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Gender-Based and Age-Related Peculiarities of Lipid Metabolism in Chronic Heart Failure Secondary to Overweight and Obesity

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Keywords: heart failure; lipid metabolism; overweight; gender; age

Abstract.

Chronic heart failure is often accompanied by comorbidities including obesity being the major one. It significantly aggravates the course of the disease and clinical outcome. Changes in the plasma concentration of lipids in chronic heart failure were demonstrated by many studies. Recently a considerable number of works has appeared in which a negative influence of both high and low levels of lipids on the course, consequences and survival in patients with chronic heart failure was observed.

The objective of the research was to study gender-based and age-related peculiarities of lipid metabolism in chronic heart failure secondary to overweight and obesity.

Material and methods. There were examined 212 patients with chronic heart failure functional class I-III having normal body weight, I-III degree abdominal obesity or being overweight. Patients underwent complete blood count and biochemical blood analysis; instrumental examination was performed according to the existing guidelines for the diagnosis and treatment of chronic heart failure. Statistical processing of the obtained material was performed using an advanced analytics software package Statistica 6.0.

Results and discussion. Both atherogenic and antiatherogenic components of lipid metabolism predominated in females. Age-related changes were presented by higher levels of atherogenic indices and prevalence of dyslipidemia in young patients reducing with age in parallel with the deepening of chronic heart failure.

Problem statement and analysis of the recent research

Chronic heart failure (CHF) is often accompanied by comorbidities including obesity being the major one. It significantly aggravates the course of the disease and clinical outcome [1]. Changes in the plasma concentration of lipids in CHF were demonstrated by many studies [2-6]. The epidemiological studies demonstrated that dyslipidemia can directly influence the development and progression of CHF [11]. Low levels of atherogenic lipids and elevated levels of anti-atherogenic ones are of undoubted importance in the development and progression of atherosclerosis and ischemic heart disease (IHD) which is especially important considering the fact that up to 70% of cases of CHF are of ischemic genesis [9]. Therapeutic tactics in dyslipidemia aimed at reducing the concentration of atherogenic and increasing the anti-atherogenic fractions of lipids is the basis for primary and secondary prevention [3]. Several preclinical and clinical studies allowed the use of statins in patients with CHF [4, 7, 10] concentrating their arguments on pleiotropy effect, ability to improve endothelial dysfunction of blood vessels as well as to reduce inflammatory processes – the main links in the pathogenesis of CHF independently of cholesterol lowering [6, 8]. However, recently a considerable number of works has appeared in which a negative influence of both high and low levels of lipids on the course, consequences and survival in patients with chronic heart failure was observed [2, 5].

Considering the continuous incidence of CHF with concomitant overweight and obesity, a small number of research works related to study of lipid metabolism, polarity of views regarding the prognostic significance of lipid levels in these patients, the chosen direction of research is timely and relevant.

The objective of the research was to study gender-based and age-related peculiarities of lipid metabolism in chronic heart failure secondary to overweight and obesity.

Material and methods

There were examined 212 patients with CHF functional class (FC) I-III having normal body weight, I-III degree abdominal obesity or being overweight. Patients were treated in the Central Clinical Hospital No 4, Zaporizhzhya. The diagnosis of CHF was made according to the Guidelines of the Ukrainian Association of Cardiology and the Ukrainian Association of Specialists in Heart Failure on the diagnosis and treatment of CHF (2012) [1]. FC of CHF was determined according to the New York Heart Association (NYHA) Functional Classification. The presence of normal body weight, overweight, obesity and its degree was determined by calculation of the body mass index (BMI). CHF was induced by arterial hypertension (AH), chronic forms of ischemic heart disease (IHD) (stable angina, post-infarction (PICS) and diffuse cardiosclerosis), and their combinations.

The study was conducted according to the standards of Good Clinical Practice and the principles of the Helsinki Declaration. The Ethical Committee of Zaporizhzhya State Medical University approved the protocol; only patients who gave written informed consent were included in this study.

Patients underwent complete blood count and biochemical blood analysis, instrumental examination was performed according to the existing guidelines for the diagnosis and treatment of CHF. The levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) were determined. The level of low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula: LDL-C=TC–HDL-C–(0.45 x TG). The level of very-low-density lipoproteins cholesterol (VLDL-C) was determined according to the formula: VLDL-C=TG/2.2. The atherogenic coefficient (AC) was calculated by the formula proposed by Klimov AM – AC = (TC–HDL-C)/HDL-C. Integral indicators of atherogenic and anti-atherogenic fractions of lipids were determined as the TG/HDL-C and LDL-C/HDL-C ratios.

Statistical processing of the obtained material was performed using an advance analytics software package Statistica (version 6.0, Stat Soft Inc, USA, license number AXXR712D833214FAN5). The hypothesis of normality of distribution of parameters was checked by the Shapiro-Wilk test. According to the sample size and distribution of values parametric (Student's t-test) and nonparametric statistical methods (Mann-Whitney U test) were used. The comparison of categorical variables was performed using bilateral Fisher's exact test or chi-square test. The relations between the indicators were assessed using correlation analysis and calculating the Spearman's rank correlation coefficient (r). The results are presented as mean value ± standard deviation (M±S). The difference was considered significant at $p<0.05$

Results

General characteristics and lipid profile in CHF secondary to overweight and obesity according to gender are presented in Table 1. It should be noted that women were older (4.4 years, $p<0.05$). CHF FC did not have any gender-based differences, and the BMI in men was significantly lower than that in women (5.9%). In women the levels of TC, HDL-C, VLDL-C and TG were higher than in men – by 8.3%, 11.6%, 8.9% and 9.3%, respectively ($p<0.05$). The level of LDL-C in women was unreliable higher. The indicator of the AC, the LDL-C/HDL-C and TG/HDL-C ratios insignificantly dominated in men.

Table 1

General characteristics and lipid profile in patients with CHF secondary to overweight and obesity according to gender

Parameter	Women (n=128)	Men (n=84)
Age, years	65.6±10.1	61.2±13.4*
CHF, FC	2.02±0.81	2.01±0.74
BMI, kg/m^2	32.3±5.78	30.5±6.18*
TC, mmol/l	5.47±1.49	5.05±1.36*
HDL-C, mmol/l	1.35±0.34	1.21±0.30*
LDL-C, mmol/l	3.26±1.29	3.11±1.13
VLDL-C, mmol/l	0.86±0.60	0.79±0.73*
TG, mmol/l	1.89±1.32	1.73±1.60*
AC	3.17±1.08	3.34±1.35
LDL-C/ HDL-C ratio	2.48±0.88	2.68±1.11
TG/ HDI-C ratio	1.54±1.20	1.62±2.14

Note:

*- the difference between indicators is statistically significant ($p<0.05$)

When analyzing the prevalence of changes in laboratory parameters in CHF there were no significant gender-based differences (Table 2). Elevated levels of atherogenic TC, LDL-C, VLDL-C, TG, and low levels of anti-atherogenic HDL-C predominated in women. The frequency of normal and low levels of TC, HDL-C, LDL-C, VLDL-C and TG was greater in men. Elevated levels of the AC, the LDL-C/HDL-C ratio were more often observed in men, and the TG/HDL-C ratio was more prevalent among women.

Table 2

Prevalence of changes in parameters of lipid metabolism in patients with CHF secondary to overweight and obesity according to gender

Parameter	Women (n=128)	Men (n=84)
TC>5 mmol/l, n (%) TC 3.2 - 5 mmol/l, n (%) TC<3.2 mmol/l, n (%)	81 (63.28) 40 (31.25) 7 (5.47)	43 (51.2) (41.67) 6 (7.0%)
HDL-C<1.0 in men, and <1.3 in women n (%) HDL-C>1.0 in men, and >1.3 in women n (%)	53 (41.4) 75 (58.6)	19 (22.6) 65 (77.4)
LDL-C>3 mmol/l, n (%) LDL-C 2-3 mmol/l, n (%) LDL-C<2 mmol/l, n (%)	71 (55.5) 38 (29.7) 19 (14.8)	38 (45.2) 31 (36.9) 15 (17.9)
VLDL-C>1.0 mmol/l, n (%) VLDL-C<1.0 mmol/l, n (%)	28 (21.9) 100 (78.1)	16 (19.0) 68 (81.0)
TG>1.7 mmol/l, n (%) TG 0.5-1.7 mmol/l, n (%) TG<0.50 mmol/l, n (%)	50 (39.1) 78 (60.9) -	27 (32.1) 55 (65.5) 2 (2.4)
AC>3.0, n (%) AC<3.0, n (%)	61 (47.7) 67 (52.3)	47 (56.0) 37 (44)
LDL-C/HDL-C ratio >2.26, n (%) LDL-C/HDL-C ratio<2.26, n (%)	72 (56.3) 56 (43.7)	49 (58.3) 35 (41.7)
TG/HDL-C ratio>1.48, n (%) TG/HDL-C ratio<1.48, n (%)	45 (35.2) 83 (64.8)	28 (33.3) 56 (66.7)

The results of studying age-related peculiarities of lipid metabolism in patients with CHF secondary to overweight and obesity are presented in Table 3. Among young patients men (38%) dominated; women (54.4%) were more often observed among elderly patients. Equal distribution of patients according to gender was observed among middle-aged patients; among senile patients women dominated. The number of women among elderly patients was greater compared to young and middle-aged patients - 41.7% and 22.7%, respectively, $p<0.05$. The opposite changes were observed among men. The progression of CHF with age manifested as a reliable increase in the average value of FC of the disease was observed. In the first two age groups there was a tendency to an increase in FC of CHF. The indicators of elderly and senile groups being different between themselves (29.8%, $p<0.05$) were significantly higher – by 33.1% and 23.5% and by 72.7% and 60.2%, respectively. The BMI in the first three groups had a tendency to decrease; in senile patients it was the lowest and yielded the values of young and middle-aged patients – 14.7% and 9.8%, respectively, $p<0.05$. There was no significant difference in the levels of TC and LDL-C; maximum values were observed in young patients; minimum values were detected in senile patients. There was a tendency to increase in the concentration of HDL-C with increasing age. Maximum values of VLDL-C were observed in young and middle-aged patients significantly yielding those in elderly (by 49.3% and 33.3%, respectively) and senile (by 69.7% and 51.5%, respectively) patients. The level of TG in young patients exceeded that in elderly and senile patients - by 48.5% and 67.8%, respectively, ($p<0.05$). The concentration of TG in middle-aged patients significantly exceeded that in elderly

patients – by 33.9% and 51.4%, respectively. With increasing age there was a decrease in the AC; in young patients this parameter exceeded that in elderly and senile patients – by 27.2% and 31.5%, respectively ($p<0.05$). The LDL-C/HDL-C ratio tended to decrease with aging while the TG/HDL-C ratio decreased significantly. Maximum value of TG/HDL-C ratio was observed in young patients; it was significantly higher than that in elderly and senile patients – by 63% and 78.9%, respectively. The TG/HDL-C ratio in middle-aged patients exceeded that in elderly and senile patients - by 47.4% and 61.8%, respectively, $p<0.05$. There were significant correlations of age with the following parameters of lipid metabolism: VLDL-C (r=-0.17), TG (r=-0.17), AC (r=-0.16), TG/HDL-C ratio (r=-0.19).

Table 3

General characteristics and parameters of lipid profile in patients with CHF secondary to overweight and obesity depending on age

Parameter	<45 years (n=13)	45-59 years (n=62)	60-74 years (n=99)	75-89 years (n=38)
Women, n (%)	4 (31)	31 (50)	72 (72.7)*[1]	21 (55.3)
Men, n (%)	9 (69)	31 (50)	27 (27.3)*[1]	17 (44.7)
CHF, FC	1.54±0.78	1.66±0.75	2.05±0.71*[1]	2.66±0.58*[12]
BMI, kg/m^2	34.3±5.43	32.7±6.66	31.2±5.70	29.9±5.24*[1]
TC, mmol/l	5.68±1.38	5.29±1.30	5.34±1.64	5.09±1.18
HDL-C, mmol/l	1.17±0.32	1.26±0.35	1.33±0.33	1.32±0.32
LDL-C, mmol/l	3.38±1.07	3.15±1.12	3.25±1.40	3.10±0.99
VLDL-C, mmol/l	1.12±0.72	1.0±0.98	0.75±0.41*[1]	0.66±0.32*[1]
TG, mmol/l	2.45±1.58	2.21±1.17	1.65±0.90*[1]	1.46±0.70*[1]
AC	3.97±0.94	3.41±1.35	3.12±1.08*	3.02±1.20*
LDL-C/HDL-C ratio	2.95±0.86	2.64±1.11	2.50±0.91	2.46±0.95
TG/ HDI-C ratio	2.20±1.70	1.99±2.57	1.35±0.90*[1]	1.23±0.80*[1]

Notes:
the difference between indicators is statistically significant compared to:
*- in Group I;
1 – in Group II,
2 - in Group III ($p<0.05$).

There were no significant age-related differences in the prevalence of changes in TC, HDL-C and LDL-C significant differences in age are not established. The increase in parameters was observed in young patients. Maximum prevalence of elevated VLDL-C levels was also detected in young patients exceeding those in middle-aged, elderly and senile patients - by 20.4%, 29% and 33%, respectively, $p<0.05$. There were observed the opposite changes in frequency of normal levels of VLDL-C increasing with age. The prevalence of elevated TG levels was most often observed among young patients exceeding that among middle-aged, elderly, and senile patients – by 28.9%, 34.9%, and 45.5%, respectively, $p<0.05$. With age, the prevalence of normal level of TG increased; in elderly and senile patients it was significantly greater compared to young patients – by 34.9% and 42.9%, respectively. Low levels of TG were detected in 1 middle-aged patient and 1 senile patient. The percentage of patients with high AC in the first three age groups had a tendency to decrease.

The AC in senile patients yielded that in young patients (by 32.2%, p<0.05). There were observed the opposite changes in the prevalence of normal levels of AC increasing with age. There were no significant differences in the prevalence of the LDL-C/HDL-C ratio. The increase in the TG/HDL-C ratio was more frequently observed in young patients exceeding that in middle-aged, elderly and senile patients – by 32.1%, 37.9% and 42.9%, respectively, p<0.05. The prevalence of normal TG/HDL-C ratio changes increasing with age had the opposite changes.

Table 4

Prevalence of changes in parameters of lipid metabolism in patients with CHF secondary to overweight and obesity depending on age

Paremeter	<45 years (n=13)	45-59 years (n=62)	60-74 years (n=99)	75-89 years (n=38)
TC>5 mmol/l, n (%) TC 3.2 - 5 mmol/l, n (%) TC<3.2 mmol/l, n (%)	9 (69.2) 4 (30.8) -	37 (59.7) 21 (33.8) 4 (6.5)	56 (56.6) 38 (37.3) 6 (6.1)	22 (57.9) 13 (34.2) 3 (7.9)
HDL-C<1.0 in men, and <1.3 in women n (%) HDL-C>1.0 in men, and >1.3 in women n (%)	6 (46.2) 7 (53.8)	19 (30.6) 43 (69.4)	34 (34.3) 65 (65.7)	13 (34.2) 25 (65.8)
LDL-C>3 mmol/l, n (%) LDL-C 2-3 mmol/l, n (%) LDL-C<2 mmol/l, n (%)	8 (61.5) 4 (30.8) 1 (7.7)	32 (51.6) 30 (32.3) 10 (16.1)	49 (49.5) 33 (33.3) 17 (17.2)	20 (52.6) 12 (31.6) 6 (15.8)
VLDL-C>1.0 mmol/l, n (%) VLDL-C<1.0 mmol/l, n (%)	6 (46.2) 7 (53.8)	16 (25.8) 46 (74.2)	17 (17.2)* 82 (82.8)*	5 (13.2)* 33 (86.8)*
TG>1.7 mmol/l, n (%) TG 0.5-1.7 mmol/l, n (%) TG<0.50 mmol/l, n (%)	9 (69.2) 4 (30.8) -	25 (40.3) 36 (58.1) 1 (1.6)	34 (34.3)* 65 (65.7)* -	9 (23.7)* 28 (73.7)* 1 (2.6)
AC>3.0, n (%) AC<3.0, n (%)	10 (76.9) 3 (23.1)	33 (53.2) 29 (46.8)	48 (48.5) 51 (51.5)	17 (44.7)* 21 (55.3)*
LDL-C/HDL-C ratio >2.26, n (%) LDL-C/HDL-C ratio<2.26, n (%)	9 (69.2) 4 (30.8)	33 (53.2) 29 (46.8)	56 (56.6) 43 (43.4)	23 (60.5) 15 (39.5)
TG/HDL-C ratio>1.48, n (%) TG/HDL-C ratio<1.48, n (%)	9 (69.2) 4 (30.8)	23 (37.1)* 39 (62.9)*	31 (31.3)* 68 (68.7)*	10 (26.3)* 28 (73.7)*

Note:

*- the difference between indicators is statistically significant (p<0.05)

Discussion

Thus, in CHF secondary to overweight and obesity more significant disorders of lipid metabolism manifested themselves as a predominance of atherogenic TC, VLDL-C and TG occurred in women. At the same time, a significantly higher level of antiatherogenic HDL-C was observed in women, which may be due to the higher range of normal values, the prevalence of the BMI and compensatory reaction of the organism to elevated levels of atherogenic components of lipid metabolism. With age, there was a significant reduction in the concentration of atherogenic VLDL-C, TG, AC and the TG/HDL-C ratio which was accompanied by a significantly higher FC of CHF in elderly and senile patients. The prevalence of high levels of VLDL-C, TG, AC and the TG/HDL-C ratio

significantly decreasing with age was the highest among young patients. As a consequence, the opposite picture regarding the frequency of detection of normal levels of these parameters significantly increasing with age was observed. The obtained age-related changes in the parameters of lipid metabolism can be explained by the decrease in functional activity of the liver with aging and more severe course of CHF, which according to current literature are accompanied by lower levels of studied parameters.

Conclusions

In CHF secondary to overweight and obesity gender-based and age-related changes in the parameters of lipid metabolism are represented by the following:

1. Both atherogenic and antiatherogenic components of lipid metabolism predominate in females.

2. Age-related changes are presented by higher levels of atherogenic indices and prevalence of dyslipidemia in young patients reducing with aging in parallel with the deepening of CHF.

Prospects for further research

We plan to study the features of lipid metabolism in patients with CHF depending on degree of excess weight and the severity of the disease as well as the correlation of these parameters with structural and functional indices of the heart, concentration of adipocytokines, carbohydrate metabolism and coagulation hemostasis.

References

1. Voronkov LH, et al. Guidelines for the diagnosis and treatment of chronic heart failure (2012). Ukrainskiy kardiologicheskiy zhurnal. 2013;1:6–44.
2. Kravchun PP. The role of lipid metabolism in the pathogenesis of CHF in patients with post-infarction cardiosclerosis, diabetes mellitus type 2 and obesity. Odeskyi medychnyi zhurnal. 2015;1(147):41-44.
3. AHA Scientific Statement. Prevention of heart failure. Circulation. 2008;117:2544–2565.
4. Charach G, George J, Roth A, et al. Baseline Low-Density Lipoprotein Cholesterol Levels and Outcome in Patients with Heart Failure. Am. J. Cardiol. 2010;105:100-104. doi: 10.1016/j.amjcard.2009.08.660.
5. Charach G, George J. LDL- Cholesterol and Outcome Prediction in Patients with Congestive Heart Failure. J. Cardiol. Curr. Res. 2014;1(2):100-107. doi: 10.15406/jccr.2014.01.00007
6. Domanski M, Coady S, Fleg J, et al. Effect of statin therapy on survival in patients with non-ischemic dilated cardiomyopathy (from the Beta-blocker Evaluation of Survival Trial [BEST]). Am. J. Cardiol. 2007;99:1448-1450.
7. Raina A, Pickering T, Shimbo D. Statin use in heart failure: a cause for concern? Am. Heart J. 2006;152:39-49.
8. Sakatani T, Shirayama T, Suzaki Y, et al. The association between cholesterol and mortality in heart failure. Comparison between patients with and without coronary artery disease. Int. Heart J. 2005;46:619-629.
9. Strandberg TE. Lipid-lowering drugs and heart failure: where do we go after the statin trials? Current Opinion in Cardiology. 2010;25:385-393.
10. Tousoulis D, Charakida M, Stefanadi E, et al. Statins in heart failure. Beyond the lipid lowering effect. Int. J. Cardiol. 2007;115:144-150. doi: 10.1016/j.ijcard.2006.03.094

11. Velagaleti RS, Massaro J, Vasan RS, et al. Relations of lipid concentrations to heart failure incidence: the Framingham Heart Study. Circulation. 2009;120:2345-2351. doi: 10.1161/CIRCULATIONAHA.109.830984.