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THE IMPACT OF ARTERIAL STIFFNESS ON COGNITIVE STATUS IN ELDERLY DIABETIC PATIENTS

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Abstract

With age, arteries become more rigid and pulse waves propagate faster. The pathogenic mechanisms that causes vascular stiffness in type 2 diabetes are complex but incompletely understood. An important element in the development of this phenomenon appears to be insulin resistance. One of the first line health problems that persist in the present is the failure to detect cardiovascular diseases in the preclinical stage which is important since more frequent cardiac events (myocardial infarction, sudden death) occur in people without obvious cardiovascular pathology in the medical history. One of the degenerative diseases with the greatest impact on the autonomy is dementia of elderly people. Recent studies have shown the association and even the possible involvement of cardiovascular risk factors and arterial stiffness in the pathogenesis of dementia and cognitive impairment. Although pulse wave velocity in the aorta is related to subclinical coronary atherosclerosis (being an important biomarker of cardiovascular risk in asymptomatic individuals), arterial stiffness is also a predictor of cognitive performance, cognitive decline or dementia.

key words: *arterial stiffness, diabetes, cognitive status.*

Introduction

With age, arteries become more rigid and pulse waves propagate faster [1]. The most obvious clinical consequences of arterial stiffness, as O'Rourke et al. mentioned, are increased pulse pressure (which is caused by an increased systolic pressure and diastolic pressure drop which increases the LV afterload) and the decrease of coronary perfusion [2].

In the elderly patients, the structure of the elastic layer (medium lamina) of the blood vessels becomes disordered due to thinning and drainage of fibers followed by the accumulation of collagen in the arterial wall [2]. The stiffness means the resistance of an elastic body against deformation caused by an applied force. Arterial stiffness translates as stiffness of the arteries. The vascular stiffness occurs prior to atherosclerosis and its appearance can be regarded as a risk factor for atherosclerosis. The

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pathogenic mechanisms that cause vascular stiffness in type 2 diabetes (T2DM) are complex but incompletely understood. An important element in the development of this phenomenon appears to be the insulin resistance. Usually this appears before the onset of diabetes and is accompanied by cardiovascular risk factors specific to metabolic syndrome. Recent studies have shown the fact that vascular stiffness could be a new feature of insulin resistance [3].

Increased arterial stiffness is the consequence of the modifications to the properties of the extracellular matrix (elastin, collagen) and of the function of vascular smooth muscle cell. These structures are especially affected by high blood pressure but also by the normal aging process [4]. Advanced glycation products of proteins have been also associated to the increase of arterial stiffness in diabetic patients [5].

One of the first line health problems that persist in the present is the failure to detect cardiovascular diseases in preclinical stage. This is important since cardiac events (myocardial infarction, sudden death) occur more frequently in people without evident cardiovascular pathology in the medical history [6]. The ability to achieve early diagnosis of vascular injuries includes as prime factor the estimation of the elasticity of the arterial system [7]. Noninvasive methods to determine atherosclerosis are: 1) ankle-brachial index (ABI): easy to measure - detects later stages (peripheral artery disease); 2) IMT (intima-media thickness): expensive, difficult - detects early stages; 3) cardio-CT (artery calcium score and coronary vessels assessment): expensive, difficult - detects later stages; 4) Magnetic Resonance: expensive, difficult - detects later stages; 5) Flow Mediated Vasodilatation (FMD): difficult, expensive - detects early stages; and 6) arterial stiffness measurements with oscillometric methods. The measurement of pulse wave velocity (PWV) is established as the most simple, non-invasive and reproducible method to determine arterial stiffness [8].

Arterial stiffness and cognitive status

One of the degenerative diseases with the greatest impact on the autonomy of humans is dementia in elderly people. Recent studies have shown the association and even the possible involvement of cardiovascular risk factors and arterial stiffness in the pathogenesis of dementia and cognitive impairment. Thus, recent data revealed that increased pulse pressure is associated with increased risk of Alzheimer's dementia [9]. As a result of increased arterial stiffness, cerebral vascularization is exposed to the potentially harmful pressure forces of the pulse pressure augmentation [10].

The incidence of dementia doubles every five years after the age of 65 and one in three person shows this pathology, the prevalence being higher among women (two thirds of patients with dementia are women) [11]. Detection and early diagnosis is important and it is therefore necessary to use methods for the early detection of vascular injury. Subclinical changes can be highlighted by increasing IMT, by increasing peripheral resistance or carotid artery stiffness [12,13].

Recently a meta-analysis on the correlation between arterial stiffness and cognitive decline was conducted. In the most significant longitudinal studies with an average duration of five years, arterial stiffness has been shown to be a predictor for cognitive decline, fact noticed in 5 of the 6 studies [14].

Although aortic pulse wave velocity (PWVao) is related to subclinical coronary atherosclerosis (being an important biomarker of cardiovascular risk in asymptomatic individuals), arterial stiffness is also a predictor

of cognitive performance, cognitive decline or dementia [15]. Thus, in the Baltimore study (which included patients without a history of stroke or dementia) conducted over a period of 11 years, significant associations between PWVao and modification of verbal fluency or learning ability were reported [16], although no correlation between arterial stiffness and prediction of MMSE score (Mini-Mental State Examination) could be established. However, MMSE test is weakly sensitive to small changes in cognitive functioning, especially in young people, or people with significant cognitive impairment [14]. It is desirable that further research in this field applies also other neuropsychological tests for the early detection of cognitive decline in order to validate the hemodynamic indices of central pressure as predictors of cognitive decline [15].

The PARTAGE study investigated 1128 patients that were followed for a period of 1 year and indicated that arterial stiffness causes cerebral suffering expressed by cognitive decline, with cerebral small vessels not being protected by pressure pulsatile flow [17]. In support of this hypothesis come the studies demonstrating the association between arterial stiffness and stroke and the cerebral lacunars state [18].

Methods for arterial stiffness measurement

Many non-invasive methods have been developed to measure arterial stiffness.

One of the indexes used to identify the stiffness is pulse wave propagation velocity (PWV), which measures the pulse propagation velocity between two selected measurement locations, the difference between the detected values increasing with the increasing of the arterial stiffness (Figure 1).

Measurement of pulse wave propagation velocity between the carotid artery and femoral artery (cf-PWV) reflects arterial stiffness along the aorta, the major site of arterial stiffening with aging. This approach is considered to be the gold standard in non-invasive assessment of large artery stiffness [20,21].

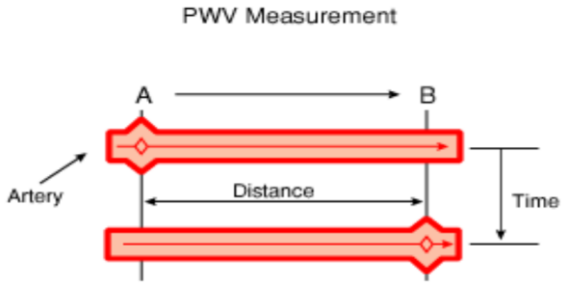

Figure 1. Pulse Wave Velocity Measurement (Adapted after Weber T [19]).

Arteriograph TensioMed ™ offers the possibility of determining these indexes of cardiovascular prognosis by a new method: noninvasive, oscillometric. The method uses Arteriograph (ARG) and is based on the fact that the information signals occurring during brachial artery oscillometric measurement are valid not only for the brachial artery, but also for the whole arterial system, providing information regarding the atherosclerosis. The calculation of the parameters is based on the phenomenon of aortic pulse wave reflection (triggered by ventricular contraction) in the aorto-iliac bifurcation. Determination of arterial stiffness using Arteriograph involves measurement of three parameters: aortic augmentation index (Aix), the speed of the aortic pulse wave propagation (PWVao) and central systolic pressure (SBPao). Thus, a complete characterization of central and peripheral arteries is made.

Another parameter measured by the oscillometric method is the central pressure at the aortic emergence (SBPao). This is different from the peripheral blood pressure due to histological differences between aorta and brachial artery. Central pressure measured non-

invasively has a closer relationship with vascular hypertrophy, accelerated atherosclerosis and cardiovascular events than the pressure measured at the brachial artery. According to Grassi and Borghi (2008), non-invasive measurement of central hemodynamic profile increases the likelihood of a more accurate estimation of the general cardiovascular risk than traditional measurement of blood pressure [22]. This is in conformity with the guidelines of the European Society of Hypertension and European Society of Cardiology 2007 [22]. Measurement of central hemodynamic parameters can also help define the therapeutic plan, with the main target to reduce cardiovascular risk.

Prognostic value of increased arterial stiffness in diabetes was investigated primarily at the level of elastic arteries (aorta and carotid). One prospective study has suggested that the stiffness of the central arteries (and not the muscular ones) is an independent predictor for death in diabetic patients with undergoing hemodialysis [23]. However, peripheral arterial stiffness appears to have significant clinical relevance on peripheral blood pressure, which is an important prognostic factor for patients with diabetes [24].

Speed measurement of pulse wave velocity from the aorta (PWVao) through the oscillometric method proposed by Arteriograph shows a decrease in arterial wall flexibility that occurs in the early stages of atherosclerosis. PWVao was reported to be a predictive factor for cognitive decline in many studies, but the practical utility of this determination will depend on the availability of effective treatment for reducing aortic stiffness and the demonstration of the hypothesis that reducing stiffness after treatment can lead to improved cognitive performance [14].

Conclusion

At this time there is insufficient evidence to implicate arterial stiffness in the etiology of dementia either vascular or non-vascular, but by upgrading the technology for an easily measure of arterial stiffness parameter, the way to new research will be available.

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