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Skeletal muscle changes and incidence of sarcopenia in patients with hypertension

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Abstract. Background. The research on sarcopenia and arterial hypertension (HTN) suggests that there is a relationship between left ventricular dysfunction and the severity of sarcopenia. This research **purposed** to study the skeletal muscle changes and sarcopenia prevalence in patients with HTN. **Materials and methods.** 180 patients with HTN stage II with preserved ejection fraction, aged 63.8 ± 6.2 years, were examined. 50 % of patients (60 women and 30 men) had a SARC-F score of more than 4 points (study group), the others consisted of the comparison group. To diagnose sarcopenia, muscle strength was assessed using a hand dynamometry and a sit-to-stand test; muscle mass was determined by calf circumference (CC); skeletal muscle function was assessed by a walking speed test. Sarcopenia was diagnosed based on the EWGSOP2 (2019) criteria. **Results.** In the study group, reduced hand strength was observed in 88.3 % of women and 60 % of men. The sit-to-stand test was increased by 25.2 ± 1.2 s/5 times. The significant correlations were between hand dynamometry indices and the age of women ($r = -0.53$) and men ($r = -0.18$), and with BMI ($r = -0.77$ in women and $r = -0.88$ in men). In 58.3 % of women and 33.3 % of men, a decrease in CC < 31 cm was found. Correlations between BMI and CC were established in women ($r = 0.87$) and men ($r = 0.41$). A reduction in the functional capacity of skeletal muscles was noted in 53.3 % of women and 23.3 % of men. The significant correlations were between walking speed and age in women ($r = -0.41$) and men ($r = -0.35$), and BMI in women ($r = -0.46$) and men ($r = -0.39$). **Conclusions.** The prevalence of sarcopenia in patients with stage II HTN was 38.3 %. Among the subjects of the study group, sarcopenia was detected in 70 %, and severe sarcopenia in 35.6 % of cases. Although the total score on the SARC-F scale in the comparison group did not exceed 4 points, sarcopenia was diagnosed in 14.4 % of cases.

Keywords: hypertension; left ventricular hypertrophy; skeletal muscle dysfunction; sarcopenia; age; sex

Introduction

Hypertension (HTN) is a fairly common disease, with a prevalence of up to 33.3 % in the general population. In Ukraine, there are almost 12 million people with HTN, which is about 30 % of the adult population [1, 2]. HTN affects more than 70 % of elderly people [3–5]. To date, the pathogenetic relation between sarcopenia in older adults and HTN has been controversial [6] and has not been systematically summarised [3]. Ageing, sarcopenia, and cardiovascular disease share common risk factors, such as age, obesity, physical inactivity, insulin resistance, and metabolic syndrome [7], haemodynamic disorders and target organ damage in HTN [8], neurodegenerative diseases, malignant tumours and chronic multiple endocrine disorders [9].

Sarcopenia is based on several pathological processes: a decrease in the number of muscle fibres, a reduction in their size, impaired innervation of myofibrils, and fatty infiltration of muscles (myosteatosis) [10]. It is believed that age-related muscle atrophy is the result of a decrease in their

ability to self-repair, which depends on myogenic stem (satellite) cells located on the surface of the muscle fibre under its basal lamina [11, 12].

The traditional view of cardiovascular ageing is that age-related cardiac adaptation is characterised by an increase in LV and LVG mass, which are often secondary to the rise in HTN [13]. In older adults, there may be an interaction between skeletal muscle sarcopenia and LV mass [9, 14], although this relationship is not always age-dependent. The impact of cardiovascular health on the incidence of sarcopenia has been demonstrated not only in older adults but also in younger individuals. The authors showed similar results in subgroups based on sex, ethnicity, and education level [15]. Analysis of NHANES data showed that involutive changes in muscle tissue in elderly patients with HTN, combined with changes in carbohydrate metabolism and obesity, determine energy homeostasis disorders due to a decrease in glucose uptake in heart and skeletal muscle cells [16]. In another study the dietary inflammation index (DII) was sig-



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nificantly associated with sarcopenia in patients with HTN: the group with higher DII levels had a higher risk of sarcopenia (Q2: odd ratio (OR): 1.23, 95% confidence interval (CI): 0.89–1.72, $p = 0.21$). At the same time, sarcopenia was promoted by inflammation-induced activation of the nuclear factor kappa-B (NF- κ B) and NOD-like receptor protein 3 (NLRP3) pathways [17]. Recent studies have confirmed that sarcopenia is a risk factor for cardiovascular disease [18]. Sarcopenia and the composite myocardial index were strongly and positively associated with LV and LVH dysfunction, and LV and LVH dysfunction were positively correlated with the severity of sarcopenia [9].

It has been shown that skeletal muscle, together with cardiomyocytes and adipose tissue, belongs to the endocrine organs [19]. During contraction, it produces several autokines, including myokines (myostats), which inhibit myocyte differentiation [20] and also play an essential role in controlling HTN and heart rhythm [21]. Cells of the cardiovascular system are direct targets for certain myokines. For example, fibroblast growth factor 21 (FGF21), muslin and apelin have beneficial effects, including anti-atherosclerotic and antihypertensive effects [18, 19, 22]. Therefore, the reviewed literature sources provide an understanding that there is a close relationship between the components of the body and the structure and function of the heart [23–25]. Both skeletal muscles and the myocardium are made of striated muscle tissue; it is currently unclear whether a decrease in heart mass and function accompanies skeletal muscle loss. Recent data suggest that pathological changes in skeletal muscle may reduce the effects of cardiac protective factors [26, 27]. Thus, patients with HF develop secondary sarcopenia [9]. Peripheral skeletal muscle loss in most patients with HF occurs earlier than in healthy individuals, regardless of whether LV ejection fraction (EF) is reduced or preserved, and is closely associated with decreased physical activity and correlates with cardiovascular risk factors [23].

Taking all of that into account, it is worthwhile to investigate the link between HTN and sarcopenia and their mutual influence on the clinical course of HTN. This complex approach opens a possibility to put previous results in a common context and create a uniform platform for the advanced development of prevention and treatment strategies.

The **purpose** was to investigate the skeletal muscle changes in patients with HTN and determine the relationship of anthropometric and demographic factors with sarcopenia.

Materials and methods

Population and design

A prospective cohort study was conducted as part of the research work of the Department of Internal Medicine No. 2 of the National Pirogov Memorial Medical University at the Vinnytsia City Clinical Hospital. The study was approved by the Bioethics Committee at the National Pirogov Memorial Medical University (protocol No. 1 dated January 3, 2024). After signing informed consent, 180 patients from the clinic with stage II HTN (heart damage as a target organ with confirmed LVH and preserved LVEF) (120 women (66.7 %) and 60 men (33.3 %)) were aged 63.76 ± 6.18 years.

Patients were diagnosed with controlled HTN, corresponding to stage 1 HTN. From this study, we excluded the patients with additional pathologies that can affect skeletal muscle (old age, rheumatoid arthritis, diabetes mellitus, chronic obstructive pulmonary disease, any glucocorticoid prescriptions, etc.).

Methods

All patients underwent a clinical interview, physical examination and biochemical tests. Anthropometric parameters were measured at the beginning of the study with an accuracy of 1 mm using a tape measure (height, body weight and calf circumference). Body weight was measured using calibrated scales with an accuracy of 0.1 kg.

To determine the degree of development of adipose tissue, the body mass index (BMI) was defined as body weight (kg) divided by the squared height (m^2). The optimal BMI values were considered within the range of 18.5–24.9 kg/m^2 , overweight — 25.0–29.9 kg/m^2 ; obesity ≥ 30.0 kg/m^2 . 58 patients (32.2 %) with hypertension had normal body weight, 52 (28.9 %) had excess weight, and 70 (38.9 %) were diagnosed with obesity.

The SARC-F questionnaire (A Simple Questionnaire to Rapidly Diagnose Sarcopenia) and the “Find-Assess-Confirm-Severity” (F-A-C-S) algorithm for diagnosing sarcopenia (EWGSOP, 2019) [28].

Following the sarcopenia diagnosis algorithm, muscle strength was assessed using handgrip dynamometry (a decrease was considered to be < 27 kg for men and < 16 kg for women) and the “Sit-to-Stand” test (duration > 15 s/5 times). In the next step, we assessed the muscle mass (a decreased value was considered to be a calf circumference below 31 cm) and skeletal muscle function (assessment test of the walking speed ≤ 0.8 m/s). The confirmed sarcopenia was diagnosed in cases of decreased skeletal muscle mass and its quality; severe sarcopenia was established when all three major criteria were decreased (mass, strength, and function) (EWGSOP2, 2019).

Statistical processing of the research results was performed using Microsoft Office Excel and Statistica software. For mathematical data processing, methods of primary descriptive statistics, Student’s t-test, and Spearman’s rank correlation coefficient were used. A level of $p < 0.05$ was considered statistically significant.

Results

As a result of the survey, a total SARC-F score of more than 4 points was found in 50 % of patients (60 women and 30 men), which was the basis for further forming the main (study) group of patients. The other respondents with SARC-F scores of less than 4 formed the comparison group. In terms of age, gender, biochemical parameters, duration of HTN, and BMI, patients in both groups were homogeneous and did not differ significantly ($p > 0.05$) (Table 1).

In the study group, reduced hand strength was found in 53 (88.3 %) women and 18 (60 %) men. The mean handgrip strength values were 8.7 ± 5.7 kg and 18.64 ± 5.25 kg, respectively. For these patients, we also observed increased duration of the “Sit-to-Stand” test — 25.2 ± 1.2 s/5 times (Table 2).

In the comparison group, the handgrip strength was 18.7 ± 4.3 kg in women and 28.6 ± 4.2 kg in men ($p > 0.05$). The time to complete the “Sit-to-Stand” test was 15.2 ± 2.2 s/5 times. In general, a decrease in skeletal muscle strength was found in 5 (8.3 %) women and 2 (6.7 %) men.

A measurement of women hand strength with respect to the degree of obesity revealed a decrease in 16 (94.1 %) patients with normal body weight, in 14 (87.5 %) with overweight, and in 19 (86.4 %) with obesity. Among men, hand strength was reduced in 9 (75.0 %) individuals with normal body weight, 6 (60 %) with overweight, and 7 (53.8 %) with obesity. Reverse correlations were found between age and handgrip strength indices among women ($r = -0.53$; $p < 0.05$) and men ($r = -0.18$; $p < 0.05$), and BMI ($r = 0.77$; $p < 0.05$ in women and $r = 0.88$; $p < 0.05$ in men), reflecting a tendency towards a decrease in hand strength with age and an increase in BMI of patients in the study group.

In patients of the study group, the calf circumference in women was equal to 32.3 ± 5.4 cm and 34.2 ± 4.3 cm ($p > 0.05$) in men. While in the comparison group, it was measured as 34.4 ± 4.4 cm in women and 36.4 ± 4.1 cm in men ($p > 0.05$). In 35 women of the study group (58.33 %), a decrease in calf circumference < 31 cm was found, indicating a decline in skeletal muscle mass, of which 19 (31.7 %) women had a normal BMI. Among men, a decrease in calf circumference was found in 10 individuals (33.3 %), of whom six (20 %) had a normal BMI. It should be noted that this indicator tended to decrease following an increase in BMI. In the comparison group, a decrease in calf circumference was found in 5 (8.3 %) women and 2 (6.7 %) men.

Direct correlations were also found between BMI and calf circumference in women ($r = 0.87$, $p < 0.05$) and ($r = 0.41$; $p < 0.05$) in men.

A decrease in the functional capacity of skeletal muscles was observed in 32 women (53.3 %) and 7 men (23.3 %) in the study group. The average walking speed was 0.26 ± 0.09 m/s and 0.26 ± 0.08 m/s, respectively ($p > 0.05$). In the comparison group, the walking speed was 0.87 ± 0.91 m/s for men and 0.78 ± 0.91 m/s for women (Table 2). Since no significant difference between men and women was found when comparing walking speed indices, in the further analysis, we pooled this data together and considered only the degree of obesity. In individuals with nor-

mal body weight, the walking speed was 0.46 ± 0.28 m/s, in those with pre-obesity (0.25 ± 0.13 m/s), and in those with obesity (0.16 ± 0.17 m/s; $p < 0.05$). A decrease in walking speed was observed in 19 (65.5 %) individuals with normal body weight, 20 (76.9 %) individuals with overweight, and 25 (71.4 %) individuals with obesity.

Moderate inverse correlations were found between walking speed and age in women ($r = -0.41$; $p < 0.05$) and men ($r = -0.35$; $p < 0.05$) and BMI in women ($r = -0.46$; $p < 0.05$) and BMI in women ($r = -0.39$; $p < 0.05$) and men ($r = -0.39$; $p < 0.05$).

A decrease in skeletal muscle strength allowed us to identify probable sarcopenia in 78.88 % of the study group and 7.8 % of the comparison group. A decrease in both skeletal muscle mass and quality allowed us to establish confirmed sarcopenia in 34.4 % of respondents in the study group (40 % of women and 23.3 % of men) and 7.78 % of individuals in the comparison group (16.1 % of women and 5 % of men). Severe sarcopenia was diagnosed in cases of a simultaneous decrease in all three criteria (mass, strength, and function), and its occurrence was equal to 35.6 % in the study group and 6.7 % in the comparison group.

Discussion

The link between sarcopenia and HTN is attracting considerable attention. The first systematic review (2020) summarises the relation between sarcopenia and HTN based on a meta-analysis of 19 studies involving 21,301 participants. The eight studies examined the relationship between sarcopenia and HTN and concluded that sarcopenia is a risk factor for HTN [3]. In addition, several prospective and cross-examination studies have established a correlation between sarcopenia and HTN [3, 6], among older adults (OR 1.39, 95% CI: 1.15–1.67, $p < 0.01$) [29], and a cross-sectional association between sarcopenia and HTN [4, 6, 16]. Eleven studies that focused on the relationship between handgrip strength and HTN did not find such a relationship [3]. In a study [8], individuals without sarcopenia demonstrated higher handgrip strength (men: 33.8 ± 7.4 , women: 23.2 ± 4.6 kg) compared to individuals with sarcopenia (men with probable sarcopenia: 9.5 ± 3.3 kg, women with probable, confirmed, and severe sarcopenia: 11.7 ± 2.5 , 12.2 ± 3.0 , 11.8 ± 1.8 kg, respectively). In another study, low handgrip strength was significantly associated with HTN in both men and women [30], however, no correlation was found between hand strength and HTN in older people [3]. In contrast, our study found significant inverse correlations between age, BMI, and handgrip strength in patients

Table 1. Clinical characteristics of the patients ($M \pm SD$)

Indices	Study group	Comparison group
Men/women, n	30/60	30/60
Men's age, years	62.7 ± 6.8	62.9 ± 7.2
Women's age, years	61.8 ± 8.1	64.5 ± 6.4
Male BMI, kg/m ²	30.7 ± 5.0	30.3 ± 5.3
Female BMI, kg/m ²	29.8 ± 6.0	30.3 ± 4.4
Duration of HTN, years	21.6 ± 11.4	22.1 ± 10.0
Total lipids, g/l	5.5 ± 0.8	6.1 ± 1.1
Triglycerides, mmol/l	2.2 ± 1.2	2.4 ± 1.3
Cholesterol, mmol/l	6.0 ± 1.1	6.0 ± 1.3

Table 2. Indices of skeletal muscle mass, strength, and function in patients with HTN ($M \pm SD$)

Indices	Study group	Comparison group
Hand grip dynamometry, kg	$13.8 \pm 3.2^*$	23.7 ± 3.2
Sit-to-stand test, s/5 times	$25.2 \pm 1.2^*$	15.2 ± 2.2
Calf circumference, cm	32.9 ± 3.0	35.1 ± 5.0
Walking speed test, m/s	$0.3 \pm 0.1^*$	0.9 ± 0.1

Note: * — significant differences between groups, $p < 0.05$.

with HTN, reflecting a tendency toward decreased skeletal muscle strength with age and obesity. Although the relationship between HTN and sarcopenia is very complex and the mechanisms are not fully understood, a meta-analysis of 10 studies involving 14,804 patients shows that sarcopenia is associated with a 39 % higher probability of HTN compared to individuals of the same age without sarcopenia [29]. Multivariate statistical analysis showed that HTN was the second most significant factor associated with sarcopenia, after adjusting for factors such as age, sex, BMI, and smoking [15].

The RaNCD cohort study showed that the combination of obesity, HTN, and muscle insufficiency is determined by a decrease in both muscle mass and strength. At the same time, obesity and ageing are independent risk factors for functional decline [31]. In confirmation of our findings, moderate inverse correlations were established between age, BMI, and walking speed among women and men with HTN.

It has been suggested that the relation between sarcopenia and HTN may involve a common mechanism of chronic inflammation and the associated production of catabolic cytokines and oxidative stress [4, 22, 29, 32]. At the same time, chronic inflammation accelerates protein breakdown and contributes to sarcopenia by activating the ubiquitin-proteasome system, caspase 3, lysosomes, and myostatin [17, 29]. Recent studies have shown that myokine deficiency in sarcopenia (including relative deficiency) may increase the risk of cardiovascular diseases, including HTN. These disorders may amplify each other, leading to a synergetic effect. Upon HTN, changes in the renin-angiotensin-aldosterone system contribute to the development of sarcopenia, and activation of mineralocorticoid receptors potentiates the progressive loss of cardiac myocytes due to apoptosis. Decreased synthesis of sex hormones, insulin, insulin-like growth factor 1 and increased cortisol synthesis simultaneously affect both the development of sarcopenia and HTN [24].

In the study of the relationship between sarcopenia and conditions related to the renin-angiotensin system, it has been found that HTN can negatively affect muscle mass, physical function, and double the risk of sarcopenia [29]. It has also been shown that low skeletal muscle capillarization is another factor that may contribute to sarcopenia and reduced physical ability in older adults due to limited diffusion of substrates, oxygen, hormones, and nutrients [4]. In addition, there is growing evidence linking insulin resistance to sarcopenia [33]. Insulin resistance not only exacerbates muscle strength loss but also increases the risk of HTN through various mechanisms, including increased activity of angiotensin II and aldosterone, the sympathetic nervous system, and oxidative stress [34], thus closing a vicious circle of interaction.

A potential direction for future research involves longitudinal monitoring of patients with HTN to clarify the causal pathways linking HTN and sarcopenia. Particular emphasis should be placed on the combined influence of sarcopenia and obesity, as this overlap may contribute to the development of metabolic disorders, cardiovascular disease, and adverse long-term outcomes.

The *limitations* of the study were related to the specifics of the sampled cohort: it was a single-centre study, and it included a relatively small number of patients who were hospitalised.

Conclusions

The overall prevalence of sarcopenia in the cohort of patients with stage II arterial HTN was equal to 38.3 %. Among the subjects of the study group, sarcopenia was detected in 70.0 %, of which severe sarcopenia was diagnosed in 35.6 % of cases. Even though the total SARC-F score in the comparison group did not exceed 4 points, sarcopenia was diagnosed in 14.4 % of cases. We established inverse correlations between age, BMI and functional indices of skeletal muscles. The secondary form of sarcopenia in HTN is the result of several mutually aggravating mechanisms that create a vicious circle of interaction.

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Зміни скелетних м'язів та частота саркопенії у хворих на артеріальну гіпертензію

Резюме. Актуальність. Дослідження саркопенії та артеріальної гіпертензії (АГ) стало підставою припущення про взаємозв'язок дисфункції лівого шлуночка з тяжкістю саркопенії. **Мета:** вивчити зміни скелетних м'язів та частоту саркопенії у хворих з АГ. **Матеріали та методи.** Обстежено 180 пацієнтів віком $63,8 \pm 6,2$ року з АГ II стадії зі збереженою фракцією викиду. 50 % пацієнтів (60 жінок і 30 чоловіків) за анкетой SARC-F мали показник більше 4 балів і становили основну групу, решта — групу порівняння. Для діагностики саркопенії м'язову силу оцінювали за допомогою кистьової динамометрії і тесту «встати зі стільця», м'язову масу — за окружністю гомілки, функцію скелетних м'язів — за тестом оцінки швидкості ходьби. Саркопенію встановлювали на основі критеріїв EWGSOP2 (2019). **Результати.** В основній групі визначено знижену силу кисті у 88,3 % жінок та 60 % чоловіків, а також збільшений час виконання тесту «встати зі стільця» ($25,2 \pm 1,2$ с/5 разів). Вірогідні кореляційні зв'язки встановлено між показниками кистьової динамометрії та віком жінок ($r = -0,53$; $p < 0,05$) і чоловіків ($r = -0,18$; $p < 0,05$),

а також індексом маси тіла (ІМТ) ($r = -0,77$; $p < 0,05$ у жінок і $r = -0,88$; $p < 0,05$ у чоловіків). У 58,3 % жінок і 33,3 % чоловіків відмічено зменшення окружності гомілки < 31 см. Виявлено кореляційні зв'язки між ІМТ та окружністю гомілки в жінок ($r = 0,87$, $p < 0,05$) та чоловіків ($r = 0,41$; $p < 0,05$). Зниження функції скелетних м'язів відмічали в 53,3 % жінок і 23,3 % чоловіків. Вірогідні кореляційні зв'язки встановлено між швидкістю ходи та віком жінок ($r = -0,41$; $p < 0,05$) і чоловіків ($r = -0,35$; $p < 0,05$), а також ІМТ ($r = -0,46$; $p < 0,05$ у жінок і $r = -0,39$; $p < 0,05$ у чоловіків). **Висновки.** Поширеність саркопенії в когорті хворих на АГ II стадії становить 38,3 %. У досліджуваній групі саркопенія виявлена в 70 % осіб, тяжка її форма — у 35,6 %. Незважаючи на те, що загальна оцінка за шкалою SARC-F у групі порівняння не перевищувала 4 бали, саркопенія була діагностована в 14,4 % випадків.

Ключові слова: артеріальна гіпертензія; гіпертрофія лівого шлуночка; дисфункція скелетних м'язів; саркопенія; вік; стать