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Editorial

Impact of Multidetector Computed Tomography Noninvasive Coronary Angiography on Epidemiology: Toward Direct Evidence of Cardiovascular Risk

Impacto de la coronariografía no invasiva por tomografía computarizada con multidetectores en epidemiología: hacia una evidencia directa del riesgo cardiovascular

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Ischemic heart disease, one of the most prevalent diseases in the developed world, carries high morbidity and mortality requiring the use of numerous economic resources.[1] An estimated one-third of patients with acute myocardial infarction and no relevant medical history present with sudden death and very few patients receiving medical assistance survive such a serious event.[2] Moreover, those patients that are admitted to hospital due to acute coronary syndrome require highly specialized medical attention and may develop serious short- and medium-term complications that incur a considerable health cost. Given such a dramatic situation, it is understandable that there is widespread social and political awareness that justifies the considerable resources allocated to the treatment of ischemic heart disease. However, because health spending is limited, it is imperative to boost research to find new and more refined methods of primary prevention of this disease that, above all, are effective in each individual.

In the middle of the last century, the epidemiological relationship between coronary atheromatosis and the now well-recognized cardiovascular (CV) risk factors was described, with the Framingham study as an international benchmark.[3] The possible health and economic importance of this association in the development of ischemic heart disease increased interest in primary prevention policies.

The European Society of Cardiology was the driving force behind studies that revealed the regional prevalence of CV disease in Europe.[4] A north–east to south–west gradient in CV disease incidence was identified, with Mediterranean countries showing a much lower incidence of CV disease than northern Europe.[5] At the same time, local epidemiological studies appeared in Spain, such as the RICORNA[6] study in Navarre, the MONICA-Catalunya[7] study, and the REGICOR[8,9] registry, which has now been in existence for over 35 years. The results of the latter study led to the REGICOR CV risk function. This function was initially valid only for the local population studied, but, after adaptation to the Framingham equation and validation for the Spanish population (VEFICA study), it became the first and only CV risk function validated for the Spanish population.[10]

Although these CV risk functions are useful for designing population-wide strategies, one drawback is that they fail to adequately predict individual risk. Not all acute myocardial infarction patients have a high CV risk, while not all people with significant risk have an acute myocardial infarction. Moreover, a considerable proportion of the population (about 40%) is included in the intermediate risk group. Thus, to improve the individual predictive value of CV risk functions, their results should be refined by other tests, particularly imaging techniques.[11]

High-resolution radiographic techniques now allow noninvasive examination of the anatomy of the coronary tree with a low level of radiation, much lower than the first systems used for this purpose. Electron beam computed tomography (EBCT) was the first imaging technique that allowed identification of calcified atherosclerotic plaques in the coronary tree without the use of iodine contrast to identify those asymptomatic individuals at risk of cardiac events.[12] Calcium deposition in atherosclerotic plaques is a consequence of their natural process of repair. Initially, the plaques have a marked inflammatory component, high lipid content, and vascularization. The appearance of microbleeds, with their subsequent repair processes, makes the plaques particularly vulnerable, because the intraluminal structural integrity can be affected, providing a location for the cascade of events that leads to acute myocardial infarction. However, the repeated phenomena of bleeding and repair usually occur in the interior of the plaque, with a progressive reduction in the lipid component and decrease in vascularization, as well as fibrosis and the final repair phenomenon of calcification.

Thus, the greater the quantity of calcified plaques, the greater the probability of concomitant lipid or fibrolipid plaques. The possibility afforded by EBCT to quantify the amount of calcium present in the coronary tree, made possible by the method proposed by Agatston in 1990,[13] gave rise to the concept of "plaque burden". The next step was to quantify the (calcified) plaque burden in extensive series of the general population to determine the normal distribution of the amount of coronary calcium present in asymptomatic individuals distributed by sex and age. The availability of normality tables of the general asymptomatic population allows individuals to be placed

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within the normal distribution of plaque burden, unless they occupy a higher percentile than desired, with a consequent increase in coronary risk.[14] Observational clinical studies performed in the general population for follow-up and prognostic evaluations showed a clear relationship between the occurrence of CV events and survival, both with the absolute values of the Agatston score (amount of coronary calcium accumulated in the arteries) and with the percentile occupied in the distribution tables by sex and age. The independent prognostic value of the Agatston score allowed refinement of the classification of the CV risk group for a specific individual, which was very useful for reclassifying those persons included in the intermediate risk group to higher or lower categories.[15] Similarly, the prognostic importance of the absolute value of the Agatston score is noteworthy, because an individual with an Agatston <100 has a much better prognosis, given identical risk factors, than someone with higher values.[16]

The drawback of requiring a highly sophisticated system such as EBCT to calculate coronary calcium, rarely available due to its high cost and low yield, was rapidly resolved with high-resolution multidetector computed tomography (MDCT) systems synchronized with the electrocardiogram. Within a few years, during the first decade of this century, MDCT underwent a dramatic technological development aimed at improving the spatial resolution to obtain submillimeter-thick sections and minimize the radiation dose, which in some current systems is less than 1 mSv. These technological advances vastly exceeded those of EBCT, which was also much more expensive, and MDCT validation of the Agatston method was swift. Nonetheless, the emergence of clinical studies begun in the era of EBCT, which related the coronary calcium score to the CV risk, whether combined[17] or not[18] with classical risk factors, provided irrefutable evidence of the relationship between coronary calcium and CV risk. A result of these studies was the use of this parameter to refine the classification of CV risk in those persons with intermediate risk according to classical risk functions, and the selection of subgroups of patients that would require a more aggressive lipid-lowering therapy according to their plaque burden.[19] Likewise, recent guidelines published by the European Society of Cardiology[20] also consider the information provided by MDCT (or EBCT) to be useful for reclassifying coronary risk in individual patients. Nonetheless, coronary calcium is still just a rough indicator of total coronary atheromatosis, because contrast-free examinations overlook noncalcified plaques. Accordingly, a lack of coronary calcium is not synonymous with an absence of coronary atheromatosis, because noncalcified soft plaques or those with minimal focal calcification are precisely those plaques that are more likely to be vulnerable; nonetheless, studies indicate that in the general population, the risk of a coronary event without indications of calcified plaques is negligible.[21]

With the arrival on the scene of the latest generation of MDCT systems, noninvasive coronary angiography (NCA) can be performed with a similar level of irradiation as that of a coronary calcium scan. The only difference is that the angiography technique requires the administration of iodine contrast. The images obtained by NCA are of high quality and, although conventional coronary angiography has a higher temporal and spatial resolution, they include information not available from invasive light-based imaging.In addition to quantification of vascular obstruction, NCA allows multiple slices and projections of the coronary tree to be obtained (some of which are unavailable in invasive coronary angiography), as well as permitting visualization of the coronary tree in 3D or 4D integrated with other anatomical structures. The technique allows evaluation of not only the coronary lumen, but also identification of the distribution of atherosclerotic plaques in the vascular wall, acquisition of basic information on tissue characteristics (lipid content, fibrosis, and calcification), and quantification of plaque extent.[22]

NCA via MDCT is a recent diagnostic imaging technique that, given the clinical impact of the information provided, has featured prominently in research and opinion articles in the few short years of its existence. Due to the almost complete absence of false negatives in the detection of atherosclerotic plaques, NCA is indicated in current guidelines due to its high negative predictive value. An NCA that rules out the existence of coronary atheromatosis, allows a practically nil short-/medium-term probability of cardiac events to be predicted with a high degree of certainty. NCA has already demonstrated its economic utility by avoiding unnecessary invasive diagnostic coronary angiography examinations that would show normal results, particularly in those patients that present to the emergency department with atypical chest pain or with inconclusive results for ischemia detection[23] or in those patients that systematically require a preoperative coronary angiography.[24] In contrast, the number and degree of obstructions caused by the atherosclerotic plaques directly identified by NCA have an independent prognostic value for coronary events, in relation to both classical risk factors[25] and coronary calcium score.[26] Also noteworthy is the psychological effect on patients of knowing the status of their coronary arteries, which can significantly increase adherence to the treatment of modifiable risk factors.

In short, the information provided by the CV risk functions has allowed and continues to allow the development of large-scale public health strategies, with visible reductions in the incidence of ischemic heart disease in the general population. Nevertheless, the current ability to noninvasively study coronary anatomy opens new doors to the investigation of the etiopathogenesis of coronary atheromatosis and its clinical consequences. Although the technique is still new, the accumulation of case series in the general asymptomatic or largely symptomless population is growing. Just as studies on coronary calcium were previously performed, several multicenter studies are currently underway that aim to use MDCT to determine the distribution and characteristics of coronary atheromatosis in the general population. Following this line of investigation, and after the promising results of a pilot study,[27] the multicenter Secure Prevention with Imaging of the Coronary Arteries (SPICA) study is about to begin in Spain, supported by the Working Group on Cardiac Imaging of the Spanish Society of Cardiology (*Sección de Imagen Cardiaca de la Sociedad Española de Cardiología*), with the collaboration of the IMIM (*Instituto Hospital del Mar d'Investigacions Mèdiques*) with the aim of determining the distribution and degree of obstruction of coronary lesions with a 5-year clinical follow-up of events in a representative sample of the general asymptomatic population at intermediate risk. The results of this study are likely to permit more precise classification of CV risk groups, which, given that coronary calcium quantification and the high negative predictive value of the absence of lesions on NCA are accepted by current guidelines, would affect primary prevention strategies. Moreover, an important field has been opened by combining, in a single individual, the characterization of coronary lesions with the characteristics of a genetic analysis, which would undoubtedly improve personal and familial risk predictions.

Performing NCA at a population level in primary prevention programs has been suggested to be an unacceptable expense for publicly-funded health systems. We believe this contention to currently be premature because it lacks a solid foundation, with no definitive data for or against the suggested approach. Given that a third of cases of acute coronary syndrome present as sudden death in patients with no relevant medical history, it is surprising that the cardiological community is reluctant to accept, even hypothetically, that NCA could come to be a fundamental diagnostic tool in primary prevention strategies, particularly for individuals at intermediate risk or with a family history of ischemic heart disease. The argument of the economic cost of NCA for primary prevention is also surprising, given the huge expense that would otherwise be spent

on each patient admitted for acute myocardial infarction. It is nothing new that the best way to combat a disease is to prevent it,[28] and current evidence indicates that NCA is a revolutionary diagnostic technique for primary prevention.

CONFLICTS OF INTEREST

None declared.

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