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Hydration status in patients hospitalized with acute decompensated heart failure depending on the severity of glucose metabolism disorder

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ABSTRACT

Aim. To study the hydration status according to clinical parameters and laboratory and instrumental research findings at admission and discharge in patients hospitalized with acute decompensated heart failure (ADHF), depending on the severity of glucose metabolism disorder.

Materials and methods. The study included 280 patients (53% men, average age 70.1 ± 10.8 years) with ADHF. 72.5% of patients had arterial hypertension in the medical history, 60% of patients had coronary artery disease. In all patients, the level of glycated hemoglobin (HbA1c) was determined to assess the glucose metabolism status. The patients were divided into groups depending on the results obtained: at HbA1c values < 5.7%, patients were included in the group without glucose metabolism disorders, at HbA1c of 5.7–6.4% – in the prediabetes group, at HbA1c ≥ 6.5% – in the type 2 diabetes group. The patients underwent a standard physical examination at admission and at discharge, as well as a clinical and comprehensive assessment of congestion (determination of N-terminal pro B-type natriuretic peptide (NT-proBNP), lung ultrasound, liver Fibroscan testing, including calculation of a controlled attenuation parameter, bioimpedance analysis of the body).

Results. The frequency of glucose metabolism disorders in patients hospitalized with ADHF was 57.5% (n = 161), while prediabetes was detected in 17.1% of patients (n = 48) and type 2 diabetes – in 40.4% (n = 113) of cases. Congestion at admission was detected in all patients. A significantly higher frequency of residual (61%) and a lower frequency of subclinical congestion (10%) were revealed in patients with ADHF and type 2 diabetes, compared to patients without glucose metabolism disorders (39% for residual congestion, 27% for subclinical congestion) and prediabetes (40% for residual congestion, 25% for subclinical congestion), respectively. There were no significant differences in the frequency of euvolemia at discharge, depending on the glucose metabolism disorder.

Conclusion. To assess congestion phenomena at discharge, it is necessary to use clinical, laboratory, and instrumental assessments for patients with ADHF and glucose metabolism disorders. However, in patients with ADHF and prediabetes, it is preferable to focus on the laboratory and instrumental assessment of congestion, while in patients with ADHF and type 2 diabetes, both clinical and laboratory and instrumental assessment of congestion should be performed.

Keywords: heart failure, congestion assessment, NT-proBNP, lung ultrasound, liver Fibroscan testing, glucose metabolism disorder

Conflict of interest. The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article.

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Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the local Ethics Committee at RUDN University (Protocol No. 28 of 15.04.2021).

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Статус гидратации у пациентов, госпитализированных с декомпенсацией острой сердечной недостаточности в зависимости от степени нарушения углеводного обмена

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РЕЗЮМЕ

Цель: изучить статус гидратации по клиническим и лабораторно-инструментальным параметрам при поступлении и выписке у пациентов, госпитализированных с острой декомпенсацией хронической сердечной недостаточности (ОДХСН), в зависимости от степени нарушения углеводного обмена (НУО).

Материалы и методы. В исследование были включены 280 пациентов (53% мужчин, средний возраст 70,1 ± 10,8 лет) с ОДХСН. Артериальную гипертонию в анамнезе имели 72,5%, ишемическую болезнь сердца – 60% пациентов. Всем пациентам для оценки статуса углеводного обмена проводили исследование уровня гликозилированного гемоглобина (HbA1c). Пациенты были разделены на группы в зависимости от полученных результатов: при значениях HbA1c < 5,7% включали в группу без НУО, 5,7–6,4% – в группу предиабета, ≥6,5% – в группу с сахарным диабетом 2-го типа (СД2). Пациентам проводили стандартное физическое обследование при поступлении и при выписке, а также делали клиническую и комплексную оценку застоя (определение концентрации мозгового натрийуретического пептида (NT-proBNP), ультразвуковое исследование (УЗИ) легких, фибросканирование печени, включая расчет контролируемого параметра затухания ультразвука, биоимпедансный анализ состава тела).

Результаты. Частота НУО у пациентов, госпитализированных с декомпенсацией хронической сердечной недостаточности (ХСН), составляет 57,5% (*n* = 161), при этом предиабет был выявлен в 17,1% (*n* = 48), СД2 – в 40,4% (*n* =113) случаев. Застойные явления при поступлении отмечены у всех пациентов. Выявлены достоверно более высокая частота остаточного (61%) и более низкая частота субклинического застоя (10%) у пациентов с ХСН и СД2 в сравнении с пациентами без НУО (39% остаточный, 27% субклинический застой) и предиабетом (40% остаточный, 25% субклинический застой) соответственно. Не показано достоверных различий по частоте эуволемии при выписке в зависимости от НУО.

Заключение. Пациентам с ОДХСН и НУО для оценки застойных явлений при выписке необходимо использовать клиническую и лабораторно-инструментальную оценку застоя. Однако у пациентов с ОДХСН и предиабетом предпочтительно сделать акцент на лабораторно-инструментальной оценке застоя, а пациентам с ОДХСН и СД2 – на клинической и лабораторно-инструментальной оценке застоя.

Ключевые слова: сердечная недостаточность, оценка застоя, NT-proBNP, УЗИ легких, фибросканирование печени, нарушение углеводного обмена

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании. Исследование одобрено этическим комитетом Медицинского института РУДН (протокол № 28 от 15.04.2021).

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) and heart failure (HF) are common comorbid conditions. In addition, new-onset T2DM and prediabetes are often found in patients hospitalized with acute decompensated heart failure (ADHF) and are independently associated with an increased risk of both all-cause and cardiovascular mortality [1].

The leading pathophysiological mechanism in ADHF and the reason for hospitalization is systemic congestion, which is associated with an unfavorable disease prognosis [2]. Systemic congestion leads to dysfunction of target organs, which has an important clinical and prognostic value. Quite often, congestion phenomena can go unnoticed, since in some cases, they do not manifest clinically [3], but can only be detected by laboratory and (or) instrumental methods. The instrumental methods for assessing congestion, which have a prognostic value according to literature data, include determining the level of brain-natriuretic peptide (NT-proBNP), assessing the number of B-lines according to lung ultrasound, estimating liver density by transient elastography, and assessing the hydration status by the bioelectrical impedance vector analysis (BIVA). Patients with T2DM with both heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) are characterized by a more advanced NYHA functional class of the disease and have more symptoms and signs associated with HF than patients without T2DM [4, 5]. In the CHARM, DIG, and I-PRESERVE trials, high frequency of symptoms and signs of congestion was found in patients with T2DM. Similar data in patients with prediabetes have not been presented in the literature.

Thus, the aim of this work was to study the hydration status according to clinical parameters and laboratory and instrumental research findings at admission and discharge in patients hospitalized with ADHF, depending on the severity of glucose metabolism disorder (prediabetes, T2DM) and without metabolism disorders.

MATERIALS AND METHODS

A prospective, observational study on investigating the features of chronic heart failure (CHF) in patients with glucose metabolism disorder included 280 people hospitalized with ADHF.

ADHF was diagnosed on the basis of current clinical guidelines: rapid aggravation of symptoms and signs of HF requiring emergency hospitalization of the patient and intensive therapy in combination with objective signs of heart failure (systolic and (or) diastolic dysfunction, left ventricular hypertrophy (LVH), left atrial enlargement according to echocardiography, and an increase in the NT-proBNP level).

Patients with acute coronary syndrome, terminal hepatorenal syndrome, non-cardiogenic edematous disorder, active cancer, exacerbation of chronic obstructive pulmonary disease (COPD), bronchial asthma (BA), pneumonia, type 1 diabetes mellitus, severe cognitive impairments, suspected or conformed COVID-19, verified hepatitis (cirrhosis of the liver), immobilized patients, and those who could not undergo BIVA (due to amputated limbs, ulcers or pronounced trophic changes in the skin of the limbs, the presence of metal implants) were not included in the study.

Glycated hemoglobin (HbA1c) was determined in all patients to assess the status of glucose metabolism. The patients were divided into groups depending on the results obtained: at HbA1c values < 5.7%, the patients were included in the group without glucose metabolism disorders, at HbA1c of 5.7–6.4% – in the prediabetes group, at HbA1c ≥ 6.5% – in the T2DM group.

In the first 24 hours from the moment of hospitalization and at discharge, all patients included in the study underwent standard physical, laboratory and instrumental examinations, including lung ultrasound, determination of the NT-proBNP level, liver Fibroscan testing with the calculation of a controlled attenuation parameter (CAP), and BIVA of body composition (Fig. 1).

The clinical and demographic characteristics of patients are presented in Table 1.

Therapy of patients in the outpatient setting included loop diuretics 72.8%, mineralocorticoid receptor antagonists (MRA) – 55%, ACEi /ARB / ARNI – 77.1%, beta-blockers – 70.0%, cardiac glycosides – 18.5%, and oral anticoagulants – 55%. In the in-patient setting, all patients received loop diuretics, MRA – 74.2%, ACEi / ARB / ARNI – 94.2%, beta blockers – 95.3%, cardiac glycosides – 18.5%, and oral anticoagulants – 66%.

To assess clinical congestion, the Composite Congestion Score (CCS) was used. Orthopnea, swelling of the cervical veins, and peripheral edema were evaluated in points. Each clinical symptom and sign were evaluated at admission and at discharge. When summing up the scores, the score ≥ 1 was considered as clinical congestion at admission and as residual congestion with clinical manifestations at discharge.

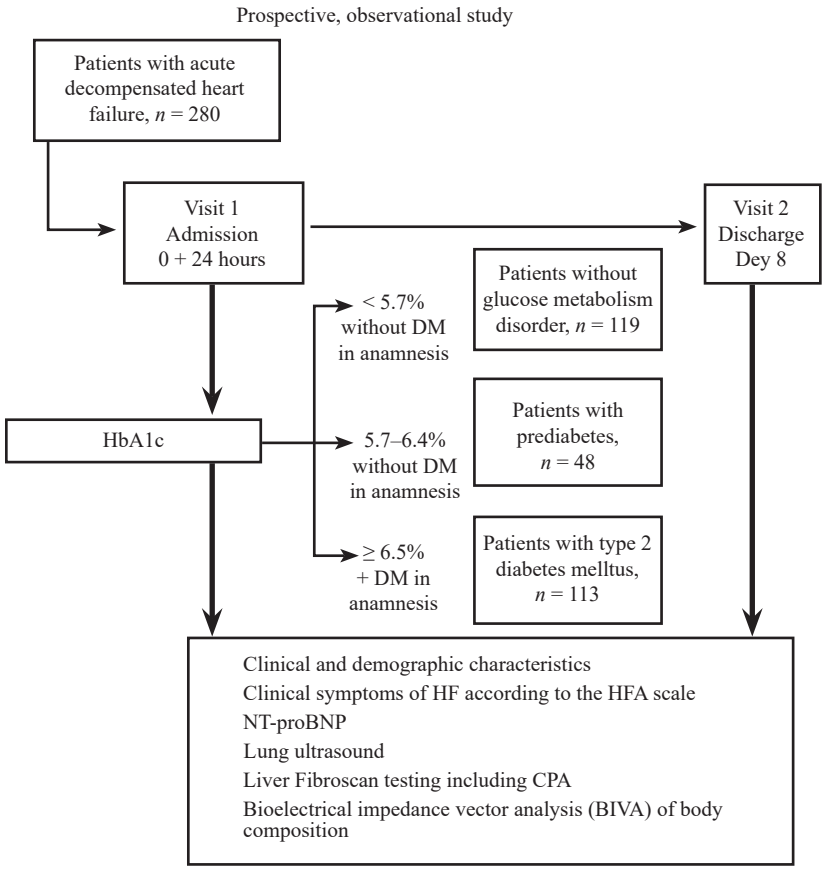

Fig. 1. Design of the study

Table 1

Clinical and demographic characteristics of patients included in the study, *n* = 280

Parameter	Value
Gender (male / female), *n* (%)	148 (53%)/132 (47%)
Age, years, *M*±*SD*	70.1 ±10.8
BMI, kg/m², *M*±*SD*	32.1 ±5.7
NYHA functional class of HF, *n* (%) II III IV	 90 (32%) 123 (44%) 67 (24%)
LVEF, %, *n* (%)	45.1 ±11.9
LVEF: <40% 40–49% ≥50%	 84 (30%) 71 (25%) 125 (45%)
Arterial hypertension, *n* (%)	203 (72.5%)
History of stroke, *n* (%)	36 (13%)
Coronary heart disease, *n* (%)	167 (60%)
History of myocardial infarction, *n* (%)	106 (38%)
Atrial fibrillation (flutter), *n* (%)	185 (66%)
Chronic kidney disease, *n* (%)	73 (26%)
COPD / BA, *n* (%)	47 (17%)

Note: BMI – body mass index, LVEF – left ventricular ejection fraction.

The concentration of NT-proBNP was determined by the enzyme-linked immunosorbent assay (ELISA) using the NT-proBNP-ELISA-BEST test systems, the A-9102 reagent kit (Vector-Best, Russia). Lung ultrasound (VIVID iq, GE) with the calculation of the sum of B-lines was performed in 8 zones. Transient elastography (TE) was performed using the FibroScan ® 502 Touch device (Echosens, France) according to the standard procedure. BIVA was performed using the ABC-01 analyzer (Medass, Russia).

Liver ultrasound was regarded as a method for assessing congestion in the pulmonary circulation, transient elastography – as a method for assessing congestion in the systemic circulation, BIVA and determining NT-proBNP – as methods for assessing systemic congestion.

At discharge, the following groups of patients were differentiated: patients with residual congestion (clinical and laboratory and instrumental assessments), patients with subclinical congestion, and euvolemic or well compensated patients.

Residual congestion at discharge was evidenced by clinical and instrumental and laboratory data confirming

the presence of congestion. Subclinical congestion was evidenced by the absence of clinical and the presence of instrumental research findings confirming the presence of congestion. The absence of clinical and instrumental research findings confirming congestion was regarded as a state of euvolemia or compensation.

For statistical data processing, MedCalc Software's VAT Version 19.0 and IBM SPSS Statistics (version 26.0) were used. Quantitative variables were presented as the arithmetic mean and the standard deviation ($M \pm SD$) for normal distribution and as the median and the interquartile range $Me\ (Q_1; Q_3)$ for non-normal distribution.

RESULTS

The frequency of glucose metabolism disorders in patients hospitalized with ADHF was 57.5% (n = 161), while prediabetes was detected in 17.1% of cases (n = 48), and T2DM – in 40.4% (n = 113) of cases.

The status of congestion phenomena at admission and discharge was analyzed in all patients hospitalized with ADHF. Congestion at admission was detected in all patients. Patients with glucose metabolism disorders at admission had significantly higher frequency of typical clinical symptoms and signs of CHF, such as wheezing in the lungs, orthopnea, swollen cervical veins, and edema of the lower extremities. They also had significantly higher values of liver density, CAP, the number of B-lines on lung ultrasound, and the level of NT-proBNP and significantly lower 6-min walk test values (6MWT) and active resistance and impedance according to BIVA, which indicates more pronounced manifestations of congestion compared to patients without glucose metabolism disorders (Table 2).

The clinical and laboratory and instrumental assessments of congestion in patients with ADHF, depending on the degree of glucose metabolism disorders at discharge, are presented in Table 3. At discharge, the frequency of residual congestion in patients with glucose metabolism disorders was significantly higher (55% vs. 39%, $p < 0.01$), and the frequency of subclinical congestion was significantly lower (14% vs. 27%, $p < 0.01$) than in the group of patients without glucose metabolism disorders. At the same time, the frequency of congestion in the prediabetes group was comparable with that in the group without glucose metabolism disorders. The differences in the frequency were revealed due to the group of patients with T2DM (Fig. 2). There were no significant differences in the frequency of euvolemia or compensation at discharge, depending on glucose metabolism disorders.

Table 2

Clinical and laboratory and instrumental assessment of congestion in patients with ADHF, depending on the degree of glucose metabolism disorders at admission, n = 280

Parameter	CHF without glucose metabolism disorders, n = 119	CHF with prediabetes, n = 48	CHF with type 2 diabetes, n = 113
6MWT, m	255.2 ± 111.4	211.3 ± 116.2*	227.7 ± 9.3*#
Clinical assessment of congestion			
Dyspnea, n (%)	113 (94.9)	46 (95.8)	111 (98.2)
Wheezing in the lungs, n (%)	50 (42.0)	37 (77.1)***	78 (69)*
Orthopnea, n (%)	79 (66.4)	35 (72.9)***	78 (69)
Swollen cervical veins, n (%)	46 (38.7)	23 (47.9)**	52 (46)
Edema of the lower extremities, n (%)	73 (61.3)	41 (85.4)**	105 (92.9)*
Laboratory and instrumental assessment of congestion			
NT-proBNP, pg / ml, $Me\ (Q_1; Q_3)$	1,700 (690; 2,901)	1,797 (1,040; 2,941)	2,130 (1,150; 3,201)*
Number of B-lines, $M \pm SD$	31,4 ± 17	34.9 ± 15.4	36 ± 17.9*
Liver density, кPa, $M \pm SD$	10.6 ± 8.9	14.3 ± 10.2**	14.3 ± 10.8**
CAP, dB / m, $M \pm SD$	231 ± 72.1	254.9 ± 51.4**	256.9 ± 55.3**
Active resistance, Om, $M \pm SD$	403.5 ± 76.9	382.5 ± 74.9	377.8 ± 73.48
Reactance, Om, $M \pm SD$	35.6 ± 9.3	32.5 ± 10.7	33.2 ± 9.8
Impedance Z, BIVA, $M \pm SD$	405.2 ± 77.1	383.9 ± 75.4	379.3 ± 73.9*

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ compared to the group of CHF patients without glucose metabolism disorders; #$p < 0.05$, ##$p < 0.01$, ###$p < 0.001$ compared to the prediabetes group and T2DM group (here and in Table 3).

Table 3

Clinical and laboratory and instrumental assessment of congestion in patients with ADHF, depending on the degree of glucose metabolism disorders at discharge, *n* = 280

Parameter	CHF without glucose metabolism disorders, *n* = 119	CHF with prediabetes, *n* = 48	CHF with type 2 diabetes, *n* = 113
Clinical assessment of congestion			
Dyspnea, *n* (%)	55 (46.2%)	26 (54.1%)	65 (57.5%)
Wheezing in the lungs, *n* (%)	15 (12.6%)	12 (25.0%)	40 (35.3%)***
Orthopnea, *n* (%)	25 (21.0%)	11 (22.9%)	30 (26.5%)
Swollen cervical veins, *n* (%)	19 (15.9%)	9 (18.7%)	24 (21.2%)
Edema of the lower extremities, *n* (%)	24 (20.1%)	17 (35.4%)	59 (52.2%)***#
Laboratory and instrumental assessment of congestion			
NT-proBNP, pg / ml, *Me* (Q_1; Q_3)	693.5 (341; 1,501)	957 (659; 1,727)***	1,252 (904; 2,146)***
Number of B-lines, *M* ± *SD*	16.5 ± 11.9	21.9 ± 15.6**	21.8 ± 11.1**
Liver density, кPa, *M* ± *SD*	5.6 ± 2.2	7.6 ± 4.4	7.8 ± 4.6
CAP, dB / m, *M* ± *SD*	454.0 ± 74.7	417.4 ± 81.1***	415.8 ± 80.0***
Active resistance, Om, *M* ± *SD*	42.8 ± 9.2	38.4 ± 11.6**	38.4 ± 9.8**
Reactance, Om, *M* ± *SD*	456.0 ± 75.1	419.2 ± 81.7**	417.7 ± 80.5**

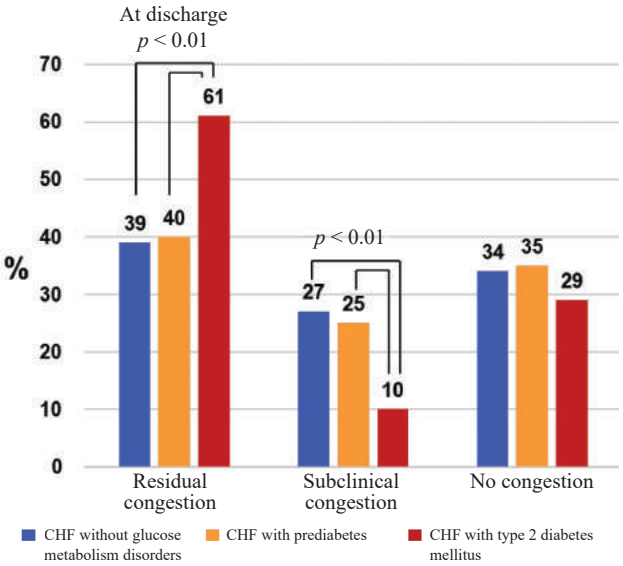

Fig. 2. Frequency of congestion at discharge in the studied groups

DISCUSSION

CHF and DM are quite common diseases. In the general population, HF is associated with higher prevalence of T2DM compared to patients without HF [4–6]. In our study, the incidence of glucose metabolism disorders in patients hospitalized with ADHF was 57.5%, while prediabetes was detected in 17.1% of cases, and T2DM – in 40.4% of cases, which is consistent with the literature data. In the registers of hospitalized patients with HF in North America and Europe, the prevalence of T2DM is about 40–45% [7]. According to a large European registry, DM is diagnosed in 36% of outpatient patients with CHF [8], while among patients hospitalized for acute HF, DM is detected in < 50% [9].

In clinical studies of patients with CHF, the prevalence of T2DM was about 30%, regardless of the HF phenotype (i.e. HFrEF and HFpEF) [3, 5, 8, 10–16]. It is important to note that in patients with HF without DM, the risk of developing DM is higher and increases with increasing severity of HF and the use of loop diuretics [17]. In addition, newly diagnosed T2DM and prediabetes are often found in patients hospitalized with ADHF. In the PARAGON-HF study, which involved 4,796 patients with HFpEF, 50% of patients had T2DM, and 18% of patients had prediabetes, that is 2/3 of the patients had glucose metabolism disorders. In the PARADIGM-FH study, it was shown that among 8,274 patients with systolic HF, 35% had a history of T2DM. The examination conducted before the start of the study revealed an additional 13% of patients with newly diagnosed T2DM (HbA1c > 6.5%) and 25% with prediabetes (HbA1c 6.0–6.4%). That is, in 38% of patients who lived to HF with LVEF ≤ 40%, clinically significant glucose metabolism disorders (prediabetes and T2DM) were not detected in time [5].

Fluid volume overload and congestion remain common causes of hospitalizations with HF. Patients with DM have increased neurohumoral activation and changes in sodium absorption, which may predispose to congestion, cardiorenal syndrome, and decreased sensitivity to diuretics. Hyperglycemia in the context of DM causes increased regulation of sodium – glucose cotransporter-2, which leads to an

increase in sodium absorption by the proximal parts of the kidneys, an increase in the fluid volume, and a decrease in sensitivity to diuretics [18].

In the CHARM, DIG, and I-PRESERVE studies, greater frequency of symptoms and signs of congestion was shown in patients with DM. Despite the fact that the status of congestion was not directly studied in the GWTG-HF study, it revealed a more frequent need for mechanical ventilation and dialysis / ultrafiltration and deterioration of kidney function in patients with T2DM, which may indicate an increase in the fluid volume load. The SOLVD-Prevention study showed that patients with asymptomatic left ventricular systolic dysfunction and T2DM had a higher probability of disease progression to symptomatic HF than those without T2DM [19].

Our study shows that not only patients with T2DM, but also patients with prediabetes were characterized by significantly higher frequency of typical clinical symptoms and signs of CHF, such as wheezing in the lungs (69 and 77.1 versus 42%), orthopnea (69 and 72.9 versus 66.4%), swollen cervical veins (46 and 47.9 versus 38.7%), and edema of the lower extremities (92.9 and 85.4 versus 61.3%) compared to patients without glucose metabolism disorders, respectively. In addition, patients with glucose metabolism disorders were characterized by significantly more pronounced laboratory and instrumental signs of congestion. Thus, in patients with T2DM and prediabetes, in contrast to patients without glucose metabolism disorders, we detected significantly higher values of liver density (14.3 ± 10.8 kP and 14.3 ± 10.2 versus 10.6 ± 8.9 kPa, $p < 0.01$), CAP (256.9 ± 55.3 and 254.9 ± 51.4 versus 231 ± 72.1 dB/m, $p < 0.01$), the number of B-lines on lung ultrasound (36 ± 17.9 and 34.9 ± 15.4 versus. 31.4 ± 17, $p < 0.05$), and NT-proBNP (2,130 and 1,797 versus 1,700 pg / ml, $p < 0.05$) and significantly lower impedance values in BIVA (379.3 ± 73.9 and 383.9 ± 75.4 versus 405.2 ± 77.1, $p < 0.05$).

Patients with CHF and T2DM at discharge were characterized by significantly higher frequency of residual congestion (61%) and lower frequency of subclinical congestion (10%), compared to patients without glucose metabolism disorders (39% for residual congestion, 27% for subclinical congestion) and prediabetes (40% for residual congestion, 25% for subclinical congestion), respectively. There were no significant differences in the frequency of achieving euvolemia at discharge, depending on glucose metabolism disorders.

CONCLUSION

To assess congestion phenomena at discharge, it is necessary to use clinical and laboratory and instrumental assessments for patients with ADHF and glucose metabolism disorders. However, in patients with ADHF and prediabetes, it is preferable to focus on the laboratory and instrumental assessment of congestion, while in patients with ADHF and T2DM, both clinical and laboratory and instrumental assessment of congestion should be performed.

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Tolkacheva V.V. – conception and design, analysis and acquisition of the data, drafting of the manuscript. Diane M.L., Khutsishvili N.I., Nazarov I.S., Smirnov I.P. – collection and processing of the materials. Cabello Montoya F.E., Galochkin S.A. – analysis and acquisition of the data, drafting of the manuscript. Kobalava Zh.D. – conception and design.

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