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Commentary: Use of EBCT in epidemiological studies: the effect of noise and body size on coronary calcium scores

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Electron beam computerized tomography (EBCT) is a non-invasive scanning technique that allows both detection and quantification of coronary artery calcium. Although only 20% of atherosclerotic plaque is calcified, the presence of coronary artery calcium in post-mortem specimens is a marker for the presence of atherosclerotic plaque and the quantity of calcium correlates with total atheroma burden.[1]

Available for over a decade, EBCT has been used extensively in the clinical assessment of patients at high risk of coronary heart disease, predominantly in the US.[2] Another promising application for EBCT is as a screening tool for coronary atheroma in epidemiological studies, particularly in young asymptomatic cohorts. Although fewer in number than those studies utilizing EBCT in clinical settings, there have been a number of recent reports of epidemiological studies using EBCT in participants with no evidence of pre-existing coronary heart disease.[3–6] Sekikawa *et al.* report on such a study in this issue, where they used EBCT to address the question of whether men born after the Second World War in America and Japan show differences in levels of atherosclerosis taking into account differences in cardiovascular risk.[7]

The validity of EBCT has been tested primarily in clinical patients who have high pre-test probability of disease.[2] The validity of the technique in populations with a low prevalence of disease has not been systematically studied, but there are indications that it is less robust in these groups.

Chest diameter and other measures of body size correlated with it are positively correlated with image noise on coronary EBCT scans.[8] Thus, unless adequately accounted for, noise can be mistaken for calcium on EBCT images leading to false positive scores, particularly in those with a high body mass index. The Agatston score,[9] the most widely used method for quantifying calcium on EBCT scans, which was utilized in Sekikawa's study, attempts to eliminate the effect of image noise by employing both a minimum density and a minimum area threshold when identifying calcium in coronary artery CT images. The density threshold of 130 Hounsfield Units has been used consistently in subsequent studies. There has however been considerable variation in the minimum area threshold employed in subsequent studies, from the 1 mm^2 in Agatston's original study to a sensitive 0.52 mm^2 and a more specific 2.05 mm^2.[4,5] This variation has usually been in response to concerns about false positive coronary calcium scores or poor inter-scan variability attributable to image noise when sensitive thresholds are used to define calcium in patients with low coronary calcium scores.

Many of the studies in younger cohorts have reported a positive association between body mass index and positive coronary calcium scores.[3–6] One reported that the association observed between body mass index and a positive coronary calcium score in a cohort aged 28–40 years diminished as the area threshold used

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to define calcium increased.[5] However in this study the positive association between body mass index and coronary calcium score remained significant, even when a relatively high six pixel threshold was used to define calcium (OR 1.64: 1.24, 2.48).

Another approach to minimize the effect of noise that has recently been suggested is to alter the density threshold used to identify calcium on a slice-by-slice basis, according to the noise evident on the EBCT scan. In a study of young people with type 1 diabetes each potential calcific lesion was reviewed by a radiologist, and only considered calcified if the lesion density exceeded the highest Hounsfield Unit measurement of non-coronary tissue in each CT slice.[10] Thus the effective density threshold increased as noise in the scan increased. The association between body mass index and a coronary calcium score greater than zero in this study was small and non-significant (OR 1.13: 0.93, 1.38). The logical consequence of this approach however, is that the more obese a person, with presumably a greater risk of coronary atheroma, the less likely it is that true calcium will be identified as such.

As many coronary heart disease risk factors are associated with and may mediate the effect of obesity on coronary heart disease, this association between body size, noise, and coronary calcium score has implications for the interpretation of epidemiological studies such as Sekikawa's. In those studies using sensitive thresholds to define coronary calcium, associations between body mass index, obesity-related coronary risk factors, and positive calcium scores may be exaggerated due to confounding by noise. In those studies where the definition of calcium is altered according to the noise observed on the scan, associations between body mass index, obesity-related coronary risk factors, and positive calcium scores may be underestimated or missed. It is therefore imperative that when these studies are reported, the area and density thresholds used to define calcium are also reported, the method used (if any) to take account of noise when scoring the scan is made explicit, and the relationship between various measures of body size and positive coronary scores is explored.

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