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Screening for cardiovascular disease risk in asymptomatic patients

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Abstract: Cardiovascular diseases (CVD) are the leading cause of death in Western countries and one of the leading causes of death in the world. The lifetime risk of atherosclerosis-related CVD in persons aged 50 years averages 52% for men and 39% for women, with large differences depending on the severity of risk factors. Cardiovascular risk assessment may be useful for targeting preventive treatment in patients who are asymptomatic but at high risk for CVD. Stratification of patients according to CVD risk remains challenging, especially in cases with low or intermediate short-term risk.

Key words: cardiovascular disease, risk scale, prevention, myocardial infarction

Introduction

CVD is the leading cause of death in Western countries and one of the leading causes of death worldwide. It is estimated that one in three American adults has one or more of the vascular diseases associated with atherosclerosis (coronary artery disease, cerebrovascular disease, or peripheral artery disease) [1]. The lifetime risk of atherosclerotic CVD for persons aged 50 years averages 52% for men and 39% for women, with wide variations depending on the severity of risk factors [2]. Assessing individual cardiovascular risk may be useful for targeting preventive treatment in patients who are asymptomatic but at high risk for CVD [3]. To facilitate individual risk assessment in patients, several algorithms have been proposed. Most risk scores included age, sex, blood pressure, smoking status, diabetes mellitus, and lipid levels. Some recently proposed scores include additional risk factors, including use of antihypertensive therapy, C-reactive protein (CRP), family history of premature CAD, low socioeconomic status, and glycated hemoglobin (hemoglobin A1c). .

Although obesity is a cardiovascular risk factor, it is often overlooked because its effect is largely mediated by other risk factors in the short term (5-10 years in most risk assessment algorithms). Chronic kidney disease, another obvious risk factor for CVD, has not yet been included in risk assessment methods. The majority of the population has one or more CVD risk factors [4]. The importance of cardiovascular risk factors was demonstrated in the INTERHEART study (a case-control study conducted in 52 countries), which showed that optimization of 9 easily measured and potentially modifiable risk factors could lead to a 90% reduction in the initial risk of MI [5].

CVD prevention strategies may vary in effectiveness depending on baseline CV risk. To properly assess the risk-benefit ratio of any prevention strategy, it is important to estimate the absolute risk reduction. If the relative risk reduction is the same in all risk groups, the absolute risk reduction will be greater in the high-risk cohort than in the low-risk cohort. For this reason, it is very important to accurately assess cardiovascular risk. Depending on the risk assessment scale used, the same patient may be classified at different levels of risk. However, one should not confuse the

precise quantitative values obtained by risk scoring with the largely arbitrary definitions that are assigned to them by preventive algorithms. For example, although 9.8% may represent a lower risk and 10.2% an intermediate risk, these estimates differ only slightly; however, when comparing different risk assessment scales, in most cases, based on such values, patients can be classified into different risk groups.

In this context, various risk assessment scales have been proposed as possible means of quantitative risk assessment in individuals without CVD symptoms (Table 1). It is important to note that implementing a "high-risk" strategy alone is unlikely to reduce the overall prevalence of CVD, since the "lower-risk" population, which by virtue of its sheer size is the largest group affected by heart disease, will be the source of the majority of cardiovascular events . Thus, it is important for social purposes to implement both high-risk prevention and population-based approaches.

Framingham Risk Score (FRS). Framingham Study Heart Study is an important achievement [6], widely known for its developed risk score for predicting the occurrence of events related to CAD over 10 years in people without symptoms of this disease [7]. Risk factors used in the Framingham score include age, gender, total cholesterol, high-density lipoprotein cholesterol (HDL -C), blood pressure and smoking. It is important to note that the Framingham grading scale is valid and can be easily used in clinical practice. FRS for assessing "hard" end points associated with coronary artery disease is included in a number of recommendations for the prevention of CVD [3,8,9] and is used to select tactics for influencing risk factors (Table 1).

The adapted FSR was included by a panel of experts in the National Educational Program on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults in the United States (III Report of the Panel on the Evaluation and Treatment of Hypercholesterolemia in Adults - Adult Treatment Panel III - ATP III) for use in recommendations for screening and treatment of dyslipidemias [3]. Although adequate risk assessment by the FRS has been validated in many populations, including European Americans and African Americans [10], its accuracy is somewhat limited in some European and Asian populations, and some risk markers are not included in the FRS. A systematic review of 27 studies using the Framingham scoring system found that the ratio of predicted to observed events ranged from an underestimation of about 0.43 in a high-risk population to an overestimation of about 2.87 in a low-risk population [11]. The FRS has been widely evaluated in a variety of settings, and many of the issues identified may also be relevant to other risk assessment systems.

In addition to the coronary event risk score, the FRS has been developed for the totality of all CVD associated with atherosclerosis (CHD, including angina, cerebrovascular accidents, peripheral arterial disease and heart failure) [2], as well as separate risk scores for each of these diseases , including the risk of peripheral artery disease [12], stroke [13] and heart failure [14]. In addition to assessing 10-year risk, scales for assessing risk over the entire subsequent life [15,16] and risk over the next 30 years of life [17] have also been developed. These latter risk assessment scales require further validation.

III report of the expert group on the assessment and treatment of hypercholesterolemia in adults - Adult Treatment Panel III - ATP III. This document provides updated recommendations for the assessment and treatment of hypercholesterolemia in adults [3]. ATP III identifies three risk categories for coronary artery disease, depending on which the goals and forms of therapy that reduce low-density lipoprotein cholesterol (LDL cholesterol) levels are determined. The highest risk category (>20% over 10 years) includes patients with CAD and diseases equivalent to CAD (atherosclerotic lesions of other arteries and diabetes mellitus). In this category, it is recommended to maintain a target LDL cholesterol level of <100 mg/dL.

In the second risk category, which includes patients with multiple (>2) risk factors, a target LDL cholesterol level of <130 mg/dL is recommended. Major risk factors include smoking, blood pressure >140/90 mmHg . or taking antihypertensive drugs, low HDL cholesterol, family history of premature IHD, age >45 years in men or >55 years in women. The ATP III algorithm stratifies patients into groups with a 10-year risk of developing CAD >20%, 10% to 20%, and <10%. The third category includes people with no or 1 risk factor, and the recommended target LDL- C level in this category is <160 mg/dL.

In 2004, a modification of the risk categories was proposed [18] with the division of the category with multiple risk factors into a moderate-high risk group (> 2 risk factors with a 10-year risk of developing CAD from 10% to 20%) and a moderate risk group (> 2 risks factors with a 10-year risk of CAD <10%). In the moderately high-risk group, an additional treatment goal may be to reduce LDL- C <100 mg/dL, based largely on the results of the **ASCOT** Lipid Lowering Trial in Adults Treated for Hypertension (Anglo-Scan-dinavian Cardiac Outcomes Trial) [19].

SCORE scale . Project SCORE (Systematic Coronary Risk Evaluation) was intended to improve the accuracy of risk assessment in patients in Europe. The SCORE scoring system was developed based on data from over 200,000 patients pooled from 1 to 2 European cohort studies [20]. The SCORE score assesses the 10-year risk of a first fatal atherosclerosis-related event, including myocardial infarction, stroke, or aortic aneurysm. This score is important because it assesses the risk of any fatal event associated with atherosclerosis, although it does not assess the risk of nonfatal events.

LDL cholesterol ratio , systolic blood pressure, and smoking. A unique aspect of the SCORE system is the separate risk scores for high- and low-risk regions of Europe. However, the predictive value of the SCORE system was high in each of the European study cohorts. There are currently several country-specific versions of the SCORE scale available.

Reynolds Risk Score. The Reynolds Risk Score was originally intended to develop and validate an algorithm for assessing total cardiovascular risk in healthy women [21]. Thirty-five factors were assessed in a clinical study in the United States of approximately 25,000 initially healthy female health care professionals. The Reynolds Risk Score assesses the 10-year cumulative risk of cardiovascular events (MI, ischemic stroke, coronary revascularization , and cardiovascular death).

It should be noted that risk factors such as blood pressure and body weight were not measured directly during this study; these indicators were self-reported by study participants. This could lead to a decrease in the assessment of the prognostic significance of these factors and cause an increase in the prognostic significance of other variables. In addition, this risk assessment scale has only been validated in the population in which it was developed.

The authors proposed 2 models of the risk assessment scale: the most accurate and simplified clinical (Reynolds risk scale). The Reynolds risk score includes age, systolic blood pressure, hemoglobin A1c in the presence of diabetes, smoking, total and LDL cholesterol , C-reactive protein as assessed by a high-sensitivity assay, and parental history of MI before age 60 years. Unlike the FRS and the SCORE score, the Reynolds risk score evaluates and takes into account risk factors such as parental history of premature CAD and precise CRP levels.

The Reynolds risk score with male-specific adjustment was used with good results in healthy men without diabetes mellitus [22]. The authors showed that in a population of male health professionals enrolled in a clinical trial, the addition of CRP and a parental history of myocardial infarction under age 60 years, as in women, improved prediction of total cardiovascular risk and risk reclassification compared with classification according to the traditional FSR included in ATP III.

ASSIGN scale. ASSIGN scale (Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network /SIGN to Assign Preventative Treatment was developed using a representative database in Scotland [23]. The scale was obtained in a population of men and women aged 30 to 74 years without symptoms of cardiovascular disease. The ASSIGN score assesses the 10-year risk of developing cardiovascular disease, including death from cardiovascular disease, diagnosis of coronary artery disease, cerebrovascular disease at hospital discharge, or coronary artery intervention.

Important risk factors for this scale include traditional factors such as the number of cigarettes smoked, low social class and family history, but not obesity. New to the ASSIGN scale is the inclusion of an assessment of an index of social status, which may explain social disparities in CVD.

QRISK Risk Score . QRISK CVD risk score (QRE-SEARCH Cardiovascular Risk Algorithm was developed based on data from a large primary health care population in the UK. This cohort consisted of 1.3 million people aged 35 to 74 years without symptoms of diabetes mellitus or cardiovascular disease [24,25]. The QRISK score assesses the 10-year risk of developing cardiovascular diseases, including myocardial infarction, coronary artery disease, stroke and transient cerebrovascular accident. Risk factors assessed were age, sex, smoking, systolic blood pressure, total cholesterol to LDL cholesterol ratio, body mass index, family history of coronary artery disease, socioeconomic status, and treatment with antihypertensive drugs.

This was the first study to use data from a general practice population rather than an observational study in a predefined population cohort. The QRISK score, like the ASSIGN score, includes low socioeconomic status, which is an important step in recognizing the importance of social deprivation in assessing cardiovascular risk. The main drawback of this scale is that the validity of the scale was tested in the same population from which the scale was developed.

Additional prognostic indicators

Although risk scoring models can improve predictive accuracy, their implementation in clinical practice leaves much to be desired. In addition, these models are developed from data obtained in different populations, but are used in the context of patients. However, this is quite consistent with our practice of healthcare and the use of medical interventions; Evidence-based medicine is based on applying to patients when prescribing drug therapy or preventive treatment the average effects observed in clinical trials. The use of a number of non-invasive tests, such as the ankle-brachial index , has been proposed to assess asymptomatic atherosclerosis. index ABI), calcification of the coronary arteries, thickness of the intima-media complex of the carotid artery (intima media thickness , IMT) and electrocardiographic studies with physical activity [26,27]. Many of these noninvasive tests are touted as potential means of improving and perhaps simplifying the assessment of cardiovascular risk in people without symptoms of CVD. However, the feasibility of their use in CVD screening remains controversial [28,29].

The ankle-brachial index , which is the ratio of systolic blood pressure measured at the ankle to systolic blood pressure measured at the upper arm, is quickly and easily measured and is an indicator of peripheral arterial disease in the lower extremities, which is overwhelmingly due to atherosclerosis. A recently published analysis pooling results from 16 international cohorts [30] showed that the ankle-brachial index provides additional independent risk information beyond the Framingham score , and a low ankle-brachial index approximately doubles the risk of all-cause and cardiovascular mortality and major coronary events in all FSR categories. The authors of this analysis proposed a new risk assessment formula that includes the ankle-brachial index and FRS markers and anticipate further development and validation of this model.

Computed tomography can non-invasively detect and quantify coronary artery calcification . Coronary artery alcinosis and its degree appear to be a very useful factor for risk assessment, as it essentially provides a visual representation of coronary atherosclerosis. According to MESA research (Multi-Ethnk Study of Atherosderosis), there was a strong association between coronary calcification and incident CAD, with an adjusted relative risk of coronary events ranging from 3.6 to 9.7 depending on the severity of calcification [31]. The C-index (discriminant accuracy) when assessing risk factors with the addition of arterial calcification was high - 0.83 for MI and death and 0.82 for all manifestations of CAD (while when assessing only risk factors was 0.79 and 0.77, respectively; $p < 0.01$ when comparing these assessment options) [31].

The intima-media complex of the carotid arteries is considered a marker of early atherosclerosis. This indicator has been used in large population studies, but the results of its measurement are very dependent on the specialist performing the vascular ultrasound examination. A number of studies have reported a modest, graded association between carotid intima-media thickness and the presence of coronary atherosclerosis, as well as the risk of future cardiovascular events [32]. However, when adjusted for traditional risk factors, the importance of intima-media thickness for risk assessment is weakened. In addition, this test is only available at selected centers, and when used in routine clinical practice, the results of intima media thickness measurements vary widely between specialists.

Abnormal results of exercise electrocardiographic studies are associated with an increased risk of MI and sudden cardiac death [33]. Exercise testing has a significant diagnostic and prognostic advantage compared to changes in the -segment during a conventional ECG study, including for assessing physical performance, restoration of heart rate, the presence or absence of arrhythmias and hemodynamic reactions.

A cohort study of asymptomatic patients followed for more than 20 years showed that exercise testing had a strong predictive value, over and above the Framingham score , for the risk of cardiovascular death in patients in categories with a risk of CAD events less than 20% for 10 years (when classified according to the Framingham scale) [27]. According to the Framingham Study, exercise testing provided additional prognostic information when assessed in models adjusted for age and other Framingham scores, especially in the highest risk group (with a predicted 10-year risk of CAD of 20%) [34].

Conclusions : Should the risk be assessed over the next 10 years or throughout the rest of life? Recently, emphasis has been placed on the risk of CVD throughout life. Among people without CVD at age 50, more than 50% of men and almost 40% of women will develop CVD in their later lives. Should we place more emphasis on assessing risk over a lifetime than over the next 10 years? Patients aged 50 years or younger may have a very high lifetime cardiovascular risk that may be reduced by reducing risk factors; but such patients may have a low 10-year cardiovascular risk (due to the weighting of age in the 10-year risk formula) and may therefore be classified as low risk.

Assessing risk across the life course may enable policymakers to more actively engage public interest in the prevention, diagnosis and treatment of CVD, especially in young people who are at high long-term risk. In addition, lifetime risk has the potential to guide resource allocation to improve population health and CVD prevention services, as well as be useful in the design of epidemiological studies. However, assessment of short-term (10-year) risk is useful in identifying patients who require active risk reduction in the short term. This level of risk may justify the use of aggressive pharmacologic agents and must be determined to balance the effectiveness, cost, and safety of therapy.

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