Assessment of Cardiovascular risk

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ATHEROSCLEROSIS

Atherosclerosis is a generalized disease of the arterial wall resulting from a complex interaction of arterial wall damage, cell modification and thrombotic factors. The origin of atherosclerosis, mainly characterised by the intracellular and extracellular build-up of modified LDL cholesterol, is a result of interaction between various elements in blood and the walls of the larger arteries, involving different cell types. Dysfunction of the endothelium, for example, as a result of unfavorable hydrodynamic forces and elevated LDL concentrations leads to the formation of macrophages with radically altered functions. These cells, together with endothelium and smooth muscle cells, can form oxygen radicals so that infiltrated lipoproteins can be modified. The excessive uptake of such particles by macrophages gives rise to foam cells. After the necrosis of these cells an atherosclerotic plaque is formed.

Though atherosclerosis can be viewed as a systemic disorder, the expression of the disease in specific preferred locations is striking. Haemodynamic factors play an important role in this context, but there is no adequate explanation for the fact that in some people atherosclerotic changes mainly occur in leg arteries, or in coronary arteries in others, and mainly in cerebral arteries in yet other people.

It is obvious that numerous other factors may have an impact on the processes mentioned above. The presence of circulating vaso-active substances, toxic agents like cigarette smoke, viral infections, and circulating immuno-complexes can all result in the dysfunction of the endothelium. The concentrations of lipoproteins that can be modified, such as LDL and lipoprotein (a), have an impact, but so do the immune system, the presence of free radicals, anti-oxidants, and a large number of growth factors, including those of platelets.

Thus it can be concluded that though lipoprotein concentrations play a predominant role, a large number of factors have a major influence on the origin and development of the atherosclerotic process. More recently, an increasing number of genes has been determined that predispose individuals to cardiovascular disease by either increasing risk factor levels, impairing response to thrombosis or raising vulnerability to ischemic damage of the heart and the brain.

RISK FACTORS

Literally, risk factors are factors that increase risk. Some characteristic being a risk factor does not necessarily imply that the factor plays a role in the etiology of disease. Epidemiological research since the fifties has found an increasing number of factors whose presence increases the risk of cardiovascular diseases. During the course of time various characteristics have been attached to the term risk factor. These can be factors that have a statistical correlation with cardiovascular disease. It can also be a factor that lies at the root of a disorder. Finally, factors can predetermine whether someone will develop cardiovascular disease, because they make an organism more sensitive to the influence of other factors.

While there is much overlap between these three groups, a causal relationship can be demonstrated with cardiovascular disease for some risk factors, while this is far less clear in other cases. Determining a causal relationship is not a precondition for the use of risk factor in establishing the risk level of an individual. A division can be made into at least four categories of risk factors:

Biological risk factors that cannot be influenced: increasing age, male sex, and hereditary load.

Risk factors as an expression of pathophysiological mechanisms: high blood pressure, high serum cholesterol and certain cholesterol fractions, elevated plasma glucose, reduced glucose tolerance, elevated plasma uric aid, elevated plasma homocysteine, changes in certain parameters of coagulation (e.g. elevated fibrinogen), or elevated pulse rate. These risk factors may possibly be changed through medication or other means.

Acquired risk factors that depend on the social environment or certain living habits: smoking, excessive use of alcohol, unbalanced diet, lack of

physical exercise, stress, and certain features of one's personality (e.g. type A behavior).
Risk factors that are an expression of damage already present in the heart and arteries: ECG deviations, left ventricular hypertrophy, a previous myocardial infarction, a low ankle/arm blood pressure ratio, calcification of the aorta, and changes in the wall of the carotid artery for example.
Up until now, the most important or strongest risk factors are high age, male sex, smoking, elevated serum cholesterol, impaired glucose tolerance and diabetes, and high blood pressure (**Neaton, 1992**). Smoking, elevated serum cholesterol, glucose intolerance and high blood pressure are factors that can in principle be influenced by diet or medication.

RISK FACTOR MODIFICATION

The gradual recognition of risk factors for cardiovascular disease has stimulated research to find ways to positively influence these factors, thereby reducing the risk of cardiovascular diseases. A distinction has to be made between the three ways in which the problem can be approached: the population approach in which an effort is made to reduce the average risk of the entire population, the high-risk approach in which a selective effort is made to reduce the elevated risks of some people, and the population approach in which the objective is to influence risk factors at a young age to reduce the increase in these factors when people grow older.
Theoretically, cardiovascular diseases could be strongly reduced by banning smoking and by bringing about a drop in the serum cholesterol and blood pressure. One problem here is the possibility that to a certain extent atherosclerotic changes of the cardiovascular system are not or only partially reversible.
This problem also arises in the second approach, in which people with higher risks are traced through screening or case finding, after which specific treatment of this high-risk group occurs. This approach was taken in a number of large-scale intervention trials, in which one or more factors were influenced and then the effects of intervention on the development of cardiovascular diseases and mortality were examined. As a rule, the effects of intervention on illness and mortality in these studies are not as large as could be expected from the reduction achieved in the risk factors. This particularly applies to the effects of blood pressure reduction on coronary heart disease. This finding lends support to the earlier hypothesis that part of the atherosclerotic process cannot be influenced after a certain age via changes made to the classic risk factors. In addition, it is possible that some of the therapies presently available not only reduce risk but may also result in other risks. One example is the treatment of high blood pressure with diuretics affecting potassium, in which the side effect of the treatment is that there is a higher risk of fatal cardiac arrhythmia (**Hoes et al, 1995**).
Logically, this leads to the third approach. It is based on a change in environmental factors from a young age, so that high blood pressure, elevated cholesterol, and smoking can be prevented. This potentially seems to be the best road to take, but there is hardly any research regarding this option, due to the huge logistical and financial efforts attached to this strategy. In such an approach, we first need to determine in what way and to what extent changes in environmental factors, such as nutrition, influence the development of high blood pressure and serum cholesterol. Moreover, we need to know whether such changes can have negative consequences for growth and development.
Another way to reduce the incidence of cardiovascular disease is offered through the recognition of a number of biochemical and/or other characteristics that lead to heightened risk of cardiovascular disease in the presence of an atherosclerotically altered vascular system. The number of people who actually develop symptoms of coronary heart disease is only a fraction of the number of people with atherosclerotic damage to the coronary arteries. It is striking that an important percentage of the persons in the highest quartile of the distribution of one of more risk factors remain free of cardiovascular disease. There is no proper explanation for this. On the one hand, it can be assumed that some of the factors that determine cardiovascular disease are not yet known. On the other hand, it is possible that the known risk factors form the basis on which an atherosclerotic vascular lesion can develop but that the fatal occlusion requires a set of circumstances in which the contribution of classic risk factors is less important.
Oliver (1986) has stated that it is important to consider the relationship of risk factors for atherosclerosis and coronary heart disease together

with a number of factors that elicit respective symptoms or make the heart more sensitive to the consequences of atherosclerosis.

SECONDARY PREVENTION

Once an episode of symptomatic cardiovascular disease has occurred, as for example a myocardial infarction, attempts can be made to prevent its reoccurrence. This is considered secondary prevention. As regards the treatment of coronary heart disease, much progress has been made in supporting patients in the acute phase. In addition, the prognosis of patients with chronic coronary heart disease and heart failure can be positively influenced. It is highly likely that the mortality due to cardiovascular disease can be reduced, or at least be delayed. Prevention of relapses in patients who have suffered a heart attack may for example be achieved by the favourable effect of certain changes in one's lifestyle and diet, quitting smoking, and by various forms of medical treatment (i.e. beta-blockers) (**Soriano et al, 1997**). Medicines that influence coagulation also have an important part to play. Secondary prevention using aspirin leads to a drop in new myocardial infarction events by about 25% (**Antiplatelet Trialists' Collaboration, 1988**). However, it is obvious that these options will raise the costs of health care, while only a limited part of the large group of people who will suffer from a myocardial infarction or heart disease can be helped. To bring about major changes in the occurrence of coronary heart disease, a change has to be made to the risk profile of the population at large, and a start should preferably be made with younger people.

RISK PROFILING

There is now general consensus that diagnosis and treatment of elevated blood pressure and serum cholesterol will reduce the occurrence of coronary heart disease. The decision to apply a medicinal intervention should however be based on the level of absolute risk of complications, e.g., based on risk profiling. Risk profiling implies the careful assessment of all indicators of an increased risk, whether causal or not. A risk profile is made by assigning weights to these various factors. Next, implicitly or explicitly, these weights are converted to probabilities of disease occurrence. The assessment of individual risk factors contradicts the fact that risk factors can enhance each other and that the elevation of several risk factors has more impact than the sum of the individual parts. The overall absolute cardiovascular risk determines the absolute net benefit a patient is likely to experience. Absolute benefits, and risks, are the most relevant expression of preventive efficacy in the practice of medicine.
Existing atherosclerotic disease is the most important predictor for new complications. This pertains to symptomatic as well as asymptomatic disease. Several new methods for non-invasive assessment of pre-symptomatic atherosclerotic arterial disease have recently come available. For example, it has been shown that thickness of the wall of the carotid artery, measured by ultrasound as an indicator of generalized atherosclerosis, is strongly related to subsequent symptomatic coronary heart disease and stroke (**Bots et al, 1997**).The importance of being able to detect early disease rests in the notion that prevention of symptoms may be achieved by prevention of atherosclerosis through risk factor modification but also by preventing triggers for sudden arterial occlusion and reduction of sensitivity for ischemia of myocardial tissue that is already suffering from a compromised coronary circulation.
It is obvious that the medicinal treatment of patients and persons with a high risk of cardiovascular complications should be part of a strategy aimed to prevent the disorder in the entire population. The exclusive treatment of persons with the highest risk will not lead to the disappearance of the disorder, nor to a reduction in the risk of cardiovascular diseases in future generations (**Rose, 1981**). From a population perspective, public health should consider the constellation of risk factor distributions and changes over time in a population. Similarly, in clinical medicine and individual prevention, physicians should appreciate the overall absolute risk as a reflection of various risk factors. The overall absolute risk determines the need for risk factor modification which should subsequently be targeted at the risk factor that is most amenable to change, by diet or drugs, in that individual.

Note

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Salt sources and occurences

General geology – diaperism

Geochemistry