

<http://dx.doi.org/10.35630/2199-885X/2022/12/2.18>

EVALUATION OF THE PROGNOSTIC VALUE OF URINARY CREATININE LEVEL IN PATIENTS HOSPITALIZED WITH THE DIAGNOSIS OF CHRONIC SYSTOLIC HEART FAILURE IN SEYED AL-SHOHADA HOSPITAL IN URMIA, IRAN

Received 01 January 2022;
Received in revised form 18 February 2022;
Accepted 21 February 2022

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ABSTRACT — **INTRODUCTION:** Heart failure patients have frequent hospitalization leading to decreased quality of life and life expectancy. The purpose of this study was to evaluate the prognostic value of urinary creatinine test in immunocompromised patients with systolic heart failure.

MATERIAL AND METHODS: This study was conducted on 122 patients hospitalized in Urmia. The inclusion criterion was according to cardiac EF obtained from echocardiography and patients with EF less than 45% were considered. In the morning, urine samples were taken from them and the amount of urinary creatinine and other parameters were registered. **RESULTS:** According to the Pearson correlation test, there was no significant relationship between body weight, height, and body mass index with urinary creatinine, but there was no significant relationship between urinary creatinine and serum creatinine ($p > 0.05$). There is a positive and significant relationship between urinary creatinine level and GFR. There is also a significant relationship between diastolic blood pressure and urinary creatinine.

CONCLUSION: The results of the present study indicate the importance of paying attention to urinary creatinine as an effective underlying factor in predicting the symptoms of heart failure.

KEYWORDS — Urinary creatinine, Serum creatinine, Ventricular ejection fraction, Urinary albumin, GFR.

INTRODUCTION

Today, heart failure is one of the most common heart problems worldwide. According to the latest statistics, more than 26 million people in the world have heart failure. There are more than 6.2 million

people in the United States alone, which will increase to more than 8 million by 2030. Chronic heart failure causes mental and physical problems including fatigue, anxiety, depression and anemia. Heart failure eventually leads to increased hospitalization, lower quality of life, and lower life expectancy. The latest meta-analysis results show that most heart failure patients have moderate and poor quality of life. In Iran, over one million people suffer from heart failure (1–3).

Heart failure is associated with various symptoms such as shortness of breath, swollen ankles and fatigue. Symptoms of heart failure are often nonspecific and do not help differentiate heart failure from other problems. Identifying and interpreting signs and symptoms may be particularly difficult in obese, elderly, and patients with chronic lung disease (5). Some diagnostic tests include echocardiography and electrocardiography. Another test is the use of serum B-type natriuretic peptide.

The kidney is important in renal failure because the kidney controls fluid volume and sodium homeostasis, and progressive renal dysfunction often limits aggressive treatment. Despite this, in addition to measuring urine volume in response to prescribed diuretics, less attention has been paid to urinalysis in patients with heart failure. Recent advances in a large number of urinary biomarkers that can predict acute kidney damage in the days before elevated serum creatinine levels have led to the addition of urine samples to laboratory data collected in clinical trials.

However, it seems that the value of urine samples in patients with heart failure has not been well understood so far and their use has been limited to the measurement of urinary creatinine, which as a statistical finding has received little attention. Used solely as a measure of protein and biomarker ratios to calculate differences in urine concentration and volume. Ter Maaten and colleagues evaluated the prognostic value of urinary creatinine and its association with clinical variables and concluded that low urinary creatinine measured in the morning urine test in patients with heart failure, with lower renal function, was smaller.

Body size, more severe heart failure, and is independently associated with an increased risk of death (for all causes) and hospitalization (11).

Chronic heart failure is associated with treatment failure and high complications. In order to choose an effective and targeted treatment path and assess the prognosis of patients' clinical condition, simple and accurate prognosis models are needed. This model should be such that it is relatively widely available and has a high predictive value. Measurement of urinary creatinine can be considered as an available and inexpensive test. Therefore, the aim of this study was to evaluate the prognostic value of urinary creatinine test in patients with systolic heart failure.

METHODS AND MATERIALS

Design and participants

This cross-sectional study was performed on 134 patients suffering from chronic systolic heart failure from February 1 to December 10, 2020, in an educational hospital (Seyed Al-Shohada) in northwest Iran (Urmia). Patients were selected through the available sampling method. The required information was collected in the first visit and followed up one month later and three months later. The inclusion criterion was according to cardiac EF obtained from echocardiography and patients with EF less than 45% were considered. Suffer patients to chronic kidney failure in stages 4 and 5, as well as patients with normal serum creatinine who underwent dialysis and patients who did not consent to participate in this research project were excluded from the study. (Patients with GFR 30 and more are present in the study). The final study score of each patient was equal to the mortality due to the complications of this disease. The number of participants was calculated using Cochran's formula with an error of 0.05, which was appropriate for 178 participants

Data collection

Data collection checklist included demographic characteristics (age, sex (male / female)), BMI, serum and urine creatinine level (mg/dL), EF (%), serum urea, serum and urine albumen (mg/dL Deciliters), GFR, period of hospital stay and mortality. After obtaining the license and concordance with the hospital, the study purposes were first explained to the participants. Patients willing to participate in the study were considered in the study. Then, at the first visit of the patient, blood and urine tests were taken and the results were entered in the checklist.

Ethical Considerations

This study has been approved in the ethics committee of Urmia University of Medical Sciences with

the ethics code IR.UMSU.REC.1398.427 and the dissertation number: 3019-32-09-96. Before the start of the study, all participants gave written consent. Participants were assured that their information would be kept confidential. The STROBE checklist was used to report the study.

Data analysis

The collected data were entered into SPSS V21 software for analysis. Descriptive (mean, percentage, frequency) and analytical (Pearson correlation) tests were used to analyze the data. Pearson correlation test was used to determine the relationship between urinary creatinine and quantitative outcomes. Significance level was considered less than 0.05.

Results

In the present study, data of 122 participants was assessed in the final analysis. The mean age of participants was 67.36 years, weight 75.52, height 166.08, and BMI was 27.11. Most participants were male (n=68). (Table 1)

The results of Pearson correlation test show that there is no significant relationship between weight, height and body mass index with urinary creatinine ($p < 0.05$). The results also showed that there was no significant relationship between serum creatinine and urinary creatinine ($p < 0.05$). Also, independent t-test showed that there was no statistically significant relationship between fraction ejection and urinary creatinine ($P = 0.915$). Regarding the relationship between mortality and urinary creatinine, analysis of variance showed a non-significant relationship. Pearson correlation coefficient showed that there is a positive and significant relationship between GFR and urinary creatinine, so that with decreasing GFR level, urinary creatinine level also decreases. According to Pearson correlation coefficient, the results showed that there is a significant positive relationship between diastolic blood pressure and urinary creatinine. But there is no significant relationship between systolic blood pressure and heart rate with urinary creatinine (Table 2).

DISCUSSION

Edema of the wrists and feet is a major manifestation in patients with heart failure. However, there are several non-cardiac causes for this symptom. In general, right heart failure may present with edema, right hypochondriac pain (liver distance), abdominal swelling (ascites), and loss of appetite. In general, peripheral edema has a sensitivity of 10% and a specificity of 93% in the diagnosis of heart failure (18). In general, pulmonary crackles are heard in elderly patients with asymptomatic cardiovascular disease, even in the ab-

Table 1. Demographic characteristics of participants

		Mean or N(%)	Variable
		67.36	Age (y)
		27.11	BMI
		75.52	Weight
		166.08	Height
N (%)	Variables	68 54	Gender Male Female
68(55.7%) 54(44.3%)	Blood pressure Yes No	12(9,8) 25(20.5) 85(69..7)	NYHA class I II III IV
44(36.1%) 78(63.9%)	Diabetes Yes No	34(27.9%) 88(72.1)	EF 31-45% >30%
44(36.1%) 78(63.9%)	COPD Yes No	92(75.4%)	Ascites Yes No
6(4.9%) 116(95.1%)	CVA/TIA YES NO	38(31.1%) 84(68.9%)	Smoking Yes No
62(50.8%) 68(55.7%) 73(59.8%) 34(27.9%)	Consumption of HF drugs ARB or ACEI Beta-blockers Furosemide Spironolactone	57(46.7%) 65(53.3%)	History of MI Yes No
21 101	Mortality Yes No	98	History of hospitalization Yes No
49.82	GFR	85.11	HR
12.43	HB	1.50	Creatinine (serum)
106.52	T.G	57.13	Urea

sence of overt heart disease or associated lung disease (20, 19). In a study by Kataoka et al. The incidence of pulmonary crackles in patients with heart failure was 42% (21); In our study, this amount was reported more; This is probably due to the average age of most of the people we studied compared to the above study.

In present study the mean urinary creatinine level was 81.19 ± 50.01 mg / dl, There was no significant relationship between weight, height, body mass index, functional class, mortality, in-hospital or out-of-hospital mortality with urinary creatinine. Also, in this study, mean urinary creatinine level in patients was lower with class 4 compared to classes 3 and 2 (75.89 vs. 93.72) but this relationship was not significant and also in our study the mean urinary creatinine level in patients with a history of 3 hospitalizations was higher than other patients. But no significant relationship was observed between hospitalization rate and

urinary creatinine level. In this study, the mean urinary creatinine level in EF was less than 30 and between 31 and 45 were 81.50 50 50.80 and 80.42 48 48.65 mg / dl, respectively, and also there was a significant relationship between urinary creatinine level and EF.

In the study by Ter Maaten et al., 2130 patients with heart failure were included in the study. They reported that there was no significant relationship between body mass index and cardiac ejection fraction with urinary creatinine level, which is consistent with the results of our study, but there is a significant relationship between height, weight, serum creatinine level, functional class, which is in line with our study. Although in our study there was also a weak correlation between serum and urinary creatinine levels; As the serum creatinine level increases, the urinary level decreases.

Also, the mean urinary creatinine level in our study was lower in patients with higher functional

Table 2. Relationship between urinary creatinine and study indicators

	Correlation coefficient	P.value
Urinary creatinine with weight	-03/0	68/0
Urinary creatinine with weight	07.0	43.0
Urinary creatinine with body mass index	07.0	38.0
Urinary creatinine with serum creatinine	-17.0	0.06
EF <30 31-45	81.50±5.41 80.42±8.34	0.915
Has no history hospitalization First times Two times three times	76.47±44.50 88.42±59.66 83.17±41.27 127.87±115.78	0.73
Mortality situation alive Death while hospitalization Mortality in follow-up after a month Mortality in follow-up after three month	83.61±50.72 63.50±46.50 65.43±16.27 76.75±132.25	0.65
GFR with urinary creatinine	0.31	0.0001
Blood pressure Systolic blood pressure Diastolic blood pressure Heart rate	0.22 0.14 0.008	0.01 0.14 0.008

class; Which is in line with the results of the above study. The findings of our study showed a positive and significant relationship between urinary creatinine level and GFR, so we expect that with decreasing GFR, urinary creatinine level will also decrease, which is a significant relationship between Maaten et al. Urinary creatinine levels and renal function achieved are correlated. On the other hand, the results of our study showed that the mean level of urinary creatinine in patients with and without spironolactone was not different from the results of Maaten et al. In this study, we also found a significant relationship between diastolic blood pressure and urinary creatinine.

Different studies in different patients have shown that lower 24-hour urinary creatinine excretion is associated with all causes of mortality and major cardiovascular events (22–24). A small cohort study of patients with chronic heart failure found that lower 24-hour creatinine excretion was associated with a higher risk of clinical side effects (mortality, heart transplantation, myocardial infarction, or readmission) (25). The prognostic value of urinary creatinine has been studied in two community-based groups. In a cohort study conducted by Carter and colleagues on 2,627 population-based individuals; They reported that low urinary creatinine concentration was associated with an increased risk of cardiovascular complications (26). In another recent

study by Carter et al. In 6770 population-based individuals; Reported that there was no significant relationship between urinary creatinine level and cardiovascular complications (27). The results also showed that the level of urinary creatinine in patients was not significantly related to the number of hospitalizations, which is in line with the results of the Carter study.

CONCLUSION

The results showed that low urinary creatinine levels in patients with heart failure were not associated with high functional levels and readmission. Also, no relationship was found between urinary creatinine and weight, height, body mass index, functional class, mortality, in-hospital or out-of-hospital mortality rate, functional level, readmission and EF. But urinary creatinine level has a positive and significant relationship with GFR and diastolic blood pressure. The results of the present study indicate the importance of paying attention to urinary creatinine as an effective underlying factor in predicting the symptoms of heart failure.

Ethics approval and consent to participate

This study has been registered in the ethics committee of Urmia University of Medical Sciences with the ethics code IR.UMSU.REC.1398.427, and written consent was taken from each subject.

Competing interests

No conflict of interest.

Authors' contributions

SA, MHAPR, AR: Concept and design, SE: Data collection, RAG: Revision of the manuscript, SA, MHAPR, AR: Data collection and drafting of initial manuscript, AR: data interpretation, AR: Statistical analysis and critical revision of the manuscript. All authors have read and approved the manuscript.

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