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Sex-related echocardiographic changes in the hearts of healthy young adults

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Abstract

Background. Transthoracic echocardiography (TTE) using M-mode, 2D-modality and 12-lead electrocardiogram (ECG) are widely available diagnostic tools in cardiology. The *aim of the study was to compare the cardiac structure and function of young healthy men and women.* ***Material and methods.*** 108 volunteers (56 female (F) and 52 male (M), median age 23 ± 2 (19-29) and 24 ± 2 (19-29) respectively) underwent TTE assessing M-mode, 2D-mode and Doppler parameters. The following TTE parameters were measured: aortic bulb (Ao), left atrium (LAS), right ventricle – diastole (RVEDd), intraventricular septum (IVSd), left ventricle – diastole (LVEDd), posterior wall of LV (PWd), left ventricle – systole (LVESd), right atrium area (RAS) diameters, LVM (left ventricular mass), LVMI (left ventricular mass index), LVEF (left ventricular ejection fraction) and RWT (relative wall thickness). In Doppler examination E and A (early and late diastolic mitral filling velocity), E/A index, diastolic filling period (DFP) and hemodynamic parameters of pulmonary outflow acceleration time of pulmonary artery (AcT) and mean pulmonary artery pressure (MPAP). BSA was considered in the comparison of results. Heart rate (HR), LV hypertrophy (Sokolow-Lyon Index) and conduction disorders were assessed using 12-lead ECG. ***Results.*** The examined groups differed in body weight, height, BMI and BSA ($p < 0.001$). In TTE examination males had larger IVSd, PWd, LVEDd, LVESd, LAS, Ao, RAS also LVM and LVMI ($p < 0.001$). CO and LVEF (M: 65 ± 5.5 vs. F: 64.5 ± 5.5%) were statistically not significant (NS). There was no sex-related difference in diastolic function of LV (NS). Physiological regurgitation was mostly present in the tricuspid valve (M: 64% vs. F: 68%, NS). LVEDd, RVEDd and LAS in correction to BSA were statistically significant in women group ($p < 0.05$). The difference in HR (M: 66 ± 11 vs. F: 70 ± 13 bpm) was NS. Sokolov-Lyon voltage was higher among males ($p < 0.001$). Incomplete Right Bundle Brunch Block was found in 17% of M and 14% of F (NS). ***Conclusions.*** Morphology of the heart is a sex-related feature. Some of the noted sex-related differences disappear after correcting for BSA. There is no difference in the systolic and diastolic function of LV in both groups of the young adults. *Geriatria 2019; 13: 141-146.*

Keywords: transthoracic echocardiography, left ventricular function, physiological valve insufficiency, sex

Background

Echocardiography and 12-lead electrocardiogram (ECG) are widely available diagnostic tools in contemporary cardiology [1]. Ultrasonography of the heart began in the 1950's when Edler and Hertz used this technology to clinically assess patients with mitral valve diseases, thus pioneering the single-dimension imaging (M-Mode) [2]. Two-dimensional (2D) imaging and pulse wave Doppler were developed in the 1970's, while color Doppler followed in 1980's [2]. All of the above-mentioned modalities are currently routinely used during echocardiographic assessment. However, the commonly accepted reference values in transthoracic echocardiography (TTE) often do not consider variations due to age or sex.

The aim of the study was to compare the selected echocardiographic parameters of heart structure and function in terms of sex in a population of healthy young adults with normal BMI. Furthermore, we aimed to compare indices (corrected TTE parameters) in terms of anthropomorphic parameters.

Material and methods

A cross-sectional study was conducted on 108 consecutive volunteers in Northern Poland, mostly university students: 56 females 23 ± 2 (19-29) years old and 52 males 24 ± 2 (19-29) years of age. Inclusion criteria were: age (19-29) and no history of illness. 27 males and 31 females declared sedentary lifestyle, whereas the rest of the group claimed to maintain regular recreational physical activity. In order to avoid confounding the measurements with possible structural changes (athlete's heart), those who intensively trained any sports were excluded from the study. TTE was performed at rest in left lateral decubitus position using Acuson Sequoia C512 (Siemens, Germany) using a 4V1c probe (3.75 MHz frequency) with simultaneous ECG monitoring. All TTE examinations were performed in accordance with the standards of the American Society of Echocardiography (ASE) and the Echocardiography Section of the Polish Cardiac Society (Sekcja Echokardiografii Polskiego Towarzystwa Kardiologicznego, SEPTK) [3,4]. Measurements of cardiac structures were performed in standard locations in M-mode using 2D images. Systolic measurements of chambers were performed on the descending arm of the T wave, whereas the diastolic measurements were taken on the peak of the ECG's R wave [4].

In the long axis of the left ventricle (LV) in the parasternal projection we measured the: left atrial systolic diameter (LAS), aortic bulb diameter (Ao), right ventricular end-diastolic diameter (RVEDd), intraventricular septum diastolic diameter (IVSd), left ventricular end-diastolic diameter (LVEDd), left ventricular end-systolic diameter (LVESd) and posterior wall diastolic diameter (PWd) [6]. Planimetric assessment of the right atrial size (RAS) was performed during systole in the four-chamber apical view [7]. We also compared our participants' LV relative wall thickness (RWT) calculated using the following formula:

$$RWT = (IVSd + PWd) / LVEDd.$$

We used the Devereux formula to assess the left ventricular mass (LVM) [8]:

$$LVM (g) = 0.8 \times \{1.04 \times [(LVEDd + IVSd + PWd)3 - (LVEDd)3]\} + 0.6.$$

Using the Simpson's biplane method of disks we measured the left ventricular end-diastolic and end-systolic volumes (LVEDV and LVESV) in order to calculate the stroke volume (SV), minute cardiac output (CO) and left ventricular ejection fraction (LVEF) [6]. All LV volumes were measured in the four-chamber apical view.

Using the pulsed wave Doppler (PW) we assessed selected parameters of LV diastolic function: peak early mitral inflow velocity (E wave), peak early filling (E wave) and late diastolic filling (A wave) velocities, E/A index and LV diastolic filling period (DFP) in miliseconds and in relation to the time of R-R interval (DFP/RR). Furthermore, we used the PW-Doppler to measure the acceleration time of the maximal flow in the pulmonary artery (AcT) and on its basis we calculated the mean pulmonary artery pressure (MPAP) using the following formula:

$$MPAP (mmHg) = -0.5 \times AcT(ms) + 80.$$

Valve regurgitation was assessed using the semi-quantitative color Doppler flow.

Basic anthropometric parameters such as height, weight, body mass index (BMI) and body surface area (BSA, calculated using the Mosteller formula) were also assessed [9]. We corrected selected echocardiographic parameters for BSA and compared them between the male and female participants. We used the same approach with the left ventricle and calculated the left ventricle mass index (LVMI).

We performed a resting 12-lead electrocardiogram (ECG) on all participants using an Aspel (Poland) electrocardiograph with 25 mm/s paper speed and amplitude set at 1mV/cm. We used the ECG to assess the heart rate (HR) LV hypertrophy (Sokolow-Lyon Index, SV1 + RV5) and conduction disorders [10].

Statistical analysis was performed using the Statistica software (StatSoft Inc., USA). The results were presented as arithmetic mean and standard deviation (SD) and in case of categorical variables as the number and percentage of participants with the particular parameter. A variable's distribution was assessed using the Shapiro-Wilk test. Parametric variables with normal distribution were assessed using the t-Student test, whereas those without normal distribution using the Mann-Whitney U test. Non-parametric variables were assessed using Pearson's χ^2 test. P value < 0.05 was considered statistically significant.

Results

As mentioned earlier, the participants in our study were of similar age however they significantly differed in terms of height, weight, BMI and BSA ($p < 0,001$). Male participants were on average 11 cm taller and 16.73 kg heavier, with BSA 0.28 m^2 greater than the female participants' (see Table I for details). BSA is considered as the best basis for correcting size-dependent echocardiographic measurements.

Statistical analysis demonstrated significantly greater systolic and diastolic diameters of the LV, septum and posterior wall, both atria and bulb of aorta among the males ($p < 0.001$). However, such difference was not noted for RVEDd (NS). The LV minute volume also was not significantly different, despite the fact that young males have greater LVESV and LVEF LV ($p < 0.005$). The LVEF was 65.0 ± 5.5 % among males and 64.4 ± 5.4% among females (NS). The calculated RWT was also similar between both sexes (NS). LV mass was significantly different before and after correcting for BSA, respectively: 170.9 ± 46.8 g for males and 119.3 ± 29.4 g for females ($p < 0.001$) and 86.8 ± 20.7 g/m^2 and 70.7 ± 15.1 g/m^2 ($p < 0.001$). After correcting for BSA the measured echocardiographic measurements are greater among females: RVEDd/BSA ($p < 0.001$), LAS/BSA ($p < 0.05$) i LVEDd/BSA ($p < 0.005$). See Tables II and III for detailed TTE measurements.

The E and A waves and their index all fit within the accepted normal reference values and statistically significant difference was not noted. Maximal early mitral inflow velocity (E wave) appears to be significantly greater among males (51.5 ± 10.2 % of single cardiac cycle's duration) than females (48.0 ± 10.6%, $p < 0.05$). No significant differences were noted for AcT and MPAP (NS). Using the semi-quantitative color Doppler method we noted a rather significant amount of physiological regurgitation, most often of the tricuspid valve 33 (63%) males, 38 (68%) females and rarely of the aortic valve 3 (6%) males, 3 (5,5%) females. However those differences were not statistically significant (see Table IV for details).

ECG at rest did not reveal statistically significant difference in heart rate: 65.7 ± 10.6 /min in males and 70.2 ± 13.9 /min among females (NS; using the Mann-Whitney U test). However sex-related differences were noted in terms of cardiac muscle hypertrophy (assessed using the Sokolow-Lyon index): 2.86 ± 0.75 mV in males and 2.22 ± 0.53 mV among females ($p < 0,001$; using the t-Student test). Other abnormalities noted in the ECG were Incomplete Right Bundle Brunch Block: 9 (17.3%) males and 8 (14.3%) females, left axis deviation (2 males and 2 females), right axis deviation (1 male, 2 females), all NS.

Table I. Descriptive characteristics of subjects

	Mean	SD	Minimum	Maximum
Female (n = 56)				
Age (years)	23,2	2,2	19	29
Body mass (kg)	60,1*	7,2	40	75
Height (m)	1,69*	0,07	1,47	1,84
Body mass index, BMI (kg/m²)	21,0*	2,1	17,1	27,2
Body surface area, BSA (m²)	1,68*	0,12	1,28	1,91
Male (n = 52)				
Age (years)	23,8	2,0	19	29
Body mass (kg)	76,8*	9,9	60	100
Height (m)	1,80*	0,06	1,68	1,98
Body mass index, BMI (kg/m²)	23,5*	2,4	18,5	29,2
Body surface area, BSA (m²)	1,96*	0,15	1,68	2,27

*p < 0,001 (t-Student test); SD – standard deviation;

Table II. Comparison of selected echocardiographic parameters in the groups of women and men

Parameter	Female n = 56	Male n = 52	p
Aortic bulb, Ao (mm)	27,5 ± 3,1	30,9 ± 3,7	< 0,001*
Left atrium, LAS (mm)	28,9 ± 3,9	31,9 ± 4,7	< 0,001*
Right ventricle - diastole, RVEDd (mm)	22,2 ± 3,8	22,5 ± 4,0	NS*
Intraventricular septum, IVSd (mm)	8,8 ± 1,8	10,1 ± 1,7	< 0,001**

Left ventricle – diastole, LVEDd (mm)	44,5 ± 4,1	49,3 ± 4,6	< 0,001*
Posterior wall of LV, PWd (mm)	7,8 ± 1,7	9,0 ± 1,8	< 0,001*
Left ventricle – systole, LVESd (mm)	31,9 ± 4,6	35,3 ± 4,8	< 0,001**
Right atrium – area, RAS (cm²)	12,6 ± 2,8	14,8 ± 3,2	< 0,001*
Hemodynamic parameters			
End-diastolic volume of LV, LVEDV (ml)	78,3 ± 24,8	93,0 ± 28,7	< 0,005**
End-systolic volume of LV, LVESV (ml)	27,7 ± 9,3	33,1 ± 12,8	< 0,05**
Ejection fraction of LV, LVEF (%)	64,4 ± 5,4	65,0 ± 5,5	NS**
Stroke volume, SV (ml)	50,6 ± 17,4	60,0 ± 17,8	< 0,005**
Cardiac output, CO (l)	3,7 ± 1,3	4,1 ± 1,3	NS**
Other			
Relative wall thickness, RWT	0,37 ± 0,07	0,39 ± 0,06	NS*
LV mass, LVM (g)	119,3 ± 29,4	170,9 ± 46,8	< 0,001*

Values are presented as mean ± SD; * t-Student test; ** Mann-Whitney U test

Table III. Comparison of selected echocardiographic parameters corrected by body surface area (BSA)

Parameter	Female n = 56	Male n = 52	p
Ao/BSA (mm/m²)	16,5 ± 1,9	15,8 ± 1,9	NS*
LAS/BSA (mm/m²)	17,2 ± 2,2	16,3 ± 2,1	< 0,05*
RVEDd/BSA (mm/m²)	13,3 ± 2,3	11,5 ± 2,1	< 0,001*
IVSd/BSA (mm/m²)	5,3 ± 1,1	5,2 ± 0,9	NS**
LVEDd/BSA (mm/m²)	26,5 ± 2,0	25,2 ± 2,2	< 0,005*
PWd/BSA (mm/m²)	4,7 ± 1,1	4,6 ± 0,9	NS*
LVESd/BSA (mm/m²)	19,0 ± 2,3	18,1 ± 2,4	NS**
RAS/BSA (mm/m²)	7,5 ± 1,5	7,5 ± 1,5	NS*
SV/BSA (ml/m²)	29,9 ± 9,4	30,5 ± 8,5	NS**
CO/BSA (l/m²)	2,2 ± 0,7	2,1 ± 0,6	NS**
LVM/BSA (g/m²))	70,7 ± 15,1	86,8 ± 20,7	< 0,001*

Values are presented as mean ± SD; * t-Student test; ** Mann-Whitney U test

Table IV. Comparison of Doppler parameters in tested groups

Parameter	Female n = 56	Male n = 52	p
Pulsed wave Doppler			
E (m/s)	0,79 ± 0,11	0,76 ± 0,12	NS*
A (m/s)	0,46 ± 0,09	0,47 ± 0,09	NS**
E/A	1,78 ± 0,45	1,67 ± 0,33	NS**
Diastolic filling period, DFP (ms)	413 ± 136	460 ± 119	< 0,01**
Diastolic filling period, DFP/RR (%)	48,0 ± 10,6	51,5 ± 10,2	< 0,05**
Acceleration time of pulmonary artery, AcT (ms)	146 ± 27	143 ± 20	NS**
Mean pulmonary artery pressure, MPAP (mmHg)	12 ± 8	10 ± 8	NS**
Color Doppler – physiological regurgitation			
Pulmonary valve insufficiency, PI (%)	52% (29)	60% (31)	NS***
Mitral valve insufficiency, MI (%)	27% (15)	38% (20)	NS***
Tricuspid valve insufficiency, TI (%)	68% (38)	63% (33)	NS***
Aortic valve insufficiency, AI (%)	5% (3)	6% (3)	NS***

* t-Student test; ** Mann-Whitney U test; *** χ^2 test;

Discussion

Although echocardiography is widely used in clinical practice, there are numerous disparities in the normal reference values. The currently accepted reference values are based on research published in 1970-1990's [11-13]. For the sake of comparison, it is worth mentioning some of the values regarded as upper-normal: LA 36-47 mm, LVEDd 52-70 mm, LVESd 30-40 mm, LV walls 11-13 mm [14]. Another issue is the fact that reference values do not take into account age, sex, ethnicity or other variables. Nearly 20 years ago Vasan et al. discussed the lack of standardization in echocardiography and emphasized that large samples (120-200 participants, depending on the particular variable's distribution) are needed in order to credibly assess any of the above-mentioned differences [14]. However such methodological criteria exclude a large amount of research published on this subject so far.

The influence of sex on the size of cardiac structures examined via TTE is the subject of numerous studies. Majority of them concluded that females have smaller hearts than males [14-16]. As part of the Framingham Heart Study Lauer et al. suggested echocardiographic reference values based on a sample of young (20-45 years of age) 288 males and 524 females with BMI 19-26 kg/m² and without chronic illness [13]. The significant differences were obtained between the parameters describing the anatomy of LV: diastolic and systolic dimension (50,8±3,6 mm vs. 46,1± 3,0 mm, and 32,9±3,4 mm vs. 28,9±2,8 mm, respectively), the sum of the intraventricular septum and posterior wall thickness (18,1±2,0 mm vs. 15,5±1,5 mm), as well as LA dimension (37,5±3,6 mm vs. 33,1±3,2 mm). All these measurements were greater among men. In the study by Gerstenblith et al. the sizes of heart structures were assessed among healthy volunteers aged 24 to 85 years. Only men were qualified to the study. In the age group 24-45 years the LVEDd was 51,8±1,03 mm and LV wall thickness 8,7±0,3 mm [17].

The rapidly developing imaging method cardiovascular magnetic resonance (CMR) might become an interesting alternative to echocardiography. Its advantages include precision of measurements, less subjectivity than in echocardiography and lack of ionizing radiation.

On the basis of a healthy subsample of the Framingham Heart Study (79 women and 63 men, 57 ± 9 years of age, without cardio-vascular illness or hypertension), Salton et al conducted a CMR analysis of sex-related differences in the structure and function of the heart [18]. Except for LVEF, all of the LV parameters were greater among men ($p < 0.001$): LVM 155.1 g vs. 103.0 g, LVEDV 114.9 ml vs. 84.4 ml, LVESV 36.3 ml vs. 25.1 ml, PWd 9/9 mm vs. 8.7 mm, IVSd 10.1 mm vs. 8.9 mm, LVEDd 50.2 mm vs. 45.6 mm. Average LVEF among men was 69% and 70% among women. After correcting for BSA, the LVM, LVEDV and LVESV were all significantly greater among men ($p < 0.001$), however women had noticeable greater LVEDd, IVSd and Pwd indexes. Finally, the calculated LV mass index was 77.9 g/m² for males and 60.8 g/m² for females. Our results are rather similar to those mentioned above, however Salton et al. unfortunately did not measure more TTE parameters. Furthermore, we must be cautious in comparing those results because CMR and TTE are completely different imaging methods. Further studies on larger samples are needed to fully explore the differences in measurements between CMR and TTE, considering that CMR might become more commonly used in clinical practice.

The literature published so far indicates that LVM calculated using CMR is lower compared to LVM obtained via TTE [19]. Depending on the authors, the accepted cut-off value for normal LVMI in TTE range from 117-134 g/m² for males and 104-110 g/m² for females [20,21]. The results published by Saltona et al re based on a significantly older age group than ours, though it seems that sex-related differences are noted at any age.

Valve regurgitation in the healthy population is an interesting phenomenon. Using PW Doppler Takao et al noted small pulmonary valve regurgitation in 39 of 50 (875) healthy adults aged 35 on average [22]. Using color Doppler to examine 110 healthy adults (65 females, 45 males, 24-64 years of age), Macchi et al noted PI in 42.7%, TI in 33,6%, MI in 10%, AI in 8,2% and described all of the above regurgitations as physiological [23].

Conclusions

TTE of healthy young adults reveals sex- and body surface-related differences in the majority of linear echocardiographic parameters. Males have significantly larger aortas, atria, heart wall thickness and left ventricles. However those differences disappear upon correction for body surface. We did not find any differences in the valve function, systolic or diastolic left ventricle function.

Conflict of interest
None

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