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Cardiovascular Disease Risk Factors Part XI -- Age By
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Your Life Your Health *The*
***Examiner* September 8,**
2005

The fact is that age is a major risk factor for cardiovascular disease. About four out of five people who die of a heart attack are over 65. As we age, our hearts tend not to work as well. The heart's walls may thicken, arteries may stiffen and harden, and the heart is less able to pump blood to the muscles of the body. Because of these changes, the risk of developing cardiovascular disease increases with age.

Age is a non-modifiable, but major risk factor in the anticipation of cardiovascular disease risk. The Framingham Study has looked at the cardiovascular disease risk of residents of the town of Framingham, Massachusetts over the past 50+ years. From the Framingham data, a scoring system has been developed which allows the estimation of the cardiovascular disease risk of patients, based on:

- Age
- Gender
- Systolic Blood Pressure
- Total Cholesterol
- HDL Cholesterol
- Smoking
- Diabetes
- Enlarged Heart

Obviously, age, gender and whether or not you have diabetes are not under your control. Subsequently, a Global Cardiovascular Risk Score has been developed using the Framingham data but eliminating the non-modifiable risk factors. Instead of the presence or absence of diabetes, the patient’s hemoglobin A1C is used in the Global Cardiovascular Risk Score. The A1C is an estimate of the average blood sugar over the past three months. A value above 6% is abnormal, but for every tenth of a point above 5%, there is a linear increase in cardiovascular disease risk. And, while the American Diabetic Association has established below 7% as the standard of excellence for treatment of diabetes, having an A1C between 6-7% leaves you at increased risk of cardiovascular disease.

It is possible to see the influence of age on cardiovascular disease risk by looking at the changes in the Framingham Cardiovascular Disease Risk Score at different ages when the same values are assigned to the other variables in the score. The following data, derived from the Framingham Cardiovascular Risk Score is based on the following values:

- Systolic blood pressure of 140 mmHg

- Blood Pressure is untreated
- HDL of 30 mg/dl
- Total Cholesterol of 220 mg/dl
- No treatment of the blood pressure
- No smoking
- No Diabetes
- No enlargement of the heart

At the following ages, the cardiovascular disease risk of an individual with the above values is:

- Age 23, less than 1%
- Age 36, less than 3%
- Age 43, 8%
- Age 61, 16%
- Age 84, 25%

These scores mean that an eighty-four year old with the above laboratory values and habits has a 25% chance of having a fatal heart attack in the next ten years, while a 23 year old with the very same values has virtually no risk.

Why is Age a Risk Factor?

While it is obvious that age is a factor for cardiovascular risk, the reason is not. With age, the following changes take place in otherwise healthy people:

- Increases in large artery wall thickening
- Increases in large artery wall stiffness
- Endothelial dysfunction

Each of these confers risk for subsequent cardiovascular disease.

Successful" and "Unsuccessful" Vascular Aging

The aging process alters blood eventually producing cardiovascular disease. Age- associated changes in arteries become "partners" with disease to determine the severity and prognosis of cardiovascular disease in older persons. Of course, the true interactions are more complex and involve age, multiple risk factors, lifestyle, diet, and genetics.

Vascular Aging as the "Risky" Component of Aging

For twenty five years, an attempt has been made to define the effects of aging on arteries. In the Baltimore Longitudinal Study on Aging, study volunteers were screened to detect both clinical and sub-clinical cardiovascular disease and were also characterized with respect to lifestyle (e.g., diet and exercise habits) in an attempt to identify and clarify the interactions of

these factors and those changes that resulted specifically from aging.

Intimal Medial Thickening

Age-associated changes in arteries of individuals who are otherwise considered healthy may be important in the dramatic increase in vascular disease. Studies in humans have found that arterial wall thickening (intimal medial thickening) and dilatation are prominent structural changes that occur within large elastic arteries during aging.
Noninvasive measurements indicate that the carotid wall intimal medial (IM) thickness increases nearly three fold between 20 and 90 years of age.

The age-associated increase in IM thickness may represent an early stage of atherosclerosis. Increased IM thickness is an independent predictor of future cardiovascular events. Thus, those older persons with greater IM thickness may be considered to have aged "unsuccessfully" or to have "sub-clinical" vascular disease. The potency of IM thickness as a risk factor in other individuals equals or exceeds that of most other, more "traditional" risk factors.

Endothelial Dysfunction and Alterations in Vascular Structure and Function

The endothelium is the lining of the arteries in the body. When it does not function normally, it is said to dysfunction. Endothelial dysfunction is a systemic disorder and a key variable in the development of cardiovascular disease. Interventions like risk factor modification and treatment with various drugs, including statins and angiotensin- converting enzyme inhibitors, may improve endothelial function and thereby, potentially prognosis.

Endothelial dysfunction is characterized by a reduction of substances which dilate arteries. On the other hand endothelium-derived contracting factors are increased. This imbalance leads to an impairment of endothelium-dependent vasodilation, which represents the functional characteristic of endothelial dysfunction.

Therapeutic Strategies to Improve Endothelial Function

Endothelial dysfunction is a reversible disorder, and strategies aimed at reducing cardiovascular risk factors, such as:

- cholesterol lowering
- antihypertensive therapy
- smoking cessation
- estrogen replacement therapy in postmenopausal women
- supplementation with folic acid
- physical exercise

also translate into an improvement in endothelial health, further supporting the association between risk factors and endothelial dysfunction.

Aging and Endothelial Function

Endothelial function becomes altered in apparently healthy persons at about the 6th decade of life. The age-associated increase in IM thickening and endothelial dysfunction are accompanied by both artery dilatation and increased vessel stiffness. This is a vicious cycle: altered mechanical properties of the vessel wall influence the development of atherosclerosis and the latter, via endothelial cell dysfunction and other mechanisms, influences vascular stiffness.

Systolic, Diastolic and Pulse Pressure

Blood pressure is determined by the interplay of peripheral vascular resistance and arterial stiffness. Peripheral vascular resistance indicates whether the arteries are dilated or constricted, and it raises both systolic and diastolic pressure to a similar degree. Whereas, arterial stiffness raises systolic but lowers diastolic pressure. Framingham investigators and others have reported an age-dependent rise in average systolic blood pressure across all adult age groups. In contrast, average diastolic pressure was found to rise until 50 years of age, level off from age 50 to 60, and decline thereafter.

Thus, pulse pressure (systolic minus diastolic) which, is a useful indicator of vascular stiffness, increases with age. The age-dependent changes in systolic, diastolic and pulse pressures are consistent with the notion that in younger people, blood pressure is determined largely by peripheral vascular resistance, while in older individuals it is determined to a greater extent by central vessel stiffness.

Owing to the decline in diastolic pressure in older men and women in whom systolic pressure is increasing, isolated systolic hypertension emerges as the most common form of hypertension in individuals over the age of 50. Isolated systolic hypertension, even when mild in severity, is associated with an appreciable increase in cardiovascular disease risk.

Vascular Stiffness

Increased vascular stiffness, over and above blood pressure, is an independent predictor of stroke, hypertension, atherosclerosis, cardiovascular events and mortality. This suggests that altered structure/function of the stiff vessel wall, in addition to the associated increase in systolic and pulse pressures, is a risk factor for future vascular events. Recent studies, in fact, have demonstrated that increased vascular stiffness precedes the development of hypertension.

Individuals with normal blood pressure, yet who have increased arterial stiffness are more likely to subsequently develop hypertension. Observations such as this give rise to the notion that hypertension is, in part at least, a disease of the arterial wall. There are compensatory mechanisms to normalize blood pressure that fail with advancing age. For example, endothelial function becomes apparently altered at about the 6th decade, i.e., when pulse pressure begins to appreciably elevate. Thus, altered endothelial function with aging may be a mechanism that not only permits arterial pulse pressure to rise but

also underlies the importance of pulse pressure as a risk factor for cardiovascular events, even after accounting for systolic pressure.

Can Vascular Aging be Prevented or Delayed?

Progressive vascular damage can continue to occur even when blood pressure is controlled. It is conceivable that drugs that retard or reverse age-associated vascular wall remodeling and increased stiffness will be preferable to those that lower pressure without affecting the vascular wall properties. For example, angiotensin converting enzyme inhibitors have been shown to delay remodeling of the arterial wall that occurs during aging in rodents by retarding the age-dependent intimal thickening and medial smooth muscle cell hypertrophy.

These agents have been shown to decrease vascular stiffness. Similar considerations pertain to treating intimal medial thickening in older persons who are otherwise healthy. Drug/diet interventions have been shown to reduce or retard IM thickening in humans. In particular, statins have been shown to significantly retard the progression of intimal medial thickening in patients with coronary artery disease and in hypercholesterolemic subjects. Importantly, many of the beneficial cardiovascular effects of statins are thought to be non lipid-related, and include favorable effects on endothelial function, plaque architecture and stability, inflammation, and inhibition of cellular proliferation. Thus, by targeting the arterial wall, statins deserve further testing as modulators of vascular aging.

With respect to life style, the risk factor of lack of vigorous exercise increases dramatically with age in otherwise healthy persons. Exercise conditioning also improves endothelial function in older persons. There is also evidence to indicate that diets reduced in sodium are associated with reduced arterial stiffening with aging. Whether lifestyle interventions or pharmacotherapy can "prevent" or retard unsuccessful aging of the vasculature in younger-middle age individuals who exhibit excessive sub-clinical evidence of unsuccessful aging remains unknown.

You can’t change your age – surprise – but you can change how you age! Remember it is your life and it is your health.