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Prognostic Value of Acute Kidney Injury in Patients Hospitalized with Acute Decompensation of Chronic Heart Failure

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ABSTRACT

Aim. To study the effect of acute kidney injury in patients hospitalized with acute decompensation of chronic heart failure (ADCHF) in relation to combined renal and cardiovascular outcomes during 1 year of follow-up.

Materials and methods. A total of 108 patients hospitalized with ADCHF (mean age 68.3 ± 10.0 years, 60% men) were included in a single-center prospective study. All patients included in the study underwent a standard physical and laboratory instrumental examination, including an assessment of the clinical condition according to the Rating Scale of Clinical State (RSCS) and laboratory tests (including serum creatinine level, glomerular filtration rate (GFR) using the CKD-EPI 2021 equation, albumin to creatinine ratio in urine, natriuretic peptide (NT-proBNP) upon admission and discharge. Acute kidney injury (AKI) was diagnosed based on the KDIGO guidelines (Kidney Disease: Improving Global Outcomes). The total rate of all-cause mortality and repeated hospitalizations from ADCHF was evaluated as cardiovascular outcomes. Renal outcomes included deterioration of renal function in the form of a decrease in GFR >15% of baseline and a decrease in GFR < 30 ml/min/1.73 m^2. Combined renal and cardiovascular outcomes were assessed during outpatient visits 3, 6, 12 months after discharge.

Results. The incidence of AKI during hospitalization in patients with ADCHF was 14% (n = 15). The groups with and without AKI were comparable in terms of clinical and demographic parameters and clinical assessment scale parameters. However, patients in the AKI group had higher baseline values of NT-proBNP and more pronounced impaired renal function, which persisted for 6–12 months of follow-up. There were no differences in clinical and laboratory data during the follow-up period. In patients with ADCHF, the presence of AKI during hospitalization significantly increases the risk of combined renal and cardiovascular outcomes during 1 year of follow-up (HR = 7.6; 95%CI = 2–29; p = 0.003).

Conclusion. The development of AKI during hospitalization in patients with ADCHF is a predictor of an unfavorable prognosis for combined renal and cardiovascular outcomes during 1 year of follow-up.

Keywords: acute decompensation of chronic heart failure, acute kidney injury, prognostic value

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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 of RUDN University.

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Прогностическое значение острого повреждения почек у пациентов, госпитализированных с острой декомпенсацией хронической сердечной недостаточности

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РЕЗЮМЕ

Цель: изучить влияние острого повреждения почек (ОПП) на прогноз у пациентов, перенесших госпитализацию по поводу острой декомпенсации хронической сердечной недостаточности (ОДХСН), в отношении комбинированных почечных и сердечно-сосудистых исходов в течение 1 года.

Материалы и методы. Включены 108 пациентов, госпитализированных по поводу ОДХСН. Мужчины составляли 60%, средний возраст 68 ± 11 лет. Проводилось стандартное физическое обследование по шкале оценки клинического состояния (ШОКС), лабораторные исследования (определялся уровень креатинина сыворотки, скорость клубочковой фильтрации (СКФ) CKD-EPI 2021, натрийуретический пептид (NTproBNP), альбумин/креатининурия) при поступлении, выписке. Диагноз ОПП устанавливался согласно критериям KDIGO (Kidney Disease: Improving Global Outcomes, Болезнь почек: улучшение глобальных результатов). В качестве сердечно-сосудистых исходов оценивали суммарный показатель смертности от всех причин и повторных госпитализаций с ОДХСН. Почечные исходы включали ухудшение функции почек в виде снижения СКФ > 15% от исходного, снижение СКФ < 30 мл/мин/1,73м^2. Почечные и сердечно-сосудистые исходы оценивались во время амбулаторных визитов через 3, 6, 12 мес после выписки.

Результаты. Частота развития ОПП во время госпитализации у пациентов с ОДХСН составила 14% (n = 15). Группы с наличием и без ОПП были сопоставимы по клинико-демографическим показателям, клиническому состоянию.

Пациенты в группе ОПП на момент госпитализации имели более высокий уровень NT-proBNP, более выраженные нарушения функционального состояния почек, которые сохранялись в течение 1 года. В течение периода наблюдения не выявлено различий по клиническим и лабораторным данным.

Наличие ОПП в период госпитализации у пациентов с ОДХСН достоверно повышает риск возникновения комбинированных почечных и сердечно-сосудистых исходов в течение 1 года наблюдения (отношение рисков 7,6; 95%-й доверительный интервал: 2–29; p = 0,003).

Заключение. Развитие ОПП у пациентов с ОДХСН является предиктором неблагоприятного прогноза в отношении комбинированных почечных и сердечно-сосудистых исходов в течение 1 года.

Ключевые слова: острая декомпенсация сердечной недостаточности, острое повреждение почек, прогноз

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.

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INTRODUCTION

Acute kidney injury (AKI) is a sudden decline in kidney function, which is a common problem in people admitted to hospital. The incidence is estimated between 7 and 18% amongst in-patients with the incidence reaching 70% in intensive care units [1], making AKI one of the most common complications following hospital discharge. AKI is a common concomitant syndrome in patients with heart failure (HF), with an average incidence of 13–20% [2, 3]. According to the meta-analysis, which included 37 studies, it was found that the overall incidence of AKI in patients with HF is even higher and amounts to 33% [4]. The high incidence of AKI in patients with HF may be due to multiple reasons. First, patients with HF are more likely to have reduced renal perfusion due to systolic or diastolic dysfunction. Second, a considerable number of patients may have had underlying chronic HF, a condition associated with chronic renal impairment [4].

A number of studies have shown that AKI is a robust independent predictor of both in-hospital and one-year mortality for HF patients [2, 5]. AKI is independently associated with a higher risk of cardiovascular complications and recurrent hospitalizations due to ADCHF after hospital discharge [6–8]. This relationship is also associated with a higher likelihood of chronic kidney disease (CKD), expedited progression to end-stage renal disease, and a decline in health-related quality of life [3, 9]. Thus, early detection of patients at risk of AKI is essential for improving outcomes [5]. However, most of these studies were conducted mainly in patients with stable HF.

Thus, it is important to determine the prognostic value of AKI in relation to combined renal and cardiovascular outcomes during one year follow-up in patients who were hospitalized for ADCHF.

MATERIALS AND METHODS

The study included 108 patients hospitalized with ADCHF in Vinogradov Clinical Hospital in Moscow. The study did not include patients with chronic kidney disease (CKD) stage 5 receiving renal replacement therapy, acute coronary syndrome, malignant neoplasms receiving active antitumor treatment, and mobility impairment with serious medical state, which makes it impossible to discharge a patient.

The study was performed in accordance with the standards of Good Clinical Practice and the principles of the Helsinki Declaration. The research protocol was approved by the local ethics committee. All patients signed an informed consent prior to the examination procedures.

All patients underwent a standard physical examination and laboratory and instrumental examinations. The clinical condition of the RSCS was assessed, the serum creatinine level was determined with the calculation of GFR according to the formula CKD-EPI 2021, the level of natriuretic peptide (NTproBNP), and the ratio of albumin to creatinine in urine at admission and discharge.

AKI was diagnosed according to the KDIGO criteria (Kidney Disease: Improving Global Outcomes) when serum creatinine increased by 0.3 mg/dl (26.5 mcmol/l) for 2 days or by 50% for 7 days.

Renal and cardiovascular outcomes were assessed during outpatient follow-up 3, 6, and 12 months after discharge. The total mortality and repeated hospitalizations for ADCHF were determined by the combined cardiovascular outcome. Renal outcomes included deterioration of renal function in the form of a decrease in GFR > 15% of baseline and a decrease in GFR < 30 ml/min/1.73 m^2. The clinical and demographic characteristics of the patients who were included in the study are presented in Table 1.

Table 1

Clinical and Demographic Characteristics of Patients Included in the Study, *n* = 108

Parameter	Value
Gender (male), *n* (%)	64 (60%)
Age, years *M*±*SD*	68±11
BMI, kg/m^2, *M*±*SD*	30 ± 6
Left ventricular ejection fraction, %, *M*±*SD*	43 ±12
Left ventricular ejection fraction <40%, *n* (%)	44 (41%)
Arterial hypertension, *n* (%)	99 (92%)
Obesity, *n* (%)	44 (41%)
Coronary heart disease, *n* (%)	55 (51%)
Atrial fibrillation or flutter, *n* (%)	64 (59%)
Chronic kidney disease before hospitalization, *n* (%)	28 (26%)
Diabetes mellitus, *n* (%)	38 (35%)
Anemia, *n* (%)	20 (19%)
Chronic obstructive pulmonary disease or bronchial asthma (without exacerbation), *n* (%)	16 (15%)

The statistical analysis was carried out using the StatTech v. 3.1.8 software (developed by Stattech LLC, Russia). Quantitative variables with a normal distribution were described using arithmetic mean and standard deviations *M*±*SD*. In case of an asymmetric distribution, they were described using the median and the interquartile range *Me* (*Q1; Q3*). Categorical data were described as absolute values and percentages

(*n* (%). In case of a normal distribution of data, the statistical significance of the differences was assessed using the Student's *t*-test, and the Mann–Whitney test was used for a distribution other than normal. Pearson's $\chi 2$ test was used to compare groups by frequency of qualitative variables. Differences were considered statistically significant at $p < 0.05$.

When constructing Kaplan-Meier curves, the frequency of reaching the combined endpoint was estimated. Differences in reaching the primary endpoint were assessed using the likelihood-ratio test. To assess the prognostic significance of AKI in relation to the onset of the combined endpoint, univariate Cox regression analysis models were used, the hazard ratio (HR) and 95% confidence interval (CI) were calculated. Differences were considered statistically significant at $p < 0.05$.

RESULTS

The incidence of AKI during hospitalization in patients with ADCHF was 14% (*n* = 15). Then, clinical, demographic, and laboratory parameters were analyzed depending on the presence of AKI (Table 2). The groups were comparable in terms of the main clinical and demographic characteristics, as well as clinical profile (RSCS). Patients from the AKI group had higher serum creatinine and NT-proBNP levels, as well as albumin/creatinuria.

Table 2

Clinical, Demographic and Laboratory Parameters of Patients with ADCHF Depending on the Presence of AKI at Admission

Parameter	Patients with AKI (*n* = 15)	Patients without AKI (*n* = 93)
Clinical and demographic parameters		
Gender (male), *n* (%)	11 (78.6)	53 (57.0)
Age, years, *M* ± *SD*	67.0±10.0	68.0±11.0
Left ventricular ejection fraction, %, *M* ± *SD*	40,2±13.1	43.1±12.1
Left ventricular ejection fraction <40%, *n* (%)	6 (40.0)	38 (40.8)
RSCS score upon admission, points, *Me* (Q_1; Q_3)	6.5 [6; 8]	7.0 [5; 9]
RSCS score at discharge, points, *Me* (Q_1; Q_3)	4.0 [1; 5]	4.0 [2; 5]
Arterial hypertension, *n* (%)	15 (100)	84 (90.3)
Obesity, *n* (%)	8 (53.3)	36 (38.7)
BMI, kg/m^2, *M* ± *SD*	33.2±7.3	30.0±6.1
Coronary heart disease, *n* (%)	10 (66.7)	45 (48.4)
Atrial fibrillation or flutter, *n* (%)	6 (40.0)	58 (61.14)
Chronic kidney disease before hospitalization, *n* (%)	2 (13.3)	26 (28)
Diabetes mellitus, *n* (%)	8 (53.3)	30 (32.3)
Anemia, *n* (%)	5 (33.3)	15 (16.1)
Chronic obstructive pulmonary disease or bronchial asthma (without exacerbation), *n* (%)	4 (26.7)	12 (12.9)
Laboratory parameters		
Creatinine, mcmol/l	186.73 ± 34.02	99.45 ± 23.70*
GFR-EPI, ml/min/1.73 m^2	29.00 [25.5; 33.5]	63.00 [45.4; 65.6]***
Albumin/creatinine in urine, mg/g	49 [3.5; 128.5]	17 [4; 64]*
NT-proBNP, pg/ml	1,370.5 [996; 1,975]	1,042 [288; 1,675]*

End of table 2

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ when comparing groups.

The dynamics of laboratory parameters during one-year follow-up is shown in Table 3. In the group of patients who developed AKI during hospitalization, significantly higher creatinine values were noted after 3, 6, and 12 months, lower GFR values after 3 months, higher values of the albumin/creatinine ratio in urine after 3 and 6 months of follow-up. There were no significant differences in the clinical condition assessed on the RSCS and the level of NT-proBNP during follow-up. After 3 months of follow-up, 43.5% (*n* = 47) of patients were diagnosed with CKD, while 17.5% (*n* = 19) of patients were diagnosed with *de novo* CKD. After 6 and 12 months of follow-up, no new cases of CKD were detected.

Table 3

Changes in Laboratory Parameters during One-Year Follow-Up, *Me* (Q_1; Q_3)

Parameter	Patients with AKI (*n* = 15)	Patients without AKI (*n* = 93)
Creatinine, mcmol/l		
3 months	121 [102; 132.5]	91 [77; 109]**
6 months	117 [89; 139]	91,5 [77; 114.03]*
12 months	122 [94; 142]	94 [79; 166]**
GFR, ml/min/1.73 m^2		
3 months	59 [41; 71]	70 [54; 89]*
6 months	61 [38.5; 76.5]	69 [52; 90]
12 months	52 [36.5; 70]	66 [48; 86]
Albumin/creatinine in urine, mg/g		
3 months	38 [19; 118]	13 [4; 33]**
6 months	26 [13; 87.5]	11 [4.25; 30]*
12 months	22 [4.5; 51.5]	12 [3; 31]
NT-proBNP, pg/ml		
3 months	425 [85; 933.3]	601 [296.7; 942.2]
6 months	1,067 [510; 1,486]	716 [349.8; 1,440.5]
12 months	1,290 [781.8; 1,400]	1,133 [466.5; 2,400]

End of table 3

Parameter	Patients with AKI (n = 15)	Patients without AKI (n = 93)
RSCS score, points		
3 months	2.5 [2; 4.75]	3.5 [2; 5]
6 months	2 [2; 3.75]	3 [2; 4]
12 months	2.5 [1; 4.25]	3 [2; 4]

*p < 0.05, **p < 0.01, ***p < 0.001 when comparing groups.

The incidence of adverse cardiovascular outcomes for one-year follow-up was 38% (n = 41), including 5 deaths and 36 hospitalizations for ADCHF, and 30.5% (n = 33) had an unfavorable renal outcome in the form of a decrease in GFR by more than 15% per year. At the same time, 14% (n = 15) of patients had both renal and cardiovascular outcomes.

To identify the main predictors of combined renal and cardiovascular outcomes, Cox regression analysis was performed during one-year follow-up. It revealed that the development of AKI during hospitalization was significantly associated with a higher probability of developing combined renal and cardiovascular outcomes during one-year follow-up (HR = 7.6; 95% CI: 2–29; p = 0.003).

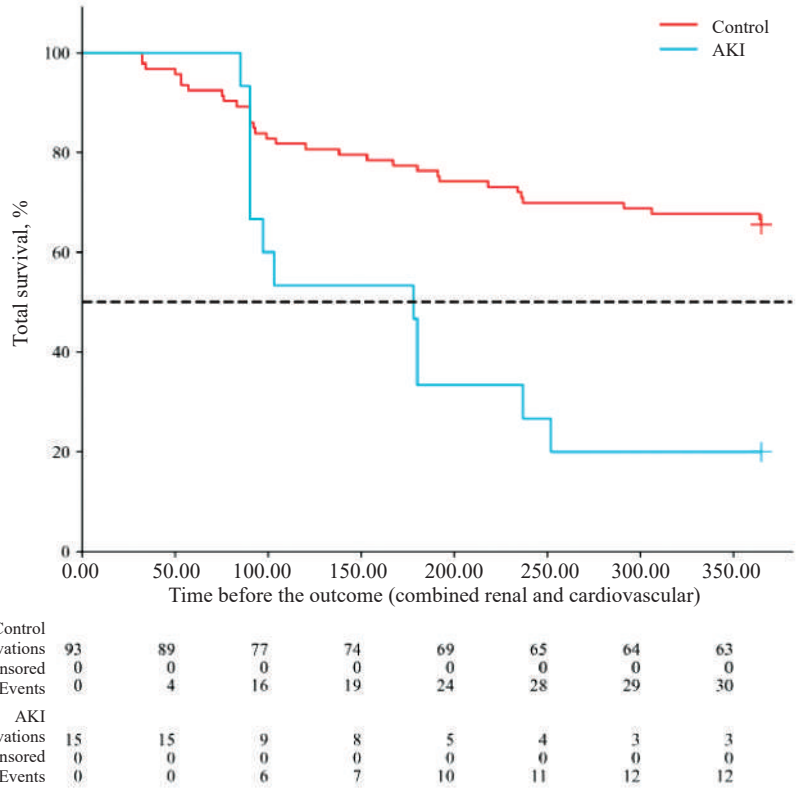

Fig. Kaplan-Meier curves (renal and cardiovascular outcomes) depending on the development of AKI during hospitalization in patients with ADCHF, n = 108

DISCUSSION

AKI is characterized by a sudden decrease in renal function, which is manifested by an increase in serum creatinine or a decrease in the level of diuresis [10]. The presence of AKI is highly common among patients admitted to the hospital for ADCHF. In a cohort of 30,529 patients with acute and chronic HF, the incidence of AKI was 10.4% [2]. In this study, the incidence of AKI in patients hospitalized for ADCHF was consistent with literature data and amounted to 14%.

Congestive phenomena in ADCHF affect pathophysiological regulation of kidney function. Venous hypertension leads to a decrease in perfusion, an increase in interstitial pressure in the kidneys, a decrease in the gradient of arterial and venous renal pressure, a decrease in GFR, inadequate autoregulatory reactions, and other neurohumoral imbalances. Higher renal pressure weakens glomerular filtration, causes tubular collapse and tubulointerstitial fibrosis [11].

A number of studies have shown that AKI is associated with serious long-term problems in patients, including the development or progression of CKD [12, 13], renal failure, cardiovascular complications [14, 15], and decreased survival [16].

AKI is generally associated with the development of CKD in the future [13], although the long-term prognosis after AKI in HF requires clarification. In the cohort of patients admitted with ADCHF, deterioration of renal function was associated with a significant increase in hospital mortality, more frequent complications, and an increase in the duration of hospitalization [17]. The transition of AKI to acute kidney disease is associated with mortality within 1 year and the development of *de novo* CKD [18]. In this study, *de novo* CKD was diagnosed in 18% (n = 19) patients after 3 months of follow-up. The association of acute kidney disease with short-term (90 days) [19] and long-term (5 years) [20] adverse prognosis (risk of mortality and adverse renal events) has been demonstrated.

This study showed that the development of AKI during hospitalization in patients with ADCHF was associated with a higher probability of developing combined renal and cardiovascular outcomes during one-year follow-up (HR = 7.6; 95% CI = 2–29; p = 0.003), which is consistent with the literature data. A meta-analysis of 11 studies showed that hospital mortality is higher in patients with AKI than in patients without AKI (HR = 3.65; 95% CI: 3.04–4.39, $p < 0.001$). Mortality was assessed in five studies, and it was found that the mortality rate remained high during one-year follow-up after AKI (HR = 1.85; 95% CI: 1.54–2.22, $p < 0.001$) [4]. AKI was associated with a higher mortality rate within 30 days after hospitalization for HF (HR = 5.3; 95% CI: 2.2–13.2) [21]. In patients with HF and normal initial renal function admitted with acute renal failure who developed AKI, increased hospital mortality was observed: 4.9% vs. 1.6%, adjusted odds ratio (OR) 3.21; $p \leq 0.001$ [3].

CONCLUSION

The development of AKI during hospitalization in patients with ADCHF is a predictor of an unfavorable prognosis for combined renal and cardiovascular outcomes during one-year follow-up.

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Author contribution

Kobalava Zh.D.— conception and design. Tolkacheva V.V.— analysis of the received data, drafting of the manuscript. Kontareva N.I., Karapetyan L.V. – collection and processing of materials.

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