

Correlation between middle cerebral artery pulsatility index and optic nerve sheath diameter with intracranial pressure in traumatic and non-traumatic brain injury patients of Dr. Soetomo General Hospital Surabaya

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Abstract

Background: Patients with brain injury experience pathology of increased intracranial pressure (ICP), which is the cause of secondary brain injury, brain herniation at the risk of brain damage. Intracranial pressure control and monitoring is one of the most important strategies in managing patients in the neurosurgery and neurointensive care fields. Intracranial pressure monitoring in Dr. Soetomo General Hospital Surabaya is still limited by intraventricular catheter installation, which is invasive. The middle cerebral artery pulsatility index (PI) and sonographic optic nerve sheath diameter enable non-invasive monitoring of intracranial pressure. This study aimed to find out the correlation between middle cerebral artery pulsatility index and optic nerve sheath diameter with intracranial pressure.

Methods: Transcranial doppler measurement was made transtemporally to measure middle cerebral artery pulsatility index. Optic nerve sheath diameter was measured 3 mm behind the globe using 12 MHz US probe. Intracranial pressure was measured using intraventricular catheter. The correlation and regression between intracranial pressure, pulsatility index,

and optic nerve sheath diameter were investigated.

Results: Thirty patients with various intracranial pathology, who underwent intraventricular catheter placement, were included in the study. A total of 86 intracranial pressure examinations, middle cerebral artery pulsatility index, and optic nerve sheath diameter were conducted. A significant correlation was found between pulsatility index and intracranial pressure with a correlation coefficient of 0.639; intracranial pressure = $9.23 \times \text{PI} + 4$ mmHg. Pulsatility index sensitivity was 93.2% with specificity 75.0%. Cut-off point was >1.11 for pulsatility index to detect increased intracranial pressure. The optic nerve sheath diameter and intracranial pressure correlation coefficient is 0.746; intracranial pressure = $7.88 \times \text{optic nerve sheath diameter} - 26.84$ mmHg with sensitivity 92.3% and specificity 95.83%. Optic nerve sheath diameter cut-off value was 5.4 mm.

Conclusion: There was a correlation between middle cerebral artery pulsatility index and optic nerve sheath diameter with intracranial pressure. Pulsatility index and optic nerve sheath diameter can be used as alternative for ICP monitoring.

Key words: Pulsatility index, middle cerebral artery, optic nerve sheath diameter, intracranial pressure.

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Introduction

Intracranial pathologies such as traumatic brain injury (TBI), stroke, meningitis, and brain tumor are a cause of high mortality. The incidence of stroke in United States of America (USA) is mentioned every 40 seconds and death occurs every 4 minutes. (1) Estimated, around 1.5 million people suffer from TBI every year in USA. More than 50,000 people die every year as a result of TBI, and other 80,000 have disability. (2) Whilst in Indonesia, the incidence is still not known certainly. (3) Data from resuscitation room in Emergency

Department Dr. Soetomo General Hospital Surabaya stated that during period of July until December 2018 as many as 6.49% from total 2035 patients who entered resuscitation room were TBI patients with a mortality rate of 16.7%.

Patient with brain trauma has an increased intracranial pressure (ICP), which is the cause of secondary brain injury, brain herniation, and a risk of brain damage and related to bad outcome. (4) ICP monitoring and controlling are essential component of neurocritical care patient management. ICP monitoring is increasingly included in protocols for management of subarachnoid haemorrhage (SAH) and intracranial haemorrhage (ICH) critical care. (5) Increased ICP can cause impaired blood circulation, decreased perfusion pressure, venous reflux obstruction, intracranial delayed blood flow, brain damage, brain shifting, and brain herniation. (6) ICP monitoring in traumatic brain injury patients were reported to decrease mortality and resulted in overall better outcome. (7) ICP monitoring can also reduce the rate of electrolyte imbalance and renal failure. (8)

The standard ICP monitoring technique uses ventricular catheter, however, due to its invasive technique, which requires surgical procedure in an operating theater, the monitoring is not commonly done. In addition, placing intraventricular catheter poses multiple potentially fatal complications including infection and bleeding. The procedure is also contraindicated in patients with hematological abnormalities and thrombocytopenia. (9) It is, therefore, crucial to find an alternative to the invasive technique, preferably using a non-invasive technique.

The non-invasive technique to monitor ICP is transcranial Doppler (TCD). TCD is one of the non-invasive tool used to assess flow velocity (FV) that represents cerebral blood flow (CBF) value. TCD can be referred to as a stethoscope and become one of the main non-invasive CBF examination methods. (10) TCD allows to a real-time examination, portable, and inexpensive compared to other methods. (11) TCD can be used to evaluate and monitor changes in cerebral blood vessel circulation, subarachnoid haemorrhage (SAH) diagnostic test, vasospasm monitoring and increased ICP detection, evaluating cerebral hemodynamic on brain injury, and to determine brain death. (12)

Pulsatility index (PI) is a difference between systolic and diastolic flow velocity divided by the mean flow velocity of middle cerebral artery (MCA), also known related to the result of invasive ICP measurements. (13) Increased ICP causes resistance to CBF and decreasing flow velocity diastolic (FVd),

resulting in increasing PI. (14) Furthermore, increased ICP can cause diameter changes of optic nerve sheath, which can be visualized using ultrasound. Optic nerve is a part of the central nervous system and coated with duramater. Subarachnoid space including cerebrospinal fluid (CSF) separate white matter and duramater for about 0.1-0.2 mm. Some studies have shown an association between diameter of optic nerve sheath with measurement of ICP invasively. (15)

As to the author knows, until now monitoring and examination of ICP in Dr. Soetomo General Hospital Surabaya still limited by performed intraventricular catheter requiring operating procedure in operating theatre. TCD and sonography of optic nerve sheath diameter (ONSD) still not used in Emergency Department of Dr. Soetomo General Hospital in management of brain injury patient, thus it is not possible to examine ICP for emergency patient. (2) There are no studies that assess correlation between PI and ONSD with ICP in brain injury patients in Intensive Observation Room. For that, the author intend to make this research.

Methods

This research is observational analytic with cross-sectional design. The study population were patients age 17 to 65-year-old diagnosed with brain injury with ICP monitoring in Intensive Observation Room Dr. Soetomo General Hospital Surabaya. Sampling technique using consecutive sampling. Furthermore, inclusion criteria were patient age 17 to 65-year-old diagnosed with brain injury with ICP monitoring in Intensive Observation Room Dr. Soetomo General Hospital Surabaya and willing to sign the consent form to take part in the research, whilst the exclusion criteria were post cardiac arrest patient, eye injury, post decompressive craniectomy patient, and patient with cranial base fracture associated with CSF leakage. The amount of sample using formula $n = \left[\frac{Z_{\alpha} + Z_{\beta}}{0.5 \ln \frac{1+r}{1-r}} \right]^2 + 3$, which n =minimum sample value, $\alpha=0.05$, so $Z_{\alpha}=1.96$; $\beta=20\%$, so $Z_{\beta}=0.84$; r =correlation coefficient of previous research 0.529²⁷, then from the formula obtained a sample of 26, fulfilled to 30. The variable of this study was independent variable, ICP, and dependent variables were PI and ONSD. The instruments of this study were ultrasonography (GE Vivid Q) and intraventricular catheter (Phycon ventricular drainage tube [Fuji System Corporation]) with M size (2.0-3.3 mm) and length 40 cm. This research was conducted in Intensive Observation Room Emergency Department Dr. Soetomo General Hospital Surabaya in April-May 2019. The data collection

procedure of PI using TCD, examined by one person who had attended a TCD examination training using ultrasound with a low-frequency probe. ONSD measurement using linear probe with 7-10 MHz by one person who had attended an ONSD examination training. ICP measured by looking at the undulation of CSF in an ICP monitor catheter with zero point as high as the acousticus externus meatus. Data was collected through a specific data collection sheet. The results were presented in table, diagram/chart, text/writing that explained the chart/diagram, then the collected data was processed using computer software with Pearson correlation test. This research has had a permission from Research Ethics Committee Dr. Soetomo General Hospital Surabaya. The confidentiality of research data subject was maintained by only including the respondent's initial. This data was only used for scientific purposes.

Results

This study was an observational analytic done to the patient with intracranial abnormalities that underwent intraventricular catheter insertion. Thirty patients with various intracranial abnormalities (trauma, stroke, and infection) underwent intraventricular catheter placement were included in this study. The subject characteristic in this study was listed on the **Table 1**.

There were thirty patients with intracranial abnormalities in this study. They were divided into 3 groups intracranial abnormalities including trauma 36.7%, stroke 50%, and infection 13.3%. Intracranial pathology due to trauma dominated by male, which was 81.8% with an average age 37.73 ± 15.96 year.

Table 2 shows that each sample run three examinations, so that the total examination was 87 times because one sample was only examined once and one outlier was discarded. Mean TCD profile in normal and increased ICP showed a significant difference in the two groups, except on peak systolic velocity (PSV). Result on ONSD also showed a statistically significant differences between two groups.

Correlation between middle cerebral artery pulsatility index and intracranial pressure

The Kolmogorov-Smirnov statistic test to PI variable and ICP indicated that both data were normally distributed with p value =0.08 for PI and 0.07 for ICP, so correlation test between PI and ICP was performed using the Pearson correlation test. Pearson correlation test showed a positive relation between PI and ICP with the value of the correlation coefficient R 0.639 and p value 0.0001 (**Figure 1**).

Simple linear regression analysis showed that mathematically ICP value was 9.23 times of PI plus 4. Receiver operating characteristic (ROC) curve between PI and ICP showed that PI sensitivity on detecting increased ICP (ICP>15 mmHg) was 92.3% (95% CI 79.1-98.4, $p < 0.0001$), and specificity 75.0% (95% CI 60.4-86.4, $p < 0.0001$). Area under the curve (AUC) 0.884 (95% CI 0.798-0.943, $p < 0.0001$) (**Figure 2**). Youden's index maximum value for ROC curve between PI and ICP was 0.673 on PI criteria >1.11 with sensitivity level 92.3% and specificity level 75.0%.

Correlation between optic nerve sheath diameter with intracranial pressure

The Kolmogorov-Smirnov statistic test to ONSD variable and ICP variable showed that both data normally distributed with p value =0.25 for ONSD and 0.07 for ICP, so correlation test between ONSD and ICP was done using the Pearson correlation test.

Pearson correlation test showed that a positive relation between ONSD and ICP with coefficient correlation R 0.746 and p value 0.0001 (**Figure 3**). Simple linear regression analysis showed that mathematically ICP value was 7.88 times of ONSD minus 26.84.

ROC curve between ONSD and ICP showed that ONSD sensitivity in detecting increased ICP (ICP>15 mmHg) was 92.3% (95% CI 79.1-98.4, $p < 0.0001$), and specificity 95.83% (95% CI 85.7-99.5, $p < 0.0001$). AUC 0.982 (95% CI 0.927-0.999, $p < 0.0001$) (**Figure 4**). Youden's index maximum value for ROC curve between ONSD and ICP was 0.897 on ONSD criteria >5.4 mm with sensitivity 89.74% and specificity 100%.

Discussion

Increasing ICP can cause impaired blood circulation, decreasing perfusion pressure, venous reflux obstruction, delayed intracranial blood flow, brain damage, brain shifting, and cerebral herniation. In the sector of neurointensive care, ICP is one of the crucial parameter for management and treatment the patient. ICP monitoring using invasive method with external ventricular drainage (EVD) is the gold standard for ICP examination. The catheter placement is associated with the risk of infection and bleeding. Hematology abnormality, for example prolong hemostasis function and thrombocytopenia, is also contraindicated in installation of ICP monitoring. (9)

Development in medical technology have made it possible to detect an increased ICP by using non-invasive instrument, which possibly to do in limited health facility that do not have neurosurgeons to do

ICP monitoring invasively. TCD is one of non-invasive instrument used to assess FV referred to CBF values. In this study, the author found that there was linear correlation between PI and MCA with ICP. Statistical test using Pearson's correlation showed that the correlation coefficient between PI and MCA with ICP was 0.639. This result showed there was a potent positive correlation between PI and MCA with ICP. Simple linear regression analysis showed that mathematically ICP can be written as $9.23PI + 4$ mmHg. This equal with a result of a former study showing that there was a significant correlation between PI and ICP ($p < 0.0001$) with a correlation coefficient of 0.938. (13) Gura et al (2011) mentioned that correlation coefficient between PI and ICP varied with potent correlation, mentioned that correlation coefficient PI and ICP were 0.567, 0.529, and 0.779 on the first day, third day, and fifth day post operative. (14,16) Some studies showed that PI and ICP had potent correlation and had some linear correlation between PI and ICP. (17)

Some study reported that decreased blood flow indicating increased ICP and intracranial hypertension related to increased PI. (18) This corresponded to result of this study showing that PSV and EDV values on patient with increased ICP were significantly lower than patient with normal ICP. ROC curve between PI and ICP showed that PI sensitivity for detection of increased ICP ($ICP > 15$ mmHg) was 92.3% (95% CI 79.1-98.4, $p < 0.0001$, and specificity 75% (95% CI 60.4-86.4, $p < 0.0001$) for PI value > 1.11 . Based on Youden's index, this PI value > 1.11 could be used as cut-off point on detecting increased ICP.

Optic nerve is a part of the central nervous system and coated with duramater. Increased PI will be transmitted to subarachnoid space, mainly retrobulbar segment, and causing changes of optic nerve sheath diameter that can be visualized with ultrasound. (19) Dilated myelin optic nerve sheath has

been proven as initial manifestation of increased ICP. (11) In this study ONSD on patient with normal ICP were in range between 4.35-5.35 mm, with mean 5.0 mm. Patient with increased ICP, mean ONSD was 5.8 mm with range 5.2-6.5 mm. This is similar with research by Lee et al (2016) showed that patient with increased ICP mean ONSD was 5.9 (5.8-6.2), while patient with normal ICP mean ONSD was 4.9 (4.6-5.2). (5,20) Pearson coefficient correlation show $R = 0.746$ between ONSD and ICP mentioned that potent correlation. This was bigger if compared with PI.

Simple linear regression analysis showed that $ICP = 7.88 \times ONSD - 26.84$. Geeraerts et al (2008) mentioned that there was a potent correlation ($r = 0.74$) between ONSD changes and ICP variety. (21,22) ROC curve between ONSD and ICP showing ONSD sensitivity in detection of increased ICP ($ICP > 15$ mmHg) was 92.3% (95% CI 79.1-98.4, $p < 0.0001$), and specificity 95.83% (95% CI 85.7-99.5, $p < 0.0001$). AUC was 0.982 (95% CI 0.927-0.999, $p < 0.0001$). Based on Youden's index, ONSD value > 5.4 mm can be used as cut-off point on detecting increased PI.

Conclusion

MCA-PI has positive correlation with ICP ($R = 0.639$) and simple linear regression analysis shows that $ICP = 9.23PI + 4$ mmHg. Whilst ONSD has positive correlation with ICP ($R = 0.746$) and simple linear regression analysis shows that $ICP = 7.88 \times ONSD - 26.84$ mmHg. This study can be a reference to future research with more homogenous and bigger sample. This can be a clinical application for the use of PI and ONSD to detect and evaluate ICP on patient in emergency room who has not performed the placement of invasive ICP monitoring, and a study to determine ONSD and PI normal value to Indonesian people.

Table 1. Subject characteristic

Subject characteristic	n/mean
Age (year)	46.4±17.11
Sex	
- Male	16 (53.3)
- Female	14 (46.7)
Comorbidity factor	
- Diabetes mellitus	3 (10)
- Hypertension	12 (40)
- Anemia	3 (10)
- Obesity	1 (3.3)
Type of intracranial pathology	
- Brain injury	11 (36.7)
- Stroke	15 (50.0)
- Infection	4 (13.3)
Early GCS	7.47±1.76
Transcranial Doppler	
- PSV (cm/s)	78.05±27.61
- EDV (cm/s)	27.36±12.97
- FVm (cm/s)	44.63±18.85
- PI	1.25±0.38
ONSD (mm)	5.37±0.52
ICP (mmHg)	15.49±5.45
- Normal (<15 mmHg)	48 (55.17)
- Increased (>15 mmHg)	39 (44.83)
MAP (mmHg)	94.53±9.51
CPP (mmHg)	79.04±11.27
PaCO ₂ (mmHg)	36.67±5.29
Hematocrit (%)	34.26±6.39

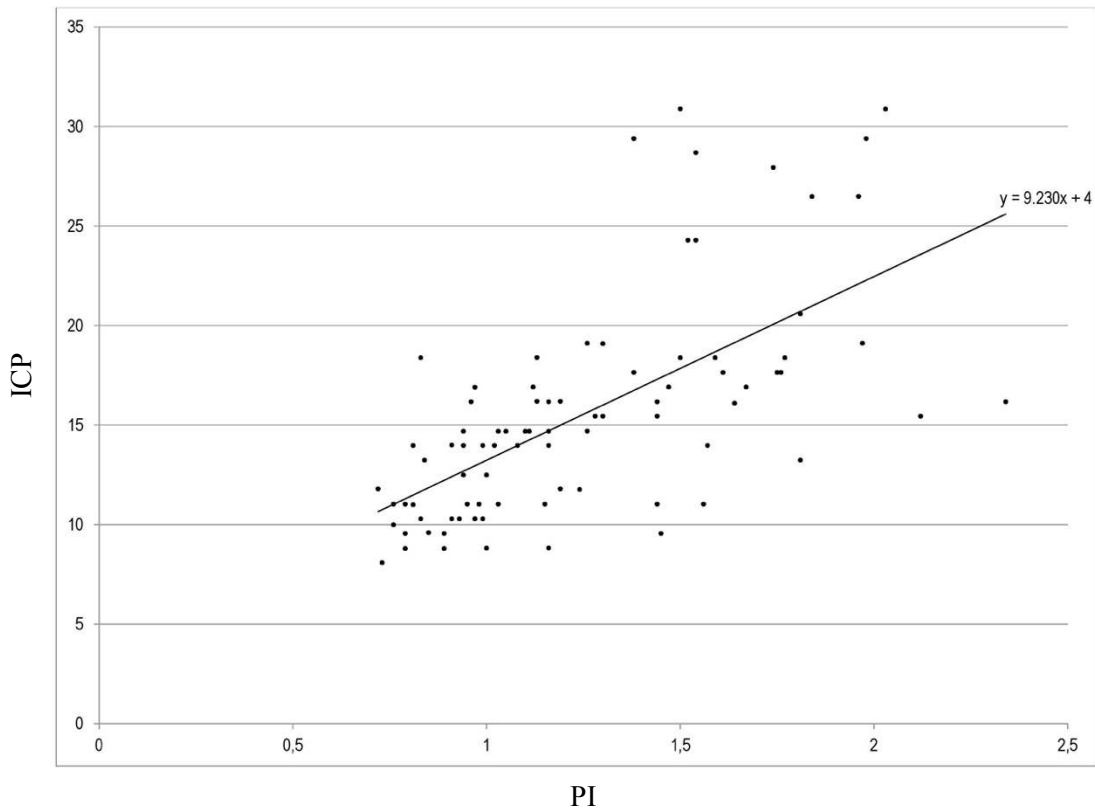
Legend: GCS=Glasgow coma scale; PSV=peak systolic velocity; EDV=end diastolic velocity; FVm=mean flow velocity; PI=pulsatility index; ONSD=optic nerve sheath diameter; ICP=intracranial pressure; MAP=mean arterial pressure; CPP=cerebral perfusion pressure; PaCO₂=arterial partial pressure of carbon dioxide

Table 2. TCD and ONSD profile based on ICP category

Profile	ICP		p
	<15 mmHg	>15 mmHg	
TCD			
- PSV (cm/s)	78.95±27.14	76.94±28.5	0.738
- EDV (cm/s)	31.68±11.88	22.04±12.37	0.0001
- FVm (cm/s)	49.13±18.74	39.10±17.68	0.013
- PI	1.03±0.23	1.52±0.35	0.0001
ONSD (mm)	5.00±0.27	5.84±0.34	0.0001

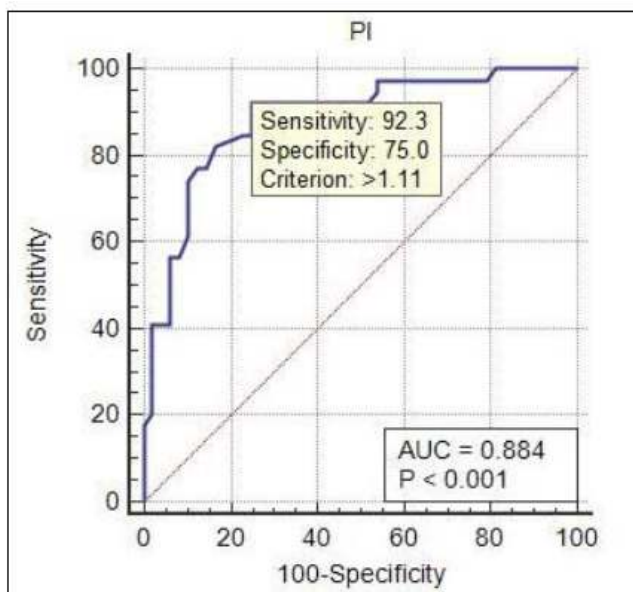
Legend: TCD=transcranial Doppler; PSV=peak systolic velocity; EDV=end diastolic velocity; FVm=mean flow velocity; PI=pulsatility index; ONSD=optic nerve sheath diameter; ICP=intracranial pressure

Figure 1. Simple regression between MCA-PI (X) and ICP (Y)



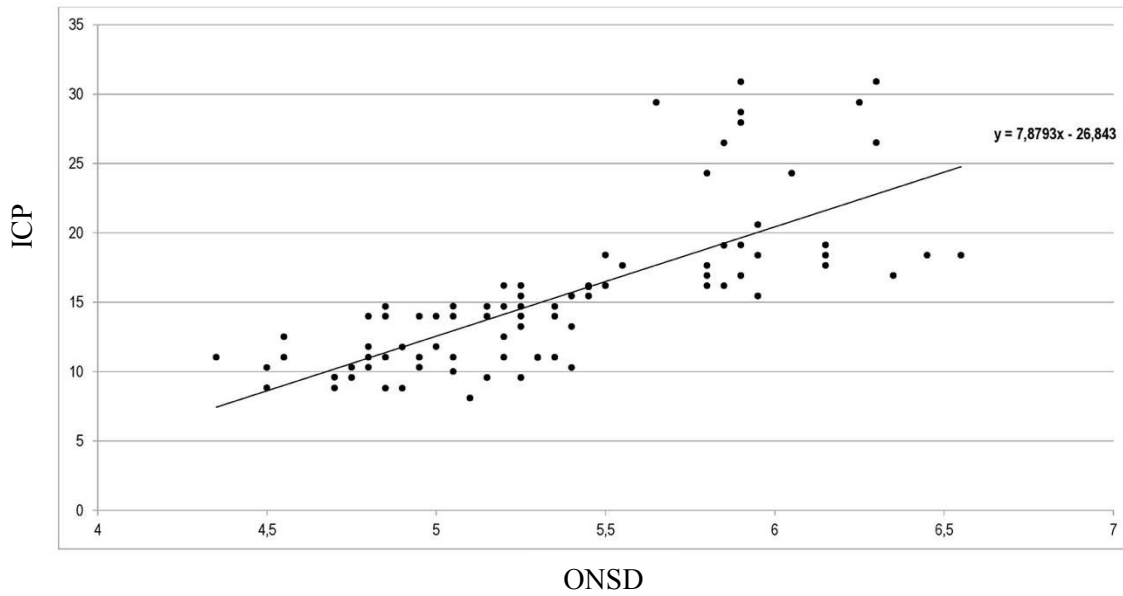
Legend: MCA=middle cerebral artery; PI=pulsatility index; ICP=intracranial pressure

Figure 2. ROC curve PI to ICP



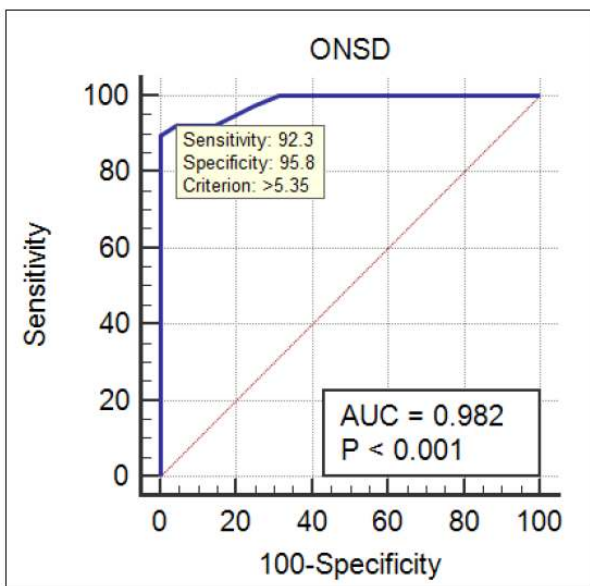
Legend: ROC=receiver operating characteristic; PI=pulsatility index; ICP=intracranial pressure

Figure 3. Simple regression between ONSD (X) and ICP (Y)



Legend: ONSD=optic nerve sheath diameter; ICP=intracranial pressure

Figure 4. ROC curve of ONSD and ICP



Legend: ROC=receiver operating characteristic; ONSD=optic nerve sheath diameter; ICP=intracranial pressure

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