Determining Your Patient's Cardiac Risk

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A 45-year-old nonsmoking woman with diabetes comes to your office for a new patient visit. Her medical history is notable for diabetes that has been diagnosed for 5 years, two normal vaginal deliveries, and a tubal ligation. For exercise, she walks for 30 minutes three times per week. Her medications include glipizide, 10 mg per day, and loratadine for allergic rhinitis. Physical exam reveals a blood pressure of 130/80 mmHg and a BMI of 27 kg/m^2 and is otherwise normal. A recent workplace health screening exam revealed a total cholesterol level of 230 mg/dl, an HDL cholesterol level of 60 mg/dl, an LDL cholesterol level of 130 mg/dl, and triglycerides of 200 mg/dl. Her hemoglobin A_{1c} (A1C) is 7.2%. In the course of your visit, she asks you if she is at risk for heart disease and if she needs to do anything to lower her risk.

Later that day, you see another new patient, a 50-year-old nonsmoking man. He has had diabetes for 15 years and has treated hypertension. He is physically inactive. His medications include glipizide, 10 mg per day, and metformin, 1,000 mg twice daily. His blood pressure is 140/70 mmHg, and his BMI is 32 kg/m^2. The physical exam is otherwise unremarkable. A recent workplace health screening exam revealed a total cholesterol level of 170 mg/dl, an HDL cholesterol level of 30 mg/dl, an LDL cholesterol level of 90 mg/dl, and triglycerides of 200 mg/dl. His A1C is 8.2%. What additional heart disease prevention strategies would you recommend?

Cardiovascular disease (CVD), including coronary heart disease (CHD) and stroke, are the most important causes of mortality in the general population and particularly in people with diabetes. Current U.S. guidelines recommend aggressive screening of patients to identify CVD risk factors and treatment to prevent cardiovascular events.[1] In adults > 40 years of age, recent U.S. guidelines have recommended considering diabetes as a "CHD equivalent" calling for treatment similar to that of patients with previous cardiovascular events.[2] However, the range of CVD risk levels in adults with diabetes varies considerably, leading others to suggest that patients should have their risk of CHD events calculated using a validated cardiac risk calculator, as is recommended by the American Heart Association for nondiabetic patients.[3]

Recent studies from the United Kingdom have suggested that an approach of calculating risk and treating with statins above a defined risk threshold is similarly effective in identifying patients who will go on to have a CHD event as a strategy of prescribing statins for all people > 40 years of age with an LDL cholesterol level > 100 mg/dl. Under the strategy of calculating risk, fewer patients who will not go on to have an event would be subjected to taking medication unnecessarily.[4]

If one wishes to calculate CHD risk in patients with diabetes, several risk prediction equations and calculators are now available, most of which are based on the Framingham Heart Study or the U.K. Prospective Diabetes Study (UKPDS)[5–7] (Table 1). The Framingham Risk Score (FRS) has been shown to perform well in U.S. white and African-American populations, but its performance in patients with diabetes is less well validated, in part because of the relatively small number of patients with diabetes in the Framingham cohort and because diabetes is included only as a dichotomous (yes/no) variable. Some versions of the FRS use estimates of total CHD events (angina, myocardial infarction [MI], and sudden death); others estimate only "hard" events, including MI and sudden death.[6]

The UKPDS risk engine was developed specifically to estimate CVD risk in patients with diabetes.[7] It relies on data from the UKPDS and incorporates a slightly different set of risk factors, including a continuous measure of blood glucose control and a term for the duration of diabetes. It can provide information about risk of CVD events, defined as fatal or nonfatal MI, sudden death, and the risk of stroke.

Both the FRS and the UKPDS risk engine omit several factors that have been shown to predict future cardiovascular events, including weight, family history of early MI, C-reactive protein level, LDL cholesterol level, or triglyceride level. These decisions are based on whether the model has sufficient increased accuracy when an additional factor is included to justify requiring its measurement. In many cases, addition of other risk factors does little to increase the model's ability to predict future events once the basic risk factors have been considered. For example, triglyceride level may be associated with CHD risk, but it adds little in terms

Table 1. CHD Risk Estimation for Patients With Diabetes

	Framingham Equation	UKPDS Equation
Website	http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof (hard events) or www.med-decisions.com (total events)	www.dtu.ox.ac.uk/index.html?maindoc=/riskengine/index.html
Outcome measured	Total CHD events in some versions; hard CHD events in others	Hard CHD events
Time horizon (default)	10 years	10 years
Measure of glycemia	Diabetes (yes/no)	A1C, duration of diabetes
Race	Not considered	Included (but based on U.K. data and classifications)
Other risk factors measured	Systolic blood pressure Smoking Total cholesterol HDL cholesterol Age Sex	Systolic blood pressure Smoking Total cholesterol HDL cholesterol Age Sex Atrial fibrillation
Diabetic population used to validate	337 patients with diabetes within the larger U.S. Framingham cohort	4,540 patients with diabetes from the United Kingdom
Estimate of uncertainty	None	Confidence intervals

of predictive ability once HDL cholesterol is considered. Thus, model developers have chosen to retain the simpler models for ease of use.

Several recent studies have compared the ability of the Framingham and UKPDS risk equations to estimate cardiovascular risk. In general, they evaluate two characteristics of test performance: discrimination and calibration. Discrimination is the probability that the test will assign higher values of risk to patients who will go on to have events compared with those who will not. It is measured with the c-statistic, which ranges from 0.50 (no discrimination) to 1.0 (perfect discrimination). Calibration is the ratio of predicted risk to observed risk. Stephens et al.[8] found that the UKPDS- and Framingham-based estimates were similar in terms of discrimination (c = 0.76 and 0.74 , respectively) but that both models underestimated CHD events. Guzder et al.[4] studied a cohort of 428 newly diagnosed diabetic patients during a period of 4 years. They found that a Framingham-based estimation had modest discrimination (c = 0.66) and poor calibration because of substantial underestimation of CHD events; the UKPDS equation had similar discrimination (c = 0.67) and only slightly better calibration.

In the case of the first patient described above, both the FRS and UKPDS risk tools estimate the risk of CHD events to be relatively low (6 and 4%, respectively) for that patient. The second, higher-risk patient described above produced higher estimates of risk in both models. The UKPDS estimate of hard CHD events (20.5%) was greater than the FRS estimate of 16% for total CHD events.

Treatment Implications

The primary importance of estimating CHD risk is for its use in treatment decision making and patient counseling. U.S. treatment guidelines for nondiabetic patients recommend the use of aspirin for heart disease prevention among patients with a CHD risk ≥ 10%;[3] lipid guidelines recommend using CHD risk calculation for determining treatment thresholds for intermediate-risk patients.[2]

The rationale for these recommendations is that consideration of CHD risk is necessary for balancing the potential benefits and drawbacks of treatment. It can be argued that such recommendations should be applied to lower-risk patients with diabetes as well. In our first example patient, the risks of adverse events from aspirin therapy, for example, may outweigh its potential benefits, even in the face of diabetes. Calculating risk and the potential benefits of treatment allows both providers and patients to better understand the magnitude of potential benefit.

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