Original Articles

APPLANATION TONOMETRY FOR ASSESSMENT OF LEFT VENTRICULAR SYSTOLIC LOAD

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Summary

Vascular-ventricular coupling is a major determinant of left ventricular load. The aim of our study was to assess non-invasively left ventricular load and its dependency on central hemodynamics. Sixty-five healthy and gender-matched individuals were divided in two groups according to their age: 20y/o and 50y/o. Applanation tonometry was performed using the Sphygmocor device. Central pressures and pulse wave analysis indices were computed. Central systolic (120±3 vs. 98±2 mm Hg) and pulse pressures (43±3 vs. 29±1 mm Hg) as well as the augmentation index (AIx75) (23±3 vs. 6±2%) were significantly higher in the 50y/o group ($p<0.01$). These parameters are relevant markers of arterial stiffness and evidenced the development of central arterial morphological and functional alterations in the older subjects. The time-tension index (TTI) computed from the systolic pressure area was significantly higher in the 50y/o subjects as compared to the 20y/o group (2378±66 vs. 1954±73 mmHg×s, $p<0.01$). Moreover, we have shown the presence of significant correlation between TTI and AIx75 ($p<0.01$) in both age groups. This finding confirmed the contribution of arterial stiffness for the impaired vascular-ventricular coupling. In conclusion, applanation tonometry might be utilized for non-invasive evaluation of the left ventricular load, which is an important parameter of cardiovascular risk.
Keywords: arterial stiffness, time-tension index, pulse wave analysis, vascular-ventricular coupling, applanation tonometry

Introduction

Cardiovascular diseases (CVD) still remain the leading cause of morbidity and mortality worldwide [1]. The awareness of this fact necessitates the implementation of better and novel methods for early screening and prevention of CVD. So far studies have been mostly directed towards revealing the risk factors for development of coronary artery disease and endothelial dysfunction leading to cardiac failure. Less attention has been paid to the role of impaired vascular-ventricular coupling in the generation of disequilibrium between oxygen supply and oxygen demands of the cardiac muscle. The compromised interaction between left ventricular and large cushioning vascular function

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might produce a large number of hemodynamic consequences that would interfere with the energetic state of the left ventricle [2].

Ventricular systolic stress as well as its duration is the major determinant of myocardial oxygen demands. The systolic heart load might be estimated with the help of the tension-time index (TTI), a parameter firstly introduced in the seminal paper of Sarnoff [3, 4]. Sarnoff et al. defined TTI per minute (measured in mm Hgxs) as the area under the systolic portion of the aortic pressure curve (systolic pressure time integral, SPTI) times the heart rate. They showed in a smart way that oxygen consumption in the heart was a function of TTI for any filling pressure. Tension time index depends mostly on the ventricular wall stress T, as specified by LaPlace's law $T = \frac{P \times r}{2h}$, where P is left ventricular pressure, r – radius of the left ventricular cross section, h – left ventricular wall thickness.

Left ventricular peak systolic pressure is determined by several parameters, vascular function being an important determinative factor as well. Vessels in the systemic circulation exert two types of load to the left ventricle: vascular resistance, generated predominately by the small muscular arteries, and the arterioles and pulsatile load that depends mostly on the aortic stiffness [5].

Arterial stiffness was recently recognized to be a relevant cardiovascular risk factor [6, 7]. It is an irreversible characteristic of aging and it is presumed to be a composite measure of the effect of various harmful influences on the vascular wall [8].

A significant progress in understanding the impact of arterial stiffness on central hemodynamics was achieved with the introduction of the non-invasive method applanation tonometry. This method is based on the detection of radial arterial pressure using a highly sensitive tonometer. The sophisticated Sphygmocor software computes the aortic pulse waveform from radial pressure data using a validated generalized transfer function [9, 10]. The aortic pressure waveform (Figure 1) reflects the rapid oscillations of the aortic walls resulting from the stroke volume ejection into the finite compartment of the proximal aorta filled with incompressible fluid.

The amplitude of the first peak, P1 or incident wave, is mainly determined by the ventricular contractility and the compliance of the ascending aorta. The amplitude of the second peak, P2, depends on the timing of the reflected pulse wave return, i.e. its propagation velocity [11]. The stiffening of the arterial walls causes earlier pulse wave return due to the augmented pulse wave velocity combined with a decreased compliance of the large arteries. These changes underlie the elevation of isolated systolic pressure and the appearance of a second, higher than P1 pressure peak P2 late in systole (Figure 1). On the contrary, in young healthy persons aortic compliance is preserved, pulse wave velocity is slower and the maximum of the reflected wave occurs in diastole. Consequently, the peak systolic pressure is minor for a given stroke volume and P2 is lower than P1 [12].

Important markers of arterial stiffness are the augmentation pressure (AP) and the augmentation index (AIx). AP is defined as the difference between P2 and P1 (positive in older adults), AIx is calculated as $AIx = \frac{P2-P1}{PP} \times 100\%$ (Figure 1). These two indices are directly dependent on the characteristics of arterial wall. In addition, both AP and AIx depend on the heart rate and on the height of the individual [13]. This is the reason why the derived indices AP75 and AIx75 are corrected for standard resting heart rate of 75 beats per minute.

The relevance of the above parameters was confirmed by numerous studies [14, 15]. In a large systematic review, the data from 5648 subjects with mean follow up of 45 months were analyzed. Central pressures and indices were shown to possess a significant predictive value of cardiovascular events and all-cause mortality [16]. The AIx was evidenced to be of particular informative value in subjects aged less than 60 years [17]. Less information exists on the association between the tension-time index (TTI) and these relevant indices of arterial stiffness.

An additional parameter provided by applanation tonometry and pulse wave analysis is the subendocardial viability ratio (SEVR), which is assumed to estimate myocardial oxygen supply non-invasively. This evaluation is based on the index introduced in 1971 by Buckberg [18]. The Buckberg index was calculated from invasive cardiac catheterization data as the ratio of the area enclosed between the diastolic aortic

and left ventricular pressure curves (presumed to characterize left ventricular coronary oxygen supply) to the systolic left ventricular pressure area (as a measure of ventricular oxygen demands).

Applanation tonometry offered the surrogate index SEVR, which was computed as the ratio of the diastolic pressure time integral (DPTI) to the SPTI [19, 20]. The DPTI (in mm Hgxs) incorporates coronary driving pressure and diastole duration thus representing subendocardial blood supply. The SPTI (in mm Hgxs) reflects ventricular systolic load, hence oxygen demands. A cutoff value of 100% is recommended as a measure of a potential mismatch between the above parameters and a sign of subendocardial hypoperfusion.

The aim of our study was to assess and compare non-invasively the systolic left ventricular load and its dependency on central arterial hemodynamics in individuals of two age groups.

Materials and Methods

Sixty-five clinically healthy and gender-matched individuals were divided in two groups according to their age: 20y/o and 50y/o. The group 20 y/o consisted of 32 individuals (14 females and 18 males) with mean age 21±0.7 years. The group 50 y/o was composed of 33 individuals (21 females and 12 males) with mean age 53±2 years. All examined subjects signed their informed consent to participate in the study, which was conducted according to the principles of the declaration of Helsinki [21]. The experimental protocol was approved by the Ethics Committee at our University.

Applanation tonometry was performed using the Sphygmocor device (AtCor Medical, Sidney, Australia) after resting in supine position for 10 minutes. The right radial pulse waveform was adjusted to the brachial arterial pressure estimated using a semi-automated Omron sphygmomanometer. Radial arterial pressure was recorded by means of the high-fidelity handheld probe (Millar Instruments, Houston, TX, USA). Only high quality measurements according to the standards of AtCor Company were utilized. Central aortic pressures and the derivative indices were computed with the help of the Sphygmocor software based on the generalized transfer function. In addition to the central (aortic) systolic and pulse pressure, the Sphygmocor software estimated the AP and AIx as well as their standardized for resting heart rate of 75 beats per minute values. The TTI and SEVR were computed and analyzed as well. We applied regression analysis looking for correlation between TTI and AIx75 in order to find the impact of arterial stiffness on the left ventricular load as estimated by TTI.

Statistical analysis was performed using the Data Analysis ToolPak of the Excel software and Vassar Statistics Software. The Wilcoxon-Mann-Whitney test, ANOVA and regression analysis were applied. The level of significance for p was assumed to be at least 0.05.

Results

The general characteristics and the applanation tonometry data of the two age groups of are presented on Table 1.

Table 1. General characteristics and applanation tonometry parameters of the two age groups Data are presented as means ± SEM. ** P<0.01, * P<0.05 (Mann Whitney test).

Groups	20 y/o (n=32)	50 y/o (n=33)
Age (years)	21±0.7	53±2
Heart rate (bpm)	68±2	70±1
Radial SAP (mm Hg)	116.9±2	131.4±3**
Radial PAP (mm Hg)	49.1±2	55±3
Aortic SAP (mm Hg)	98±2	120±3**
Aortic PAP (mm Hg)	29±1	43±3*
AIx75 (%)	-6±2	23±3**
TTI (mmHg x s)	1954±73	2378±66**
SEVR (%)	161.4 ± 6.8	144.6 ± 4.1*

Resting heart rate in supine position did not differ between the studied individuals. Radial systolic pressures were in the normal range for both age groups. Yet, radial systolic pressure was significantly higher in the 50 y/o group as compared to the 20 y/o individuals ($p<0.01$). On the other hand radial pulse pressure did not differ considerably between groups (Table 1).

Aortic systolic and pulse pressures were significantly higher in the older individuals ($p<0.01$, $p<0.05$ respectively). The indexes AIx75 and TTI in the 50 y/o group were significantly higher as compared to the younger individuals ($p<0.01$) while SEVR was lower ($p<0.05$) – Table 1, Figure 1.

Regression analysis showed statistically significant positive correlation between TTI and the AIx75 ($R=0.60$, $p< 0.001$) – Figure 2.

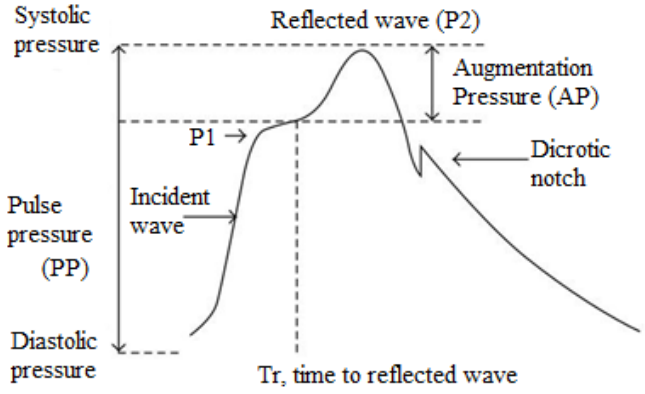

Figure 1. Aortic pressure waveform.

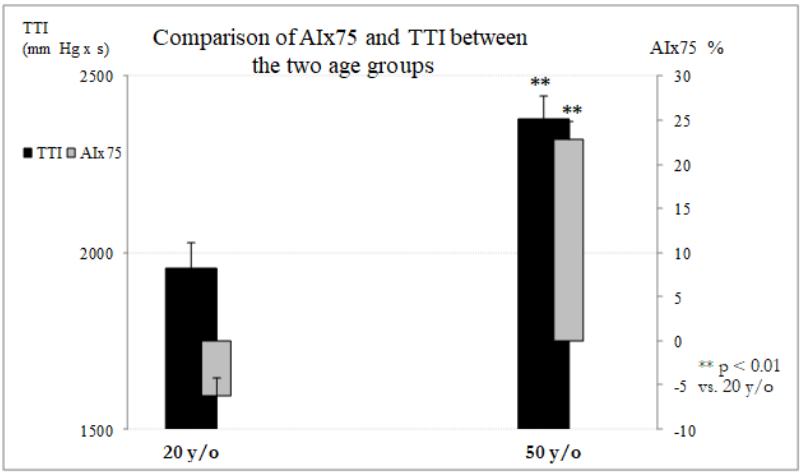

Figure 2. Augmentation indices (Aix75) and tension-time indices (TTI) in the two age groups
** $p<0.01$ vs. 20 y/o

Discussion

As already described applanation tonometry was widely recognized as a precise and informative non-invasive method for estimation of central arterial condition and putative cardiovascular risk. Our study was planned to explore and reveal certain details of the natural evolution of arterial stiffening with aging.

Our 50 y/o subjects were normotensive according to the European guidelines [22]. However, if we focus our attention on the central pressures and indices provided by the Sphygmocor software, we might notice an obvious difference between the two age groups. Both aortic systolic and pulse pressures were significantly higher in the older subjects. We interpreted this finding as an evidence of arterial 'hardening' and of

the consequent decreased arterial distensibility. Arterial stiffening is the result of alterations in the vascular media properties; it generates reduced arterial compliance. Arterial stiffening was shown to decrease central arterial buffering ability to pulsatile cardiac performance [6, 11]. This concept was confirmed by our aortic pulse pressure data. Although radial pulse pressures did not differ markedly between groups, central pulse pressure was significantly higher in the 50 y/o individuals as compared to the 20 y/o group (Table 1). The arterial system performs not only conduit but dampening function as well. Even without narrowing of the vascular diameter arterial stiffness decreases the capacity of large arteries to accommodate the stroke volume ejected by the left ventricle [11]. The reduced arterial distensibility or compliance causes a huge rise in aortic systolic pressure. The pulse pressure value depends on the timing of the superimposed reflected pulse wave from the periphery as well. Arterial stiffness not only reduces arterial compliance, it also accelerates pulse wave velocity. Therefore, the reflected pulse wave returns earlier in systole and further increases pulse pressure value in the stiff arteries [13, 14]. Hence, the evaluation of central pulse pressure is essential since it was shown that central pulse pressure had a better predictive value concerning cardiovascular risk than peripheral pulse pressure [23].

Correspondingly, the AIx75 was significantly higher in our older group as compared to the younger individuals due to the increased reflected pulse wave amplitude and its earlier return in systole (Figure 1) [14]. The larger AIx75 was an additional evidence for the development of arterial stiffness as it was proposed to be a relevant marker by the Expert consensus document [24].We have specially selected our older individuals to be less than 60 years of age (mean age 53±2) since it was evidenced that AIx changed only slightly above this age and was no more of informative value. It was shown that in the elderly the central arterial stiffness is increased to such an extent that it surpasses the normally larger peripheral arterial stiffness (the stiffness of the muscular or resistive vessels). The resulting loss of stiffness gradient between peripheral and central elastic arteries reduces the reflection wave amplitude and permits the transmission of bigger forward pressure wave with damaging impact on the microcirculation of the target organs (heart, brain, kidneys) [25].

An important finding of our study was the evidenced positive and statistically significant correlation between AIx75 as marker of arterial stiffness and TTI as index of ventricular load. This correlation positively showed that vascular function was an important modifier of ventricular load since the more manifested arterial stiffness was the larger got TTI. The augmented afterload produces unfavourable effects in the myocardium. It is well-known that chronically elevated ventricular load promotes development of ventricular remodelling and augmentation of oxygen demands [23].

An additional evidence of the negative effect of arterial stiffening and augmented ventricular load, i.e. of the consequent alterations in central hemodynamics, was the significantly lower SEVR in the older individuals as compared to the young group. We find of interest these data as our older subjects were apparently healthy and the reduction of SEVR could only be attributed to the alterations caused by the arterial stiffening. In normal hemodynamic conditions the reflected pulse wave returns back in diastole and thus maintains diastolic perfusion pressure in the coronary circulation [25]. The earlier return of the reflected wave produces larger systolic load and reduced diastolic aortic pressure with the subsequent imbalance between myocardial oxygen delivery and demands.

In conclusion, we believe to have shown in a definite manner that in our clinically healthy individuals aging produced essential alterations of the central arterial vessels with a negative impact on central hemodynamics, ventricular-vascular coupling and on myocardial energetics.

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