

Diabetes and Coronary Risk Equivalency

What does it mean?

The National Cholesterol Education Program Adult Treatment Panel III (ATP III) listed diabetes as a coronary heart disease (CHD) risk equivalent for setting therapeutic goals for LDL cholesterol (1). A goal for LDL cholesterol of <100 mg/dl was recommended for patients with CHD and CHD risk equivalents. The latter included individuals with noncoronary forms of atherosclerotic cardiovascular disease (ASCVD), diabetes, and patients with a 10-year risk for major coronary events (myocardial infarction + coronary death) of >20%. For the majority of patients with diabetes, this LDL cholesterol goal would evoke the use of cholesterol-lowering drugs, particularly statins. Some investigators have questioned whether most or all patients with diabetes have a CHD risk equivalent and thus require cholesterol-lowering drugs (2). One approach to this issue is to examine epidemiological data relating to absolute risk for developing CHD in various populations of persons with diabetes.

In the present issue of *Diabetes Care*, Howard et al. (3) reported the incidence of CHD in the Strong Heart Study, a cohort study of cardiovascular disease (CVD) in 13 American-Indian tribes/communities conducted in three study centers in southwestern Oklahoma, central Arizona, and North and South Dakota. The population of the Strong Heart Study has a high prevalence of type 2 diabetes and CVD associated with diabetes. The findings of this study showed wide variation in rates of CHD in patients with diabetes, depending in part on coexisting risk factors. Most individuals had 10-year risk >20%, the threshold for ATP III's CHD risk equivalency, but only those with multiple risk factors had rates of CHD events equivalent to patients with established CHD. The authors conclude that it may be prudent to consider therapeutic goals for risk factors based on the entire risk factor profile, rather than just the presence of diabetes.

Other studies likewise have found considerable variability in risk for major coronary events when diabetes is present. Some reports (4–10) suggest that patients

who have diabetes but not CHD do not carry as high a risk for major coronary events as do those with established CHD. Other studies (11–14) find that risk for CHD is similar in patients with diabetes and those with established CHD. The ATP III report (1) indicated that diabetes in general can be viewed as a high-risk state (CHD risk equivalent); this is generally true and adds simplicity to cholesterol management, just as it does for patients with established ASCVD. An alternate approach is to attempt to estimate 10-year risk for individuals with diabetes and to adjust LDL cholesterol goals accordingly. An example of individualized risk assessment is the U.K. Prospective Diabetes Study risk engine (15), which calculates risk for individuals with diabetes analogous to the risk algorithm of the Framingham Heart Study (8). Of interest, several reports suggest that Framingham scoring for patients with diabetes often underestimates absolute risk (16–18). If so, the choice of the risk assessment tool for estimating risk for CHD becomes an important issue when using an individualized approach.

Of course, there is variability in risk for major coronary events in patients with established CHD; therefore risk assessment could be carried out in individuals with CHD to tailor secondary prevention therapies. This approach however has been widely rejected by guideline panels for CHD prevention (1,19–21). For most cardiovascular guidelines, a diagnosis of ASCVD triggers a full therapeutic response for secondary prevention. The rationale is that the clinical simplicity of this approach will yield a net benefit that exceeds individual risk assessment based on problematic risk-assessment tools. This simplified strategy has been widely accepted by the cardiovascular community and appears to have improved implementation of secondary prevention therapies.

The National Cholesterol Education Program (1) proposed the same approach for patients with diabetes who as a group are known to be at high risk for ASCVD events. The concept is that most patients with diabetes in the U.S. are at least at

high enough risk that a simple tactic for cholesterol-lowering therapy will be both efficacious and cost-effective. Even though an individualized risk assessment in patients with diabetes is reasonable in the hands of specialists, a broad application of risk assessment and adjustment of goals for LDL cholesterol on a patient-by-patient basis by most practitioners will be difficult to implement, just as it would be in management of patients with ASCVD. Moreover, beyond the simplicity of guidelines, several other reasons were given in the ATP III report for identifying patients with diabetes as having a CHD risk equivalent. These reasons can be summarized briefly.

First, in ATP III, CHD risk equivalent defines the risk of developing a major coronary event (myocardial infarction + coronary death) over 10 years of >20%. The 20% risk was that of patients with stable angina who have not sustained a myocardial infarction (22,23). This risk is lower than for those who have a history of acute myocardial infarction, which is about 26% (24,25). Many subsequently assumed that the risk accompanying a history of myocardial infarction defined a CHD risk equivalent and not stable angina. This was not the position of ATP III (1), which identified the 20% level. Moreover, cost-effectiveness analysis showed that cholesterol-lowering drugs are highly cost-effective at the risk level of 20% (1). In fact, as the costs of cholesterol-lowering drugs decline, acceptable cost-effectiveness reaches down to 10% risk or even lower (1).

Beyond 10-year risk estimates, there were other reasons for applying the term of CHD risk equivalent to patients with diabetes. A common misconception is that this term came exclusively from the study of Haffner et al. (11), which reported that Finnish patients with type 2 diabetes have a risk for future major coronary events similar to that of patients with previous myocardial infarction. In ATP III, this was not the only rationale, although reference was made to this report (11) and others with similar findings

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