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LETTER TO THE EDITOR

Comments on association of HbA1c with carotid artery plaques in patients with coronary heart disease

Dear Editor,

Diabetes and carotid arterial plaque (CAP) incidence are related. In a study involving 9,275 patients with coronary disease, Cheng et al. showed a correlation between HbA1c levels and CAP incidence in both pre-diabetic and diabetic subjects. This study also addresses plaque echogenicity, showing a higher prevalence of hyperechoic and heterogeneous plaques in diabetic patients compared with non- and pre-diabetic subjects [1]. These findings highlight the fact that atherosclerosis begins early, in the pre-diabetic phase. The authors also emphasise the influence of increased HbA1c on cardiovascular disease (CVD) risk. As suggested, this relationship could mean that patients with higher HbA1c have had plaques for a longer period or that the development from hypoechoic to hyperechoic plaque is accelerated in those patients. The paper draws attention to the need for detection and management of patients with increased HbA1c, even in the pre-diabetic phase.

But this study also raises other questions: How can ultrasounds help us to assess the CVD risk of our patients? What about the use of multi-modality imaging techniques in the assessment of arterial plaques?

As carotid ultrasound imaging provides a unique 'window' into the identification and evaluation of atherosclerosis, two distinct approaches have been proposed: carotid intima-media thickness (CIMT) measurement and CAP assessment. Due to a lack of precision and specificity of CIMT, quantification of CAP is currently considered as a more powerful predictor of CVD risk [2] and proposed in the guidelines.

However, plaque definition also varies from consensus to consensus. The European Mannheim consensus defined a plaque as a focal thickening that encroaches into the lumen by 0.5 mm or by 50% of the surrounding intimal-medial thickness or where CIMT is >1.5 mm [3]. For the European Society of Cardiology (ESC), a plaque is defined as a focal wall thickening that is $>50\%$ greater than the surrounding vessel wall or as a focal region with an intima-media thickness measurement >1.5 mm that protrudes into the lumen. For the ESC, patients with CAP are considered as at very high risk of CVD [4]. In 2020, the American Society of Echocardiography (ASE) proposed a slightly different definition:

- Any focal thickening thought to be atherosclerotic in origin and encroaching into the lumen (protuberant-type plaque)

Or

- CIMT $\geq$1.5mm in any segment (diffuse-type plaque) [5].

They proposed recommendations for standardisation of the quantification of CAP for the purposes of CVD risk stratification and proposed a CVD risk pathway using plaque grading by two-dimensional/three-dimensional (2D/3D) ultrasound. Unlike the ESC [4], the ASE algorithm divides patients into three CVD risk groups, according to the plaque height: low risk (no plaque or plaque height <1.5 mm), intermediate risk (plaque height or CIMT $\geq$ 1.5 mm) and high risk (plaque height or CIMT $\geq$2.5 mm) [5] (Figure 1).

Assessing the CVD risk more accurately could guide physicians in the management of their patients. It is an important but challenging issue because CVD risk scores are imperfect, especially for patients classified as at intermediate risk. Combining established CVD risk scores with imaging appears reasonable. Coronary artery calcium (CAC) score and ankle-brachial index are good tools, but they also have their faults. Carotid and femoral plaques are strongly linked to atherosclerosis and are good risk markers. Several plaque scores have been proposed (total plaque score, atherosclerosis burden score …), but these scores may be complicated and time-consuming. Plaque area, 3D measurement of plaque volume or plaque vascularity assessment by contrast enhanced ultrasound (CEUS) seem to be more sensitive in assessing CVD risk than mere assessment of plaque presence. Unfortunately, these techniques are also time-consuming and not readily available.

Plaque characterisation has been studied using CEUS, multidetector computer tomography, magnetic resonance imaging or ^{18}fluoro-deoxyglucose positron tomography. As these imaging techniques are more able to detect unstable carotid plaques, their main value lies in

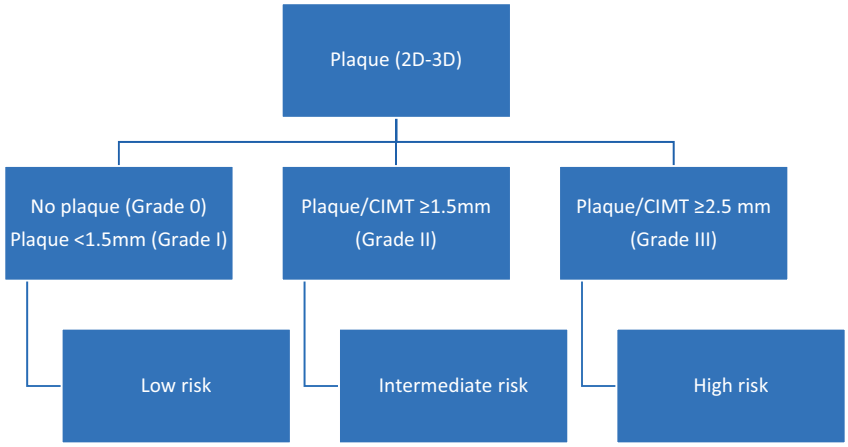

Figure 1. Stepwise CVD risk stratification pathway using plaque grading by 2D/3D ultrasound (proposed by the American Society of Echocardiography for reclassification of low-intermediate risk patients). Intermediate risk may be reclassified as high risk according to patient or plaque vulnerability (neovascularisation and echolucency) [5].

strokeprevention, but given their higher cost, they cannot currently be recommended for serial clinical assessment of atherosclerosis [5].

As proposed by the ESC, it currently looks reasonable to include plaque imaging or CAC score as potential, but not systematic, modifiers in CVD risk assessment (class IIb, level B) [6]. However, head-to-head comparisons of CVD risk assessment methods are still needed.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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