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Cardiomyopathies: echocardiographic profiles based on principal component factor analysis in men and women

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Aim. To determine echocardiographic profiles and their prognostic value using factor analysis in men and women with various types of cardiomyopathies (CMP).

Material and methods. The study involved 100 people with CMP — 69 men with a median age of 53 years and 31 women with a median age of 58 years. Among the subjects, six nosological types corresponding to ICD 10 classification were revealed: dilated CMP (DCM), ischemic CMP (ICM), alcoholic CMP, mixed CMP, hypertrophic CMP (HCM) and myocarditis. All persons underwent an echocardiography. Echocardiography results as variables were included in factor analysis. The resulting two factors are presented as the first and second echocardiographic profiles.

Results. The first echocardiographic profile was characterized as the degree of myocardial contractile function reduction. A strong association of the first profile with DCM, alcoholic CMP and myocarditis in men (p=0,001) and DCM in women (p=0,05) was obtained. In some individuals with ICM and mixed CMP, there was no association with the first profile. The second echocardiographic profile reflected the degree of myocardial mass increase and had significant differences only in women (p=0,04). A strong correlation with the second profile was observed in HCM, in the majority of women with ICM and in some persons with mixed CMP. Fatal outcomes in men were recorded in patients with ICM (66,7%), alcoholic CMP and myocarditis, and in women with mixed CMP (11,1%).

Conclusion. For patients with DCM, myocarditis, and alcoholic CMP, the first echocardiographic profile with a risk of death is characteristic. The second echocardiographic profile was inherent in HCM and was associated with a protective effect in women with ICM. The revealed echocardiographic profiles can be extrapolated to nosological types of CMP in men and women in order to verify the diagnosis and prognosis.

Key words: cardiomyopathies, echocardiography, factor analysis, sex differences.

Relationships and Activities: none.

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Cardiomyopathies (CMP) are a large group of non-coronary myocardial diseases with various etiological and pathogenetic mechanisms. CMPs are widespread and often lead to heart failure, arrhythmias and sudden cardiac death [1, 2]. Recent international studies show that CMPs in men and women have different prevalence and frequency of complications [3-7]. This is due to the influence of sex on cardiac metabolism, different signaling pathways and gene expression [8]. Currently, verification of certain CMP types is possible only with molecular genetics and cellular testing, myocardial biopsy and modern visualization methods (magnetic resonance imaging, computed tomography and cardiac positron emission tomography), of which transthoracic echocardiography remains the leading technique in the diagnosis of CMPs. In order to obtain the qualitative characteristics of echocardiography in the differential diagnosis of CMPs, we used the factor analysis separately in men and women.

The aim was to determine echocardiographic profiles and their prognostic value using factor analysis in men and women with various types of cardiomyopathies.

Material and methods

We performed a retrospective analysis of medical records of 123 patients with CMP discharged from the hospital during 2018. According to the International Classification of Diseases 10th Revision (ICD-10), a total of 6 CMP types were registered: dilated CMP (DCM) (I42.0), ischemic CMP (ICM) (I25.5), alcoholic CMP (I42.6), mixed CMP (I43.1-43.8; I42.7-42.9), hypertrophic CMP (HCM) (I42.1-42.2) and myocarditis (I40.0-40.9). After hospitalization and examination, 111 patients were discharged with CMP, while 12 patients died. Of the 123 registered CMP cases, 100 medical records were available for analysis, of which 8 were lethal cases. There were 69 men with a mean age of 52,7±12,8 years and 31 women with a mean age of 58,6±14,7 years. Data on coronary angiography were available in 35 people out of 100 (35,0%). In all cases, no coronary artery stenosis was detected. Autopsy data were available in 6 of 8 deceased patients with CMP.

All patients underwent standard echocardiography. The following echocardiographic parameters were taken into account: ejection fraction (EF), left ventricular (LV) end diastolic dimension (EDD), LV end systolic dimension (ESD), LV end diastolic volume (EDV), LV end systolic volume (ESV), right ventricle dimension, interventricular septal thickness, LV posterior wall thickness, LV relative wall thickness, left atrial transverse diameter, right atrial transverse diameter, post-systolic shortening, pulmonary artery systolic pressure, LV mass index, presence of hypokinetic regions, and pericardial effusion.

Statistical analysis was carried out using the SPSS 17.0. Comparison of mean values was carried out according to Student's t-test. Differences were considered significant at $p<0,05$. The arithmetic mean was presented as M±SD, where M is the mean and SD is the standard deviation. The varimax rotated two-factor analysis was carried out. The obtained factor values for each case of CMP were ranged into 4 groups of percentiles depending on the trait t for men and women. The analysis of contingency table was carried out using the chi-squared test.

Table 1

Prevalence of different CMPs in men and women

		CMP types						Total
		DCM	ICM	Alcoholic CMP	Myocarditis	Mixed CMP	HCM	
Men	n	21	6	5	12	24	1	69
	%	30,4	8,7	7,2	17,4	34,8	1,4	100,0
	% CMP	91,3	46,2	100,0	85,7%	57,1	33,3	69,0
Women	n	2	7	0	2	18	2	31
	%	6,5	22,6	0,0	6,5	58,1	6,5	100,0
	% CMP	8,7	53,8	0,0	14,3	42,9	66,7	31,0
Total	N	23	13	5	14	42	3	100
	%	23,0	13,0	5,0	14,0	42,0	3,0	100,0
	% CMP	100,0	100,0	100,0	100,0	100,0	100,0	100,0
P		0,01*	0,05*	>0,5	>0,5	0,03*	>0,5	0,05*

Note: * — differences in the prevalence of CMP between men and women.

Abbreviations: HCM — hypertrophic cardiomyopathy, DCM — dilated cardiomyopathy, ICM — ischemic cardiomyopathy, CMP — cardiomyopathy.

Results

Among patients with CMP (n=100), there were more men (n=69) (69,0%) than women (n=31) (31,0%), which was significant (p<0,001). In men, compared with women, DCM was significantly more common (p=0,01), and in women, mixed CMP (p=0,03) and ICM were more often recorded (p=0,05). The distribution of CMP types by sex is presented in Table 1.

The group of CMP men was younger than women with CMP: the median age for men was 53 years, for women — 58 years (p=0,04). By age, the oldest among men and women were patients with ICM (66,3±4,0 years and 79,2±8,8 years, respectively), while the youngest were patients with myocarditis (45,9±10,6 years and 41,5±13,4 years, respectively). Comparative analysis of the groups of men (n=69) and women (n=31) revealed sex differences in almost all parameters of echocardiography, which coincide with other studies [9] (Table 2).

Comparative analysis of echocardiographic data in patients with the same type of CMP between men and women revealed that among those with DCM, myocarditis and HCM, there were no sex differences in any echocardiographic parameter (p>0,5), while there were significant differences between men and women only with ICM and mixed CMP (Table 3).

Among men (n=69), there were 6 deaths (8,7%): 4 (66,7%) patients with ICM (n=6), 1 (20,0%) patient with alcoholic CMP (n=5) and 1 (8,3%) patient with myocarditis (n=12). The difference in mortality with ICM in men (n=6) compared to women with ICM (n=7) was significant: 66,7% and 0% (p=0,009). The deceased and surviving men with ICM did not differ in age (p>0,5) and echocardiographic parameters (p>0,5).

Among women (n=31), 2 (6,5%) people with mixed CMP died, which amounted to 11,1% in the mixed CMP group of women (n=18). The 2 women who died differed from the surviving women with mixed CM by lower ejection fraction (p=0,002), LV reduced contractility fraction (p=0,001) and the presence of hypokinetic regions (p=0,024). There were no differences in mortality in patients with mixed CMP and in general between women and men (8,7% and 6,5%) (p>0,5).

Principal factor analysis was carried out separately for men and women. Three factors have been identified that explain 83,7% of the total variance of studied variables in men, of which the first factor explained 45,9%, the second factor — 21,9% and the third factor — 15,8% of the variance. In women, the total variance was 80,8%, where the first factor explained 43,1% of the total variance, the second factor — 19,4%, and the third factor — 18,3%. Fac-

Table 2

Comparative analysis of echocardiographic data in CMP among men and women

Parameters	Men (n=69) M±SD	Women (n=31) M±SD	p
EF (%)	47,3±14,8	53,4±12,1	0,046
LA (cm)	4,8±1,0	4,5±0,8	>0,5
RA (cm)	4,5±0,8	4,2±0,9	>0,5
RV (cm)	3,8±0,7	3,3±0,6	0,001
CF (%)	24,8±8,6	28,7±7,5	0,032
RWT	0,31±0,08	0,37±0,10	0,002
EDD (cm)	6,0±1,0	5,2±0,8	0,001
ESD (cm)	4,6±1,2	3,9±0,8	0,004
EDV (ml)	189,3±77,5	146,7±45,3	0,008
ESV (ml)	107,9±71,9	63,1±34,8	0,002
IVS (cm)	0,9±0,2	1,0±0,3	0,028
LVPW (cm)	0,9±0,1	0,9±0,2	>0,5
LVMI	125,5±45,2	123,9±43,6	>0,5
RVSP (mm Hg)	41,2±11,5	39,1±8,2	>0,5
Pericardial fluid (n)	3 (5,4%)	5 (16,1%)	0,06
Hypokinesia (n)	31 (52,5%)	9 (29,0%)	>0,5

Abbreviations: LVPW — left ventricular posterior wall, LVMI — left ventricular mass index, EDV — end-diastolic volume, ESV — end-systolic volume, EDD — end-diastolic dimension, ESD — end-systolic dimension, LA — left atrium, IVS — interventricular septum, RWT — relative wall thickness, RV — right ventricle, RA — right atrium, RVSP — right ventricular systolic pressure, EF — ejection fraction, CF — contractility fraction.

Table 3

Comparative analysis of echocardiographic data in men and women with ICM and mixed CMP

CMP type	Parameters	Men, M±SD	Women, M±SD	p
ICP	RV (cm)	4,0±0,6, n=6	3,2±0,5, n=7	0,04
	EDD (cm)	6,7±0,7, n=6	5,8±0,7, n=7	0,07
Mixed CMP	RV (cm)	3,6±0,6, n=24	3,2±0,5, n=18	0,02
	EDD (cm)	5,7±0,6, n=24	5,1±0,6, n=18	0,01
	ESV (ml)	79,8±50,6, n=24	51,4±21,5, n=18	0,04

Abbreviations: ICM — ischemic cardiomyopathy, EDD — end-diastolic dimension, CMP — cardiomyopathy, ESV — end-systolic volume, RV — right ventricle.

Table 4

Rotated factor matrix in men and women with CMP

Factor loadings							
Variables	Units	Men			Women		
		Factor 1	Factor 2	Factor 3	Factor 1	Factor 2	Factor 3
LA	cm			0,801			0,872
RA	cm			0,953			0,953
EF	%	-0,892			-0,875		
CF	%	-0,878			-0,879		
EDD	cm	0,870			0,864		
ESD	cm	0,948			0,773		
EDV	ml	0,834			0,898		
ESV	ml	0,901			0,929		
IVS	cm		0,910			0,859	
LVPW	cm		0,936			0,895	
LVMI	n		0,692			0,789	
Hypokinesia	n	0,780			0,788		

Abbreviations: LVPW — left ventricular posterior wall, LVMI — left ventricular mass index, EDV — end-diastolic volume, ESV — end-systolic volume, EDD — end- diastolic dimension, ESD — end-systolic dimension, LA — left atrium, IVS — interventricular septum, RA — right atrium, EF — ejection fraction, CF — contractility fraction.

Table 5

Contingency table of Factor 1 with different CMP types in men

CMP type		Factor 1: reduced MCF				Total
		No	Mild	Strong	Very strong	
DCM	n	1	0	6	8	15
	%	6,7%	0,0%	40,0%	53,3%	100,0%
ICM	n	1	3	2	2	8
	%	12,5%	37,5%	25,0%	25,0%	100,0%
Alcoholic CMP	n	0	0	2	0	2
	%	0,0%	0,0%	100,0%	0,0%	100,0%
Myocarditis	n	0	0	0	1	1
	%	0,0%	0,0%	0,0%	100,0%	100,0%
Mixed CMP	n	9	12	5	3	29
	%	31,0%	41,4%	17,2%	10,3%	100,0%
HCM	n	3	0	0	0	3
	%	100,0%	0,0%	0,0%	0,0%	100,0%
Total	n	14	15	15	14	58
	%	24,1%	25,9%	25,9%	24,1%	100,0%

Abbreviations: HCM — hypertrophic cardiomyopathy, DCM — dilated cardiomyopathy, ICM — ischemic cardiomyopathy, CMP — cardiomyopathy.

tor analysis created a rotated matrix of factor loadings with three main components (Table 4).

The first component (Factor 1) included variables same for men and women: EF, post-systolic shortening, EDD, ESD, EDV, ESV, hypokinetic myocardium. Factor 1 had a strong inverse relationship with EF and contractility fraction variables and a strong direct relationship with LV dimension, volume, and hypokinesis, as a result of which Factor 1 was characterized as *the first echocardiographic profile with reduced myocardial contractile function* (MCF). The second component (Factor 2) in men and women consisted of the variables of the interventricular septum, LV posterior wall, LV mass index, reflecting the LV myocardium walls' thickness and was designated as *the second echocardiographic*

Table 6

Contingency table of Factor 1 with different CMP types in women

CMP type		Factor 1: reduced MCF				Total
		No	Mild	Strong	Very strong	
DCM	n	0	0	0	2	2
	%	0,0%	0,0%	0,0%	100,0%	100,0%
ICM	n	0	2	1	2	5
	%	0,0%	40,0%	20,0%	40,0%	100,0%
Mixed CMP	n	2	3	4	1	10
	%	20,0%	30,0%	40,0%	10,0%	100,0%
HCM	n	2	0	0	0	2
	%	100,0%	0,0%	0,0%	0,0%	100,0%
Total	n	4	5	5	5	19
	%	21,1%	26,3%	26,3%	26,3%	100,0%

Abbreviations: HCM — hypertrophic cardiomyopathy, DCM — dilated cardiomyopathy, ICM — ischemic cardiomyopathy, CMP — cardiomyopathy.

Table 7

Contingency table of Factor 2 with different CMP types in women

CMP type		Factor 2: increased MM				Total
		No	Mild	Strong	Very strong	
DCM	n	2	0	0	0	2
	%	100,0%	0,0%	0,0%	0,0%	100,0%
ICM	n	0	1	3	1	5
	%	0,0%	20,0%	60,0%	20,0%	100,0%
Mixed CMP	n	2	4	2	2	10
	%	20,0%	40,0%	20,0%	20,0%	100,0%
HCM	n	0	0	0	2	2
	%	0,0%	0,0%	0,0%	100,0%	100,0%
Total	n	4	5	5	5	19
	%	21,1%	26,3%	26,3%	26,3%	100,0%

Abbreviations: HCM — hypertrophic cardiomyopathy, DCM — dilated cardiomyopathy, ICM — ischemic cardiomyopathy, CMP — cardiomyopathy.

profile with increased myocardial mass (MM). The third component (Factor 3) is defined as the degree of *atrial load*, since in men and women this factor included the variables of the left and right atria.

When analyzing contingency tables with analysis of relationship strength of factor values of *the first echocardiographic profile* with individual CMP types, the chi-squared test in men was significant at the level of p=0,001, and in women it was equal to p=0,05. Among men, association with *the first echocardiographic profile* were obtained for alcoholic CMP, myocarditis, DCM, ICM, and mixed CMP (Table 5).

In women, the relationship of *the first echocardiographic profile* with DCM, ICM and mixed CMP (Table 6).

The second echocardiographic profile with increased MM among men did not have a significant relationship with CMP (p>0,5). On the contrary, in women, *the second echocardiographic profile* had a significant difference (p=0,04) with HCM and ICM (Table 7).

Factor 3 (*degree of atrial load*) showed no differences either in men (p>0,5) or in women (p>0,5), which indicated a comparatively equal atrial load in all types of CMP in both sexes.

Discussion

The first echocardiographic profile with reduced MCF was characteristic of patients with DCM, alcoholic CMP, myocarditis and, in general, corresponded to morphological abnormalities in these

CMPs. Among these individuals, deaths were reported in men. *The second echocardiographic profile with increased MM* was present in women with HCM, since they did not have *the first echocardiographic profile*. There were no sex differences in the echocardiographic parameters (p>0,5) in DCM, myocarditis and HCM, which may indicate the dominance of etiological and genetic mechanisms of the development of these CMP types over sex influence. To confirm these conclusions, it is necessary to study a large population of patients with CMP due to the differences between our results and a number of other studies [5-7].

With ICM, the majority of men had an association with *the first echocardiographic profile* and high mortality (66,7%) compared with women (p=0,009). This confirms the literature data [8] about a poor prognosis in men with ICM. There were no differences in echocardiographic parameters between the deceased and surviving men with ICM (p>0,5), which indicates the morphological homogeneity of this group. Comparison of men with ICM with women with ICM revealed sexual dimorphism of echocardiographic parameters with a significant increase in heart chambers among men (p<0,05). All women with ICM, as well as men, had an association with *the first echocardiographic profile*, but women also had a significant association with *the second echocardiographic profile*. It can be assumed that *second echocardiographic profile* had a protective effect in women with ICM and prevented deaths among them. This conclusion is supported by other studies [8, 10] on the prevalence of concentric myocardial remodeling in women with cardiac hypertrophy, which prevents a decrease in myocardial contractility. All lethal cases in women were registered with mixed CMP, as other papers [8], which revealed a high mortality rate in women with metabolic (mixed) CMP in comparison with men. In our study, in some women with this CMP type, there was an association with *the first echocardiographic profile* and less often there was an association with *the second echocardiographic profile* compared with women with ICM.

Thus, factor analysis of a large number of echocardiographic variables reduces them to complex factors and allows classification by selection of several echocardiographic profiles. Two echocardiographic profiles with different prognostic values revealed in our study indicate associations of different strength with certain CMP types. The results obtained can be extrapolated to patients with CMP in order to verify the diagnosis and determine the prognosis.

Conclusion

1. Among patients with CMP, there were 2 main echocardiographic profiles: *first profile with reduced MCF* and *the second profile with increased MM*.

2. *The first echocardiographic profile* in men had significant differences (p=0,001) and was closely associated with DCM, myocarditis, alcoholic CMP and was present in the majority of patients with ICM and mixed CMP.

3. Among women, a clear relationship (p=0,05) with *the first echocardiographic profile* was in all individuals with DCM and in some with ICM and mixed CMP.

4. *The second echocardiographic profile* with increased MM in women had a strong relationship with HCM and the majority of individuals with ICM (p=0,04).

5. High mortality was found in men with ICM (66,7%) and among women with mixed CMP (11,1%).

6. Comparative analysis of echocardiographic profiles and outcomes in patients with ICM and mixed CMP suggests a protective effect of *the second echocardiographic profile* in women with ICM.

Relationships and Activities: none.

References

1. Cardiology: national guideline. Ed. Shlyakhto EV. 2-nd edition. M.: GEOTAR-Media, 2019. p. 800. (In Russ.) ISBN: 978-5-9704-4810-6.
2. Braunwald E Cardiomyopathies: An Overview. Circulation Research. 2017;121(7):711-21. doi:10.1161/CIRCRESAHA.117.311812.
3. Seyler C, Meder B, Weis T, et al. TranslatiOnal Registry for CardiomyopatHies (TORCH) — rationale and first results. ESC Heart Fail. 2017;4(3):209-15. doi:10.1002/ehf2.12145.
4. Masarone D, Kaski JP, Pacileo G, et al. Epidemiology and Clinical Aspects of Genetic Cardiomyopathies. Heart Fail Clin. 2018;14(2):119-28. doi:10.1016/j.hfc.2017.12.007.
5. Meyer S, van der Meer P, van Tintelen JP, et al. Sex-related differences in cardiomyopathies. European Journal of Heart Failure. 2014;16(3):238-47. doi:10.1002/ejhf.15.
6. Pelliccia F, Limongelli G, Autore C, et al. Sex-related differences in cardiomyopathies. Int J Cardiol. 2019;286:239-43. doi:10.1016/j.ijcard.2018.10.091.
7. Norris CM, Yip CYY, Nerenberg KA, et al. State of the Science in Women's Cardiovascular Disease: A Canadian Perspective on the Influence of Sex and Gender. J Am Heart Assoc. 2020;9(4):e015634. doi:10.1161/JAHA.119.015634.
8. Murphy E, Amanakis G, Fillmore N, et al. Sex differences in metabolic cardiomyopathy. Cardiovasc Res. 2017;113(4):370-7. doi:10.1093/cvr/cvx008.
9. Filatova OV, Chursina VI. Characteristic features of Echo parameters in men and women with different geometric configurations. Human Physiology. 2016;42(5):63-72. (In Russ.) doi:10.7868/s0131164616050064.
10. Phua AlH, Le T-T, Tara SW, et al. Paradoxical Higher Myocardial Wall Stress and Increased Cardiac Remodeling Despite Lower Mass in Females. J Am Heart Assoc. 2020;9(4):e014781. doi:10.1161/JAHA.119.014781.