Zhou *et al.*
European Journal of Medical Research (2025) 30:190
https://doi.org/10.1186/s40001-025-02371-3

European Journal
of Medical Research

RESEARCH Open Access

Napkin-ring sign plaques are associated with cerebral small vessel disease

Hui Zhou[1], Qiao Lin[2], Xinwei He[2], Rui Huang[2*] and Linkao Chen[2*]

Abstract

Background Few studies have investigated the association between the carotid artery napkin-ring sign (NRS) and cerebral small vessel disease (CSVD). This study aimed to investigate whether carotid NRS plaque burden and CSVD are associated.

Methods This retrospective, single-center, cross-sectional study following STROBE guidelines enrolled patients with symptoms or clinical suspicion of anterior circulation acute ischemic stroke (AIS). Plaques were evaluated using preoperative cervicocerebral computed tomography angiography (CTA). Imaging markers of CSVD, such as white matter hyperintensities (WMHs) and perivascular spaces (PVSs), were assessed.

Results A total of 575 patients (64.9 ± 8.0 years, 378 men) were evaluated. Patients with AIS had a higher percentage of total NRS plaques than those in the control group (144 (37.1%) vs. 45 (24.1%), P = 0.002), and the total NRS amount increased the risk of AIS after adjusting for confounding factors (odds ratio 1.717; 95%CI 1.141–2.584; P = 0.009). A higher WMHs grade was associated with the presence of NRS plaques (P < 0.001) and a higher total NRS area (P < 0.001). A higher PVSs grade was associated with positive remodeling (PR) on the NRS (P = 0.006).

Conclusions An increased incidence of NRS plaques on CTA was associated with the occurrence of AIS, and the area and PR of NRS plaques were associated with the risk stratification of CSVD.

Keywords Napkin-ring sign plaque, Cerebral small vessel disease, Acute ischemic stroke

Background

Cerebral small vessel disease (CSVD) is a disease of small perforated arterioles, capillaries, and possibly venules in the brain that is very common, especially in the elderly, and plays an important role in the occurrence of acute ischemic stroke (AIS) [1, 2]. CSVD includes white matter hyperintensities (WMHs), perivascular spaces (PVSs), and other features that are often accurately detected using magnetic resonance imaging (MRI) [3].

The napkin-ring sign (NRS) is defined as a high-density ring structure around a low-density center. This is often observed in coronary arteries [4]. Recently, we found that this sign is often present in the carotid artery [5]. A variety of noninvasive imaging methods, such as ultrasound, computed tomography (CT), and high-resolution magnetic resonance images (HRMRI), can detect NRS plaques. Ultrasound has shown low accuracy in the assessment of carotid plaque, while computed tomography angiography (CTA) and HRMRI have similar accuracy in the assessment of carotid plaque, HRMRI has higher technical requirements, and CTA is more popular in the population, so we chose CTA for plaque assessment [6–9].

*Correspondence:
Rui Huang
babadou97@163.com
Linkao Chen
a15757193810@163.com
[1] Department of Radiology, Taizhou Central Hospital (Taizhou University Hospital), School of Medicine, Taizhou University, Taizhou 318000, Zhejiang, China
[2] Department of Neurology, Taizhou Central Hospital (Taizhou University Hospital), School of Medicine, Taizhou University, Taizhou 318000, Zhejiang, China

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Previous studies have shown that many factors, such as old age, hypertension, diabetes, hyperlipidemia, and smoking, are associated with CSVD, and some studies have suggested that intracranial and carotid artery plaques are associated with CSVD [10–12]. In addition, intracranial arterial plaques combined with CSVD may be strong predictors of AIS [13]. Currently, no study has reported on the correlation between NRS plaques and CSVD. Therefore, we hypothesized that NRS plaques may be associated with an increase in AIS and risk stratification for CSVD.

Materials and methods

Patient recruitment

The studies involving human participants were reviewed and approved by the Ethics Committee of Taizhou Central Hospital [2025L-01–06]. Written informed consent for participation was not required for this study, in accordance with national legislation and institutional requirements.

Patients with symptoms or clinical suspicion of anterior circulation AIS who presented at Taizhou Central Hospital (Taizhou University Hospital) and underwent neck CTA and cranial MRI between January 2017 and June 2021 were recruited. AIS was diagnosed based on symptoms (e.g., paralysis, limb weakness, headache, and vomiting), along with imaging results from MRI within 12 h of symptom onset, according to the American Heart Association or American College of Cardiology guidelines [14].

The exclusion criteria were as follows: (1) prior carotid endarterectomy or stenting; (2) common carotid artery occlusion; (3) severe malacic lesion, extensive or old infarction, hemorrhage, atrophy, or tumor; (4) other diseases that may cause white matter lesions, such as multiple sclerosis, vasculitis, and connective tissue diseases; and (5) poor image quality.

Neuroimaging acquisition and processing

CTA was performed on a 64-slice Discovery CT750 HD (GE Healthcare, USA) with the following parameters: 100 kVp, 3 mAs; section thickness, 0.625 mm; interval, 0.625 mm; and display field of view (DFOV) 250 mm × 250 mm. An intravenous iodinated contrast agent (Ioversol Injection, 1.5–2 mL/kg; Hengrui Medicine Co., Ltd., China) was administered at a rate of 4.0 mL/s.

MRI was performed using a 1.5 T MR-Signa HDx MRI system (GE, USA). MRI images were obtained after axial scanning using the following parameters: time repetition (TR)/time echo (TE) = 8200/109 ms, slice thickness (ST) = 5 mm, DFOV = 165 × 240 mm for T2-weighted images; TR/TE = 464/14 ms, ST = 4 mm, and DFOV = 225 × 240 mm for T1-weighted images; TR/TE = 3400/94 ms, ST = 5 mm, and DFOV = 230 × 230 mm for diffusion-weighted imaging (DWI).

CTA image analysis

After scanning, all CTA data were transferred to a post-processing workstation for image analysis. Reconstruction was performed in the axial, coronal, and sagittal planes, including volume rendering of different segments of the measured artery, maximum intensity projection, and multiplane and curved plane reformatting. An example of this is shown in Fig. 1.

The atherosclerotic lesions were distributed across certain segments [15]. Because blood vessels in the intracranial segment are often occluded, we selected images of

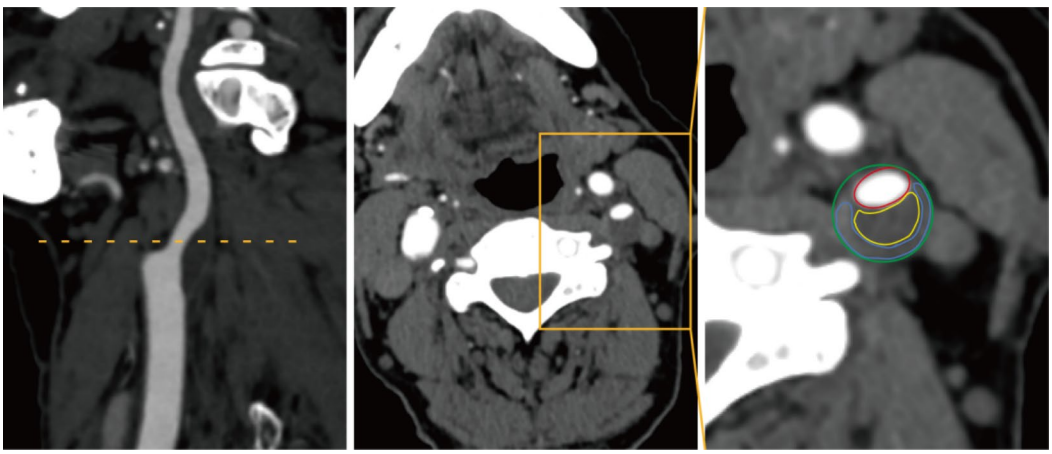

Fig. 1 Napkin-ring sign plaque analysis. A 67-year-old man had a plaque with NRS at the left common carotid artery identified on CTA. The yellow round demonstrates the low-attenuation area of the plaque surrounded by a high-attenuation rim (blue round), and the red area represents the lumen filled with contrast

the bilateral common carotid arteries up to the initiation of the internal carotid artery.

NRS on CTA has been defined in previous studies as an inner low-density core surrounded by an outer high-density ring with no more than 130 Hounsfield units [16]. Additionally, when counting the area, the largest section that was not near the calcifications was selected to avoid beam-hardening artifacts. The NRS area represents the total area on the ipsilateral side, calculated as the maximum cross-section if more than one NRS patch was present. Two independent neurologists blinded to the patients' clinical data evaluated the areas. The intraclass correlation coefficient (ICC) values of the right- and left-sided scores from the two neurologists were 0.857 ($P<0.001$) and 0.841 ($P<0.001$), respectively. The average values of the two observers were used in the final analysis.

The remodeling index was calculated as the maximum narrow cross-sectional area of the NRS site with the greatest plaque burden divided by the average cross-sectional area of the proximal reference segment and the remote reference segment ($\leq$10 mm). A remodeling index $\geq$ 1.05 indicates PR [17].

Assessment of MRI markers

All CSVD imaging markers were defined according to usual neuroimaging standards [12, 18]. The presence of lacunes, WMHs, and PVSs was independently observed outside the acute infarct area (based on DWI). Cerebral WMHs were defined as a focal $\geq$3 mm lesion without definite hypointensity on T1-weighted images and with hyperintensity on fluid-attenuated inversion recovery (FLAIR) and T2-weighted images, rated according to the Fazekas scale from 0 to 3 [19]. PVSs were defined as cerebrospinal fluid (CSF)-like signal lesions that were round, ovoid, or linear and 1–3 mm in diameter, situated in the centrum semiovale and basal ganglia, and rated on a validated semi-quantitative scale from 0 to 4 [20]. In this study, we counted PVSs only in the basal ganglia because the PVSs in this region seem to be specifically associated with cerebral small vessel disease [2].

The severity of WMHs and PVSs was trichotomized because of the small number of samples with a more severe degree (mild [degree 0], moderate [degree 1], severe [degree 2–3 for WMHs and degree 2–4 for PVSs]).

Statistical analysis

The Kolmogorov–Smirnov test was used for normality testing. Normally distributed data are presented as the mean ± standard deviation (SD), and nonnormally distributed data are presented as the median (interquartile range). Categorical data were presented as frequencies and percentages. The clinical and neuroimaging characteristics between the groups were compared using Student's t-test, paired t-test, analysis of variance with Bonferroni correction, Mann–Whitney U test, or Pearson's chi-square test, as appropriate. We calculated the ICC and the corresponding 95% CI to evaluate the degree of inter-reader reliability. Multivariate analyses were performed using logistic regression models adjusted for potential influencing factors, which were selected based on univariate analyses ($P<0.05$) including age, hypertension, and diabetes mellitus. After adjusting for confounding factors (age, hypertension, and diabetes mellitus), multivariate logistic regression analysis revealed that the total NRS amount increased the risk of AIS (odds ratio 1.717, 95%CI 1.141–2.584, $P=0.009$). All data were analyzed using SPSS 20.0 (IBM, Chicago, IL, USA). Two-sided P values of <0.05 were considered statistically significant if not otherwise specified.

Results

Patient characteristics

A total of 575 participants were included in the study. The basic patient characteristics are summarized in Table 1. The mean age of the patients was 64.9 ± 8.0 years, and 378 (65.7%) of the patients were males. Approximately, 388 patients with AIS and 187 patients without AIS. Patients with AIS were older and had a higher prevalence of hypertension and diabetes mellitus than those without AIS (Table 1).

Napkin-ring sign plaques characteristics

A total of 189 patients had NRS and 40 had PR of NRS, and the mean total NRS area was 10.7 (7.6, 14.3). Patients with AIS had a higher percentage of total NRS plaques than controls (144 (37.1%) vs. 45 (24.1%), $P=0.002$; Table 1, Fig. 2A). After adjusting for confounding factors(including age, hypertension, and diabetes mellitus), multivariate logistic regression analysis revealed that the total NRS score increased the risk of AIS (odds ratio 1.717, 95% confidence interval [CI], 1.141–2.584; $P=0.009$).After considering potential confounders based on existing literature (including age, sex, hypertension, diabetes mellitus, dyslipidemia, Atrial fibrillation, smoking, and drinking), multivariate logistic regression analysis suggested that total NRS amount remained an independent predictor of AIS (odds ratio 1.869, 95%CI 1.183–2.951, $P=0.007$). No difference was found between patients with AIS and the control group in the PR of the NRS and NRS areas (Table 1, Fig. 2B, C).

Table 2 summarizes the NRS characteristics of the symptomatic and contralateral sides in patients with AIS. The percentage of NRS plaques on the symptomatic side was higher than that on the contralateral side (115 (29.6%) vs. 59 (13.0%), $P<0.001$, Fig. 2D). A higher

Table 1 Baseline characteristics of patients

Variables	Total N = 575	Control N = 187	AIS N = 388	*P*
Age, years	64.9 ± 8.0	63.6 ± 8.1	65.5 ± 7.8	**0.005**
Male, n (%)	378 (65.7%)	132 (70.6%)	246 (63.4%)	0.089
Hypertension	412 (71.7%)	116 (62.0%)	296 (76.3%)	**< 0.001**
Diabetes mellitus	208 (36.2%)	56 (29.9%)	152 (39.2%)	**0.031**
Dyslipidemia	281 (48.9%)	94 (50.3%)	187 (48.2%)	0.642
Coronary heart disease	57 (9.9%)	14 (7.5%)	43 (11.1%)	0.176
Atrial fibrillation	127 (22.1%)	38 (20.3%)	91 (23.5%)	0.399
Smoking	169 (29.4%)	49 (26.2%)	120 (30.9%)	0.244
Drinking	98 (17.0%)	28 (15.0%)	70 (18.0%)	0.359
Medicine				
Antihypertensive therapy	245 (42.6%)	71 (38.0%)	174 (44.8%)	0.118
Antidiabetic therapy	114 (19.8%)	34 (18.2%)	80 (20.6%)	0.492
Statins	82 (14.3%)	33 (17.6%)	49 (12.6%)	0.107
Antithrombotic therapy	71 (12.3%)	28 (15.0%)	43 (11.1%)	0.184
Napkin-ring sign				
NRS plaques	189 (32.9%)	45 (24.1%)	144 (37.1%)	**0.002**
PR of NRS	40 (7.0%)	6 (13.3%)	34 (23.6%)	0.224
NRS area(mm^2)	10.7 (7.6, 14.3)	10.8 (7.7, 13.1)	10.7 (7.5, 14.7)	0.606

Bold values indicate statistical differences

The values are presented as the mean ± SD or median (interquartile range) for continuous variables and as a number (percentages) for categorical variables

AIS acute ischemic stroke, *NRS* napkin-ring sign, *PR* positive remodelling

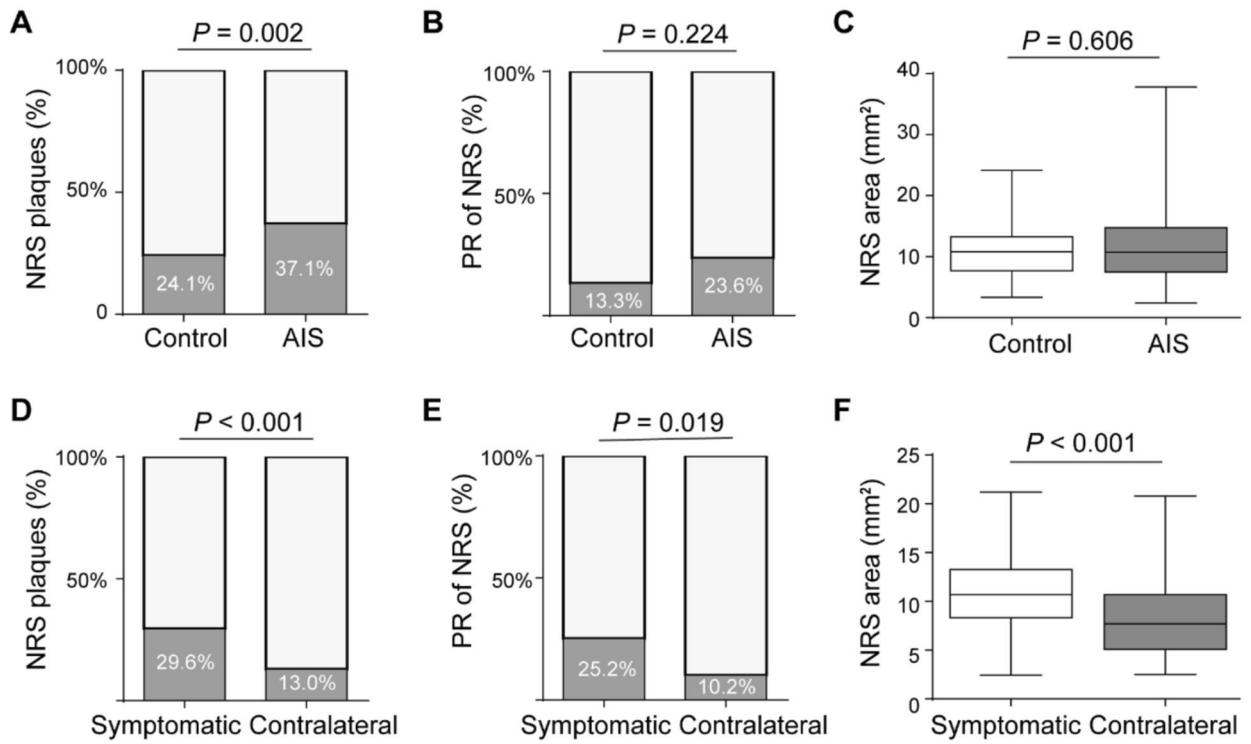

Fig. 2 Napkin-ring sign plaque characteristics between symptomatic and contralateral sides of in acute ischemic stroke patients. **A**–**C** NRS plaques were higher in AIS patients; No difference was found between patients with AIS and the control group in the PR of the NRS and NRS areas; **D**–**F** NRS plaques, PR of NRS and NRS area were higher in the symptomatic sides. *NRS* napkin-ring sign, *AIS* acute ischemic stroke

Table 2 Comparison of the plaque with napkin-ring signs counts between symptomatic and contralateral sides in AIS patients

Characteristics	Symptomatic	Contralateral	*P*
NRS plaques	115 (29.6%)	59 (13.0%)	**< 0.001**
PR of NRS	29 (25.2%)	6 (10.2%)	**0.019**
NRS area(mm^2)	10.7 (8.3, 13.2)	7.7 (5.2, 10.4)	**< 0.001**

Bold values indicate statistical differences

NRS plaques and NRS area were higher on the symptomatic side

NRS napkin-ring sign, *PR* positive remodelling

percentage of PR was observed on the symptomatic side than on the contralateral side (29 (25.2%) vs. 6 (10.2%), P = 0.019; Fig. 2E). In addition, the NRS area was higher on the symptomatic side than on the contralateral side [10.7 (8.3, 13.2) vs. 7.7 (5.2, 10.4) mm^2, P < 0.001; Fig. 2F].

Napkin-ring sign plaques and WMHs

Table 3 summarizes the association between the NRS characteristics and WMHs. A total of 124 patients had WMHs grade 0, 225 had WMHs grade 1, and 226 patients with grade 2–3. A higher WMHs grade was associated with the presence of NRS plaques (P < 0.001; Fig. 3A) and a higher total NRS area (P < 0.001; Fig. 3C). No association was found between the PR of the NRS and WMHs in the combined data on both sides (P = 0.105, Fig. 3B).

On the symptomatic side, a higher WMHs grade was associated with the presence of NRS plaques (P < 0.001). On the contralateral side, there was no significant difference in the NRS plaques. No association was found between the PR of the NRS plaques and WMHs on either side. A higher WMHs grade was associated with a higher NRS area, both on the symptomatic (P < 0.001) and contralateral sides (P = 0.001).

Napkin-ring sign plaques and PVSs

Table 4 summarizes the association between NRS characteristics and PVSs. A total of 133 patients had PVSs grade 0, 316 had PVSs grade 1, and 126 had PVSs 2–4. A higher PVSs grade was associated with PR of NRS (P = 0.006; Fig. 3E). No association was found between NRS plaques, NRS areas, and PVSs in the combined data on both sides (P = 0.066 for NRS plaques, Fig. 3D; P = 0.421 for NRS area, Fig. 3F).

A higher PVSs grade was associated with the presence of plaques on the contralateral side (P = 0.002). A higher PVSs grade was associated with the presence of PR of NRS plaques both on the symptomatic (P = 0.016) and contralateral sides (P = 0.004). No significant difference was observed in the NRS area across the different grades of PVSs.

Discussion

Our study found that an increase in NRS plaque was associated with an increase in AIS incidence. In addition, we found that higher WMHs grades were associated with the appearance and area of NRS plaques and that the PR of NRS was associated with the grade of PVSs.

NRS plaques, defined as high-risk plaque features, are associated with cholesterol crystallization and thin-cap atherosclerosis and may cause further inflammatory responses [17, 21]. Angiogenesis and inflammation are thought to be major causes of atherosclerotic plaque

Table 3 Association between the napkin-ring sign plaques and WMHs

Characteristics		WMHs			*P*
		Grade 0 N = 124	Grade 1 N = 225	Grade 2–3 N = 226	
Bilateral side					
NRS plaques	N (%)	30 (24.2%)	60 (26.7%)	99 (43.8%)	**< 0.001**
PR of NRS	N (%)	2 (4.5%)	14 (22.9%)	24 (23.2%)	0.105
Total NRS area	mm^2	6.6 (4.8, 10.0)	9.5 (7.1, 12.9)	13.3 (9.7, 16.0)	**< 0.001**
Symptomatic side					
NRS plaques	N (%)	22 (17.7%)	48 (21.3%)	82 (36.3%)	**< 0.001**
PR of NRS	N (%)	1 (4.5%)	11 (22.9%)	19 (23.2%)	0.112
NRS area	mm^2	5.8 (4.5, 10.4)	9.2 (6.8, 11.0)	11.9 (10.1, 14.1)	**< 0.001**
Contralateral side					
NRS plaques	N (%)	12 (9.7%)	25 (11.1%)	38 (16.8%)	0.090
PR of NRS	N (%)	1 (8.3%)	3 (12%)	6 (15.8%)	0.176
NRS area	mm^2	6.6 (4.0, 9.1)	6.7 (5.0, 7.7)	9.2 (7.4, 13.0)	**0.001**

Bold values indicate statistical differences

NRS napkin-ring sign, *PR* positive remodeling, *WMHs* white matter hyperintensities

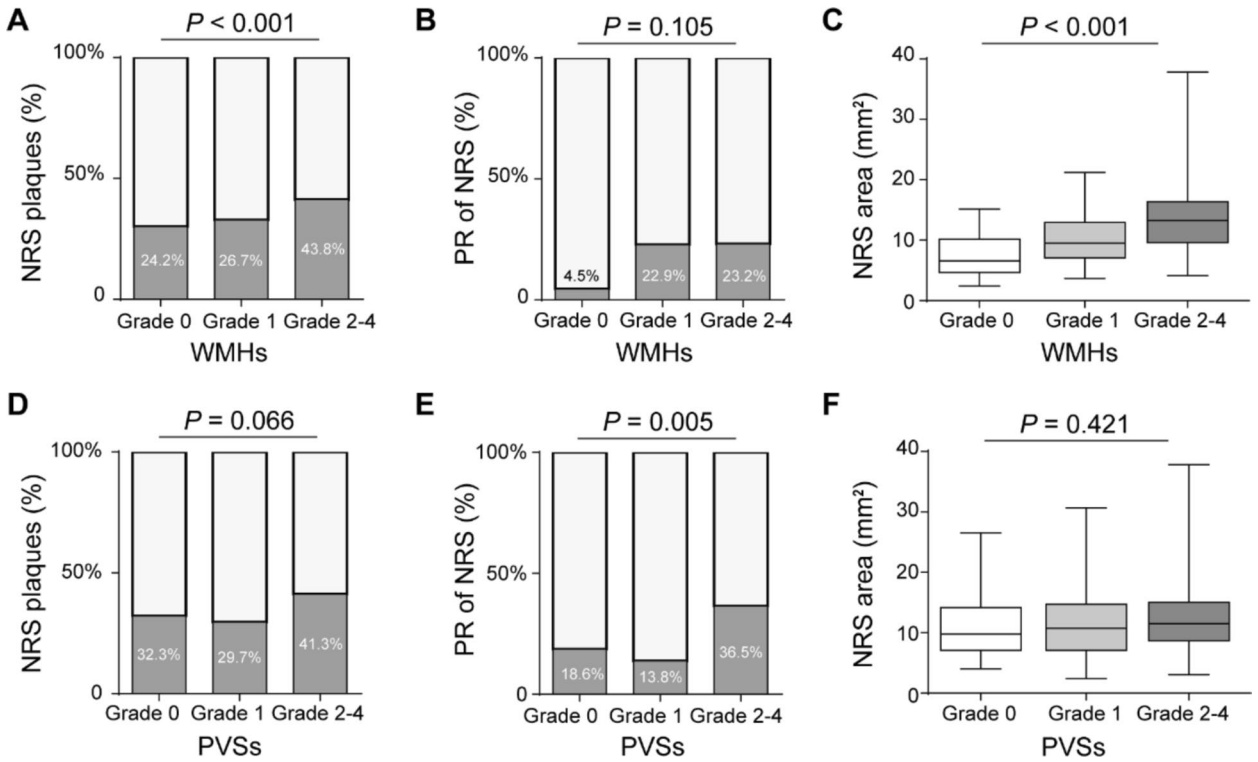

Fig. 3 Association between napkin-ring sign plaque and MRI markers of cerebral small vessel disease combined on both sides. **A**–**C** NRS plaques and NRS area were higher in higher WMHs grade patients. No association was found between the PR of the NRS and WMHs in the combined data on both sides. **D**–**F** PR of NRS was higher in higher PVSs grade patients. No association was found between NRS plaques, NRS areas, and PVSs in the combined data on both sides. *NRS* napkin-ring sign, *PR* positive remodeling, *WMHs* white matter hyperintensities, *PVSs* perivascular spaces

Table 4 Association between the napkin-ring sign plaques and PVSs

Characteristics		PVSs			*P*
		Grade 0 N = 133	**Grade 1 N = 316**	**Grade 2–4 N = 126**	
Bilateral side					
NRS plaques	N (%)	43 (32.3%)	94 (29.7%)	52 (41.3%)	0.066
PR of NRS	N (%)	8 (18.6%)	13 (13.8%)	19 (36.5%)	**0.005**
Total NRS area	mm^2	9.8 (7.6, 14.0)	10.8 (7.1, 14.5)	11.5 (8.4, 15.0)	0.421
Symptomatic side					
NRS plaques	N (%)	34 (25.6%)	79 (25.0%)	39 (31.0%)	0.426
PR of NRS	N (%)	7 (20.6%)	11 (13.9%)	13 (33.3%)	**0.016**
NRS area	mm^2	10.1 (8.7, 11.2)	10.5 (7.1, 13.1)	11.5 (9.4, 13.2)	0.135
Contralateral side					
NRS plaques	N (%)	19 (14.3%)	29 (9.2%)	27 (21.4%)	**0.002**
PR of NRS	N (%)	1 (5.3%)	2 (6.9%)	7 (25.9%)	**0.004**
NRS area	mm^2	7.1 (5.0, 9.7)	8.1 (6.6, 11.2)	6.9 (4.7, 10.2)	0.371

Bold values indicate statistical differences

NRS napkin-ring sign, *PR* positive remodeling, *PVSs* perivascular spaces

vulnerability and rupture. Since these features are histologically associated with advanced atherosclerotic and ruptured lesions, NRS may be a marker of advanced disease on coronary CT angiography (CCTA) [22]. An increased incidence of plaques was an independent and important risk factor for AIS [23]. We found that patients

with AIS had a higher occurrence of NRS plaques, higher PR, and a larger plaque area on the symptomatic side, which further supported the association of NRS plaques and PR with AIS. Therefore, suggesting that NRS plaques may be an imaging marker reflecting plaque vulnerability.

Typical brain MRI findings in CSVD include WMHs, lacunes, and PVSs. Arterial asphyxia, systemic low-grade inflammation, vascular oxidative stress, and intestinal dysbiosis can lead to dysfunction of cerebral vascular endothelial cells [24, 25]. As a result, CBF (Cerebral Blood Flow) regulation is impaired and the blood–brain barrier breaks down, leading to neuroinflammation, neuronal damage, and increased blood–brain barrier permeability, which often leads to the formation of CSVD [26]. Simultaneously, CBF decline is the basis for the development of WMHs and PVSs. We also found in a study that intracranial pulsation of small blood vessels is also associated with CSVD [27]. These findings suggest that changes in intracranial blood flow affect the occurrence of CSVD, and that carotid artery plaques often affect intracranial blood flow, especially vulnerable plaques such as NRS plaques.

An earlier study reported no direct causal relationship between carotid atherosclerosis and WMH severity but suggested an indirect relationship between the characteristics of carotid plaques [28, 29]. In addition, we found reports that WMH progression was more strongly associated with systemic risk factors than plaque features or circulating cell biomarkers [10]. However, in other studies we found that carotid atherosclerotic plaque characteristics, especially calcification, may be independently associated with the severity of WMHs, and at the same time, carotid intraplaque hemorrhage was also associated with the total burden of CSVD [30, 31]. To date, no study has reported NRS plaques association with CSVD imaging markers such as WMHs and PVSs. Our study revealed that a higher WMHs grade was associated with the presence of NRS plaques and higher total NRS area. In AIS patients, on the symptomatic side, the higher the WMHs grade, the higher the corresponding NRS plaque occurrence, and the NRS plaque area was positively correlated with WMHs grade on both sides.

We found that the PR of NRS plaques seemed to have a greater correlation with PVS. PVSs are anatomical structures that follow a typical dilation process as blood vessels pass through the gray or white matter, which is considered passive, secondary to transient vasoconstriction and dilation of blood vessels [32, 33]. PVSs are more common in older adults, hypertensive patients, and those with carotid plaques [20]. In patients with AIS, a higher grade of PVSs was found to be associated with the presence of PR of NRS plaques, observed on both the symptomatic and contralateral sides. PR is characterized as an atherosclerotic plaque feature that denotes an increase in arterial caliber at the site of an atheroma, which occurs in response to escalating plaque burden [34]. This is observed in atherosclerotic plaques of the neck and is an important feature of NRS plaques [35]. PR may cause a lateral increase in the arterial diameter, thereby increasing PVSs.

At the same time, another study pointed out that intracranial atherosclerotic plaques, especially complex plaques, are correlated with CSVD, and NRS plaques were not mentioned, possibly because observing NRS plaques in the intracranial blood vessels is difficult [3]. In addition, we found that the co-occurrence of intracranial atherosclerotic plaques and small cerebral vascular disease may be a strong predictor of AIS [13], suggesting the need to further explore the correlation between NRS plaques combined with CSVD and AIS.

This study has some limitations. First, this was a single-center cross-sectional study that explored the relationship between NRS plaques and CSVD at specific time points, and there are limitations to the size of the sample, which may make it impossible to establish complete causality. Longitudinal studies can better determine whether NRS plaque is a precursor or a consequence of CSVD and AIS. Secondly, due to limitations in sample size and selection criteria, patients with asymptomatic CSVD typically did not undergo CTA examinations, conversely, most patients who did receive CTA often presented with compromised vascular conditions, which may introduce a selection bias. Consequently, the majority of AIS patients in our study were primarily those suffering from atherosclerosis of large arteries. Additionally, owing to restricted vascular evaluation capabilities, all participants included in our research had anterior circulation infarctions, thereby excluding certain cases of posterior circulation AIS. Future randomized trials involving multi-center collaborations and larger datasets may be necessary to investigate whether different TOAST classifications of cerebral infarction are more closely associated with NRS plaques. Third, assessing NRS across the entire vessel, rather than just the common carotid artery, may be more relevant, and future prospective studies examining the entire vessel may help us assess its association with CSVD more comprehensively.

In conclusion, our study suggests that the increased incidence of napkin-ring sign plaques on CTA is positively correlated with the occurrence of AIS, and the areas of NRS plaques and PR may be correlated with a higher degree of imaging markers of CSVD, such as WMHs and PVSs, and may indicate risk stratification of CSVD. To the best of our knowledge, this is the first study to examine the relationship between NRS plaques and CSVD, and we believe it has the potential to lay the groundwork

for further exploration of potential biological pathways between NRS plaques and CSVD. Earlier observation of NRS plaques on CTA may help identify patients who are more prone to AIS and determine the risk stratification of CSVD, thus facilitating us to better guide the subsequent medication regimen of patients. When NRS plaques are identified, we may be able to implement more aggressive strategies, such as intensive lipid reduction. Additionally, carotid artery stenosis associated with relevant plaques could potentially be addressed earlier through interventions like carotid stenting or endarterectomy. However, these approaches will require further validation in future studies.

Acknowledgements
Not applicable.

Author contributions
HZ contributed to the study design, acquisition, drafting and revising the article, and final approval of the version to be published. QL and XH contributed to revising the article for important intellectual content, analysis and interpretation of data, and final approval of the version to be published. RH contributed to acquisition of data and final approval of the version to be published. LC contributed to conception and design, analysis and interpretation of data, revising the article for important intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

Funding
This study was supported by the Special Start-up Fund Program for Young Physicians in Research and Teaching, Department of Medicine, Taizhou University (yxbz202401).

Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was approved by the ethical review committee of Taizhou Central Hospital waived of the requirement for informed consent and approved the study (ZFPH No: 2025L-01-06). All subject records and data were deidentified and anonymized prior to analysis. This study was conducted in accordance with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 9 January 2025 Accepted: 9 February 2025
Published online: 21 March 2025

References

1. Bushnell C, Kernan WN, Sharrief AZ, et al. 2024 guideline for the primary prevention of stroke: a guideline from the American Heart Association/American Stroke Association. Stroke. 2024;55(12):e344–424. https://doi.org/10.1161/STR.0000000000000475.
2. Bos D, Wolters FJ, Darweesh SKL, et al. Cerebral small vessel disease and the risk of dementia: a systematic review and meta-analysis of population-based evidence. Alzheimers Dement. 2018;14(11):1482–92. https://doi.org/10.1016/j.jalz.2018.04.007.
3. Zhu KL, Shang ZY, Liu BJ, et al. The association of intracranial atherosclerosis with cerebral small vessel disease imaging markers: a high-resolution magnetic resonance imaging study. Sci Rep. 2023;13(1):17017. https://doi.org/10.1038/s41598-023-44240-1.
4. Seifarth H, Schlett CL, Nakano M, et al. Histopathological correlates of the napkin-ring sign plaque in coronary CT angiography. Atherosclerosis. 2012;224(1):90–6. https://doi.org/10.1016/j.atherosclerosis.2012.06.021.
5. Murgia A, Erta M, Suri JS, Gupta A, Wintermark M, Saba L. CT imaging features of carotid artery plaque vulnerability. Ann Transl Med. 2020;8(19):1261. https://doi.org/10.21037/atm-2020-cass-13.
6. Cheng L, Zheng S, Zhang J, et al. Multimodal ultrasound-based carotid plaque risk biomarkers predict poor functional outcome in patients with ischemic stroke or TIA. BMC Neurol. 2023;23(1):13. https://doi.org/10.1186/s12883-023-03052-6.
7. Li J, Tian Y, Shi Y, Cui Y, Lian J, Liu P. Association of vulnerable plaques with white matter hyperintensities on high-resolution magnetic resonance imaging. Quant Imaging Med Surg. 2024;14(5):3606–18. https://doi.org/10.21037/qims-23-1856.
8. Pakizer D, Kozel J, Taffe P, et al. Diagnostic accuracy of carotid plaque instability by noninvasive imaging: a systematic review and meta-analysis. Eur Heart J Cardiovasc Imaging. 2024;25(10):1325–35. https://doi.org/10.1093/ehjci/jeae144.
9. Xu S, Zhang J, Yang J, et al. Evaluating the association between vascular remodeling and plaque calcification patterns of the carotid artery and its effects on ischemic symptoms using CT angiography. Cardiovasc Diagn Ther. 2024;14(2):229–39. https://doi.org/10.21037/cdt-23-428.
10. Hannawi Y, Vaidya D, Yanek LR, et al. Association of vascular properties with the brain white matter hyperintensity in middle-aged population. J Am Heart Assoc. 2022;11(11): e024606. https://doi.org/10.1161/JAHA.121.024606.
11. Zhai FF, Yang M, Wei Y, et al. Carotid atherosclerosis, dilation, and stiffness relate to cerebral small vessel disease. Neurology. 2020;94(17):e1811–9. https://doi.org/10.1212/WNL.0000000000009319.
12. Zhai FF, Yan S, Li ML, et al. Intracranial arterial dolichoectasia and stenosis: risk factors and relation to cerebral small vessel disease. Stroke. 2018;49(5):1135–40. https://doi.org/10.1161/STROKEAHA.117.020130.
13. Li Q, Yu M, Yang D, et al. Association of the coexistence of intracranial atherosclerotic disease and cerebral small vessel disease with acute ischemic stroke. Eur J Radiol. 2023;165: 110915. https://doi.org/10.1016/j.ejrad.2023.110915.
14. Bushnell C, Kernan WN, Sharrief AZ, et al. 2024 Guideline for the primary prevention of stroke: a guideline from the American Heart Association/American Stroke Association. Stroke. 2024. https://doi.org/10.1161/STR.0000000000000475.
15. Savastano L, Brinjikji W, Lutsep H, Chen H, Chaturvedi S. Symptomatic nonstenotic carotids: a topical review. Stroke. 2024. https://doi.org/10.1161/STROKEAHA.123.035675.
16. Maurovich-Horvat P, Schlett CL, Alkadhi H, et al. The napkin-ring sign indicates advanced atherosclerotic lesions in coronary CT angiography. JACC Cardiovasc Imaging. 2012;5(12):1243–52. https://doi.org/10.1016/j.jcmg.2012.03.019.
17. Finck T, Stojanovic A, Will A, et al. Long-term prognostic value of morphological plaque features on coronary computed tomography angiography. Eur Heart J Cardiovasc Imaging. 2020;21(3):237–48. https://doi.org/10.1093/ehjci/jez238.
18. Wardlaw JM, Smith E, Biessels GJ, Cordonnier C, Fazekas F, Frayne R, Lindley RI, O'Brien JT, Barkhof F, Benavente OR, Black SE, Brayne C, Breteler M, Chabriat H, Decarli C, de Leeuw FE, Doubal F, Duering M, Fox NC, Greenberg S, Hachinski V, Kilimann I, Mok V, Oostenbrugge RV, Pantoni L, Speck O, Stephan BC, Teipel S, Viswanathan A, Werring D, Chen C, Smith C, van Buchem M, Norrving B, Gorelick PB, Dichgans M. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol. 2013;12(8):822–38. https://doi.org/10.1016/S1474-4422(13)70124-8.
19. Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. Am J Roentgenol. 1987;149:351. https://doi.org/10.2214/ajr.149.2.351.
20. Maclullich AM, Wardlaw JM, Ferguson KJ, Starr JM, Seckl JR, Deary IJ. Enlarged perivascular spaces are associated with cognitive function in healthy elderly men. J Neurol Neurosurg Psychiatry. 2004;75(11):1519–23. https://doi.org/10.1136/jnnp.2003.030858.

21. Kolossvary M, Karady J, Szilveszter B, et al. Radiomic features are superior to conventional quantitative computed tomographic metrics to identify coronary plaques with napkin-ring sign. Circ Cardiovasc Imaging. 2017;10(12): e006843. https://doi.org/10.1161/CIRCIMAGING.117.006843.
22. Maurovich-Horvat P, Ferencik M, Voros S, Merkely B, Hoffmann U. Comprehensive plaque assessment by coronary CT angiography. Nat Rev Cardiol. 2014;11(7):390–402. https://doi.org/10.1038/nrcardio.2014.60.
23. Wu J, Zou Y, Meng X, et al. Increased incidence of napkin-ring sign plaques on cervicocerebral computed tomography angiography associated with the risk of acute ischemic stroke occurrence. Eur Radiol. 2024;34(7):4438–47. https://doi.org/10.1007/s00330-023-10404-w.
24. Dupre N, Drieu A, Joutel A. Pathophysiology of cerebral small vessel disease: a journey through recent discoveries. J Clin Invest. 2024;134(10). https://doi.org/10.1172/JCI172841.
25. Rouhl RP, Damoiseaux JG, Lodder J, et al. Vascular inflammation in cerebral small vessel disease. Neurobiol Aging. 2012;33(8):1800–6. https://doi.org/10.1016/j.neurobiolaging.2011.04.008.
26. Blair GW, Thrippleton MJ, Shi Y, et al. Intracranial hemodynamic relationships in patients with cerebral small vessel disease. Neurology. 2020;94(21):e2258–69. https://doi.org/10.1212/WNL.0000000000009483.
27. Shi Y, Thrippleton MJ, Blair GW, et al. Small vessel disease is associated with altered cerebrovascular pulsatility but not resting cerebral blood flow. J Cereb Blood Flow Metab. 2020;40(1):85–99. https://doi.org/10.1177/0271678X18803956.
28. Ammirati E, Moroni F, Magnoni M, et al. Relation between characteristics of carotid atherosclerotic plaques and brain white matter hyperintensities in asymptomatic patients. Sci Rep. 2017;7(1):10559. https://doi.org/10.1038/s41598-017-11216-x.
29. Wardlaw JM, Allerhand M, Doubal FN, et al. Vascular risk factors, large-artery atheroma, and brain white matter hyperintensities. Neurology. 2014;82(15):1331–8. https://doi.org/10.1212/WNL.0000000000000312.
30. Shen R, Tong X, Zhao C, et al. Atherosclerotic plaque characteristics in extracranial carotid artery may indicate closer association with white matter hyperintensities than intracranial arteries: a CARE-II study. Eur J Radiol. 2024;170: 111208. https://doi.org/10.1016/j.ejrad.2023.111208.
31. Fan X, Zhang X, Lai Z, et al. Cerebral small vessel disease burden related to carotid intraplaque hemorrhage serves as an imaging marker for clinical symptoms in carotid stenosis. Front Neurol. 2021;12: 731237. https://doi.org/10.3389/fneur.2021.731237.
32. Liu H, Yang S, He W, et al. Associations among diffusion tensor image along the perivascular space (DTI-ALPS), enlarged perivascular space (ePVS), and cognitive functions in asymptomatic patients with carotid plaque. Front Neurol. 2021;12: 789918. https://doi.org/10.3389/fneur.2021.789918.
33. Gutierrez J, Rundek T, Ekind MS, Sacco RL, Wright CB. Perivascular spaces are associated with atherosclerosis: an insight from the Northern Manhattan Study. AJNR Am J Neuroradiol. 2013;34(9):1711–6. https://doi.org/10.3174/ajnr.A3498.
34. Onnis C, Virmani R, Madra A, et al. Whys and wherefores of coronary arterial positive remodeling. Arterioscler Thromb Vasc Biol. 2024;44(12):2416–27. https://doi.org/10.1161/ATVBAHA.124.321504.
35. Kinoshita D, Suzuki K, Usui E, et al. High-risk plaques on coronary computed tomography angiography: correlation with optical coherence tomography. JACC Cardiovasc Imaging. 2024;17(4):382–91. https://doi.org/10.1016/j.jcmg.2023.08.005.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.