Cardiovascular and Metabolic Science www.ancam.org.mx

Vol. 32 Suppl. 3
July-September 2021

doi: 10.35366/100807

Coronary atherosclerosis diagnosis by non-invasive studies: echocardiography, computed tomography

Diagnóstico de aterosclerosis coronaria mediante estudios no invasivos: ecocardiografía, tomografía computarizada

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INTRODUCTION

Coronary artery disease (CAD) represents an important cause of morbidity and mortality worldwide.[1] Noninvasive cardiac imaging studies (NICIS) are fundamental for appraisal. Choosing a cardiac imaging test demands knowledge and understanding of diagnostic and prognostic accuracy, advantages and drawbacks. Establishing presence of CAD will determine the implementation of measures to avoid an acute coronary event as well as secondary prevention. In the event that CAD is ruled out, will allow reinforcing adherence to primary prevention.[2]

Patients are referred to a NICIS due to the presence of different both; typical and atypical symptoms. There is no enough evidence in open population demonstrating that a test is significantly better than any other for CAD diagnosis. Appropriate criteria, pretest probability, availability, accessibility, center expertise and cost, will facilitate clinicians´ decision for the use of a specific imaging modality.[2] For the purpose of this section, only stress echocardiography (SE) and computed tomography will be considered.

STRESS ECHOCARDIOGRAPHY

Background. Due to its versatility, technological advances in acquiring images, echo borders enhancement agents, lack of radiation and diagnostic accuracy, SE has become a reliable tool in CAD diagnosis and stratification. It is also indicated in preoperative risk assessment, evaluation of exertional dyspnea, after revascularization and for ischemia localization. It is an operator-dependent technique and a high level of training is needed to adequately perform and interpret results.[3]

Technical principles. The detection of wall motion abnormalities (WMA) is the core of SE. For didactic purposes, it is considered that WMA appear before symptoms and electrocardiographic (EKG) changes, and after perfusion abnormalities.[4] The protocol consists in acquiring base, low dose, peak dose and recovery phases images in four-screen setup. Either exercise (treadmill or bicycle) or pharmacologically (dobutamine or dipyridamole) SE can be used, the target heart rate will be at least 85% of the age-predicted heart rate. Eventually, atropine and/or handgrip strength can be used to enhance chronotropic response.

The left ventricle is divided in 17 segments. Basal wall motion is compared with intermediate and mainly with peak stress. Rationale of this test is inducing a chronotropic and inotropic response to induce myocardial ischemia. Normal segments will present hypercontractile responses while ischemic segments will become hypo-contractile. A necrotic segment has dysfunction at rest and remains fixed during stress. A hypokinetic segment may show either improvement during stress indicating a stunned myocardium or improve during early stress and later deterioration with peak stimulation

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Received:
01/07/2021
Accepted:
09/07/2021

How to cite: Gutiérrez-Fajardo P, Sierra-Galán LM. Coronary atherosclerosis diagnosis by non-invasive studies: echocardiography, computed tomography. Cardiovasc Metab Sci. 2021; 32 (s3): s253-s257. https://dx.doi.org/10.35366/100807

(biphasic response) suggesting viability and ischemia. During the test, EKG, blood pressure, oxygen saturation and symptoms are monitored. Indications for stopping SE protocol are presence of new or worsening of WMA, significant rhythm abnormalities, hypertensive response, significant hypotension and intolerable symptoms.[5]

Diagnostic accuracy and prognostic information. Accuracy of SE refers to detection of coronary artery disease and myocardial viability. Different stressors such as exercise (ES), dobutamine (DBS) and dipyridamole (DYS), have similar accuracies and sensitivities for CAD and results will be related to percentage of coronary stenosis. The more stenotic and greater number of affected coronary arteries, the more probability to provoke wall motion abnormalities. In general, sensitivity and specificity for ES, DBS and DYS are 85% and 77%, 80% and 86%, and 78% and 91%, respectively. On the other hand, a normal SE has been associated with a good prognosis with an event rate for cardiac events less than 1% per year. In terms of myocardial viability detection, DBS is widely used for assessing contractile reserve.[5]

Advantages and disadvantages

Due to its versatility, echocardiography represents the first imaging technique to approach different clinical scenarios. SE maintains these advantages: availability, accessibility, portability, reproducibility, low cost, no radiation, border enhancement agents, rational time protocol and immediate results. Main disadvantages are related with both; patient (poor acoustic window due to thinness, obesity, thorax over distention in some pulmonary diseases and exercise capacity) and operator (level of expertise, left ventricle foreshortening).

Highlights

SE is a reliable NICIS for risk stratification and diagnosis of CAD.

Normal wall motion does not rule out significant CAD.

Abnormal wall motion could be secondary to ischemic or non-ischemic origin.

Negative SE in a high probability pretest patient could be associated to circumflex disease, two non-significant vessel disease or small vessel disease.

CONCLUSIONS

SE remains as a robust NICIS, either with exercise or with a pharmacological agent, allowing the assessment and stratification of patients with diagnosed or suspected CAD. Also, can be used to detect functional viable myocardium.

COMPUTED TOMOGRAPHY

Background. There are mainly two different types of atherosclerotic coronary artery disease (CAD) that can cause acute coronary syndromes (ACS), the obstructive CAD (OCAD) and non-obstructive CAD (NObCAD). OCAD is traditionally clinically recognized by causing a ST-segment elevation during myocardial infarction, by sensitive biomarkers, by high-grade coronary stenosis in coronary computed tomography angiography (CCTA), and by the luminography of the invasive coronary angiography (ICA). However, the identification of NObCAD remains challenging if we study the patients only with «standard imaging modalities» and criteria. It is imperative to learn how to recognize the NObCAD since it contributes to the burden of atherosclerosis. In some groups, such as young women, it represents the majority of cases of ACS. NObCAD causes ACS with significantly lower cardiovascular risk at baseline in those patients, typically categorized as low-risk patients, and a subsequently lower likelihood of death or MACE. However, they are still at high risk for cardiovascular mortality and morbidity based on their underdiagnoses and undertreatment.[6]

Some of these cases are currently included as MINOCA or INOCA syndromes, which include several pathophysiological entities beyond the scope of this text.

Technical principles. The non-invasive evaluation of OCAD and NObCAD relies upon the decision to investigate anatomy vs function. If we decide to investigate CAD functionally, we have to use techniques that look for myocardial perfusion or function at stress, such as echocardiography, nuclear –SPECT

and PET– computed tomography perfusion, and cardiovascular magnetic resonance. If we opt to investigate CAD anatomically, we have to look inside the vessels; the more common, widely available, and reproducible method for that purpose is CCTA.

CCTA is performed in a multidetector CT scanner with the possibility of at least 64 slices. A lower number of detectors is feasible, but the image quality and the amount and type of artifacts refrain from widely used and recommended. The main requirements of this study from the technical point of view are; 1) the intravenous access, it is crucial to have good access to allow a high pressure of a rapid bolus of a considerable amount of viscous iodine contrast media, 2) heart rate control, around 60 bpm, in scanners with a higher number of detectors this requirement is less crucial and even could not be necessary, 3) good patient cooperation with breath-holding during images acquisition.

The presence of arrhythmias and some intravascular-intracardiac devices limits the acquisition, produces several artifacts and reduces image quality; however, it is challenging but feasible in experienced hands.[7]

Radiation dose is important however, we cannot see it, and some personnel is not aware of the risks of the radiation to the patients. We should scan patients having the ALARA principle[8] (as low as reasonably achievable) in mind. Specific data about radiation dose reduction protocols used worldwide and the information from Latin America is shown in detail in the PROTECTION VI study.[9]

Diagnostic accuracy and prognostic information for OCAD *(Figure 1A)*, in the real world, as demonstrated by the PICTURE study, without the bias of patients with a high

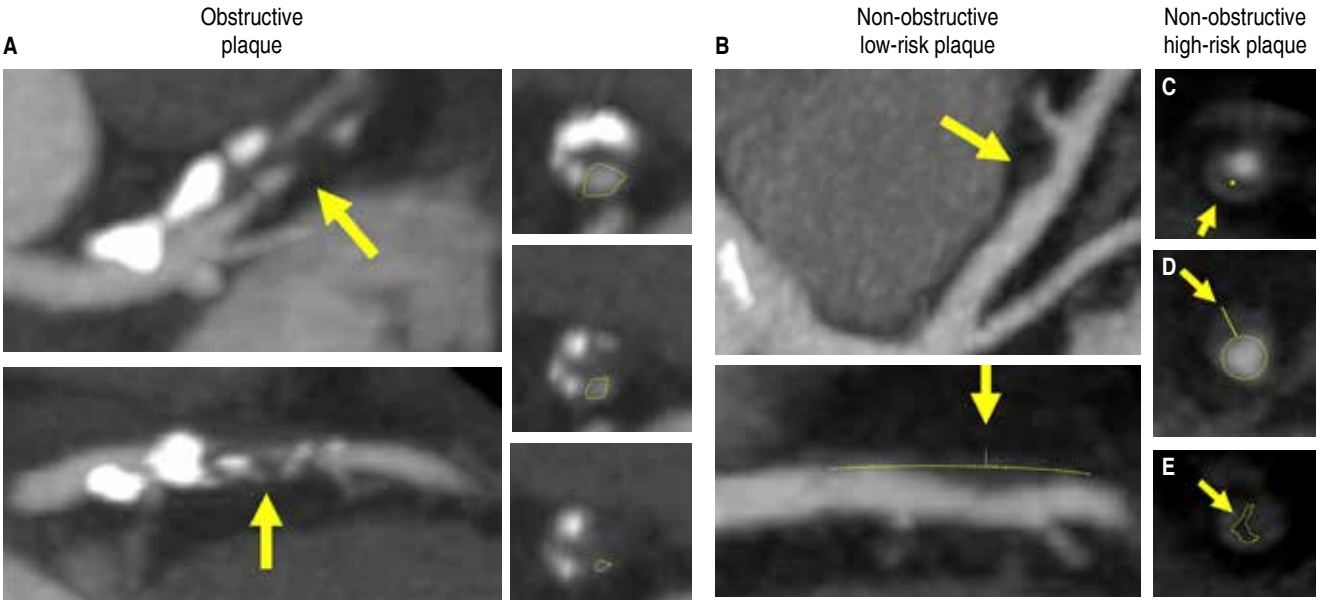

Figure 1: A) The left panel shows high-grade stenosis of the proximal LAD, with stable characteristics such as intense focal calcification, absence of significant positive remodeling, progressive reduction of the lumen, absence of areas of plaque rupture, and napkin ring sign. The right panel shows two different types of non-obstructive plaques. **B)** Shows two orthogonal MPR projections of the proximal LAD. The superior image shows the non-obstructive non-calcified plaque. The lower image shows its positive remodeling (a dashed thin line highlighted the border of the «normal» arterial wall, and the small vertical line marked with the arrow indicates the volume of the non-calcified plaque that expands outwards from the external wall of the artery, representing the positive remodeling. **C-E)** Shows thin axial MPR of the artery with a non-obstructive plaque and different high-risk features. **C)** Shows a plaque that has the napkin ring sing (marked with the tiny asterisk). **D)** Shows a plaque that significant positive remodeling marked with the slim perpendicular line above the lumen (circle). **E)** Shows a low-attenuation plaque of 40 HU delineated and marked with the arrow.
LAD = left descending coronary artery; MPR = multiplanar reconstruction; HU = Hounsfield.

prevalence of the disease, in a prevalence of 52% with a stenosis ≥ 50% by ICA, CCTA has a sensitivity of 92%, and a specificity of 87%. If the stenosis is defined as ≥ 70% by ICA, CCTA has a sensitivity of 93% and a specificity of 89%.[10] The main strength of CCTA is its negative predictive value of 99%, as shown in the ACCURACY trial,[11] giving the ability to discard with confidence and with no additional risk to the patient for future events after an episode of chest pain even from the Emergency Department.[12]

NObCAD *(Figure 1B)* remains challenging since those are the type of lesions that could produce an ACS without being rule out by myocardial perfusion studies and by calling «non-significant» lesions in the CCTA. However, some key features of those lesions have an excellent prognostic value by being associated with the future development of ACS.[13,14] Those features allow to call an atherosclerotic lesion a high-risk plaque and are the equivalent of the histological characteristics of a vulnerable plaque, such as the «napkin ring sing» *(Figure 1C)* that is defined as the presence of a ring of high attenuation around certain coronary artery plaques; and attenuation of the ring presenting higher than those of the adjacent plaque and no > 130 Hounsfield units.[15] This sign has a specificity of 97%, a negative predictive value for future ACS of 99%, and a hazard ratio of 5.55. Therefore, it has significant prognostic importance for ACS. It is independent of other CCTA features such as positive remodeling *(Figure 1D)* and low-attenuation plaque *(Figure 1E)*, which has a hazard ratio of 5.25 and 3.75, respectively; even higher than the presence of an obstructive plaque that has a hazard ratio of 1.62.[14] This information gives us a clue if we do not identify OCAD and the suspicion remains high for ischemic heart disease, the possibility is the presence of one or more features of NObCAD as a surrogate of the presence of an unstable, vulnerable atherosclerotic plaque.

Advantages and disadvantages

The main benefits of CCTA are the ability to evaluate the coronary anatomy non-invasively, its high negative predictive value,[15] and the possibility to identify high-risk plaques with certainty. The main disadvantages are its low positive predictive value, the prompts to further test if the clinical suspicion remains high, and the absence of functional information[15] if following the ALARA principle's current recommendations.

Highlights

CAD, obstructive, or non-obstructive can cause ACS.

There are currently imaging modalities that allow non-invasively the proper identification of each one.

CCTA implies radiation and should be considered when order one to a patient, balancing the benefit to the risk, and using the ALARA principle at all times.

CONCLUSIONS

CCTA should be part of the diagnostic algorithm for patients with dyslipidemia, in intermedia risk[16] and with chest pain, using the ALARA principle in the setting of stable ischemic heart disease and also in the Emergency Department, always taking advantage of its main strength, the negative predictive value to rule out obstructive lesions, and the characterization of vulnerable, non-obstructive plaques.

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