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THE EFFECT OF YOGA PRACTICE ON LIPID PROFILES IN PATIENTS WITH CHRONIC HEART FAILURE

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Abstract. The effect of yoga practice on lipid profiles in patients with chronic heart failure. Babkina T.M., Smyrnova G.S., Mykhailenko L.A., Kozarenko T.M., Globa M.V., Kundina V.V. *The aim of the present study was to assess the efficiency of yoga practice in addition to the standard medical therapy in patients with chronic heart failure (HF) and dyslipidemia. One hundred and two patients with chronic HF and dyslipidemia were divided into the control group (CG) – 54 patients and the yoga group (YG) – 48 patients. The CG was prescribed standard therapy for chronic HF (angiotensin converting enzyme inhibitors, β-blockers, aldosterone antagonists, digoxin, loop diuretics, statins, antiplatelet agents) and dyslipidemia. The YG additionally followed lifestyle modification in the form of 1 h daily practice of yoga for a period of 3 months. All patients completed the questionnaire reporting on their age, gender, medical history and treatment. The fasting blood samples were analyzed for total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol, C-reactive protein, interleukin-8 and tumor necrosis factor -α on admission to the department and after 3 months of treatment. The pre-specified duration of the enrollment period was two years and during that time we interviewed 168 patients. Forty-two did not meet the inclusion criteria for the study, 24 patients refused to participate. A total of 102 patients were enrolled, of them, 54 were included into the control group and 48 into the yoga group. At baseline, there were no significant ($p>0.05$) differences between the groups in clinical characteristics of the patients. On admission to hospital the patients of both groups received standard therapy in comparable doses. By the end of the study, a significant ($p<0.05$) reduction in TC, TG and LDL-C levels was observed in both groups with a tendency to more considerable changes in YG. Correlation analysis revealed the positive correlation relationship between TC, LDL-C levels and cytokines. The present study has shown that the practice of yoga in addition to the standard therapy in patients with HF and dyslipidemia could be associated with lipid profile improvements.*

Реферат. Вплив йоги на ліпідні профілі в пацієнтів з хронічною серцевою недостатністю. Бабкіна Т.М., Смирнова Г.С., Михайленко Л.А., Козаренко Т.М., Глоба М.В., Кундіна В.В. *Мета дослідження – оцінити ефективність йоги в пацієнтів із хронічною серцевою недостатністю (СН) та дисліпідемією. Сто два пацієнти з хронічною СН та дисліпідемією були розподілені в контрольну групу (КГ) з 54 пацієнтів та групу йоги (ЙГ) із 48 пацієнтів. КГ було призначено стандартну терапію хронічної СН (інгібітори ангіотензинперетворюючого ферменту, β-адреноблокатори, антагоністи альдостерону, дигоксин, петльові діуретики, статини, антиагреганти) та дисліпідемії. У ЙГ додатково проводили модифікацію способу життя у вигляді 1 години щоденної практики йоги протягом 3 місяців. Усі пацієнти заповнювали анкету, повідомляючи про свій вік, стать, історію хвороби та лікування. Пацієнтам аналізували рівні загального холестерину (ЗХ), тригліцеридів (ТГ), холестерину ліпопротеїдів низької щільності (ЛПНЩ-Х), холестерину ліпопротеїнів високої щільності, С-реактивного білка, інтерлейкіну-8 та фактора некрозу пухлини -α при надходженні у відділення та через 3 місяці лікування. Нами було обстежено 168 пацієнтів, з них 42 – не відповідали критеріям включення в дослідження, 24 – відмовились брати участь у дослідженні. Усього розподілено 102 пацієнти, з них 54 були включені до КГ та 48 до ЙГ. На початку дослідження не було виявлено значущих ($p>0,05$) відмінностей між групами за клінічними характеристиками пацієнтів. Під час госпіталізації пацієнти обох груп отримували стандартну терапію в порівняних дозах. Наприкінці дослідження в обох групах спостерігалось значне ($p<0,05$) зниження рівня ЗХ, ТГ*

та ЛПНЩ-Х з тенденцією до більш значних змін у ЙГ. Кореляційний аналіз виявив позитивний взаємозв'язок між рівнем ЗХ, ЛПНЩ-Х та концентрацією цитокінів. Результати нашого дослідження продемонстрували, що додавання йоги до стандартної терапії в пацієнтів із хронічною СН та дисліпідемією може асоціюватися з поліпшенням ліпідного профілю.

Chronic heart failure (HF) is associated with high morbidity and mortality, and an enormous economic burden on the healthcare system [7]. The hospitalization rate due to this disease is still reported high and the number of patients with HF is increasing annually. The timely detection of modifiable risk factors for chronic HF will help determine and adopt optimal prevention strategies.

It is well known that dyslipidemia, defined as dysfunction and/or lipid imbalance (of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) levels, high-density lipoprotein cholesterol (HDL-C), triglyceride (TG)), is an important risk factor for coronary heart disease (CHD) and stroke. Statins have been shown to be highly effective, particularly in treating persons at high risk of CHD. Moreover, according to clinical trial results, statin treatment has been proven to reduce the incidence of chronic HF [4]. These data suggest that dyslipidemia is also a risk factor for chronic HF. Recent investigation detected a direct association between the ratio of TC and HF risk [5].

Numerous studies show that immune cells play a main role in cardiac injury and are present in cardiac tissue early in disease [12]. Immune cells, identified in the heart, include macrophages, monocytes, neutrophils, B cells, T cells, etc. Inflammation in non-immune-mediated cardiac injury leads to a secretion of inflammatory cytokines and chemokines such as interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF) -α, etc. An increase in levels of cytokines and chemokines leads to the recruitment of neutrophils and monocytes. Initially, the immune cells infiltrated the cells to scavenge dead and dying cardiomyocytes by digesting the tissue with proteolytic enzymes. The inflammatory cascade is amplified by the dead cells causing a release of inflammatory cytokines which further amplify inflammation through their effect on leukocytes, endothelial cells, and cardiomyocytes.

A possible role of proinflammatory cytokines in chronic HF was first reported by Levine *et al* [8]. Subsequently, other studies suggested that concentrations of TNF-α, IL-6, IL-1β and C-reactive protein (CRP) in patients with HF were significantly higher than in the control subjects. Results of numerous studies indicated that serum proinflammatory cytokines were associated with an increased risk for chronic HF [2]. In recent years, it has become evident that systemic inflammation is also the main driver for atherosclerosis and inflammatory markers have a strong association with dyslipidemia. Hence, it is highly essential to identify the cytokines released by various cells and understand their role in the inflammatory cascade.

Taking into account the abovementioned, the improvement of dyslipidemia treatment strategies in patients with HF is obvious. During the last decades, traditional medicine has been actively introducing additional methods of non-pharmacological treatment, including yoga practice. This system of physical and breathing exercises as well as meditation techniques has been known for more than 4 thousand years. Since the second half of the XX century some scientific findings have shown that yoga can be useful in the prevention of cardiovascular disease among healthy individuals. However, no data are currently available for studying the efficiency of yoga practice in the treatment of patients with HF and dyslipidemia.

Therefore, the aim of the present study was to evaluate the effect of yoga practice on the lipid profiles in patients with chronic HF and dyslipidemia.

MATERIALS AND METHODS OF RESEARCH

We conducted a prospective, single-center, non-blinded trial in the National Medical University at the Department of the Urgent Cardiology and Rehabilitation of the Institute of Emergency and Recovery Surgery between September 2013 and November 2015. A total of 102 participants were enrolled. The study participants were included if they met the following criteria: age ≥18 years; stable ischemic heart disease in history and chronic HF with symptoms leading to hospitalization; dyslipidemia. Chronic HF was diagnosed with the presence of chronic HF history and typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema).

Dyslipidemia was defined as the presence of one or more abnormal serum lipid concentrations (TC level above 5.0 mmol/L and/or LDL-C level above 4.8 mmol/L; HDL-C lower than 1.68 mmol/L in men and 1.42 mmol/L in women). Hypertriglyceridemia was defined as TG level higher than 1.7 mmol/L.

One hundred and two patients with chronic HF and dyslipidemia were divided into the control group (CG) of 54 patients and the yoga group (YG) of 48 patients. The CG was prescribed standard therapy for chronic HF (angiotensin converting enzyme

inhibitors, β-blockers, aldosterone antagonists, digoxin, loop diuretics, antiplatelet agents) and dyslipidemia (statins). The YG additionally followed lifestyle modification in the form of 1 h daily practice of yoga for a period of 3 months.

All patients completed the questionnaire reporting on their age, gender, medical history and treatment. The 8 ml blood samples of each patient were collected in test tubes after an overnight fasting under all aseptic conditions. The fasting blood samples were analyzed for TC, TG, LDL-C and HDL-C on admission to the department and after 3 months of treatment. TC, TG, LDL-C, HDL-C levels were determined by colorimetric and photometric methods using the automatic analyzer AU480 (Beckman Coulter, USA) [9]. CRP level was determined by an immunoturbidimetric method with latex amplification using the Cobas 6000 automatic biochemical analyzer (Roche Diagnostics, Switzerland) [10]. IL-8 and TNF-α concentrations were determined by enzyme-linked immunosorbent assay using the Multiscan programmed apparatus (LabSystem, Finland) and the Bender MedSystems commercial test systems from Bioscience (Austria). CRP and pro-inflammatory cytokines were determined on admission to the department and after 3 months of treatment.

Yoga classes were conducted under control of an experienced yoga teacher twice a week and lasted for 60 minutes. During each session, patients completed the following: a 5-min warm-up phase including breathing exercises (pranayama), a 40-min period of standing and/or seated yoga postures (asanas), and finally, a 15-min relaxation phase. Sessions were conducted on an individual basis according to individual medical and orthopedic limitations. Breathing exercises consisted of slow, deep inhalation and exhalation through the nasal passageways in a one-to-longer-than-one ratio, without breath retention. Inhalation was taught to begin with sequential involvement of the abdomen, lower chest, and then upper chest, with the same sequence in reverse, during exhalation. Meditation and relaxation were performed in a supine or seated position according to the patient's comfort level. After 2 weeks of supervised yoga training, each patient was given instructions for the ongoing medical and non-medical treatment to follow it regularly at home up to 3 months. The posthospital control over patients' adherence to doctors' instructions was carried out by phone or during routine check-ups.

The study was approved by the biomedical ethics commission of Shupyk National Healthcare University of Ukraine and was conducted in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – "Ethical principles for medical research involving human subjects" and "Universal Declaration on Bioethics and Human Rights" (UNESCO).

The obtained results were processed on a personal computer using statistical analysis package STATISTICA ver. 10.0.1011.0 (StatSoft Inc., serial number BXXR210F561922FA-8) [1]. The D'Agostinho & Pearson, Shapiro-Wilk and Kolmogorov-Smirnov tests were used to assess the normality of the data distribution. The paired and unpaired Student's t-test was used to compare normally distributed continuous variables between the groups. Descriptive statistics parameters for continuous variables were presented as the arithmetic mean and standard deviation. The χ^2 (Pearson) criterion was used to assess the statistical significance of the differences between two relative data. The relationship between two variables was measured by using Spearman correlation coefficient (r). The significant association was defined by p value <0.05.

RESULTS AND DISCUSSION

The pre-specified duration of the enrollment period was two years and during that time we interviewed 168 patients. Forty-two did not meet the inclusion criteria for the study, 24 patients refused to participate. A total of 102 patients were enrolled, of them, 54 were included into the CG and 48 into the YG.

At baseline, there were no significant (p>0.05) differences between the groups in clinical characteristics of the patients (Table 1). On admission to hospital the patients of both groups received standard therapy in comparable doses.

By the end of the study, a significant (P < 0.05) reduction in TC, TG and LDL-C levels was observed in both groups with a tendency to more considerable changes in YG if compared to controls (Table 2).

No difference was found in *HDL-C levels*. Correlation analysis revealed the positive correlation relationship between TC, LDL-C levels and cytokines (Table 3).

Multiple studies have noted that dyslipidemia plays a significant role in the development of abnormal cardiac structure and function [6]. Elevated TC and decreased HDL-C levels are associated with increased blood pressure levels, arterial stiffness related to left ventricular mass and wall thickness [14]. Experimental evidence from the animal-based research shows that diet-induced hypercholesterolemia leads to a decrease in systolic and diastolic functions, an increase in the end-diastolic volume and pressure of the left ventricle, and a decrease in the sensitivity of myocardial perfusion to stress. That is why it is important to find effective ways to correct the lipid profile in such patients.

Clinical characteristics of the groups of patients

Parameter	CG (n=54)	YG (n=48)	p values
Age, years	67.2±6.1	69.3±5.6	p=0.67
Gender (M:F)	32:22	26:22	χ^2=0.1, p=0.75
BMI (kg/m2)	26.6±0.9	25.8±0.5	p=0.09
FC II (NYHA)	n=9 (17%)	n=10 (22%)	χ^2=0.04, p=0.84
FC III (NYHA)	n=35 (65%)	n=30 (62%)	χ^2=0.01, p=0.96
FC IV (NYHA)	n=10 (18%)	n=8 (16%)	χ^2=0.01, p=0.96
Diabetes mellitus	n=12 (22%)	n=9 (19%)	χ^2=0.01, p=0.91
Arterial hypertension	n=45 (83%)	n=35 (73%)	χ^2=1.07, p=0.3
Hypercholesterolemia	n= 28 (52%)	n= 27 (56%)	χ^2=0.06, p=0.8
History of myocardial infarction	n=35 (65%)	n=35 (73%)	χ^2=0.05, p=0.82

Notes: CG – control group; YG – yoga group; BMI – body mass index; HF – heart failure; FC – functional class; NYHA – New York Heart Association.

The results of our work showed that the yoga practice in addition to the standard therapy has a positive effect on the lipid profile in patients with chronic CH and dyslipidemia that is consistent with literature data [3]. The beneficial effect of yoga in the management of hyperlipidemia cannot just be attributed only to the caloric expenditure as there is no rapid muscle activity and energy generation involved in yoga. Different kinds of chronic stress are known to lead to persistent cortisol elevation which causes central obesity and dyslipidemia. The yoga practice reduces stress- induced sympathetic over-activity that *leads* to a *lowering* of the *cortisol levels* [11]. Better ability to overcome stress resulting in lowered cortisol levels can be cited as a possible mechanism for improvements in lipid profiles of patients who practice yoga exercises. Therefore, in the perspective of our further work we can determine the study of the stress impact on the course of chronic HF and dyslipidemia, as well as the yoga role in these processes.

Dynamics of lipid profile in both groups (M±m)

Parameter	Patients			
	CG (n=54)		YG (n=48)	
	at baseline	after 3 m	at baseline	after 3 m
TC, mmol/l	6.23±0.81	5.75±0.56*	6.34±0.61	5.28±0.74*
LDL-C, mmol/l	3.78±0.55	3.46±0.34*	3.76±0.44	3.20±0.82*
HDL-C, mmol/l	1.24±0.21	1.29±0.19	1.26±0.22	1.31±0.24
TG, mmol/l	2.69±0.34	2.31±0.25*	2.73±0.42	2.16±0.31*

Notes: CG – control group; YG – yoga group; TC - total cholesterol; TG - triglycerides; LDL-C – low-density lipoprotein-cholesterol; HDL-C – high-density lipoprotein-cholesterol; * – results are statistically significant if compared to the baseline.

The results of a correlation analysis between lipoproteins and cytokines

Parameter	IL-8	TNF-α	CRP
TC, mmol/l	r=0.31, p<0.05	r=0.26, p<0.05	r=0.36, p<0.05
LDL-C, mmol/l	r=0.39, p<0.05	r=0.28, p<0.05	r=0.42, p<0.05
HDL-C, mmol/l	r=0.17, p>0.05	r=0.13, p>0.05	r=0.09, p>0.05
TG, mmol/l	r=0.09, p>0.05	r=0.07, p>0.05	r=0.1, p>0.05

Notes: TC – total cholesterol; TG – triglycerides; LDL-C – low-density lipoprotein-cholesterol; HDL-C – high-density lipoprotein-cholesterol; IL-8 – interleukin-8; TNF-α – tumor necrosis factor-α; CRP – C – reactive protein.

In addition, recent scientific findings have implicated multiple inflammatory mediators in the progression of HF and cardiovascular disease. During chronic diseases, inflammation can also cause various changes in lipid metabolism, including a decrease in HDL-C, increases in TG and LDL-C levels [13]. We found such confirmation in our study: a positive correlation between TC, LDL-C and cytokines may explain one of the pathogenetic mechanisms of dyslipidemia in patients with chronic HF. It is known that yoga decreases body fat percentage and fat is a source of pro-inflammatory cytokines. Through this mechanism the yoga practice can lead to the normalization of levels of TC and LDL-C.

CONCLUSIONS
The present study has shown a significant reduction in TC, TG and LDL-C levels was observed in both groups with a tendency to more considerable changes in YG if compared to controls. The causes of this phenomenon have not been fully studied. It opens up prospects for the further work.

Contributors:
Babkina T.M. – supervision;
Smyrnova G.S. – conceptualization, investigation;
Mykhailenko L.A. – writing – review & editing;
Kozarenko T.M. – methodology, resources;
Globa M.V. – writing – original draft, and supervision;
Kundina V.V. – investigation, validation.

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