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Review paper

Assessment of aortic stiffness in computed tomography – methodology of radiological examination from 2000 to 2020

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Abstract

Introduction: Vascular elasticity may be a predictive factor of various diseases. Although stiffening is thought to be a natural consequence of ageing, it can be accelerated by a number of pathological conditions such as hypertension, diabetes, or renal diseases. Aim of the study was to discuss the methodology used to assess aortic stiffness, with particular emphasis on radiological examination.

Material and methods: The PubMed and Google Scholar databases were screened from inception to the year 2000 by 2 independent analysts initially working separately and then comparing their results.

Results: Assessment of stiffness can be divided into methods not requiring computed tomography scan, such as tonometry of carotid femoral pulse wave velocity, bioelectrical impedance analysis, and cardio ankle vascular index, and methods requiring it, such as multidetector row computed tomography – ECG gated, in which indexes such as aortic distensibility, aortic stiffness, and aortic compliance can be obtained with simultaneous calcification evaluation based on the Agatston score.

Discussion: Aortic stiffness was corelated with left ventricular afterload, prehypertension, coronary artery plaques, prediction of coronary artery diseases, bone demineralization, chronic obstructive pulmonary diseases, and diabetes mellitus.

Conclusions: Being a factor of various severe diseases, aortic stiffness may play an important role in the early detection of patients requiring additional medical care.

Key words: aorta, tomography, pulse.

Introduction

General information on elasticity

Arterial elasticity is a very important functional property of vessels. More recently, it has also been used as a predictive factor in the prediction of cardiovascular diseases and their complications, and the assessment of pharmacological treatment [1-3]. Asterial stiffness increases cardiac afterload and contributes to left ventricular hypertrophy, and it is an independent predictor of coronary artery disease [4]. It has also been associated with increased epicardial adipose tissue [5]. The artery elasticity index aortic distensibility (AD) is particularly useful in assessing level of atherosclerosis [1]. Because elasticity is a natural property of the arteries, its decrease is a manifestation of abnormal function. It should be noted, however, that general stiffening of aorta is thought to be a natural consequence of ageing [2]. This physiological process can be accelerated by several pathological conditions, such as hypertension, diabetes, and renal disease [6].

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Authors' contribution:

A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

General information about the structure of the aorta

All diseases of the aorta are related to changes in the microstructure of blood vessel walls, in the content and architecture of the connective fibres: elastin and collagen, which give the aorta elasticity and strength, respectively [2]. The consequences of aging are numerous changes in the structure of blood vessel walls: thickening, increases in collagen, degeneration and fragmentation of elastin, damage of endothelium, and progressive dilation of the vessels [6]. All this causes a decrease in the elasticity of the arteries, which is a symptom of abnormal functioning of vessels [1]. The structure of the aorta, including elasticity and dimensions, can be assessed by ultrasound, X-ray, computed tomography, and cardiac magnetic resonance [7].

Information about biomechanics

The wall of aorta is a dynamic composite structure consisting of matrix macromolecules and vascular cells. Each component plays a role in determining the structure of the tissue, and therefore a disruption of each of these components can change the mechanical behaviour of the vessel wall. The relative amounts and organization of these components are believed to have the greatest impact on the normal function of the aortic wall and any pathologies that may occur [8].

Physiologically the pressure wave is reflected from the periphery and reaches the heart on diastole. As the aorta stiffens, the speed of the pressure wave increases, and the reflected pressure wave eventually returns to the heart earlier, i.e. during the end of the systole instead of diastole, causing an increase of the heart afterload and systolic blood pressure. Isolated systolic hypertension is a common phenomenon in people over 80 years old, and it occurs as a manifestation of aortic stiffness that causes the pulse pressure to widen [6].

Why it is important to assess aortic elasticity

Vascular calcification is a factor that is also associated with arterial stiffness, which can be used as a predictor of cardiovascular diseases. The mechanisms of arterial calcification are complex, and one of the identified significant risk factors for developing calcification is chronic kidney disease, which is associated with the process of differentiation of smooth muscle cells into osteoblast-like cells in this disease. Calcification occurs in the intimal and medial layers of the walls of arteries and causes decreased vascular elasticity [9]. Aortic stiffness is predictor of cardiovascular mortality [3].

Flexibility versus aneurysms

Ascending aorta aneurysm is a serious health problem, and its complications are one of the leading causes of death (in the top 20 leading causes of mortality in the United States) [10]. It often grows slowly and is often asymptomatic, which makes it very difficult to detect [11].

Parameters identified as useful for assessing aortic flexibility include regional distensibility, pulse-wave velocity, and the maximum rate of systolic distension. The latter is relatively new and is currently considered the most adequate parameter for assessing changes in the properties of the aortic wall [10].

Aortic stiffness is a risk factor for stroke

One of the main risk factors for cardiovascular diseases is hypertension, while the development of arterial hypertension is influenced by an increase in aortic stiffness. The increased aortic stiffness results in increase of systolic blood pressure and reduction of diastolic blood pressure, and it leads to arterial hyperpulsatility and increased pulse pressure [12]. In recent years, there has been growing interest in assessing arterial stiffness as a means of assessing total cardiovascular risk and for a non-invasive evaluation of it, the aortic pulse wave velocity is used [13]. Previous studies have shown that PWV is an independent marker of cardiovascular risk [12,13].

Research conducted in recent years shows a strong link between increased pulse wave velocity and stroke [12]. The connection of these 2 phenomena can be explained by a number of mechanisms. Firstly, increased aortic stiffness causes an increase of pulse pressure, which leads to remodelling of arteries, increased thickness of the walls of the arteries, the development of atherosclerosis, and increased risk of plaque rupture. Secondly, the increase in arterial stiffness is generally associated with age-related systemic arterial damage and other cardiovascular risk factors. Thirdly, arterial stiffness and high pulse pressure promote the development of heart failure and coronary artery disease, and these are also risk factors for stroke. Therefore, based on the studies conducted so far, pulse wave velocity can be considered an important haemodynamic parameter in determining the risk of stroke because it is an independent risk factor [12].

Purpose

The purpose of the article was to discuss the methodology of aortic stiffness assessment, with emphasis on radiological examination. Although methods involving magnetic resonance can measure vessel function accurately, its long imaging time and low spatial resolution limits the evaluation during cardiac cycle [14], so in this review we focused on computed tomography, and we mention conventional ways to measure aortic stiffness that do not require a CT scan.

Material and methods

To prepare this manuscript, the PubMed and Google Scholar databases were screened from the inception until

2000 with use of the following keywords: aortic, stiffness, evaluation, computed, tomography, assessment, methodology. To find the most relevant paper, 2 independent analysts (WH and AŻ) initially worked separately by screening the mentioned databases, then each of the analysts prepared their list of chosen abstracts and presented it to the other, so that each abstract was read by both analysts. Then the full text was acquired and read, and consequently, by discussion, 43 papers were found to be the most relevant and were included in this review.

Results

Methods – a general description of the most common ways to assess aortic stiffness and flexibility

Classical methods to measure flexibility that do not require a CT scan

Aortic stiffness can be measured by noninvasive techniques, one of which is **tonometry of the carotid-femoral pulse wave velocity**. In this technique the pulse wave speed, which relates to aortic stiffness, is estimated by measuring the pulse on the carotid artery and femoral artery. Pulse wave velocity can be measured by pressure transducer, doppler flow, and echo tracking. The pathway is commonly measured by tape measure or calliper. However, because the pulse wave moves in 2 opposite directions (to the carotid artery and in the opposite way to the femoral artery) direct measure leads to overestimation and appropriate corrections are needed, most commonly the distance is multiplied by a factor of 0.8:

$$PWW = 0.8\, L/\Delta T,$$

where *L* is distance and *ΔT* transit time. This issue can be limited by using MRI to measure PWW [3,15].

The other method is **bioelectrical impedance (BI) analysis**, the basis of which is the measurement of changes in the BI signal generated by the variation of blood volume conductivity in the artery, then an impedance wave transit time is determined between the chest and the thigh. BI is measured by an electrode impedance device [3].

Due to blood pressure dependency the pulse wave velocity method was further developed to the **cardio-ankle vascular index** (CAVI):

$$CAVI = a \left\{ \frac{2\rho}{\Delta P} \times \ln\left(\frac{Ps}{Pd}\right) PWW^2 \right\} + b$$

where *Ps* is systolic blood pressure, *Pd* is diastolic blood pressure, *PWW* is pulse wave velocity, $\Delta P = Ps - Pd$ ρ is blood density, and *a* and *b* are constants (required due to scale conversion that enables convenient comparison of CAVI with PWV – Hasagawa's method). CAVI reflects the stiffness of the aorta tibial and femoral artery as a whole [16]. High CAVI values are associated with increased wall thickness of the descending aorta, and CAVI has been found to be useful for aortic atherosclerosis evaluation [17] and to reflect coronary atherosclerosis as a useful screening tool [18], and it was found to corelate with stiffness measured by ECG-gated multidetector row computed tomography [19].

Computed tomography methods – how mathematical equations let us see more

Measuring the stiffness can be based on the maximum change of aorta cross-sectional diameter *ΔDi* and the corresponding maximum change in blood pressure *ΔPi* during a particular cardiac cycle at a particular section *i* of the aorta. One of the stiffness indexes of the aorta is the Young modulus E, which is defined by the ratio between the stress increment *Dσ* and the strain increment *Δε*. This can be expressed by the formula:

$$E = \frac{\Delta\sigma}{\Delta\varepsilon} = \left(\frac{P_{max} - P_{min}}{2h\,(D_{max} - D_{min})/D_{min}^{\;2}} \right)$$

where *P* stand for blood pressure, *h* for thickness of the aorta wall, and *D* for the cross-sectional diameter. As well as classical deterministic methods of calculating the stiffness indexes, there are also more complex solutions concerning a stochastic approach to the problem [20].

The image quality of the tomography can be improved by using electrocardiographic assistance to reduce cardiac motion artifacts during the imaging of the thoracic aorta. This is important because aortic movement potentially contributes to misinterpretation of the image of aortic dissection [21].

To measure aortic stiffness, **ECG-gated multidetector-row computed tomography** can be used. One study of this method used porcine aortic specimens and cardiac CT coronary angiography scans of 2 patients. In this method the authors measured elasticity using the following equation:

$$D = \frac{\Delta A}{A_0 \times \Delta p}$$

The result of this equation is *D*, which stand for distensibility and quantifies the elasticity of the aorta. Than *ΔA* is the difference (a relative change) between the maximum and minimum cross-sectional area *A* that occurs during the cardiac cycle. This is then divided by the corresponding change in the blood pressure *Δp* multiplied by the minimum vessel area A_0 [22]. This was named the **aortic distensibility** index [23,24].

One study described the use of **computed tomography angiography** (CTA) to measure aorta elastic properties on an aortic model made from polydimethylsiloxane (PDMS). The model was particularly useful because once removed from its location during autopsy the aorta changes its properties, which can contribute to measuring errors. In this study a 64-slice ECG-gated multidetector CT was used to gather the row data, then a discrete wavelet transformation technique was applied with the use of MATLAB software to calculate variations of the cross-sectional area of aorta and changes in wall thickness over time. Then these variations were used to compute the aorta elasticity. The strain calculation was based on the difference between maximal and minimal cross-sectional area between diastole and systole, whereas the stress affecting the vessel was calculated on the basis of pressure, inner radius, and wall thickness of the model [25].

The authors of another study used a different equation to measure the **aortic stiffness index**:

$$AoSI = \ln\left(\frac{Ps}{Pd}\right)/\left(\frac{Ds - Dd}{Dd}\right)$$

where *AoSI* is the stiffness index, *Ps* and *Pd* are systolic and diastolic pressure, and *Ds* and *Dd* are the maximum and minimum average diameter of the aorta. In this study the authors used **retrospective ECG-gated dual-source CT (DSCT)**. The elasticity was defined as "the change in arteria blood volume within an aortic segment chosen by a given change in arterial blood pressure". The authors state that using the DSCT method allows temporal resolution to be increased by up to 83 ms, which leads to greater precision. In their discussion the authors raised the important issue that different age groups of patients present different elasticity of aorta, which should be considered when it comes to choosing suitable candidates for endovascular procedures. The authors claim that age is an important factor for aortic elasticity. It is important to emphasize that during the study an age-dependent decrease of elasticity was reported in the group of patients without known vascular diseases [14]. It is also worth mentioning that other results indicate that using prospective ECG-triggering data acquisition (gating) instead of retrospective analysis allows the radiation dose to be reduced with only a slight increase in scanning time. However, it is also important to note that the best result can be achieved with lower patient's heart rate (particularly lower than 80 beats per minute) [26].

Apart from aortic distensibility and stiffness index, another index can be used to assess the aorta, i.e. **aortic compliance (AC):**

$$AC = \left(\frac{Ss - Sd}{Ps - Pd}\right)$$

where *Ss* and *Sd* stand for maximum and minimum cross-sectional area, and *Ps* and *Pd* are systolic and diastolic blood pressure [23].

Aorta elasticity – its connection to calcification and metabolic risk

Arterial stiffening was associated with arterial calcification [27-30], which can be measured by the **Agatston score (AS),** and because it was initially designed to assess coronary artery calcification a certain technique has to be used to measure aorta calcification. One study introduced the technique of "simultaneous quantification and 3-D visualization of aortic calcification using the volume rendering method". In this research calcification was measured by use of 3 methods: slice-by-slice pixel based, voxel based, and volume rendering voxel based. In the pixel-based method a special semi-automatic analysis software identifies areas with at least 130 Hounsfield Units (HU). Then manually each of the arterial calcification lesion is selected, and then each lesion score (pixel area in mm^2 and lesion density scored as 1 when 130-199 HU, 2 when 200-299 HU, 3 when 300-399 HU, and 4 when more then 400 HU) is calculated. Then all of them are summed and the AS is obtained. Similarly, in the voxel-based method the difference is calculated by summing selected voxels (ml). In the volume-rendering method the calculation was based on a reconstructed image of the whole trunk and then extraction of the aortic calcifications [31]. Aortic calcification was associated with aging, hypertension, diabetes mellitus, smoking, and renal impairment [32]. It was observed that aortic calcification was an independent prognostic factor for progression of arterial stiffness, and it was suggested that anti-calcification therapies have the potential to ameliorate arterial stiffness [28]. However, it should also be pointed out that one multivariate analysis found the association between brachial-ankle pulse wave velocity for aortic calcification negative, but the authors admit the possibility that their data did not reach statistical significance owing to the small number of studied groups [32]. Aortic stiffness was also found to be associated with aortic inflammation in a hybrid PET/CT imaging study [33], and in patients with diabetes mellitus type 2 subclinical arterial inflammation was a determinant of arterial stiffness in PET/CT [34.]

Discussion

Clinical significance of arterial elasticity assessment

Due to the change in a stiffened aorta's backward waves of reflected blood, the early return overlaps with the systolic ejection period, which increases the peak left ventricle pressure, consequently increasing the LV afterload and systole length, which in turn leads to a decrease in coronary perfusion. In this study CAVI was also significantly higher in patients with vascular calcification [35]. Reduced ascending aortic elasticity was found in prehypertension groups of patients, and changes in elasticity preceded the appearance of morphological ones with aortic distensibility (assessed in CT) as the most sensitive index (in particular, changes in aortic distensibility were observed before any changes to the aorta diameter – elasticity damage proceeded morphology damage). It was also found to be an important factor causing hypertension, which subsequently leads to a further decrease in elasticity. The study emphasises the significance of the early detection value of elasticity assessment, particularly in prehypertensive patients [23]. Furthermore, aortic distensibility correlated with the presence of coronary artery plaque in longitudinal assessment of changes in coronary artery atherosclerosis, and the authors claim that routine assessment of aortic stiffness during gated cardiac CT may improve risk stratification strategies and monitoring of CVD progression [24]. Measurement of aortic stiffness index was found to be an applicable and safe method to predict subclinical atherosclerosis guiding the referral of patients to individual preventive strategies [36]. Moreover, aortic stiffness was also found to be a factor improving the prediction of both the diagnosis and severity of coronary artery diseases, and the pulse wave velocity index was suggested to be clinically useful in decreasing the number of unnecessary angiographies [37]. Increased aortic stiffness was also correlated with calcified descending thoracic aortic atherosclerosis [38]. Vascular stiffness was also associated with epicardial and pericardial adipose tissue [39]. In addition, increased aortic stiffness was corelated with left ventricular volume index, which is a marker of early stages of cardiac remodelling in patients with suspected coronary artery disease, and its early detection may play an important role in the prevention of CV disease [40]. Furthermore, arterial stiffness was also associated with demineralization of cortical bone in women [41]. Also, aortic stiffness was also found to participate in the mechanism of chronic obstructive pulmonary disease (COPD) vascular risk, and patients with COPD presented with increased aortic stiffness [42]. Additionally, it was found that diabetes mellitus type 1 has a slight effect on descending aorta elasticity [43]. Thus, as can be seen, the assessment of arterial stiffness has wide clinical application and can be used as an independent predictor of cardiovascular events.

Conclusions

Aortic stiffness may play an important role in the selection of patients in need of additional medical care. The studies conducted so far have provided abundant evidence suggesting that arterial stiffness is an independent cardiovascular risk factor and, at the same time, probably the best prognostic indicator for predicting the occurrence of cardiovascular events. In particular, due to its predictive possibility aortic elasticity may help in indicating patients in early stages of diseases in which early intervention could decrease further progression. Radiological methods of stiffness assessment appear to be more precise due to a lack of the overestimation encountered in classical pulse wave velocity measuring methods. Different indexes can be used to define aortic elasticity, from which the aortic stiffness index is commonly corelated with various diseases.

Conflict of interests

The authors declare no conflict of interest.

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