

Editorial

Coronary computed tomography angiography in asymptomatic patients with diabetes



Angiografía coronaria por tomografía computarizada en diabéticos asintomáticos

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Ischemic heart disease is the main cause of mortality in patients with diabetes. The probability of coronary artery disease (CAD) and cardiovascular risk is higher among these patients than among nondiabetic controls. Given the high prevalence of silent CAD and its association with future cardiac events, screening in asymptomatic patients with diabetes is an attractive option, especially if is performed using a noninvasive imaging technique such as coronary computed tomography angiography (CCTA), which has recently seen significant reductions in costs, radiation dose administered, and scanning time required.

In a recent article published in *Revista Española de Cardiología*, Hyun et al.¹ analyzed the additive value of CCTA for risk stratification in asymptomatic patients with diabetes. Briefly, these authors found that the addition of CCTA information (obstructive CAD, stenosis more than 50%) to the United Kingdom Prospective Diabetes Study (UKPDS) risk category improved the c-index and reclassification rate for predicting the primary outcome (a composite of cardiac death, nonfatal infarction, unstable angina, and coronary revascularization). The study is particularly notable for its long follow-up (a median of 10 years), and its results complement and expand those of previous studies on the prognostic value of CCTA in asymptomatic patients with diabetes.^{2,3}

The study does, however, have some limitations. First, coronary revascularization was included in the primary composite outcome and was performed in about 50% of patients experiencing this outcome. The study excluded revascularizations performed during the first 3 months after CCTA. However, given that patients were asymptomatic, the initial approach to many of those showing evidence of obstructive CAD on CCTA would probably have been conservative. Nevertheless, the presence or absence of such a finding would influence, or even be decisive, regarding the adoption of a subsequent invasive strategy (eg, in the case of the onset of atypical symptoms), with the consequent risk of incurring a self-fulfilling prophecy. Furthermore, the UKPDS scale

was developed to predict the risk of hard cardiovascular events, and therefore direct comparisons would be facilitated by removing coronary revascularization from the primary outcome. Irrespective of how information on these patients was handled after revascularization (whether censoring or continued follow-up), it would obviously affect the interpretation of the results and their clinical implications. However, excluding revascularization would have markedly reduced the number of events and the power of the study, which may be why the authors ruled out this option.

On the other hand, CCTA performed quite well, in that evidence of obstructive CAD was found in about 40% of the patients included. This result may be related to way in which referrals to CCTA are implemented in this particular hospital, which would make it difficult to generalize to other hospitals. Furthermore, the low adoption of current cardiovascular prevention recommendations at the start of the study raises the question of how the results may have been different in an era of more intense treatment of cardiovascular risk factors in patients with diabetes.

Finally, the degree of coronary stenosis was taken into account, but not its extent. Previous studies have shown that the predictive power of risk scales (eg, the Segment Involvement Score or the CT-Leaman score) is better improved by adding the extent of CAD to them than by adding the presence of obstructive CAD and/or coronary calcification alone.^{4,5}

In addition to the issue of whether the detection of atherosclerotic plaques by CCTA provides additive prognostic information over and above clinical risk scores in asymptomatic patients with diabetic, the key question is whether the increased cost and use of radiation and contrast media would translate into a clinically relevant decrease in the future risk of serious cardiac events. The usefulness of a systematic screening technique is based precisely on the assumption that detecting an abnormal result will improve the prognosis of the disease; unfortunately, we still lack compelling evidence regarding this assumption. The FACTOR-64⁶ trial included 900 asymptomatic patients with diabetes randomized to CCTA vs optimal medical treatment. No significant differences were found between groups in the primary endpoint (a composite of death, infarction, or unstable angina) or the secondary endpoint (coronary death, nonfatal infarction, or unstable angina). Of note, the study was stopped before reaching

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the initially planned number of patients (1100), and although follow-up was conducted over a long period, the event rate in the control group was very low, which definitely detracted from the statistical power of the study. However, other studies using stress tests have, in general, obtained negative results,⁷ resulting in the absence of clear indications in clinical practice guidelines.^{8,9}

The use of CCTA could only improve prognosis through changes in treatment and, to date, only seems to be associated with better adherence to medical treatment and stricter control of cardiovascular risk factors.¹⁰ The available evidence seriously calls into question the power of coronary revascularization to improve prognosis outside the setting of acute ischemic heart disease. Thus, the BARI 2D trial¹¹ randomized 2368 patients with type 2 diabetes mellitus and evidence of CAD to revascularization or medical treatment. After a mean follow-up of 5 years, no significant differences were found between groups in mortality rates or serious cardiovascular events; around 18% of the patients enrolled were asymptomatic.

If revascularization is not beneficial for asymptomatic patients with diabetes, why screen with CCTA instead of simply offering maximal medical treatment to all such patients? The most relevant argument in favor of screening for CAD with CCTA is based on the fact that considering diabetes as a coronary risk equivalent requiring the most aggressive approach at all stages of the disease without taking into account the heterogeneity in risk in these patients could be an outdated approach.¹² In fact, 21% of the patients included in the study by Hyun et al. had no evidence of CAD.¹ The use of computed tomography in this context could facilitate the personalization of preventive lipid-lowering and/or cardiometabolic treatments¹³ and identify candidates for antiplatelet therapy. Its simplest and most widely studied modality, coronary calcium scan (CCS), has the advantages of reduced costs and radiation dose and no need for contrast. Coronary calcium scan is a reliable predictor of cardiovascular events in patients with diabetes and has been shown to be superior to the UKPDS scale in predicting cardiovascular risk.¹⁴ However, it cannot detect noncalcified atherosclerotic plaque or the extent of CAD; even a CCS score of 0 is not an accepted reason for discontinuing statin therapy in these patients,¹⁵ which almost leaves us where we started. The additive value of CCTA over CCS was not evaluated in the study by Hyun et al.; nevertheless, the CCTA information for CAD provided significant discriminatory power.¹

Although evidence is still very scarce on the use of computed tomography to identify subgroups of asymptomatic patients with diabetes who might benefit from personalized treatment strategies, relevant studies are underway. The SCOT-HEART 2 trial (NCT03920176), currently in the inclusion phase, will enroll 6000 patients with cardiovascular risk factors (including diabetes) and no known atherosclerotic disease and randomize them to CCTA vs conventional treatment based on a risk score. This trial will undoubtedly shed more light on the potential role of CCTA in primary prevention.

In conclusion, CCTA is an excellent tool for cardiovascular risk stratification of asymptomatic patients with diabetes. Although its applicability in primary prevention is limited by the use of contrast media, upcoming technical improvements and reduced radiation

doses make it a promising technique in the assessment of such patients. However, in a value-based health care system, further studies are needed to determine which specific patient subgroups might derive the maximum net benefit from the use of this technique.

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CONFLICTS OF INTEREST

None declared.

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