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Predictive value of magnetic resonance angiography combined with serum ischemia-modified albumin for secondary cerebral infarction after transient ischemic attack

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Abstract

Objective This study investigated the diagnostic value of magnetic resonance angiography (MRA) combined with serum ischaemia-modifier albumin (IMA) testing in predicting secondary cerebral infarction (CI) following transient ischemic attack (TIA).

Methods All TIA patients underwent MRA and IMA level assessments, along with $ABCD^2$ scoring (a TIA risk stratification tool). Patients were categorized into secondary CI and non-CI groups based on the occurrence of CI within a 90-day follow-up period. Vessel stenosis, serum IMA levels, the predictive value of MRA and IMA levels for secondary CI after TIA, and the independent factors associated with secondary CI in TIA patients were analyzed.

Results The high-risk and intermediate-risk groups showed a higher proportion of moderate-severe vessel stenosis and elevated IMA levels compared to the low-risk group, with IMA levels significantly higher in the high-risk group than in the intermediate-risk group ($P<0.05$). The secondary CI group exhibited a greater proportion of moderate-severe vessel stenosis and higher IMA levels compared to non-CI group ($P<0.05$). The combined predictive model using MRA and IMA demonstrated a significantly higher area under the curve (AUC = 0.908) compared to MRA alone (AUC = 0.798; z = 3.083, $P=0.002$), but only slightly higher than IMA alone (AUC = 0.875; z = 1.226, $P=0.220$). Independent factors associated with secondary CI included advanced age, moderate-severe vessel stenosis, $ABCD^2$ scores, and elevated IMA levels (OR > 1, $P<0.05$).

Conclusion Changes in MRA and IMA levels were correlated with disease severity in TIA patients. MAR combined with serum IMA demonstrated high predictive efficacy for secondary CI after TIA, making it a valuable tool for CI risk assessment. Independent factors associated with secondary CI included advanced age, moderate-severe vessel stenosis, intermediate-high-risk $ABCD^2$ scores, and elevated IMA levels.

Keywords Transient ischemic attack, Secondary cerebral infarction, Magnetic resonance angiography, Ischaemia modifier albumin, Predictive value

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Introduction

Transient ischemic attack (TIA) is defined as a reversible neurological deficit resulted from transient focal and temporary ischemia of the central nervous system [1]. Common symptoms of TIA are sudden and transient, including unilateral paresis, monocular blindness, and speech disturbance [2]. TIA is a significant risk factor for cerebral infarction (CI) [3], with approximately one-third of TIA patients progressing to CI [4]. As TIA servers as an early warning for CI, identifying sensitive biomarkers for its diagnosis and prognosis is crucial for developing optimal intervention strategies. Early detection of ischemia modified albumin (IMA) has proven valuable in the diagnosis of posterior circulation TIA and the prediction of secondary CI [5].

Magnetic resonance angiography (MRA) is a powerful tool for evaluating arterial and venous pathologies in both upper and lower extremities [6]. It encompasses various imaging techniques based on magnetic resonance imaging to assess arterial and venous systems [7]. MRA is widely utilized in predicting ischemic stroke [8], and can provide insights into the mechanisms of TIA [9]. IMA is a modified form of serum albumin produced under oxidative stress conditions [10]. It serves as an oxidative stress marker, reflecting the presence and severity of oxidative stress [11]. A previous study has demonstrated that IMA is a sensitive and rapid biomarker for early ischemic stroke screening [12]. Monitoring IMA levels in acute ischemic stroke patients may aid in predicting clinical outcomes and disease progression [13]. Elevated serum IMA levels have been observed in patients with acute ischemic stroke and are correlated with ischemic tissue volume [14]. IMA has also been shown to be a useful diagnostic marker for ischemic diseases and cerebrovascular disorders. Moreover, IMA measurement can differentiate between subarachnoid hemorrhage and brain infarction during the acute phase of cerebrovascular events [15]. Building upon these findings, we recognized a gap in research regarding the combined role of MRA and serum IMA in predicting and diagnosing secondary CI after TIA. Therefore, this study aims to evaluate the predictive and diagnostic value of combining MRA with serum IMA testing for secondary CI in patients with TIA.

Materials and methods

Ethics statement

This study was approved by the Ethics Committee of Cangzhou Central Hospital (approval number: 2021-219-02 (z)), and the patients and their families signed written informed consent. The study was performed in accordance with the Helsinki declaration.

Study subjects

Ninety-eight TIA patients admitted to our hospital between December 2021 and June 2022 were enrolled, comprising 57 males and 41 females, with a mean age of 63.27 ± 5.04 years. Inclusion criteria: ① patients with a sudden onset of neurological deficits whose symptoms and signs completely resolved within 24 h; ② patients who underwent MRA examination within 24 h of symptom onset; ③ patients without hemorrhage, mass effect, or other lesions that could account for the clinical symptoms, as confirmed by the examination; ④ patients with complete clinical data. Exclusion criteria: ① patients with symptom duration exceeding 24 h; ② those with a history of coronary artery disease, valvular heart disease, stroke, pulmonary embolism, or systemic embolic diseases; ③ those with prosthesis, stent implants, or claustrophobia; ④ those with a history of major surgery or trauma within one month before symptom onset. ⑤ those with severe liver or kidney dysfunction or malignant tumors; ⑥ those with abnormal stress test results within 24 h; ⑦ Pregnant individuals.

MRA examination

All patients underwent MRA examination using a 3.0T magnetic resonance imaging machine (GE, USA) equipped with an 8-channel head coil. The scanning protocol employed the 3D time-flight method with the following parameters: echo time (TE) 7.9 ms, repetition time (TR) 3196 ms, and inversion time (TI) 960 ms; T2-FLAIR scanning parameters included TE115 ms, TR10024 ms, and TI2300 ms, while the T2-fast spin echo (FSE) sequence parameters were TE118 ms, and TR5100 ms. The slice thickness, matrix, and spacing were set to 5 mm, 128 × 128, and 1.0 mm, respectively. The main trunk and branches of the anterior, middle, and posterior cerebral arteries, as well as the basilar and vertebral arteries, were scanned. The location, size, and degree of infarction of lesions were carefully observed. Images were processed using a workstation and independently viewed by two experienced radiologists. Disagreements were resolved through consultation to reach a consensus. Based on MRA findings, stenosis was assessed by measuring lumen diameter shortening and signal loss: Severe stenosis-occlusion: Diameter shortening > 75% or complete signal loss. Moderate stenosis: Diameter shortening of 50-75%. Normal-mild stenosis: Diameter shortening < 50%.

$ABCD^2$ scoring system and grading methods

The $ABCD^2$ scoring system included the following parameters: age ≥ 60 years (1 point); first systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg after TIA onset (1 point); unilateral limb weakness (2 points); speech disorder without

Table 1 MRA and IMA in patients with different $ABCD^2$ scores

Grouping	*N*	Moderate-severe vessel stenosis	IMA (U/L)
The low-risk group	34	11 (32.35%)	64.16 ± 7.12
The intermediate-risk group	36	28 (77.78%)*	70.19 ± 14.59*
The high-risk group	28	26 (92.86%)*	86.22 ± 10.66*#

Note: *$P < 0.05$ vs. the low-risk group; #$P < 0.05$ vs. the intermediate-risk group

Table 2 MRA and IMA between patients with secondary CI and those without CI

Grouping	*N*	Moderate-severe vessel stenosis	IMA (U/L)
The secondary CI group	34	32 (94.12%)	89.04 ± 9.07
The non-CI group	64	33 (51.56%)	63.98 ± 7.30
P value		< 0.001	< 0.001

limb weakness (1 point); symptom duration ≥ 60 min (2 points); symptom duration of 10–59 min (1 point); diabetes mellitus (1 point). The total score ranged from 0 to 7 points. Patients were categorized into three risk groups: low-risk (≤ 3 points), intermediate-risk (4–5 points), and high-risk (≥ 6 points) groups [16].

IMA test

At the time of admission, 4 mL of venous blood was collected from each patient. The serum was centrifuged at 3000 r/min for 10 min and stored at -80 ℃ for subsequent measurement. IMA levels were measured using the albumin-cobalt binding (ACB) method, with the IMA assay kit supplied by Medicalsystem Biotechnology Co., Ltd. (Ningbo, Zhejiang, China).

Secondary CI follow-up

After admission, all patients received appropriate treatment based on their condition and were registered for follow-up. Patients were monitored for the occurrence of secondary CI within 90 days after TIA. Secondary CI was diagnosed by a neurologist based on the presence of a new infarct in the same responsible vessel observed during MRA examination, accompanied by corresponding clinical symptoms and signs. Patients were categorized into a secondary CI group or a non-CI group according to the presence or absence of secondary CI during the follow-up period [17].

Statistical analysis

Data were processed using SPSS 22.0 software (SPSS Inc, Chicago, IL, USA) and GraphPad Prism 6.0 software (Graph Pad Inc., La Jolla, CA, USA). Measurement data were assessed for normality and homogeneity of variance. Variables meeting the assumptions of normal distribution and homogeneity of variance were depicted as mean ± standard deviation ($\overline{x} \pm s$). Categorical data were expressed as n (%). For between-group comparisons, measurement data were analyzed by the t-test. Categorical data were analyzed by the χ^2 test. The predictive value of MRA and IMA for secondary CI in TIA patients was evaluated using receiver operating characteristic (ROC) curves. Logistic regression analysis was implemented to identify independent factors affecting secondary CI in TIA patients. A significance level of $\alpha = 0.05$ was applied, and a *P*-value < 0.05 was considered statistically significant.

Results

Patient baseline data and secondary CI follow-up results

Among the 98 patients, 51 (52.04%) had hypertension; 21 (21.43%) had diabetes mellitus; 31 (31.63%) had lipid metabolism disorders, 27 (27.55%) were cigarette smokers, and 20 (20.41%) consumed alcohol. The mean $ABCD^2$ scores were 4.42 ± 1.51. Within 90 days after TIA, 34 patients (34.69%) developed CI.

MRA findings and IMA levels in patients with different $ABCD^2$ scores

Based on the $ABCD^2$ scores, the 98 TIA patients were categorized into low-risk ($n = 34$), intermediate-risk ($n = 36$), and high-risk ($n = 28$) groups. The proportion of moderate-to-severe vessel stenosis and IMA levels in the high-risk and intermediate-risk groups were significantly higher than in the low-risk group, while IMA levels in the high-risk group were significantly higher than those in the intermediate-risk group ($P < 0.05$). However, no significant difference in the proportion of moderate-to-severe vessel stenosis was observed between the high-risk and intermediate-risk groups ($P > 0.05$). These results suggest that MRA indicators and changes in IMA levels are associated with the severity of disease in TIA patients (Table 1).

MRA findings and IMA levels in patients with and without secondary CI

Patients in the secondary CI group exhibited a higher proportion of moderate-to-severe vessel stenosis and elevated IMA levels compared to the non-CI group ($P < 0.05$), suggesting that changes in MRA and IMA levels had potential reference value for assessing TIA progression (Table 2).

Table 3 Predictive value of MRA and IMA for secondary CI in TIA patients

Items	AUC	95% CI		Sensitivity	Specificity	Youden index	Cutoff value
		Lower limit	Upper limit				
MRA	0.798	0.712	0.884	76.5	71.9	0.484	> 53%
IMA	0.875	0.798	0.951	88.2	76.6	0.648	> 77.25U/L
The combined diagnosis	0.908	0.849	0.966	91.2	85.9	0.771	-

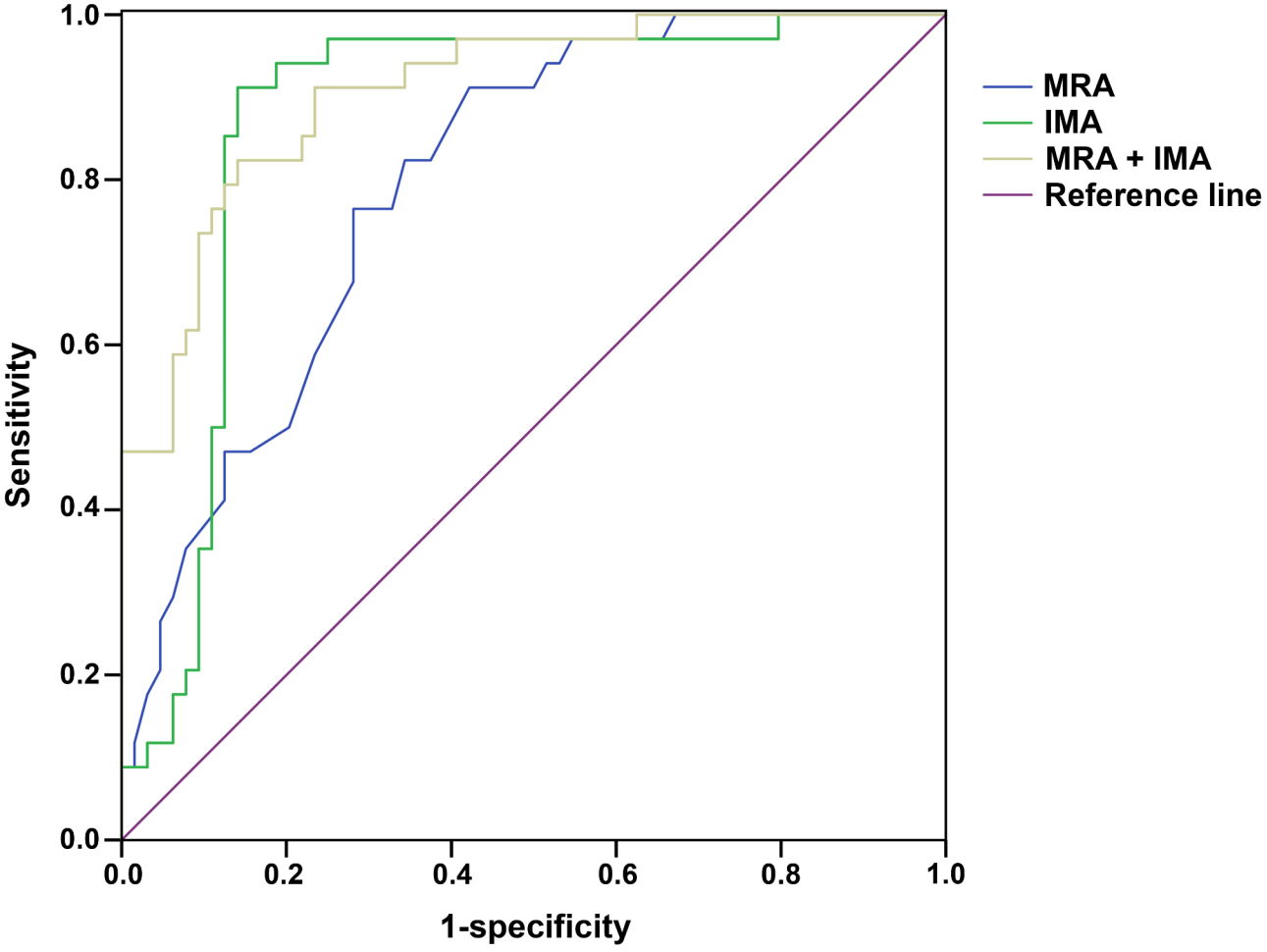

Fig. 1 ROC curves of MRA and IMA levels predicting secondary CI in TIA patients

Predictive value of MRA and IMA levels for secondary CI in TIA patients

The area under the curve (AUC) for predicting secondary CI was 0.798 (95% CI: 0.712–0.884) for MRA alone and 0.875 (95% CI: 0.798–0.951) for IMA alone. When combining MRA and IMA, the AUC increased to 0.908 (95% CI: 0.849–0.966). Further comparisons of the AUC values revealed that the combined prediction (MRA + IMA) had a significantly higher AUC than MRA alone ($z = 3.083$, $P = 0.002$). However, the combined prediction was only slightly higher than IMA alone, and the difference was not statistically significant ($z = 1.226$, $P = 0.220$), which suggested that the combination of MRA and IMA has certain predictive value for secondary CI in TIA patients. (Table 3; Fig. 1).

Uni-variate analysis of factors affecting secondary CI in TIA patients

Univariate analysis revealed that age, hypertension, lipid metabolism disorders, moderate-severe vessel stenosis, $ABCD^2$ scores, and IMA levels were associated with the progression of TIA to CI ($P < 0.05$). Gender, diabetes, smoking, and alcohol consumption were not associated with the progression of TIA to CI ($P > 0.05$) (Table 4).

Table 4 Uni-variate analysis of factors affecting secondary CI in TIA patients

Items	The secondary CI group ($n=34$)	The non-CI group ($n=64$)	*P* value
Gender			0.831
Male	19 (55.88%)	38 (59.38%)	
Female	15 (44.12%)	26 (40.63%)	
Age	65.76 ± 4.76	61.94 ± 4.70	< 0.001
Hypertension			0.011
Yes	24 (70.59%)	27 (42.19%)	
No	10 (29.41%)	37 (57.81%)	
Diabetes mellitus			0.797
Yes	8 (23.53%)	13 (20.31%)	
No	26 (76.47%)	51 (79.69%)	
Lipid metabolism disorders			< 0.001
Yes	20 (58.82%)	11 (17.19%)	
No	14 (41.18%)	53 (82.81%)	
Smoking			0.814
Yes	10 (29.41%)	17 (26.56%)	
No	24 (70.59%)	47 (73.44%)	
Drinking			0.301
Yes	9 (26.47%)	11 (17.19%)	
No	25 (73.53%)	53 (82.81%)	
Vessel stenosis degree			< 0.001
Normal-mild vessel stenosis	2 (5.88%)	31 (48.44%)	
Moderate-severe vessel stenosis	32 (94.12%)	33 (51.56%)	
$ABCD^2$ scores			< 0.001
Low-intermediate-risk	9 (26.47%)	61 (95.31%)	
High-risk	25 (73.53%)	3 (4.69%)	
IMA (U/L)	89.04 ± 9.07	63.98 ± 7.30	< 0.001

Table 5 Multivariate analysis of factors affecting secondary CI in TIA patients

Items	β	SE	Wald	*P* value	Exp(B)	95% CI	
						Lower limit	Upper limit
Age	9.084	0.602	8.471	0.008	10.941	3.169	12.258
Hypertension	0.290	0.288	0.051	0.822	0.748	0.060	9.345
Lipid metabolism disorders	1.053	1.414	0.550	0.456	0.349	0.022	5.572
Moderate-severe vessel stenosis	5.373	1.424	4.230	0.006	7.114	2.105	7.906
$ABCD^2$ scores	9.294	1.747	8.299	0.047	5.331	3.082	7.779
IMA	4.657	1.566	6.040	0.010	5.685	2.513	6.956

Multivariate analysis of factors affecting secondary CI in TIA patients

Using the progression of TIA to CI as the dependent variable (assigned 1 for progression to CI and 0 for no progression), and the statistically significant indicators from Table 4 as independent variables, logistic regression analysis was performed. The analysis revealed that age, moderate-severe vessel stenosis, $ABCD^2$ scores, and IMA levels were independent factors for secondary CI in patients with TIA ($P<0.05$). These findings highlight that these factors significantly influence the progression of TIA to CI (Table 5).

Discussion

TIA is a crucial risk factor for acute CI [18]. This paper aimed to evaluate the diagnostic value of MRA combined with serum IMA testing for predicting secondary CI after TIA. As previously reported, IMA has a significant association with the secondary CI, with serum IMA levels increased after TIA onset [5]. Serum IMA levels have been shown to correlate with artery stenosis and short-term prognosis in acute CI patients. In addition, elevated serum IMA levels are observed in CI patients, with higher serum IMA levels in those exhibiting severe stenosis compared to those with mild stenosis [19]. The $ABCD^2$ scoring system (incorporating age, blood pressure, clinical presentation, diabetes mellitus, and duration of symptoms) is commonly used in the initial evaluation to assess the immediate risks of repeat

ischemia and stroke [2]. In this study, TIA patients were categorized into low-risk, intermediate-risk, and high-risk groups according to the $ABCD^2$ scores. Our findings revealed that the proportion of moderate-severe vessel stenosis and serum IMA levels were significantly higher in the high-risk and intermediate-risk groups compared to the low-risk group. Additionally, IMA levels in the high-risk group were significantly higher than those in the intermediate-risk group, suggesting that MRA findings and changes in IMA levels are associated with disease severity in TIA patients. Further analysis grouped patients into secondary CI and non-CI groups based on the occurrence of secondary CI. Patients in the secondary CI group showed higher proportions of moderate-to-severe vessel stenosis and elevated IMA levels compared to the non-CI group, indicating the potential value of MRA and IMA in assessing disease progression in TIA patients.

A previous study has demonstrated that combining $ABCD^2$ scores, diffusion weighted imaging (DWI), and MRA improves prediction accuracy for CI after TIA [4]. In our study, the combined prediction using MRA and IMA showed a significantly higher AUC than MRA alone, with a statistically significant difference. However, the combined prediction was only marginally superior to IMA alone, with no statistically significant difference. Existing research also suggests that $ABCD^2$ scores and carotid stenosis assessment via ultrasound are effective strategies for predicting CI in patients with TIA [3]. High $ABCD^2$ score, DWI lesions, and carotid artery stenosis are associated with a high risk of early ischemic stroke recurrence [1]. In our study, univariate analysis identified age, hypertension, lipid metabolism disorders, moderate-to-severe vessel stenosis, ABCD2 scores, and elevated IMA levels as factors influencing prognosis in TIA patients. Multivariate analysis revealed that advanced age, moderate-to-severe vessel stenosis, moderate-to-high-risk $ABCD^2$ scores, and elevated IMA levels were independent risk factors for secondary CI in TIA patients.

This study has notable strengths and limitations. On the positive side, the combination of MRA and serum IMA testing demonstrated high efficacy in predicting secondary CI after TIA. This approach effectively enhances prediction sensitivity, aiding in the clinical identification of high-risk CI patients and facilitating timely preventive and therapeutic interventions to improve prognosis. However, the study's findings are based on a limited dataset, restricting their generalizability to a broader TIA population. Future research with larger and more diverse cohorts is needed to further validate these findings.

Conclusion

In conclusion, this study highlights that changes in MRA findings and serum IMA levels are correlated with disease severity in TIA patients. The combination of MRA and serum IMA testing provides high predictive efficacy for secondary CI after TIA, offering a valuable tool for CI risk assessment. Advanced age, moderate-to-severe vessel stenosis, moderate-to-high-risk $ABCD^2$ scores, and elevated IMA levels were identified as independent risk factors for secondary CI in TIA patients, emphasizing the need for closer clinical supervision of such patients. This research provides a foundation for further investigation into the combined diagnostic value of MRA and serum IMA testing in secondary CI prediction following TIA.

Abbreviations

TIA	Transient ischemic attack
CI	Cerebral infarction
IMA	Ischemia modified albumin
MRA	Magnetic resonance angiography
TE	Echo time
TR	Repetition time
TI	Inversion time
FSE	Fast spin echo
ROC	Receiver operating characteristic
AUC	Area under the curve
DWI	Diffusion weighted imaging

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Author contributions

Lige Liu contributed to study design; Qiuyue Yan contributed to manuscript editing; Jingyi Ai and Rudong Jiao contributed to experimental studies; Meng Li contributed to data analysis. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethical approval and consent to participate

This study was approved by the Ethics Committee of Cangzhou Central Hospital (approval number: 2021-219-02 (z)), and the patients and their families signed written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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