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Research Article

Application of High-Resolution MRI and Contrast-Enhanced Ultrasound in The Stability of Carotid Atherosclerotic Plaque

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Abstracts

Purpose: Compare the evaluation value of high-resolution magnetic resonance (HRMRI) and contrast-enhanced ultrasound (CEUS) in the stability of carotid atherosclerotic plaque.

Method: We selected 71 patients with carotid artery color plaques in the Affiliated Hospital of Inner Mongolia Medical University from november2019 to november2020 and divided them into AIS group and non-AIS group according to whether they had internal carotid artery derived acute ischemic stroke (AIS). The patients in the two groups were examined by HRMRI and CEUS respectively to compare the detection of carotid vulnerable plaques and evaluate the consistency of the two examination methods.

Results: 1. There were 106 plaques in AIS group and 65 plaques in non-AIS group. Compared with the two groups, AIS group had more plaques and a larger proportion of vulnerable plaques. 2. HRMRI and CEUS can effectively identify vulnerable plaque. There is a significant difference in the detection rate of vulnerable plaque between the two groups (55.70%vs36.90%, 47.20%vs30.80%) (p=0.017, p=0.034). 3. In AIS group, the detection rate of vulnerable plaques in HRMRI was significantly higher than that in CEUS (55.70%vs36.90%) (p=0.005). The consistency of the two examinations was poor (kappa=0.269). HRMRI had a higher detection rate of vulnerable plaques.

Conclusion: HRMRI and CEUS can effectively distinguish vulnerable plaques. HRMRI has a higher detection rate of vulnerable plaques, and can refine plaque components, provide more valuable information for clinical diagnosis.

Keywords: Acute ischemic stroke; High resolution magnetic resonance imaging; Contrast-enhanced ultrasound; Plaque stability

Introduction

Acute ischemic stroke (AIS) is one of the main causes of disability and death all over the world [1]. Its high incidence rate, disability rate, recurrence rate and mortality rate have brought a heavy burden to people's lives. In recent years, with the in-depth study of cryptogenic stroke, the role of vulnerable plaque is gradually known. Many studies have proved that different components of vulnerable plaque are closely related to the occurrence of AIS from histology, morphology and other aspects.The presence of vulnerable plaque led to the reclassification of up to 15% of AIS etiological subtypes [2], which not only opened a new direction of AIS etiology research, but also put forward more thoughts for AIS risk stratification and intervention indication evaluation [3].With the emergence of “vulnerable plaque”, various examination methods emerge in endlessly. Whether it is a new ultrasonic examination method [4], or a new magnetic resonance examination sequence [5], they have played a great role in the detection of vulnerable plaque. This has made great progress in dynamically observing the pathological changes of plaques, evaluating the vulnerability of plaques, and predicting the occurrence of stroke.In this paper, the technology of high resolution magnetic resonance imaging (HRMRI) and contrast enhanced ultrasound (CEUS), which are currently the fastest-growing, are selected for the first comparative study. Our aim is to optimize the clinical vulnerable plaque examination program, realize the early screening of high-risk groups of cerebrovascular disease, and guide the clinical early intervention measures, so as to reduce the occurrence and development of ischemic stroke.

Materials and Methods

Research object

From November 2019 to November 2020, 71 patients (55 males and 16 females, aged 45-82 years, with an average age of 65.48 ± 6.68) with carotid plaque diagnosed by color Doppler ultrasound in the Affiliated Hospital of Inner Mongolia Medical University were included, including 40 patients with AIS and 31 patients without AIS. Inclusion criteria: 1 AIS patients who meet the latest diagnostic guidelines [6] and have an onset time of <3 days due to atherosclerosis of the internal carotid system; 2. Carotid endarterectomy, stent implantation and radiotherapy were not performed; 3. Patients who are not AIs are ordinary physical examiners with carotid plaque confirmed by color Doppler ultrasound;Exclusion criteria: 1 Patients with MRI contraindications; 2. Those who are allergic to contrast media and have renal insufficiency; 3. Patients with cerebral infarction caused by intracranial infection, tumor, cardiogenic, immune and vasculitis; 4. Patients with serious diseases who cannot cooperate with the examination;All patients completed CEUS and HRMRI examination within 1 week after the discovery of carotid plaque. The interval between the two examinations was less than 5 days, and they did not receive any plaque treatment during the examination. This study was approved by the hospital ethics committee (no. wz2022003), and all subjects knew and agreed to this study.

Hrmri examination

Philips intera Achieva 3.0T superconducting magnetic resonance scanner of Shanghai Hanfei and 8-channel coil for neck were used. The subject lies on his back with his head tilted back later, keeping still, while reducing the swallowing action and amplitude, and fully exposing the blood vessels of the neck. With the subject’s bilateral mandibular angle as the center to fix the coil, first perform 3D-TOF scanning of bilateral carotid arteries to determine the location of carotid bifurcation, and then scan the plaques within 3cm above and below with the carotid bifurcation as the center. The scanning sequences are T1WI (repetition time TR: 800.0 ms, echo time TE: 9.3 ~ 11.0 ms, repetition chain length ETL: 8, acquisition time 8 min, a total of 12 layers) T2WI (TR 2500 ~ 3700 ms; TE 40 ~ 70 ms, ETL 8, acquisition time 4 min, a total of 18 layers), 3D-TOF (TR 23.0 ms, TE 3.5 ms, turning angle 25, acquisition time 3 min, a total of 40 layers) and 3D MP-RAGE (TR 8.8 MS, TE 5.3ms, acquisition time 3 min, a total of 40 layers). The whole scanning process lasts for 40 minutes. Upload the images to the semi-automatic image processing software (MRI plaque view) for parameter measurement and quantitative analysis. Two imaging physicians above the level of deputy director use blind method to analyze all images independently, and the patient’s clinical information and image sequence information are hidden. Readers can adjust the window width and window level by themselves. According to the different signal intensity of different components of plaque on different sequences, the plaque components are evaluated (Table 1); According to the AHA plaque classification standard (type I-II: the thickness of the pipe wall is close to normal, and the pipe wall has no calcification; type III: the vascular intima is diffusely thickened or small eccentric plaque without calcification; type IV-V: large necrotic lipid core, plaque covered with fiber cap, with a small amount of calcification; type VI: plaque surface ulcer, plaque hemorrhage, thrombosis; type VII: calcified plaque; type VIII: fibrous plaque without lipid core, with a small amount of calcification) The plaque stability was evaluated. Type IV-VI was vulnerable plaque, and the other types were stable plaque. If the interpretation result is controversial, the final result shall be agreed by the two doctors through consultation (Table 1).

Table1: Comparison of signal intensity between different plaque components and ipsilateral sternocleidomastoid muscle.

Plaque Component	MRI Sequence			
	3D-TOF	T1W1	T2W2	3D MP-RAGE
Lipid necrosis core	0	+	+	0/-
Fiber cap	-	0/+	0/+	+/-
intra-plaque hemorrhage (Related to bleeding time)	+	+	+/-/0	+
Calcification in plaque	-	-	-	-
Loose matrix	0	-/0	+	0

*Note + High signal - Low signal 0 and other signals

Ceus examination

Toshiba aplio 500 ultrasonic diagnostic instrument, 11L4 probe, frequency of 4~11MHZ, double screen display, mechanical index of 0.07 was used for the inspection. When the examiner finds carotid plaque, fix the probe at the plaque, bolus inject 1.6ml of sonovane contrast agent with sufficient vibration through the median elbow vein, and push 5ml of normal saline at the same time, start the timer and start dynamic image acquisition at the same time. After 15~20s of timing, microbubble perfusion of contrast agent appears in the carotid lumen, and then record the perfusion of the shoulder (upper shoulder, lower shoulder), base and top of carotid plaque. For plaques with complex components, it is necessary to inject 0.8-1.0ml of contrast agent again through the middle elbow vein about 1.5min after injection of contrast agent, repeat the above observation process, observe whether there is dot and linear contrast agent enhancement in the plaques, record the image change process, and save the image with obvious plaque enhancement [7]. If the patient has multiple plaques in the same vessel, the above process needs to be repeated to ensure the accuracy of the observation results. The whole operation process was completed with the cooperation of an ultrasound doctor with more than 7 years and a technician with more than 5 years. Image post-processing analysis was performed by two associate chief physicians with more than 7 years of experience using the imaging grading semi quantitative analysis method. Plaque evaluation was carried out according to deyama plaque classification standard. Grade 0: no contrast microbubbles are found in the plaque; Grade I: microbubbles of contrast medium are limited to the shoulder and / or lateral membrane of the plaque; Grade II: diffuse microbubbles, linear, or blood flow sign in the plaque. Plaques with grade I-II characteristics are unstable plaques, and plaques with grade 0 characteristics are stable plaques.

Statistical method

SPSS 22.0 statistical software was used to analyze the data. The quantitative data in line with the normal distribution was expressed by $\bar{x}\pm S$. In the counting data, the ordered data used nonparametric rank sum test, and the disordered data used chi square test. $P < 0.05$ means that the difference is statistically significant; To judge the difference and consistency between CEUS and HRMRI, chi square test and kappa test were used.

Result

General information

A total of 71 patients were studied, including 40 patients in AIS group and 31 patients in non-AIS group. There was no significant difference in the age, sex, hypertension, diabetes, history of coronary heart disease, stroke and smoking between the two groups. The risk factors of the two groups were balanced and comparable ($P > 0.05$) (Table 2)

Table 2: Comparison of clinical data between AIS group and non-AIS group *n*%)

Project	AIS group (*n*=40)	non-AIS group (*n*=31)	*t/X² value*	*P value*
Age [years, x̄±s]	65.28±7.17	65.68±6.18	/	0.807
Male [number (%)]	29 (72.5)	26 (83.9)	1.294	0.255
Female [number (%)]	11 (27.5)	5 (16.1)	1.294	0.255
Hypertension [number (%)]	26 (65.0)	18 (58.1)	0.356	0.55
Diabetes [number (%)]	7 (17.5)	8 (25.8)	0.723	0.395
coronary heart disease [number (%)]	9 (22.5)	10 (32.3)	0.848	0.357
History of stroke [number (%)]	11 (27.5)	10 (32.3)	0.19	0.663
Smoking history [number (%)]	27 (67.5)	20 (64.5)	0.069	0.792

Detection of plaque on HRMRI

A total of 106 plaques were found in 40 patients in AIS group, including 32, 39, 20, 3 and 12 plaques of type I-II/III, IV-V, VI, VII and VIII, respectively. Therefore, 47 stable plaques and 59 vulnerable plaques were detected by HRMRI (the detection rate of vulnerable plaques was 55.7%, 59/106); There were 31 people in the non-AIS group, with a total of 65 plaques, of which 22, 14, 10, 10 and 9 were type I-II/III, IV-V, VI, VII and VIII plaques respectively. Therefore, 41 stable plaques and 24 vulnerable plaques were detected by HRMRI (the detection rate of vulnerable plaques was 36.9%, 24/65) (Figure 1); There was a significant difference in the detection rate of carotid plaque between AIS group and non-AIS group (p=0.017) (Figure 1 to 2, Table 3).

Table 3: Comparison of HRMRI plaque detection between AIS group and non-AIS group.

Group	Number of patches (PCs.)	Number of stable patches (PCs.)	Number of vulnerable patches (PCs.)	Detection rate of vulnerable plaque (%)	X^2 value	P value
AIS group	106	47	59	55.7	5.663	0.017
non-AIS group	65	41	24	36.9		

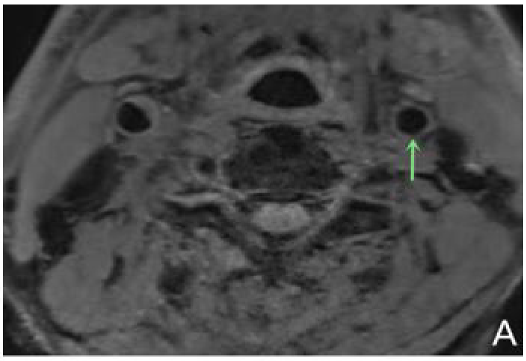
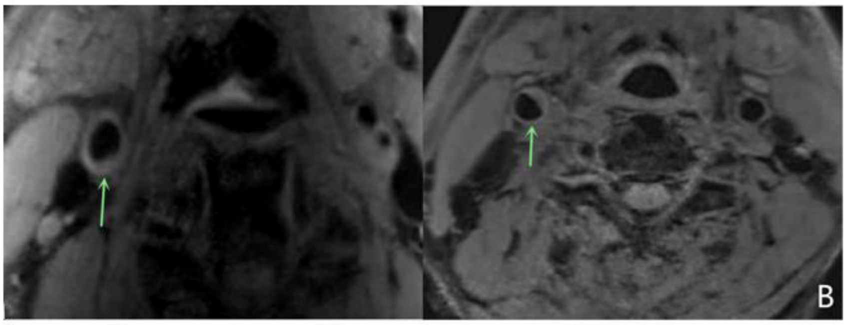
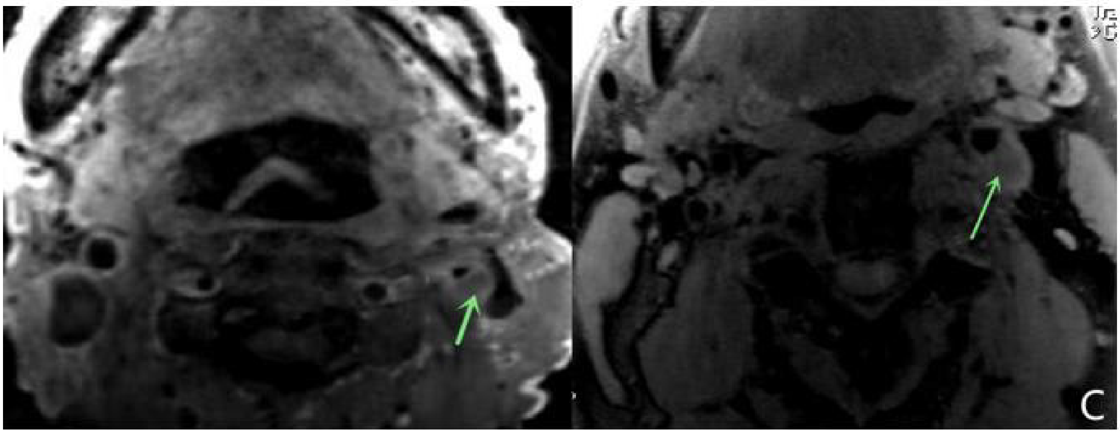


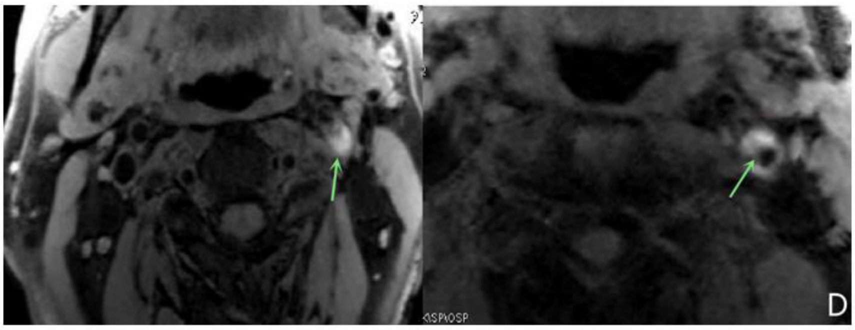
Figure 1: HRMRI:(I-II/III) Almost normal carotid wall thickening without calcification(A)



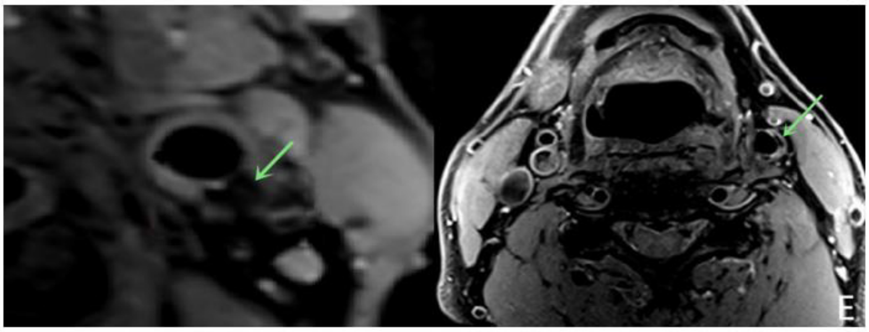
(III)Diffusely thickened carotid wall (Left of B) and Small eccentric calcified plaque in carotid lumen (right of B)



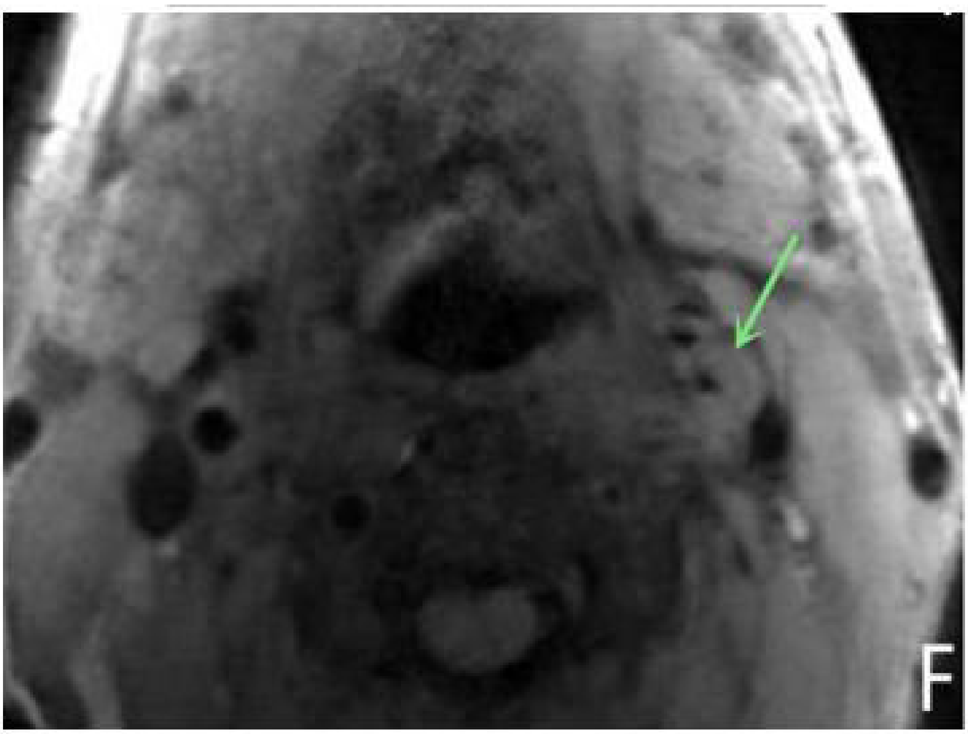
(IV-V) The plaque contains lipid core and thin fiber cap (Left of C) and Thick fiber cap (right of C)



(VI)The plaque contains ulcer and bleeding (Left of D) and Plaque contains hemorrhage and calcification (right of D).



(VII) Calcified plaque in carotid artery (E)



(VIII)The wall of carotid artery is significantly thickened, the lumen is narrow, and fibrous plaque is formed (F)

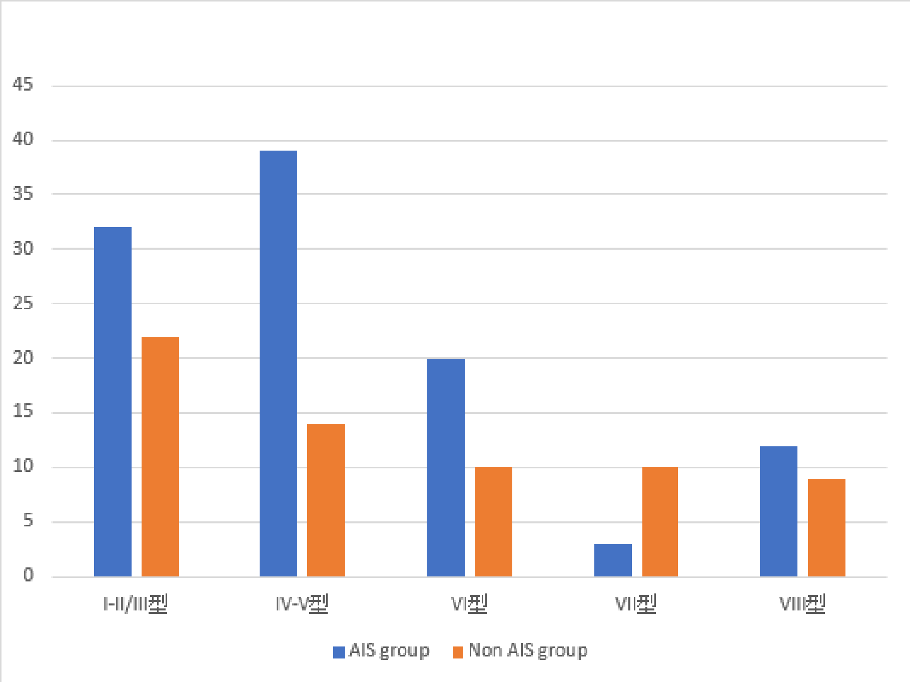


Figure 2: Detection of plaque on HRMRI

Plaque detection of ceus

In AIS group, there were 40 patients with a total of 106 plaques, of which 56 were grade 0, 23 were grade I, and 27 were grade II plaques. CEUS detected 56 stable plaques and 50 vulnerable plaques (the detection rate of vulnerable plaques was 47.2%, 56/106); There were 31 people in the non-AIS group, with a total of 65 plaques, of which the number of grade 0, grade I and grade II plaques were 45, 9 and 11 respectively. CEUS detected 45 stable plaques and 20 vulnerable plaques (the detection rate of vulnerable plaques was 30.8%, 20/65) (Figure 3); There was a significant difference in the detection rate of carotid plaque between AIS group and non-AIS group (p=0.034) (Figure 3 to 4, table 4).

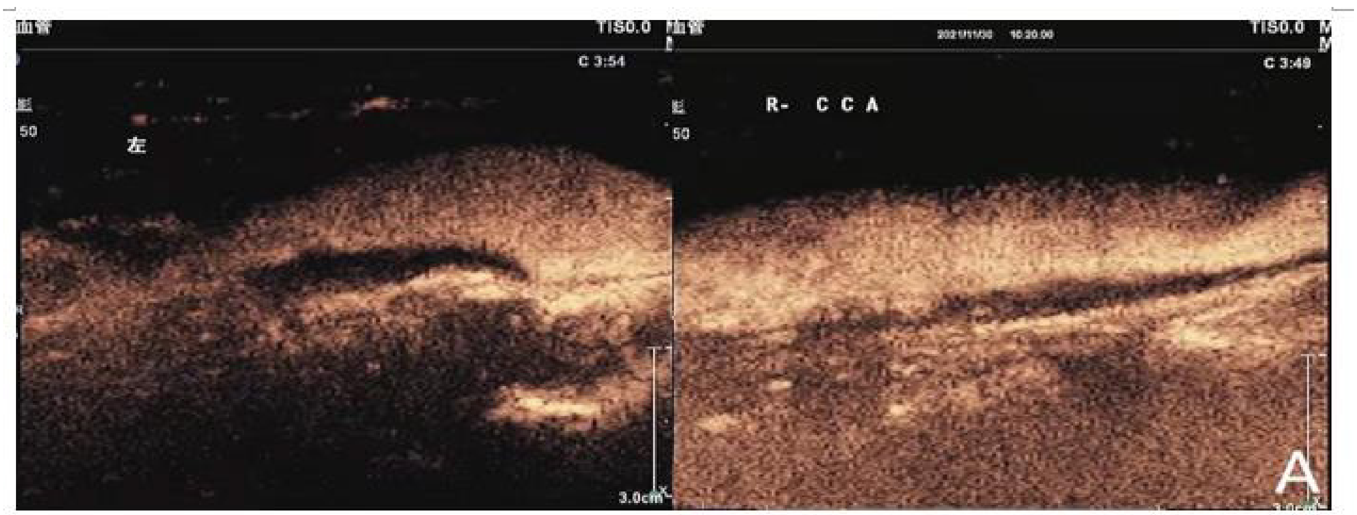


Figure 3: CEUS: (Level 0) Plaque on the distal anterior wall of the left common carotid artery (Left of A) and plaque on the posterior wall of the distal segment of the right common carotid artery(right of A) were no microbubbles of ultrasound contrast agent were found.

Table 4: Comparison of CEUS plaque detection between AIS group and non-AIS group.

group	Number of patches (PCs.)	Number of stable patches (PCs.)	Number of vulnerable patches (PCs.)	Detection rate of vulnerable plaque (%)	X^2 value	P value
AIS group	106	56	50	47.2	4.482	0.034
non-AIS group	65	45	20	30.8		

Figure 3. CEUS: (Level 0) Plaque on the distal anterior wall of the left common carotid artery (Left of A) and plaque on the posterior wall of the distal segment of the right common carotid artery (right of A) where no microbubbles of ultrasound contrast agent were found. 。

(Level I) Dot shaped contrast-enhanced ultrasound microbubbles can be seen in both plaque on the posterior wall of the right carotid bulb (Left of B) and plaque on the posterior wall of the distal segment of the left common carotid artery (right of B).

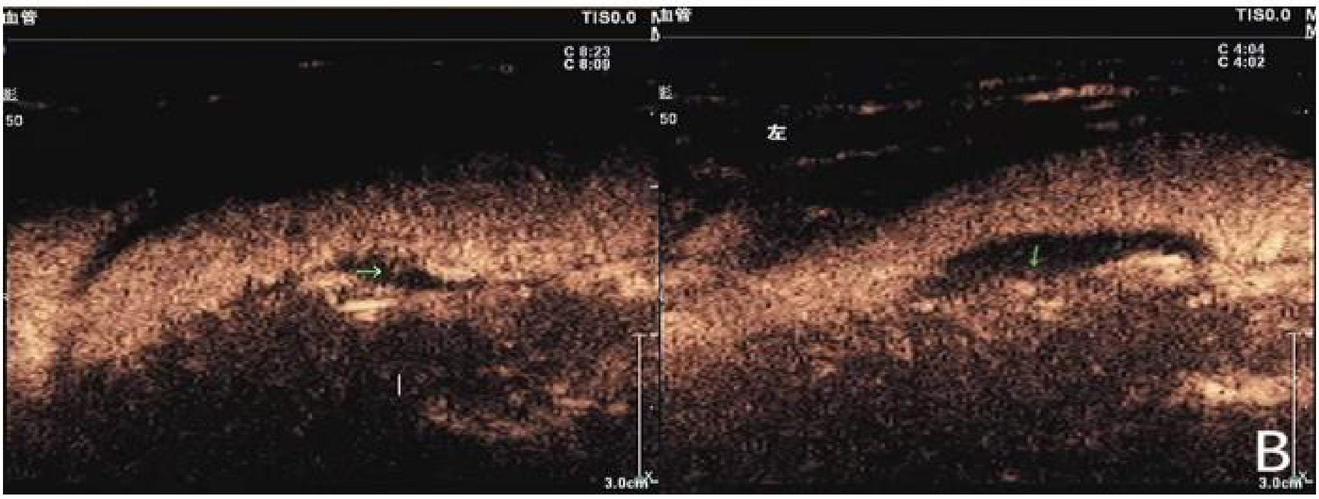
(Level II) An isoechoic flat plaque (Left of C) was found on the posterior wall of the left common carotid artery, and punctate and linear contrast medium microbubbles were seen at the top, lower shoulder and upper shoulder of the plaque; Plaque was found on the posterior wall of the distal segment of the left carotid artery (right of C) and punctate and linear contrast-enhanced ultrasound microbubbles were seen at the base.

Comparison of detection of vulnerable plaque between HRMRI and CEUS in ais group

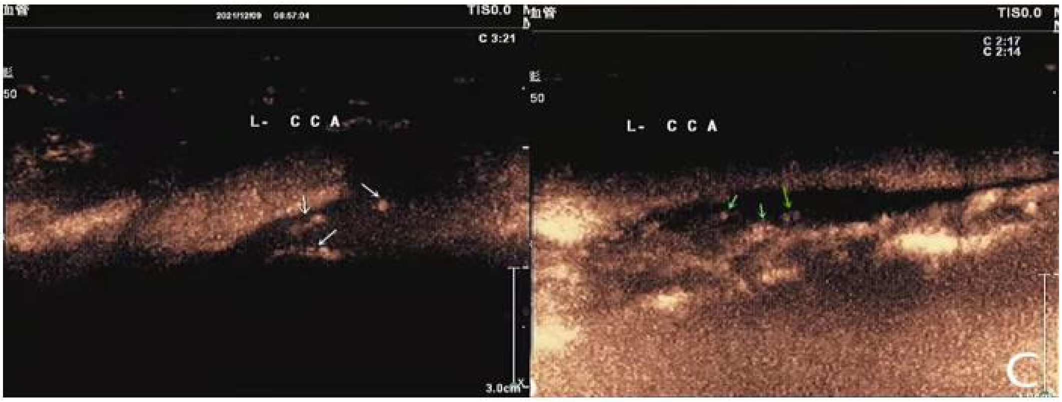
Among the 106 plaques in AIS group, 59 vulnerable plaques were detected by HRMRI, of which 24 were considered as stable plaques by CEUS evaluation; Among the 50 vulnerable plaques diagnosed by CEUS, 15 were regarded as stable plaques by HRMRI. There was significant difference between the two methods in the detection rate of vulnerable plaque (p=0.005), and the consistency was poor (kappa=0.269) (Table 5).

Table 5: Comparison of plaque detection between HRMRI and CEUS in AIS group.

Vulnerable Plaques		Ceus		Total
		Stable Plaques		
HRMRI	Vulnerable Plaques	35	24	59
	Stable Plaques	15	32	47
Total		50	56	106



(Level I) Dot shaped contrast-enhanced ultrasound microbubbles can be seen in both plaque on the posterior wall of the right carotid bulb (Left of B) and plaque on the posterior wall of the distal segment of the left common carotid artery(right of B).



(Level II) An isoechoic flat plaque (Left of C) was found on the posterior wall of the left common carotid artery, and punctate and linear contrast medium microbubbles were seen at the top, lower shoulder and upper shoulder of the plaque; Plaque was found on the posterior wall of the distal segment of the left carotid artery (right of C) and punctate and linear contrast-enhanced ultrasound microbubbles were seen at the base.

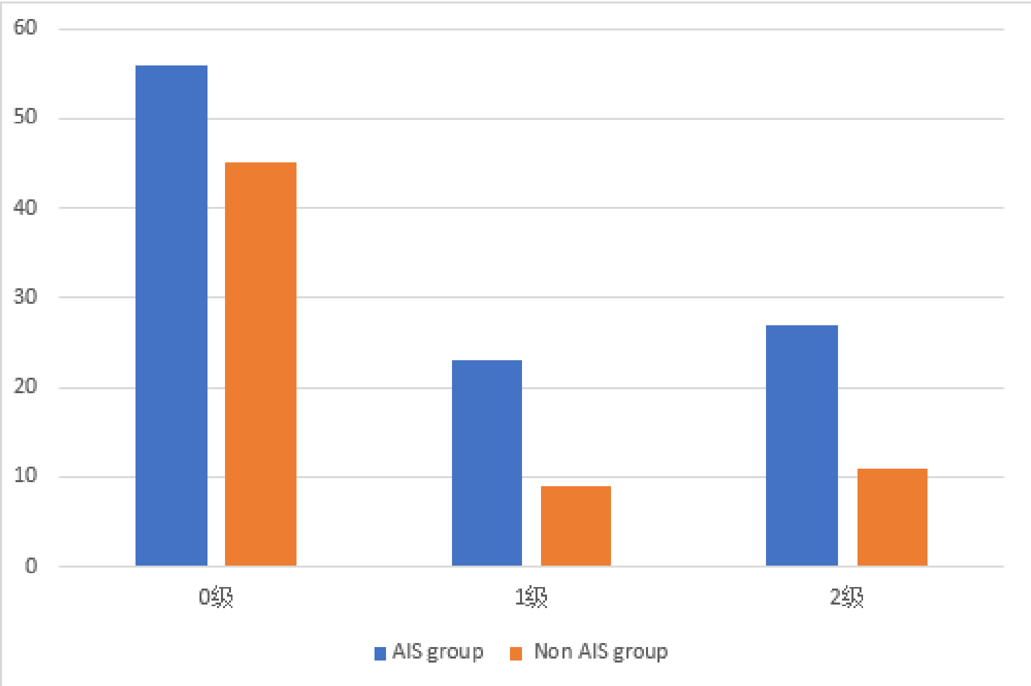


Figure 4: Detection of plaque on CEUS

Discussion

AIS is the type of stroke with the highest clinical incidence rate, accounting for 3/4 of acute cerebrovascular disease. Various secondary changes caused by the formation of vulnerable carotid plaques have exacerbated the occurrence and development of AIS [8]. The study found that the different histological characteristics of vulnerable plaque (including plaque thrombosis, low fiber content, macrophage infiltration, microvessel density, etc.) are closely related to the occurrence of stroke[9]; Through the comparative study of plaque in AIS group and non AIS group, it is found that the total number of plaque and the proportion of vulnerable plaque in AIS group are significantly higher than that in non AIS group, which indicates that the existence of vulnerable plaque is closely related to the occurrence of AIS. Therefore, early identification of vulnerable plaque composition and assessment of plaque vulnerability are of great significance for the prevention and treatment of AIS.

HRMRI is one of the most extensive imaging examination methods for vulnerable plaque research at present. It can not only refine and quantify the plaque components, but also realize the dynamic observation of nutrient vessels in the plaque and the tracking monitoring of active inflammation and can effectively evaluate the occurrence and development of cerebrovascular disease [10-12]. Zhao Ke qiang [12] and others have shown that HRMRI has a sensitivity and specificity of 83.30% and 71.4% in the qualitative diagnosis of vulnerable plaque. In this study, the AIS group and the non-AIS group were examined with HRMRI at the same time. According to the improved AHA carotid plaque classification, the nature of carotid plaque was analyzed. It was found that the AIS group had more vulnerable plaques, the detection rate of vulnerable plaques was significantly higher than that of the non-AIS group, and most vulnerable plaques had the characteristics of large necrotic lipid core, fibrous cap, surface ulcer, and even combined with bleeding and thrombosis. There is evidence that [13], patients with fiber cap rupture are more likely to cause AIS events in the short term; The existence of intra plaque hemorrhage will accelerate the process of atherosclerotic plaque and increase the risk of AIS events [14]; HRMRI can accurately analyze the composition and structure of plaque and has important evaluation value for plaque stability.

CEUS is one of the emerging arterial imaging technologies in recent years. By injecting microbubble contrast agent into human body, CEUS can observe the enhancement intensity of microbubbles in the plaque, reflect the neovascular density in the plaque, and then evaluate the stability of the plaque. The study found that CEUS' evaluation of the degree of neovascularization in the plaque is positively correlated with the density of neovascularization shown by histopathological examination and has high accuracy in evaluating neovascularization in the plaque [15]; At present, studies at home and abroad [16] have confirmed that CEUS is an important way to evaluate the neovascularization of carotid plaque. It mainly uses two methods: semi quantitative analysis of development grading and quantitative analysis of contrast-enhanced ultrasound tic. In view of the fact that CEUS examination in our hospital is in the development stage and tic quantitative analysis technology is not perfect, this study mainly adopts CEUS development grading semi quantitative analysis method to study the target plaque. The results showed that more plaques with neovascularization were found in the AIS group, and the vulnerability rate of plaques was higher. Similar studies in the literature [17] also reached the same conclusion. However, due to the different restrictions of the enrolled cases, the CEUS detection rate data were significantly different, but they all confirmed the close correlation between the development and grading of neovascularization in plaques and the occurrence of cerebral infarction, as well as the good evaluation effect of CEUS on neovascularization in plaques.

This study found that HRMRI and CEUS have significant differences and poor consistency in the detection rate of carotid vulnerable plaques. CEUS, as an extended imaging technology of conventional two-dimensional ultrasound, needs to further analyze the enhancement of plaque contrast agent on the basis of conventional ultrasound detection, which can better identify the neovascularization information in soft plaque, but it is poor for the identification of stable hard plaque and mixed plaque with complex components [18], which is well supplemented by HRMRI. Different sequences of HRMRI have a good identification effect on various components of plaque. On the other hand, it may also be related to the limited sample size. CEUS technology in our hospital has just been developed, and the detection rate is low. At the same time, the degree of patient cooperation also affects the detection of vulnerable plaque to a certain extent. At present, HRMRI has many disadvantages, such as expensive equipment, long examination time and many contraindications, which greatly limit its wide clinical application. For patients with MRI contraindications, ultrasound may be a good choice.

Conclusion

In conclusion, this study preliminarily explored the application value of HRMRI and CEUS in evaluating the stability of carotid plaque. Both of them have a better evaluation effect on vulnerable carotid plaque. HRMR has a better evaluation effect than CEUS, plays a stronger role in the refinement of plaque components, can better evaluate the status of plaque, clarify the risk stratification of high-risk patients, and reduce the incidence of stroke, The role of effectively guiding plaque treatment still needs further research.

Acknowledgement

None.

Disclosure of Interest

The authors declare that there is no conflict of interest.

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