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REVIEW

Diagnostic and predictive value of radiomics-based machine learning for intracranial aneurysm rupture status: a systematic review and meta-analysis

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Abstract
Currently, the growing interest in radiomics within the clinical practice has prompted some researchers to differentiate the rupture status of intracranial aneurysm (IA) by developing radiomics-based machine learning models. However, systematic evidence supporting its performance remains scarce. The purpose of this meta-analysis and systematic review is to assess the diagnostic performance of radiomics-based machine learning for the early detection of IA rupture and to offer evidence-based recommendations for the application of radiomics in this area. PubMed, Cochrane, Embase, and Web of Science databases were searched systematically up to March 2, 2024. The Radiomics Quality Score (RQS) was employed to assess the risk of bias in all included primary studies. We separately discussed the diagnostic or predictive performance of machine learning for IA rupture status based on task type (diagnosis or prediction). We finally included 15 original studies covering 9,111 IA cases. In the validation cohort, radiomics demonstrated a sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, as well as SROC curve of 0.84 (95% CI: 0.76–0.90), 0.82 (95% CI: 0.77–0.86), 4.7 (95% CI: 3.7–5.8), 0.19 (95% CI: 0.13–0.29), and 24 (95% CI: 15–40), respectively, for the diagnostic task of aneurysm rupture status. Only 2 studies (3 models) addressed predictive tasks, with sensitivity and specificity ranging from 0.77 to 0.89 and from 0.69 to 0.87, respectively. Radiomics-based machine learning exhibits promising accuracy for early identification of IA rupture status, whereas evidence for its predictive capability is limited. Further research is needed to validate predictive models and provide insights for developing specialized strategies to prevent aneurysm rupture.

Keywords Unruptured intracranial aneurysm · Radiomics · Machine learning · Meta-analysis

Introduction

Intracranial aneurysm (IA) is a common condition featuring significant death and morbidity rates among cerebrovascular diseases. The overall prevalence of unruptured intracranial aneurysm (UIA) is approximately 3.2% (95% CI 1.9–5.2) [1]. With advancements in imaging technology, the detection rate of UIA continues to rise. The rupture of IA is a critical concern, with an annual rupture rate estimated at 1–2% [2]. Rupture leads to aneurysmal subarachnoid hemorrhage (aSAH), which accounts for approximately 80–85% of non-traumatic subarachnoid hemorrhages [7]. aSAH is associated with high mortality and morbidity, and the median mortality rate for ruptured aneurysms is 32% in the United States, 43-44% in Europe, and 27% in Japan [8].

Early detection of IA and prediction of their rupture risk are thus crucial. Current diagnostic methods for assessing the rupture status of IA encompass Computed Tomography Angiography (CTA), Magnetic Resonance Angiography (MRA), and Digital Subtraction Angiography (DSA). CTA is a primary tool for IA detection owing to its speed, cost-effectiveness, and relative non-invasiveness, and has become the preferred diagnostic method at some centers [9]. However, its capability to detect aneurysms with diameters less than 3 mm remains limited; even with 320-row CT, the sensitivity for detecting

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aneurysms less than 3 mm is only 81.8% [10], leaving a likelihood for missed diagnoses of small aneurysms. Similarly, MRA has a sensitivity of only 74.1% for aneurysms less than 3 mm in diameter [11], and its diagnostic efficacy is compromised by longer examination times and lower contrast enhancement [12]. DSA, as the "gold standard" for diagnosing IA, exhibits superior specificity, sensitivity, and accuracy compared to non-invasive methods like MRA and CTA. However, DSA involves prolonged examination times, with patients and healthcare professionals exposed to X-ray radiation, and may lead to complications such as contrast agent allergy, puncture site hematoma, cortical blindness, or cerebral infarction [13].

In recent years, radiomics has garnered significant attention in clinical practice. Some studies have explored its potential for differentiating IA rupture status and predicting IA rupture risk. However, systematic evidence validating the effectiveness of radiomics for detecting IA rupture status and predicting IA rupture risk remains lacking. Therefore, this study seeks to review the accuracy of radiomics in detecting and predicting the status of IA rupture, thereby providing evidence to support the further application of radiomics in IA.

Methods

Study registration

This study was performed in adherence to the guidelines for systematic reviews and meta-analyses (PRISMA 2020). The protocol has been prospectively registered with PROSPERO (Registration No: CRD42024537872).

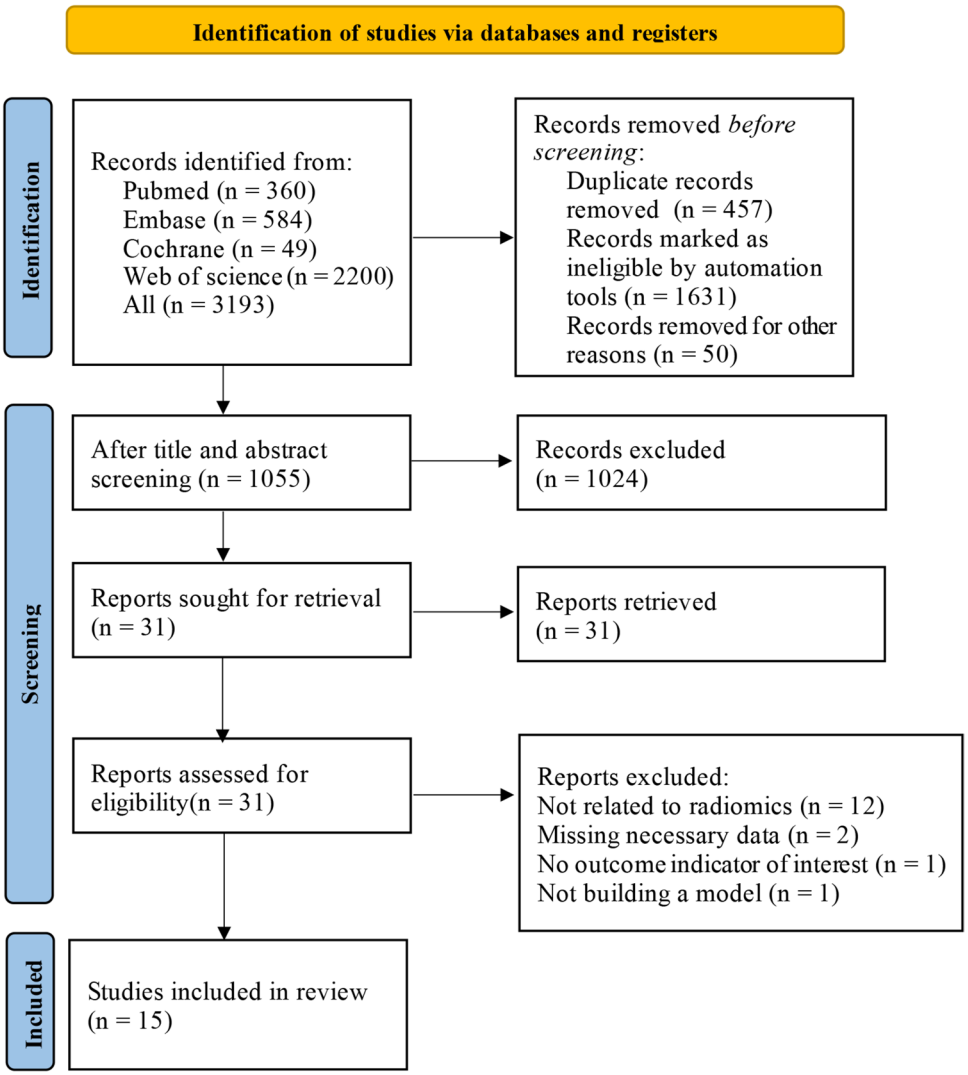

Fig. 1 Literature selection process

Eligibility criteria

Inclusion criteria

(1) The subjects in the paper are patients with IA;
(2) A comprehensive machine learning model encompassing radiomics has been developed for detecting IA rupture state or predicting rupture risk;
(3) The included studies are reported in English.

Exclusion criteria

(1) The study types were meta-analyses, reviews, guidelines, expert opinions, conference abstracts without peer review;
(2) Only differential factor analyses were carried out, and a complete machine learning model was not constructed;
(3) Studies of machine learning constructed for radiomics were not covered;
(4) There is a lack of outcome indicators related to the prediction accuracy of the machine learning model (e.g., ROC, c-statistic, c-index, sensitivity, specificity, accuracy, recall, precision, confusion matrix, diagnostic fourfold table, F1 score, calibration curve).

Data sources and search strategy

PubMed, Cochrane, Embase, and Web of Science were systematically searched until March 2, 2024. The search strategy in our search involved the employment of "subject headings + free terms". No constraints were placed on region or language. The detailed strategy is presented in Table S1.

Study selection and data extraction

We imported the retrieved studies into EndNote, and after removing duplicates, screened titles and abstracts of the remaining studies to select those preliminarily eligible ones. Full texts were then downloaded, and final inclusion in the systematic review was determined based on the full text. Before data extraction, we created a standard electronic data extraction spreadsheet. The extracted information included: title, first author, publication year, country, study type, patient source, task type, radiological source, if a complete imaging protocol was recorded, number of participating investigators, whether measurements were performed repeatedly at different times, regions of interest (ROI) for imaging segmentation software, total number of IA ruptures, total number of cases, number of IA ruptures and cases in the training set, generation methods, number of cases and cases with outcome events in the validation set, variable selection methods, types of models used, if radiomics scoring was constructed, overfitting assessment, whether code and data were accessible, and model evaluation metrics.

The study screening and data extraction were independently performed by two investigators (J. Z and J. Y), who cross-checked their results. When there were discrepancies, the third investigator (S. Y) assisted in judgment.

Table 1 Basic characteristics of included studies

No.	First author	Year of publication	Country	Study type	Patient source	Task type	Total number of ruptured intracranial aneurysm cases	Total number of cases
1	Hyeondong Yang	2022	Korea	Case-control	Single center	Diagnosis	44	123
2	Jinjin Liu	2018	China	Case-control	Single center	Diagnosis	540	594
3	Masayuki Yamanouchi	2022	Japan	Case-control	Single center	Diagnosis	18	28
4	Xiaoyuan Luo	2023	China	Case-control	Multicenter	Diagnosis	375	676
5	Hyeondong Yang	2023	Korea	Case-control	Single center	Diagnosis	45	125
6	Yi Yang	2021	China	Cohort study	Multicenter	Prediction	18	37
7	Jun Hyong Ahn	2021	Korea	Case-control	Multicenter	Diagnosis	177	457
8	Xin Tong	2021	China	Case-control	Multicenter	Diagnosis	106	254
9	Chubin Ou	2022	China	Cohort study	Multicenter, registration database	Prediction	120	947
10	QingLin Liu	2021	China	Case-control	Single center	Diagnosis	216	719
11	Mirzat Turhon	2023	China	Case-control	Multicenter	Diagnosis	437	1809
12	Felicitas J. Detmer	2020	USA	Case-control	Multicenter, registration database	Diagnosis	558	1880
13	Heshan Cao	2024	China	Case-control	Multicenter, registration database	Diagnosis	211	623
14	Wenjie Li	2023	China	Case-control	Multicenter	Diagnosis	192	576
15	Tao Hu	2023	China	Case-control	Single center	Diagnosis	125	263

Table 2 Basic characteristics of included studies

No.	First author	Radiomics source	Image segmentation personnel and qualifications	Image area of interest (ROI) region segmentation software	Number of cases in training set	Number of cases in the training set	Generation method of the validation set	Number of outcome event cases in the validation set	Number of cases in the validation set	Model type
1	Hyeondong Yang	DSA	Not Applicable	ANSYS Workbench Fluent	22	75	Random sampling	22	48	CNN
2	Jinjin Liu	CTA	Not Applicable	Not Applicable	373	577	Random sampling	76	123	ANN
3	Masayuki Yamanouchi	MRA	Not Applicable	MATLAB	10	113	Leave-one-out cross validation	Not Applicable	Not Applicable	SVM
4	Xiaoyuan Luo	CTA/MRA	3(Qualified radiologists)	3D Slicer	252	293	Random sampling	105	258	ANN/SVM
5	Hyeondong Yang	DSA	Not Applicable	ANSYS Workbench Fluent	31	84	Random sampling	14	41	ANN
6	Yi Yang	CTA	2(Experienced neurosurgeon)	MIMICS 17.0	16	32	Random sampling	Not Applicable	Not Applicable	ANN
7	Jun Hyong Ahn	DSA	3(Experienced neurosurgeon)	Not Applicable	133	364	Random sampling	47	93	CNN
8	Xin Tong	DSA	4(15-year veteran neurointerventionalist)	3D Slicer	63	176	Random sampling	43	78	LR
9	Chubin Ou	DSA/CTA/MRA	5(Experienced neurosurgeon)	3D Slicer	29	120	Cross validation	Not Applicable	Not Applicable	DL
10	QingLin Liu	DSA	2(Interventional physician)	3D Slicer	147	504	Random sampling	69	215	LR
11	Mirzat Turhon	DSA	3(Neurointerventionist)	PyRadiomics	272	1157	Internal validation (random sampling 20%) + external validation	165	652	SBDT
12	Felicitas J. Detmer	DSA	Not Applicable	Not Applicable	492	1631	External validation	66	249	SVM/KNN
13	Heshan Cao	DSA	Not Applicable	Not Applicable	124	464	Internal validation + external validation	87	159	LR
14	Wenjie Li	CTA	2(Trained interventional radiologists)	ITK-SNAP	125	403	Random sampling	67	173	LR
15	Tao Hu	DSA	Not Applicable	Not Applicable	89	187	Random sampling	36	76	Generalized Hessian

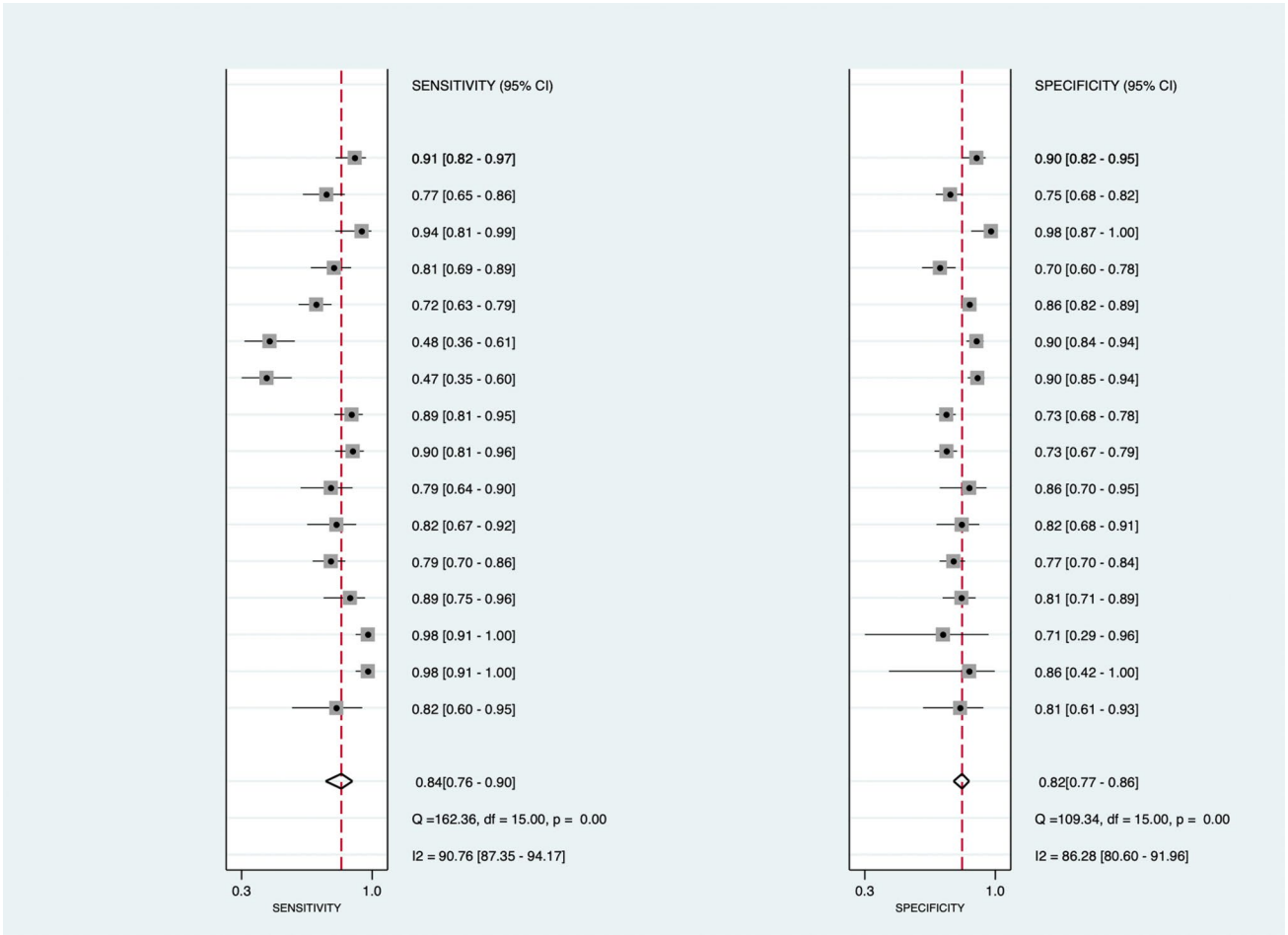

Fig. 2 Forest plot of meta-analysis for sensitivity and specificity of radiomics in distinguishing IA rupture status in the training set

Assessment of study quality

Two researchers (J. Z and J. Y) employed the Radiomics Quality Score (RQS) to evaluate the methodological quality and risk of bias of the eligible studies. Following their assessment, a cross-check was conducted. When any dispute arose, a third researcher (S. Y) was involved in making a decision.

Synthesis methods

A bivariate mixed-effects model was utilized for a meta-analysis of sensitivity and specificity. This model summarized sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio(NLR), diagnostic odds ratio(OR), and the summary receiver operating characteristic (SROC) curve along with its 95% confidence interval. During the analysis, it was necessary to perform meta-analyses of sensitivity and specificity based on diagnostic contingency tables. Nevertheless, because these tables were not reported in the majority of original studies, we adopted two approaches to calculate the tables: (1) Calculating by sensitivity, specificity, precision, and case numbers; (2) Extracting sensitivity and specificity in terms of the optimal Youden's index and calculating based on case numbers. Our meta-analysis was carried out with the help of R version 4.2.0 (R Development Core Team, Vienna, 网址http://www.R-project.org).

Results

Study selection

In the current study, 3,193 studies were retrieved from online databases. Duplicates were removed, leaving 2,736 studies. After reviewing abstracts, 31 articles were obtained. After excluding 12 studies unrelated to radiomics, 2 studies lacking necessary data, 1 study with irrelevant outcome measures, and 1 study not related to model construction, a total of 15 studies were selected for this meta-analysis (Fig. 1).

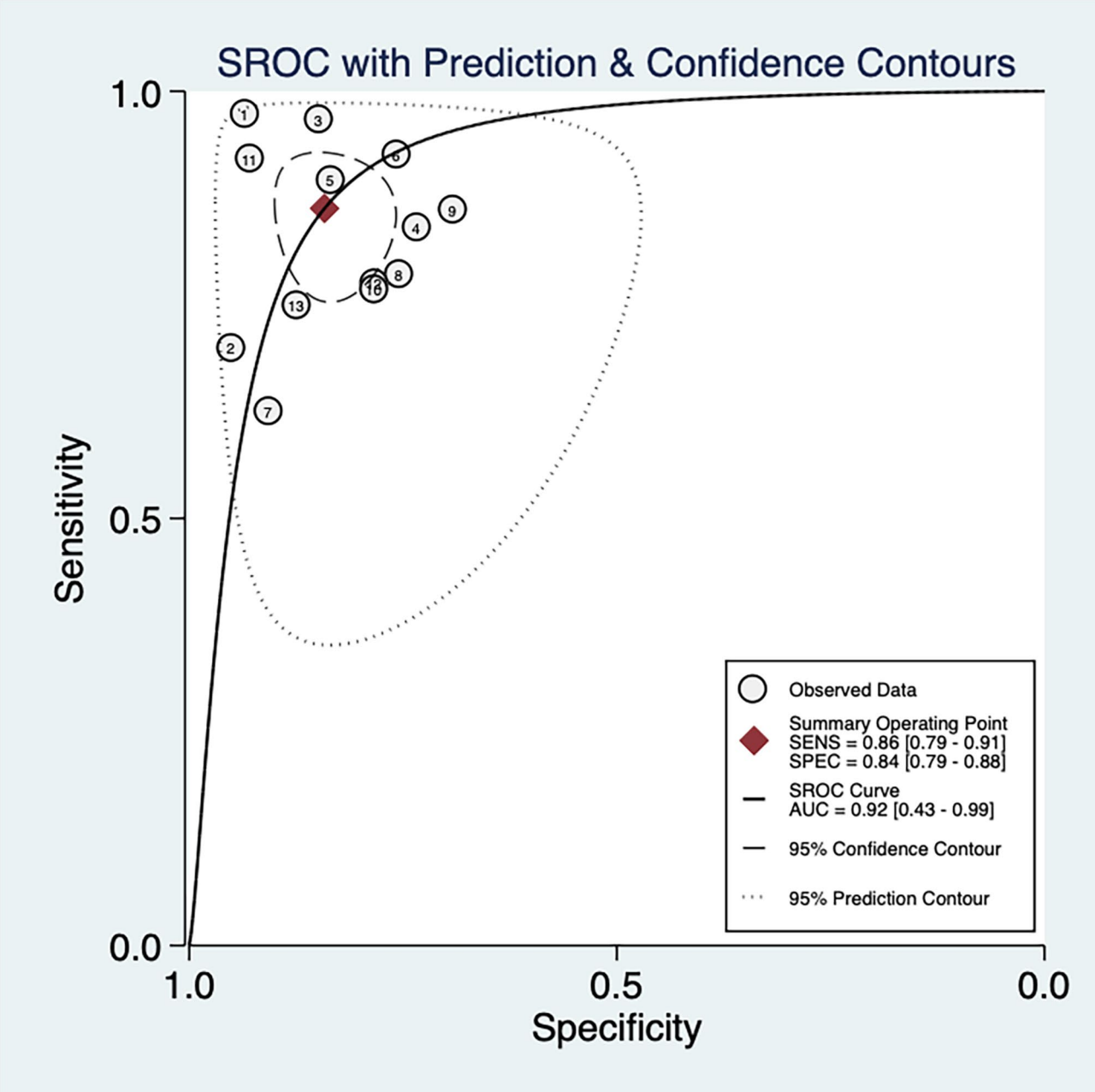

Fig. 3 SROC curve of meta-analysis for radiomics in identifying IA rupture status in the training set

Study characteristics

The 15 eligible articles were published between 2018 and 2024 and encompassed a total of 9,111 IA, of which 3,182 were ruptured IA. Of these studies, 10 [15] were from China; 3 [25] were from South Korea; the remaining two studies were from Japan [28] and the United States [29]. Among the included studies, 13 [15] focused on the diagnosis of ruptured IA and were case-control studies; 2 [17] were cohort studies predicting the risk of rupture. Of the included studies, 13 employed retrospective designs, and 2 used prospective designs. Nine studies were conducted across multiple centers (three of which utilized data from registries), while the remaining six studies were single-center ones. Among the studies, radiomics data sources included 5 from CTA [15], 10 from DSA [16], and 3 from MRA [28] Among these, 3 were externally validated, and the rest were internally validated through random sampling. The models used were primarily based on machine learning (Tables 1 and 2).

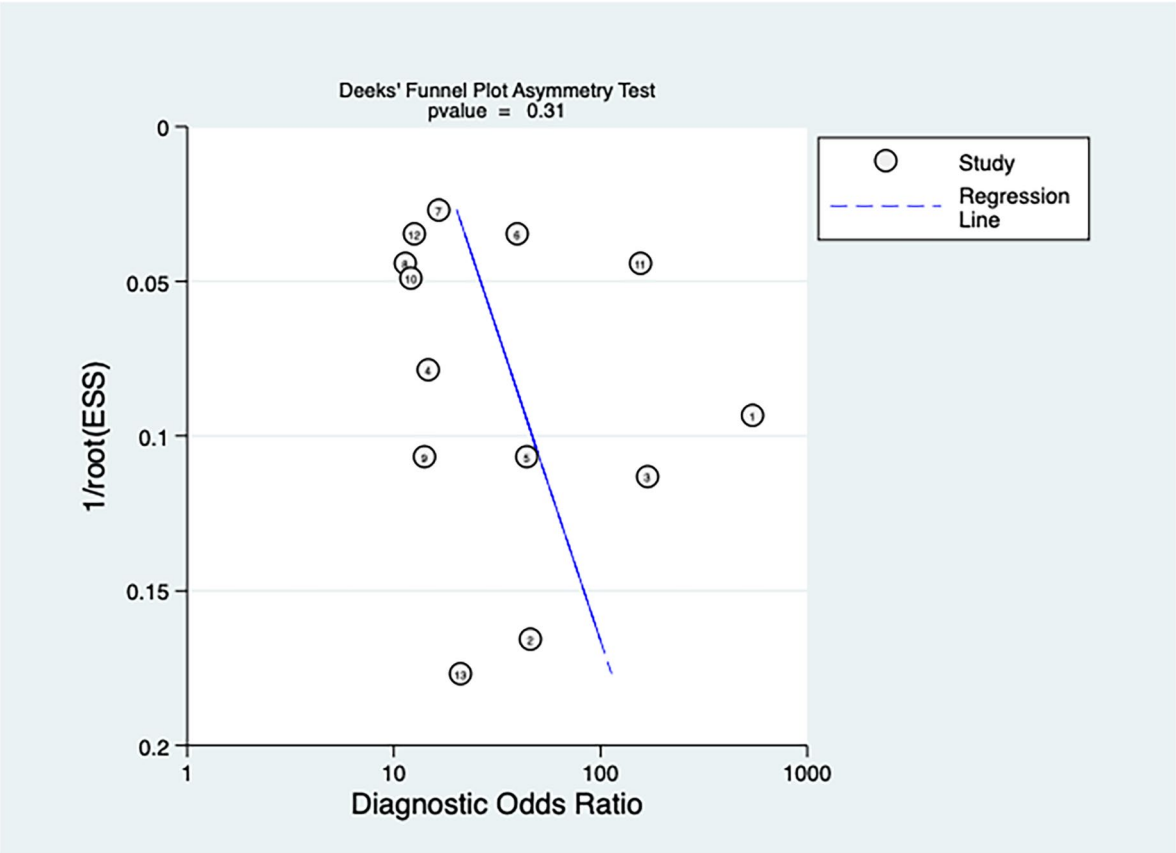

Fig. 4 Deek's funnel plot of meta-analysis for radiomics in detecting IA rupture status in the training set

Meta-analysis of diagnostic accuracy

Training set

In the training set, we performed a meta-analysis of 10 diagnostic 2 × 2 tables. The pooled results for sensitivity, specificity, PLR, NLR, diagnostic OR, and SROC curve were 0.87 (95% CI: 0.78–0.92), 0.85 (95% CI: 0.79–0.90), 5.9 (95% CI: 4.0–8.6), 0.16 (95% CI: 0.09–0.27), and 37 (95% CI: 17–83), respectively (Figs. 2 and 3). No publication bias was observed in the detection of IA rupture status by radiomics in the training set according to Deek's funnel plot ($P = 0.31$) (Fig. 4). Approximately 36% of patients in the included studies had ruptured IA, which was used as the prior probability. With a PLR of 5.9, the model predicted a 72% probability that a rupture status indicated by the model was indeed a ruptured IA. Conversely, if the model indicated a non-ruptured aneurysm, the probability that the aneurysm was truly non-ruptured was 93% (Fig. 5).

Validation set

In the validation set, a meta-analysis of 16 validation cross-tables was conducted, yielding the following summary statistics for sensitivity, specificity, PLR, NLR, diagnostic OR, and SROC curve: 0.84 (95% CI: 0.76–0.90), 0.82 (95% CI: 0.77–0.86), 4.7 (95% CI: 3.7–5.8), 0.19 (95% CI: 0.13–0.29), and 24 (95% CI: 15–40), respectively (Figs. 6 and 7). Deek's funnel plot indicated no publication bias in the assessment of radiomics for detecting IA rupture status in the validation set ($P = 0.05$) (Fig. 8). Approximately 36% of patients in the eligible studies had ruptured IA, which was used as the prior probability. Given a PLR of 4.7, if the model suggests a ruptured status, the probability of an actual ruptured IA is 72%; if the model suggests a non-ruptured aneurysm, the probability of an actual non-ruptured aneurysm is 90% (Fig. 9).

Review of predictive accuracy

Among the studies included, only two reported predictions of rupture risk for UIA based on radiomics. In light of the limited studies, only a summary could be provided. In the

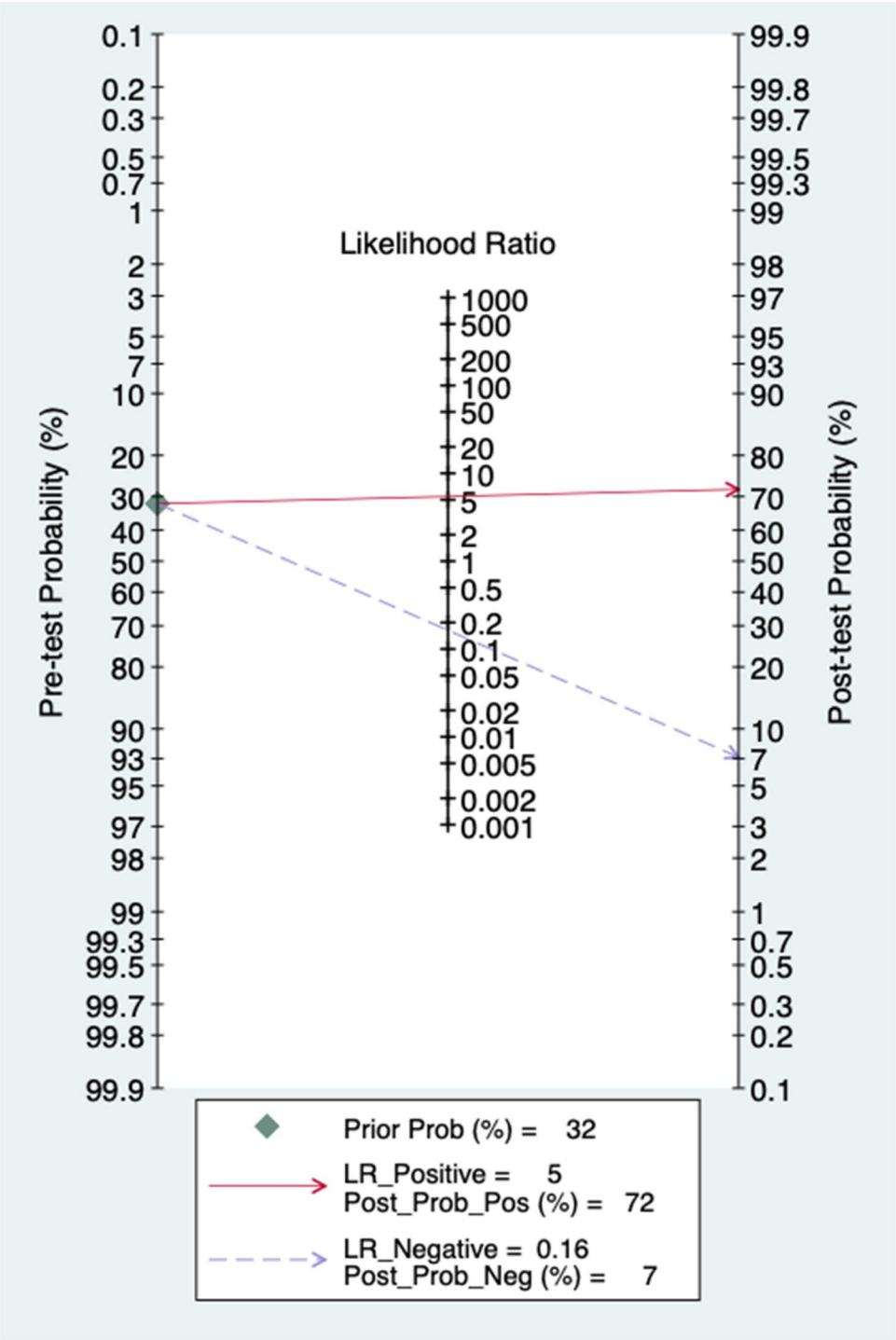

Fig. 5 Nomogram of meta-analysis for radiomics in determining IA rupture status in the training set

study by Chubin Ou et al. [19], radiomics showed a sensitivity of 0.865, specificity of 0.687, PLR of 2.764, NLR of 0.197, and diagnostic OR of 14.064 for predicting aneurysm rupture risk. The study by Yi Yang et al. [17] reported an AUC of 0.816 in the training set, with sensitivity and specificity of 0.7667 and 0.8658, respectively, demonstrating significant statistical relevance.

Assessment of study quality

Of the 15 studies, nine did not offer detailed imaging protocols, thus scoring zero points for the first criterion. Seven studies did not mention methods for segmenting multiple images, resulting in zero points for the second criterion. None of the studies employed repeated

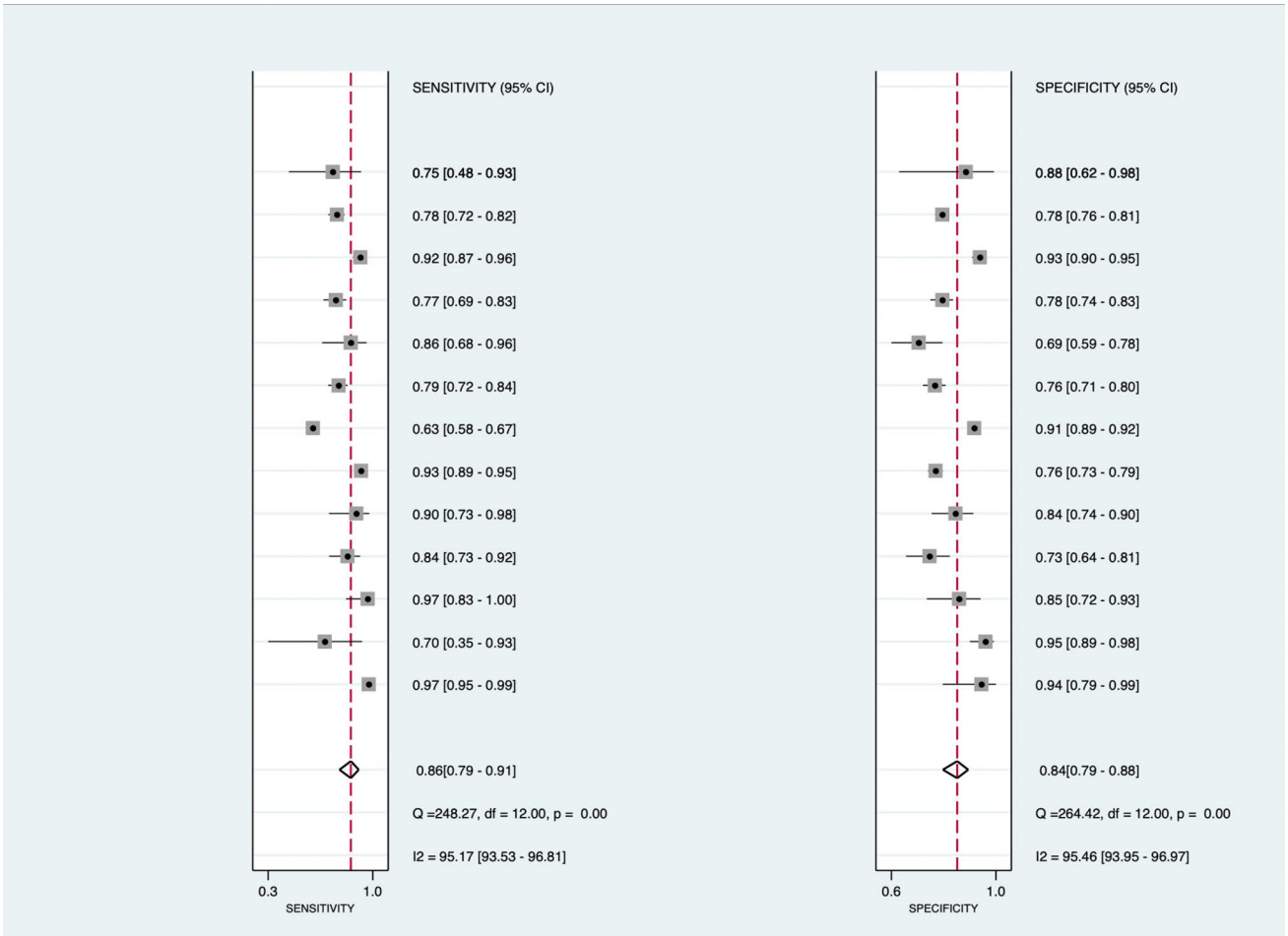

Fig. 6 Forest plot of meta-analysis showing sensitivity and specificity of radiomics for differentiating IA rupture status in the validation set

measurements across different images or imaging at multiple time points, leading to zero points for the third, fourth, and fifth criteria. Six studies did not address multivariable analysis with non-radiomic features, thus scoring zero for the sixth criterion. None of the studies examined or discussed biological relevance, leading to zero points for the seventh criterion. Twelve studies did not perform cutoff value analysis, resulting in zero points for the eighth criterion. Twelve studies did not calibrate statistical data, thus scoring zero for the tenth criterion. Fourteen studies did not register prospective studies in trial databases, resulting in zero points for the eleventh criterion. All studies did not compare with a "gold standard", leading to zero points for the thirteenth criterion. Twelve studies did not report potential clinical applications, thus scoring zero for the fourteenth criterion. None of the studies conducted a cost-effectiveness analysis, leading to zero points for the fifteenth criterion. Three studies did not publicly disclose corresponding codes and data, resulting in zero points for the sixteenth criterion. The final average score for the included studies was 7.4 points.

Discussion

Summary of the main findings

Radiomics-based machine learning models demonstrated relatively ideal accuracy in diagnosing IA rupture, with sensitivity and specificity of 0.84 (95% CI: 0.76–0.90) and 0.82 (95% CI: 0.77–0.86), respectively. For predicting the future rupture risk in UIA, only a small number of studies have been included, yet they also exhibited relatively satisfactory accuracy.

Comparison with previous reviews

Previous research has also reviewed various potentially viable methods for diagnosing IA rupture status. For instance, a systematic review and meta-analysis were carried out by Mohammad Amin Habibi et al. [30] to assess the potential of artificial intelligence algorithms in forecasting the risk of cerebral aneurysm rupture. Their study reported sensitivity, specificity, diagnostic OR, diagnostic score, and AUC

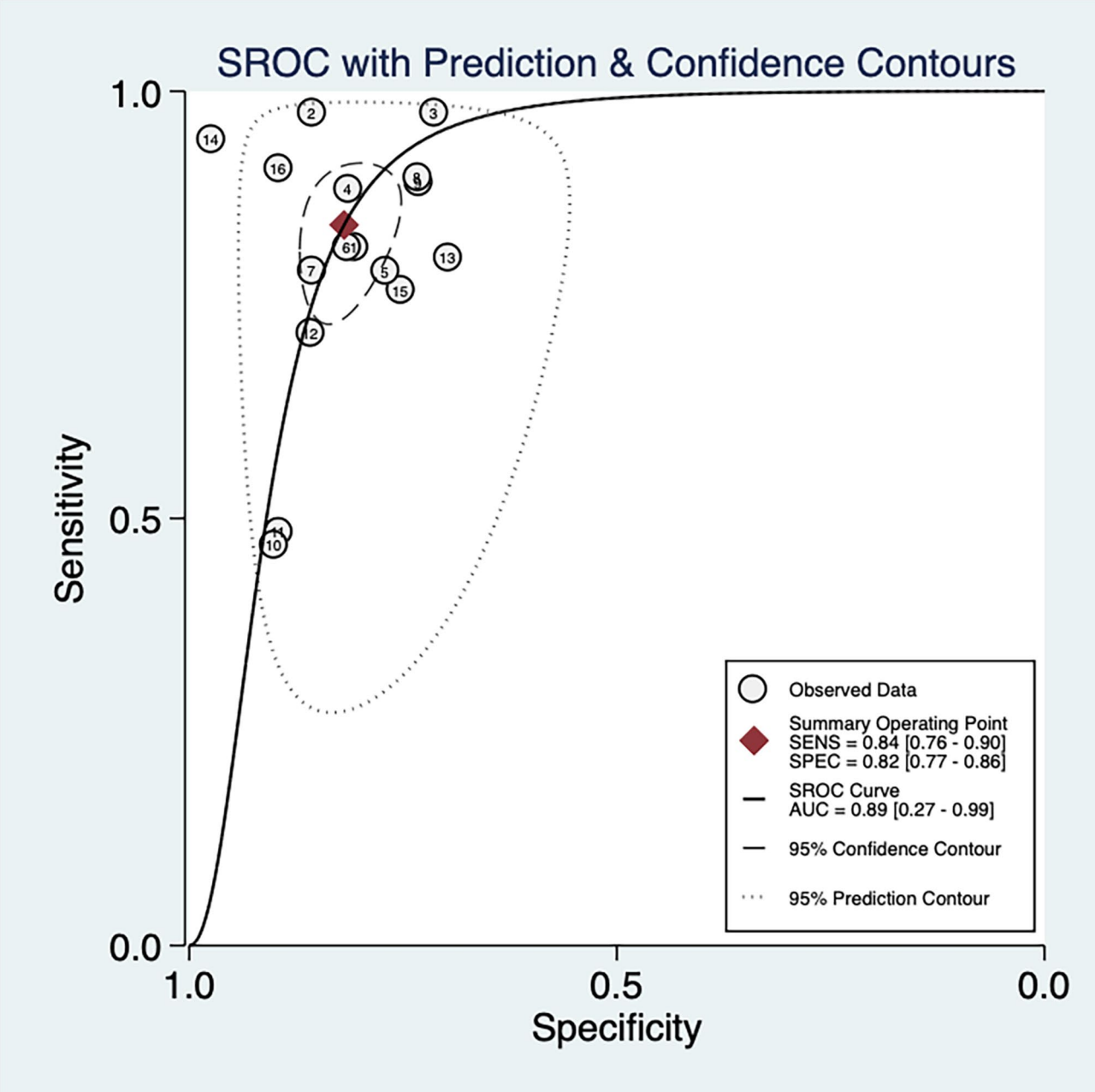

Fig. 7 SROC curve from meta-analysis assessing radiomics for differentiating IA rupture status in the validation set

of 0.83, 0.83, 23.7, 3.2, and 0.90, respectively. Their findings prove that ML algorithms are effective for predicting aneurysm rupture risk, with good sensitivity, specificity, AUC, and accuracy. However, further research is needed to enhance these algorithms' diagnostic performance for aneurysm rupture.

Wei Zhu et al. [31] performed a stability study using clinical and imaging data of IA, revealing significant advantages of machine learning models in stability analysis of unruptured aneurysms, with the AUC, specificity and accuracy being 0.867, 92.9% and 82.4%, respectively.

Yu Ye et al. [32] constructed and validated a classification model combining CTA radiomics data with clinical factors for differentiating between ruptured and unruptured small IA (< 5 mm). The model was able to predict the rupture state with an AUC of 0.87 in the training cohort and 0.85 in the test cohort.

Furthermore, a diagnostic meta-analysis of machine learning algorithms for assessing rupture risk in IA [33] provided summary diagnostic values as follows: sensitivity, 0.84 (95% CI: 0.75–0.90); specificity, 0.78 (95% CI: 0.68–0.85); PLR, 3.8 (95% CI: 2.4–5.9); and NLR, 0.21

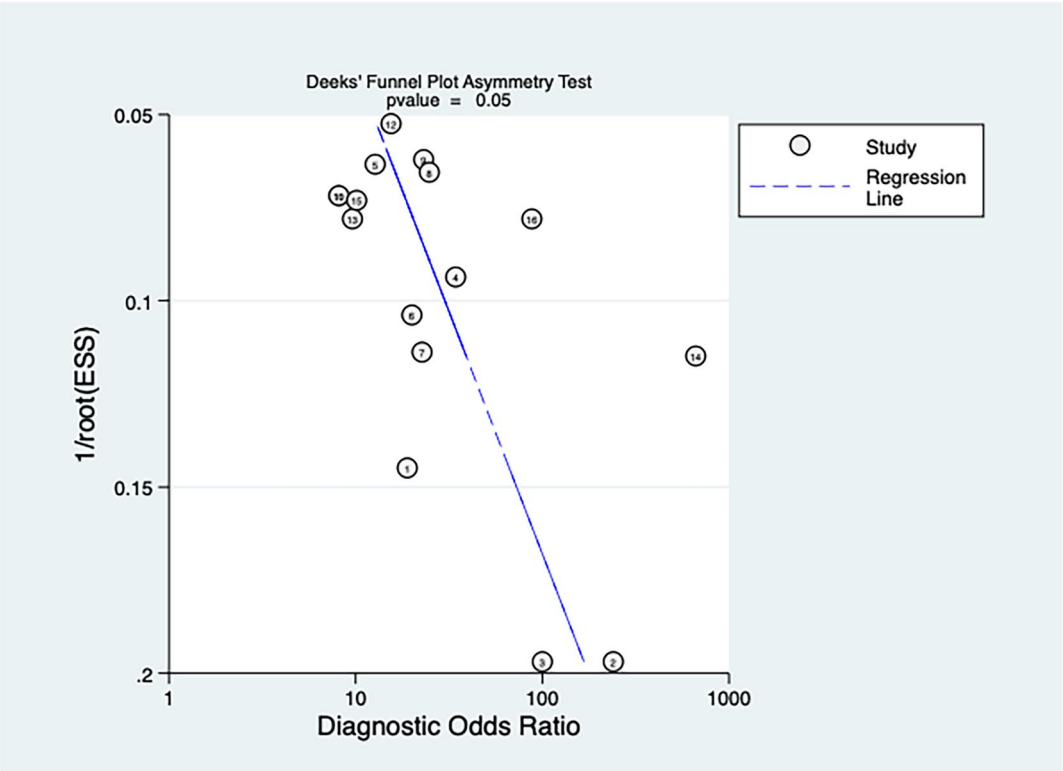

Fig. 8 Deek's funnel plot from meta-analysis evaluating radiomics for IA rupture status in the validation set

(95% CI: 0.12–0.35). This supports the prospect of artificial intelligence algorithms for the IA rupture risk evaluation. Currently, machine learning models for IA rupture mainly involve hemodynamics, clinical features, and radiomics. Although many researchers have applied machine learning to diagnose IA, the accuracy appears significantly influenced by varying modeling variables. Therefore, our study focused solely on radiomics-based methods.

In carrying out research on radiomics, it is crucial to thoroughly consider the significance of clinical characteristics in disease diagnosis and prediction. The RQS scale recommends integrating clinical factors, gene-protein expressions, and other relevant factors. However, in practical studies, there is a greater emphasis on incorporating clinical factors, as they may serve as interpretable variables for certain diseases. Yet, among all selected studies, few explored the integration of radiomics with clinical features. Since there are a very limited number of such studies, no further discussion was provided.

In clinical practice, real-time monitoring of the rupture risk for UIA holds significant clinical value. This allows clinicians to devise early preventive strategies based on the patient's rupture risk. However, current research seems to focus on only a rather limited set of studies concerning the rupture risk prediction in UIA during the patient's future life. Our meta-analysis included only two studies that assessed the risk of rupture in patients with UIA. The results of these studies exhibited relatively ideal accuracy, suggesting that radiomics-based machine learning might be feasible for the early prediction of rupture risk in UIA. Nevertheless, this conclusion is drawn from limited evidence and necessitates further validation.

Limitations of the study

Our study has several limitations: (1) Although we undertook a systematic search, the inclusion of radiomics-based machine learning studies remains relatively limited; (2) A significant amount of the included studies involved internal validation from random sampling, which may constrain the result interpretation; (3) The selected articles were primarily on diagnostic tasks, and only a few addressed predictive tasks. More research is needed to verify the accuracy. (4) The included studies were mainly retrospective studies, which may have cause biased results. It is impossible to determine the consistency of image acquisition settings or the specific scanners used across studies, which may cause some bias in the results. (5) The original studies did not report whether all scans came from different devices in their unit. Hence, we did not discuss it deeply, which may have caused some bias in the results. (6) In addition,

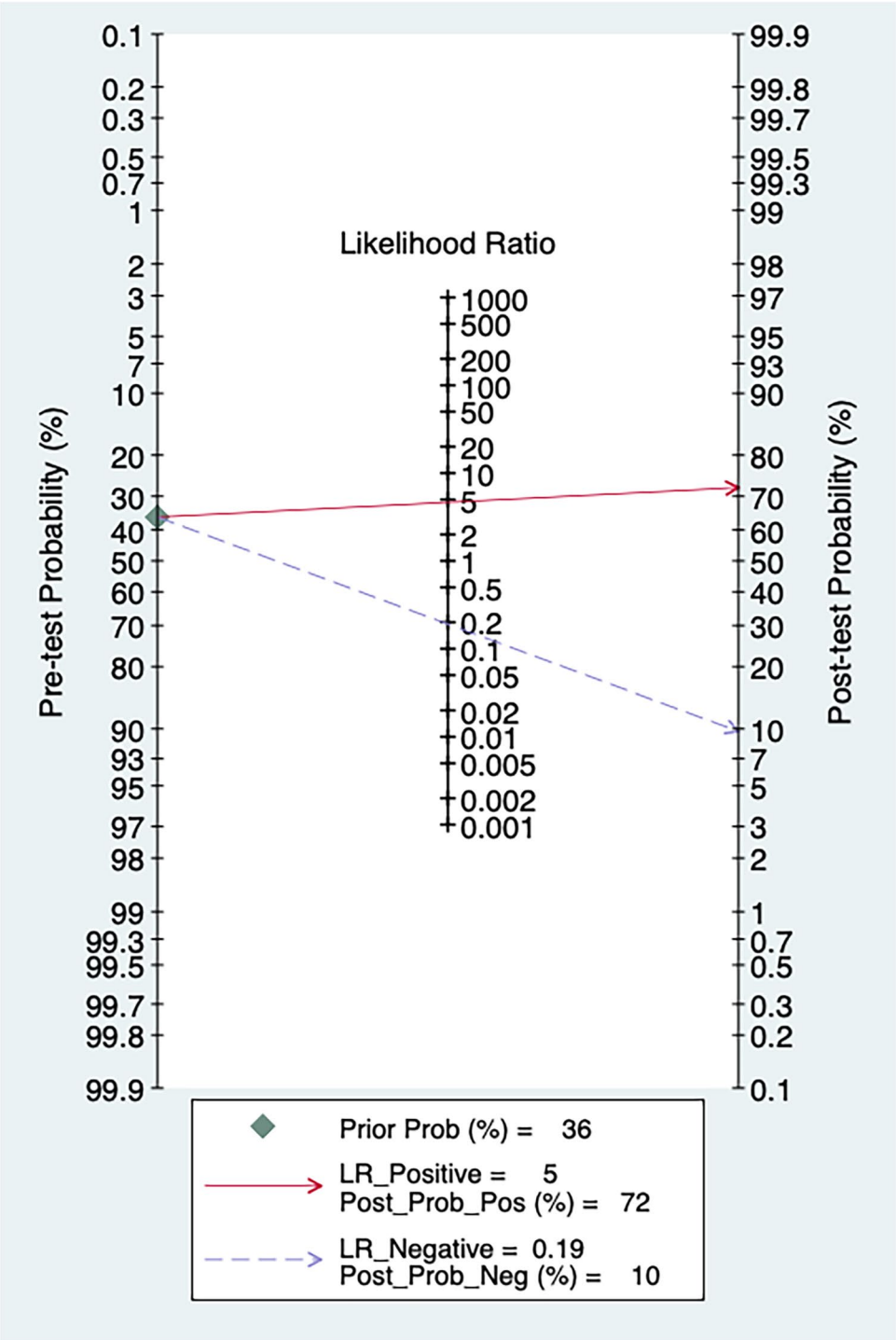

Fig. 9 Nomogram of meta-analysis for radiomics in determining IA rupture status in the validation set

due to the extremely limited number of included studies, which mainly used DSA and CTA data, we did not deeply discusse the resolution and image quality of these three types of data. Therefore, future studies should evaluate the advantages of radiomics based on DSA and CTA. The above limitations may have a certain impact on the interpretation of our results. In future studies, we should consider adjusting these potential limitations.

Conclusions

Our research suggests that radiomics-based machine learning demonstrates promising accuracy for early differentiation of rupture status in IA. Aggregated results reveal that radiomics-based machine learning is both sensitive and specific for early identification of rupture status in IA. However, evidence for predicting rupture status is

exceedingly sparse. Therefore, future research should further validate the prediction of rupture status in IA. Additionally, in light of the limited volume of studies employing deep learning models, future studies should prioritize the development of machine learning and deep learning models for predicting and diagnosing the rupture risk of IA to enable intelligent differentiation.

Supplementary Information The online version contains supplementary material available at 网址https://doi.org/10.1007/s10143-024-03086-5.

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Author contributions All authors contributed to the study conception and design. Writing - original draft preparation: Jianguo Zhong, Yu Jiang, Qiqiang Huang, Shaochun Yang; Writing - review and editing: Jianguo Zhong; Conceptualization: Jianguo Zhong, Yu Jiang; Methodology: Jianguo Zhong; Formal analysis and investigation: Jianguo Zhong, Yu Jiang, Qiqiang Huang; Funding acquisition: Shaochun Yang; Resources: Shaochun Yang; Supervision: Shaochun Yang, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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