Evaluation of Diastolic Heart Function Using Echocardiography and Pulse Wave Analysis in Patients After Anthracycline Therapy

Magdaléna Šudáková[1], Ksenia Budinskaya[1], Zuzana Nováková[1]

[1]Department of Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic

Abstract

Diastolic dysfunction plays a crucial role in heart failure. In routine clinical practice, echocardiography is the standard for cardiac examination. The applanation tonometry is the golden standard for measuring pulse wave velocity, but thanks to pulse wave analysis it is possible to determine parameters of heart function as well. The aim of this study was to determine the correlation between the parameters of heart function measured by echocardiography and obtained by applanation tonometry.

92 pediatric cancer survivors were measured with echocardiography and applanation tonometry with estimation of the diastolic heart function parameters. All analyzed parameters were in physiological range. Correlation between echocardiography parameters and applanation tonometry parameters shows us opportunity to use applanation tonometry parameters for evaluation diastolic heart function.

1. Introduction

Diastolic dysfunction plays a crucial role in heart failure, regardless of its cause. It affects symptoms, treatment, and prognosis (1). In routine clinical practice, echocardiography, which assesses the structure and function of the heart, is the standard for cardiac examination. Pulse Doppler analysis parameters are used to evaluate diastolic function. These include the mitral peak blood flow during early diastole (E wave) and during atrial contraction (A wave). Subsequently, the E/A ratio is calculated and physiologically the A-wave should not be higher than the E-wave. However, the E/A ratio may be "pseudonormal", therefore the isovolumic relaxation time (IRT) and the deceleration time of passive filling during early diastole (DT), which indicates the deceleration of the mitral blood flow velocity during early diastole, are also evaluated. When assessing individual parameters, it is necessary to consider whether the patient's ejection fraction is maintained or reduced.

The applanation tonometry is the golden standard for measuring pulse wave velocity and assessing arterial stiffness. Physiologically, the reflected pulse wave travels back to the heart during diastole, increasing the perfusion pressure of the coronary arteries. In the case of increased arterial stiffness, the reflected pulse wave reaches the heart at the end of the systole leading to an increase of the pressure against which the heart works, i.e. afterload. Thanks to the analysis of the central pulse wave of the aorta (PWA), it is possible to determine whether there is such an increase in pressure at the end of the systole. The parameters which are used for this are augmentation pressure and augmentation index. They indicate the stiffness of the arteries as well as the condition of the cardiovascular system as a whole. However, this non-invasive examination can also provide us with other parameters that are not yet commonly used, even though they provide additional valuable information about the function of the heart. Such parameters are the area under the pressure-time curve during systole (TTI) and during diastole (DTI). By calculating their ratio, we get the Subendocardial Viability Index (SVI), also called the Buckberg Index, which gives us the pressure and time of oxygen supply in relation to the pressure and time of oxygen consumption by the heart.

The aim of this study was to determine the correlation between the parameters of diastolic heart function measured by echocardiography and obtained by applanation tonometry.

2. Methods

92 respondents (41 women and 51 men) aged 11-36 years were enrolled in the study. All of them have been previously treated for hemato-oncological disease (acute lymphoblastic leukemia, Hodgkin's or non-Hodgkin's lymphoma) with anthracycline antibiotics with a cumulative dose of doxorubicin or daunorubicin 220 (180-240) mg/m^2, cyclophosphamide 3.000 (2.800 / 3.300) mg/m^2 or vincristine 12 (12-15) mg/m^2). The time since the end of treatment in patients was 6-30 years at the time of the study. We chose this group of patients because of presumed subclinical cardiac dysfunction due to the late cardiotoxic consequences of anthracycline therapy (2).

Pulse wave measurements were performed by

applanation tonometry with a SphygmoCor device (Sphygmocor; AtCor Medical, Australia). Peripheral pulse waves were measured from a. radialis on a dominant hand with the palm facing up in a sitting patient. At least 21 pulses were recorded, of which we used the 10 highest quality ones. The measurements were repeated three times, each measurement being calibrated by oscillometric measurement of blood pressure (Omron HEM-907-E, Japan). These peripheral pressure waves were transformed into central aortic pressure waves using a validated generalized transfer function of the SphygmoCor Px system (3). From the analysis of the peripheral pulse wave we obtained the values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) and from the analysis of the central pulse wave we obtained Tension-Time Index (TTI), Diastolic Time Index (DTI), (Fig. 1). The Subendocardial Viability Ratio (SVI) is the ratio of DTI and TTI in percentage.

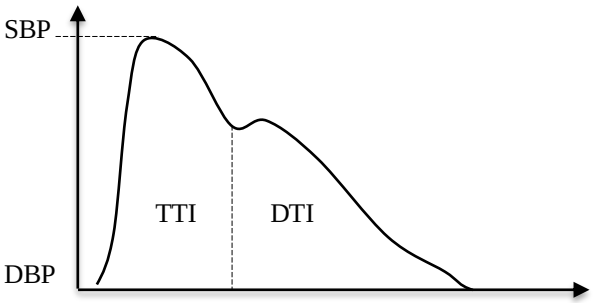

Figure 1: Parameters of central pulse wave analysis: SBP – systolic blood pressure, DBP - diastolic blood pressure, DTI - diastolic time index, TTI - tension-time index.

Echocardiographic measurement (Nemio XG, TOSHIBA, Japan) was performed on persons in lying position in 4 – chamber apical projection. We used 2D imaging and Pulsed Doppler analysis of transmitral filling of the left ventricle (4).

Table 1. ECHO parameters of diastolic function.

E [m/s]	passive filling of the left ventricle in early diastole
A [m/s]	active filling of the left ventricle in atrial systole
E/A	ratio between E and A
IRT [ms]	isovolumic relaxation time
DT [ms]	deceleration time of passive filling during early diastole

For statistical analysis was used program Statistica 13.5 (StatSoft). From the methods of descriptive statistics, we used the mean and standard deviation. Spearman correlation coefficients were used to detect a correlation between ECHO parameters and parameters that were obtained with applanation tonometry.

3. Results

Tables 2 and 3 show the obtained parameters of diastolic heart function. All analyzed values were in the physiological range. The IRT value is at the lower border of the physiological range.

Table 2. Parameters of diastolic heart function obtained using PWA.

Parameters	Average value	Standard deviation
SBP [mmHg]	112	± 12.12
DBP [mmHg]	66	±8.77
TTI	1842	±299.56
DTI	2974	±370.20
SVI [%]	165	±28.71

Table 3. Parameters of diastolic heart function measured by echocardiography.

Parameters	Average value	Standard deviation
E [m/s]	92	±15.54
A [m/s]	51	±12.06
DT [ms]	164	±29.07
E/A	1.89	±0.48
IRT [ms]	59	±11.30

We did not find a significant correlation between age and SVI, but we found a negative significant correlation between age and E (r: -0.21; $p < 0.05$) (Fig. 2). In case of correlation between PWA parameters and ECHO parameters we found a negative significant correlation between A and SVI (r: -0.277; $p < 0.05$), and positive significant correlation between E/A and SVI (r: 0.256; $p < 0.05$).

We did not find a statistically significant correlation in the other surveyed parameters. We also did not find a correlation between the parameters of diastolic function and time since the end of treatment.

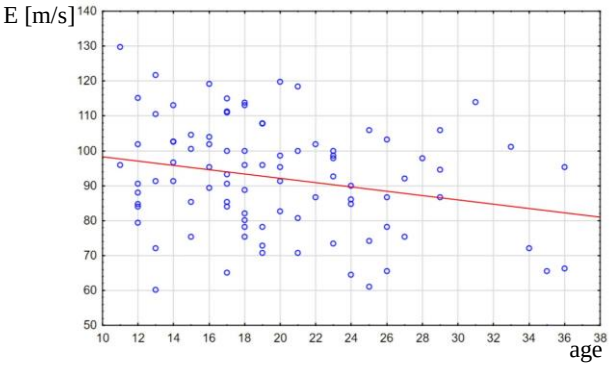

Figure 2: Correlation between age and E: E – passive filling of the left ventricle in early diastole. Correlation is significant with $p<0.05$, index of correlation is $r=-0.21$. The red straight line shows the trend of negative correlation.

4. Discussion

Anthracycline antibiotics usage increases the survival ratio from 30% to 70% (5). At the same time anticancer treatment can be associated with other organ impairment, for example, very often impact on cardiovascular disease (CVD) (6). In spite of cardio protection therapy there is a higher risk of cardiac damage, including left ventricular dysfunction (LVD) and heart failure. Impairment of cardiovascular system could be reversible (more frequently) or irreversible and cause progressive CVD (7).

ECHO is a non-invasive method for studying the function of the heart. It is based on uses ultrasound waves reflected from the heart to generate images of cardiac structure and function. For evaluation of left ventricular function could be used parameters of systolic, diastolic function and parameters describing the size of left ventricle.

It had been shown that isovolumic relaxation time, deceleration time and mitral E/A ratio are impaired in patients treated by anthracyclines with preserved normal EF[8]. In comparison with other similar studies, parameters of our patients are located in physiological range. The probable explanation is age of respondents during measuring. The manifestation of cardiotoxicity directly depends on the age of the patient. In our case we measured respondents who had hemato-oncological disease in early age (2 – 6 years old). Manifestation of cardiotoxicity of anthracycline antibiotics in case of older patients appears earlier and with the strongest significance (8).

In spite of significant role of ECHO in the evaluation of systolic and diastolic heart function, this technic has a certain disadvantage. It is the inability to detect the initial stages of heart failure before achieving structural changes. Unlike echocardiography, applanation tonometry makes it possible to identify changes in the parameters of the cardiovascular system at the subclinical level (9). The indirect parameter that determines the predisposition of the left ventricle to diastolic dysfunction is SVI that reflects the subendocardial viability. The values under 140% reflect lower coronary perfusion. Moreover, our results shown that it could be age-independent parameter for the evaluation of heart function. But at this moment applanation tonometry usage has been limited to determining only the parameters of arterial stiffness.

Unfortunately, there is no available published data about TTI, DTI and SVI that was measured with applanation tonometry as parameters of the systolic or diastolic function. Owing to this fact, we set ourselves the goal of finding out whether there is a statistically significant correlation between the individual methods.

5. Conclusion

From the observed correlation between echocardiography and applanation tonometry, we can assume that the SVI parameter is suitable for the assessment of diastolic heart function. However, this finding should be verified also in other groups of patients.

Acknowledgments

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Address for correspondence:

Ksenia Budinskaya
Department of Physiology
Faculty of Medicine
Masaryk University
Kamenice 5
625 00 Brno
Czech Republic
409542mail.muni.cz