

## Editorial

# Is a picture worth a thousand words in cardiovascular risk assessment? ¿Mejor una imagen que mil palabras también en la valoración del riesgo vascular?

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Cardiovascular disease (CVD) events are responsible for more than 4 million deaths in Europe each year.<sup>1</sup> In Spain, although cardiovascular mortality has been decreasing in the last 15 years, it continues to be the main cause of death among the national population.<sup>2</sup> The most useful measures to prolong life expectancy and, consequently, to reduce cardiovascular mortality are the following: *a*) no smoking; *b*) maintain a body mass index of between 18.5 and 22.9 kg/m<sup>2</sup>; *c*) follow a high-quality dietary plan (ie, Mediterranean diet); *d*) maintain moderate alcohol intake (5–14.9 g of ethanol/d); and *e*) practise moderate to vigorous exercise > 30 minutes a day.<sup>3</sup> Although these recommendations work for the general population, more intensive lifestyle efforts and the use of evidence-based preventive pharmacotherapy (ie, statins) should be prescribed for persons at high risk of atherosclerotic CVD, since, in this case, the benefits of medical therapy outweigh the risk of any adverse effects.<sup>1</sup> In this setting, to select persons who merit inclusion in special preventive cardiovascular programs, criteria are currently based on absolute predicted risk for atherosclerotic CVD (typically, a 10-year estimated risk).

Currently, cardiovascular risk assessment uses different scales adapted to each region or country, according to their own cohort data. The Framingham general CVD profile is the most common risk assessment tool used worldwide.<sup>4</sup> In Europe, the most commonly used scale is the European Systematic Coronary Risk Evaluation (SCORE), because it is based on analysis of large representative European cohorts,<sup>1</sup> in which risk estimates have been differentiated into high- and low-risk regions. This fact explains why the Framingham-REGICOR (*Registre Gironí del Cor*) is also recommended in Spain.<sup>5</sup> Based on the 2019 ESC/EAS guidelines, patients are classified according to their SCORE as very high risk (SCORE  $\geq$  10% for 10-year risk of fatal CVD), high risk ( $\geq$  5% and  $\leq$  10%), moderate risk ( $\geq$  1% and  $\leq$  5%), or low risk ( $<$  1%). To estimate the total risk of CVD (fatal and nonfatal event) we must multiply by 3 the value obtained in the SCORE scale.<sup>1</sup>

Estimation of absolute risk of developing a CVD event is useful to assist health professionals in selecting which patients are likely to benefit from statin therapy. This estimation can be performed rapidly in daily practice with the use of clinical

calculators. However, the scales may sometimes overestimate (especially in older people and countries with low CVD mortality) or underestimate (especially in young people and countries with high CVD mortality) vascular risk.<sup>1</sup> To minimize mismatches, risk assessment tools should be recalibrated to suit different populations. Both laboratory tests (ie, plasma lipoprotein(a) and the results of -omics techniques) and imaging techniques such as vascular 2-dimensional (D) and 3D ultrasonography, coronary artery calcification (CAC) score, multidetector cardiac computed tomography angiography, cardiac magnetic resonance imaging, and cardiac positron emission tomography are very useful for quantifying atherosclerotic burden.<sup>6–8</sup> However, up to now, only vascular ultrasonography has been used to evaluate the general population because of its feasibility and relatively low cost.<sup>6</sup>

Focusing on this area of research, in the current issue of *Revista Española de Cardiología*, Bermúdez-López et al.<sup>9</sup> evaluated the prevalence of subclinical atheromatosis by vascular ultrasound examination in 12 territories of the carotid and femoral arteries in a cohort of 8330 middle-aged asymptomatic participants (51% women) with 1 or more cardiovascular risk factors (CVRF). The participants were recruited by stratified sampling from the primary care electronic clinical history database of the Catalan Health Institute. All were found to have low-to-moderate cardiovascular risk, since patients with a clinical history of diabetes, chronic kidney disease, or a previous cardiovascular event were excluded. Interestingly, a new chronic disease such as dyslipidemia, hypertension, kidney disease, obesity, or diabetes was diagnosed in a significant proportion (10%–21%) of this sample. However, the results of ultrasonography were even more sound since the authors detected subclinical atheromatosis, especially in common femoral and carotid bifurcation, in a high percentage of the participants (70%), whereas intermediate and generalized atheromatosis were found in 1 in 3 and 1 in 5 participants, respectively. Total plaque area was higher in the femoral artery and increased with the number of CVRF.

The article by Bermúdez-López et al. highlights the shortcomings of cardiovascular risk assessment scales, especially when they are applied to persons with low-to-moderate cardiovascular risk, since a huge amount of persons with subclinical atheromatosis who should be candidates for therapeutic intensification were not captured using standard risk assessment scales.<sup>9</sup> Formerly, the absence of classic CVRF was considered evidence of low atheromatosis risk, but some previous studies, such as the PESA (Progression of Early Subclinical Atherosclerosis) study,

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which included 3869 participants (age  $45.8 \pm 4.3$  years; 63% men) have shown the presence of atherosclerotic plaques in different territories in up to 30% of patients without known CVRF and 60% of participants in tertile 3 of global plaque burden analysis had no or only 1 CVRF.<sup>10,11</sup> Likewise, the AWHs (Aragon Workers' Health Study), which enrolled 1423 middle-aged men (mean  $51.0 \pm 3.7$  years), > 60% with no or 1 CVRF, also found a higher prevalence of subclinical atherosclerosis (72%) together with a high CAC score (38%).<sup>12</sup> Therefore, besides a classic vascular risk assessment score, other tools must be used to obtain a better classification of persons and more precisely define those with risk of future cardiovascular events.<sup>13</sup>

The validity of certain alternative assessment tools, however, has been questioned. The United States Preventive Services Task Force provided a Recommendation Statement about the routine use of ankle-brachial index, high-sensitivity C-reactive protein, or CAC score measurement in clinical risk assessment and decision-making.<sup>14</sup> The main conclusion was that there was insufficient evidence to recommend any of these markers to be used in the general population, although CAC score used in selective patients could reclassify patients to high or low cardiovascular risk.<sup>14</sup> In this sense, Baber et al.<sup>15</sup> enrolled 5808 asymptomatic adults (mean age, 69 years) to prospectively assess the role of vascular imaging (CAC score and 3D carotid ultrasound) on cardiovascular risk prediction over a median follow-up of 2.7 years. The authors concluded that detection of subclinical carotid or coronary atherosclerosis improves risk predictions and reclassification compared with conventional risk factors, although cost-effective analyses are necessary to define the optimal role of these techniques in CVD prevention. It is precisely in this population of moderate or low cardiovascular risk that serum or urine markers (apolipoprotein B, lipoprotein (a), triglycerides, C-reactive protein, and albuminuria) or imaging studies (ultrasonography to detect atherosclerotic plaque in the carotid or femoral arteries or coronary tomography to measure CAC score) may improve risk classification.<sup>1</sup>

In summary, there is consensus that there is an urgent need to improve our tools for cardiovascular risk assessment, especially in those patients who are considered to be at low or moderate risk. Therefore, the current approach to primary prevention of CVD would need to be fundamentally reconsidered. Using scales such as SCORE or Framingham-REGICOR should be the first step, but due to the frequent discrepancies between risk assessments based on CVRF and atherosclerotic burden, complementary tests are needed, mainly imaging techniques such as vascular ultrasonography and/or CAC score. Henry Ibsen coined the adage that 'a picture is worth a thousand words' in the fields of journalism and publicity. Perhaps we should apply the same adage in the screening of patients at different vascular risk, and imaging techniques should substitute clinical examination of CVRF in order to optimize estimation of

individual cardiovascular risk and, thus, enter in the era of precision cardiovascular medicine.

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