

Type of the Paper (Research Article)

# Hyponatremia Negatively Affects the Outcome of Patients with ST Elevation Myocardial Infarction Treated with Primary Angioplasty

Mohammed G. Mohammed<sup>1\*</sup>, Aly M. Elsheimy<sup>1</sup>, Khaled A, Elkhashab<sup>1</sup>, Ahmed M. Elebiary<sup>2</sup>, Gomaa A. Ahmed<sup>1</sup>

<sup>1</sup>Cardiology Department, Faculty of Medicine, Fayoum University, Fayoum, 63514 Egypt.

<sup>2</sup> Physiology Department, Faculty of Medicine, Fayoum University, Fayoum, 63514 Egypt.

\*Correspondence: Mohammed G. Mohammed, <u>mgmmosa@gmail.com</u>, Tel: (002) 01006829570.

Received:	2 December, 2024	Reviewed:	15 March, 2025
Accepted:	13 May, 2025	Published online:	26 June 2025

# Abstract:

**Introduction:** Serious health consequences such as increased mortality, morbidity, and longer hospital admissions are linked to hyponatremia. Cardiovascular mortality is correlated with hyponatremia in individuals with HF. Myocardial infarction may lead to hyponatremia due to the stimulation of the reninangiotensin system and elevated production of catecholamines.

Aim of the study: To evaluate the influence of hyponatremia on results in cases with ST-segment elevation myocardial infarction handled by 1st angioplasty during hospitalization and thirty days following discharge.

**Subjects and Methods:** The research involved 100 cases (65 with hyponatremia and 35 with normal sodium levels) hospitalized with STEMI and treated with primary angioplasty. The following were done for all cases: ECG, cardiac biomarkers, admission sodium level, and glomerular filtration rate (GFR). The intervention involved the use of stents and glycoprotein IIb/IIIa inhibitors during coronary angiography. In-hospital problems like mechanical complications, heart failure, arrhythmia and cardiac arrest, and follow-up for thirty days following discharge.

**Results:** Hyponatremia was associated with lower left ventricular Ejection fraction (47.4  $\pm$ 10.2 versus 51.7  $\pm$ 6.2, *p* =0.011) and was more frequent in HF cases compared to in non-HF cases in the ICU (90.3% vs. 53.6%, *p* < 0.0001). 33% of individuals suffered problems within 30 days. Complications occurred in 19% of cases with HF, 10% with re-infarction, and 2% with death or VT. (93,9% vs. 50,7% for those without complications) p 0.0001. In cases that developed difficulties within thirty days, there is a strong correlation between hyponatremia and an elevated risk of mortality.

**Conclusions:** In cases with STEMI treated with primary angioplasty, hyponatremia is correlated to lower left ventricular Ejection fraction, ICU HF, and complications thirty days following hospital discharge.

Keywords: primary angioplasty, hyponatremia, STEMI.

# 1. Introduction

Sodium is the most prevalent extracellular cation and an electrolyte with a positive charge, which aids in maintaining fluid balance and proper neuromuscular function in the human body [1]. Serious health consequences such as increased mortality, morbidity, and longer hospital admissions are linked to hyponatremia (serum sodium content lower than one hundred thirty-five mmol per Liter) [2].

The frequency of hyponatremia is around 20% among cases with heart failure (HF) that are admitted to the hospital, according to the American Heart Association. Alterations in water homeostasis are often linked to ageing and chronic illness [3]. Treatment of hyponatremia mainly involves treatment of the underlying cause, if possible. In acute marked hyponatremia, intravenous saline may be used with symptomatic treatment.

As many as 30% of hospitalized cases are affected by hyponatremia, the most

prevalent electrolyte imbalance. Compared to cases with normonatremia, those hospitalized with hyponatremia have a mortality risk that is more than twice as high [4].

The frequency of hyponatremia in patients with STEMI varies between 12.5% and 23.2% [5] and close to 25% in cases with HF [6].

Cardiovascular mortality is correlated with hyponatremia in people with HF. As an outcome of this, the reninangiotensin-aldosterone pathway, catecholamines, and arginine vasopressin are all recognized as being overactive [7].

During myocardial infarction, the renin-angiotensin system becomes active, and there is an increase in the production of catecholamines, which may exacerbate hyponatremia. The glomerular filtration rate reduces as a result of the aforesaid causes, and tubular fluid is sent to the diluting section of the nephron [8].

# 2. Subjects and Methods

#### 2.1 Subjects

This is an observational research study that involved one hundred cases hospitalized with STEMI and managed by 1st angioplasty between April 2021 and April 2022. The research was done with the permission of the local institution's ethics committee.

#### Inclusion criteria

- Cases admitted with acute ST-segment elevation myocardial infarction.
- Cases managed with primary percutaneous coronary intervention (PCI).

#### Exclusion criteria

- Cases with concurrent renal impairment.
- Cases with concurrent hepatic impairment.
- Cases known to be Cardiomyopathic.
- Cases known to be suffering from pituitary gland issues
- Cases using any treatments influencing sodium level, for example, diuretics, as well as certain antidepressant medications.

#### 2.2 Methods

All cases were evaluated as follows:

- Age and Sex.
- History of IHD.
- Cases have a medical history that includes diabetes mellitus, hypertension, and smoking.
- Family history of cardiovascular illnesses and hypercholesterolemia
- Electrocardiography (ECG) (ischemic alterations include T wave, ST segment, QRS complex)
- Cardiac biomarkers (Creatinine kinase-MB (CK-MB) and troponin).
- Admission sodium level.
- Admission glomerular filtration rate (GFR).
- Culprit artery thrombolysis in myocardial infarction flow before and following PCI, the number of coronary arteries with higher than 50% stenosis on coronary angiography, the utilization of glycoprotein IIb/IIIa inhibitors and stents during the intervention.
- The intervention was followed by the continuation of medical therapy in the critical care unit and, subsequently, the cardiac ward.
- In-hospital problems like arrhythmia, heart failure, any mechanical complications and cardiac arrest.

- The outpatient department obtained followup data through either a telephone call or a visit.
- Echocardiographic examination of cases after PCI in the critical care unit and assessment of: PASP, LA diameter, left ventricle (LV) diameters, any valvular lesion, and ejection fraction (EF).

#### 2.3 Statistical analysis

The data were collected and analyzed by appropriate statistical approaches with the computer program Statistical Package for the Social Sciences

(SPSS) version sixteen software. The categorical data have been presented as percentages and numbers, while the quantitative data have been defined as range and mean  $\pm$  standard deviation (SD). The numerical parameters in the research groups have been compared utilizing a Student (ttest). This test compares the means of two independent groups when the data is normally distributed. The t-value is the ratio of the variance between the two means to the estimated standard deviation of this difference. Statistical significance has been defined as *p*-values less than 0.05.

# **3. Results**

This study included 100 STEMI patients admitted and treated with primary angioplasty at Fayoum University Hospital and the National Heart Institute (NHI). 65% of study patients were hyponatremic on admission, while 35% were normonatremic. Hyponatremia was found to be significantly higher in females than males, p = 0.004 (**Table 1**). Patients with hyponatremia had a mean age of 54.3+10.3 years, and there was no statistically significant difference in age between patients with hyponatremia and those with normal sodium (**Table 1**).

**Table 1:** Socio-demographics about hyponatremia.

		Hyponatremia (N=65)	No hyponatremia (N=35)	<i>P</i> -value
A	ge	54.3±10.3	53.1±12.9	0.615
Cor	Female	13 (100.0%)	0 (0.0%)	0.004*
Sex	Male	52 (59.8%)	35 (40.2%)	- 0.004**

There was no statistically significant difference in risk factors for atherosclerosis between patients with hyponatremia and those with normal sodium levels, p>0.05 (**Table 2**).

**Table 2:** Relation between hyponatremia and risk factors of MI.

		Hyponatremia (N=65)	No hyponatremia (N=35)	<i>P</i> -value
RBG		216.5 ±95.8	$189.9 \pm 88.6$	0178
Admission GFR		86.9 ±34.9	99.1 ±30.6	0.085
Smoking	No	31 (72.1%)	12 (27.9%)	0.106
	Yes	34 (59.6%)	23 (40.4%)	0.190
Family history	No	53 (65.4%)	28 (34.6%)	0.952
of CAD	Yes	12 (63.2%)	7 (36.8%)	0.832
Diabetes	No	37 (58.7%)	26 (41.3%)	0.086
Mellitus (DM)	Yes	28 (75.7%)	9 (24.3%)	0.080
Hypertension	No	27 (64.3%)	15 (35.7%)	0.800
	Yes	38 (65.5%)	20 (34.5%)	0.099

GFR: Glomerular filtration rate, CAD: coronary artery disease.

Hyponatremia was not significantly linked with cardiac enzyme levels or the type of STEMI, p>0.05 (**Table 3**).

Table 3: Cardiac enzymes, ECG findings, and hyponatremia.

	Hyponatremia (N=65)	No hyponatremia (N=35)	P-value	
CKMB level	$106.8 \pm 64$	117.5 ±55.3	0.406	
Anterior STEMI	44 (67.7%)	21 (32.3%)	0.442	
Inferior STEMI	21 (60%)	14 (40%)		
	CKMB level Anterior STEMI Inferior STEMI	Hyponatremia (N=65)           CKMB level         106.8 ±64           Anterior STEMI         44 (67.7%)           Inferior STEMI         21 (60%)	Hyponatremia (N=65)         No hyponatremia (N=35)           CKMB level         106.8 ±64         117.5 ±55.3           Anterior STEMI         44 (67.7%)         21 (32.3%)           Inferior STEMI         21 (60%)         14 (40%)	Hyponatremia (N=65)         No hyponatremia (N=35)         P-value           CKMB level         106.8 ±64         117.5 ±55.3         0.406           Anterior STEMI         44 (67.7%)         21 (32.3%)         0.442           Inferior STEMI         21 (60%)         14 (40%)         0.442

STEMI: ST-segment elevation myocardial infarction.

Patients with hyponatremia had significantly lower left ventricular EF than those with normal sodium levels (47.4  $\pm$ 10.2 vs. 51.7  $\pm$ 6.2, *p* =0.011), but other

echocardiographic parameters (LA diameter, EPASP and valvular complications) and occurrence of arrhythmia showed no significant difference (**Tables 4 and 5**).

		Hyponatremia (N=65)	No hyponatremia (N=35)	P-value
Ejection fraction		$47.4 \pm 10.2$	51.7 ±6.2	0.011*
LA diameter		3.5 ±0.5	3.4 ±0.4	0.456
EPASP		30.4 ±6	29.1 ±5	0.276
Valuation lasions	No	60 (63.2%)	65 (36.8%)	0.150
varvular lesions	Yes	5 (100%)	0 (0%)	- 0.139

**Table 4:** Echocardiographic findings and hyponatremia.

EPASP: Estimated pulmonary artery systolic pressure.

**Table 5:** Relation between hyponatremia and arrhythmia.

		Hyponatremia (N=65)	No hyponatremia (N=35)	P-value
Amberthania	No 23 (69.7%) 10 (30.3%)	0.480		
Amyunnia	Yes	42 (62.7%)	25 (37.3%)	0.489

Patients with hyponatremia developed HF during hospital stay higher

rate than patients with normal sodium (*p* <0.0001) (**Table 6**).

**Table 6:** Relation between hyponatremia and ICU Heart failure.

		Hyponatremia (N=65)	No hyponatremia (N=35)	P-value
	No	37 (53.6%)	32 (46.4%)	<0.0001*
ЮПГ	Yes	28 (90.3%)	3 (9.7%)	- <0.0001*

ICU HF: heart failure in the intensive care unit.

33% of the patients in the present study suffered problems after 30 days. Complications occurred in 19% of patients with HF, 10% with re-infarction, and 2% with death or VT-HF. In patients who developed difficulties within 30 days, hyponatremia was shown to be substantially linked with an increased risk of death (93,9% vs. 50,7% for those without complications) (p = 0.0001) (**Tables 7 & 8** and Figure 1).

#### **Table 7:** 30-day complications according to hyponatremia.

		Hyponatremia (N=65)	No hyponatremia (N=35)	P-value
	No	34 (50.7%)	33 (49.3%)	<0.0001*
ICU HF	Yes	31 (93.9%)	2 (6.1%)	- <0.0001*

#### Table 8: 30-day complications in patients with hyponatremia.

		N (%)
30-day complications	No	67 (67%)
	Yes	33 (33%)
	Death	2 (2%)
	HF	19 (19%)
	Re-infarction	10 (10%)
	VT	2 (2%)

HF: heart failure, VT: ventricular tachycardia.



Figure 1: 30-day complications.

# 4. Discussion

Hyponatremia, which is characterized by blood sodium concentrations lower than one hundred thirty-five mg per deciliter, is commonly observed in hospitalized cases and has been linked to a variety of clinical outcomes. Cases with an AMI that have hyponatremia are more likely to die. In cases with hyponatremia and AMI, the non-osmotic production of vasopressin and the stimulation of renin-angiotensinthe aldosterone system, and activation of the sympathetic nervous system are all observed. The survival of the cases may be adversely impacted by these procedures [9].

Activation of neurohormonal during hospitalization may be influenced by variables, for example, the restoration of flow in the stenosed artery, which is the preferred primary care technique for acute myocardial infarction in the era of primary angioplasty. Drugs that involve angiotensin blockers, beta-blockers, receptor and angiotensin converting enzyme inhibitors similarly reduce the activity of neurological and hormonal systems. As a result, many cases that survive the acute incident may have abnormal blood sodium concentrations throughout their hospitalizations [10].

When the renal excretion of solutefree water deteriorates, diluting the blood and lowering the serum sodium level, hyponatremia occurs [11]. A better result for STEMI cases was achieved with 1st angioplasty; the correlation among sodium concentrations at outcomes and admission in cases treated with this procedure should be examined [12]. We examined cases with STEMI who had primary angioplasty to see whether hyponatremia affected their outcomes in the hospital and 30 days after release.

Hundred cases with STEMI have been hospitalized and managed with primary angioplasty in this research. The research demonstrated that hyponatremia was significantly higher in females, p = 0.004, while according to Devi et al., there was no gender difference in hyponatremia in STEMI cases [13]. This can be because of a relatively small sample size.

Cases with hyponatremia (65%) had an average age of 54.3 +10.3 years, and there was statistically insignificant variance in age among those with hyponatremia and those with normal sodium in our research. It was also demonstrated that hyponatremia has been found in 43% of MI cases in a research conducted by Mati et al [14]. Elderly individuals were more likely to have hyponatremia than younger individuals, according to Hasoor and colleagues [15], while hyponatremia cases were not significantly older than individuals with normal salt levels in another study (60.3 vs 59.8 years) [16].

In terms of risk variables (DM, HTN, smoking, dyslipidemia, and family history

of CAD), we found no variance among cases with hyponatremia and those with normal sodium concentrations (p > 0.05), regarding our results. Also, Klopotowski et al. found statistically insignificant variances in renal function, smoking history, hypertension, diabetes mellitus, and Killip class among hyponatremic and normonatremic individuals [12]. Vikas et al. demonstrated that hyponatremia has been correlated with hypertension among the many risk variables evaluated (smoking, diabetes, hypertension, past diuretic medication, and prior history of IHD) [17]. But a statistically significant variance was observed in baseline clinical features among hyponatremic and normonatremic individuals within some studies [18]. According to Goldberg et al., hyponatremia is more prevalent among smokers, with a statistically significant variance [19].

Hyponatremia in our study was not linked to cardiac enzyme levels or the kind of STEMI in a statistically significant way. But hyponatremia has been correlated with an elevated risk of anterior wall MI and a greater CK-MB level in cases, as demonstrated by Devi et al [13].

We found that cases with hyponatremia had a lower EF percentage

than those with normal sodium (47.4  $\pm$ 10.2 vs. 51.7  $\pm$ 6.2, *p* =0.011). Hyponatremia upon admission was also observed to be related to reduced ejection percentage, according to Vikas et al [17]. Also, the mean ejection fraction in hyponatremic and normonatremic cases was 37.8% and 41.1%, respectively, according to studies by Hasoor et al [15].

Hyponatremia in our research was more frequent in cases who acquired HF in the ICU compared to those who didn't develop HF (90.3% versus 53.6%, p<0.0001).

Heart failure cases had greater amounts of renin, angiotensin II. catecholamines, vasopressin and aldosterone in their blood compared to individuals with hyponatraemia. Hyponatremia no can indicate cardiac stress in cases of acute myocardial infarction, regardless of the volume status or presence of other medical conditions [20]. After discharge, hyponatraemia may be a sign of severe neurohormonal activation, which would lead to heart failure and a poor long-term result [21].

Hyponatremia has been linked to a longer hospital stay and a higher risk of rehospitalization in cases with HF [22].

Thirty days after discharge, 30% of cases had difficulties, according to the results of our research. Complications occurred in 19% of cases with HF, 10% with re-infarction, and 2% with death or VT. Problems occurred in 93.9% of cases with hyponatremia, compared to 50.7% of cases that did not have complications (p < 0.0001). Hyponatremia has been demonstrated to be an indicator of death in STEMI cases managed angioplasty with 1st by Klopotowski et al [12]. Following primary angioplasty, hyponatremia wasn't associated with long - or short-term death in STEMI cases, according to research by Lazzeri et al [16]. Choi et al. found hyponatremia at discharge was the best indicator of longterm death in cases with AMI, according to other time points [23]. Klopotowski et al., Tang and Hua both used large samples and found a link between hyponatremia and mortality [12, 24].

Hyponatremia is significantly correlated with long-term death in both STEMI and NSTEMI cases. According to Burkhardt et al., non-ST-segment elevation myocardial infarction cases with lower blood sodium concentrations had an even greater risk of death compared with STsegment elevation myocardial infarction cases, according to their research [25]. According to Hoorn et al. and Vikas et al., in cases with STEMI, higher thirty-day mortality was shown to be linked to hyponatremia [2, 17].

# **5.** Conclusion

In cases with STEMI managed with 1<sup>st</sup> angioplasty, hyponatremia is linked to failure, ICU heart and cases with hyponatremia had lower EF percentages compared to those with normal sodium concentrations. In cases that developed difficulties within 30 days, hyponatremia was shown to be substantially linked with an elevated risk of death. Serum sodium levels could be used as a simple diagnostic test to identify individuals with a high risk of having negative outcomes. The study was limited to the relatively low number of examined cases and single-center research; moreover, the limited follow-up up for only thirty days after discharge. However, as a final recommendation, Serum sodium levels could be used as a simple diagnostic test to identify individuals with a high risk of having negative consequences in cases with STEMI managed with 1st angioplasty, and patients with hyponatremia with STEMI should be considered for close follow-up and condensed treatment.

Ethical committee approval: Before the research, conducting we obtained ethical acceptance from the review committee of our Faculty. Additionally, each case has been provided with an informed written consent in line with the guidelines of the Local Ethical Committee.

### References

 Hariprasad S, Basavaraj M. Electrolyte dysfunction in myocardial infarction patients. Int J Adv Med. 2018;5(5):1–5.

doi:10.18203/2349-3933.ijam20183872.

- Hoorn EJ, Zietse R, Pereira R, Hoekstra MO, van der Lubbe N, Zietse R, et al. Hyponatremia and mortality: moving beyond associations. Am J Kidney Dis. 2013;62(1):139–49. doi:10.1053/j.ajkd.2012.09.019.
- 3. Grodin JL, Simon JA, Hachamovitch R, Wu Y, Jackson G, Halkar M, et al. Pharmacologic approaches to electrolyte abnormalities in heart failure. Curr Heart Fail Rep. 2016;13(4):181–9. doi:10.1007/s11897-016-0295-7.
- 4. Zilberberg MD, Exuzides A, Spalding J, Foreman A, Jones AG, Colby C, Shorr AF. Epidemiology, clinical and economic outcomes of admission hyponatremia among hospitalized patients. Curr Med Res Opin. 2008;24(6):1601–8. doi:10.1185/03007990802081675
- 5. Madan VD, Novak E, Rich MW. Impact of change in serum sodium concentration on mortality in patients hospitalized with heart failure and hyponatremia. Circ Heart Fail. 2011;4(5):637–43. doi:10.1161/CIRCHEARTFAILURE.111.961011

**Competing interests:** There are no conflicts of interest for the authors.

**Funding:** No particular grants from public, commercial, or nonprofit funding organizations were given to this research.

AI declaration statement: None declared.

6. Mohan S, Gu S, Parikh A, Radhakrishnan J. Prevalence of hyponatremia and association with mortality: results from NHANES. Am J Med. 2013;126(12):1127–37.e1.

doi:10.1016/j.amjmed.2013.07.021

 Szatalowicz VL, Arnold PE, Chaimovitz C, Bichet D, Berl T, Schrier RW. Radioimmunoassay of plasma arginine vasopressin in hyponatremic patients with congestive heart failure. N Engl J Med. 1981;305(5):263–6.

doi:10.1056/NEJM198107303050506

- 8. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. N Engl J Med. 1999;341(8):577-85. doi: 10.1056/NEJM199908193410806.
- Winzeler B, Jeanloz N, Nigro N, Suter-Widmer I, Schuetz P, Arici B, Bally M, Blum C, Bock A, Huber A, Mueller B, Christ-Crain M. Long-term outcome of profound hyponatremia: a prospective 12 months follow-up study. Eur J Endocrinol. 2016;175(6):499-507. doi: 10.1530/EJE-16-0500.
- 10. Volpe M, Tocci G, Battistoni A, Rubattu S. Angiotensin II Receptor Blocker Neprilysin Inhibitor (ARNI): New Avenues in Cardiovascular Therapy. High Blood Press Cardiovasc Prev. 2015;22(3):241-6. doi: 10.1007/s40292-015-0112-5.

- 11. Gheorghiade M, Abraham WT, Albert NM, Gattis Stough W, Greenberg BH, O'Connor CM, She L, Yancy CW, Young J, Fonarow GC; OPTIMIZE-HF Investigators and Coordinators. Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry. Eur Heart J. 2007;28(8):980-8. doi: 10.1093/eurheartj/ehl542.
- 12. Klopotowski M, Kruk M, Przyluski J, Kalinczuk L, Pregowski J, Bekta P, Malek LA, Kepka C, Ciszewski A, Chmielak Z, Demkow M, Karcz M, Witkowski A, Ruzyllo W. Sodium level on admission and in-hospital outcomes of STEMI patients treated with primary angioplasty: the ANIN Myocardial Infarction Registry. Med Sci Monit. 2009;15(9):CR477-83.
- 13. Devi KB, Chanu KJ, Ram R, Narayanaswamy G, Singh K-B, Chongtham DS. Profile of acute ST-elevation myocardial infarction patients with hyponatremia. J Med Soc. 2017;31(2):119–22. DOI: 10.4103/jms.jms\_83\_15.
- 14. Mati E, Krishnamurthy N, Ashakiran S, Sumathi ME, Raghavendra P. Dyselectrolytemia in acute myocardial infarction a retrospective study. J Clin Biomed Sci. 2012;2(3):167–74. DOI: 10.58739/jcbs/v02i3.9.
- 15. Hasoor S, Kinagi A, Afiya S. A prospective study of in-hospital outcome of acute phase of STEMI with hyponatremia. J Evol Med Dent Sci. 2014;3(36):14483–92. DOI: 10.14260/jemds/2014/3943.
- 16.Lazzeri C, Valente S, Chiostri M, Attanà P, Picariello C, Gensini GF. Usefulness of hyponatremia in the acute phase of ST-elevation myocardial infarction as a marker of severity. Am J

Cardiol. 2012;110(10):1419-24. doi: 10.1016/j.amjcard.2012.07.004.

- 17. Vikas, Kaur G. Prognostic importance of hyponatremia in acute ST elevation myocardial infarction (STEMI). J Med Sci Clin Res. 2018;6(8):142–51. Doi: 10.18535/jmscr/v6i8.24
- 18. Singla I, Zahid M, Good CB, Macioce A, Sonel AF. Effect of hyponatremia (<135 mEq/L) on outcome in patients with non-ST-elevation acute coronary syndrome. Am J Cardiol. 2007;100(3):406-8. doi: 10.1016/j.amjcard.2007.03.039.
- 19. Goldberg A, Hammerman H, Petcherski S, Zdorovyak A, Yalonetsky S, Kapeliovich M, Agmon Y, Markiewicz W, Aronson D. Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. Am J Med. 2004;117(4):242-8. doi: 10.1016/j.amjmed.2004.03.022.
- 20. Klein L, O'Connor CM, Leimberger JD, Gattis-Stough W, PiñA IL, Felker GM, Adams KF, Califf RM, Gheorghiade M. Lower serum sodium is associated with increased Short-Term mortality in hospitalized patients with worsening heart failure. Circulation. 2005;111(19):2454–60. Doi: 10.1161/01.cir.0000165065.82609.3d
- 21.Lilly LS, Dzau VJ, Williams GH, Rydstedt L, Hollenberg NK. Hyponatremia in congestive heart failure: implications for neurohumoral activation and responses to orthostasis. J Clin Endocrinol Metab. 1984;59(5):924-30. doi: 10.1210/jcem-59-5-924.
- 22. Bettari L, Fiuzat M, Shaw LK, Wojdyla DM, Metra M, Felker GM, O'Connor CM. Hyponatremia and long-term outcomes in chronic heart failure--an observational study from the Duke Databank for Cardiovascular Diseases. J Card Fail. 2012;18(1):74-81. doi: 10.1016/j.cardfail.2011.09.005.

doi:

- 23. Choi JS, Kim CS, Bae EH, Ma SK, Ahn YK, Jeong MH, Kim SW. Prognostic impact of hyponatremia occurring at various time points during hospitalization on mortality in patients with acute infarction. myocardial Medicine (Baltimore). 2017;96(23):e7023. doi: 10.1097/MD.000000000007023.
- 24. Tang Q, Hua Q. Relationship between hyponatremia and in-hospital outcomes in Chinese patients with ST-elevation myocardial infarction. Intern Med.

2011;50(9):969-74.

10.2169/internalmedicine.50.4703.

25. Burkhardt K, Kirchberger I, Heier M, Zirngibl A, Kling E, von Scheidt W, Kuch B, Meisinger C. Hyponatraemia on admission to hospital is associated with increased long-term risk of mortality in survivors of myocardial infarction. Eur J Prev Cardiol. 2015;22(11):1419-26. doi: 10.1177/2047487314557963.