

IFG), 14% met the NCEP definition, and 12% met the WHO definition of metabolic syndrome.

IGT and the NCEP definition had a higher sensitivity than the modified WHO definition (51.9%, 52.8%, and 42.8%, respectively). IGT had a higher positive predictive value than the NCEP and WHO definitions (43.0%, 30.8%, and 30.4%, respectively). Combining the NCEP and IGT definitions increased sensitivity to 70.8% and had a positive predictive value of 29.7%. When the NCEP definition of an abnormal fasting glucose level was lowered to 5.4 mmol/L (100 mg/dL) or higher, it performed even better, with a sensitivity of 62% and positive predictive accuracy of 31%.

The authors concluded that the metabolic syndrome predicts diabetes independently of other factors; that the NCEP definition of metabolic syndrome predicts incident diabetes better than the modified WHO definition; and that a further lowering of the definition of IFG to 5.4 mmol/L or higher further improves the prediction of diabetes by the metabolic syndrome. ■

Atherosclerosis

Conventional Risk Factors and Cardiac Events—Debunking an Old Myth About Prevalence

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Major Risk Factors as Antecedents of Fatal and Nonfatal Coronary Heart Disease Events

Greenland P, Knoll MD, Stamler J, et al.

JAMA. 2003;290:891-897.

This analysis evaluated subjects from the Chicago Heart Association Detection Project, the Multiple Risk Factor Intervention Trial, and the Framingham Heart Study, who had documented cardiac events (n = 20,995). At least 1 conventional risk factor (cigarette

smoking, hypertension, diabetes, or hypercholesterolemia [cholesterol > 240 mg/dL]) was present in 91.1% of those who experienced a fatal coronary heart disease (CHD) event. This analysis did not take obesity, sedentary lifestyle, the dysmetabolic syndrome, high-density lipoprotein cholesterol, or low-density lipoprotein cholesterol, into account. If these variables had been considered, virtually all of those with fatal CHD events would have had at least 1 modifiable cardiac risk factor. Furthermore, these data antedate the acceleration of the U.S. obesity pandemic.

The “take-home message” from this study is that virtually all patients with cardiac events have longstanding, modifiable, and potentially reversible cardiac risk factors. Because modern technologies (ie, coronary revascularization) have been largely unsuccessful in halting and reversing the CHD epidemic, more emphasis must be placed on novel approaches such as primary prevention. This will require attacking conventional risk factors and their underlying environmental causes—diets high in sugars, fats, and simple carbohydrates for the majority who are overweight or obese; cigarette smoking; hypertension; and physical inactivity.

Prevalence of Conventional Risk Factors in Patients with Coronary Heart Disease

Khot UN, Khot MB, Bajzer CT, et al.

JAMA. 2003;290:898-904.

With methods similar to those employed by Greenland and coworkers, this analysis combined patient data for ST-segment elevation myocardial infarction (STEMI), unstable angina (UA) /non-STEMI, and percutaneous coronary intervention from 14 clinical trials (n = 122,458). Presumably, not all subjects in this sample had CHD, especially in the UA/non-STEMI group, where, typically, ~20% are found to have normal coronary arteries at angiography. Taking this limitation into consideration, the investigators found at least 1 conventional risk factor was present in 82.6% of subjects. Although hyperlipidemia was classified differently from trial to trial, and could not be distilled into a single number, the other likely risk factors had similar definitions in all of the epidemiological studies, though they were not specifically stated in the article. Importantly, the investigators noted that if obesity was considered as a risk factor, then ~90% of cases would have had at least 1 risk factor. Again, the current obesity pandemic would lead us to believe that, in this analysis of primarily non-fatal CHD events, virtually all such patients have modifiable or reversible risk factors that can be addressed with weight reduction and

regular exercise, along with the application of pharmacotherapies, if necessary.

Emerging Risk Factors for Atherosclerotic Vascular Disease: A Critical Review of the Evidence

Hackam DG, Anand SS.

JAMA. 2003;290:932-940.

This careful review of emerging or novel cardiac risk factors found that, after distilling the literature since 1990 (373 papers), 4 conventional risk factors had consistent relationships with cardiovascular disease. However, few data were available regarding the additive yield of screening for novel factors (high-sensitivity C-reactive protein [hs-CRP], fibrinogen, lipoprotein(a), homocysteine). Furthermore, randomized trials of individuals specifically treating these novel factors with available therapies are lacking. The authors concluded that the explanatory power of the conventional cardiovascular risk factors has been systematically underestimated—creating an artificial or exaggerated case for novel risk factors. The other major challenge is that each novel risk factor poses a validation dilemma. For example, lipoprotein(a) and fibrinogen do not have proven reduction therapies available. Homocysteine is typically only modestly elevated in a subset of the general population but markedly elevated in those with renal dysfunction, an independent risk state in its own right.¹ Lastly, hs-CRP is fraught with problems as an independent risk factor because it is heavily confounded by conventional risk factors such as obesity, sedentary lifestyle, and dyslipidemia. To make matters worse, interventions that have been proven to reduce cardiovascular risk such as aspirin, exercise, weight reduction, and lipid-lowering therapy all reduce levels of hs-CRP. So the critical issue with this risk factor, as measured in populations, is that those with low hs-CRP values have low cardiovascular event rates, probably due to their risk reducing strategies (particularly aspirin and statin use).² Because epidemiological studies of hs-CRP have not taken these factors into account, the relationship between hs-CRP and CHD may be entirely due to confounding and effect modification—much like the previously observed relationship between estrogens and CHD.

Collectively, these studies discount the traditional notion that 50% of cardiac events occur in patients with no cardiovascular risk factors. In fact, virtually all patients with cardiac events have modifiable or reversible risk factors. These risk factors largely have their origins in excess body fat and a sedentary lifestyle. Efforts to modify or reverse conventional risk factors should take priority over attempts to identify novel risk factors at this time. ■

References

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Angina Pectoris

Ranolazine: A New Drug and a New Paradigm for Management of Myocardial Ischemia and Angina

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Recurrent symptomatic myocardial ischemia (angina pectoris) resulting from reduced coronary blood flow relative to myocardial oxygen requirements is a common manifestation of ischemic heart disease. Angina is frequently treated with interventions that reduce myocardial workload and/or improve myocardial blood flow, such as drugs (nitrates, β -blockers, calcium channel blockers), risk-factor modification, and invasive revascularization with percutaneous coronary interventions or bypass surgery. A number of patients with ischemic heart disease continue to suffer from recurrent angina despite

A new paradigm for treating myocardial ischemia has been introduced: the use of novel compounds to improve the metabolic efficiency of myocardium.

maximally tolerated medical therapy, and a certain proportion of them are unsuitable for invasive revascularization because of coronary anatomic considerations (eg, diffuse disease, small-caliber vessels, chronic total occlusions not amenable to or with failed attempts to revascularize) or very high-risk status. These patients, estimated to number approximately 26 million in the United States, have impaired quality of life and few viable options. Although a number of alternative approaches, such as