



Can artificial intelligence accurately predict the risk of hematoma expansion in intracerebral hemorrhage? A systematic review and Meta-analysis of 7,665 patients

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Abstract

Early prediction of hematoma expansion (HE) in patients with intracerebral hemorrhage (ICH) is critical for improving clinical outcome and guiding timely interventions. This study focuses on assessing the effectiveness of artificial intelligence (AI) models, specifically those utilizing machine learning (ML) and deep learning (DL) in predicting HE. The search strategy for this study was conducted in PubMed, Scopus, Embase, and Web of Science to identify eligible studies. Metrics such as sensitivity, specificity and area under the curve (AUC) were extracted and analyzed. Out of 1,235 studies initially screened, 14 met the inclusion criteria with totally 7665 patients. AI algorithms demonstrated significant predictive capabilities. The pooled sensitivity and specificity across studies were 0.82 [95% CI: 0.74–0.88] and 0.83 [95% CI: 0.78–0.87], respectively. The pooled positive DLR was 4.91 [95% CI: 3.73–6.47], while the negative DLR was 0.21 [95% CI: 0.14–0.32]. The diagnostic score was 3.14 [95% CI: 2.55–3.72], and the overall diagnostic odds ratio was 23.01 [95% CI: 12.83–41.24]. The pooled AUC was 0.89, suggesting a potentially useful diagnostic performance, although the high heterogeneity limits the robustness of this finding. Subgroup analysis revealed that AI models performed better in predicting HE, in patients with spontaneous ICH compared to patients with traumatic brain injury-related ICH, with a higher AUC (0.90 vs. 0.87), sensitivity (0.85 vs. 0.76) and diagnostic odds ratio (28 vs. 16). AI-based models may serve as potentially useful tools in predicting HE and supporting clinical decisions in ICH care. However, due to the high heterogeneity across studies, these findings should be interpreted with caution, and rigorous external validation with standardized imaging protocols is essential before clinical implementation.

Keywords Intracerebral hemorrhage · Hematoma expansion · Artificial intelligence · Machine learning · Deep learning · Diagnostic performance

Introduction

Intracerebral hemorrhage (ICH) is a life-threatening neurological condition associated with high morbidity and mortality rates, accounting for about 20% of all strokes worldwide [1, 2]. One of the significant complications of this disease is hematoma expansion, which typically occurs within the first 24 to 48 h after onset and represents one of the critical

clinical challenges in the treatment and management of spontaneous and traumatic ICH [3, 4]. Traumatic hematomas usually result from external forces causing a traumatic brain injury with intracranial hemorrhage [5, 6]. In contrast, spontaneous hemorrhages can have multiple non-traumatic causes, such as hypertension or vascular abnormalities [3, 7]. In both categories, the gradual enlargement of the hematoma can cause an elevation of the intracranial pressure associated with serious neurologic deficits, poor prognosis, and high rates of disability and mortality [3, 8, 9].

Artificial intelligence models, especially machine learning (ML) and deep learning (DL) have been widely used in many fields of medicine, including diagnosing and treating

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cerebrovascular disease [10–14]. Studies demonstrated that AI models have higher sensitivity and specificity in predicting early hematoma expansion [15]. AI has different algorithms to predict hematoma expansion. These algorithms are based on features such as baseline hematoma volume, imaging biomarkers, and clinical variables to predict the expansion of hematoma [16]. Several studies have investigated the value of AI for diagnosis [17], radiographic evaluation and management of ischemic and hemorrhagic strokes, arteriovenous malformations, and aneurysms [10]. Although AI has shown significant improvements in the predictability of hematoma expansion, variability in imaging protocols and feature extraction techniques has raised concerns about the validity of those studies.

Therefore, this study evaluates the application of AI models in predicting HE risks among patients with ICH. By systematically assessing the effectiveness and accuracy of AI algorithms, this study aims to provide valuable tools for clinical decision-making and offers the potential to assist physicians and emergency care providers by delivering faster, more reliable predictions of HE, enabling timely interventions and leading to improved risk stratification, better prioritization of high-risk patients, and more effective resource allocation in emergency settings. Ultimately, this review focuses specifically on the role of AI in forecasting the risk of HE rather than diagnosing ICH or differentiating between types of ICHs.

Methods

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [18] guidelines. It is registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the ID CRD42024627887.

Search strategy

We searched PubMed, Embase, Scopus, and Web of Science databases to ensure no relevant articles were missed, the first 100 results from Google Scholar were reviewed as a supplementary search. The following search terms were included: (“expansion” OR “progression”) AND (“intra cerebral hematoma” or “ICH”) AND (“Artificial intelligence” OR “Machine learning” OR “Deep learning”). The described search strategy was applied to all aforementioned databases. The Medical Subject Headings (MeSH) and Emtree were used in PubMed and Embase, respectively, in combination with several similar keywords to develop the

unique search strategy for each database. This search was performed from the inception of the respective databases until December 2, 2024. The full search strategy syntax for each database is outlined in Supplementary file 1 (Table S1).

Inclusion criteria

1) English language, 2) Conducted on humans, 3) Involving patients with HE, 4) Reporting the use of ML and DL algorithms; including Random Forest (RF), Extreme Gradient Boosting (XGBoost), Categorical Boosting (CatBoost), Deep Neural Network (DNN), Random Neural Network (RNN), Chi-squared Automatic Interaction Detection (CHAID), Decision Tree (DT), Extreme Gradient Boosting (EGB), K-nearest neighbors (KNN), Support Vector Machine (SVM) in predicting poor outcomes, and 4) Original articles including cohort studies, randomized clinical trials, non-randomized clinical trials, observational case-series (> 20 cases), and case-control studies.

Exclusion criteria

(1) Non-original articles, case reports, (2) Studies focusing on subarachnoid hemorrhages, subdural or epidural hematomas, or hematomas secondary to vascular malformations, aneurysms, tumors, or surgical complications (3) Hematomas with an unclear etiology or unspecified type (4) Hematomas occurring in pediatric populations or pregnant.

Study selection

The extracted articles were added to EndNote version 21. According to the eligibility criteria, three reviewers (AN, SM and PP) independently evaluated the studies. Following the exclusion of duplicate records, screening was carried out in two phases: first, by examining the title and abstract, and then by selecting the most relevant studies for a full-text review. The investigations that satisfied the criteria for eligibility were selected for the phase of data extraction. In a dispute between three reviewers, a fourth reviewer (IM) participated.

Data extraction

Two reviewers (AN and PP) separately extracted the intended data from included articles, including, first name, year of publication, country, number of patients, mean age, gender composition, design of the study, reference imaging study (e.g., digital subtraction angiography (DSA), computed tomography (CT), and magnetic resonance imaging (MRI)), ML and DL algorithm, sensitivity, specificity,

accuracy, precision, F1score, and AUC. The information from the articles was imported into a predesigned Excel sheet. HE, which was bolded as the main outcome, is considered in this data collection. Any discrepancies between the two reviewers were resolved through discussion, and if consensus was not reached, a third senior reviewer adjudicated the decision.

Quality assessment

The PROBAST tool was used to evaluate the risk of bias (ROB) and the applicability of the included studies [19]. This tool evaluates four primary aspects: participants, predictors, results, and analysis. Each domain was assessed for risk of bias and categorized as low, high, or unclear risk. Additionally, the appropriateness of the forecasting models was evaluated within the same subject domains to determine if the research studies aligned with the research question.

Statistical analysis

The metrics for true positives, true negatives, false positives, and false negatives for each high-performing algorithm in the included studies were collected for analysis. Sensitivity and specificity data were combined using a meta-analysis diagnostic model. Given the substantial heterogeneity across studies, all pooled estimates were calculated using random-effects models. All statistical analyses were conducted using the MIDAS package in STATA version 17.

Results

Study characteristics and selection process

In this systematic review, our initial search in the databases identified 1235 records. Duplicate records, including 179 papers, were removed. After an initial screening of titles and abstracts, 48 papers were chosen for additional assessment. Finally, 14 articles were included in the qualitative analysis, and meta-analysis, one of the studies included two different datasets with distinct outcomes. Since both datasets met the eligibility criteria for our study, we analyzed them as two separate studies [20]. The studies in our analysis were conducted across several countries. The PRISMA flow diagram showing the study selection process is provided in Fig. 1.

Altogether, the included studies comprised 7665 patients with a mean age of 58.7 years, of whom 41.26% were women. The mean time between the second CT scan and the initial CT scan was 36.92 h. Among all AI algorithms, 13 were DL and 10 were ML (Fig. 2) (Table 2).

XGBoost was the best-performing algorithm with the highest average values for accuracy (0.9), sensitivity (0.62) and AUROC (0.96) followed by MLP; with accuracy of 0.92, sensitivity of 0.89, specificity of 0.92, and AUROC of 0.921 (Fig. 3) (Table 2).

Among our included studies, the majority were from China (11 studies), while the remaining studies were from South Korea (2), Taiwan (1), and Spain (1). 10-fold cross-validation was utilized in 5 studies (35.7%), followed by 5-fold cross-validation in 4 studies (28.6%), while 5 studies (35.7%) did not report their validation method. All studies focused on CT-based radiomic features, with 6 studies (42.9%) using semi-automated methods, 5 studies (35.7%) employing automated methods, 2 studies (14.3%) relying on manual methods, and 1 study (7.1%) not specifying the extraction approach (Tables 1 and 2).

Sensitivity and specificity

The analysis showed that the pooled sensitivity was 0.82 [95% CI: 0.74–0.88], with considerable heterogeneity (I^2 of 83.35%, p-value of 0). Regarding pooled specificity, the result was 0.83 [95% CI 0.78–0.87], with significant heterogeneity observed between the studies (I^2 of 88.04%, p-value of 0) (Fig. 4).

Positive and negative diagnostic likelihood ratio (DLR)

The analysis showed a combined positive likelihood ratio of 4.91 [95% CI: 3.73–6.47], with a significant heterogeneity found among the studies (I^2 value of 83.74%, p-value of 0). On the other hand, the pooled negative likelihood ratio was 0.21 [95% CI: 0.14–0.32], and there was notable heterogeneity observed between the studies (I^2 value of 83.92%, p-value of 0) (Fig. 5).

Diagnostic score and diagnostic odds ratio

The diagnostic score obtained from the pooled data was 3.14 [95% CI: 2.55–3.72], indicating significant heterogeneity (I^2 of 99.29%, p-value of 0). The diagnostic odds ratio of the pooled data was 23.01 [95% CI: 12.83–41.24], with significant variation observed between the studies (I^2 of 100%, p-value of <0.001) (Fig. 6).

Area under curve

The pooled SROC curve, which combines sensitivity and specificity data, resulted in an AUC of 0.89 (95% CI: 0.86–0.92) (Fig. 7).

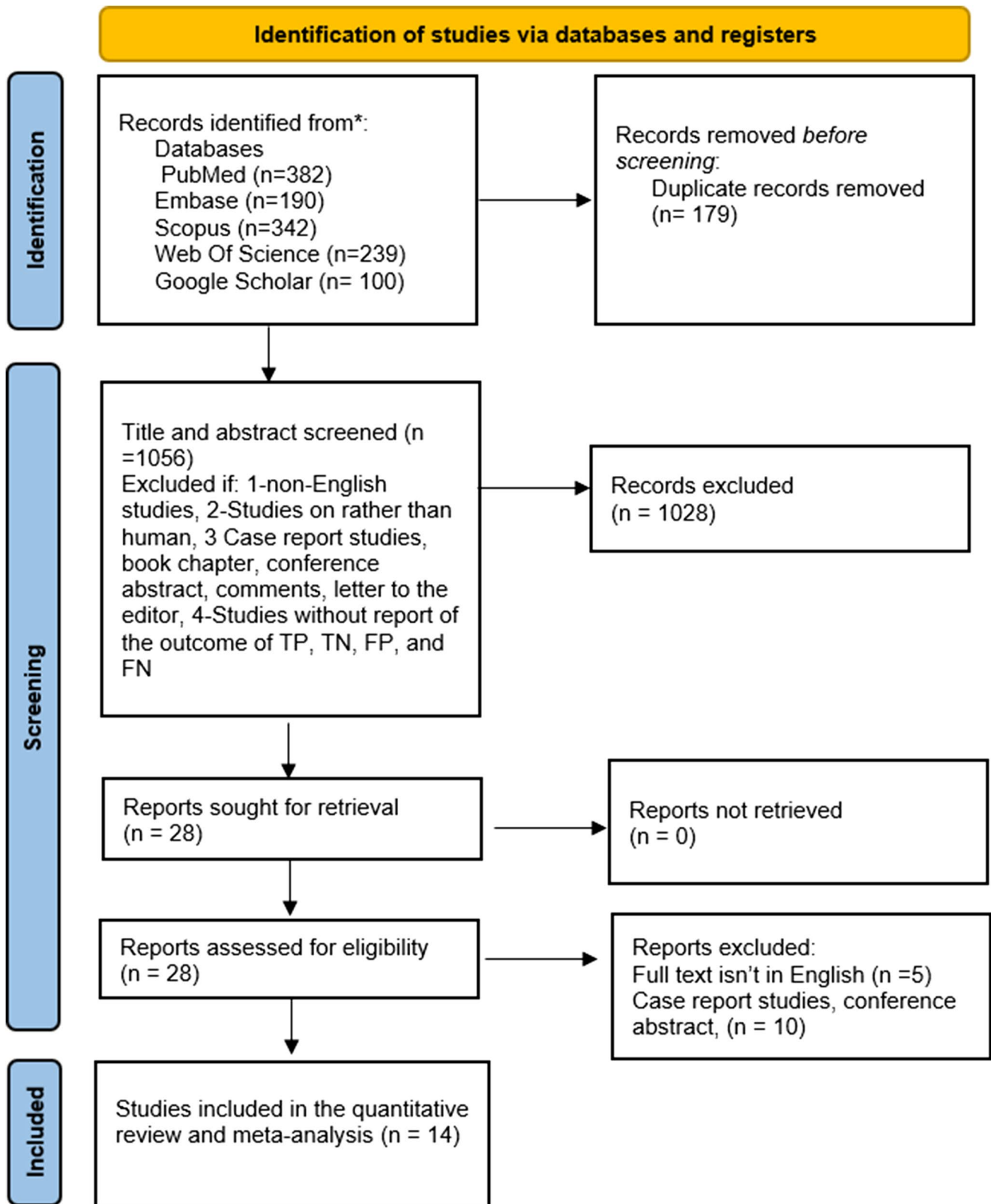


Fig. 1 PRISMA flowchart of the study selection process

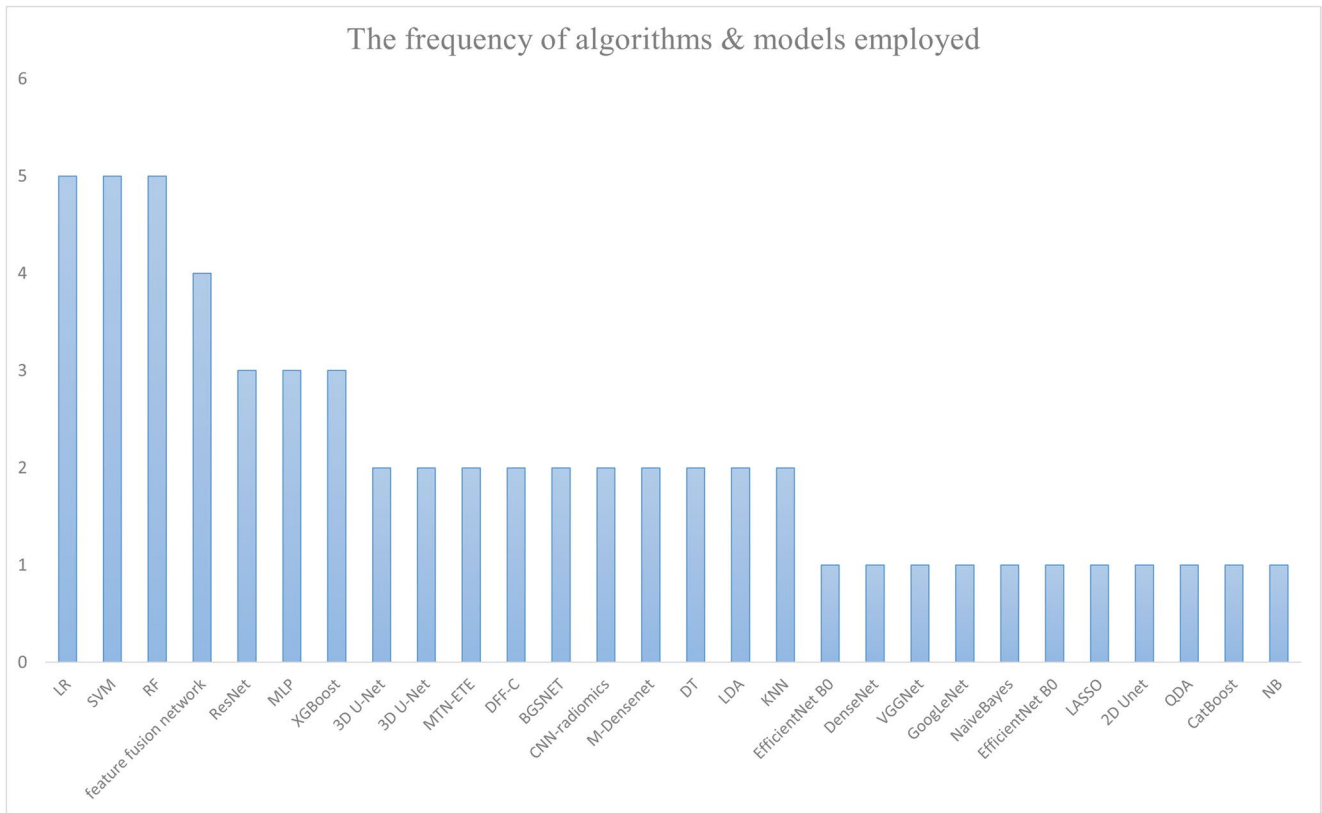


Fig. 2 Frequency of algorithms used in the analyzed studies

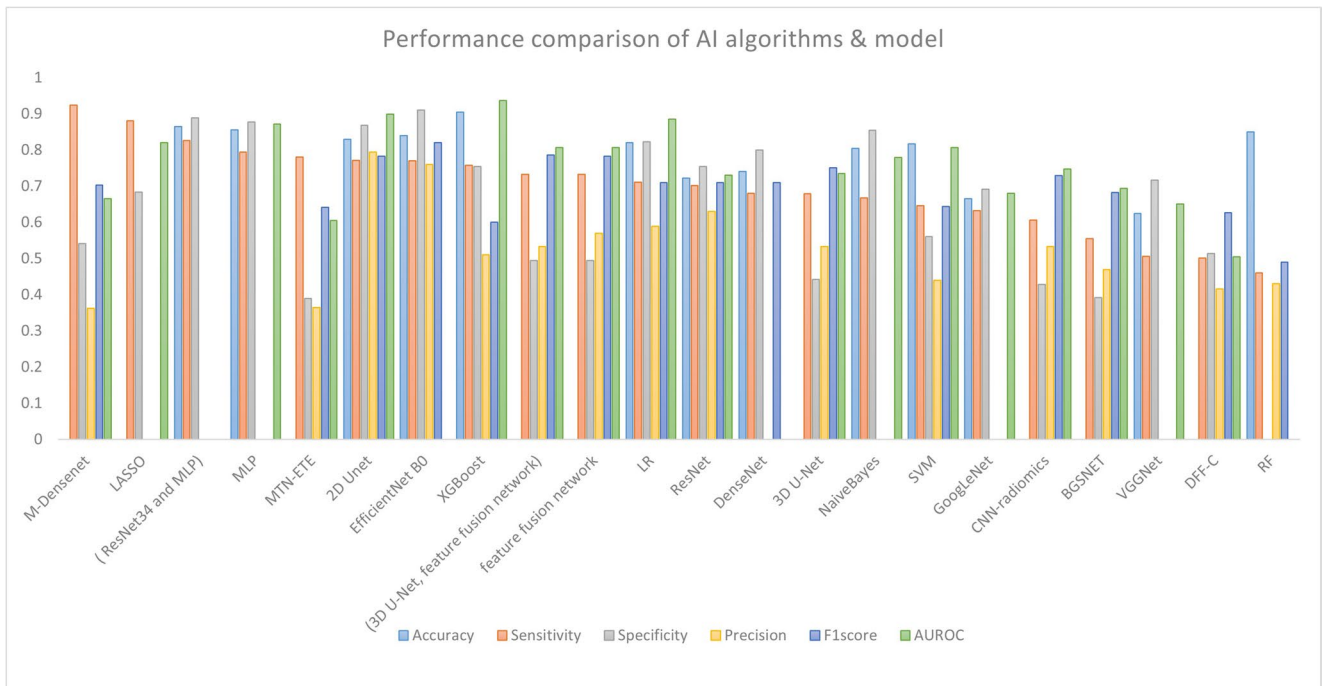


Fig. 3 Performance comparison of ML algorithms, including accuracy, sensitivity, specificity and AUROC

Table 1 Demographic and HE characteristics

Author/year	Type of study	Country	Progression criteria	Hematoma causes	Follow up CT (hr)	Mean age/female%	Inclusion criteria	Exclusion criteria
Xu et al. [38]	R	China	Hematoma volume increase > 33% within 24 h	spontaneous	24	62.7/68.3%	ICH within 6 h of symptom onset, Follow-up CT within 24 h,	Secondary causes of ICH, Poor-quality imaging, Surgery/intervention before follow-up CT
Cheng et al. [39]	R	China	a proportional increase of hematoma volume > 33% or an absolute growth of hematoma volume > 12.5 ml from baseline CT scans to follow-up CT scans	spontaneous	48	59.64/35%	age > 18 years; baseline CT scans performed within 6 h after ICH symptoms; ICH confirmed on NCCT showing parenchymal hematoma; follow-up CT scans performed within 48 h after the baseline CT scan	patients with secondary ICH caused by an arteriovenous malformation, cerebral aneurysm, traumatic brain injury, brain tumor, or hemorrhagic infarction and anticoagulant-associated ICH patients; patients who had surgical intervention before the follow-up CT scan
Chen et al. [24]	R	China	increase of 33% or 6ml in the hematoma volume from baseline to follow-up	spontaneous	72	61.1/34%	patients aged > 18 years with spontaneous ICH, Patients with baseline and follow-up cranial CT within 6 h and 72 h of symptom onset	traumatic ICH or hemorrhagic transformation of ischemic stroke, tumor, aneurysm or arteriovenous malformation presumed to be the potential cause of the bleeding, primary intraventricular hemorrhage or multiple ICH, usage of anticoagulant drugs prior to ictus, surgical intervention before the follow-up CT and severe artifacts on the original image
Zhang et al. [5]	R	China	follow-up CT scan showing 15% increase in size or number of hemorrhagic lesions, including newly developed ones	TBI	12	54.9/23.9%	(1) brain contusion with intraparenchymal hemorrhage in CT scan, (2) brain contusions without evidence for neurological compromise, controlled ICP and no significant signs of mass effect on CT scan, (3) arrival at the emergency department within 12 h after injury and the first head CT completed within 2 h after arrival; and (4) age ≥ 18 years.	penetrating brain injury, combined epidural hematoma > 10 ml, combined thickness of subdural hematoma > 5 mm and/or a midline shift > 5 mm and/or volume > 10 ml, unilateral or bilateral loss of pupil reactivity or herniation syndrome, and pupil asymmetry of > 2 mm
Y.-J. Shih et al. [6]	R	Taiwan	relative volume increase of more than 30% or an absolute volume increase of more than 10 mL compared to the initial CT.	TBI	96	52.8/NA	Adults (≥ 18 years) with blunt TBI; Initial CT showing IPH; Follow-up CT within 96 h	Extra-axial hemorrhages only, Midline shift > 5 mm, Herniation syndromes, Surgical intervention between CTs

Table 1 (continued)

Author/year	Type of study	Country	progression criteria	Hematoma causes	Follow up CT (hr)	Mean age/female%	Inclusion criteria	Exclusion criteria
Q. Yang et al. [40]	R	China	the increase of the volume of intracranial hematoma by 25% or more when compared with the initial CT. The hematoma volume was calculated as ABC/2.	TBI	6	58.14/79.71%	NA	patients < 18 years old; patients with a history of skull surgery; patients with a baseline head CT more than 6 h after trauma; patients who did not undergo repeated CT within 3 days of baseline; severe artifacts on the baseline images; patients with penetrating TBI; (7) patients with brain surgery or interventional therapy before the follow-up head CT and patients with anticoagulant therapy before trauma; and patients with non-traumatic brain diseases, such as tumor, discovered on CT
Ko et al. [41]	R	South Korea	relative hematoma growth > 33% or absolute hematoma growth > 6 mL from baseline hemorrhage volume	spontaneous	24	58.6/36%	primary spontaneous ICH with baseline volume ≤ 60 mL, presentation to the emergency department within 6 h from symptom onset, availability of baseline and follow-up NCCT data within 48 h after symptom onset, and the absence of anticoagulant treatment	secondary ICH, hemorrhagic transformation of ischemic stroke, primary intraventricular hemorrhage, and NCCT images of insufficient quality
Li et al. [20]	R	China	absolute increase in hematoma volume of more than 6 mL on follow-up NCCT scans	spontaneous	6–48	60.1/33.5%	ICH patients with or without hematoma expansion, Baseline and follow-up NCCT scans conducted within 6 h and 48 h from symptom onset	no follow-up NCCT, no hematoma, secondary ICH, poor preprocessed NCCT
Li et al. [20]	P	China	absolute increase in hematoma volume of more than 6 mL on follow-up NCCT scans	spontaneous	6–48	60.6/39%	ICH patients with or without hematoma expansion, Baseline and follow-up NCCT scans conducted within 6 h and 48 h from symptom onset	no follow-up NCCT, no hematoma, secondary ICH, poor preprocessed NCCT
Wu et al. [31]	R	China	hematoma volume increases by > 6 mL or > 33% compared with the initial hematoma volume at reexamination	spontaneous	24	NA/29.9%	age over 18 years old; conformed to the diagnostic criteria for cerebral hemorrhage; first CT examination and first CT reexamination both less than 24 h; the clinical data, complete imaging examination, and laboratory test results; and informed consent form of the patient	secondary cerebral hemorrhage; implementing interventions such as surgery and intervention before CT reexamination; poor image quality, which affected judgment and measurement; and minimal cerebral hemorrhage (maximum diameter < 3 mm) and multiple cerebral hemorrhage.

Table 1 (continued)

Author/year	Type of study	Country	progression criteria	Hematoma causes	Follow up CT (hr)	Mean age/female%	Inclusion criteria	Exclusion criteria
Yalcin et al. [30]	R	Spain	NA	spontaneous	NA	NA	Patients older than 18 years; Diagnosis of acute spontaneous and anticoagulation associated supratentorial ICH within 12 h of symptom onset; Informed consent signed by the patient or relatives; Availability of both baseline and follow-up CTs for the calculation of volumetric differences in hematomas and label assignment; Baseline hematoma volume not less than 5 ml	Known secondary ICH etiology (trauma, underlying vascular malformation); Surgical hematoma evacuation; Life expectancy under 6 months; Pregnancy; Suboptimal imaging acquisition; Outlier cases based on IQR of baseline hematoma volume
C. Du et al. [42]	R	China	Hematoma volume increase > 6 ml in follow-up CT	spontaneous	24	59.4/46.0	Baseline CT scan within 24 h and follow-up CT within 24 h; supratentorial hemorrhage	Secondary ICH, history of stroke, anticoagulant therapy, primary intraventricular hemorrhage
H. He et al. [33]	R	China	Hematoma volume increase > 6 mL or > 33% within 72 h	TBI	72	NA	Age ≥ 18, 5-mm CT scan within 12 h post-trauma, Follow-up CT within 72 h, Clear traumatic intracerebral hematoma	Incomplete records, Severe CT artifacts, Pre-existing neurological deficits, Anticoagulant therapy
H. Lee et al. [34]	R	South Korea	A 20% or greater increase in the initial ICH area on follow-up CT scans within 12 h of the initial scan	TBI	NA	57.2/28.5%	patients with mild to moderate traumatic brain injury (TBI), a Glasgow Coma Scale (GCS) score above 8, who had an initial non-contrast CT scan and did not require immediate neurosurgical intervention.	ever TBI (GCS score ≤ 8) and patients requiring immediate neurosurgical intervention for acute subdural or epidural hematoma
F. Yu et al. [32]	R	China	Hematoma volume increase by > 33% or > 6 mL	spontaneous	24	59.7/NA	patients with hypertension, who had their first CT scan within 24 h of disease onset, and a hemorrhage located in the brain parenchyma (including basal ganglia, thalamus, brain lobes, brainstem, or cerebellum).	patients with secondary ICH (due to trauma, cerebrovascular malformations, aneurysms, or tumors), ischemic cerebral infarction hemorrhagic transformation, those who underwent surgical treatment before CT examination, poor quality CT images, or hematomas with unclear borders preventing accurate ROI delineation.

Abbreviations: NA: Not Applicable, R: Retrospective Study, P: Prospective Study, TBI: Traumatic Brain Injury, NCCT: Non-Contrast Computed Tomography, ICH: Intracerebral Hemorrhage, CT: Computed Tomography, hr: Hours, ICP: Intracranial Pressure, ROI: Region of Interest

Table 2 AI algorithms characteristics and performance metrics

Author/year	Validation	Type of reference Sequence	Input characteristics	Method of radiomics	No of extracted/final radiomics (radiomics features) group	No of patients in train/test group	AI algorithm & model	Best predictor	Accuracy	Sensitivity	Specificity	Precision	F1 score	AUROC
Xu et al. [38]	10 - fold cross - validation	CT	Radiomics (texture, shape) and imaging markers (satellite sign) radiomics and clinical features	semi-automated	396/4	68/61	LASSO, LR	LR	NA	0.95	0.766	NA	NA	0.857
Cheng et al. [39]	10 - fold cross - validation	CT	radiomics and clinical features	automated	10/4	105/21	ResNet34, MLP, VGGNet, GoogLeNet	combined (ResNet34 and MLP)	0.865	0.826	0.889	NA	NA	NA
Chen et al. [24]	10 - fold cross- validation	CT	radiomics and clinical features	semi-automated	15/3	864/289	LASSO	LASSO	NA	0.881	0.683	NA	NA	0.82
Zhang et al. [5]	NA	CT	radiomics and clinical features	manual	NA	66/22	2D Unet	2D Unet	0.829	0.771	0.868	0.794	0.783	0.899
Y.-J. Shih et al. [6]	10-fold cross-validation	CT	radiomics features and clinical features.	Manual	107/NA	107	SVM, KNN	SVM	0.776	0.622	0.887	NA	NA	0.76
Q. Yang et al. [40]	5-fold cross-validation	CT	radiomic features extracted from NCCT	semi-automated	201/712	145/62	SVM, RF, LR, CatBoost, XGBoost	SVM	0.806	0.818	0.793	NA	0.818	0.853
Ko et al. [41]	NA	CT	radiomics	automated	NA	197/50	EfficientNet B0, DenseNet, ResNet	EfficientNet B0	0.84	0.77	0.91	0.76	0.82	NA
Li et al. [20]	NA	CT	radiomics	automated	NA	1876/608	3D U-Net, feature fusion network, MTN-ETE, DFF-C, BGSNET, CNN-radiomics, M-Densenet	combined two stages	NA	0.784	0.666	0.663	0.711	0.767
Li et al. [20]	NA	CT	radiomics	automated	NA	NA/500	3D U-Net, feature fusion network, MTN-ETE, DFF-C, BGSNET, CNN-radiomics, M-Densenet	combined two stages	NA	0.646	0.8	0.326	0.354	0.806
Wu et al. [31]	NA	CT	radiomics and clinical features	automated	NA	204/50	MLP, Naive-Bayes, LR	MLP	0.92	0.889	0.927	NA	NA	0.921
Yalcin et al. [30]	5-fold cross-validation	CT	radiomics	semi-automated	NA	73/24	EfficientNet B0, DenseNet, ResNet	EfficientNet B0	0.84	0.77	0.91	NA	0.82	NA
C. Du et al. [42]	NA	CT	Clinical features and radiomics (CT markers)	Manual	NA	NA	XGBoost, SVM, RF, LR	XGBoost	0.9	0.62	NA	0.51	0.6	0.96
H. He et al. [33]	5-fold cross-validation	CT	Radiomics (CT-based) and clinical features	Semi-automatic	1,502/7	315/137	LR, SVM, RF, LDA, DT	LR	0.797	0.744	0.861	NA	0.8	0.848
H. Lee et al. [34]	NA	CT	Radiological + clinical	manually extracted radiological features	7/7	520/65	XGBoost, RF	XGBoost	0.91	0.8958	0.7549	NA	NA	0.913
F. Yu et al. [32]	10-fold cross-validation	CT	Radiomics + clinical + conventional imaging feature	Semi-automated	1218/29	555/77	LR, KNN, SVM, DT, RF, LDA, QDA, NB	LR	0.883	0.85	0.894	0.739	0.791	0.917

Abbreviations: NA: Not Applied, CT: Computed Tomography, NCCT: Non-Contrast Computed Tomography, MLP: Multi-Layer Perceptron, SVM: Support Vector Machine, RF: Random Forest, LR: Logistic Regression, LASSO: Least Absolute Shrinkage and Selection Operator, KNN: K-Nearest Neighbors, AUROC: Area Under the Receiver Operating Characteristic Curve, F1 Score, ResNet: Residual Network, VGGNet: Visual Geometry Group Network, CNN: Convolutional Neural Network, 2D Unet/3D Unet: Two-/Three-Dimensional U-Net Model, XGBoost: Extreme Gradient Boosting, LDA: Linear Discriminant Analysis, DT: Decision Tree, QDA: Quadratic Discriminant Analysis, EfficientNet: Efficient Convolutional Neural Network Model

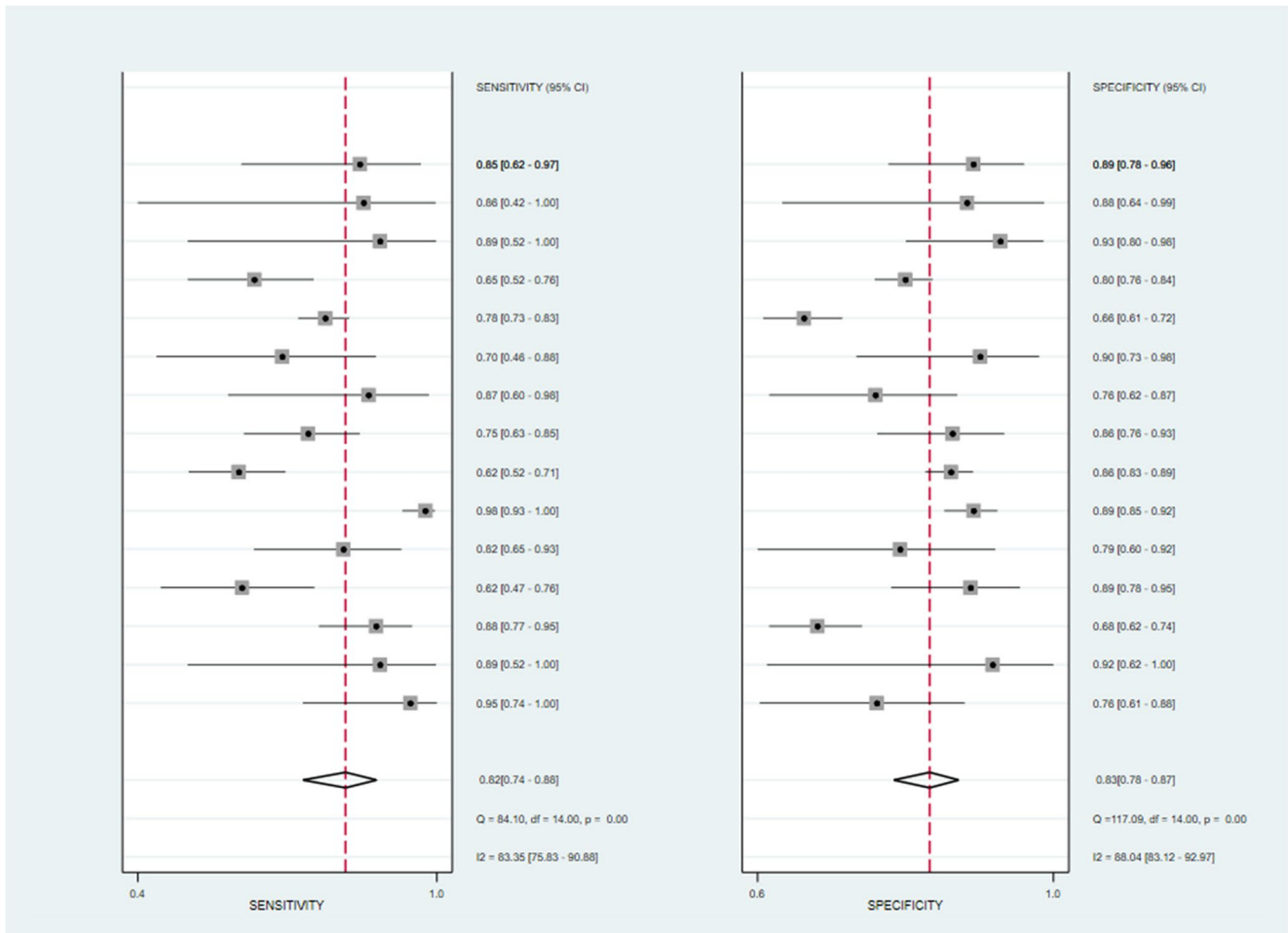


Fig. 4 Sensitivity and specificity of ML algorithms

Sub-group between TBI (Traumatic brain Injury) and spontaneous

Among the 14 included studies, 5 studies (35.7%) focused on TBI, while the remaining 9 studies (64.3%) investigated spontaneous ICH. Regarding the total 7,665 patients, 1,925 patients (25.1%) had TBI-associated ICH, whereas the remaining 5,740 patients (74.9%) belonged to the spontaneous ICH subgroup.

The comparison between ICH, HE following TBI, and spontaneous subgroups revealed that the spontaneous group demonstrated superior diagnostic performance with a higher AUROC (0.90 vs. 0.87), sensitivity (0.85 vs. 0.76), and diagnostic odds ratio (28 vs. 16). Specificity was comparable between the two groups (0.83 in both). The spontaneous group also showed a lower negative likelihood ratio (0.18 vs. 0.29), indicating better exclusion of false negatives. However, the spontaneous subgroup exhibited significant

heterogeneity ($I^2 = 96\%$), while the TBI subgroup had no heterogeneity ($I^2 = 0\%$), suggesting variability in the spontaneous ICH studies.

Publication bias assessment

The regression-based analysis estimated the bias coefficient at 6.85 (95% CI: -13.84 to 27.54, $P=0.487$), showing no statistically significant bias. The wide confidence interval suggests uncertainty in the estimate. However, the intercept of 2.52 (95% CI: 0.86 to 4.18, $P=0.006$) was statistically significant, potentially indicating some degree of bias despite the lack of strong evidence for small-study effects.

A Deeks' test for funnel plot asymmetry showed no significant publication bias, with a P-value of 0.49. Visual inspection and the regression line confirmed no substantial small-study effects, indicating that the studies in the meta-analysis were not influenced by selective reporting (Fig.S1).

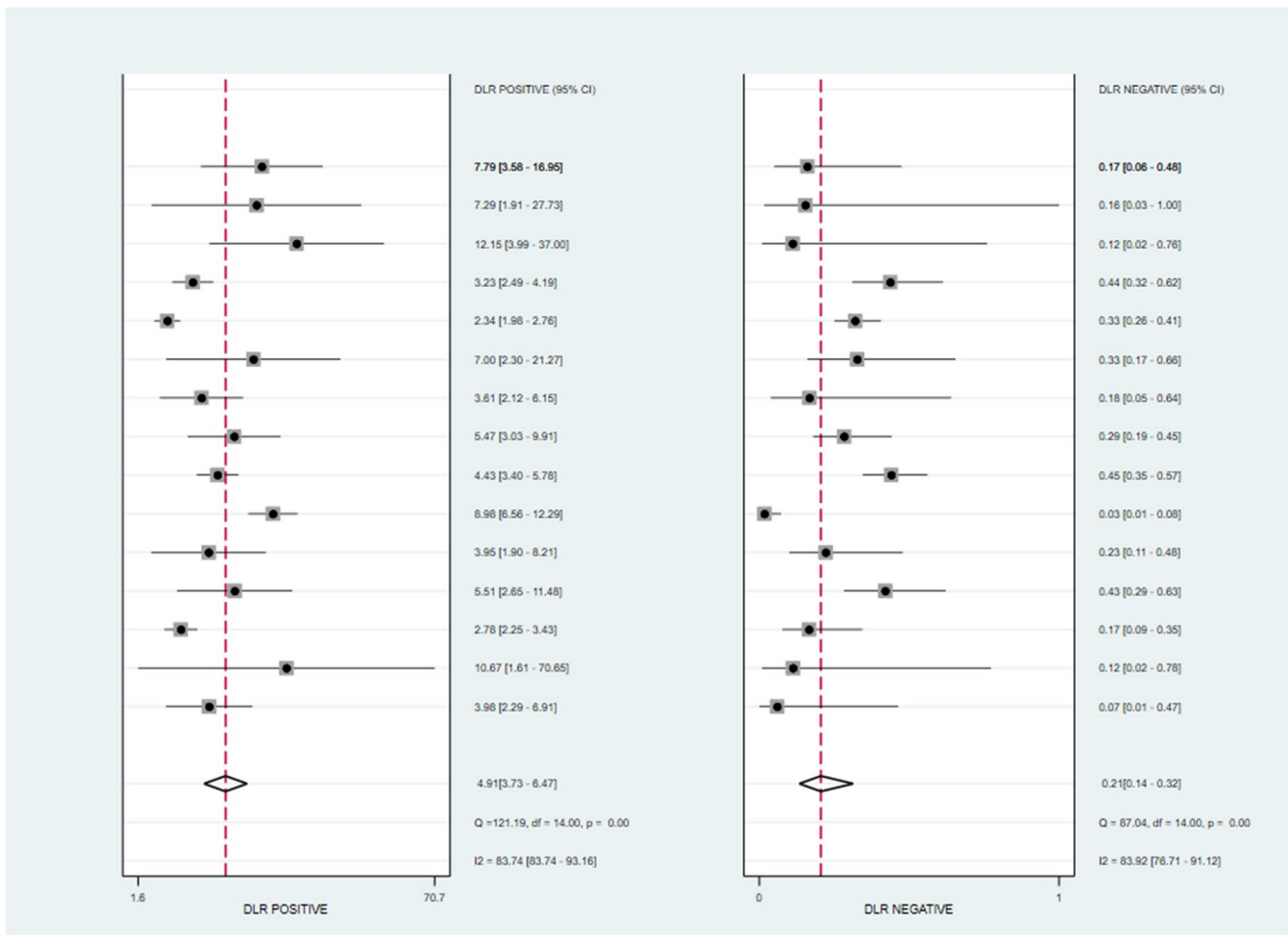


Fig. 5 Positive and negative DLR of ML algorithms

Risk of bias (PROBAST)

Across the four domains of participants, predictors, outcomes, and analysis, 93% of studies demonstrated low risk of bias. In 7% of studies, the ROB was unclear, particularly in the predictor and analysis domains. No studies were rated as having a high ROB (Fig.S2).

Applicability of the ML tools (PROBAST)

For applicability, 94% of studies showed low concern in the participants domain, and 92% in the predictor domain. Similarly, 93% of studies demonstrated low concern in the outcome's domain, and 95% in the analysis domain. A small percentage (6–8%) across domains was classified as unclear. No domains were noted as having high concern (Fig.S3).

Discussion

The application of AI-based models to predict HE in ICH represents a promising advancement in neurocritical care. This systematic review and meta-analysis evaluated the current evidence on the predictive performance of AI-based models in this regard. The pooled sensitivity of 82% [95% CI: 74–88%] shows that AI models can accurately identify most cases of HE, thus decreasing the chances of missed diagnosis and enabling early interventions. Moreover, the pooled specificity of 83% [95% CI: 78–87%] indicates that these models can also exclude non-HE cases effectively, which reduces false positives and unnecessary treatments. The positive DLR of 4.91 [95% CI: 3.73–6.47] indicates that when the prediction is positive, this will increase the odds of HE by almost fivefold. On the other hand, the

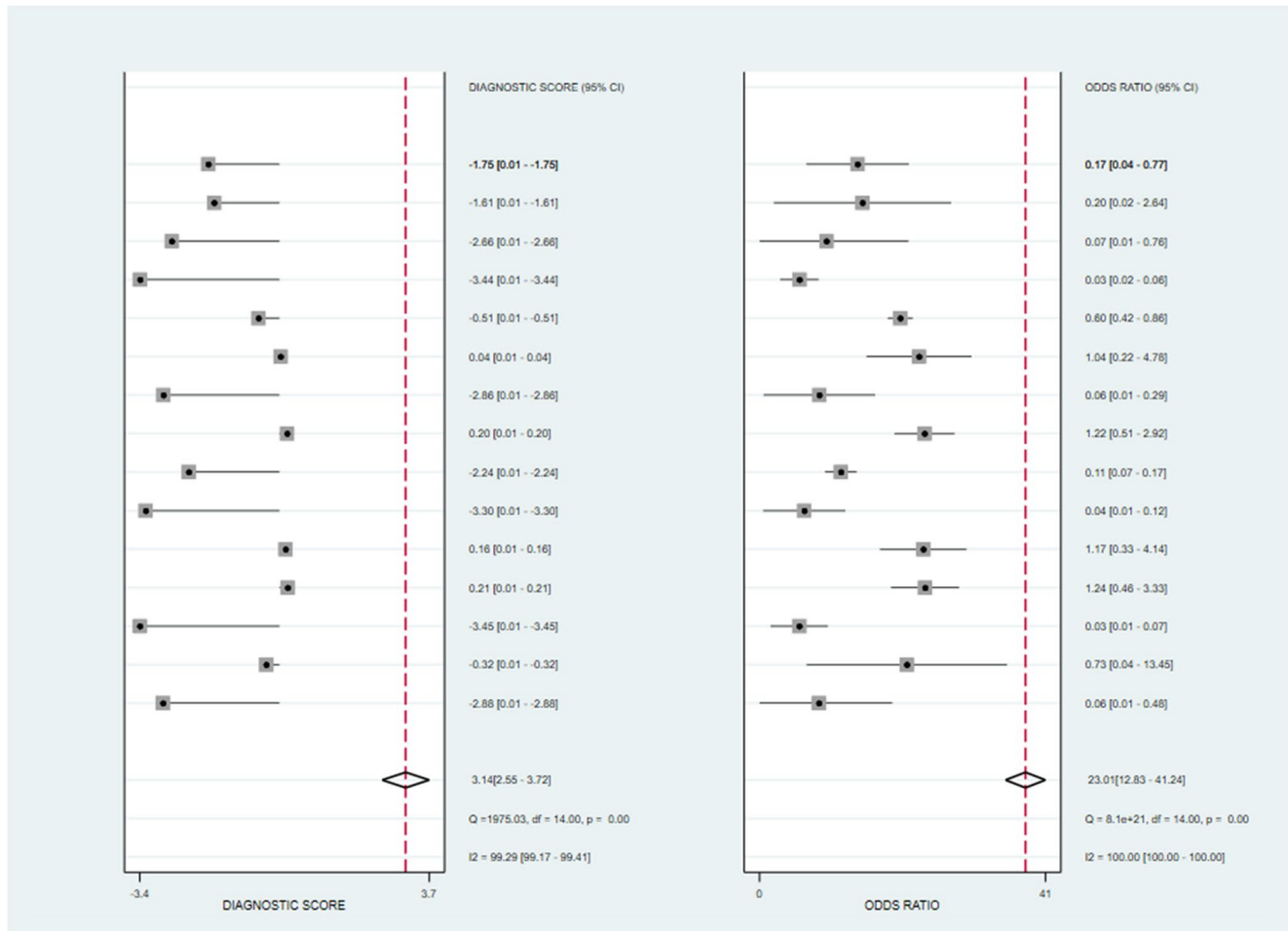


Fig. 6 Diagnostic score and diagnostic odds ratio of ML algorithms

negative DLR of 0.21 [95% CI: 0.14–0.32] significantly reduced the probability of having an HE when the prediction is negative. Further, the DOR of 23.01 [95% CI: 12.83–41.24] pools sensitivity and specificity, reflecting the strong overall diagnostic accuracy of AI systems. Finally, the AUC of 0.89 [95% CI: 0.86–0.92] underlines the high discriminatory capability of AI-based models, supporting their clinical utility in forecasting HE and aiding critical decision-making in managing ICH patients.

Several nomograms and AI-based radiomics models have been developed to predict the HE following ICH [21–24]. Yang et al. developed a LR-based nomogram for predicting HE after ICH, identifying baseline hematoma ≥ 20 mL (OR: 4.09) and time to CT < 1 h (OR: 4.19) as key predictors [21]. Zhang et al. developed an LR-based nomogram to predict HE [22]. They showed that the National Institutes of Health Stroke Scale (NIHSS) and International Normalized Ratio (INR) were the most significant predictive factors, followed by time to baseline CT scan, CTA spot signs, and hypodensities [22]. Their model showed a sensitivity of 74% and specificity of 64% with a C-index of 0.743 [22].

Despite promising predictive outcomes of nomograms concurrent with their straightforward interpretation and daily application, These models rely on limited parameters and cannot adequately handle large datasets with multiple variables [22]. In contrast, AI-based models can analyze datasets with substantial sample sizes and identify the correlation between clinical, treatment, and radiological variables [23]. The AI-based models have demonstrated an AUC and ACC ranging from 0.5 to 0.96 and 0.624 to 0.92, respectively, which indicate these models' favorable predictive performance in HE prediction [2, 21, 22, 25–29]. Recently, the prediction of HE using only the initial scan has drawn increasing attention in research. CT imaging markers such as the island sign, hypodensity, satellite sign, black hole sign, blend sign, and swirl sign have been proposed as indicators of HE [30].

Using DL models based on admission NCCT scans, C. Yalcin et al. modeled a deep learning framework that leverages the 2D EfficientNet B0 model to predict HE. This image-based approach demonstrated superior performance compared to models like DenseNet121 and ResNet34. By

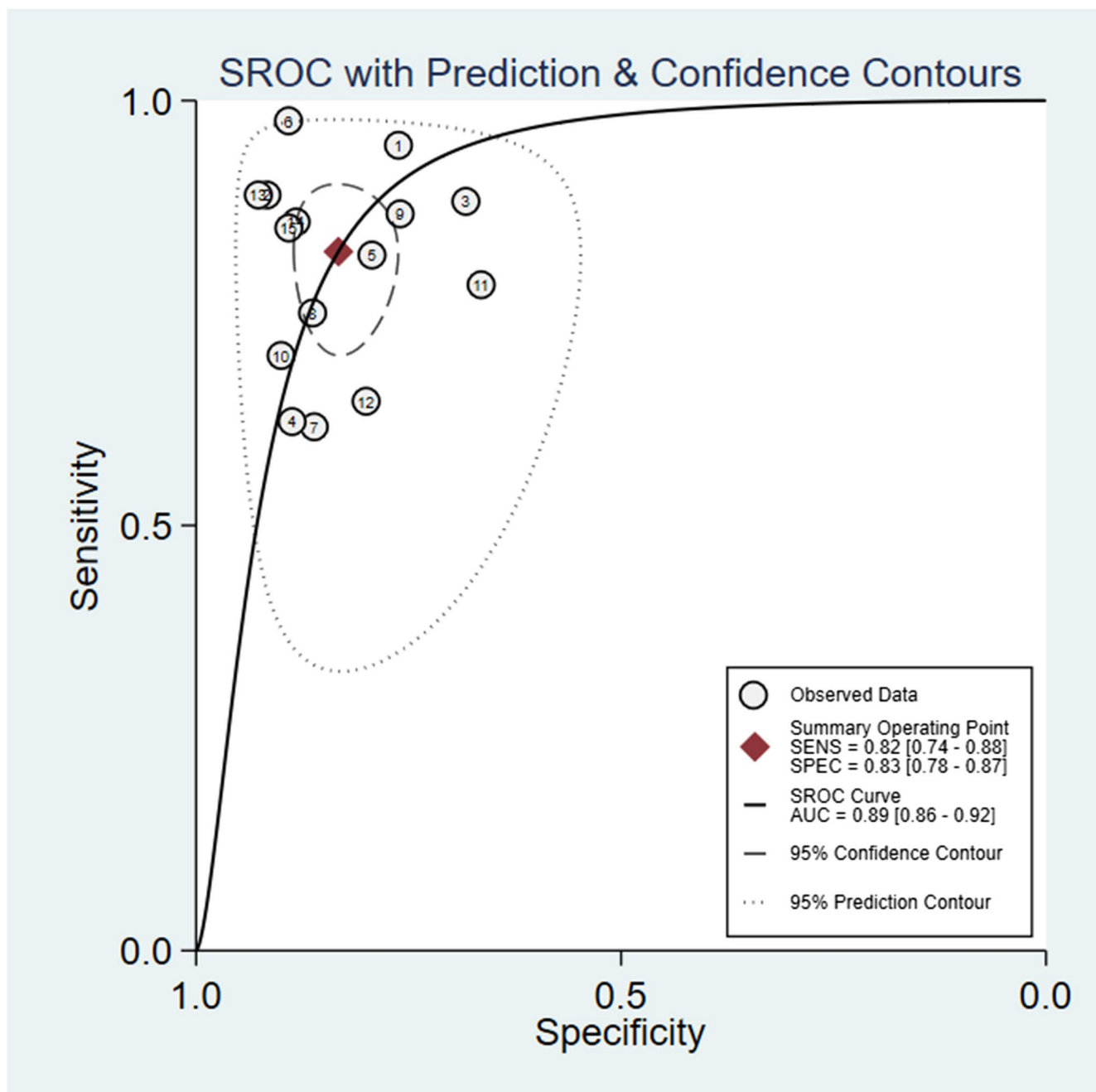


Fig. 7 Summary receiver operator characteristic curve (SROC) of ML algorithms

incorporating synthetic images alongside standard data augmentation techniques to tackle dataset and disease-related challenges, the model achieved remarkable results with an accuracy of 0.84, an F1-score of 0.82, a sensitivity of 0.77, and a specificity of 0.91 [30].

In another approach, Li et al. developed non-automatic and automatic approaches. The first phase utilized a multi-task 3D U-Net to segment hematomas and generate preliminary risk scores, leveraging hematoma segmentation for multi-scale feature learning in HE prediction. The second phase

employed a feature fusion network to refine the risk score by integrating deep features from the first phase and hematoma mask-derived features (i.e., radiomics properties and hematoma volume). AUC results show 0.767 in the first phase and 0.760 in the second. Non-automatic methods show limited performance, while CNN-radiomics achieves the highest sensitivity (0.840) but low specificity (0.558). Conversely, M-Densenet121 favors specificity over sensitivity [20].

Wu et al. utilized a joint model integrating clinical and imaging data with the VGG deep learning framework,

achieving superior predictive performance among MLP models, with a test accuracy of 0.920, and AUC scores of 0.921 [31]. The VGG-19 model is utilized for feature extraction from images, leveraging its deep convolutional layers to capture complex patterns. These extracted features are then used as input for various ML models such as LR, SVM, and RF, which are employed for validation and prediction tasks. This combination enhances the predictive accuracy by integrating deep learning and traditional ML methods.

Similarly, F. Yu et al. developed a nomogram integrating clinical data and imaging signs to assess HE risk in HICH patients. Various ML algorithms (LR, KNN, SVM, DT, RF, LDA, QDA, NB) achieved training set AUCs ranging from 0.788 to 1.000, with 10-fold cross-validation AUCs averaging between 0.645 and 0.845. The LR algorithm, considered the most stable, was used for constructing the radiomics model, achieving an AUC of 0.827 in the validation set. Key predictors—admission GCS score, hematoma volume, irregular shape, and Rad score—were identified via multivariate LR to create a hybrid model. This model achieved AUCs of 0.901, 0.838, and 0.917 in the training, validation, and test sets, respectively [32].

A three-dimensional (3D) segmentation network for the semi-automatic segmentation of traumatic intracerebral hematomas was developed based on the open-source SSL4MIS segmentation model to train popular 3D convolutional encoder-decoder networks, including 3DUNet, Attention-3DUNet, and 3DVNet. Attention-3DUNet was utilized as an assistance in segmentation to ease physicians' workload, minimize manual variations, and improve consistency. Integrated radiomic and clinical features achieved the best performance (AUC = 0.83), outperforming radiomic models (AUC = 0.8) and clinical models (AUC = 0.77) in predicting hematoma expansion [33].

In the first application of an ML model to predict HE in traumatic brain injury (TBI), LR achieved a promising AUC of 0.82. However, the SHAP value-enhanced XGBoost model significantly surpasses it with an AUC of 0.913. SHAP values improve the interpretability of individual risk factors, providing clinicians with a powerful tool for personalized analysis of ICH progression and enabling more precise, tailored decision-making [34].

Clinical implications

The clinical applicability of AI-based models for predicting hematoma expansion remains promising but faces important barriers. A major challenge is the lack of standardized imaging protocols, as variations in acquisition parameters and modalities (CT, CTA, MRI) can significantly affect reproducibility and model performance. Automated and reliable segmentation of hematomas is another critical requirement,

since manual methods are time-consuming and subject to inter-observer variability. Furthermore, most AI models operate as “black boxes,” limiting interpretability and potentially reducing clinicians' trust in their predictions. For successful integration into clinical workflows, these models must undergo rigorous external validation across diverse populations and healthcare systems, and they should be embedded within user-friendly platforms that can interact with hospital information systems. Collaboration between clinicians, radiologists, and data scientists will be essential to ensure that AI models are not only technically accurate but also clinically meaningful and feasible for real-world application.

Limitation

Despite the promising predictive outcomes of AI-based models, these novel tools are correlated with various limitations. Dependency on high-quality, large datasets for training is a major limitation for AI models, especially in neurosurgical fields, due to the rarity and heterogeneity of conditions [35]. Poor generalizability due to the overfitting of models, especially when trained on small datasets, is another limitation of the application of AI models in neurosurgery [36]. The lack of standardized metrics, imaging protocol inconsistencies, and variability in data labeling are other limitations of AI-based models that limits their reproducibility and external validation [37]. These limitations highlight that the results of the AI models should be interpreted meticulously. In addition, the included studies used heterogeneous definitions of hematoma expansion (e.g., absolute increase >6 mL vs. relative increase >33%), which may have influenced the pooled results and contributed to the high heterogeneity observed. Standardized definitions of HE will therefore be essential for future studies to allow more reliable comparisons and meta-analyses. These limitations highlight that the results of the AI models should be interpreted meticulously.

Future directions

To enhance the clinical applicability and performance of AI-based models in predicting HE in ICH, future studies should aim at increasing the diversity and size of patient datasets, integrating multi-center prospective research to enrich model robustness. Larger cohorts and more varied populations will help in addressing the potential biases of small-scale studies, ensuring that predictive models are both accurate and widely applicable.

In addition, developing standardized imaging protocols, particularly for MRI and CT scans, will be critical for improving the reproducibility and generalizability of AI models. Variations in imaging techniques and feature extraction methods have contributed to inconsistencies in

current studies, emphasizing the need for a unified approach across research centers.

Furthermore, exploring a broader range of machine learning algorithms, especially deep learning models, could help refine model predictions. Optimizing these models for different ICH subtypes, such as traumatic versus spontaneous hemorrhage, would enhance their specificity and sensitivity.

External validation using independent multi-center cohorts is also essential to confirm the robustness of AI predictions and facilitate their integration into routine clinical practice. Ensuring that these models generalize well across diverse patient populations will be crucial for translating AI advancements into tangible clinical outcomes, enabling timely and personalized interventions in ICH management.

Conclusion

This study highlights the potential of AI models, particularly ML and DL, in predicting HE in ICH. The pooled sensitivity (0.82), specificity (0.83), and AUC (0.89) indicate a potentially useful diagnostic performance; however, the high heterogeneity across studies limits the robustness of these findings. Subgroup analysis suggested better outcomes in predicting spontaneous ICH compared to traumatic ICH. While the results are encouraging, variability in imaging protocols and feature extraction methods restricts generalizability. Therefore, standardized imaging protocols and rigorous external validation are essential before AI-based models can be reliably integrated into clinical practice.

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Declarations

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