Recent Landmark Trials in Cardiovascular Disease Prevention

Gagandeep Singh Wander MD, *Gurgaon, India*

Prevention occupies the central position in our endeavors to curb the growing epidemic of cardiovascular disease (CVD) worldwide. CVD prevention heavily relies on anticipatory actions that promote better dietary and lifestyle changes as well as the corrective actions that need to be taken when various risk factors have already set in. Although it is well known that the impact of adopting a healthy lifestyle in cardiovascular disease prevention is substantial, more knowledge is needed about the interplay of various risk factors.

Low-Risk Diet and Lifestyle Habits in the Primary Prevention of Myocardial Infarction in Men: A Population-Based Prospective Cohort Study

Akesson A, Larsson S C, Discacciati A, Wolk A. *J Am Coll Cardiol.* 2014;64:1299–306.

The trial tested impact of adherence to a combination of healthy dietary and lifestyle practices on the primary prevention of myocardial infarction (MI). It was a population-based, prospective study of cohort of Swedish men aged 45 to 79 years. The study population completed a detailed questionnaire on diet and lifestyle at baseline in 1997. Thereafter, 20,721 men with no history of cancer, cardiovascular disease, diabetes, hypertension, or high cholesterol levels were followed till 2009. Low-risk behavior included five factors: a healthy diet (top quintile of Recommended Food Score); moderate alcohol consumption (10–30 g/day); no smoking; being physically active (walking/bicycling 40 min/day and exercising 1 h/week); and having no abdominal adiposity (waist circumference <95 cm).

From: Medanta Heart Institute, Medanta - The Medicity, Gurgaon India (G.S.W)

Corresponding Author: Dr. Gagandeep Singh Wander MD
Department of Clinical and Preventive Cardiology, Medanta Heart Institute, Medanta - The Medicity, Gurgaon 122001, Haryana, India

Email: drgswander@yahoo.com

In 11 years of follow up, there were 1,361 cases of MI. The low-risk dietary choice together with moderate alcohol consumption was associated with a relative risk of 0.65 (95% confidence interval [CI]: 0.48–0.87) compared with men having 0 of 5 low-risk factors. Men having all five low-risk factors compared with those with 0 low-risk factors had a relative risk of 0.14 (95% CI: 0.04–0.43). This combination of healthy behaviors could prevent 79% (95% CI: 34–93%) of the MI events on the basis of this study population.

Perspective

The trial concluded that combining five low risk behaviors (healthy diet, moderate alcohol consumption, no smoking, being physically active, and healthy weight) may prevent four of five MIs in men. However, it is noteworthy, that such healthy behavior was seen in only 1% of the entire studied population, which remains the major challenge to CVD prevention.

Very Low Levels of Atherogenic Lipoproteins and the Risk for Cardiovascular Events: A Meta-Analysis of Statin Trials

Boekholdt MS, Hovingh KG, Mora S, Arsenault BJ, Amarenco P, Pedersen TR, LaRosa JC, Waters DD, DeMicco DA, Simes RJ, Keech AC, Colquhoun D, Hitman GA, Betteridge DJ, Clearfield MB, Downs JR, Colhoun HM, Gotto AM Jr, Ridker PM, Grundy SM, Kastelein JJ. *J Am Coll Cardiol.* 2014;64:485–94.

Statin therapy leads to highly variable levels of atherogenic lipoproteins. The meta-analysis was done to evaluate (i) the interindividual variability of reductions in LDL-C, non-HDL-C, or apoB levels achieved with statin therapy; (ii) the proportion of patients not reaching guideline-recommended lipid levels on high-dose statin therapy; and (iii) the association between very low levels of atherogenic lipoproteins achieved with statin therapy and cardiovascular disease risk. Individual patient data from eight randomized controlled statin trials was used for this meta-analysis. In these trials, conventional

lipids and apolipoproteins were determined in all study participants at baseline and at 1-year follow up. High-dose statin therapy was defined as either atorvastatin 80 mg or rosuvastatin 20 mg. Usual-dose statin therapy was defined as all other statin dosing regimens. The primary outcome of this meta-analysis was time to first major cardiovascular event.

Total 38,153 patients were allocated to statin therapy; 5,387 participants had a total of 6,286 major cardiovascular events during follow-up. Fixed-dose statin led to large interindividual variability in the reductions of LDL-C, non-HDL-C, and apoB. It was seen that more than 40% of trial participants assigned to high-dose statin therapy did not reach an LDL-C target <70 mg/dL. Compared with patients who achieved an LDL-C >175 mg/dL, those who reached an LDL-C of 75 to <100 mg/dL, 50 to <75 mg/dL, and <50 mg/dL had adjusted hazard ratios for major cardiovascular events of 0.56 (95% CI: 0.46–0.67), 0.51 (95% CI: 0.42–0.62), and 0.44 (95% CI: 0.35–0.55), respectively. Similar associations were observed for non-HDL-C and apoB.

Perspective

The reductions of LDL-C, non-HDL-C, and apoB levels achieved with statin therapy has large interindividual variation; 40% of trial participants treated with high-dose statin therapy did not reach an LDL-C target <70 mg/dL. The patients who achieve very low LDL-C levels have a lower risk for major cardiovascular events than those achieving moderately low levels.

Metabolically Healthy Obesity and Coronary Artery Calcification

Chang Y, Kim B Y, Yun K E, Cho J, Zhang Y, Rampal S, Zhao D, Jung HS, Choi Y, Ahn J, Lima JA, Shin H, Guallar E, Ryu S. *J Am Coll Cardiol.* 2014;63:2679–86.

Obesity is an established risk factor for cardiovascular disease. The effect of obesity on the development of CVD is mediated through a number of metabolic abnormalities, such as dyslipidemia, hyperglycemia, and hypertension. Many obese individuals may not have obesity-related metabolic abnormalities. The risk of cardiovascular disease among obese individuals without obesity-related metabolic abnormalities, referred to as metabolically healthy obese (MHO), is controversial. The purpose of this study was to compare the coronary artery calcium (CAC) scores of MHO and metabolically healthy normal-weight individuals in a large sample of apparently healthy men and women.

In this cross-sectional study of 14,828 metabolically healthy adults with no known cardiovascular disease, estimation of CAC scores by cardiac tomography was done. Being metabolically healthy was defined as not having any metabolic syndrome component and having a homeostasis model assessment of insulin resistance <2.5.

MHO individuals had a higher prevalence of coronary calcification than normal weight subjects. In multivariable adjusted models, the CAC score ratio comparing MHO with normal-weight participants was 2.26 (95% confidence interval: 1.48–3.43). Further adjustment for metabolic risk factors markedly attenuated this association, which was no longer statistically significant (CAC score ratio 1.24; 95% confidence interval: 0.79–1.96).

Perspective

MHO participants in this trial had a higher prevalence of subclinical coronary atherosclerosis than metabolically healthy normal weight participants. This finding suggests that MHO is not a harmless condition and needs to be viewed more seriously.