PLAQUE NEOVASCULARIZATION DETECTED WITH CONTRAST-ENHANCED ULTRASOUND IS ASSOCIATED WITH INFLAMMATION MEASURED WITH 18FLUORDEOXYGLUCOSE POSITRON-EMISSION TOMOGRAPHY IN PATIENTS WITH ISCHEMIC STROKE AND CAROTID ATHEROSCLEROSIS

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Background

Neovascularization is a hallmark of carotid plaque vulnerability and is closely related to inflammation. With Contrast-Enhanced Ultrasound (CEUS) it is possible to visualize plaque neovessels *in vivo*. We hypothesized that CEUS-detected neovascularization was associated with carotid plaque inflammation measured with [18]Fluordeoxyglucose Positron-Emission-Tomography ([18]FDG PET-CT).

Methods

We conducted a prospective study of consecutive patients with an acute anterior circulation ischemic stroke and at least one atherosclerotic plaque in the internal carotid artery (ICA). All of our patients underwent a CEUS study and neovessels were identified as hyperechoic bubbles appearing within the plaque after a bolus of Sonovue® contrast (Figure 1). The patients underwent also an [18]FDG PET-CT and we determined the maximum Standardized Uptake Value (SUV) from the symptomatic ICA (Figure 2). Comparison of the SUVs between neovascularized and non-neovascularized plaques was performed using the Student's t-test. A multivariate linear regression analysis was performed to study other predictors of plaque inflammation.

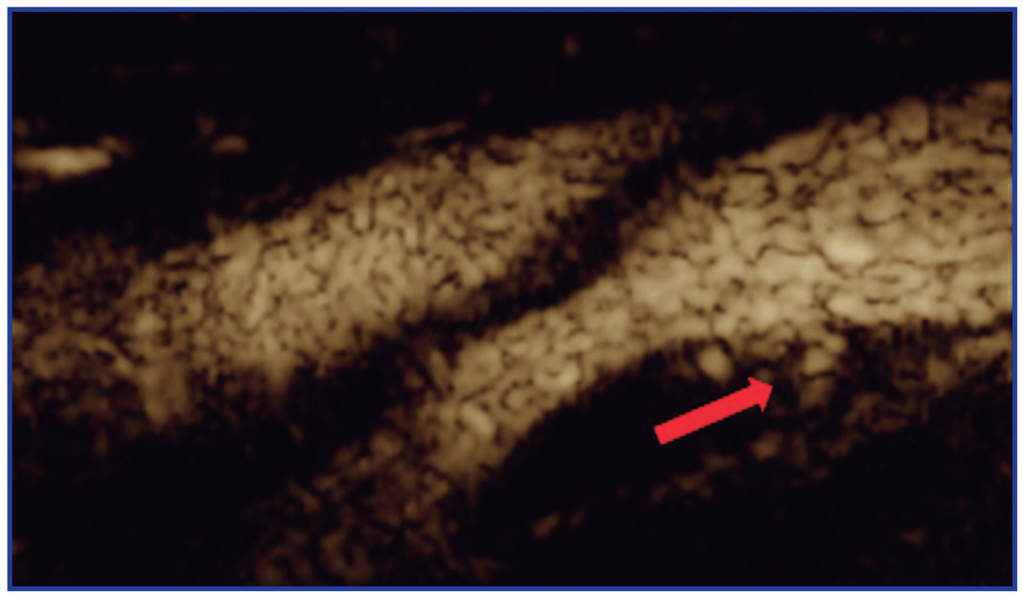
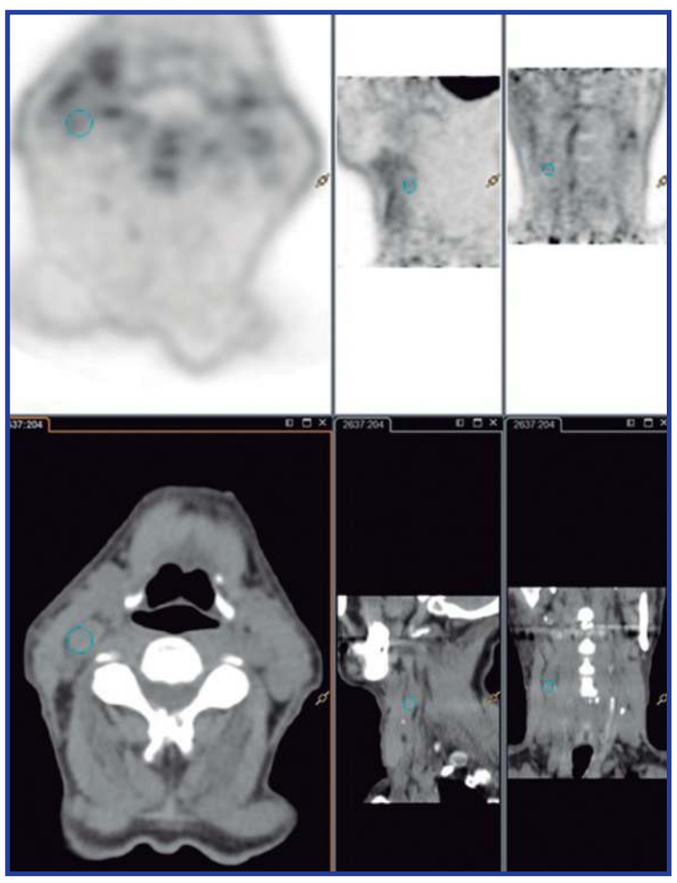


Figure 1: Example of a CEUS study. The image shows an eccentric atherosclerotic plaque from the internal carotid artery during the CEUS study. Plaque neovessels are identified as hyperechoic microbubbles (red arrow).

Figure 2: Example of a carotid [18]-FDG PET-CT quantification. Following semi-automated co-registration of PET and CT images, carotid 18FDG activity in 10 regions of interest (ROI) defined relative to the slice of maximal stenosis was quantified using standardized uptake values (SUV g/mL = measured uptake (MBq/mL)/injected dose (MBq) per patient weight).



Results

We included 50 patients whose mean age was 74.3±10.4y and 74.4% were men. There were 17 (34.0%) patients with a low-grade stenosis (<50%). The remainder presented high-grade carotid plaques. The results of the CEUS were not interpretable in 8 (16%) of the patients, mainly due to calcium shadows. We detected neovascularization in 71.4% of the plaques. The presence of CEUS-detected neovessels was associated with higher plaque inflammation (SUV=2.84±0.56 vs SUV=2.35±0.36, p=0.007). In the multivariate linear regression analysis CEUS-detected neovessels persisted independently associated with inflammation even after adjusting by the degree of stenosis (Table 1).

Table 1: Predictors of Internal Carotid Artery Inflammation

Univariate analysis	Beta Coefficient	95% CI	p
Age	0,005	(-0,009)-0,019	0,466
Sex (woman)	0,418	0,077-0,758	0,017
Current smoking	0,221	(-0,585)-0,143	0,228
Hypertension	0,197	(-0,242)-0,636	0,371
Diabetes	0,192	(-0,128)-0,512	0,234
Dyslipidemia	0,058	(-0,280)-0,396	0,731
Prior antiplatelet therapy	-0,268	(-0,583)-0,047	0,094
Prior use of statins	-0,072	(-0,403)-0,260	0,665
Hypoechoic plaque	0,256	(-0,094)-0,605	0,147
Severe carotid stenosis (≥70%)	0,426	0,127-0,731	0,006
Plaque neovascularization	0,493	0,141-0,846	0,007
Multivariable analysis	**Beta Coefficient**	**95% CI**	**p**
Plaque neovascularization	0,455	0,123-0,787	0,009
Severe carotid stenosis (≥70%)	0,388	0,083-0,695	0,014

Conclusion

CEUS-detected neovessels are associated with carotid plaque inflammation in patients with a recent ischemic stroke.