral valve replacement.

Of the total six patients with adverse neurologic outcomes, none of the patients was extubated at 6 hours postoperatively. One of the patients suffered from delayed extubation on day 3 postoperatively due to diffuse cerebral edema, which was likely on account of related hypoxic injury as evidenced on CT scan of the head. Nevertheless, this patient did not demonstrate any neurological deficits on discharge. Six patients (12%) with adverse outcomes were extubated beyond 24 hours postoperatively and developed various motor manifestations as enumerated in [Table/Fig-3]. One of the patients died within the 7<sup>th</sup> day of surgery due to quadriplegia, multiple intercurrent and consequent complications.

Out of the 50 patients studied, patients who developed postoperative adverse neurologic outcomes were either ASA PS grade two (20%), three (66%) or four (2%) [Table/Fig-4].

| Characteristics   | (n, %)   |
|---|----------|
| <b>Gender</b>   |          |
| Male  | 28 (56%) |
| Female  | 22 (44%) |
| <b>Primary diagnosis</b>  |          |
| CAD-TVD   | 20 (40%) |
| RHD-Severe aortic stenosis, MR, PAH, atrial fibrillation        | 8 (16%)  |
| CAD-DVD   | 6 (12%)  |
| BAV with severe aortic stenosis                                 | 3 (6%)   |
| Severe aortic stenosis  | 3 (6%)   |
| RSD with severe MS  | 2 (4%)   |
| CAD-SVD with aortic stenosis and aortic regurgitation           | 2 (4%)   |
| Calcific aortic stenosis with aortic regurgitation              | 1 (2%)   |
| MVP with severe MR  | 1 (2%)   |
| Post closed mitral valvotomy restenosis                         | 1 (2%)   |
| Severe calcific aortic stenosis                                 | 1 (2%)   |
| Severe MR   | 1 (2%)   |
| Severe MS and MR with left atrium clot with atrial fibrillation | 1 (2%)   |

**[Table/Fig-1]:** Baseline demographics and clinical characteristics of study population (N=50).

CAD: Coronary artery disease; TVD: Triple-vessel disease; RHD: Rheumatic heart disease; MR: Mitral regurgitation; MS: Mitral stenosis; PAH: Pulmonary arterial hypertension; DVD: Double-vessel disease; BAV: Balloon aortic valvuloplasty; RSD: Reflex sympathetic dystrophy; MVP: Mitral valve prolapsed

| Types of surgery                                | Adverse neurological outcomes |               |
|---|-------------------------------|---------------|
|   | Present (n=6)                 | Absent (n=44) |
| Aortic Valve Replacement (AVR)                  | 0 (0)                         | 6 (13.6)      |
| Coronary Artery Bypass Grafting (CABG)          | 4 (66.7)                      | 15 (34.1)     |
| CABG with AVR                                   | -                             | 5 (11.4)      |
| CABG with MVR                                   | -                             | 2 (4.5)       |
| CABG with right coronary artery end arterectomy | -                             | 1 (2.3)       |
| Double valve replacement                        | 1 (16.7)                      | 3 (6.8)       |
| Mitral valve replacement (MVR)                  | 1 (16.7)                      | 12 (27.3)     |

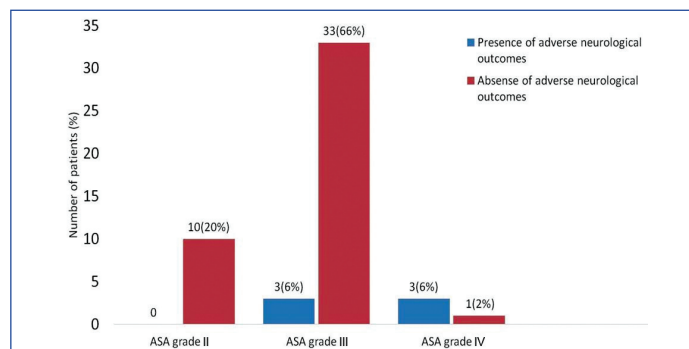
**[Table/Fig-2]:** Distribution of surgical procedures among patients with and without adverse neurological outcomes. Data are expressed as frequency and percentages

| Parameters  | n, %    |
|---|---------|
| <b>At 6 hours/postextubation neurologic deficits</b>    |         |
| Note extubated  | 6 (12)  |
| Within normal limit                                     | 44 (88) |
| <b>At 24 hours postoperative neurologic deficits</b>    |         |
| Present   | 6 (12)  |
| Delayed extubation due to diffused cerebral oedema      | 1 (2)   |
| Left-sided hemiparesis                                  | 1 (2)   |
| Left-sided monoparesis                                  | 1 (2)   |
| Paraparesis   | 1 (2)   |
| Quadriparesis   | 1 (2)   |
| Right-sided hemiparesis                                 | 1 (2)   |
| Within normal limit                                     | 44 (88) |
| <b>After 7 days/discharge/death/neurologic deficits</b> |         |
| Present   | 4 (8)   |
| Within normal limit                                     | 45 (90) |
| Died  | 1 (2)   |

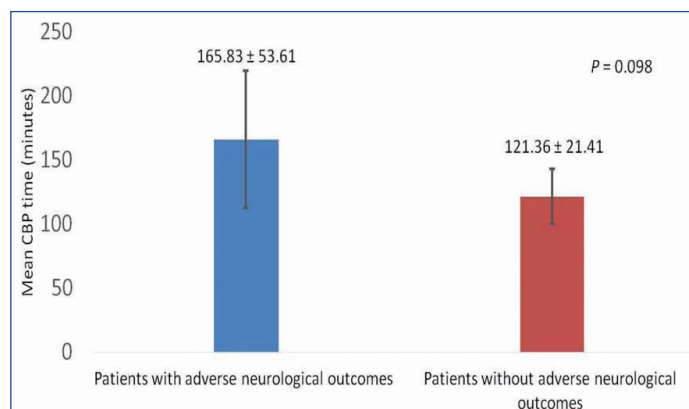
**[Table/Fig-3]:** Detection of timing of neurologic deficits postoperatively and type of manifested neurologic deficits (N=50). Data are expressed as frequency and percentages

The mean of total CPB time (in minutes) among patients with and without adverse neurological outcomes were compared, and obtained findings revealed that mean CPB time was higher in patients with adverse neurologic outcomes but the value was

not significant (165.83±53.61 minutes vs. 121.36±21.41 minutes; p-value=0.098) [Table/Fig-5].



**[Table/Fig-4]:** Distribution of the patients with and without adverse neurological outcomes according to American Society of Anesthesiologists Physical Status (ASA PS) ratings.



**[Table/Fig-5]:** Comparison of mean cardiopulmonary bypass time among patients with and without adverse neurological outcomes. P = 0.098

The ONSD values of the average of both planes (viz. sagittal and transverse) in right eye, left eye and both eyes in relation to adverse neurologic outcomes at each time point of measurement were compared. Patients with adverse neurological outcomes had significantly higher ONSD (average of both planes) on CPB from 60 minutes through 150 minutes/end of CPB timeline for right eye (p-value <0.001), left eye (p-value <0.001), and both eyes (p-value <0.001). [Table/Fig-6] demonstrating trend of mean optic nerve sheath diameter values of right eye, left eye and both eyes.

As illustrated in [Table/Fig-7], the maximum ONSD recorded anytime during CPB (average of both planes in both eyes) of ≥5.5 mm was appeared to be more likely to develop adverse neurologic outcomes postoperatively (100% vs. 4.5%, p-value <0.001). Comparison of consolidated validity measures such as sensitivity, specificity and diagnostic accuracy between maximum ONSD anytime during CPB and average ONSD of all values during CPB are compared in [Table/Fig-8]. To measure “maximum ONSD anytime during CPB (average of both eyes in both planes of each eye)”, an arbitrary cut-off of ≥5.5 mm demonstrated a sensitivity of 100%, specificity of 95%, diagnostic accuracy of 100%, and predictive value of negative test of 100% with significant p-value of <0.001.

## DISCUSSION

Ultrasonographic ONSD measurement is a relatively recent application for the assessment of optic ultrasound. In the last few decades, it has been increasingly used as a surrogate marker for elevated ICP [10].

The utility of ultrasonographic ONSD measurement has been extensively evaluated in a variety of clinical, laboratory, imaging and critical care settings as a reliable tool to predict elevated ICP. Hamilton DR et al., from his preclinical study on a porcine model, asserted the utility of ONSD to non invasively validate acute changes in ICP over one hour. Furthermore, they advocated the implementation of this approach in humans using measurement



| Variables                        | Right eye (average of both planes) |           |         | Left eye (average of both planes) |           |         | Both eyes (average of both planes in each eye) |           |         |
|----------------------------------|------------------------------------|-----------|---------|-----------------------------------|-----------|---------|--|-----------|---------|
|                                  | Adverse neurological outcomes      |           |         |                                   |           |         |  |           |         |
|                                  | Present                            | Absent    | p-value | Present                           | Absent    | p-value | Present  | Absent    | p-value |
| Baseline                         | 4.70±0.49                          | 4.54±0.46 | 0.469   | 4.58±0.48                         | 4.78±0.35 | 0.225   | 4.56±0.47                                      | 4.74±0.39 | 0.323   |
| Postintubation                   | 4.90±0.36                          | 4.86±0.40 | 0.804   | 4.87±0.37                         | 4.93±0.37 | 0.688   | 4.86±0.39                                      | 4.91±0.36 | 0.743   |
| <b>On Cardiopulmonary bypass</b> |                                    |           |         |                                   |           |         |  |           |         |
| At 0 min                         | 4.76±0.34                          | 5.06±1.03 | 0.150   | 5.11±1.08                         | 4.78±0.34 | 0.113   | 5.08±1.05                                      | 4.77±0.34 | 0.129   |
| At 15 min                        | 4.77±0.34                          | 4.97±0.81 | 0.279   | 4.99±0.85                         | 4.78±0.35 | 0.250   | 4.98±0.83                                      | 4.77±0.34 | 0.262   |
| At 30 min                        | 4.76±0.34                          | 5.01±0.47 | 0.123   | 5.08±0.49                         | 4.79±0.33 | 0.067   | 5.04±0.48                                      | 4.78±0.34 | 0.090   |
| At 45 min                        | 4.77±0.33                          | 5.08±0.49 | 0.051   | 5.07±0.51                         | 4.77±0.33 | 0.063   | 5.07±0.50                                      | 4.77±0.33 | 0.056   |
| At 60 min                        | 4.76±0.34                          | 5.23±0.41 | <0.001  | 5.25±0.39                         | 4.78±0.34 | <0.001  | 5.24±0.40                                      | 4.77±0.34 | <0.001  |
| At 75 min                        | 4.78±0.34                          | 5.42±0.22 | <0.001  | 5.47±0.22                         | 4.78±0.34 | <0.001  | 5.44±0.22                                      | 4.78±0.34 | <0.001  |
| At 90 min                        | 4.81±0.35                          | 5.52±0.15 | <0.001  | 5.58±0.16                         | 4.81±0.35 | <0.001  | 5.55±0.15                                      | 4.81±0.35 | <0.001  |
| At 105 min                       | 4.77±0.35                          | 5.58±0.04 | <0.001  | 5.63±0.12                         | 4.80±0.35 | <0.001  | 5.61±0.08                                      | 4.78±0.35 | <0.001  |
| At 120 min                       | 4.78±0.36                          | 5.04±1.28 | <0.001  | 5.63±0.08                         | 4.80±0.36 | <0.001  | 5.34±0.65                                      | 4.79±0.36 | 0.011   |
| At 135 min                       | 4.75±0.39                          | 5.65±0.11 | <0.001  | 5.68±0.08                         | 4.76±0.37 | <0.001  | 5.67±0.09                                      | 4.76±0.38 | <0.001  |
| At 150 min (End)                 | 4.77±0.33                          | 5.63±0.06 | <0.001  | 5.65±0.07                         | 4.78±0.33 | <0.001  | 5.64±0.06                                      | 4.78±0.33 | <0.001  |

**[Table/Fig-6]:** Trend of mean optic nerve sheath diameter (in mm) values of right eye, left eye and both eyes. p-value <0.05 was considered statistical significance; CPB: Cardiopulmonary bypass

| An arbitrary cut-off ONSD values  | Adverse neurological outcomes |               | p-value |
|---|-------------------------------|---------------|---------|
|   | Present (n=6)                 | Absent (n=44) |         |
| ONS average of both eyes (both planes in each eye) of all measurements during CPB |                               |               |         |
| <5.5 mm   | 0                             | 11 (25)       | 0.317   |
| ≥5.5 mm   | 6 (100)                       | 33 (75)       |         |
| Maximum ONSD recorded on CPB (average of both eyes viz. both planes in each eye)  |                               |               |         |
| <5.5 mm   | 0                             | 42 (95.5)     | <0.001  |
| ≥5.5 mm   | 6 (100)                       | 2 (4.5)       |         |

**[Table/Fig-7]:** An arbitrary cut-off values of an optic nerve sheath diameter (a) as an average of all measurements on cardiopulmonary bypass (b) maximum optic nerve sheath diameter recorded anytime during cardiopulmonary bypass. ONSD: Optic nerve sheath diameter; CPB: Cardiopulmonary bypass

| Parameters                                       | Maximum ONSD anytime during CPB (N=50) (Average of both eyes in both planes of each eye) | Average ONSD of all values during CPB (N=50) (Average of both eyes in both planes of each eye) |
|--|--|--|
| <b>Postoperative adverse neurologic outcomes</b> |  |  |
| <b>ONS &lt;5.5 mm</b>                            |  |  |
| Present  | 0  | 5 (10)   |
| Absent   | 42 (84)  | 44 (88)  |
| <b>ONS ≥5.5 mm</b>                               |  |  |
| Present  | 6 (12)   | 1 (2)  |
| Absent   | 2 (4)  | 0  |
| <b>Statistics</b>                                |  |  |
| Sensitivity (%)                                  | 100  | 16   |
| Specificity (%)                                  | 95   | 100  |
| PPV (%)  | 75   | 100  |
| NPV (%)  | 100  | 90   |
| Diagnostic accuracy (%)                          | 100  | 96   |
| Cohen's Kappa statistics                         | 0.834  | 0.260  |
| p-value  | <0.001   | 0.210  |

**[Table/Fig-8]:** Comparison of consolidated validity measures between maximum optic nerve sheath diameter anytime and average optic nerve sheath diameter of all values during cardiopulmonary bypass in both planes of both eyes. p-value <0.05 was considered as statistically significant; PPV: Positive predictive value; NPV: Negative predictive value

of direct ICP, to prove its utility as a screening tool for acute and chronically enlarged diameters caused by elevated pressure in clinical settings [11]. Širanović M et al., presented correlation between ultrasonographic measurement of ONSD and direct measurement of ICP in patients with traumatic brain injury [12].

Usefulness of ocular ultrasound scans in identifying elevated ICP was reported in diverse conditions. Geeraerts T et al., reported in severe traumatic brain injury, Hansen HC et al., in cerebrospinal fluid absorption disorders (communicating hydrocephalus or optic disc elevation of unknown origin), Baurele J et al., in idiopathic intracranial hypertension, Moretti R et al., in intracranial haemorrhage, Zaidi SJH et al., in ventriculoperitoneal shunt obstruction [6,13-16].

The mean age of the index study cohort was 56.30±11.42 years. Consistent with the literature, this analysis also showed advanced age as a robust predictor of neuropsychological injury secondary to cardiac [17,18]. In this study, six patients had adverse neurologic outcomes secondary to CABG surgery, which is consistent with the trend that most cases of adverse neurologic outcomes reported are of CABG. As such, it has been noted that the event of a clinically evident stroke secondary to CABG ranged from 0.8-5.2% [19]. A German population-based study showed that the incidence of stroke increases by 3.3% when CABG is combined with valve replacement surgery [20]. Moreover, another study claimed that the incidence of stroke increases further (upto 6.7%) in patients undergoing multiple valves replacement surgery [21]. Literature regarding the relationship between duration of bypass and adverse neurologic outcomes are conflicting. In the present study, patients with adverse neurologic outcomes had higher mean CPB duration but the value was statistically insignificant (165.83±53.61 minutes vs. 121.36±21.41minutes). The institutional protocol routinely employs non pulsatile hypothermic CPB. Many authors have presented that progressive cerebral vasoconstriction can give rise to cerebral injury during prolonged non pulsatile hypothermic CPB as an additional responsible factor [22,23], whilst others have disputed it [24,25].

There is a wide variation and a lack of consensus about the optimal cut-off values of ONSD and what measurement represents elevated ICP. Frumin E et al., measured ONSD of 24 patients in the supine position in correlation with ICP measured by external ventricular drain and concluded that the optimal ONSD for the elevated ICP of >20 mmHg was ≥5.2 mm with a sensitivity and specificity of 83.3% and 100%, respectively [26]. Findings of a study published by Rajajee V et al., demonstrated that the best cut-off value of ONSD was ≥0.48 cm, which was a good predictor of ICP >20 mmHg with sensitivity and specificity of 96% and 94%, respectively [27]. Receiver Operating Characteristic Curve (ROC) analysis demonstrated that the best cut-off for the detection of elevated ICP (> 20 mmHg) was 6.1 with a sensitivity of 100% and specificity of 83% in the study reported by Širanović M et al., and 5.9 mm with a sensitivity of 95% and specificity of 79% by

Geeraerts T et al., [6,12]. Recently, cut-off values for elevated ICP have been proposed to be 5-5.9 mm [28]. This discordance in cut-off values may be attributable to multiple reasons, including the baseline variability. But in general, if we keep higher the sensitivity, the cut-off value comes down and similarly keeping the specificity higher then cut-off value migrates towards the upper side. In the present study, maximum ONSD anytime during CPB with an arbitrary cut-off of 5.5 mm proved to be a significant parameter in predicting postoperative adverse neurologic outcomes; with a sensitivity of 100%, specificity of 95%, diagnostic accuracy of 100%, and negative predictive value of 100%.

### Limitation(s)

The present study was mainly restricted by small sample size and short-term follow-up. Moreover, the data about the duration of cardiac disease, level of control of co-morbidities, intraoperative haemodynamic trends, CPB conduct modes and practices were not adequately recorded, and hence their bearing on postoperative neurologic outcomes could not be interpreted. Further studies with greater sample size, better power of estimate, longer follow-up, ONSD acquisition, and the influence of co-morbidities are warranted to validate our arbitrary cut-off of 5.5 mm.

### CONCLUSION(S)

It is concluded that the parameter maximum ONSD anytime during CPB (average of both eyes in both planes of each cycle) has a high sensitivity, specificity, diagnostic accuracy, as well as predictive value of negative test. Hence, it is a suitable candidate for the predictor of adverse postoperative neurologic outcomes following open heart cardiac surgeries done on CPB. It may further be stated that elevated ONSD on CPB beyond cut-off serves to suggest instituting appropriate measures to reduce ICP in an attempt to halt anticipated ongoing neurologic damage and prompt further neuroimaging confirmatory modalities.

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