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Risk Factor Modification in Coronary Heart Disease:
Insights from the XVIIIth Congress of the European Society of Cardiology

Reported and discussed by: Shaun Goodman, MD

A wealth of scientific evidence shows that changes in lifestyle – stopping smoking, eating a healthy diet, and regular exercise – and drug therapies (Aspirin, beta-blockers, angiotensin converting enzyme (ACE) inhibitors, anticoagulants, and lipid lowering agents) can reduce morbidity and mortality in those patients with established coronary heart disease. Recommendations for secondary prevention of coronary heart disease in clinical practice have been formally established in Europe and North America over the past two years.

EuroASPIRE Study

On August 25, 1996, at the XVIIIth Congress of the European Society of Cardiology, Dr. David Wood presented data from the EuroASPIRE survey conducted by the European Society of Cardiology through its working group on epidemiology and prevention in nine European countries. The principal reason for the survey was to evaluate whether clinical practice reflected recent recommendations on how risk factors in coronary heart disease patients should be managed. The three main objectives of the survey, conducted in the Czech Republic, Finland, France, Germany, Hungary, Italy, Netherlands, Slovenia, and Spain were: 1) to determine whether the major coronary heart disease risk factors (cigarette smoking, obesity, high blood pressure, elevated cholesterol, diabetes, and family history of heart disease) and their management were identified and recorded in patients' medical records; 2) to interview patients 6 months after hospitalization for a coronary event (coronary artery bypass grafting, coronary angioplasty, myocardial infarction, or myocardial ischemia without infarction) and measure the modifiable risk factors and describe their management in terms of lifestyle and drug therapy; 3) to determine whether the patient's family members had been screened for coronary heart disease risk factors. 4,866 patients < 70 years of age were included in the survey. The presence of the major risk factors is indicated in Table 1. Importantly, almost 20% of all patients were still smoking, 50% of hypertensive patients had poorly controlled hypertension (systolic > 140 and/or diastolic > 90 mm Hg), and 44% of patients with total cholesterol > 5.5 mmol/L were not receiving cholesterol

St. Michael's Hospital
30 Bond St., Suite 701A
Toronto, Ontario M5B 1W8
Fax: (416) 864-5330

Table 1: Incidence of Risk Factors in EuroASPIRE		
	Overall Average	**Range Among Countries**
Diabetes	18%	12-21%
Smoking	19%	12-32%
Hypertension*	53%	41-54%
Hypercholesterolemia**	44%	36-58%

* SBP >140 mm Hg ΔBP >90 mm Hg
** Total cholesterol >5.5 mmol/L

Table 2: Prevalence of Treatment in EuroASPIRE		
	Overall Average	**Range Among Countries**
Antiplatelet	81%	72-92%
Beta-blockers	54%	35-80%
Calcium antagonists	42%	23-60%
ACE inhibitors	30%	19-49%
Lipid lowering	32%	23-43%

lowering therapy. Of note, the time during which the survey was conducted overlapped with the publication of the landmark Scandinavian Simvastatin Survival Study (4S),[1] which unequivocally demonstrated the superiority of simvastatin over placebo in the reduction of cardiovascular morbidity and mortality.

Drug therapy in these patients is outlined in Table 2. ACE inhibitor use was highest (39%) among the clinical group that had sustained recent myocardial infarction. Lipid lowering therapy use was highest (41%) in patients who were included in the survey on the basis of recent angioplasty.

Dr. Wood concluded that the European cardiology community needed to utilize an evidence based approach to the management of their patients with coronary heart disease since there is clear evidence that appropriate management of the major, modifiable risk factors results in significant reductions in morbidity and mortality.

Endothelial dysfunction

In a related presentation, Dr. Andreas Zeiher discussed the primacy of the endothelium in the initial development of atherosclerosis. Due to its strategic location positioned as the interface between the flowing blood and the underlying vessel wall, the endothelium serves as a primary mediator of any blood associated effects in the initial development of atherosclerosis. The endothelium produces and releases numerous substances that not only affect vascular tone, but also exert antithrombotic functions. One of the most important mediators released by the endothelium is nitric oxide (NO), which is produced by receptor mediated stimulation, as well as by the sheer stress exerted by the flowing blood. Experimentally, NO has been shown to have potent antiatherosclerotic effects by suppressing the activity of transcription factors of numerous genes implicated in the early pathogenesis of atherosclerosis. Clinically, the presence of risk factors for atherosclerosis (e.g., age, smoking, hypertension, and hyperlipidemia) have been shown to be associated with reduced bioactivity of NO in the absence of angiographically visible coronary stenoses, suggesting that reduced availability of NO might importantly contribute to the development of atherosclerotic lesions in humans.

Recent clinical trials have shown improved endothelial vasodilator function (change from vasoconstriction to vasodilatation in response to acetylocholine) after favourable cholesterol modification in response to diet, lipid lowering medications, and most recently angiotensin converting enzyme (ACE) inhibition. Anderson et al[2] demonstrated significant improvement in endothelial vasomotor function in response to a combination of lovastatin and probucol treatment and a trend in improvement in a lovastatin and cholestyramine combination group by comparison to a lipid lowering diet alone group. Treasure et al[3] also demonstrated significant improvement in coronary endothelial function in a lovastatin treated group after a mean of 5.5 months of therapy, and on the background of a significant reduction in LDL cholesterol of 33%. Recently, Mancini et al showed that ACE inhibition with quinapril improved endothelial dysfunction in *normotensive* patients with coronary artery disease who did not have significant hyperlipidemia.

Findings from these and other studies indicate the potential for improvement in endothelial function following either a reduction in cholesterol or intervention which enhances nitric oxide release (ACE inhibition), which in turn may result in stabilization of atherosclerotic plaque and, therefore, reduce the propensity for rupture and acute ischemic events. The key role of the endothelium and dramatic improvement in endothelial dysfunction with lipid lowering and ACE inhibitor treatment provides an explanation for two previously poorly understood "paradoxes". Coronary angiographic studies have consistently demonstrated an arrest in the progression of lesions and significant regression in others following lipid lowering therapy. However, an even more substantial decrease in cardiovascular events during follow-up was seen despite minimal absolute regression of lesions. Similarly, it is now clear that, contrary to what was previously believed, most acute coronary events (example, unstable angina and myocardial infarction) are not frequently caused by atherosclerotic lesions that result in severe stenoses. In fact, the majority of events are caused by lesions with stenoses of < 60%. Indeed, the atherosclerotic plaques in danger of rupturing and causing acute ischemic events are young ones, high in lipids and macrophages, soft in consistency with a thin, fibrous capsule. These young plaques have a very high tension at their extremity, often leading to rupture, ulceration, and thrombosis. These characteristics are more often seen in small plaques; in contrast, more severe stenoses angiographically are often more stable and, therefore, less likely to rupture.

Aggressive risk factor modification (better diabetic control, discontinuation of cigarette smoking, treatment of hypertension and hyperlipidemia) results in dramatic improvement in endothelial function (and, therefore, substantial decreases in cardiovascular events) despite important but less striking degrees of plaque regression.

Risk factor modification

Dr. Valentin Fuster also discussed the importance of the management of cardiovascular risk factors in the optimal care of patients with established cardiovascular disease or at high risk for the development of this disease. Dr. Fuster served as the co-chairman of the 27th Bethesda Conference of the American College of Cardiology (convened September, 1995); the specific goal of the conference was to match the intensity of risk factor management with the identified hazard for coronary heart disease events. Dr. Fuster outlined the conclusions of the 8 separate task forces charged with the review and clarification of the role of management of risk factors in the care of high risk patients. This extensive process has been recently published in its entirety in the *Journal of the American College of Cardiology* (1996;27:957-1047). The conference highlighted the rationale for heightened attention to cigarette smoking, lipid disorders, hypertension, thrombotic diathesis, and other risk factors in the high risk patient, and provided specific recommendations for case management and for organizational strategies to assure the optimal provision of these services.

Based on the American Heart Association consensus panel statement regarding the prevention of heart attacks and deaths in patients with coronary artery disease (*Circulation* 1995;92:2-4), the following specific recommendations were made: 1) Smoking: complete cessation. Patients and their family should be strongly encouraged to

stop smoking with the provision of counselling, nicotine replacement therapy, and/or formal cessation programs as necessary. 2) Physical activity. Minimal goal: 30 minutes 3-4 times per week. In order to assess risk level and to guide heart rate prescription, it was recommended that an exercise stress test be performed. Patients should be encouraged to engage in a minimum of 30-60 minutes of moderate intensity activity 3-4 times weekly (walking or cycling) supplemented by an increase in daily lifestyle activities (e.g. walking breaks at work, using stairs) with the maximum benefit seen at 5-6 hours per week. Moderate to high risk patients should be involved in a medically supervised exercise program. 3) Weight management. For patients whose weight is greater that 120% of ideal for their height, an intensive diet and appropriate physical activity intervention (as outlined above) should be initiated, particularly in those patients with hypertension, elevated triglycerides, and/or elevated glucose levels. 4) Blood pressure control. Goal: ≤140/90 mm Hg. Lifestyle modification, including weight control, physical activity, alcohol moderation, and moderate sodium restriction, was recommended as the first step. The addition of blood pressure medication, individualized to other patient requirements and characteristics (i.e. age, race, need for drugs with specific benefits), was recommended for patients whose blood pressure, 3 months after initial lifestyle modification, remained > 140/90 mm Hg or in those patients whose initial blood pressure was > 160 mm Hg systolic or > 100 mm Hg diastolic. 5) Medical therapy. Appropriate use of antiplatelet agents/anticoagulants, ACE inhibitors, beta-blockers, and estrogen replacement in all postmenopausal women with coronary artery disease, should be considered in patients with coronary heart disease based on strong evidence from clinical trials. 6) Lipid management. Primary goal: LDL < 2.6 mmol/L; secondary goals: HDL > 0.9 mmol/L, triglycerides <2.0 mmol/L. American Heart Associate Step 2 diet should be initiated in all patients with coronary heart disease (<30% fat, <7% saturated fat, <200 mg per day of cholesterol). A fasting lipid profile should be obtained in all patients with coronary heart disease (noting that the profile may take 4-6 weeks to stabilize following an acute coronary or other medical event). Drug therapy should be considered for all patients with an LDL >2.6 (e.g., a statin or niacin).

Conclusion

Dr. Fuster concluded that the optimal care of the patient with cardiovascular disease remains the key responsibility of the cardiovascular specialist and that risk factor management is a cornerstone of that optimal care. He emphasized a team approach, involving family physicians, general internists, other specialists such as endocrinologists and vascular surgeons, nurses, nutritionists, exercise physiologists, behavioural scientists, and cardiovascular specialists should assure the provision of this care.

References

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