Association of cardiovascular risk factors, behaviours, short stature and longevity.

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Abstract
Cardiovascular risk factors (CVRFs) and behaviours interact during adulthood with the sad privilege of being the first cause of disability and death.
CVRFs interact positively with additive effects such as of hypercholesterolaemia and high blood pressure and the risk derived from the simultaneous exposure is greater than would be expected by the simple addition of the corresponding factors.
During the last century, life expectancy increased rapidly in Europe as well as in other parts of the world.
Life expectancy is a health indicator of a given population, while the term longevity simply means an average life expectancy.
Comparative studies between Japan and some western countries clearly reveal the difference in longevity of its inhabitants.
High stature could be assessed as a late risk factor too.
Introduction

It is known that atherosclerosis is a slow, progressive disease that starts in childhood and usually manifests itself clinically much later, as it has been demonstrated by several authors [1-7], including genetic predisposition, the environment, harmful behaviours and cardiovascular risk factors (CVRFs) that produce a disease initially asymptomatic.

Identify and treat CVRFs in childhood and adolescence would be the most important value of Cardiovascular Prevention.

Long-lived patients who are still autonomous may hypothetically have protective factors and/or fewer CVRFs which afford a better quality of life.

The decline in mortality in the Japanese people is undoubtedly influenced in the general improvement of health consideration of a number of factors such as diet, work, social relations, primary health care, public health services, the economy, among others as the short stature among Okinawans who have the highest prevalence of centenarians in the world (33.6/100000 inhabitants).

Cardiovascular risk factors

The role of RFs on cardiovascular morbidity and mortality may be influenced by age [8], male gender [9], and by ethnic or geographic factors. [10]

Age is a prognostic factor of great importance, already recognized by Benjamin Gompertz (insurance actuary) in 1825, and is the most powerful independent RF for the prognosis of death and atherosclerosis disease. It is the most powerful risk factor for hypertension, and cardiovascular death. [11]

Male sex is associated with greater cardiovascular complications.

The association between high blood pressure and cardiovascular disease and mortality has been the subject of numerous observational studies.

From a long time ago it has been demonstrated that arterial hypertension is also a major RF in the elderly. [12] [13] [14]

Patients with a history of hypertension have at least six times greater risk of heart failure than those individuals without that a history. [15]

No specific guidelines exist for hypertension management for this particular elderly population.

Numerous observational studies have confirmed the predictive role and existence of a causal relationship between hypercholesterolaemia and coronary heart disease. (for example: Framingham Heart study, MRFIT study).

Hypercholesterolaemia is one of the main modifiable CVRFs.

Also, cholesterol chemically is an alcohol; hypercholesterolaemia induces a decreasing in the chromatic vision, the higher visual function, located in the areas 17, 18 and 19 of the cerebral cortex. [16]

Hypercholesterolaemia was correlated with dizziness by the action on the labyrinth as a neurotoxic effect. [17]

Evidence exists that hypercholesterolaemia is a risk factor for the neuronal aging. The findings in elderly Finnish men suggested that high serum cholesterol concentration was an independent risk factor for Alzheimer’s disease. The National Cholesterol Education Project sets no upper age limit for lipid screening; however, it recommends "caution in proceeding to drug therapy in the elderly" for primary prevention. Some authors question the utility of cholesterol as a significant risk factor for heart disease mortality in elderly people.

Unfortunately, little direct evidence exists about the benefits or burdens of screening and
treating octogenarians with high serum lipids. The epidemic of type 2 diabetes (DM) is clearly linked to increasing rates of overweight and obesity in the U.S. population, but projections by the Centers for Disease Control and Prevention suggest that even if diabetes incidence rates level off, the prevalence of diabetes will double in the next 20 years, in part due to the aging of the population. [18] The results of the observations revealed a significant association between obesity and diabetes after accounting for genetic factors. [19] Data from the Framingham study indicate that diabetic patients are at a higher risk of developing heart failure than non-diabetics. Cardiovascular mortality is double in males and quadruple in diabetic women. Diabetes is also a risk factor for sudden death. During the past decades, the prevalence of overweight and obesity in the Western world has increased by 30-50%, leading to what has been described as a global epidemic. Obesity is often associated with co-morbidities such as hypertension, diabetes, atherogenic dyslipidemia, and chronic inflammation, thereby constituting an important risk factor for cardiovascular disease and mortality. [20] [21] According to US Life Expectancy Statistics obesity decreases the average life span of males and females, 4.9 and 4.1 years, respectively. Uric acid, despite being a major antioxidant protecting tissues against the toxic effects of oxygen radicals in the human plasma, both correlates and predicts development of obesity, hypertension, and cardiovascular disease, conditions associated with oxidative stress. [22] A significant association between lower serum uric acid levels in long-lived individuals and their offspring has been observed. [23] RFs interact positively, such that cardiovascular risk derived from the simultaneous exposure to several RFs is greater than would be expected by the simple addition of the corresponding factors. [24] When other factors such as diet were analyzed the authors found a significant association between the consumption of mono and polyunsaturated fats and a lower incidence of cardiovascular diseases, suggesting that the dietary patterns of the Southern European countries, with a low intake of saturated fat and a high intake of fruits and vegetables, was a decisive factor in lower cardiovascular mortality. [25] Numerous studies have been made showing the benefits of adherence to a "healthy diet" in reducing cardiovascular disease, data have been collected from more than 12 cross-sectional studies such as: Monica Project [26], Cardia study [27], Dash diet [28], OmniHeart [29], among others. Dr. Raymond Pearl of the University of Johns Hopkins, USA, in 1938, published a paper showing that smokers live less than non-smokers. The negative effects of smoking are well-documented. Tobacco smoking is incompatible with successful aging and compromises life expectancy even in extreme longevity. [30] The alcohol intake and survival is controversial. A meta-analysis of 143 papers describing the relative drinking of alcohol and cognition found that moderate drinking seems to reduce the risk of dementia and cognitive decline in older subjects. [31] The World Health Organization has repeatedly confirmed the importance of regular physical activity in old age, in an attempt to preserve functional ability as much as possible. The most important variable in lifestyle is physical activity, it is also a very important
predictor of mortality and may actually be a superior predictor of mortality than the individual’s body mass index (BMI). Adults aged 65 years and older gain substantial health benefits from regular physical activity, and these benefits continue to occur throughout their lives. [32]

It has recently been reported that even a small amount of regular exercise can have a true impact on longevity. Favorable attitudes, emotions, personality characteristics, and self-rated health have been associated with successful aging in late life. Psychological factors may exert protective effects on mental health outcomes in advanced age. [33]

Elderly people who are optimistic have lived 7.6 years on average more than those with a negative mindset. [34]

In genetic studies the relationship between elongation of telomeres and longevity is controversial. [35] [36] [37]

In human leucocytes has been shown that the length of telomeres decreases with age and the shortening is associated with age-related illnesses such as cardiovascular disease. For several decades investigators have been trying to determine whether the body size is associated with risk for cardiovascular disease. Short/height stature is controversial about longevity.

Several studies observed an increased risk for coronary disease in shorter men. [38] [39] [40] [41] [42]

Another studies have observed an inverse association between height and risk for coronary disease. [43]

The search published in Plos One Medical Magazine, began in 1965 was conducted in between Kuakini Honolulu Heart Program and Kuakini Honolulu-Asia Aging Study, Hawaii, a 60-year long research on a sample of 8,006 Americans men of Japanese origin born between 1900 and 1919; about 1,200 of these men have reached an age of between 90 and 100 years and about 250 are still alive.

AFRICA study
(AFrica: Acronyms in Spanish of Association of coronary risk factors in old age) [44]

This is a multicenter cross-sectional study developed in Argentina in old age patients was carried out in order to know the prevalence of behavioural, and the presence or absence of CVRFs and their association. Data were collected on 322 individuals aged 90 years or more, 47% of whom had a family history of longevity, probably due to some genetic component.

In our series we found a ratio man/woman of 2.8 similar to the general population aged ≥90 years.

The majority of patients ate meals comprising mainly fruit, milk and vegetables every day and half of the participants drank a moderate amount of red wine.

On average, their BMI was normal and they regularly took some form of physical activity. The age of the menopause for the long-lived women was 48 years.

Frequently, type 2 DM was associated with obesity. No subject had insulin-dependent DM was found.

Interestingly, considering the onset of arterial hypertension started at the high average age of 72 years, it might be due to arteriosclerosis rather than to essential hypertension, a possibility that would be supported by the lack of participants in the study whose hypertension had started before the age of 50 years, time in which there were no angiotensin converting enzyme inhibitors or angiotensin receptors blockers therapy. May be, for the same reason, we detected no association between obesity and
hypertension, unlike that seen in children, adolescents and adults. According to these data essential hypertension would label a malignant disease.

Few were found to be current smokers (3.8%) and even fewer individuals had two or three concurrent CVRFs:

<table>
<thead>
<tr>
<th>HBP</th>
<th>HC</th>
<th>11%</th>
</tr>
</thead>
<tbody>
<tr>
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<td>BMI &lt; 25</td>
<td>4%</td>
</tr>
<tr>
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<td>BMI 25-30</td>
<td>7%</td>
</tr>
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<td>Diabetes +</td>
<td>BMI &gt; 30</td>
<td>25%</td>
</tr>
<tr>
<td>HBP +</td>
<td>Quintile highest of obesity</td>
<td>0%</td>
</tr>
<tr>
<td>HC +</td>
<td>Quintile highest of obesity</td>
<td>0%</td>
</tr>
</tbody>
</table>

Note: HBP: high blood pressure; HC: hypercholesterolaemia; BMI: Body mass index.

<table>
<thead>
<tr>
<th>HBP +</th>
<th>HC +</th>
<th>Smoking</th>
<th>0.4%</th>
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<tbody>
<tr>
<td>HBP +</td>
<td>HC +</td>
<td>Diabetes</td>
<td>0.8%</td>
</tr>
<tr>
<td>HBP +</td>
<td>HC +</td>
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<td>2.4%</td>
</tr>
<tr>
<td>HBP +</td>
<td>HC +</td>
<td>sedentary lifestyle</td>
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Short/high stature and longevity.

In a retrospective cross-sectional study, data were collected from 1510 hypertensive patients consecutively who were assisted at the hypertension research centre (Foggia, Italy) in the last 5 years. Female/male 896/614, each gender divided into three groups of age: 60-69/70-79/80-89 years old (average age: female 64/74/83; male: 64/74/83).

The population registered over 90 years old were women 12 and men 3, scarce amount to obtain a statistical value.

All patients enrolled in the study had not cardiovascular, endocrine, renal and metabolic decompensated diseases.

The prevalence of women was highest in each decades (60-69/70-79/80-89), and in turn, they are shorter stature than men (13.5/13.3/13.2 cm) with a statistically significant difference (p <0.0001).

From 60 to 80 years, the ratio of women to men increases from 1.3 to 1.8.

Although hormones are assumed to explain this advantage, they may play only a partial role.

The total population decreases in each decade, affirming that age is the most potent cardiovascular risk factor.

The stature and body weight, in relation to the increase of age, they were lower with a statistically significant difference in each age group.

The BMI decreases poorly in each group, but a significant difference was found in both genders between 70 and 80 years.
The systolic blood pressure increases every decade, in all groups, with a significant difference only between 60 and 70 years old, both gender. The diastolic blood pressure decrease every decade, in all groups, without statistically significant difference. Table 1

Interestingly, in each group of age, both genders, comparing the patients who were in the lowest quintile of height respect to the highest quintile, the BMI were always more higher, but statistically significant difference only in both groups of 60 years. Table 2

This could mean that the association of high stature and obesity would be a delayed CVRF. We can observed that the height of our patients over 80 years of age was 149 cm among women and 162.2 cm among men, both lower than the average height population.

Table 1

| BMI: body mass index. SBP: systolic blood pressure. DBP: diastolic BP. HR: heart rate. |
|---|---|---|---|---|---|---|---|
| **FEMALE** | N | Height | Weight | BMI | SBP | DBP | HR |
| 60 yrs | 439 | 154.5 | 74.7 | 31.4 | 134.1 | 79.4 | 70.6 |
| 70 yrs | 333 | 152.2 | 72.6 | 31.3 | 140.1 | 77.4 | 70.3 |
| 80 yrs | 124 | 149.0 | 66.2 | 29.9 | 144.2 | 76.3 | 71.3 |
| **MALE** | | | | | | | |
| 60 yrs | 346 | 168.0 | 83.9 | 29.7 | 132.6 | 80.4 | 68.8 |
| 70 yrs | 197 | 165.5 | 79.7 | 29.1 | 137.1 | 77.6 | 67.6 |
| 80 yrs | 71 | 162.2 | 72.7 | 27.6 | 138.1 | 75.2 | 69.9 |

Table 2

<table>
<thead>
<tr>
<th>Decade</th>
<th>Height</th>
<th>Low Q</th>
<th>HighQ</th>
<th>p</th>
<th>Low Q</th>
<th>HighQ</th>
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<tbody>
<tr>
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<td></td>
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<tr>
<td>60</td>
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<tr>
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</tr>
<tr>
<td>80</td>
<td>BMI</td>
<td>30.2</td>
<td>26.6</td>
<td>0.07</td>
<td>28.2</td>
<td>27.0</td>
<td>0.5</td>
</tr>
<tr>
<td>MALE</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Q: quintile

Summary

Atherosclerosis develops depending on hereditary characteristics and exposure to CVRFs, environmental factors and lifestyle. Age and male gender are very strong predictors of cardiovascular events. The low prevalence of simple RF or its associations in an individual may result in an improved quality of life.

In addition to arterial harm, we could hypothesize that hypercholesterolaemia can produce a possible damage of nervous system higher than we know. Hypertension associated to hypercholesterolaemia were as harmful as the smoking habit. Diet healthy and regular physical activity they are beneficial. Today, there is stronger evidence
that increasing adherence to the Mediterranean Diet is associated with lower blood pressure. The alcohol intake is controversial, varies according to the quantity, the time of consumption and the response of the individual. Obesity, frequently associated to hypertension, during childhood, adolescence, and adult population, is always a very major problem by health. DM is a strong RF for macro and microvascular disease. Ethnic, geographic, and socio-economic factors should be considered. Psychological attitude and methodical lifestyle should not be to excluded when evaluating longevity.

People of short stature could live longer. The tall population could live longer if it is not obese. In hypertensive patients the high stature could be a late CVRF, it is worst when associated with higher BMI and increases age. Being bipedal is the price we must pay for, or by the association of all CVRFs? The control of the several CVRFs in the population by means of cardiovascular prevention programs is one of the aims of public health and health care systems, and it may contribute to longer life expectancy and a better quality of life.
Bibliography


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