CT measurements of optic nerve sheath diameter to evaluate the outcome of acute carbon monoxide poisoning

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Abstract

Background

Thousands of people die each year from carbon monoxide poisoning. There are no clear indicators for evaluating the outcome of carbon monoxide poisoning. We aimed to evaluate the relationship between optic nerve sheath diameter (ONSD) and ONSD/ transverse eyeball diameter ((ETD)) measured by CT and the outcome of acute carbon monoxide poisoning.

Methods

We retrospectively analyzed all acute carbon monoxide poisoning patients who had received CT November 2017 to July 2020. All patients underwent cranial CT examination on the day of admission, the ONSD at 3 mm behind the eyeball on CT was measured and the ONSD/ETD ratio was calculated by ETD. According to the CPC score, the patients were divided into two groups: good outcome group and poor outcome group. ROC curve was used to evaluate the diagnostic value of each index in outcome. Logistic regression analysis was used to screen the related factors affecting the outcome of patients.

Results

We identified 146 patients who received cranial CT as the first clinical evaluation after acute carbon monoxide poisoning, which including 108 patients with good outcome and 38 patients with poor outcome. Compared with the good outcome group, there were significant differences in ONSD, ONSO/ETD, Lactic acid, CPK, NSE, PSS and APACHEII scores between the poor outcome group and the poor outcome group. An ONSD model for predicting poor outcome was established, and the corresponding ROC curve was drawn. The area under the ROC curve (AUC) was 0.925, the best prediction probability out-off value was 0.3585, the sensitivity was 89.5%, and the specificity was 94.4%. The same method obtains the prediction model of ONSD/ETD, the AUC is 0.916, the out-off value of the best prediction probability is 0.3547, the sensitivity is 89.5%, and the specificity is 92.6%.

Conclusion

ONSD and ONSD/ETD are significantly related to the outcome of patients with acute carbon monoxide poisoning. The outcome is poor when ONSD > 5.68 mm or ONSD/ETD > 0.24. Measuring the diameter of optic nerve sheath by CT may be a simple and rapid method to evaluate the clinical outcome of patients with carbon monoxide poisoning.

Introduction

Carbon monoxide (CO) is a by-product of incomplete combustion of hydrocarbons. It is a colorless, odorless, tasteless and non-irritating gas, so poisoning is very common [1]. Acute carbon monoxide still has a high incidence and mortality in remote and backward areas such as rural areas. In addition to carbon monoxide poisoning caused by coal, carbon monoxide is produced during the use of gas generators or any gas tools, which can lead to carbon monoxide poisoning if used in rooms with poor ventilation and small space. Most patients wake up soon after getting out of the poisoning environment, resulting in their lack of enough attention to carbon monoxide poisoning. Carbon monoxide poisoning is the most vulnerable to brain damage, which can easily lead to brain edema [2]. Some patients with acute carbon monoxide poisoning have a false recovery period of 2–60 days after waking up in a coma, followed by delayed encephalopathy with a variety of mental and neurological symptoms. It causes a huge burden on family life and affects the quality of life of patients [3]. Therefore, the evaluation of the outcome of carbon monoxide poisoning is very important for clinical treatment.

The optic nerve sheath is an extension of the dura mater, and the subarachnoid space extends from the intracranial space to surround the optic nerve [4]. The increased pressure in the intracranial space leads to the dilatation of the optic nerve sheath. The accumulation of cerebrospinal fluid can lead to the broadening of ONSD, which is mainly concentrated in the front of the optic nerve sheath, usually in the Retrobulbar 3 mm [5]. In recent years, the diameter of optic nerve sheath has become a convenient and non-invasive method for monitoring intracranial pressure ((ICP)). Some experiments show that there is a good correlation between optic nerve diameter and intracranial pressure measured by CT. It is considered that the widening of optic nerve sheath diameter is sensitive to the increase of early intracranial pressure [6]. It is reported that ONSD has high specificity and sensitivity (100% and 95% respectively) in the diagnosis of increased ICP. In previous studies, higher intracranial pressure was closely associated with poor outcome and significantly predicted adverse outcome [8]. The diameter of optic nerve sheath measured by CT can be obtained early and quickly. Therefore, it is inferred that the ONSD measured by CT is related to the outcome of acute carbon monoxide poisoning.

The purpose of this study is to explore the relationship between ONSD and the outcome of patients with carbon monoxide poisoning, and to provide help for clinicians to evaluate the outcome of patients with acute carbon monoxide poisoning.

Patients And Methods

We conducted a retrospective , single-centre study from November 2017 to October 2020, set in the Emergency Department of the first people's Hospital of Lianyungang CN. 146 patients with carbon monoxide poisoning treated in the Emergency Department of the first people's Hospital of Lianyungang City were selected. The age ranged from 18 to 85 years old, including 83 males and 63 females. Inclusion criteria: in accordance with the diagnostic criteria of carbon monoxide poisoning, the age is more than 18 years old. Exclusion criteria: (1)Acute stroke, intracranial space occupying, empty sella, hydrocephalus, skull base deformity, etc. (2)Subjects with increased intracranial pressure, such as eye trauma, surgery or eye diseases, such as glaucoma, cataract, optic neuritis, eye tumor and so on. (3)The data of patients

who are lack of clinical or laboratory data or without definite results. (4) The diameter of optic nerve sheath could not be measured without CT imaging data or CT data.

Study population

The clinical data of patients admitted to hospital were recorded. Including name, sex, age, time from poisoning to hospital, basic disease, systolic blood pressure, white blood cell count, neutrophils , lymphocyte, hematocrit, serum creatinine, albumin, CPK, lactic acid, NSE, acute physiology and chronic health score system (APACHE score), poisoning severity score (PSS score), GCS score and so on. The patients were evaluated with CPC score when they were discharged from hospital. The head CT was examined within 24 hours after admission, the ONSD at the retroocular 3mm and the (ETD), of the transverse diameter of the eyeball were measured and the ONSD/ETD ratio was calculated, and the CPC score at discharge was used as the basis for clinical outcome, CPC l or 2 as a good outcome and CPC3~5 as a poor outcome.

Image acquisition and imaging assessment

Within 24 hours of admission, the American General purpose company GE Optima 680Pro 64 CT machine was used to scan the skull continuously from the canthus line to the top of the skull. The scan thickness of 5mm was measured independently by two emergency doctors. The window width was adjusted to 300mm 500HU, and the window level was 30mm 50HU. Then the axial plane with the largest diameter of the retrobulbar optic nerve sheath was selected, and the target image was magnified 2 times. The distal 3mm of the origin of the optic nerve was taken as the measuring point of the optic nerve sheath diameter, and the measurement vector was perpendicular to the optic nerve axis. The maximum value of ONSD was taken as the measured value, accurate to 0.1mm, and the bilateral average value was taken. The longest transverse diameter of eyeball was measured by the largest image of eyeball volume. The transverse diameter of bilateral eyeball was measured by (ETD), and the average value was taken.

Statistical analysis

The measurement data were tested by normality test, the data in accordance with normal distribution were expressed by mean ±standard deviation, and the independent sample t-test was used for comparison between groups. The data that did not accord with the normal distribution were expressed by the median (quartile), and the Mann-Whitney U test was used for the comparison between groups. The classified counting data were expressed by the number of cases (percentage), and the comparison between groups was performed by χ 2 test. ROC curve was used to evaluate the diagnostic value of each index in poor outcome. Logistic regression analysis was used to screen the related factors affecting the poor outcome of the patients. All analyses were performed using SPSS26.0 and GraphPadPrism7. The p-value of less than 0.05 was considered statistically significant.

Results

Comparison of different prognostic data: there was no significant difference in sex, age, time from poisoning to admission, underlying disease, systolic blood pressure, leukocyte, neutrophil, lymphocyte, hematocrit, creatinine, albumin and Na + in patients with different outcome. Compared with the group with good outcome, the levels of NSD, ONSD/ETD, NSE, CPK, lactic acid, PSS and APACHEII in patients with poor outcome were higher than those in the group with good outcome. The differences were statistically significant (P < 0.05). The comparison of clinical indexes of patients with different outcome is shown in Table 1.

Table 1
comparison of patients with different outcome

Variables	**Good outcome (*n* = 108)**	**Bad outcome (*n* = 38)**	***t/Z/χ²***	***P value***
Sex(Male/Female)	62/46	21/17	0.053	0.818
Age(years)	53.85 ± 16.62	54.47 ± 18.33	0.193	0.847
ONSD	5.22 ± 0.47	5.74 ± 0.52	5.693	< 0.001
ONSD/ETD	22.85 ± 2.08	24.99 ± 2.52	5.161	< 0.001
Poisoning until admission time	5(4,7)	6(4,8)	-1.279	0.201
Basis of disease	22(20.4)	9(23.7)	0.185	0.667
Systolic blood pressure	129.63 ± 16.66	134.55 ± 21.4	1.450	0.149
White blood cells	10.79 ± 4.12	12.07 ± 5.21	1.529	0.128
Neutrophils	79.6 ± 13.98	81.35 ± 13.5	0.671	0.503
Lymphocyte	11.3(7.25,20.63)	10.6(6.4,20.1)	-1.436	0.151
Hematocrit	40.64 ± 4.51	42 ± 7.02	1.113	0.271
Serum creatinine	55.09 ± 16.03	58.84 ± 17.57	1.210	0.228
Albumin	38.73 ± 3.9	37.51 ± 3.34	1.712	0.089
Na	138.53 ± 2.76	138.82 ± 3.73	0.430	0.669
CPK	100.5(71.25,229.75)	252.5(110.25,957)	-2.999	0.003
Lactic acid	2.35(1.5,5.18)	3.9(2.1,5.33)	-2.427	0.015
PSS	2(2,3)	4(3,6)	-3.813	< 0.001
APACHEII	6(5,9)	10(7.75,17)	-5.878	< 0.001
NSE	17.3 ± 6.13	23.04 ± 6.8	4.821	< 0.001

Analysis of related factors affecting the outcome of the patients: taking the outcome of the patients (good = 0, bad = 1) as dependent variables, sex, age, ONSD, ONSD/ETD, time from poisoning to admission, underlying disease, systolic blood pressure, white blood cells, neutrophils, lymphocytes, hematocrit, creatinine, albumin, Na+, CPK, lactic acid, PSS, APACHEII, NSE as independent variables, the binary logistic regression equation was established. The results showed that there were significant correlations between ONSD, ONSD/ETD, CPK, lactic acid, PSS, APACHEII, NSE and outcome. The results of univariate logistic regression analysis of patients with poor outcome are shown in Table 2

Table 2
logistic regression analysis of univariate factors affecting poor outcome of patients

Variables	***B***	***SE***	***Waldχ2***	***P***	***OR(95% CI)***
Sex(Male/Female)	0.087	0.380	0.053	0.818	1.091(0.518 ~ 2.297)
Age(years)	0.002	0.011	0.038	0.846	1.002(0.98 ~ 1.024)
ONSD	2.563	0.564	20.677	0.000	12.975(4.299 ~ 39.162)
ONSD/ETD	0.470	0.109	18.616	0.000	1.599(1.292 ~ 1.979)
Poisoning until admission time	0.016	0.043	0.147	0.702	1.016(0.935 ~ 1.105)
Basis of disease	0.193	0.450	0.184	0.668	1.213(0.502 ~ 2.932)
Systolic blood pressure	0.015	0.010	2.057	0.152	1.015(0.995 ~ 1.036)
White blood cells	0.062	0.041	2.261	0.133	1.064(0.981 ~ 1.154)
Neutrophils	0.010	0.015	0.452	0.501	1.01(0.981 ~ 1.039)
Lymphocyte	-0.008	0.018	0.179	0.673	0.993(0.959 ~ 1.028)
Hematocrit	0.051	0.037	1.835	0.176	1.052(0.978 ~ 1.132)
Serum creatinine	0.013	0.011	1.430	0.232	1.013(0.992 ~ 1.035)
Albumin	-0.093	0.055	2.857	0.091	0.911(0.819 ~ 1.015)
Na	0.031	0.062	0.248	0.618	1.032(0.913 ~ 1.166)
CPK	0.696	0.282	6.086	0.014	2.005(1.154 ~ 3.485)
Lactic acid	0.222	0.081	7.467	0.006	1.249(1.065 ~ 1.465)
PSS	0.434	0.112	14.931	0.000	1.543(1.238 ~ 1.922)
APACHEII	0.325	0.059	30.355	0.000	1.384(1.233 ~ 1.553)
NSE	0.135	0.032	17.855	0.000	1.145(1.075 ~ 1.219)

CPK, Phosphocreatine kinase; PSS, Poisoning severity score; APACHEII, Acute Physiology and chronic Health scoring system II; NSE, Neuron-specific enolase

The binary logistic regression equation was established by conditional forward method with poor outcome (no = 0, is = 1) as dependent variable and ONSD, ONSD/ETD, CPK, lactic acid, PSS, APACHEII, NSE as independent variables. The results showed that ONSD, ONSD/ETD, lactic acid, APACHEII and NSE were statistically significant in the model, and all of them were risk factors for poor outcome (OR > 1, P < 0. 05). The results of logistic regression analysis of multiple factors affecting the poor outcome of the patients are shown in Table 3.

Table 3
logistic regression analysis of multiple factors affecting poor outcome of patients

Variables	Model1			Model2		
	OR(95% CI)	Waldχ^2	P	OR(95% CI)	Waldχ^2	P
ONSD	9.404(2.612 ~ 33.857)	11.757	0.001	-	-	-
ONSD/ETD	-	-	-	1.479(1.14 ~ 1.919)	8.699	0.003
Lactic acid	1.343(1.017 ~ 1.774)	4.323	0.038	1.317(1.011 ~ 1.716)	4.163	0.041
APACHEII	1.400(1.213 ~ 1.615)	21.305	0.000	1.390(1.208 ~ 1.600)	21.117	0.000
NSE	1.140(1.043 ~ 1.247)	8.268	0.004	1.154(1.056 ~ 1.26)	10.056	0.002
Model 1 includes ONSD, ONSD/ETD, CKM, lactic acid, PSS, APACHE II, NSE; Model 2 into ONSD, ONSD/ETD, CKM, lactic acid, PSS, APACHE II, NSE.						

From the ROC curve, the areas under the curve for ONSD, ONSD/ETD, lactic acid, APACHEII, NSE and predicting severity were 0.790, 0.777, 0.633, 0.820 and 0.736 respectively, and the corresponding P values were all less than 0.05, indicating that the areas under the curve for predicting poor outcome were statistically significant (Fig. 1.1). Among them, the area under the curve of ONSD model is the largest. The sensitivity and specificity of ONSD > 5.675 mm in predicting poor outcome were 60.5% and 89.8%, respectively (P < 0.001). The sensitivity and specificity of ONSD/ETD > 0.244 in predicting poor outcome were 73.7% and 84.3%, respectively (P < 0.001); NSE > 23.1 ng/ml, the sensitivity and specificity of predicting poor outcome were 57.9% and 78.7%, respectively (P < 0.001). The sensitivity and specificity of APACHEII > 10.5 in predicting the outcome of neurological dysfunction were 65.8% and 88.8%, respectively (P < 0.001). The sensitivity and specificity of ONSD/ETD > 0.244 in predicting poor outcome were 73.7% and 84.3%, respectively (P < 0.001). Draw ROC curves according to the established model (Fig. 2.2)the area under the ROC curve of the, ONSD prediction model (AUC) is 0.925, the best prediction probability critical value is 0.3585, the sensitivity is 89.5%, and the specificity is 94.4%. The ONSD/ETD prediction model of adverse outcome was obtained by the same method, the AUC was 0.916, the critical value of the best prediction probability was 0.3547, the sensitivity was 89.5%, and the specificity was

92.6%. ONSD has higher sensitivity and specificity for poor outcome. The results of ROC curve analysis of each index diagnosed as poor outcome are shown in Table 4.

Table 4
ROC curve of poor outcome diagnosed by each index

	AUC(95% CI)	P	Out-off value	Sensitivity	Specificity
ONSD	0.790(0.698 ~ 0.882)	< 0.001	5.675	60.5	89.8
ONSD/ETD	0.777(0.680 ~ 0.875)	< 0.001	24.44	73.7	84.3
Lactic acid	0.633(0.536 ~ 0.729)	0.015	1.85	89.5	38.0
APACHEII	0.820(0.730 ~ 0.910)	< 0.001	10.5	65.8	88.9
NSE	0.736(0.639 ~ 0.832)	< 0.001	23.1	57.9	78.7
ONSD model	0.925(0.856 ~ 0.995)	< 0.001	0.3585	89.5	94.4
ONSD/ETD model	0.916(0.840 ~ 0.991)	< 0.001	0.3547	89.5	92.6

Discussion

The results of this study showed that the optimal threshold of ONSD for predicting adverse outcome of patients with acute carbon monoxide poisoning was 5.68 mm; when ONSD > 5.68 mm, the probability of poor outcome of patients with acute carbon monoxide poisoning was significantly increased, the sensitivity was 60.5%, and the specificity was 89.8%. Amini et al. [9] found that ONSD in non-invasive patients was correlated with ICP (r = 0.88). When ONSD > 5.5 mm, it has good sensitivity and specificity for predicting the increase of intracranial pressure. At the same time, studies have shown that [10], when ONSD > 6.0 mm, it is valuable for predicting increased intracranial pressure, with a sensitivity of 97% and a specificity of 42%. This is roughly the same as the results of this paper. In addition, this study found that ONSD, ONSD/ETD, lactic acid, APACHEII and NSE are risk factors affecting the outcome of patients with carbon monoxide poisoning. This may be related to hypoxia, ischemia and brain damage caused by carbon monoxide poisoning. Lactic acid is an independent risk factor for predicting serious complications and requiring intensive monitoring and treatment. Patients with high levels of lactic acid in patients with acute carbon monoxide poisoning may have persistent coma and eventually die, patients with slightly higher levels of lactic acid may be discharged from hospital after waking up in a coma, but the incidence of delayed encephalopathy has greatly increased [10]. NSE is a biomarker for evaluating neurological function, secreted by dead neurons and glial cells. A multicenter study in Europe shows that NSE has a sensitivity of 77.3% and a specificity of 100% in predicting the outcome of neurological dysfunction [11]. Due to the poor tolerance of the brain to hypoxia, patients with carbon monoxide poisoning are prone to brain damage, which leads to the increase of NSE. When these risk factors affecting the outcome of patients were included in the analysis, the sensitivity and specificity of the ONSD model were significantly increased, with a sensitivity of 89.5% and a specificity of 94.4%. The

combination of these risk factors of carbon monoxide poisoning is helpful for emergency doctors to triage patients and follow-up treatment.

Related studies have shown that the sensitivity and specificity of measuring ONSD on CT in detecting the elevation of ICP is similar to that of ultrasound and MRI. And the ONSD measurements of CT and MRI are determined to be equivalent in direct comparison [12]. At present, ultrasound is mostly used to study ONSD. Compared with skull CT, ultrasound examination of ONSD is simple and fast, convenient for bedside examination, and helps to continuously observe the dynamic changes of intracranial pressure. However, for patients with carbon monoxide poisoning, most of them are conscious, and ultrasound measurements may make the patients feel uncomfortable. Measuring the diameter of optic nerve sheath by CT is not only convenient and rapid, but also can find the lesions in the brain and rule out other possible diseases. This paper discusses the relationship between ONSD measured by CT and carbon monoxide poisoning.

Limitations

First of all, the data may be missing in the process of collection, and the final patients may have selection bias. Secondly, in the process of data measurement, although the average value is measured many times, there are still measurement errors. Finally, this study is a retrospective single-center study, the number of patients is relatively small, lack of large sample studies. In order to make CT measurement of ONSD can be widely used in clinic, help doctors to effectively judge patients who may have a poor outcome, and guide clinical medication and rehabilitation. More samples need to be collected and analyzed in the future.

Conclusion

ONSD is significantly related to the outcome of patients with acute carbon monoxide poisoning with high sensitivity and specificity. When ONSD > 5.68 mm, the poor outcome of patients with carbon monoxide poisoning is higher. Combined with lactate, NSE and APACHEEII scores, ONSD is more valuable in predicting poor outcome. The measurement of optic nerve sheath diameter by CT may become a new index to evaluate the clinical outcome of patients with acute carbon monoxide poisoning and guide clinical treatment.

Declarations

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None

Authors' contributions

HJY, CDM, ZL and LF contributed to data collection. HSQ and SY were responsible for the statistical analyses. HJY, LXM and WYL drafted the manuscript. All authors reviewed and revised the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Hospital Trust institutional review board approved the study as minimal risk as only routine clinical data were collected from the electronic health records. Hence, the requirement for informed consent was waived.

Consent for publication

Not applicable

Competing interests

All authors declare that they have no competing interests.

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Figures

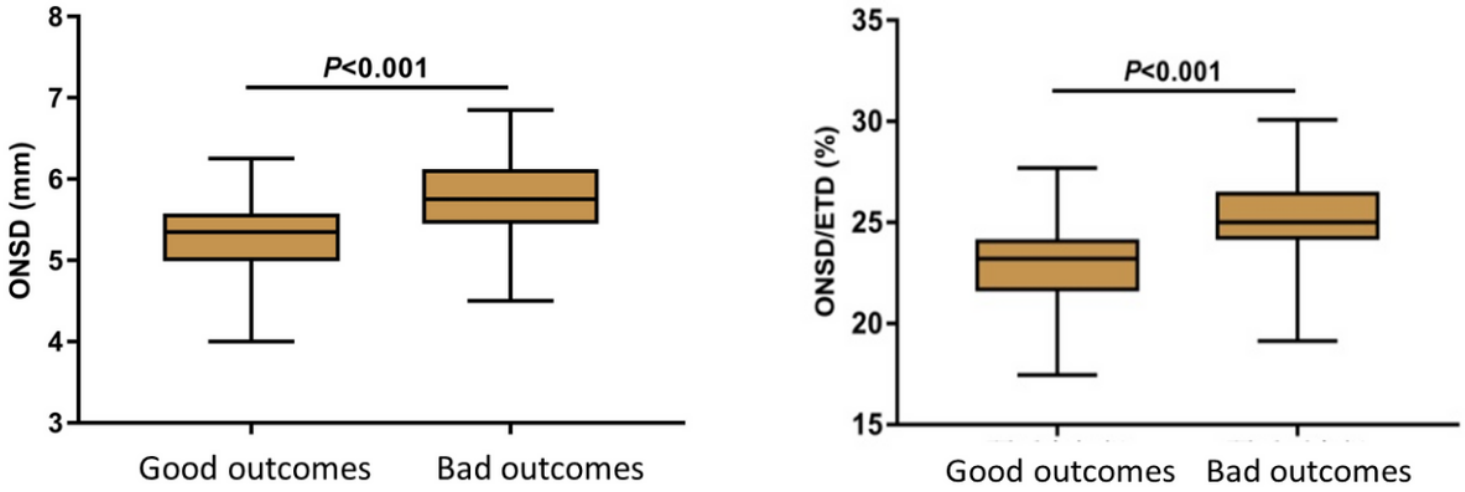

Figure 1

box diagram of ONSD and ONSD/ETD comparison with different outcome

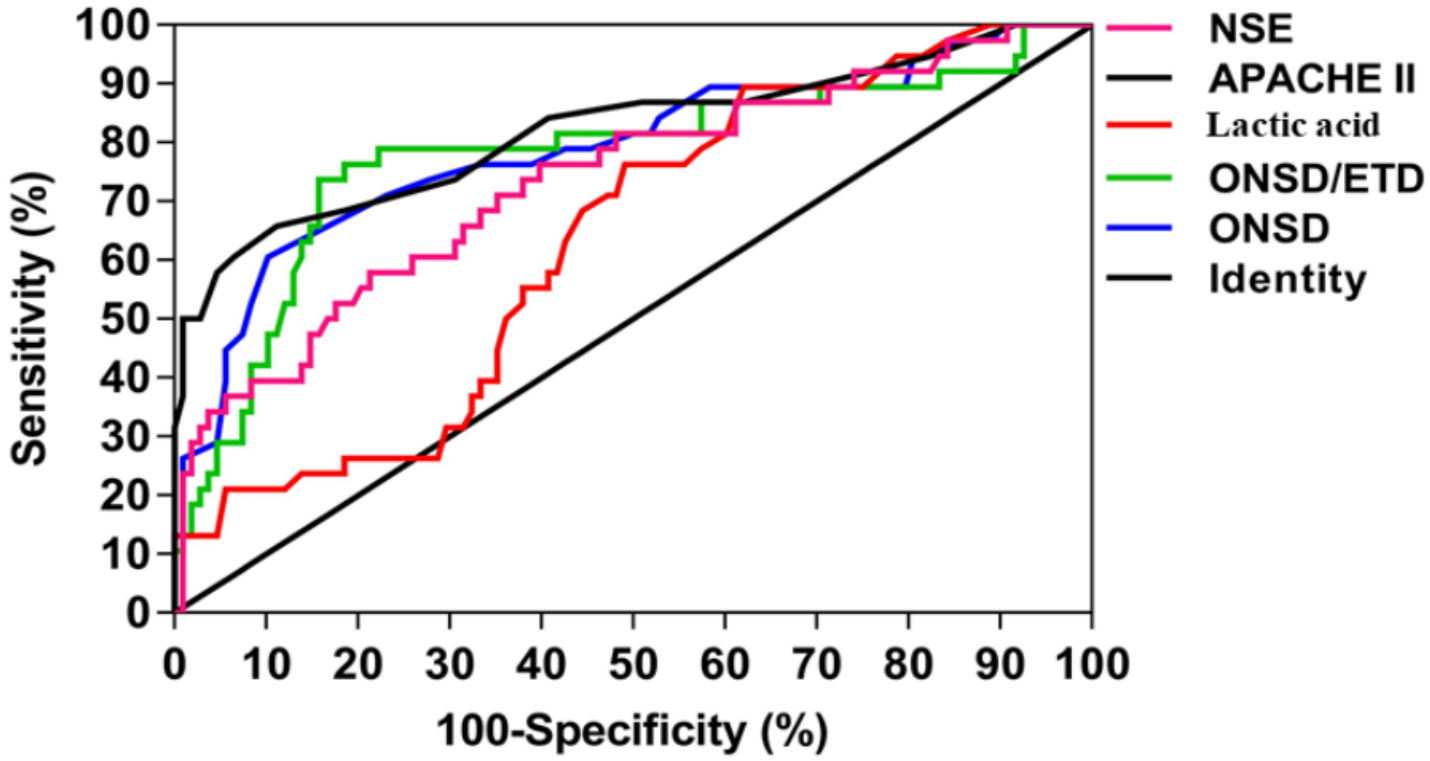

Figure 2

ROC curve of each index to predict poor outcome

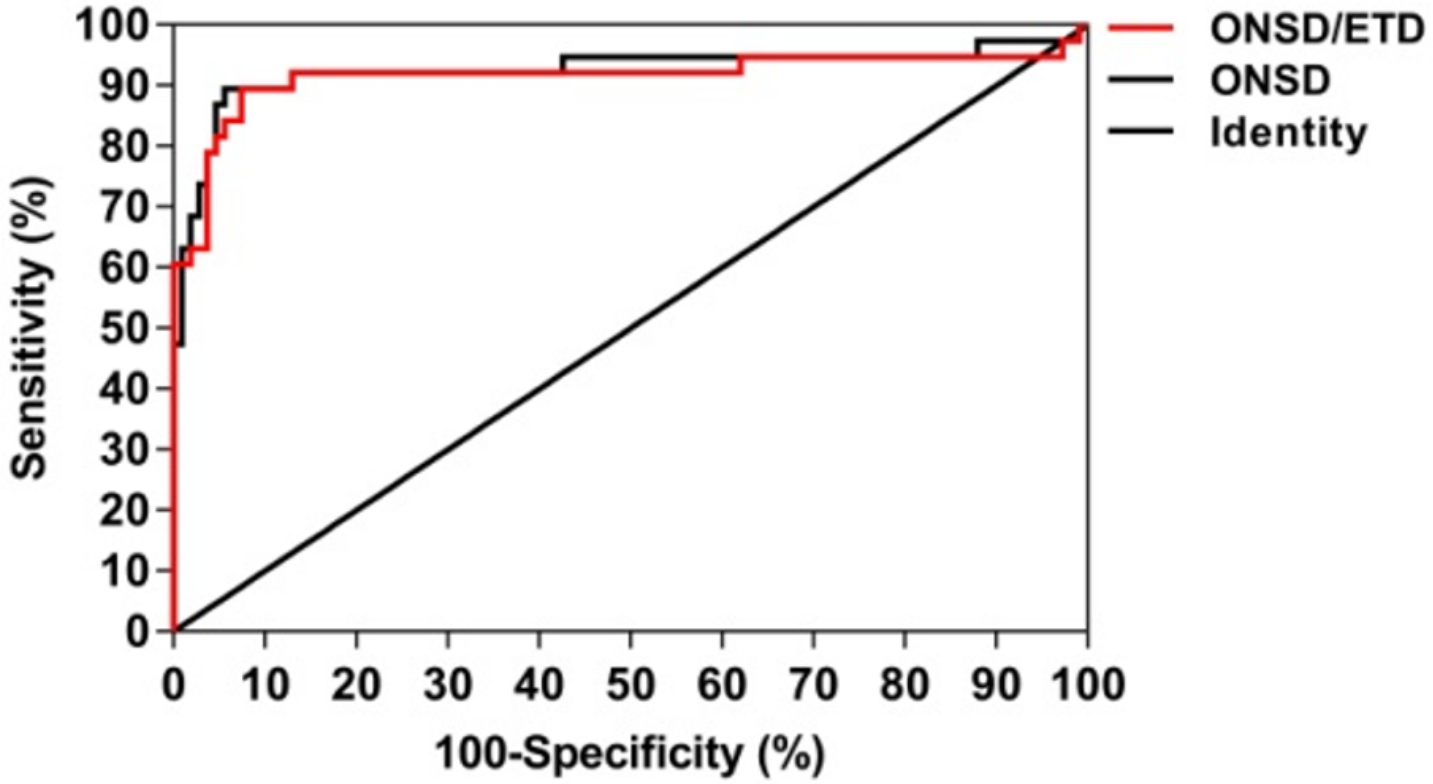

Figure 3

establishing a model to predict the ROC curve of poor outcome