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STATE-OF-THE-ART PAPER

Screening for Cardiovascular Risk in Asymptomatic Patients

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Cardiovascular disease is the number 1 cause of death in the western world and 1 of the leading causes of death worldwide. The lifetime risk of atherosclerotic cardiovascular disease (CVD) for persons at age 50 years, on average, is estimated to be 52% for men and 39% for women, with a wide variation depending on risk factor burden. Assessing patients' cardiovascular risk may be used for the targeting of preventive treatments of individual patients who are asymptomatic but at sufficiently high risk for the development of CVD. Risk stratifying patients for CVD remains challenging, particularly for those with low or intermediate short-term risk. Several algorithms have been described to facilitate the assessment of risk in individual patients. We describe 6 risk algorithms (Framingham Risk Score for coronary heart disease events and for cardiovascular events, Adult Treatment Panel III, SCORE [Systematic Coronary Risk Evaluation] project, Reynolds Risk Score, ASSIGN [Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network/SIGN to Assign Preventative Treatment], and QRISK [QRESEARCH Cardiovascular Risk Algorithm]) for outcomes, population derived/validated, receiver-operating characteristic, variables included, and limitations. Areas of uncertainty include 10-year versus lifetime risk, prediction of CVD or coronary heart disease end points, nonlaboratory-based risk scores, age at which to start, race and sex differences, and whether a risk score should guide therapy. We believe that the best high-risk approach to CVD evaluation and prevention lies in routine testing for cardiovascular risk factors and risk score assessment. We recommend that health care providers discuss the global cardiovascular risk and lifetime cardiovascular risk score assessment with each patient to better explain each patient's future risk. Appropriate intervention, guided by risk assessment, has the potential to bring about a significant reduction in population levels of risk. (J Am Coll Cardiol 2010;55:1169–77) © 2010 by the American College of Cardiology Foundation

Case Vignette

A 56-year-old woman without any cardiovascular symptoms comes to your office to establish care. She does not smoke currently, but she reports smoking until 4 years ago when her sister at age 54 had an ischemic stroke. There is no family history of myocardial infarction (MI) or sudden cardiac death. Her resting blood pressure is 138/76 mm Hg, fasting glucose is 109 mg/dl (6 mmol/l), total cholesterol is 210 mg/dl (5.4 mmol/l), high-density lipoprotein (HDL) is 42 mg/dl (1.1 mmol/l), and triglyceride level is 201 mg/dl (2.3 mmol/l). She is physically inactive, and her body mass index (the weight in kilograms divided by the square of the height in meters) is 31. She has never taken any medication. She is asking what is her risk for a future cardiovascular disease (CVD) event?

The Clinical Problem

Cardiovascular disease is the number 1 cause of death in the western world and 1 of the leading causes of death worldwide. An estimated 1 in 3 American adults have 1 or more types of atherosclerotic vascular disease (coronary heart disease [CHD], cerebrovascular disease, or peripheral artery disease) (1). The lifetime risk of atherosclerotic CVD for persons at age 50 years, on average, is estimated to be 52% for men and 39% for women, with a wide variation depending on risk factor burden (2). Assessing a patient's cardiovascular risk may be used for the targeting of preventive treatments of individual patients who are asymptomatic but at sufficiently high risk for the development of CVD (3).

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Abbreviations and Acronyms

ABI = ankle-brachial index
ASSIGN = Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network/SIGN to Assign Preventative Treatment
ATP = Adult Treatment Panel
CHD = coronary heart disease
CRP = C-reactive protein
CVD = cardiovascular disease
FRS = Framingham risk score
HDL-C = high-density lipoprotein cholesterol
hsCRP = high-sensitivity C-reactive protein
IMT = intima media thickness
LDL-C = low-density lipoprotein cholesterol
MI = myocardial infarction
QRISK = QRESEARCH Cardiovascular Risk Algorithm
SCORE = Systematic Coronary Risk Evaluation

Several algorithms have been described to facilitate the assessment of risk in individual patients. Most risk scores have included age, sex, blood pressure level, smoking status, diabetes mellitus, and lipid values. Several recent risk scores have proposed including additional risk factors, including use of antihypertensive therapy, C-reactive protein (CRP), family history of premature CHD, social deprivation, and hemoglobin A1c.

Although obesity is a risk factor, it is frequently omitted because its influence is largely mediated through other cardiovascular risk factors in the short term (5- to 10-year timeline of most risk estimation algorithms). Chronic kidney disease, another apparent risk factor for the development of CVD, has yet to be incorporated into a risk scoring method. Most persons in the general population have 1 or more risk factors for CVD (4). To demonstrate the importance of cardiovascular risk factors, the INTERHEART study, a case-control study of 52 countries, noted that optimization of 9 easily measured and potentially modifiable risk factors could potentially result in a 90% reduction in the risk of an initial acute MI (5).

Cardiovascular prevention strategies may vary in benefit depending on the underlying level of cardiovascular risk. The absolute reduction in risk is important to estimate, to adequately assess the risk versus benefit of any prevention strategy. If the relative risk reduction is equal across risk strata, the absolute reduction would be greater in a high-risk cohort than in a low-risk cohort. For this reason, it is very important to accurately estimate the cardiovascular risk. Depending on the risk score used, the same patient may be categorized into a different level of risk. However, one must not confuse the quantitative value provided by the risk score and the largely arbitrary labels put on those by prevention algorithms. For example, although 9.8% may be lower risk and 10.2% may be intermediate risk, these scores do not differ markedly, yet that is the magnitude of most reclassification that happens when comparing risk scores.

In this context, different risk scores have been proposed as potential means for quantifying the assessment of risk in asymptomatic persons (Table 1). Importantly, implementing a "high-risk" strategy alone is unlikely to reduce the overall prevalence of CVD because the "lower-risk" population, which by sheer number is the largest group affected with heart disease, would comprise most events. Thus, for societal purposes, it is important to implement both high-risk prevention and population-based approaches.

Strategies and Evidence

Framingham risk score (FRS). The Framingham Heart Study is a landmark achievement (6), well known for its 10-year risk score for prediction of CHD events in asymptomatic patients (7). Risk factors used in Framingham scoring include age, sex, total cholesterol, high-density lipoprotein cholesterol (HDL-C), blood pressure, and cigarette smoking. Importantly, the FRS is easy to apply and clinically relevant. The FRS for hard CHD events has been incorporated into several guidelines for CVD prevention (3,8,9) and been used to guide treatment of risk factors (Table 1).

The FRS was adapted and then incorporated into the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) for use in their recommendations for screening for and treatment of dyslipidemia (3). Although the FRS has been validated in many populations, including Caucasian Americans and African Americans (10), its accuracy is somewhat limited among some European and Asian populations, and some risk markers are not incorporated. In a systematic review of 27 studies using the Framingham scoring system, the predicted-to-observed ratios ranged from an underprediction of 0.43 in a high-risk population to an overprediction of 2.87 in a low-risk population (11). The FRS has been evaluated in the largest number of diverse settings, and many of these problems are likely to be relevant to the other risk scores.

In addition to the coronary event risk score, the FRS has been developed for a composite of all atherosclerotic CVD (CHD composite including angina, cerebrovascular events, peripheral artery disease, and heart failure) (2) as well as individual risk scores for each specific components, including peripheral artery disease (12), stroke (13), and heart failure (14). Risk scores have also been developed for lifetime risk (15,16) and 30-year risk (17) as opposed to 10-year risk. These latter scores require further validation.

ATP III. The ATP III document updated clinical guidelines for cholesterol testing and management (3). The ATP III identified 3 categories of risk that modify the goals and modalities of low-density lipoprotein cholesterol (LDL-C) lowering therapy on the basis of CHD as an end point. The category of highest risk (>20% per 10 years) consists of CHD and CHD risk equivalents (atherosclerotic disease of other arterial beds and diabetes mellitus). The LDL-C goal is <100 mg/dl.

The second category consists of multiple (≥2) risk factors and the LDL-C goal is <130 mg/dl. The major risk factors include cigarette smoking, blood pressure ≥140/90 mm Hg

Table 1 Characteristics of the Various Cardiovascular Risk Scores

Study (Ref. #)	Variables Included	Outcomes	Population Derived	Population Validated	ROC	Limitations
FRS (6,7)	Age, sex, BP, smoking, use of HTN medications, TC, and HDL	CHD (angina, MI, sudden death)	U.S. white men and women, ages 30–62 yrs	Men, women, blacks, Europe, Mediterranean, and Asia	0.7744 (w) 0.7598 (m)	Age <30 yrs, >65 yrs, Japanese-American men, Hispanic men, Native-American women, LVH, DM, and severe HTN
Global cardiovascular risk (2)	Age, sex, SBP, smoking, TC, HDL, DM, and use of HTN medications	CHD, stroke, CHF, or PVD	U.S. white men and women, ages 30–74 yrs	Framingham offspring	0.793 (w) 0.763 (m)	Mainly white
SCORE (20)	Age, sex, smoking, either TC or TC/HDL ratio, broken up into areas of high and low CVD risk	Fatal CV events	European men and women, ages 45–64 yrs	Europe	0.71–0.84	No nonfatal events, "single" risk factor measurements made, rather than "usual"
ASSIGN (23)	Age, sex, SBP, TC, HDL, +family history, social deprivation	CV death, CHD admission, CABG, or PTCA	Scotland men and women, ages 30–74 yrs	Scotland	0.7841 (w) 0.7644 (m)	Marginally better than Framingham, still overestimated risk
Reynolds (21)	Age, SBP, smoking, total cholesterol, HDL, hsCRP, +family history, hgbAlc if DM	MI, stroke, coronary revascularization, or CV death	U.S. women, age >45 yrs	U.S. women	0.808 (w)	Mainly white, all women, socioeconomic status not generalizable, BP, weight, and family history, all taken by self-report
QRISK (24,25)	Age, sex, SBP, smoking, ratio of TC/HDL, +family history, use of HTN medications, BMI, social deprivation	MI, CHD, stroke, TIA	United Kingdom men and women, ages 35–74 yrs	United Kingdom	0.7879 (w) 0.7674 (m)	"Home advantage," data validated from same population it was originally derived
Reynolds, men (22)	Age, sex, SBP, smoking, total cholesterol, HDL, hsCRP, +family history, hgbAlc if DM	MI, stroke, coronary revascularization, or CV death	U.S. men, ages 50–80 yrs	U.S. men	0.7–0.714 (m)	Mainly white, middle-aged, socioeconomic status and access to care not generalizable, self-reported with family history

ASSIGN = Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network/SIGN to Assign Preventative Treatment; BMI = body mass index; BP = blood pressure; CABG = coronary artery bypass graft surgery; CHD = coronary heart disease; CVD = cardiovascular disease; DM = diabetes mellitus; FRS = Framingham risk score; HDL = high-density lipoprotein; hgb = hemoglobin; hsCRP = high-sensitivity C-reactive protein; HTN = hypertension; LVH = left ventricular hypertrophy; m = men; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angiography; ROC = receiver-operating characteristic; QRISK = QRESEARCH Cardiovascular Risk Algorithm; SBP = systolic blood pressure; SCORE = Systematic Coronary Risk Evaluation; TC = total cholesterol; TIA = transient ischemic attack; w = women.

or receiving antihypertensive medication, low HDL-C, family history of premature CHD, and age ≥45 years in men or ≥55 years in women. The ATP III risk algorithm stratifies these persons into those with 10-year risk for CHD of >20%, 10% to 20%, and <10%. The third category consists of persons with 0 to 1 risk factor and the LDL-C goal of <160 mg/dl.

In 2004, a modification of the risk categories was proposed (18); the multiple risk factor category was divided into a moderately high risk group (≥2 risk factors and 10-year CHD risk 10% to 20%), and a moderate risk group (≥2 risk factors and 10-year CHD risk <10%). For the moderately high risk group, there is an optional LDL-C goal of <100 mg/dl largely based on the ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) of lipid lowering in adults with treated hypertension (19).

The SCORE project. The SCORE (Systematic Coronary Risk Evaluation) project intended to provide better predictive accuracy for European patients. The SCORE system was derived from data from >200,000 patients pooled from 12 European cohort studies (20). The SCORE system estimates the 10-year risk of a first fatal atherosclerotic event including heart attack, stroke, or aortic aneurysm. This is significant because it estimates the risk for any fatal atherosclerotic event, but is limited in that it does not consider nonfatal events.

Risk factors used in the SCORE system include age, sex, total cholesterol, total cholesterol to HDL-C ratio, systolic blood pressure, and cigarette smoking. A unique aspect of the SCORE system is that it has separate risk scores for higher risk and lower risk regions of Europe. Nevertheless, the predictive value of the SCORE system was high in each component study cohort from Europe. There are now multiple country-specific versions of the SCORE system.

Reynolds risk score. The Reynolds risk score was initially designed to develop and validate an algorithm for global cardiovascular risk in healthy women (21). Thirty-five factors were assessed among ≈25,000 initially healthy women health professionals enrolled in a clinical trial in the U.S. The Reynolds risk score estimates the 10-year risk of cardiovascular events, a composite of MI, ischemic stroke, coronary revascularization, and cardiovascular death.

Of note, risk factors such as blood pressure and body weight were not directly measured but were self-reported in categories, which may have diminished some of their utility as predictive variables, allowing opportunities for other covariates to add predictive utility. Additionally, the risk score was validated from the same population it was derived.

The authors provided 2 models: a best-fitting model and a clinically simplified model (the Reynolds risk score). The Reynolds risk score was composed of age, systolic blood pressure, hemoglobin A1c if diabetic, smoking, total and HDL-C, C-reactive protein measured by a high-sensitivity assay (hsCRP), and parental history of MI before age 60 years. In contrast to the FRS and SCORE system, the Reynolds score evaluated and incorporated the risk factors of parental history of premature CHD and hsCRP.

Recently, the Reynolds risk score, using male-specific equations, was applied to healthy nondiabetic men with good results (22). Similar to women, the authors showed that the addition of hsCRP and parental history of MI before age 60 years improved global cardiovascular risk prediction and reclassification of risk as compared with the traditional FRS employed in the ATP III in a population of male health professionals enrolled in a clinical trial.

The ASSIGN risk score. Using a representative database from Scotland, the ASSIGN (Assessing Cardiovascular Risk to Scottish Intercollegiate Guidelines Network/SIGN to Assign Preventative Treatment) risk score was developed (23). This score was derived from men and women ages 30 to 74 years and free of symptomatic CVD. The ASSIGN score estimates the 10-year risk of CVD, including cardiovascular death or any hospital discharge diagnosis of CHD, cerebrovascular disease, or coronary artery intervention.

Traditional risk factors, including number of cigarettes smoked, plus social deprivation and family history, but not obesity, were significant factors in this risk score. The ASSIGN scoring system was novel because the authors included an index of social status, which may account for social gradients in disease.

QRISK risk score. The QRISK (QRESEARCH cardiovascular risk algorithm) CVD risk score was derived from a large United Kingdom primary care population (24,25). The derivation cohort consisted of 1.3 million subjects ages 35 to 74 years free from diabetes and CVD. The QRISK score estimates the 10-year risk of CVD, including MI, CHD, stroke, and transient ischemic attack. Risk factors were age, sex, smoking status, systolic blood pressure, ratio of total to HDL-C, body mass index, family history of CHD, a measure of social deprivation, and treatment with antihypertensive agent.

This was the first study to use data from a general practice population and not use an observational study in a predefined cohort. Both the QRISK and ASSIGN risk scores include social deprivation, an important step in acknowledging inequalities in cardiovascular risk. A major limitation of this risk score was that it was validated from the same population it was derived from.

Variables With Incremental Prediction

Although risk-scoring models can improve the prediction of risk, their adoption into clinical practice is poor. Moreover, they are derived from populations and applied to patients. However, this is how we practice and apply medicine; the premise of evidence-based medicine is to apply average effects observed in clinical trials to patients in prescribing treatments and preventive therapies. The incorporation of noninvasive tests as indicators of asymptomatic atherosclerosis, such as the ankle-brachial index (ABI), coronary artery calcium, carotid artery intima media thickness (IMT),

and electrocardiographic exercise testing, has been proposed (26,27). Many of these noninvasive tests are touted as a potential means for improving and perhaps simplifying the estimation of cardiovascular risk in asymptomatic subjects. However, controversy exists regarding screening for underlying CVD (28,29).

The ABI, which is the ratio of systolic pressure at the ankle to that in the arm, is quick and easy to measure and is an indicator of lower extremity peripheral arterial disease, which is overwhelmingly due to atherosclerosis. In a recent collaboration of 16 international cohorts (30), the ABI provided independent risk information over and above the FRS, and a low ABI approximately doubled the risk of total and cardiovascular mortality and major coronary events across all FRS categories. The authors of that analysis propose a new risk equation incorporating the ABI with FRS markers and are intending to develop and validate such a model.

Computed tomography can noninvasively detect and quantify coronary artery calcification. The presence and extent of coronary artery calcification would seem to be a very useful risk factor as it essentially visualizes coronary atherosclerosis. A report from the MESA (Multi-Ethnic Study of Atherosclerosis) cohort found a strong association between coronary calcification and incident CHD, with an adjusted relative hazard for coronary events between 3.6 and 9.7, depending on the amount of calcification (31). The c-index (discriminant accuracy) for risk factors plus calcium score was excellent at 0.83 for MI and death, and 0.82 for all CHD events ($p < 0.01$ in comparison with risk factors alone, 0.79 and 0.77, respectively) (31).

Carotid artery IMT is thought to be a marker for early atherosclerosis. It has been used in large-scale population studies, but the measurements are very operator dependent. Several studies have noted a moderate, graded association between carotid IMT and the presence of coronary atherosclerosis and the risk of future cardiovascular events (32). However, much of the excess risk is attenuated when adjusted for traditional risk factors. Furthermore, IMT testing is only available at select centers, and its measurement has considerable interobserver variability when it is used in routine clinical practice.

An abnormal electrocardiographic exercise test is associated with an increased risk of MI and sudden cardiac death (33). The exercise test provides substantial diagnostic and prognostic value beyond simple ST-segment changes, including exercise capacity, heart rate recovery, presence or absence of arrhythmias, and hemodynamic responses.

A cohort study of asymptomatic patients followed up for >20 years found that exercise testing was strongly predictive of cardiovascular death, incremental to the FRS, and across FRS risk categories with <20% risk of a CHD event over 10 years (27). In a report from the Framingham Heart Study, exercise testing provided additional prognostic information in age- and FRS-adjusted models, particularly among those in the highest risk group (10-year predicted CHD risk of 20%) (34).

Areas of Uncertainty

10-year and lifetime risk. Recent emphasis has been placed on lifetime risk of developing CVD. Among people free of CVD at age 50 years, >50% of men and nearly 40% of women will have CVD during their lifetime. Should we place more emphasis on lifetime risk or 10-year risk estimates? Patients who are 50 years of age or younger may have a very high lifetime cardiovascular risk, which may be amenable to risk factor reduction, but may be considered to be at low risk because they have a low 10-year cardiovascular risk (due to the weighting of age in 10-year risk equations).

Lifetime risk may allow policy makers to better promote public interest in prevention, screening, and treatment of CVD, especially in younger people who have high long-term risks. In addition, lifetime risk can potentially guide the allocation of resources to improve public health and preventive services for CVD, and be useful in the design of epidemiological studies. Nevertheless, estimates of short-term (10-year) risk are useful for the identification of patients who need aggressive risk reduction in the near term. This level of risk may justify aggressive pharmacological agents and should be evaluated balancing efficacy, costs, and safety of therapy.

CVD versus CHD. What end point should be evaluated? Currently, there are risk scores for MI, stroke, peripheral artery disease, atrial fibrillation, cardiac revascularization, and more. There is also a composite risk score for all atherosclerotic CVD (CHD composite including angina, cerebrovascular events, peripheral artery disease, and heart failure) (2).

Although many studies are designed using "hard end points" (MI, stroke, and death), the inclusion of "softer" or more subjective end points (such as angina, claudication, heart failure, and revascularizations) are important from a patient's perspective and policy standpoint. Patients and health care policy makers may benefit from putting resources into avoiding these softer end points to risk stratify, counsel, and potentially treat with pharmacologic therapy (e.g., aspirin and statin therapy) those patients earlier than advocated by existing national guidelines in order to reduce the risk of a hard end point in the future.

Nonlaboratory-based risk score. Because of the limited resources available in certain areas of the world, finding low-cost strategies for risk scores is essential. Almost every risk score contains some laboratory test as a risk marker. In an attempt to simplify risk prediction, Framingham study (2) and NHANES (National Health and Nutrition Examination Survey) (33) data were used to develop an assessment tool using measurements readily available at the clinic or office.

Gaziano et al. (35) evaluated whether a risk score without laboratory testing could predict CVD as effectively as 1 that

includes laboratory testing. The nonlaboratory-based model used the same risk factors from the FRS but excluded HDL, and total cholesterol was replaced with body mass index. The authors demonstrated an almost identical ability to accurately discriminate CVD from a nonlaboratory-based risk score (35). For that reason, use of a nonlaboratory-based risk score should be considered in all areas where laboratory data are unavailable, and future studies should assess the predictive value of laboratory versus nonlaboratory based risk assessment.

Age at which to start. Many of these risk scores have not been evaluated or validated in younger populations. These observations are important because younger subjects may have a very high lifetime cardiovascular risk, which may be amenable to risk factor reduction, but they may be considered to be at low risk because they have a low 10-year risk. A study of risk prediction in young adults noted an inability of the FRS to classify patients <40 years of age at high 10-year risk despite substantial risk factor burden (36). In fact, younger patients are at lower risk, but this gives an incomplete picture to them regarding long-term risk and hampers risk communication, and likely diminishes motivation and adherence to recommendations. Moreover, with the ongoing obesity epidemic continuing to start at younger ages and the continued lack of physical activity in many young adults, there are likely many young adults that are at heightened long-term risk.

Given that the goal of risk stratification is to avoid bad clinical outcomes by starting behavioral change and medical therapy earlier, it is reasonable to screen when clinicians become concerned that a patient is at increased risk. Recent data suggest that younger adults (age ≤50 years) with a low-10 year risk and high lifetime risk of ≥39% (at least 1 elevated risk factor that can be treated) have a greater subclinical disease burden and greater incidence of atherosclerotic progression compared with patients with low 10-year and lifetime risk (37). This suggests a potential benefit of aggressive prevention efforts for younger age patients with low short-term risk but high lifetime predicted risk.

Race and/or sex differences. Absolute risks in any risk score may differ according to the set of risk factors present in a given population, for example, those of different racial or ethnic characteristics. This difference may be due to differential susceptibility to established risk factors along with exposure to "emerging" risk factors. Several studies have suggested that the FRS overestimates the risk of CHD events in Japanese-American and Hispanic men, in Native American women, and in European and Asian populations (10,38–40).

A 1999 workshop convened by the National Heart, Lung, and Blood Institute to evaluate the Framingham functions in non-Framingham populations noted comparable FRS estimates for CHD between white and black U.S. populations (40). However, blood pressure should ideally be given extra weight in black men and women. The authors also concluded that differences extend to various ethnic groups and will require adjustment of absolute risk estimates based on ethnicity using simple calibration adjustments to account for different underlying rates of disease incidence and prevalence of risk factors.

Sex-stratified prediction scores in each of the scoring methods discussed in the preceding text illustrate the significant differences between women and men. An important sex difference is the 10-year delay in the onset of CVD in women, which remains incompletely understood. The difference between women and men particularly stands out for which end point to analyze. Women are at higher risk for stroke earlier in life, whereas men are at higher risk for MI. Furthermore, primary prevention trials of aspirin demonstrated that aspirin was effective in the reduction of stroke for women and MI in men (41,42).

Nevertheless, in American College of Cardiology/American Heart Association recommendations for aspirin, current guidelines tend to use the 10-year FRS for CHD as a guide to treat or not to treat with aspirin therapy. It seems that women, who derive their benefit from aspirin principally by reducing the risk of stroke, should use a risk score including the risk of stroke factored into the treatment decision. In fact, the recent U.S. Preventive Services Task Force recommends aspirin for men based on the risk for CHD whereas aspirin for women should be based on the risk for stroke (8).

Should Risk Estimates Guide Therapy?

Risk stratification tools can and should be used in conjunction with commonly practiced medical guidelines. The decision to use or not to use a certain medication for cardiovascular prevention depends, in part, on the initial risk for CVD in that person. Thus, decisions about aspirin therapy for primary prevention should consider the overall risks for CVD (and potential harm of aspirin).

Available tools, as described above, provide estimates of absolute cardiovascular risk allowing for an informed decision between the patient and the medical care provider. Unfortunately, risk scoring for proper evaluation of potential side effects (e.g., major bleeding from aspirin use or hyperkalemia from blockade of the renin/angiotensin system) of certain medications is not available. Only after proper assessment for both benefit and risk can optimal decisions be made.

Nevertheless, providing a risk score for the development of CVD should promote a discussion about behavioral change and medical therapy that may decrease the likelihood of onset of disease or disease progression. A short- and long-term risk stratification tool can be of great benefit in helping the patient understand their risk and perhaps be a motivating tool as well.

Guidelines

The assessment of cardiac risk in asymptomatic patients without CVD is increasingly advocated by international organizations and by individual risk factor guidelines (3,8,9,18,43,44). Guidelines from the American Heart Association (9) recommend a 10-year risk assessment beginning at age 40 years and repeated every 5 years (or more frequently if risk factors change). Although no specific risk score was mandated, the authors supported the Framingham 10-year CHD score, while acknowledging its limitations in some race and ethnic groups.

A combined statement from the American Heart Association and American College of Cardiology (44) supported an assessment of risk for adequate primary prevention, primarily involving the FRS. In contrast, the European Society of Cardiology recommended the SCORE system (43), a 10-year risk score for cardiovascular mortality. The authors of all these guidelines express concern that any risk assessment is not perfect and should not be used to promote complacency. Rather, all patients, regardless of risk, should be counseled on proper dietary and lifestyle management.

Conclusions and Recommendations

For the patient in the case vignette, the estimated risk varies according to the risk score used (Table 2). The 10-year "hard" risk of CHD (MI/CHD death) is 2%, whereas the 10-year global cardiovascular risk ranges from 6% to 14%. Further adding complexity, her lifetime risk for CVD is estimated to be 39% (50% if we count her obesity as a major risk factor). Recently, the "heart age" (or "vascular age") was promoted to better understand the concept of risk (2). This 56-year-old woman with abnormal risk factors has the heart age of a 73-year-old woman with normal risk factors. Table 3 estimates the cardiovascular risk of this patient using stable variables from the 10-year CHD FRS, but modifying other risk factors not calculated in the FRS (e.g., family history, hsCRP, body mass index, and social deprivation).

Table 2 Risk Score of the Patient Described in Case Vignette

Risk Score	Estimated Risk
Framingham	
10-yr CHD risk score	2%
Global CVD score	10%*
Heart age/vascular age	73
Reynolds	6%
SCORE (fatal CVD)	1%–2%†
QRISK	11%
ASSIGN	14%
Lifetime risk for CVD	39%

*The risk was 10% in both the full model and the simpler nonlaboratory-based model. †One percent if population is in a country with low cardiovascular risk and 2% if in a country with high cardiovascular risk.
Abbreviations as in Table 1.

Table 3 Variation in Cardiovascular Risk Calculated on the Basis of the Results of Several Published Risk Scores

Risk Score	Estimated Risk
Framingham	
10-yr CHD risk score	2%
Reynolds	
Negative FH, hsCRP 0.5 mg/l	2%
Negative FH, hsCRP 3.0 mg/l	3%
Negative FH, hsCRP 8.0 mg/l	4%
Positive FH, hsCRP 0.5 mg/l	3%
Positive FH, hsCRP 3.0 mg/l	5%
Positive FH, hsCRP 8.0 mg/l	6%
SCORE (fatal CVD)	
Country of low cardiovascular risk	1%
Country of high cardiovascular risk	2%
QRISK	
Negative FH, BMI <23 kg/m^2	6%
Negative FH, BMI 23–32 kg/m^2	6%
Negative FH, BMI ≥33 kg/m^2	7%
Positive FH, BMI <23 kg/m^2	10%
Positive FH, BMI 23–32 kg/m^2	11%
Positive FH, BMI ≥33 kg/m^2	12%
ASSIGN*	
Negative FH, SIMD <10	7%–8%
Negative FH, SIMD 10–29	8%–10%
Negative FH, SIMD ≥30	10%–15%
Positive HH, SIMD <10	12%–13%
Positive FH, SIMD 10–29	13%–15%
Positive FH, SIMD ≥30	15%–23%
Lifetime risk for CVD	39%

*ASSIGN incorporates SIMD (Scottish Index of Multiple Deprivation) as a risk factor. The SIMD can range between 0.54 (least deprived) and 87.6 (most deprived).
FH = family history; other abbreviations as in Table 1.

The best high-risk approach for CVD evaluation and prevention lies in routine testing for cardiovascular risk factors and risk score assessment. This approach, while not perfect, is a valuable tool for identifying a population who can benefit from preventive treatments demonstrated to be effective in clinical trials. We recommend that health care providers discuss the 10-year CHD as well as global cardiovascular risk, and lifetime cardiovascular risk score assessment with each patient to better explore each individual patient's future risk. Use of a global and lifetime cardiovascular risk score will engage greater numbers of patients, at an earlier stage of their disease, and highlight the need for early and prolonged intervention on risk factors. Appropriate intervention, guided by risk assessment, has the potential to bring about a significant reduction in long-term risk.

Potential risk reduction strategies for this patient include aggressive lifestyle change, blood-pressure–lowering agents, cholesterol-lowering drugs, and aspirin. We believe that, for the purpose of deciding whether to start therapy and evaluation of benefit versus risk, global risk scores should be used. However, the validity and applicability of each risk score assessment should be evaluated in future studies, and only

adequately designed prospective trials will be able to evaluate whether the risk score improves important health outcomes and health care expenditures.

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