

CAROTID PLAQUE NEOVASCULARIZATION DETECTED WITH CONTRAST-ENHANCED ULTRASOUND PREDICTS ISCHEMIC STROKE RECURRENCE

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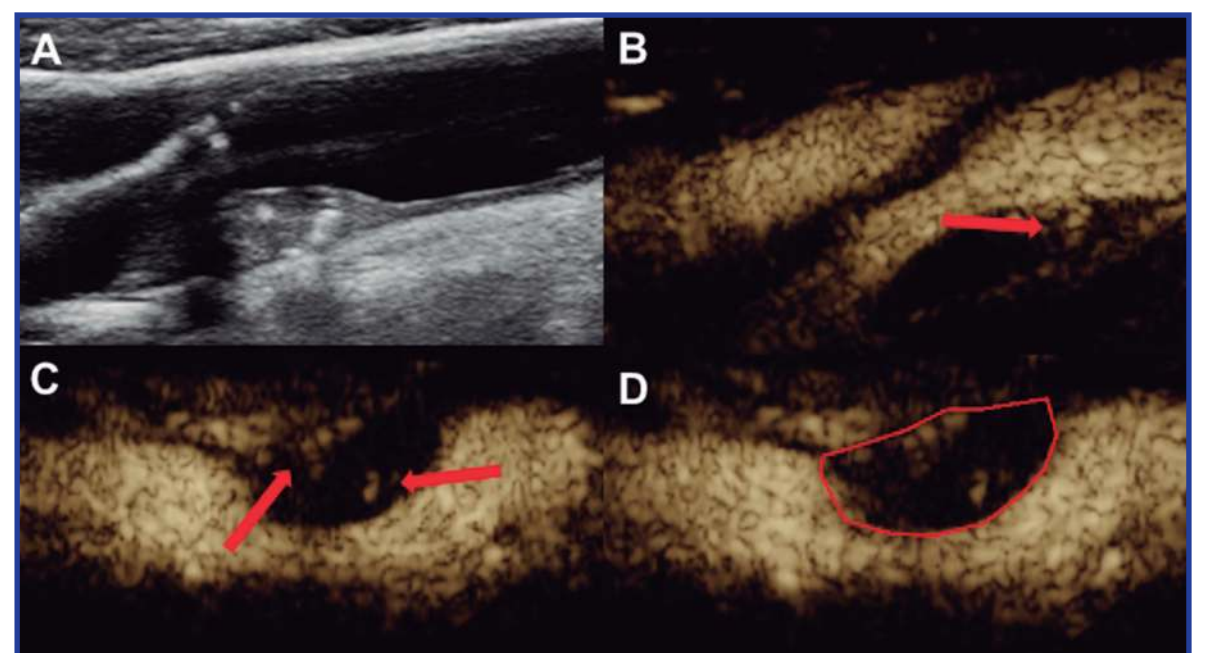
Background

Plaque neovascularization is a hallmark of carotid plaque vulnerability. With Contrast-Enhanced Ultrasound (CEUS) it is possible to visualize plaque neovessels *in vivo*. The clinical significance of CEUS-detected neovascularization is unclear. We hypothesized that CEUS-detected neovessels were associated with stroke recurrences in patients with a recent stroke and carotid atherosclerosis.

Methods

We conducted a prospective study of consecutive patients with a recent anterior circulation ischemic stroke and at least one atherosclerotic plaque in the internal carotid artery. Patients with a cardioembolic stroke etiology were excluded from our study. All of our patients underwent a CEUS examination (Figure 1). Neovascularization was graded into three categories according to the extent of neovessels: 0 (no visible microbubbles within the plaque), 1 (moderate microbubbles confined to the shoulder and/or adventitial side of the plaque) and 2 (extensive microbubbles throughout the plaque). During the follow-up, we recorded stroke recurrences. A multivariable Cox regression analysis was performed to evaluate predictors of recurrence.

Figure 1: Example of a CEUS study. Image (A) shows an eccentric atherosclerotic plaque from the internal carotid artery with a predominantly hyperechoic texture. On the upright (B) the same plaque is shown during the CEUS study. Plaque neovessels are identified as hyperechoic microbubbles (red arrows). Image (C) shows the CEUS study of a plaque with diffuse neovascularization (grade 2). On image (D) we can see the same plaque delineated with the region of interest tool from the Philips QLAB Advanced Quantification Software® to obtain the time-intensity enhancement-curve.



Results

We included 78 patients whose mean age was 74.3±10.4y and 58 (74.4%) were men. There were 29 (37.2%) patients with a low-grade stenosis (<50%). The remainder presented high-grade carotid plaques. The results of the CEUS were not interpretable in 35.9% of the patients, mainly due to calcium shadows. We detected neovascularization in 80% of the plaques. After a median follow-up of 11.1 months (IQR 3.5-16.6) there were 13 stroke recurrences. In the Cox regression analysis, CEUS-detected neovascularization was independently associated with the risk of stroke recurrence, even after adjusting for the degree of stenosis (HR=6.57 95%CI 1.66-26.01) (Table 1) (Figure 2).

Figure 2: Kaplan-Meier survival curve according to grades of carotid plaque neovascularization. The outcome measured was any recurrent ischemic stroke.

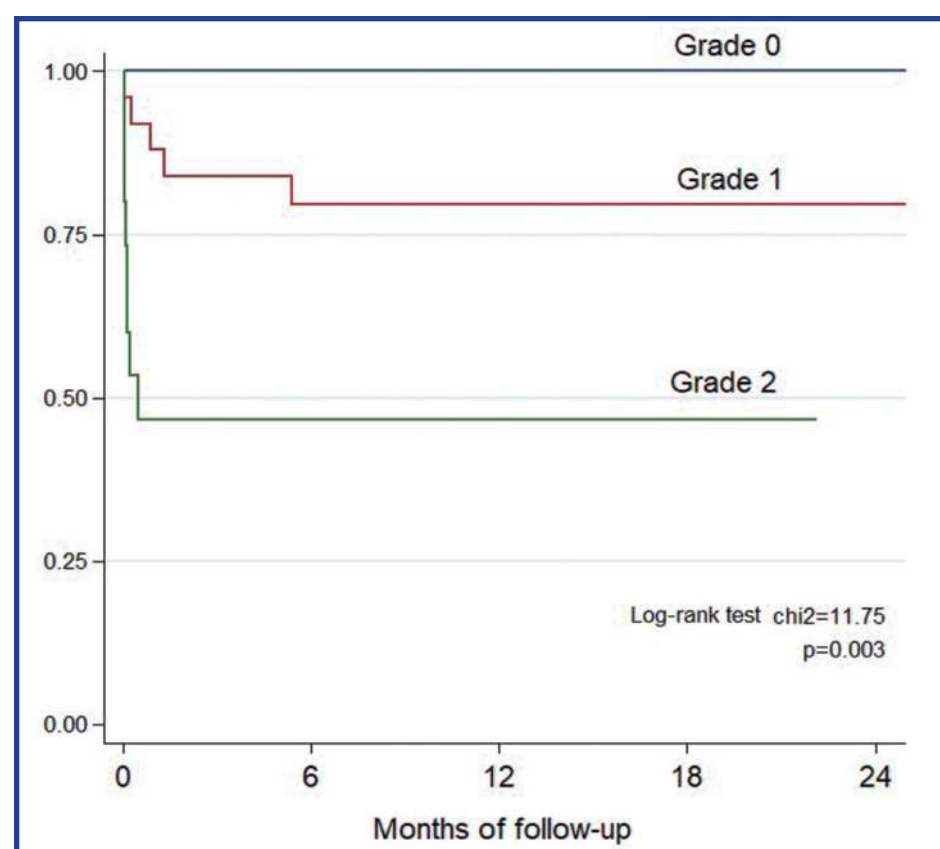


Table 1. Predictors of stroke recurrence

Univariate analysis			
	HR	95% CI	p
Age	1.03	0.98-1.09	0.261
Sex (woman)	1.74	0.58-5.19	0.323
Current smoking	1.37	0.43-4.37	0.597
Hypertension	0.60	0.20-1.84	0.371
Diabetes	3.48	1.09-11.12	0.035
Dyslipidemia	1.16	0.36-3.72	0.797
Prior antiplatelet therapy	1.05	0.36-3.02	0.933
Prior use of statins	1.66	0.52-5.31	0.391
Hypoechoic plaque	2.62	0.81-8.52	0.109
Severe carotid stenosis (≥70%)	4.86	1.35-17.46	0.015
Diffuse plaque neovascularization (Grade 2)	5.30	1.72-16.36	0.004
Carotid revascularization	1.08	0.33-3.50	0.903
Multivariable analysis			
	HR	95% CI	p
Plaque neovascularization (Grade 2)	6.57	1.66-26.01	0.007
Severe carotid stenosis (≥70%)	2.60	0.66-10.25	0.172

Conclusion

In patients with an anterior circulation ischemic stroke and carotid atherosclerosis, plaque neovascularization detected with CEUS was an independent predictor of stroke recurrence.