


Carotid plaque inflammation and calcification on somatostatin receptor PET/CT imaging predict stroke and major adverse cardiovascular events

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Purpose

Carotid atherosclerosis is a risk factor for stroke and major adverse cardiovascular events (MACE) and is characterized by inflammation and calcification at different stages. Simultaneous assessment of both features may improve risk stratification. We therefore evaluated whether combined assessment of carotid plaque inflammation and calcification on [⁶⁸Ga]DOTA-TOC PET/CT predicts stroke and MACE in a real-world oncologic population.

Methods and results

We retrospectively included patients who underwent [⁶⁸Ga]DOTA-TOC PET/CT for suspected or confirmed neuroendocrine tumours. Carotid plaques were assessed visually and semiquantitatively on PET/CT, and patients were categorized into four groups according to the patient-level presence of carotid artery calcification and/or focal [⁶⁸Ga]DOTA-TOC uptake. Median follow-up was 55 months (IQR 42–72). Stroke and MACE, defined as myocardial infarction, hospitalization for myocardial ischaemia, coronary revascularization, and all-cause death, were recorded. A total of 353 patients were evaluated. Carotid artery calcification was present in 123/353 (34.8%) patients, with a median calcification volume of 77.7 cm³ (IQR 27.9–169.8). Forty-six patients (13.0%) showed 67 foci of [⁶⁸Ga]DOTA-TOC uptake, with median SUV_{max} 1.68 (IQR 1.55–1.93) and median TBR 2.14 (IQR 1.65–2.79). Patients with both calcified and inflamed carotid plaques had the highest rates of stroke (15.2%) and MACE (12.1%) vs. all other groups (*P* < 0.05). In multivariable Cox analysis, this combined patient-level phenotype remained independently associated with stroke and MACE and remained significant in competing-risk analyses.

Conclusion

[⁶⁸Ga]DOTA-TOC PET/CT enables simultaneous assessment of macrophage-related carotid plaque inflammation and calcification and identifies a subgroup at particularly high risk of stroke and MACE.

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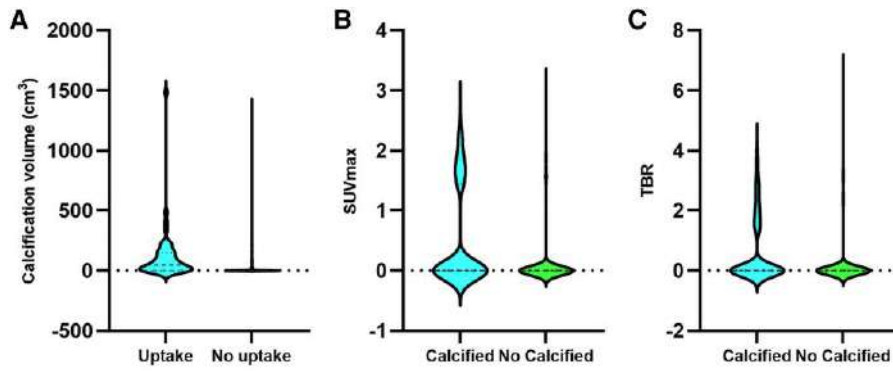


Figure 2 Correlation between carotid artery calcification and focal [⁶⁸Ga]DOTA-TOC uptake. (A) Carotid artery calcification volume was significantly larger in patients with focal [⁶⁸Ga]DOTA-TOC uptake than in those without, 47.2 (0, 149.1) cm³ vs. 0 (0, 13.4) cm³, *P* < 0.001; (B,C) [⁶⁸Ga]DOTA-TOC uptake (SUVmax and TBR) was significantly higher in patients with carotid artery calcification than in those without, (B) SUVmax: 0 (0, 1.44) vs. 0 (0, 0), *P* < 0.001, (C) TBR: 0 (0, 1.38) vs. 0 (0, 0), *P* < 0.001.

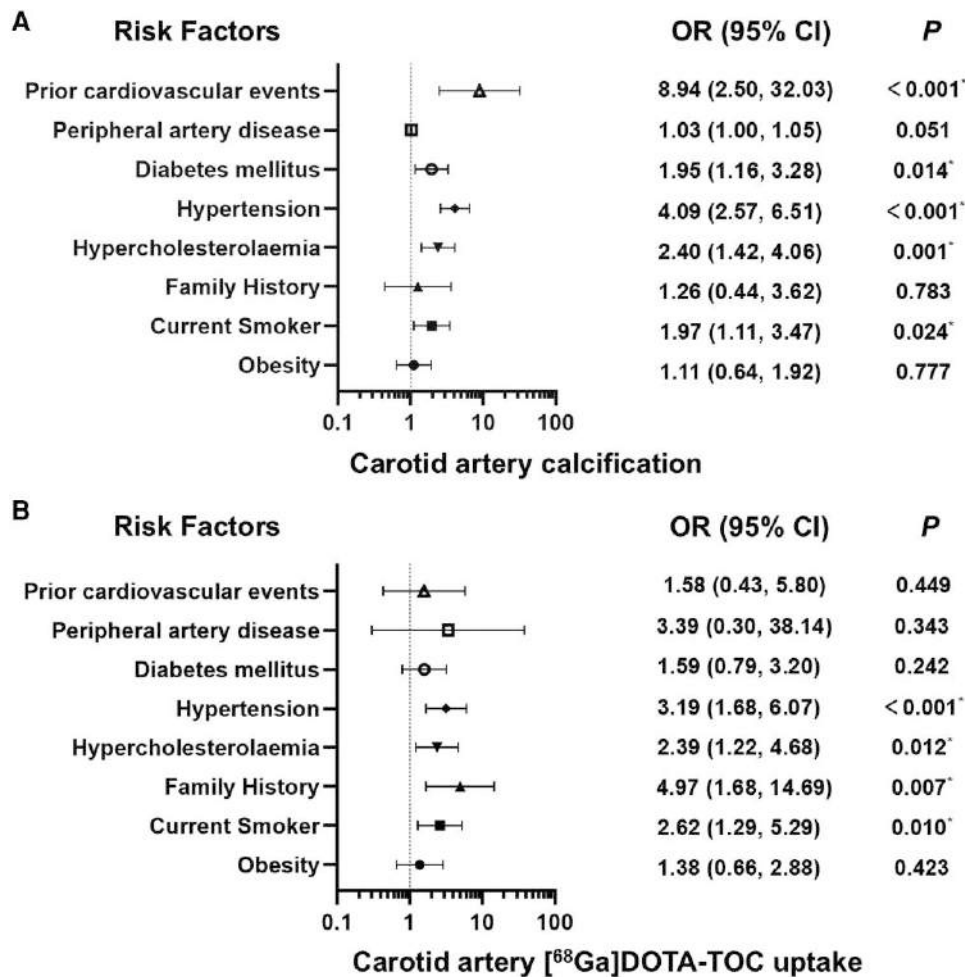


Figure 3 Relationship between cardiovascular risk factors and carotid artery calcification (A), focal [⁶⁸Ga]DOTA-TOC uptake (B). * indicates a statistically significant.

events. Consequently, it was not feasible to construct a robust prognostic prediction model based on these quantitative plaque characteristics. Given the limited number of stroke and MACE events, the multivariable Cox models are at risk of overfitting and should be interpreted as exploratory. Furthermore, only 26 focal [⁶⁸Ga]DOTA-TOC uptake sites in the carotid artery co-localized with carotid artery calcification, and due to the relatively small number of events, we were unable to explore the relationship between inflammatory calcified plaques and cardiovascular events at the lesion level.

Finally, the imaging examinations for the enrolled subjects were conducted over a considerable time span. During this period, the imaging instrumentation was upgraded. Differences in detection sensitivity and spatial resolution between the different scanner generations may introduce variability in the PET quantitative parameters.^{9,10}

Conclusions

Calcified carotid plaques represent a risk factor for the onset of cardio-cerebrovascular hard events. The combined patient-level presence of carotid calcification and M1-like macrophage-related inflammation as detected by [⁶⁸Ga]DOTA-TOC PET/CT identifies a subgroup at particularly high risk of cardio-cerebrovascular hard events. Hence, [⁶⁸Ga]DOTA-TOC PET/CT may be effectively used in order to plan an early start of an effective preventive therapy.

Supplementary data

Supplementary data are available at [European Heart Journal - Cardiovascular Imaging](https://www.ehponline.com/advance-article/doi/10.1093/ehjci/jeq110/8664281) online.

Author contributions

Xiaoliang Shao (Conceptualization, Writing—original draft [equal], Formal analysis [supporting]), Carola Maria Bregenzer (Data curation [equal], Writing—original draft [supporting]), Jiahui Wang [Formal analysis, Methodology (equal)], Yizhou Chen [Formal analysis, Methodology (equal)], Yuetao Wang (Data curation, Methodology [equal], Writing—original draft [supporting]), Luisa Maria Knappe (Data curation [equal], Writing—original draft [supporting]), Axel Rominger (Conceptualization [supporting], Writing—original draft [equal]), Kuangyu Shi (Resources [lead], Writing—original draft [equal]), and Federico Caobelli (Conceptualization, Methodology, Writing—original draft [equal], Supervision [lead])

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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