Editor's Page

Evaluation of Cardiovascular Risk in the Asymptomatic Patient: Beyond the Classical Risk Factors and Towards Vascular Age

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"A man is as old as his arteries" – Thomas Sydenham

Cardiovascular disease remains the leading cause of death in developed countries. The tremendous advances in the pharmacological and interventional management of patients with established cardiovascular disease have drastically decreased cardiovascular mortality; however, the bet that contemporary and future medicine has to win is not how to *cure* but how to *prevent* cardiovascular disease. The majority of patients visiting primary health care facilities are patients with no established cardiovascular disease, with no symptoms typical of cardiovascular disease and with usually one or more cardiovascular risk factors. Risk assessment, a critical step in decision making, is usually performed with the use of risk charts, such as the Framingham Risk Score or the European Score, which take into account the traditional risk factors for coronary artery disease. Recent developments in the European Score, according to the statistics of each European country, may provide more accurate risk prediction than the Framingham Risk Score for specific European countries with lower cardiovascular mortality than the USA.[1]

Risk scores are very useful in terms of statistical calculations and public health management; however, they provide only a crude assessment of any individual patient's risk. In addition, the management of asymptomatic patients in the intermediate or the lower risk category remains a challenge. Tools for better risk assessment than that provided by the traditional risk scores would be highly desirable and would help in the risk stratification of such patients.

These stratification tools should have specific properties: they should be safe and non-invasive, in order to be employed in large populations; they should not be expensive; and, most importantly, they should provide incremental prognostic information beyond that provided by the Framingham or the European Risk Scores. Several tools have been tested for this purpose; amongst them there are those that assess vascular function or structure in various vascular beds, which have been widely tested as surrogate markers of cardiovascular risk.

Vascular function can be estimated by the assessment of endothelial function or arterial stiffness and wave reflections.[2] Endothelial function can be assessed non-invasively by measuring post-ischaemic dilation of the brachial artery. Although this measurement has incremental prognostic value in patients with established cardiovascular disease, there are conflicting data regarding its predictive role in the asymptomatic patient or in the general population.[3] Arterial stiffness and wave reflections can be measured non-invasively by means of pulse wave velocity measurement and applanation tonometry, respectively.[4] There is strong evidence that arterial stiffness and wave reflections have incremental prognostic value in the general population or in patients with no known cardiovascular disease.[5,6]

There are several ways to assess atherosclerosis of the peripheral arteries. Imaging techniques based on ultrasound, computed tomography, or magnetic resonance imaging can image most arterial territories, including the aorta, the carotid arteries, the renal arteries and the arteries of the lower limbs.[7] The presence

of extracoronary atherosclerosis is a marker of increased risk for coronary artery disease. Of note is the measurement of carotid intima-media thickness, which can be performed easily with a high-frequency ultrasound machine. It has been shown that, even in the absence of carotid plaques, the presence of increased carotid intima-media thickness is an independent predictor of cardiovascular risk.[8]

Coronary atherosclerosis can be evaluated noninvasively by the measurement of coronary artery calcium. This is done using computed tomography without contrast administration, and with much less radiation than is used in computed tomographic angiography of the coronary arteries. Coronary calcium is related to the presence and the extent of coronary atherosclerosis, and is an independent predictor of cardiovascular risk in asymptomatic patients and in the general population.[9]

Accordingly, the concept of the *vascular age* of an individual has emerged. If vascular age is lower than chronological age, then the patient can be reclassified to a lower risk category. Conversely, should vascular age be greater than chronological age, the patient is reclassified in a higher risk category. However, there are several issues that need to be resolved. While cut-off values for "desired" and "non-desired" levels exist for the majority of these indices, true normograms are lacking for most of them. Furthermore, important questions remain to be answered. Can these methods be combined and, if so, which of them should be put together? Does any combination increase the predictive accuracy, compared to one method alone? Although studies have attempted to clarify these issues, there is no consensus regarding the combination of methods. At present, there are recommendations regarding coronary calcium score, carotid intima-media thickness and aortic pulse wave velocity issued by Cardiological and Hypertension Societies in Europe and the USA.[10,11]

The field is expanding and more data are accumulating regarding the predictive value of these parameters. Until all necessary data have been gathered, assessment of vascular function and structure in individuals will continue to be performed according to a department's expertise and facilities, and vascular age is calculated in many centres via assessment of coronary or peripheral arteries.[12] Estimation of arterial age has the potential to increase the accuracy of risk prediction and guide the management strategy of asymptomatic patients.

References

1. Panagiotakos DB, Fitzgerald AP, Pitsavos C, et al. Statistical modelling of 10-year fatal cardiovascular disease risk in Greece: the HellenicSCORE (a calibration of the ESC SCORE project). Hellenic J Cardiol. 2007; 48: 55-63.
2. Kullo IJ, Malik AR. Arterial ultrasonography and tonometry as adjuncts to cardiovascular risk stratification. J Am Coll Cardiol. 2007; 49: 1413-1426.
3. Fathi R, Haluska B, Isbel N, et al. The relative importance of vascular structure and function in predicting cardiovascular events. J Am Coll Cardiol. 2004; 43: 616-623.
4. Vlachopoulos C, Alexopoulos N, Boudoulas H, et al. Aortic function in coronary artery disease. In: Boudoulas H, Stefanadis C, editors. The aorta: structure, function, dysfunction and diseases. Informa Healthcare; 2008.
5. Laurent S, Cockcroft J, Van Bortel L, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J. 2006; 27: 2588-2605.
6. Agabiti-Rosei E, Mancia G, O'Rourke MF, et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. Hypertension. 2007; 50: 154-160.
7. Raggi P, Taylor A, Fayad Z, et al. Atherosclerotic plaque imaging: contemporary role in preventive cardiology. Arch Intern Med. 2005; 165: 2345-2353.
8. Lorenz MW, von Kegler S, Steinmetz H, et al. Carotid intima-media thickening indicates a higher vascular risk across a wide age range: prospective data from the Carotid Atherosclerosis Progression Study (CAPS). Stroke. 2006; 37: 87-92.
9. Shaw LJ, Raggi P, Schisterman E, et al. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology. 2003; 228: 826-833.
10. Greenland P, Abrams J, Aurigemma GP, et al. Prevention Conference V: Beyond secondary prevention: identifying the high-risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing Group III. Circulation. 2000; 101: E16-22.
11. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2007; 28: 1462-1536.
12. Vlachopoulos C, Aznaouridis K, Stefanadis C. Clinical appraisal of arterial stiffness: the Argonauts in front of the Golden Fleece. Heart. 2006; 92: 1544-1550.