

What We Learn From Current Cardiology: Look at the Risk Factors

Aurelio Leone

Aurelio Leone, Former Director, Department of Internal Medicine City Hospital Massa, Italy

Correspondence to: Aurelio Leone, MD, FASH, FRSPH, Former Director, Department of Internal Medicine City Hospital Massa, Massa, Italy.

Email: reliol@libero.it

Telephone: +393472272215

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ABSTRACT

This is an extensive review about the risk factors for cardiovascular disease, according to the continuous progress reported in literature. Cardiovascular risk factors show a clear evidence of increased risk of cardiovascular disease, particularly in the coronary arteries and cerebral circulation, with different results, which depend on the fact that they may act isolated or combined together. Some of them like cigarette smoking, hypertension, altered lipid and glucose profile, obesity and sedentary life are believed to be major cardiovascular risk factors and, therefore, efforts should be conducted in an attempt to control and modify their potentially adverse effects. There is evidence that preventive measures may act in this way improving cardiovascular system health and reducing the incidence of cardiovascular events in both developed and developing countries as always more current papers undoubtedly show.

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Key words: Cardiovascular risk factor; Etiologic factor; Epidemiology; Prevention; Physical activity

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INTRODUCTION

The advances of the knowledge in the physiology and pathological characteristics of the cardiovascular system are continuously in

progress and involve all the fields of the modern cardiology, although some differences may be observed in a topic rather than another one.

Today, at the beginning of the twenty-first century, there is resurgence in the etiologic approach to cardiovascular risk factors since they permit to establish the incidence of cardiovascular disease and, therefore, warrant a major control. Particularly with regard to atherosclerosis^[1], epidemiological findings go towards this direction.

Cardiovascular risk factors, whatever is the approach to their assessment-and there are different types of approach: etiological, statistical, physiological, pathological, metabolic, clinical and so others-show, however, a higher incidence specifically in some cardiovascular events mainly related to vascular pathology.

Many cardiovascular risk factors, which show a progressive increase in their number and effects, have been proposed over the last decade, although their reliability varies according to the role and power^[2-3].

Since evidence indicates that cardiovascular disease (CVD) and stroke are primarily the leading-causes of death and disability in the developed countries of the western area^[4-7] together with Japan and Middle-East, it is worth noting that each progress observed is strictly linked with cardiovascular changes and should be carefully identified.

This is an extensive review aimed to describe the relationship between metabolic patterns of cardiovascular risk factors and their influence on the cardiovascular system.

ROLE OF CARDIOVASCULAR RISK FACTORS IN THE PATHOLOGY OF THE HEART

The high mortality that characterized cardiovascular pathology of the civilized countries during the first years of the 20th century has met a dramatic decline in the recent years because of an intensive campaign addressed to recognize and treat cardiovascular risk factors and establish their role to cause cardiovascular events.

Several risk factors have been identified, although smoking^[8-12], hypertension^[13-17], high LDL-Cholesterol levels with reduced HDL-Cholesterol^[18-22], metabolic syndrome, and diabetes mellitus^[23-29] are those particularly analyzed from the various findings. In addition, current opinion is that cardiovascular risk factors may be grouped into three main classes as table 1 shows.

As it can be noted, some risk factors are strongly related to both

Table 1 Main characteristics of the cardiovascular risk factors.

Characteristics	Risk factor
1. Risk factor strongly related to heart disease	Hypertension
	LDL-Cholesterol
	Smoking
	Diabetes mellitus
	Aging Obesity Metabolic syndrome
2. Risk factor probably related to heart disease	Sedentary life
	Recurrent stress
	Inflammation Homocysteine
3. Predisposing risk factors	Family history Genetic patterns

cardiovascular disease and events, some others show a weaker link, and, finally, the group of predisposing factors is still not well defined and in progress for what concerns findings and reports.

The cardiovascular system has a considerable impact to preserve the health of individuals, allowing the normal functions of the body organs and providing metabolic energy necessary for the vital functions through the transport of oxygen and nutrients.

Three basic mechanisms as the contraction of the heart, hydraulic properties based on pressure gradients of the heart and blood vessels, and chemical reaction at the cellular level for metabolic purposes, permit the apparently simple function of the cardiovascular system. Therefore, a question arises: Why a structure as the cardiovascular system deputed to carry out apparently simple functions is affected, even today, by a higher incidence of morbidity and mortality? Undoubtedly, several factors, related to lifestyle and deeply interacting, play a predominant role in the modern society.

There are factors that favour the appearance of cardiovascular disease whose role and significance should be further clarified in both an epidemiological and pathological context. They are commonly considered cardiovascular risk factors. Assessing their exact role to determine the cardiovascular pathology is of basic significance since different opinions exist on the topic.

Different opinions support the fact that several papers do not reach similar results either on the type of damage or on the relationship with a specific cardiovascular disease and/or event. Therefore, interpreting unanimously the significance and role of a cardiovascular risk factor gives a correct setting to the pathology of the heart and blood vessel.

A simple definition identifies a risk factor as a variable associated with a major incidence of the disease than that due to its lack, although it does not play necessarily a causal role. Several factors like hypertension, high LDL-cholesterol, diabetes mellitus, and others may accompany, alone or all together, the occurrence of cardiovascular disease with a higher rate. Therefore, the conclusion is that there are some factors, which may increase, but not determine the incidence of a disease. Thus, such an assumption well explains the concept of risk.

The potential role of a risk factor can be assessed by comparing the risk of the subjects exposed who show the event to be examined with those without in a large group of individuals.

Statistical methods contribute to establish the role of a cardiovascular risk factor by comparing the percent of population affected on the total population. Therefore, a risk factor provides the global burden of disease by the analysis of many events, which involve lifestyle, age and gender, socioeconomic habit, education, geographic area and characteristics of the studied population.

The results observed by the analysis of the risk factors, are, usually, provided by epidemiological studies and as much an epidemiological

study is large as the risk may be better measured.

An emerging concept to prevent the incidence of cardiovascular disease is to carry out those strategies, which can prevent the adverse effects of a risk factor^[30]. Therefore, when a risk factor can be completely removed, even if by a great effort, there is a good reason to support the economic costs able to avoid completely its effects. An example may be the exposure to passive smoking, which should be removed because this factor is not only a risk factor, but also the leading cause of cardiovascular damage as the findings show^[1] and, legal acts forbid.

EPIDEMIOLOGICAL CHARACTERISTICS AND PREVENTIVE MEASURES

It is worth noting that there are yet no universally diagnostic and codified criteria with regard to the effects of risk factors on the cardiovascular system. This fact sufficiently explains the reasons of the lack of conclusive results assessed by statistical and epidemiological methods. In addition, the epidemiology needs some specific characteristics to be well defined as a correct approach to the study design, large sample enrolling as many subjects as it is possible, collecting data in a uniform way, assessing the best statistical method, analyzing collected data, and interpreting accordingly to the observed results. There is evidence that many of these aspects follow those methods experienced by the statistical estimate. Therefore, a correct statistical assessment may help to obtain the most useful, but not conclusive epidemiological survey.

The aim of this discussion is not that to define, in detail, all the factors involved in the epidemiological assessment, but, on the contrary analyze briefly the enormous progress obtained by the studies of some parameters, and the role played in the epidemiological survey based on the prevention of the disease. This parameter covers a fundamental importance with regard to the assessment of cardiovascular risk factors since it may provide the material for a reduction and control of the disease. Thus, each major cardiovascular risk factor exerts different effects, although often obtains similar final results. The concept of prevention is in agreement with the old aphorism “prevention is better than cure”^[31].

Some characteristics have been established to define a major cardiovascular risk factor (table 2): its implication to cause coronary heart disease, frequent appearance in the examined population and control by preventive measures.

Evidence indicates that cigarette smoking, hypertension, changes

Table 2 Characteristics of a major cardiovascular risk factor.

1. Assessment of the relationship with coronary heart disease
2. Highest rate in the examined population.
3. Control or reduced effects by preventive measures

in lipid and glucose metabolism, and obesity undoubtedly meet these criteria. However, different responses to the preventive measures characterize cardiovascular risk factors.

Smoking

The primary prevention towards cigarette smoking may be absolutely obtained by smoking cessation. It causes a dramatic fall in the incidence of coronary artery disease, although differences in the rate characterize the various reports^[32-35]. In quitting smokers, the relative risk of ischemic heart disease declines up to that of non-smokers in one year or less^[32]. According to the report of Tsevat *et al*^[33], a 35-year-old who quits smoking could gain 3 to 5 years of life and significant reduction in the rate of coronary heart disease

and death. Other reports^[34-35], primarily observational studies, would demonstrate that smokers who quit reduce their excess risk of coronary events by 50 percent in the first year or two after cessation with a maximum gain in the first months. Then, further gradual decline characterizes former smokers who approach the risk of never smokers after 5 to 10 years.

There were and are still in progress effective anti-smoking campaigns whose purpose is that to reach and maintain quitting smoking in the previous smokers^[36-37].

Secondary prevention of cigarette smoking is carried out in smokers suffering primarily from coronary artery disease.

It is worth noting that the secondary prevention in ischemic subjects has a greater importance if compared to primary prevention. The subjects suffering from coronary artery disease met a large number of heart attacks and recurrent myocardial infarction^[38-41] that were higher in rate when an association of major cardiovascular risk factors including cigarette smoking existed. Therefore, it is imperative to recommend smoking cessation because findings demonstrate a certain advantage using this behaviour. Indeed, there would be a clear evidence of that.

A reduced incidence up to 50 percent of recurrence in cardiovascular events together with health benefits can be obtained in past smokers compared to patients who continue to smoke.

Hypertension

It is worth noting that a different address should be discussed for the primary prevention of hypertension. Meanwhile, it is questionable, considering the definition of primary prevention as that to control all known and hypothesized factors responsible for the disease, if a correct approach, and rightly so, of primary prevention measures tends to prevent the complications of a disease, usually already appeared as, of course, is the high blood pressure.

A diet with reduced amounts of sodium, programmed daily physical activity, reduction of body weight, and careful control of the most important biochemical parameters related to the carbohydrate and lipid metabolism could slow down, although not prevent, the onset of high blood pressure in people who are predisposed.

In the presence of hypertension, some measures of change in lifestyle associated, often, with drugs able to lowering blood pressure seem to reduce the incidence of stroke. Similar results have not been identified with regard to the coronary heart disease with no clear reason^[42-43].

The results obtained with the secondary prevention do not differ from those observed for the primary prevention even if much confusion exists, as aforesaid, between the two types of prevention.

By the analysis of the data provided, however, it is clear that important recommendations can be carried out. First, the costs due to a satisfactory treatment of blood pressure are high and not still justified by reliable results^[44]. Secondly, the result that should be obtained is that to protect against the onset of cardiovascular complications of hypertensive subjects by lowering blood pressure in any way got. Thirdly, evidence indicates that the values of blood pressure must be stably below 130 mm Hg for the systolic and 80 mm Hg for the diastolic blood pressure^[45].

Metabolic Factors

The prevention of metabolic factors is very complex because a whole range of genetic, familial and epidemiological factors play a significant role, not always measurable and, in addition, with features that can respond in a different way, not always favourable, to the therapy. However, some interesting conclusions on the subject have been reached.

Trials^[46-48] demonstrate that lowering or correcting altered metabolism and bio-humoral parameters as well as excess in body weight could reduce the incidence of coronary heart disease with regard to both the primary and secondary prevention. In addition, evidence indicates that physical inactivity is able to double the risk of coronary heart disease as observational studies and clinical trials undoubtedly would show^[49-52].

Observational studies conducted primarily in men have identified that both physical activity of a trained exercise and leisure-time activity reduced the risk of coronary heart disease and all-cause death, although the statistical incidence achieved different levels. In addition, regular exercise would reduce the incidence of both myocardial infarction and sudden death in people performing physical activity. Finally, physical activity seems to be able to reduce blood pressure, body weight, platelet aggregation and adhesiveness with increased fibrinolysis^[53].

PROGRESSES IN THE INTERACTION BETWEEN THE MAJOR RISK FACTORS

It is worth noting that the observations on the interaction of cardiovascular risk factors derive from the results provided by different studies, of which MRFIT cohort large-study^[54] achieve a strong significance.

From the analysis of this study, there is evidence that each major coronary risk factor, namely cholesterol level, hypertension, smoking and diabetes mellitus, exerts an isolated effect of increasing the rate of coronary events for those people who are affected.

When these major factors are variously combined, the effects increase exponentially, and the degree of increase may be also measured, as some reports demonstrate^[55-56]. The table 3 shows the more frequent association among the coronary risk factors

Table 3 Prevailing association among the major cardiovascular risk factors.

Risk factor	Association
Smoking	Altered lipid profile (LDL-Cholesterol excess)
	Hypertension
	Endothelial dysfunction
Lipid Profile	Smoking
	Metabolic syndrome
	Hypertension
	Diabetes
Metabolic syndrome	Obesity
	Increased insulin resistance
	Diabetes
Hypertension	Altered lipid profile
	Smoking
	Altered lipid profile
	Age
	Endothelial dysfunction
Obesity	Metabolic syndrome
	Diabetes
	Altered lipid profile

Some differences according to the type of factors associated, age and characteristics of the population exist. The association between level of LDL-cholesterol, smoking and hypertension in young people usually shows strongly enhanced effects, while diabetes mellitus, isolated systolic hypertension and both systolic and diastolic hypertension associated play a heavy effect in elderly subjects. However, the level of risk absolutely increases when the combination of risk factors occurs.

Smoking is one of the early major cardiovascular risk factors to be documented in association since it begins as a pleasant act in

the younger population. It well relates the adverse effects on the cardiovascular system, particularly with enhanced LDL-Cholesterol concentrations because both these factors are able to induce, in time, atherosclerotic plaque formation. Thus, smoking, either active or passive, potentiates its effects when high LDL-Cholesterol levels are associated.

A study, which assessed the interaction among the major coronary risk factors^[57], analyzed the association of cholesterol, triglycerides, blood pressure, obesity and cigarette smoking. Two methods were used as a standard correlation analysis and percentile analysis methods applied to associations at higher levels of the risk factors. Percentile analysis requires that a known value of a variable has to be divided into 100 sub-sets with equal frequencies. Mathematical result of a percentile is easy to be calculated as the ratio of the number of observations below the value analyzed divided for the total number of observations multiplied 100. The study population consisted of 4,839 men and women aged from 30 to 39 years, a number statistically significant. In the percentile analysis, subjects with moderate (equal or over 70th percentile) or high (equal or over 90th percentile) levels in one of the examined risk factors showed clustering of elevations in other risk factors in that expected ratio were generally greater than unity. From these data, there is evidence that the incidence of the strongest power due to interactions of the major coronary risk factors covers significant expectations.

Data provided by the paper of Gotto^[56] emphasized that the mortality rate from coronary heart disease was from two to three times greater in those people who were heavy smokers, and such a fact, then, identified smoking as an independent major risk factor for coronary heart disease. In addition, the risk was even higher when smokers were hypertensive and with elevated cholesterol that are pathological features of frequent observation in the patients suffering from coronary artery disease.

Pooling Project^[58] provides further data about the risk factor interaction showing an additive effect of the association between cigarette smoking, hypertension and elevated cholesterol levels. In addition, in the Ni-Hon-San Study^[59] the effects of cigarette smoking on ischemic heart disease rate in the presence of hypercholesterolemia appeared to be more than an additive factor for the Japanese Americans who lived in Hawaii. The same effect, however, did not characterize Japanese men living in Japan, who, usually, had lower cholesterol levels. In addition, additive effects^[60] among the different major coronary risk factors existed in the Goteborg study. Very recently, an excellent paper^[61] developed a cardiovascular risk prediction model appropriate for the Chinese population, related mainly to the assessment of the ischemic heart disease in the presence of major cardiovascular risk factors (age, systolic blood pressure, serum total cholesterol, body mass index, smoking, and diabetes mellitus) in both men and women. Evidence indicated that in a country in very rapid socioeconomic progress like China, stroke was the predominant cardiovascular disease rather than coronary heart disease.

Multiple logistic equations have been prepared and applied to establish the role of interaction of the major coronary risk factors. These equations analyze the presence of multiple risk factors with additive effects within themselves. Thus, the estimate of the interaction, which adds the percent value of each factor, obtained results greater than that represented by the real value of the risk with no association. Such a condition shows an exponential increase instead of a mathematical addition regulates the harmful effects of coronary risk factors when they act together. Indeed, such a concept is, nowadays, universally accepted.

Analytical and methodological refinements are useful for a better knowledge of coronary risk factor association. Nevertheless, evidence exists that multiple risk factors together greatly increases the risk of cardiovascular and cerebrovascular events.

With regard to the type of cardiovascular events potentially occurring in individuals with multiple risk factors, there is no explanation about that. Cardiovascular events may be fatal or nonfatal independently of the different association of risk factors, and such a fact is still far to be interpreted. Therefore, when an association of different major risk factors exists, a global burden of the effects may be measured statistically, although quantitative results on the outcome of disease cannot be obtained.

CONCLUSION

In conclusion, several epidemiological studies permit, today, to know that a significant number of diseases and cardiovascular events correlate with a ranging rate of clinical manifestations primarily coronary disease, stroke and atherosclerotic plaque. The incidence seems to be associated with a number of factors, not yet fully defined, identified as cardiovascular risk factors.

Despite the high correlation with coronary heart disease and stroke in some geographical population^[61], the lack of homogeneity of the subjects enrolled in the various trials, whether they were heterogeneous or homogeneous groups of subjects according to environmental conditions and lifestyle, does not permit final conclusions on the role and, above, on the real number of risk factors. However, it generally agrees that in the event of standardized living habits and conditions related to the environment, individuals who have a greater number of risk factors display a higher probability of coronary heart disease. Therefore, the role and the responses provided by the preventive measures should be directed towards the control of the risk primarily in those groups of subjects with cardiovascular risk factors.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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Peer reviewers: Gao-Qiang Xie, MD, PhD, Associate Professor, Department of Data Management, Peking University Clinical Research Institute, Room 113#, Building 6#, Xueyuanlu 38#, Haidian District, Beijing, 100191, China; Antonio de Padua Mansur, Associate Professor, Clinical Department, Heart Institute (InCor), Av. Dr. Enéas C. Aguiar, 44, São Paulo/SP, 05403-000, Brazil.