Electron-Beam Computed Tomography in the Assessment of Coronary Artery Disease After Heart Transplantation

To the Editor:

In their study of electron-beam computed tomography (EBCT) for the assessment of coronary artery disease in heart transplantation, Knollmann et al. noted a significant discrepancy between the amount of calcification measured by EBCT and that measured by intracoronary ultrasound. In their discussion, they suggest a number of possible explanations for this. However, this discrepancy may be related to the different pathogenesis of intimal and medial calcification. Intimal calcification occurs within the perimeter of the internal elastic lamina within the atherosclerotic plaque. It is associated with inflammatory cells, lipids, and vascular smooth muscle cells. In contrast, medial calcification occurs as a separate process in the context of aging (Mönckeberg’s sclerosis), end-stage renal disease, neuropathy, diabetes, and a number of rare genetic syndromes. It is associated with elastin and vascular smooth muscle cells.

EBCT is unable to distinguish between medial and intimal calcification. Thus, the use of EBCT to measure intimal calcification and, therefore, atherosclerosis relies on the assumption that the amount of medial calcification in the coronary arteries is negligible. However, in the case of transplantation it is possible that the denervated heart is prone to medial calcification similar to the medial calcification that occurs in peripheral arteries in neuropathy. Using intracoronary ultrasound, the extent of deeper medial calcification may be underestimated because of the acoustic shadow of more superficial intimal calcification.

If EBCT is to be used routinely to assess coronary artery disease in transplanted hearts, it is vital that studies are conducted to determine the incidence of medial calcification within this patient group. This is because the presence of medial calcification will reduce the utility of EBCT calcium score as a measure of atherosclerosis.

Response

We certainly appreciate Dr Farzaneh-Far’s interest in our study, and we greet the opportunity to elaborate on this issue. In our investigation, 7 patients had calcifications of the left anterior descending coronary artery on electron-beam computed tomography (EBCT) only, which cannot be explained by the presence of medial calcification because intracoronary ultrasound (ICUS) did not detect any calcium in these instances. Although ICUS may underestimate the extent of calcifications deep within the arterial wall, it would still detect their presence unless they occurred in combination with thickly calcified intimal plaques. In another 7 patients, calcifications were found by ICUS only, which cannot be explained by the presence of medial calcification either, because all 7 patients displayed calcified intimal plaque formation on ICUS. Therefore, isolated medial calcification would not explain discrepancies in the rates of detecting calcified lesions between EBCT and ICUS. Accordingly, the presence of coronary calcifications on EBCT correlated with calcified plaque on ICUS (concordant result in 84% of cases, P<0.0001).

Although we agree that the EBCT calcium score cannot differentiate different sites of calcification within the vessel wall, our data offer evidence that the total calcium score may serve as a surrogate marker of coronary disease in heart transplant recipients, regardless of its cause. Established concepts of allograft coronary disease include the fact that the disease is characterized by intimal proliferation, but we have no evidence that medial calcification is a feature, neither histologically nor on ICUS. In contrast, Mönckeberg’s disease is highlighted by the absence of coronary artery involvement. ICUS investigations of conventional coronary disease have found that medial calcifications occur in more than half of all angiographically detected atherosclerotic lesions, and the detection of coronary calcifications in the general population is now accepted as proof of coronary disease with grave prognostic implications.

We conclude that isolated medial calcification is not a likely explanation for discrepancies between EBCT and ICUS, nor does it impair the diagnostic powers of EBCT for detecting coronary disease after heart transplantation.

Friedrich D. Knollmann, MD
Roland Felix, MD, PhD
Department of Radiology
Charité, Campus Virchow-Klinikum
Humoldt-University of Berlin
Berlin, Germany

Wolfgang Bocksch, MD
Department of Cardiology
German Heart Institute Berlin
Berlin, Germany

Susanne Spiegelsberger, MD
Manfred Hummel, MD
Roland Hetzer, MD, PhD
Department of Cardiothoracic and Vascular Surgery
German Heart Institute Berlin
Berlin, Germany

Afshin Farzaneh-Far, MRCP(UK)
Division of Cardiovascular Medicine
University of Cambridge
Addenbrooke’s Hospital (ACCI level 6)
Hills Road
Cambridge CR2 2QQ, UK
aff24@cam.ac.uk


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Afshin Farzaneh-Far

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