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Research Article

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Predictors of Death in Comorbid Patients with Thrombotic Complications: a Single-Center Retrospective Cross-Sectional Study

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INTRODUCTION Despite the improvements and success in the management of thrombosis, the prognosis of thrombotic complications in comorbid patients remains extremely unfavorable. Understanding this problem suggests that it is rational to pay more attention to the prevention of thrombosis in order to avoid thrombotic complications in the first place, and there is an urgent need to improve the ability to predict the development of complications and, most importantly, death. Therefore, some inexpensive, but effective methods of risk assessment need to be developed and integrated in clinical practice.

AIM OF STUDY To assess which laboratory markers can be associated with higher probability of fatal outcome in patients with thrombotic complications.

MATERIAL AND METHODS The retrospective cross-sectional study included 283 patients who were admitted to the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2021. Minimum age was 21 years, maximum age was 96 years, median age – 68 (59,0; 76,5) years. 161 (56,9%) patients were males, 122 (43,1%) – females. Group I included 226 patients with thrombotic complications; Group II included 57 (20,1%) patients who died during hospitalization. The patients were diagnosed with the following thrombotic complications: pulmonary embolism (PE) was diagnosed in 28 (9.9%), acute coronary syndrome with ST segment elevation in 38 (13.4%), arterial thrombosis in 84 (29.7%), venous thrombosis in 54 (19.1%), thrombophlebitis in 22 (7.8%), and systemic thromboembolism in 7 (2.5%) patients.

RESULTS It was established that the decrease in the estimated glomerular filtration to the levels of stage 3 (and lower) chronic kidney disease (AUC — 0,881, sensitivity — 86.92%, specificity — 85.71%), hemoglobin level — to less than 120 g/L (AUC — 0,690, sensitivity — 77,21%, specificity — 55,1%), as well as hypoalbuminemia (AUC — 0,905, sensitivity — 78,89%, specificity — 91,18%) statistically significantly increased the likelihood of death by 19 (OR 19.276, 95% CI [7,792–47.687], p<0.001), 4 (OR 4.158, 95% CI [2.177–7.939], p<0.001), and 30 (OR 30,000, 95% CI [9.93–90,610], p<0.001) times, respectively. The statistical analysis using the univariate logistic regression model revealed that such diseases as coronary artery disease (OR 8,6, 95% CI [2,6–28,466], p<0.001), chronic heart failure (CHF) (OR 13,714, 95% CI [4,784–39,313], p<0.001), atrial fibrillation (OR 3,455, 95% CI [1,830–6,525], p<0.001), type 2 diabetes (OR 2.5, 95% CI [1,286–4,858[, p=0.007), postinfarction cardiosclerosis (OR 3,734, 95% CI [1,953–7,142], p<0.001), and previous stroke (OR 3,319, 95% CI [1,519–6,490], p=0.002) made an independent contribution to death prediction. During the study, we calculated the patients' serum albumin-to-creatinine ratio (sACR). ROC analysis revealed a cut-off point for sACR to be 0.33 g/mmol as having the best predictive ability of death (AUC — 0.920, 84.3 % sensitivity, 85.29% specificity). It was established that sACR less than 0.33 g/mmol increased the probability of death by 26 times (OR 26.3806, 95% CI [9.4573.57], p<0.001).

CONCLUSION Serum albumin-to-creatinine content ratio can be used as a predictor of fatal outcome in comorbid patients with thrombotic complications.

Keywords: cardiovascular diseases, thrombotic complications, predictors of fatal outcome, prognosis

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ACS — acute coronary syndrome
ACVA — acute cerebrovascular accident
AF — atrial fibrillation
AH — arterial hypertension
AKI — acute kidney injury
ALT — alanine aminotransferase
AST — aspartate aminotransferase
AUC — area under the ROC curve
BBT — blood biochemistry test
CHF — chronic heart failure
CI — confidence interval
CLGI — chronic low-grade inflammation
CVC — cardiovascular comorbidity
CVD — cardiovascular diseases
CVE — cardiovascular events
DM — diabetes mellitus
ED — endothelial dysfunction
EE — expected events
eGFR — estimated glomerular filtration rate
FO — fatal outcome
GBT — general blood test
Hb — hemoglobin
Ht — hematocrit
IHD — ischemic heart disease
MI — myocardial infarction
OR — odds ratio
PAD — peripheral artery disease
RBC — red blood cells
RD — risk of death
PE — pulmonary embolism
RF — risk factor
RR — risk ratio
sACR — serum albumin to creatinine ratio
ST-ACS — acute coronary syndrome with ST segment elevation
uACR — urinary albumin to creatinine ratio
WBC — white blood cells

INTRODUCTION

Cardiovascular comorbidity (CVC) remains one of the pressing problems of modern cardiology. The incidence of the comorbid pathology increases with age, reaching 85% in patients of the older age group [1]. The high incidence is explained by the entity of pathogenetic mechanisms of CVC, which includes endothelial dysfunction (ED), hypercytokinemia with the development of chronic low-grade inflammation (CLGI), and increased lipid peroxidation [2-4]. Comorbidity negatively affects the prognosis of disease outcome. A.F. Verbovoy et al. (2017) reported that in patients with two or more disorders, the three-year mortality rate progressively increases, reaching 82% [5]. The above processes lead to damage to the interior wall of blood vessels, predisposing to accelerated development of atherosclerosis, with thrombotic complications in the arterial and venous beds. The most common clinical manifestations of thrombotic complications include acute coronary syndrome (ACS), peripheral arterial disease (PAD), and deep vein thrombosis. It is noteworthy that these conditions can lead to the development of even more serious complications – myocardial and cerebral infarction, pulmonary embolism (PE), aortic and peripheral artery aneurysm, critical ischemia of the lower extremities and fatal outcome (FO). L. Sin et. al. (2016) conducted a research that showed a characteristic association between thrombotic complications in the arterial bed and the risk of death (RD). The study included 1018 patients with stable ischemic heart disease (IHD). During a follow-up period of 7.2 years, 4.9% of the patients

developed symptomatic PAD. Mortality in the group with symptomatic PAD was 19% versus 5% in the group where this pathology was not observed (p<0.001, statistically significant). Also, in the group with developed symptomatic PAD, an increased risk of recurrent cardiovascular events (CVEs) was identified: stroke, transient ischemic attack, chronic heart failure (CHF), myocardial infarction (MI). Moreover, after adjustment for traditional risk factors (RFs) for symptomatic PAD, the association remained with a 70% statistically significant increased risk of recurrent CVEs (adjusted risk ratio (RR) 1.7; 95% confidence interval (95% CI) [1.0–2.9]; p=0.04), and 80% increased RD (adjusted RR 1.8; 95% CI [1.2–2.7]; p=0.0069). Factors implicated in these associations included inflammation, inadequate glycemic control, and severity of cardiac comorbidity [6]. The consequences of venous thromboembolism can also be fatal. Depending on the degree of pulmonary embolization and concomitant right heart dysfunction, the mortality rate from PE can vary from 1% to 50%, even with adequate anticoagulant therapy [7].

Despite current advances in the treatment for thrombosis of various origins, the prognosis for thrombotic complications in patients remains extremely unfavorable. Understanding of this problem suggests that at the moment there is a need to shift the focus aimed at treating thrombotic complications towards the prevention of thrombosis, as well as the ability to predict the development of complications and, most importantly, FO. In this regard, there is a sharp increase in the need to develop relatively inexpensive, but effective methods aimed at identifying the risks of adverse outcomes.

Aim of the study was to determine clinical and laboratory predictors for FO in comorbid patients with thrombotic complications.

MATERIAL AND METHODS

The retrospective cross-sectional study included 288 patients hospitalized at the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2021. Of these, Group I consisted of 219 (75.62%) patients with a favorable outcome of thrombotic complications; Group II – 69 (24.38%) patients who died. The minimum age was 21 years, the maximum – 96 years, the median age was 68 (59.0; 76.5) years; males – 164 (56.9%), females – 124 (43.1%).

Data from patient medical records were obtained using the Unified Medical Information and Analytical System (UMIAS). Further data aggregation was carried out using Microsoft Excel 2019.

Inclusion criteria:

– age over 18 years;

– presence of thrombotic complications as indications for hospitalization.

Non-inclusion criteria:

– age under 18 years.

Exclusion criteria:

– no indication of thrombotic complications in the medical history;

– incompleteness of clinical and laboratory data;

– indication of cancer in the medical history.

The distribution of thrombotic complications was as follows: PE was diagnosed in 32 (11.3%), acute coronary syndrome with ST segment elevation (ST-ACS) – in 42 (14.84%), arterial thrombosis – in 109 (38.51%), venous thrombosis – in 61 (21.55%), thrombophlebitis – in 30 (10.6%), and systemic thromboembolism – in 9 (3.6%) patients.

Upon admission, all the patients underwent a general clinical examination, which included the collection of complaints and anamnesis, and examination of the patient; general blood test (GBT), and blood biochemistry test (BBT). In the GBT and BBT, basic laboratory parameters were assessed, such as the level of hemoglobin (Hb), red blood cells (RBC), hematocrit (Ht), absolute and relative numbers of neutrophils and lymphocytes, total protein, albumin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, lactate dehydrogenase, and urea. Estimated glomerular filtration rate (eGFR) was determined using the CKD-EPI formula. The protocols of pathological autopsies were studied and analyzed.

Statistical processing. Statistical processing of the obtained data was carried out using the Jamovi 2.2.5 statistics program for the macOS Monterey operating system. Quantitative data are presented as median and interquartile range (Me (Q1; Q3)). Nominative variables are presented as absolute numbers and their percentages (n (%)). To compare quantitative variables, the Mann–Whitney U test was used. Nominative indicators were compared depending on the calculated incidence of expected events (EE). For EE less than 5, Fisher's exact test

was used, for EE from 6 to 9, the χ^2-Pearson test with Yates' correction for continuity was used, for EE more than 10, the χ^2-Pearson test was used. To determine predictors of unfavorable outcome, univariate and multivariate binomial logistic regression models were used to calculate the odds ratio (OR), and 95% confidence interval (95% CI). ROC analysis was used to determine cut-off points for quantitative variables, indicating the area under the ROC curve (AUC), and sensitivity and specificity. The level of statistical significance was 5%, differences were considered statistically significant at *p* less than 0.05.

RESULTS

Arterial hypertension (AH), ischemic heart disease (IHD), chronic heart failure (CHF), and chronic kidney disease (CKD) were the most common in the patients of both groups. Stage 4-5 CKD in the groups respectively occurred in 6 (2.7%), and 16 (28.1%) patients (p <0.001, statistically significant). Group II was characterized by a more pronounced incidence of comorbid pathology (Table 1).

The most common causes of death were the following: PE – 8 (14%), acute left ventricular failure – 16 (28%), acute kidney injury (AKI) – 5 (8.8%). As can be seen from Table 2, ST-ACS and systemic thromboembolism were statistically significantly more common in Group II.

Table 1

Distribution of comorbid pathology in patients in the study groups

Diagnosis	Group I (n=219, 75.62%)	Group II (n=69, 24.38%)	*p*-value
AH, *n* (%)	196 (89.49)	53 (76.81)	**<0.001***
IHD, *n* (%)	151 (68.95)	52 (75.36)	<0.309
CHF, *n* (%)	105 (47.94)	48 (69.56)	**<0.001***
AF, *n* (%)	37 (16.89)	23 (33.33)	**0.003***
type 2 DM, *n* (%)	36 (16.43)	18 (26.08)	0.073
Post-infarction cardiosclerosis, *n* (%)	34 (15.52)	24 (34.78)	**<0.001***
ACVA in history, *n* (%)	23 (10.50)	16 (23.18)	**0.001***
CKD (stage 3–5), *n* (%)	58 (26.48)	43 (62.31)	**<0.001***

Notes: * — statistically significant differences; ACVA – acute cerebrovascular accident; AF – atrial fibrillation; AH – arterial hypertension; CHF – chronic heart failure; CKD – chronic kidney disease; DM – diabetes mellitus; IHD – ischemic heart disease

Table 2

Distribution of the nature of thrombotic complications

Nature of thrombotic complications	Group I (n=219, 75.62%)	Group II (n=69, 24.38%)	*p*-value
PE, *n* (%)	22 (10.04)	10 (14.49)	0.306
ST-ACS, *n* (%)	24 (10.95)	18 (26.08)	**0.002***
Arterial thrombosis, *n* (%)	83 (37.89)	26 (37.68)	0.975
Venous thrombosis, *n* (%)	58 (26.48)	8 (11.59)	**0.01***
Thrombophlebitis, *n* (%)	28 (12.78)	2 (2.89)	**0.019***
Systemic thromboembolism, *n* (%)	4 (1.82)	5 (7.24)	**0.024***

Notes: * — statistically significant differences; PE — pulmonary embolism; ST-ACS — acute coronary syndrome with ST segment elevation

Group I was characterized by a decrease in hemoglobin (Hb) concentration, characteristic of anemic conditions, but the number of red blood cells (RBC), despite the intergroup statistically significant difference, remained within the reference values. Also, the group of deceased was characterized by neutrophilic leukocytosis. The number of platelets in the patients of Groups I and II did not differ statistically significantly (p = 0.733), and was within the reference values (Table 3).

The patients of Group II showed a tendency to hypoproteinemia, hypoalbuminemia, and increased concentrations of hepatic transaminases in the blood (Table 4). The above conditions, together with increased concentrations of urea and creatinine in the blood, give reason to assume functional hepatorenal

Table 3

General blood test indicators

Parameter	Group I (n=219, 75.62%)	Group II (n=69, 24.38%)	*p*-value
Hb, g/l	135 (120; 147)	117 (103; 132)	**<0.001***
RBC, $x10^{12}$/l	4.58 (4.2; 5.0)	3.96 (3.4; 4.6)	**<0.001***
Ht, %	41.2 (37.3; 44.0)	35.5 (32.1; 40.1)	**<0.001***
WBC, $x10^9$/l	7.1 (5.7; 8.7)	12.8 (10.1; 16.2)	**<0.001***
Neutrophils, %	65.0 (58.8; 75.2)	82.1 (76.3; 87.0)	**<0.001***
Neutrophils, abs.	4.6 (3.5; 7.1)	9.8 (5.9; 13.4)	**<0.001***
Lymphocytes, %	23.0 (15.9; 30.1)	9.3 (6.1; 15.8)	**<0.001***
Lymphocytes, abs.	1.7 (1.2; 2.1)	1.2 (0.8; 1.9)	**0.010***
Platelets, $x10^{12}$/l	206 (164; 248)	211 (150; 260)	0.733

Note: * — statistically significant differences; Hb – hemoglobin; Ht – hematocrit; RBC – red blood cells; WBC - white blood cells

Table 4

Biochemical blood test indicators in patients of the study groups

Parameter	Group I (n=219, 75.62%)	Group II (n=69, 24.38%)	*p*-value
Total protein, g/l	70.0 (65.2; 74.9)	62.8 (55.9; 67.0)	**<0.001***
Albumin, g/l	38.2 (35.9; 40.5)	29.6 (23.9; 32.7)	**<0.001***
AST, U/l	24.5 (18.7; 34.5)	90.7 (42; 208)	**<0.001***
ALT, U/l	27.0 (17.5; 40.0)	47.0 (28.9; 91.2)	**<0.001***
Urea, mmol/l	6 (4.7; 7.6)	11 (7.5; 17.6)	**<0.001***
Total bilirubin, μmol/l	9.9 (7.4; 13.9)	15.4 (9.5; 19.6)	**<0.001***
Bilirubin bound, μmol/l	2.5 (1.9; 3.9)	6.19 (3.9; 11.5)	**<0.001***
Free bilirubin, μmol/l	6.60 (4.8; 10.3)	7.35 (5.3; 11.8)	0.385
Glucose, mmol/l	5.64 (4.9; 6.6)	7.82 (5.9; 11.0)	**<0.001***
Creatinine, μmol/l	88.9 (77.9; 104)	136 (109; 193)	**<0.001***

Note: * — statistically significant differences; ALT – alanine aminotransferase; AST – aspartate aminotransferase

failure. Elevated glucose levels in the blood, together with the observed neutrophilic leukocytosis, probably characterize the presence of chronic low-grade inflammation.

PREDICTORS OF FATAL OUTCOME

Using a univariate logistic regression model, it was found that an independent statistically significant contribution to the prediction of FO was made by diseases such as: IHD (OR 8.6; 95% CI [2.6–28.45]; p<0.001); CHF (OR 13.7; 95% CI [4.8–39.3]; p<0.001); AF (OR 3.5; 95% CI [1.8–6.5]; p<0.001); type II diabetes (OR 2.5; 95% CI [1.3–4.9]; p=0.007); post-infarction cardiosclerosis (OR 3.7, 95% CI [1.9–7.1], p<0.001); history of ACVA (OR 3.3, 95% CI [1.5–6.5], p=0.002) (Table 5).

Reduction of eGFR to a level corresponding to stage 3 CKD and below (AUC – 0.881, sensitivity – 86.92%, specificity – 85.71%); decreased Hb concentration < 120 g/l (AUC – 0.690, sensitivity – 77.21%, specificity – 55.1%); as well as hypoalbuminemia (AUC – 0.905, sensitivity – 78.89%, specificity – 91.18%) (Fig. 1) increased the likelihood of FO by 19 (OR 19.3; 95% CI [7.8–47.7]; p<0.001), 4 (OR 4.2; 95% CI [2.2–7.9]; p <0.001), and 30 (OR 30.0; 95% CI [9.9–90.6]; p<0.001) times, respectively.

Table 5

Univariate logistic regression model for determining the probability of death

Risk Factor	OR	95% CI	*p*-value
IHD	8.6	2.6–28.5	<0.001*
CHF	13.7	4.8–39.3	<0.001*
AF	3.5	1.8–6.5	<0.001*
Type 2 DM	2.5	1.3–4.9	0.007*
Post-infarction cardiosclerosis	3.7	1.9–7.1	0.001*
ACVA in history	3.3	1.5–6.5	0.002*
eGFR of less than 50 ml/min/1.73m2	19.3	7.8–47.7	<0.001*
Hemoglobin of less than 120 g/l	4.1	2.2–7.9	<0.001*
Hypoalbuminemia (albumin of less than 35 g/l)	30.0	9.9–90.6	<0.001*

Note: * — statistically significant differences; ACVA – acute cerebrovascular accident; AF – atrial fibrillation; CHF – chronic heart failure; DM – diabetes mellitus; eGFR – estimated glomerular filtration rate; IHD – ischemic heart disease

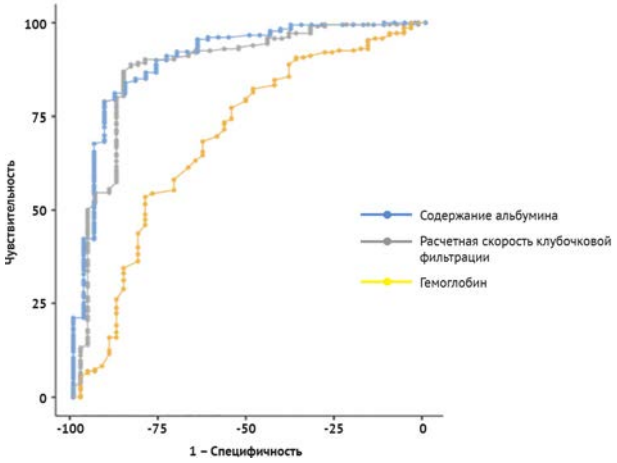

Fig. 1. ROC analysis for estimated glomerular filtration rate, blood albumin and hemoglobin levels

SERUM ALBUMIN TO CREATININE RATIO (sACR)

In Group II, the sACR indicator was statistically significantly lower compared to Group I (Table 6, Fig. 2).

Table 6

Serum content albumin to creatinine content ratio

Parameter	Group I (n=219, 75.62%)	Group II (n=69, 24.38%)	*p*-value
sACR, g/μmol	0.438 [0.355; 0.498]	0.183 [0.141; 0.272]	<0.001*

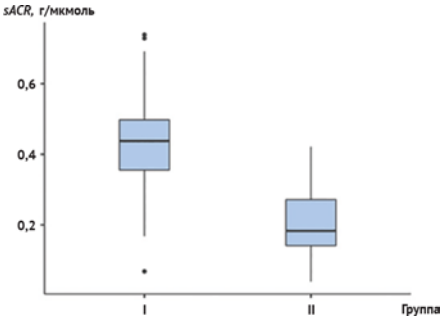

Fig. 2. Difference in sACR values between the selected groups

Using ROC analysis (Fig. 3), a threshold value of sACR=0.33 g/μmol was established at which FO was predicted. AUC for sACR was 0.920, sensitivity of the method was 84.3%, specificity was 85.29%.

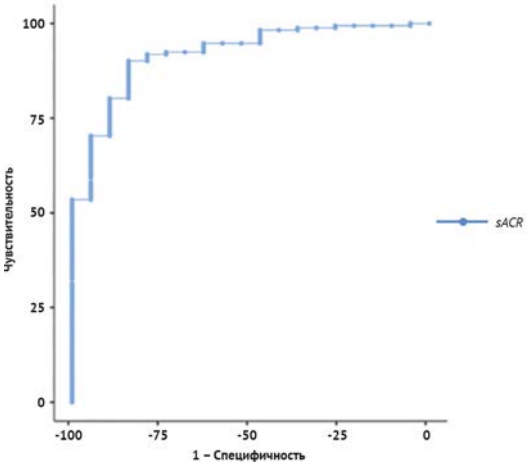

Fig. 3. ROC analysis for sACR

During the building of the univariate logistic regression model, it was found that with a sACR value of less than 0.33 g/μmol, the likelihood of FO increases by 26 times (OR 26.3806; 95% CI [9.45–73.57]; p<0.001).

DISCUSSION

As can be seen from the blood test results, the deceased patients at the time of hospitalization had indicators outside the range of reference values, which makes it possible to distinguish them into a separate category of patients who are expected to have an unfavorable prognosis. The observed changes in indicators may be a reflection of the presence in such patients of more pronounced inflammatory processes, which, however, are sluggish in nature and do not manifest themselves clinically. The connection between comorbidity and chronic inflammation has long been known. In the English-language literature, the term “inflammaging” is used, reflecting the connection between aging, the development of diseases, and the presence of inflammatory processes [8]. It is worth noting that, like any inflammatory process, inflammaging promotes increased production of pro-inflammatory cytokines, which, in turn, further damage the endothelium [9], causing thrombus formation [10]. In addition, proinflammatory cytokines, such as tumor necrosis factor (TNF-α), interleukins (IL-1, IL-8 and IL-6), can alter platelet function, resulting in increased platelet reactivity [11].

Hypoalbuminemia. The increased likelihood of FO in case of hypoalbuminemia found in our study (OR 30.000; 95% CI [9.933–90.610]; p<0.001) is not random. Albumin performs a number of important physiological functions, which include maintaining oncotic pressure, transporting some biologically active substances (fatty and bile acids, cholesterol, metal ions and drugs), and neutralizing free radicals [12]. Moreover, previous studies have proven the antiplatelet ability of albumin [13]. In addition, albumin transports sphingosine-1-phosphate which has a protective effect on the endothelium, acts as a free radical scavenger, and has immunomodulatory and anti-inflammatory effects [14]. Hypoalbuminemia, defined as plasma albumin levels less than 35 g/L, is associated with poor postoperative outcome, and although this relationship has long been known, their underlying pathophysiological mechanisms are still unclear. Theoretically, the association of hypoalbuminemia with adverse outcomes can be explained as follows. First, plasma albumin concentration can serve as a marker for adequate nutritional status. Secondly, being a transport and antioxidant protein, a lack of albumin may reflect a deficiency of the above-described properties, thereby affecting the prognosis of an unfavorable outcome. Third, albumin is an anti-inflammatory protein, thus hypoalbuminemia contributes to the development of an increased inflammatory status, affecting prognosis [12]. Endothelial dysfunction (ED), inflammation, and oxidative stress are key processes in the development of atherosclerosis and many other cardiovascular diseases (CVDs). Research has proven that low levels of plasma albumin are associated with the development of IHD, CHF, AF and venous thromboembolism, regardless of RFs such as body mass index and the presence of chronic inflammation. Hypoalbuminemia is also an independent prognostic factor in some CVDs, such

as chronic coronary syndrome, CHF, congenital heart disease, infective endocarditis, and stroke; even after adjusting for "classical" RFs and prognostic markers [15]. In a meta-analysis by Wiedermann CJ et al. (2010), the authors showed that hypoalbuminemia is a significant predictor of acute kidney injury (AKI) and death due to AKI [16]. In an updated review by Wiedermann C. J. et al. (2017), citing data from randomized controlled trials, it was concluded that albumin might have nephroprotective properties, therefore, timely monitoring and correction of albumin levels can potentially prevent the development of AKI [17]. The results of another meta-analysis conducted by Hansrivijit P. et al. (2021) showed that each subsequent decrease in plasma albumin of 1 g/dL was associated with an increased risk of AKI (OR 1.685; 95% CI [1.302–2.179]). In addition, subgroup analysis showed that age of at least 70 years, and baseline serum albumin of less than 3.2 g/dL were significant RFs for AKI. In the mortality cohort, patients with AKI and hypoalbuminemia had significantly higher mortality (OR 1.183; 95% CI [1.085–1.288]) [18].

CARDIOVASCULAR DISEASES AND KIDNEYS. THE CONCEPT OF THE CARDIORENAL CONTINUUM

The dynamic relationship between the heart and kidneys is well known in the clinic. Cardiorenal syndrome (CRS) was defined as a set of heart and kidney diseases in which acute or chronic dysfunction of one organ can cause acute or chronic dysfunction of the other. In recent years, due to the prevalence of CKD in populations worldwide, significant research efforts have been directed toward determining the mechanism of accelerated atherosclerosis and other associated disorders in this group of patients. Traditionally recognized RFs such as AH, hypercholesterolemia, obesity and hyperhomocysteinemia do not by themselves explain the high incidence of CVD in patients with CKD. Therefore, it is emphasized that non-traditional RFs may be important here, including, in addition to ED, vascular calcification, increased preload, oxidative stress, and inflammation [19]. Changes in cardiovascular function are reflected in indicators of renal function, such as urinary albumin excretion and creatinine clearance. The Prevention of Renal and Vascular Endstage Disease (PREVEND) trial [20] showed that urinary albumin excretion is a predictor of all-cause mortality in the general population. A two-fold increase in urinary albumin concentration was associated with mortality from CVD (RR=1.29; 95% CI [1.18–1.40]), and death from all causes (RR=1.12; 95% CI [1, 04–1.21]) [21]. In another study, Liu S. et al. (2021) explored the association between urinary albumin-to-creatinine ratio (uACR) and the risks of subclinical atherosclerosis, CVEs, and all-cause mortality. It was found that patients with albuminuria had a 50% risk of CVE (RR = 1.50; 95% CI [1.11–2.03]), and 87% RD from all-causes (RR = 1.87; 95% CI [1.24–2.81]) during follow-up. During stratified analysis, the association of higher uACR with the risk of CVEs and all-cause mortality was stronger among individuals with concomitant subclinical atherosclerosis, diabetes mellitus, a large number of cardiovascular RFs, respectively. The authors concluded that uACR levels were positively associated with subclinical atherosclerosis and predicted the risk of CVEs and all-cause mortality. Thus, the authors concluded that assessment of uACR levels should be integrated into risk stratification and prevention of CVEs and all-cause mortality, especially in patients with pre-existing subclinical atherosclerosis and cardiometabolic disorders [22]. Inoue K. et al. (2021) sought to examine the association between uACR within normal limits and cardiovascular or all-cause mortality. This study included a nationally representative sample of 31,413 American adults over the age of 20 years. The association of uACR with cardiovascular and all-cause mortality was explored. The analysis was performed by age, sex, race, and comorbidities (eg, hypertension, type II diabetes, other CVD, and chronic kidney disease). Over a mean follow-up period of 7.6 years, there were 2854 deaths from all causes and 454 deaths from CVD. Higher uACR (greater than 10 mg/g) was associated with an increased risk of all-cause mortality (adjusted HR=1.29; 95% CI: 1.22–1.37) and CVD mortality (adjusted HR=1.34 ; 95% CI: 1.17–1.55). Elevated, even within normal limits, uACR was associated with higher RD from all causes and CVDs, including participants without comorbidities. The results presented in the study indicate the importance of early detection of albuminuria and careful assessment of uACR, even within normal limits, to reduce RD [23].

sACR. In our study, we assessed the prognostic value of sACR for determining the risk of FOs in patients with thrombotic complications and

comorbid pathology. Patients who had low sACR values were statistically significantly associated with a multiple probability of FO (OR 26.3806; 95% CI [9.45–73.57]; p<0.001); moreover, the predictive model we built was characterized by good prognostic significance (AUC for sACR was 0.920, sensitivity of the method was 84.3%, specificity was 85.29%). The identified sACR cut-off point of less than 0.33 g/μmol appears to reflect severe hepatorenal dysfunction, which negatively affects prognosis. There are practically no works devoted to the prognostic significance of serum albumin to creatinine ratio. Liu H. et al. (2020) conducted a trial of 2250 patients with MI, of whom 229 (10.2%) died during a designated follow-up period of 10.7 (7.2–14.6) months. The authors showed that compared to patients with high sACR values, patients with the low values had higher all-cause mortality rates and an increased incidence of adverse outcomes. The Cox regression analysis showed that lower sACR levels were an independent predictor of death from all causes and death from cardiac causes. Thus, the authors concluded that sACR may be a useful biomarker for identifying patients with high-risk MI in the early period of hospitalization in the intensive care unit [24].

CONCLUSIONS

1. Concomitant comorbid pathology makes a significant contribution to the development of fatal outcome. Thus, a statistically significant contribution to the prediction of fatal outcome was made by such diseases as: coronary artery disease (OR: 8.6; 95% CI: [2.6–28.45]; p<0.001); chronic heart failure (OR: 13, 7; 95% CI: [4.8–39.3]; p<0.001); atrial fibrillation (OR: 3.5; 95% CI: [1.8–6.5]; p<0.001); type II diabetes (OR: 2.5; 95% CI: [1.3–4.9]; p=0.007); post-infarction cardiosclerosis (OR: 3.7, 95% CI: [1.9–7.1], p<0.001); history of acute cerebrovascular accident (OR: 3.3; 95% CI: [1.5–6.5], p=0.002).

2. We determined threshold values of laboratory parameters that statistically significantly increase the chances of fatal outcome: the estimated glomerular filtration rate of less than 50 ml/min/1.73 m2 increases the odds of death by 19 times (OR 19.3; 95% CI [7.8–47.7]; p<0.001), hemoglobin concentration of less than 120 g/ l – by 4 times (OR 4.1; 95% CI [2.2–7.9]; p<0.001), decrease in albumin concentration of less than 35 g/l – by 30 times (OR 30; 95% CI [9, 9–90.6]; p<0.001).

3. The prognostic significance of serum albumin to creatinine ratio in relation to the development of fatal outcome was revealed, and its threshold value was determined. When serum albumin to creatinine ratio is less than 0.33 g/μmol, the chances of developing a fatal outcome increase by 26 times (OR 26.3806; 95% CI [9.45–73.57]; p<0.001). The sensitivity of the method was 84.3%, specificity – 85.29%, AUC – 0.920.

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