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Serial Changes in CT-Derived Optic Nerve Sheath Diameter Predict Hemorrhagic Transformation in Acute Ischemic Stroke: A Prospective Observational Study

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Research Article

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Abstract

Background

Hemorrhagic transformation (HT) is a serious complication of acute ischemic stroke (AIS) and is associated with increased morbidity and mortality. Early identification of patients at risk for HT may facilitate closer monitoring and timely intervention. Optic nerve sheath diameter (ONSD) has emerged as a non-invasive surrogate marker of intracranial pressure. This study aimed to evaluate whether serial changes in CT-derived ONSD could predict hemorrhagic transformation in patients with acute ischemic stroke.

Methods

A prospective observational study was conducted in the Emergency Department of a tertiary care teaching hospital. Consecutive adult patients presenting with acute ischemic stroke were enrolled. ONSD was measured from initial CT brain images and repeated on follow-up CT performed 24 hours later. The primary outcome was the development of hemorrhagic transformation on follow-up imaging. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive performance of ONSD change.

Results

A total of 110 patients with acute ischemic stroke were included. Hemorrhagic transformation occurred in 34 patients (30.9%). Patients who developed HT demonstrated a greater increase in ONSD between baseline and follow-up imaging. ROC analysis showed that change in ONSD predicted hemorrhagic transformation with an area under the curve (AUC) of 0.754. An ONSD change threshold of 0.34 mm demonstrated a sensitivity of 88.2%, specificity of 59.2%, positive predictive value of 49.2%, and negative predictive value of 91.8% for predicting HT.

Conclusions

Serial CT-derived ONSD change is associated with hemorrhagic transformation in acute ischemic stroke. An increase in ONSD of 0.34 mm or greater demonstrated good discriminatory ability and a high negative predictive value, suggesting potential utility as an early imaging biomarker for risk stratification in patients with AIS. Larger multicentre studies are warranted to validate these findings.

Introduction

Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide and remains a major public health challenge. Despite advances in reperfusion therapies, hemorrhagic transformation (HT) remains one of the most serious complications of AIS and is associated with neurological deterioration, prolonged hospitalization, and increased mortality. Early identification of

patients at increased risk of HT is therefore essential to optimize monitoring strategies and guide timely clinical decision-making [1–4].

Hemorrhagic transformation results from a complex interplay of blood–brain barrier disruption, reperfusion injury, endothelial dysfunction, and cerebral edema. These pathological processes contribute to increased intracranial pressure (ICP), which may precede radiologically apparent hemorrhagic transformation. However, current methods for assessing elevated ICP are either invasive or rely on repeated neuroimaging, limiting their utility for serial monitoring in the emergency department [5–8].

The optic nerve sheath is anatomically continuous with the intracranial subarachnoid space, allowing changes in ICP to be transmitted to the optic nerve sheath. Consequently, optic nerve sheath diameter (ONSD) has emerged as a reliable, non-invasive surrogate marker of elevated ICP in various neurological conditions, including traumatic brain injury, intracranial hemorrhage, and acute ischemic stroke.[9–12]

Although previous studies have evaluated single ONSD measurements in patients with acute stroke, evidence regarding the role of serial ONSD measurements in predicting hemorrhagic transformation remains limited. Dynamic changes in ONSD may better reflect evolving intracranial pathophysiology than isolated measurements and could therefore provide additional prognostic information during the early course of AIS.[13–15]

While the present study evaluated serial CT-derived ONSD measurements, its clinical implications extend beyond CT imaging. Demonstrating that serial changes in ONSD are associated with hemorrhagic transformation provides a physiological basis for future studies evaluating serial point-of-care ultrasound (POCUS)-guided ONSD monitoring. Such an approach may offer emergency physicians a rapid, bedside, repeatable, radiation-free, and cost-effective method for identifying patients at increased risk of hemorrhagic transformation and guiding the need for closer neurological monitoring and repeat neuroimaging.[16–18]

Therefore, this study aimed to evaluate whether serial changes in CT-derived optic nerve sheath diameter could predict hemorrhagic transformation in patients presenting with acute ischemic stroke.

Methods

Study design and participants

This prospective observational study was conducted in the Department of Emergency Medicine at Amrita Institute of Medical Sciences and Research Centre, Kochi, India, between October 2023 and October 2026.

Consecutive adult patients (≥ 18 years) presenting to the emergency department with a diagnosis of acute ischemic stroke confirmed by neuroimaging were screened for eligibility. Patients meeting the

inclusion criteria were enrolled after obtaining informed consent from the patient or their legally authorized representative.

Patients with pre-existing ophthalmological conditions affecting the optic nerve, orbital pathology, previous neurosurgical procedures involving the optic nerve, poor-quality CT images precluding accurate ONSD measurement, or incomplete follow-up imaging were excluded from the study.

Data collection

Clinical data were collected at presentation. All enrolled patients underwent a baseline non-contrast CT brain at presentation and a repeat CT brain 24 hours later as part of the institutional stroke management protocol.

Optic nerve sheath diameter measurement

CT imaging was performed using Philips and Siemens multidetector CT scanners, and images were reviewed using the institutional imaging software (MEDVISION). Optic nerve sheath diameter (ONSD) was measured on axial CT images 3 mm posterior to the globe in both eyes.(Fig. 1) The average of the right and left ONSD measurements was considered the final ONSD value for each patient[19, 20].

All measurements were performed using the same predefined measurement technique throughout the study by a single investigator. Baseline ONSD was defined as the average ONSD measured on the initial CT scan, while follow-up ONSD was obtained from the repeat CT scan performed 24 hours later. The change in ONSD was calculated as:

Change in ONSD = Follow-up ONSD – Baseline ONSD.

Outcome measure

The primary outcome was the occurrence of hemorrhagic transformation (HT) on the 24-hour follow-up CT scan. Hemorrhagic transformation was recorded as a binary outcome (present or absent) based on radiological evidence of hemorrhage within the infarcted territory. [21, 22]

Statistical analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of serial ONSD change for hemorrhagic transformation. The area under the ROC curve (AUC) with 95% confidence intervals was calculated. The optimal cutoff value was determined using Youden's index. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated.

Ethical considerations

The study was approved by the Institutional Ethics Committee of Amrita Institute of Medical Sciences and Research Centre, Kochi (Approval No. ECASM-AIMS-2024-429). Written informed consent was obtained from all participants or their legally authorized representatives.

Results

Overall cohort

A total of 110 patients with acute ischemic stroke were included, of whom 34 (30.9%) developed hemorrhagic transformation on the 24-hour follow-up CT scan, while 76 (69.1%) did not.

Predictive performance of serial ONSD change

Receiver operating characteristic (ROC) curve analysis demonstrated that change in optic nerve sheath diameter (ONSD) predicted hemorrhagic transformation with an area under the curve (AUC) of 0.754 (95% CI 0.666–0.842; P < 0.001).(Fig. 2)

The optimal cutoff value for predicting hemorrhagic transformation was an increase in ONSD of ≥ 0.34 mm. Using this cutoff, the sensitivity was 88.2% (95% CI: 72.6%–96.7%), specificity was 59.2% (95% CI: 47.3%–70.4%), positive predictive value (PPV) was 49.2% (95% CI: 41.8%–56.6%), negative predictive value (NPV) was 91.8% (95% CI: 81.5%–96.6%), and overall diagnostic accuracy was 68.2% (95% CI: 58.6%–76.7%).

Patients with an ONSD change of ≥ 0.34 mm had a markedly higher incidence of hemorrhagic transformation than those with a smaller ONSD change (49.2% vs. 8.2%).

Diagnostic performance of serial CT-derived ONSD change for predicting hemorrhagic transformation in acute ischemic stroke is shown in Table 1.

Subgroup analyses

In the thrombolysis subgroup (n = 47), change in ONSD predicted hemorrhagic transformation with an AUC of 0.753 (95% CI: 0.613–0.893; p < 0.001)(Fig. 3). Using the same cutoff value of ≥ 0.34 mm, the sensitivity was 94.4%, specificity was 65.5%, PPV was 62.9%, NPV was 95.0%, and overall diagnostic accuracy was 76.6%.

In the thrombectomy subgroup (n = 40), ROC analysis demonstrated an AUC of 0.709 (95% CI: 0.539–0.879; p = 0.016)(Fig. 4). The optimal cutoff for ONSD change was ≥ 0.475 mm, which yielded a sensitivity of 89.5%, specificity of 61.9%, PPV of 68.0%, NPV of 86.7%, and diagnostic accuracy of 75.0%.

Overall, serial ONSD change demonstrated consistent diagnostic performance across the overall cohort as well as among patients undergoing reperfusion therapies.

Diagnostic performance of serial CT-derived ONSD change in patients undergoing thrombolysis and mechanical thrombectomy is shown in Table 2.

Discussion

In this prospective observational study of patients with acute ischemic stroke (AIS), serial changes in CT-derived optic nerve sheath diameter (ONSD) were associated with the development of hemorrhagic transformation (HT). An increase in ONSD of ≥ 0.34 mm demonstrated good discriminatory performance for predicting HT (AUC 0.754) with a high NPV of 91.8%, suggesting that serial ONSD assessment may serve as a useful non-invasive imaging biomarker for early risk stratification in AIS. [4, 5, 13–15]

Our findings are biologically plausible because HT is characterized by blood–brain barrier disruption, reperfusion injury, endothelial dysfunction, and cerebral edema, all of which contribute to increased intracranial pressure (ICP). Owing to the continuity of the optic nerve sheath with the intracranial subarachnoid space, increases in ICP are reflected by expansion of the optic nerve sheath, providing a physiological basis for serial ONSD assessment. [6–9]

Previous studies have established ONSD as a non-invasive surrogate marker of raised ICP in traumatic brain injury, intracerebral hemorrhage, and ischemic stroke. However, most investigations have focused on single ONSD measurements. In contrast, the present study evaluated serial CT-derived ONSD changes over the first 24 hours following AIS, suggesting that dynamic changes may better reflect evolving intracranial pathophysiology than isolated measurements. [10–17]

An important finding of our study was the high NPV (91.8%), indicating that patients with little or no increase in ONSD were unlikely to develop HT. Clinically, this may help identify patients at lower risk who require less intensive radiological surveillance, while patients demonstrating greater ONSD increases may benefit from closer neurological monitoring and earlier repeat neuroimaging. [3, 4]

The diagnostic performance of serial ONSD measurements remained consistent in patients undergoing reperfusion therapies. In the thrombolysis subgroup, serial ONSD change demonstrated a sensitivity of 94.4% and an NPV of 95.0%, while moderate diagnostic performance was also observed among patients undergoing mechanical thrombectomy. These findings are particularly relevant because patients receiving reperfusion therapies have an increased risk of HT and require close neurological observation during the early post-treatment period. [3, 4, 22, 23]

Although ONSD measurements in the present study were obtained from CT imaging, the clinical implications extend beyond CT itself. Our findings support the concept that serial ONSD behaves as a dynamic biomarker of evolving intracranial pathophysiology following AIS. This provides a physiological rationale for future studies evaluating serial point-of-care ultrasound (POCUS)-guided ONSD monitoring as a rapid, bedside, repeatable, radiation-free, and cost-effective strategy for identifying patients at increased risk of HT. However, as ultrasound-guided ONSD was not evaluated in the present study, this potential application requires prospective validation before routine clinical implementation. [9, 16–18]

This study has several limitations. It was conducted at a single tertiary-care centre with a relatively modest sample size, which may limit generalizability. ONSD measurements were performed by a single investigator, and interobserver variability was not assessed. Important clinical predictors of HT, including stroke severity, infarct volume, and functional outcomes, were not systematically evaluated, and multivariable analysis was not performed. Finally, only CT-derived ONSD measurements were assessed, precluding direct comparison with ultrasound-guided ONSD measurements.

Despite these limitations, this study demonstrated that serial CT-derived ONSD changes are associated with hemorrhagic transformation following acute ischemic stroke and may represent a useful adjunctive imaging biomarker for early risk stratification. Larger multicentre studies are warranted to validate these findings and to determine whether serial bedside ultrasound-guided ONSD monitoring can improve the early detection and management of hemorrhagic transformation in patients with acute ischemic stroke.

Conclusion

Serial changes in CT-derived optic nerve sheath diameter (ONSD) were associated with hemorrhagic transformation in patients with acute ischemic stroke. An increase in ONSD of ≥ 0.34 mm demonstrated good diagnostic performance and a high negative predictive value for identifying patients at low risk of hemorrhagic transformation. These findings support the concept that serial ONSD assessment may serve as a dynamic biomarker of evolving intracranial pathophysiology following acute ischemic stroke. Furthermore, they provide a physiological rationale for future studies evaluating serial point-of-care ultrasound (POCUS)-guided ONSD monitoring as a rapid, bedside, repeatable, and radiation-free approach for early identification of patients at risk of hemorrhagic transformation.

Abbreviations

AIS
Acute Ischemic Stroke
HT
Hemorrhagic Transformation
ONSD
Optic Nerve Sheath Diameter
CT
Computed Tomography
ROC
Receiver Operating Characteristic
AUC
Area Under the Curve
PPV
Positive Predictive Value
NPV

Negative Predictive Value
ICP
Intracranial Pressure
BBB
blood–brain barrier
POCUS
Point–of–care ultrasound

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of Amrita Institute of Medical Sciences and Research Centre, Kochi (Approval No. ECASM-AIMS-2024-429). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from all participants or their legally authorized representatives.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable patient information but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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No funding was received for this study.

Authors' contributions

CMJ: Conceptualization, methodology, data curation, investigation, formal analysis, writing—original draft preparation.

BP: Conceptualization, methodology, supervision, validation, writing—review and editing.

PB: ONSD measurement from CT images

A :contributed in sample collection

STP,NM,GK: supervision and validation

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References

1. World Stroke Organization. Global Stroke Fact Sheet 2022.
2. GBD 2021 Stroke Risk Factor Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2021. Lancet Neurol. 2024;23:973–1003.
3. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke. Stroke. 2019;50:e344–418.
4. Sun J, Lam C, Christie L, et al. Risk factors for hemorrhagic transformation in acute ischemic stroke: a systematic review and meta-analysis. Front Neurol. 2023;14:1079205.
5. Hong JM, Kim DS, Kim M. Hemorrhagic transformation after ischemic stroke: mechanisms and management. Front Neurol. 2021;12:703258.
6. Rosell A, Lo EH. Matrix metalloproteinases in neuroinflammation. Glia. 2002;39:279–97.
7. Jiang X, Andjelkovic AV, Zhu L, et al. Blood-brain barrier dysfunction and recovery after ischemic stroke. Prog Neurobiol. 2018;163–164:144–71.
8. Arba F, Rinaldi C, Caimano D, et al. Blood-brain barrier disruption and hemorrhagic transformation in acute ischemic stroke: systematic review and meta-analysis. Front Neurol. 2020;11:594613.
9. Hansen HC, Helmke K. The subarachnoid space surrounding the optic nerves. Surg Radiol Anat. 1996;18:323–8.
10. Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med. 2008;15:201–4.
11. Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 2018;44:1284–94.
12. Sekhon MS, Griesdale DE, Robba C, McGlashan N, Needham E, Walland K, et al. Optic nerve sheath diameter on computed tomography is correlated with simultaneously measured intracranial pressure in patients with severe traumatic brain injury. Intensive Care Med. 2014;40(9):1267–74.
13. Lee SJ, Choi MH, Lee SE, et al. Optic nerve sheath diameter change in prediction of malignant cerebral edema in ischemic stroke. BMC Neurol. 2020;20:354.

14. Xu H, Liu Y, Liu J, et al. Dilated optic nerve sheath diameter predicts poor outcome in acute spontaneous intracerebral hemorrhage. Cerebrovasc Dis. 2022;51:199–206.
15. Sivas E, Colak N, Bayram B, et al. Evaluation of optic nerve sheath diameter in acute stroke: pre- and post-thrombolytic assessment. PeerJ. 2025;13:e19197.
16. Castilho VA, Mendonça JA, Maciel RC, et al. Ultrasound and CT agreement for non-invasive ONSD measurement: a systematic review and meta-analysis. Ultrasound Med Biol. 2025;51:1660–9.
17. Parameswaran P, Venkatachalam B, Selvi T, et al. Prospective comparative study of optic nerve sheath diameter measurement by ultrasonography versus CT. Indian J Crit Care Med. 2026;30:50–6.
18. Robba C, Cardim D, Tajsic T, et al. Ultrasound non-invasive measurement of intracranial pressure in neurointensive care: a prospective observational study. PLoS Med. 2017;14:e1002336.
19. Zubair AS, Sheth KN. Hemorrhagic Conversion of Acute Ischemic Stroke. Neurotherapeutics. 2023;20(3):705–11.
20. Fiorelli M, Bastianello S, von Kummer R, et al. Hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. Stroke. 1999;30:2280–4.
21. Hacke W, Schwab S, Horn M, et al. Malignant middle cerebral artery territory infarction: clinical course and prognostic signs. Arch Neurol. 1996;53:309–15.
22. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387:1723–31.
23. Boisseau W, Fahed R, Lapergue B, et al. Predictors of parenchymal hematoma after mechanical thrombectomy. Stroke. 2019;50:2364–70.

Tables

Table 1 and 2 available in the Supplementary Files section.

Figures

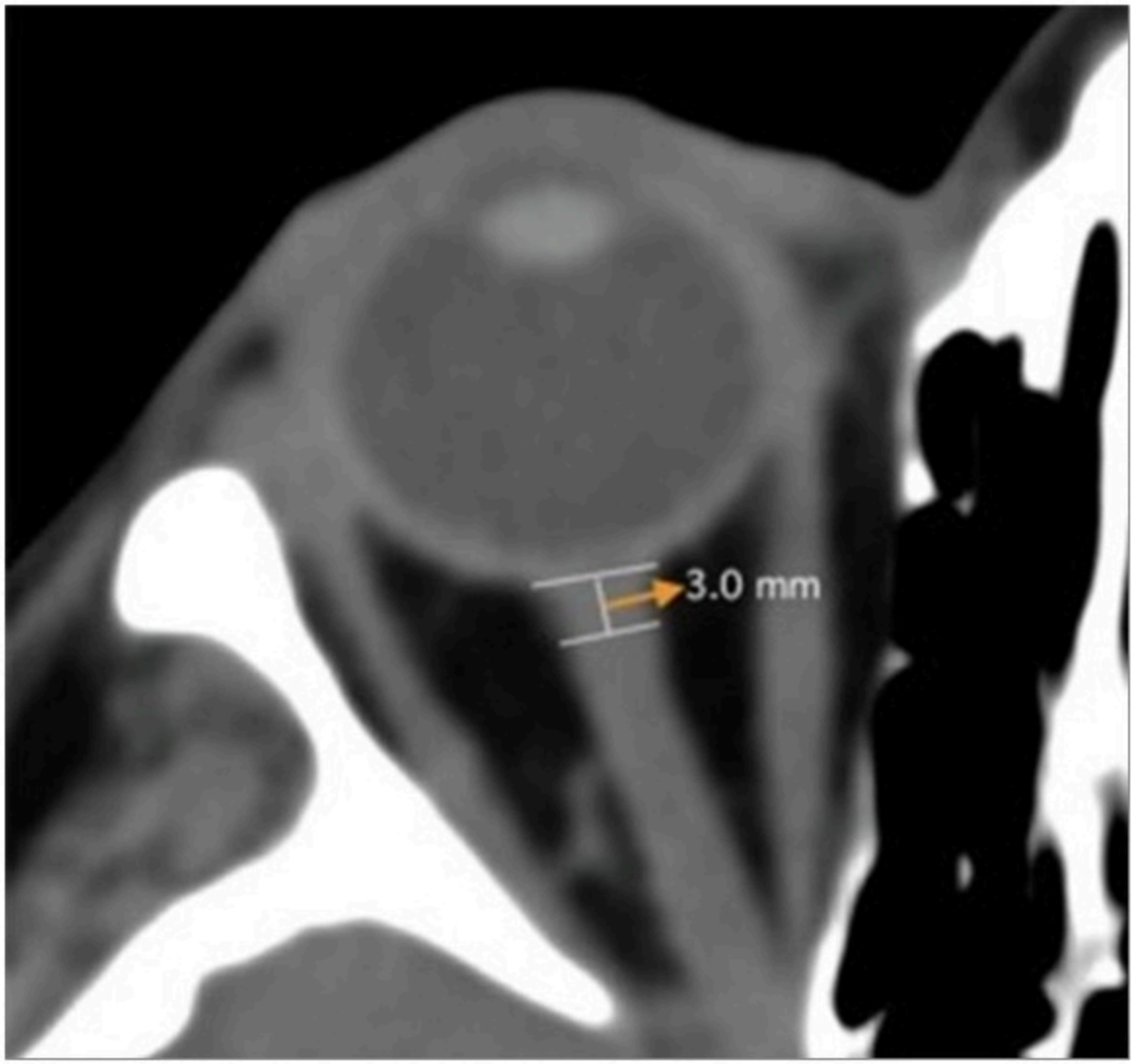


Figure 1

Measurement of optic nerve sheath diameter (ONSD) on axial computed tomography (CT) images. ONSD was measured 3 mm posterior to the globe in both eyes. The average of the right and left ONSD measurements was considered the final ONSD value for analysis.

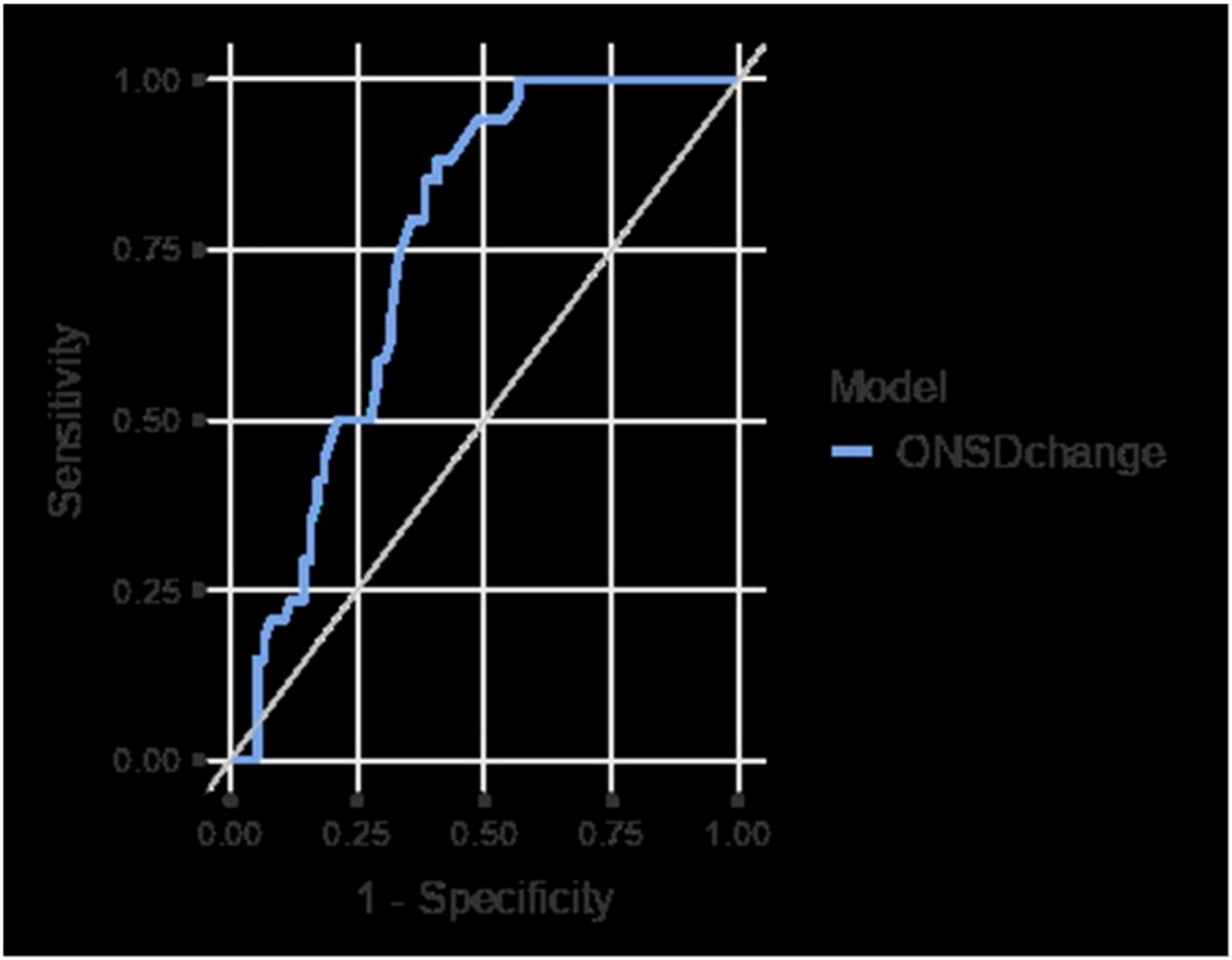


Figure 2

Receiver operating characteristic (ROC) curve demonstrating the diagnostic performance of serial CT-derived optic nerve sheath diameter (ONSD) change for predicting hemorrhagic transformation in the overall study cohort. The area under the curve (AUC) was 0.754 (95% CI 0.666–0.842; P<0.001).

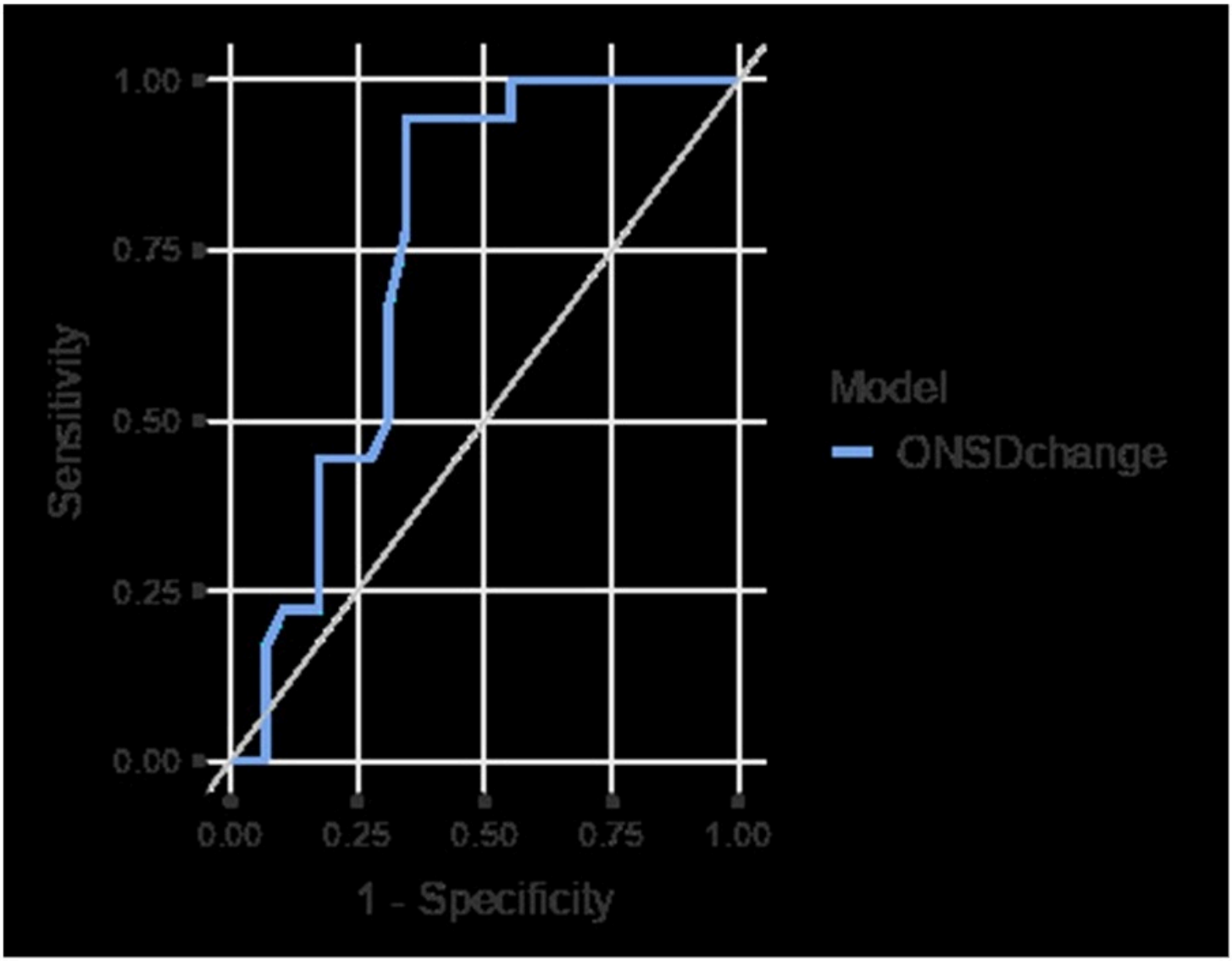


Figure 3

Receiver operating characteristic (ROC) curve demonstrating the diagnostic performance of serial CT-derived optic nerve sheath diameter (ONSD) change for predicting hemorrhagic transformation in patients who underwent intravenous thrombolysis. The AUC was 0.753 (95% CI 0.613–0.893; P<0.001).

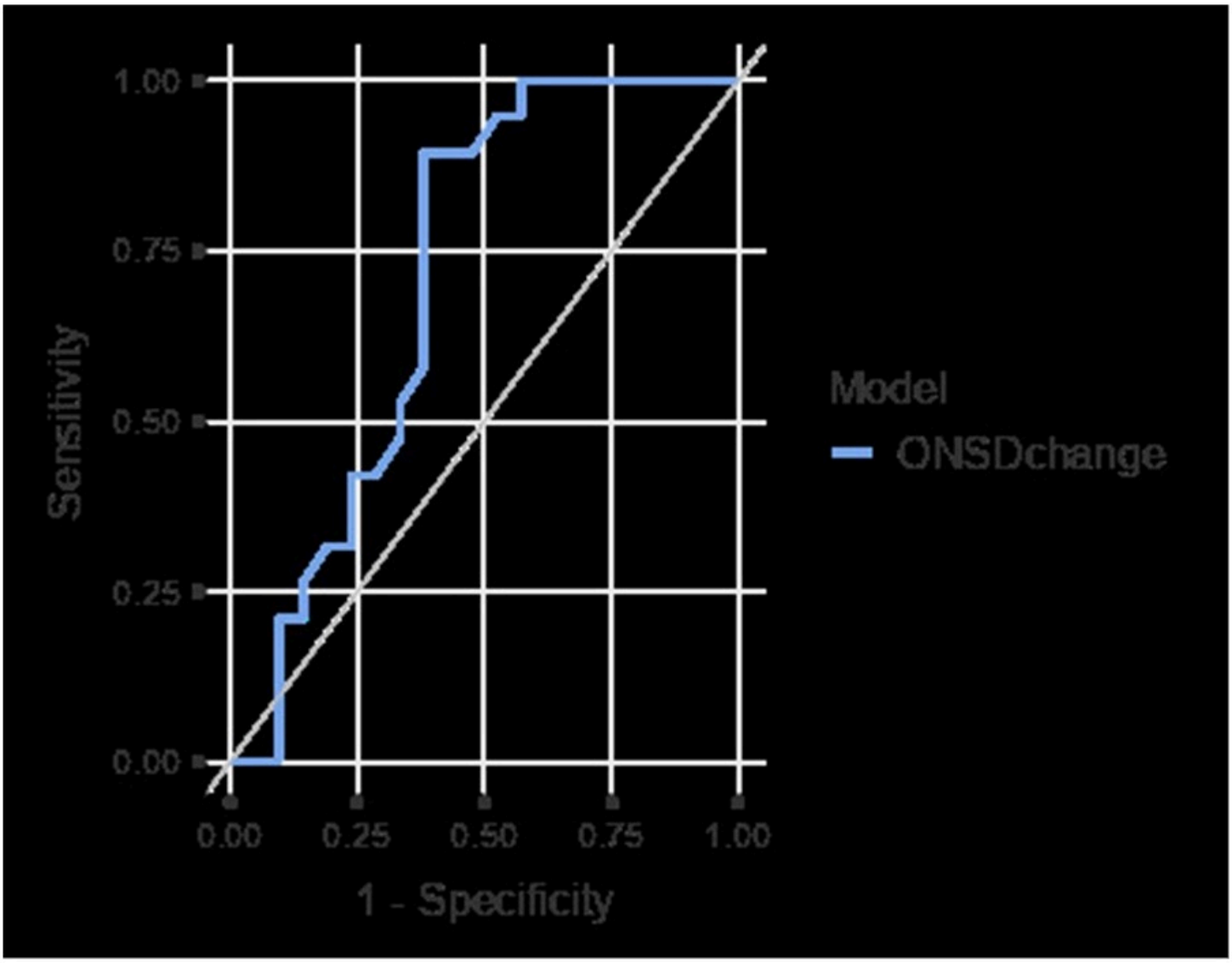


Figure 4

Receiver operating characteristic (ROC) curve demonstrating the diagnostic performance of serial CT-derived optic nerve sheath diameter (ONSD) change for predicting hemorrhagic transformation in patients who underwent mechanical thrombectomy. The AUC was 0.709 (95% CI 0.539–0.879; P=0.016).

Supplementary Files

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