DOI: https://doi.org/10.2298/SARH230921065D
UDC: 616.6-78-036.8; 616.12-008.46:616.61-78-056.24

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Factors influencing mortality in prevalent hemodialysis patients with different types of heart failure – single-center experience

Marija Dobričić[1], Vesna Pakić[1], Vesna Pejović[1], Aleksandra Kuzmanović[1], Miodrag Milić[1], Jelena Marinković[2], Višnja Ležaić[2]

[1]Special Hospital for Internal Diseases, Lazarevac, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

SUMMARY

Introduction/Objective This retrospective longitudinal study aimed to analyze survival factors in prevalent hemodialysis (HD) patients with different heart failure (HF) phenotypes.

Methods Over 36 months, 96 patients were monitored, with 51 deaths recorded. Patients were categorized into HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF), and non-HF (no HF) groups. Demographic, clinical, and laboratory parameters were analyzed to identify survival predictors within each subgroup.

Results Survival curves did not differ among HF subgroups, and mortality was as follows: 42.9% for HFrEF, 52.4% for HFpEF, and 60.6% for no-HF patients. The main causes of death were COVID-19 infection (70%), followed by *de novo* cardiovascular diseases (myocardial infarction and cerebrovascular insult) (25%). Some demographic (age, male sex, HD vintage) and laboratory differences (anemia, lipids) between the surviving and deceased subgroups of patients have been found. Multivariate analysis identified distinct survival predictors: in HFrEF: pulse rate and interventricular septum thickness; in HFpEF: primary renal disease, cardiac history, and diuretic use; in no-HF: BMI, serum sodium, and HDL/LDL ratios.

Conclusion Our results led us to suspect that COVID-19 infection might have masked the expected impact of HF phenotype on patients' survival. Obtained findings contribute to the evolving understanding of HF in prevalent HD patients in the pandemic era. As HF, dialysis, and COVID-19 intertwine, further investigation is crucial to navigate this intricate finding and optimize patient care.

Keywords: heart failure; hemodialysis; mortality; risk factors

INTRODUCTION

Patients with end-stage renal disease undergoing maintenance hemodialysis (HD) frequently encounter an array of cardiovascular complications, further exacerbated by the coexistence of heart failure (HF) [1]. Consequently, the interplay between HD and HF warrants investigation, particularly in the context of mortality outcomes.

Three types of HF in the general population are recognized: HF with preserved ejection fraction (HFpEF), HF with reduced EF (HFrEF), and HF with moderately reduced EF [2]. Their clinical presentation and risk factors are similar, but the approach to treatment and response to treatment is different. Having in mind that HF is a poor predictor of HD patient outcome [3], timely identification of HF risk factors, and clinical presentation would be helpful in prevention and their management [4]. HFrEF is characterized by a compromised left ventricular ejection fraction (EF), often resulting from structural heart damage, myocardial infarction, or dilated cardiomyopathies. On the other hand, HFpEF, characterized by preserved EF, typically involves diastolic dysfunction and is associated with comorbidities such as hypertension, diabetes, and aging [4].

Mortality rates among patients with HF undergoing HD remain a subject of concern. The concomitant presence of both conditions introduces intricate hemodynamic alterations, electrolyte imbalances, and potential medication interactions, all of which contribute to elevated mortality risk [5, 6]. Understanding the differential impact of HFrEF and HFpEF on mortality in the context of maintenance HD is essential for tailoring effective interventions and optimizing patient care.

Existing research has primarily focused on overall mortality in HD patients without distinguishing between HFrEF and HFpEF subgroups, warranting further investigation into the unique contributors to mortality in each subgroup. Thus, the present study aimed to identify specific factors that contribute to mortality in prevalent HD population with different types of HF.

METHODS

Patients

This was a single-center retrospective longitudinal analysis of data from 96 prevalent patients treated with HD. The included patients

Received • Примљено: September 21, 2023
Revised • Ревизија: June 27, 2024
Accepted • Прихваћено: August 5, 2024
Online first: August 13, 2024

Correspondence to:
Marija DOBRIČIĆ
Special Hospital
for Internal Diseases
Đorđa Kovačevića 27
11550 Lazarevac, Serbia
marija.dobricic@yahoo.com

were older than 18 years, with at least six months of HD treatment. Statins, aspirin, angiotensin-converting enzyme inhibitors (or angiotensin-receptor blockers), and beta-blockers were prescribed to all patients in accordance with current guidelines for secondary prevention of CV events independently of clinical evaluation, as well as anti-aggregation treatment and anticoagulants as needed. Parameter of anemia and mineral metabolism were controlled according to current KDIGO guidelines, which are adopted locally [7, 8]. Studied patients were all asymptomatic for chest pain and had no history of acute coronary syndrome in the previous three months. Exclusion criteria were the inability of the patients to provide signed written consent for participation in the study. According to the criteria of the American and European Society of Cardiology [2, 4] and based on signs and/or symptoms of HF, and left ventricular function indicators obtained by transthoracic echocardiography, patients were divided into the following groups: 1. those with HF and reduced EF – rEF (EF < 40%), plus moderately reduced HF marked as HFmrEF (EF = 40–50%) – 21 patients; 2. those with HF and preserved EF – HFpEF (EF ≥ 50%) – 42 patients; 3. those without overt HF – 33 patients. During the monitoring period (from March 2020 to April 2023), 51 patients died. In order to identify the factors that contributed to the mortality in the study population, we compared all the data reported in the methods below between deceased patients and survivors. For easier comparison, the basal groups of patients with HFrEF, HFpEF, and the group without HF were divided into two subgroups each i.e. those who survived and those who died, thus forming six subgroups marked with numbers 1–6.

The approval of the local ethics committee was obtained (number 110/21.1.2020) and written informed consent was obtained from all the participants.

Data collection

1. Demographic data: age, sex, renal disease, comorbidities (coronary artery disease, hypertension, diabetes mellitus, dyslipidemia, and peripheral obstructive arterial disease), residual diuresis, and body mass index (BMI) including history of coronary artery disease defined as prior revascularization (through angioplasty or coronary artery bypass). Also, each patient was physically examined and questioned for signs and/or symptoms of HF including edema of the lower extremities, (exertional) dyspnea graded by the New York Heart Association criteria (NYHA I-IV), and paroxysmal nocturnal dyspnea/orthopnea [9].

2. Dialytic data: duration of bicarbonate dialysis session (four hours three times a week), dialysis vintage, dialysis membrane (low- and high-flow polysulfone membrane, with a surface of 1.3–1.8 m^2), without change throughout the study period, single pool Kt/V [10], interdialytic weight gain, dialysis access, and systolic and diastolic blood pressure before HD session, volume status checked by bioimpedance spectroscopy, using the Body Composition Monitor – BCM (Fresenius Medical Care, Bad Homburg, Germany).

Measurements

All the measured parameters, i.e. laboratory data and transthoracic echocardiography characteristics, are described in detail in our previous work [11].

Outcomes

The main outcome of this study was all-cause and cardiovascular mortality during the 36 months of follow-up. The date and causes of death were recorded from the patient's medical files. Sudden cardiac death, heart failure, myocardial infarction, severe aortic stenosis, aortic dissection, ischemic stroke, and peripheral vascular ischemia were considered causes of cardiovascular death. Infection-related mortality included COVID-19 cases and sepsis. Also, the number and causes of hospitalizations were recorded from the patient's medical records.

Statistical analyses were performed using the IBM SPSS Statistics, Version 25.0 (IBM Corp., Armonk, NY, USA) and R software (version 3.6.1, R Core Team, 2019). Continuous variates with normal distribution were presented as mean ± SD and compared using the Student's t-test. Variables without normal distribution were presented as median with interquartile ranges and compared using the Mann–Whitney U test or for multiple comparisons Tukey post-hoc test. Categorical data were presented as the number of cases and percentages and compared using the χ^2 test. Cox multivariate logistic regression model including all significantly different characteristics in the univariate logistic regression models (at $p = 0.05$) as well as those predictors that are known to affect the patient's death were used to determine the independent association with all-cause mortality. Two-sided p-values < 0.05 were considered statistically significant.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

RESULTS

Study population

Differences in baseline characteristics between surviving and deceased patients at the entry of the study are presented in Table 1. Considering two subgroups with HFpEF, deceased patients were older, and there were more males. They had been on HD for a shorter time before the start of this study compared to patients from other groups, and had more frequent renal anemia compared to deceased persons without HF. In groups of survivors, more women were in the subgroup with HFrEF compared to the subgroup with HFpEF, and zero NYHA score was more common in HFpEF compared to no HF group. In the groups of non-survivors, the patients from the HFrEF group had

Table 1. Baseline characteristics of examined patients

Characteristics	Group 1 (HFrEF + HFmrEF)		Group 2 (HFpEF)		Group 3 (no HF)		p-value
	Survivors (N = 12 pts)	Deceased (N = 9 pts)	Survivors (N = 20 pts)	Deceased (N = 22 pts)	Survivors (N = 13 pts)	Deceased (N = 20 pts)	
Age, years	70 (61.2–76.5)	67 (52.5–75)	61.6 (52.7–71.2)	71 (61.2–81)	66 (59.2–73)	72 (65–77.5)	0.01
Sex, m/f	10/2	7/2	8/12	17/5	7/6	14/6	0.019
HD vintage, months	51 (30.2–103.2)	57 (35–224)	30.5 (15.2–63.2)	27.5 (17.75–52.5)	51.5 (32.7–82.2)	71 (28.5–130)	0.039
Co-morbidities, HTA/CVI DM2/tumor COPD/PVD IM/PCI/CABG	 2/- -/1 1/- -/-/1	 5/1 2/- -/-/1	 8/1 1/- 1/- 1/-	 9/1 4/2 2/2 8/-/5	 6/- -/1 - 1/-	 11/2 2/2 3/1 2/2/2	Non-significant
Renal anemia, yes	11	8	18	22	11	16	0.029
NYHA class: 1 2 3	 3 6 3	 1 5 3	 7 13 0	 6 10 6	 1 10 2	 3 13 4	0.021
EF %	46.33 ± 1.5	39.53 ± 5.26	59 ± 6.88	55 ± 4.53	59.12 ± 6.94	60.37 ± 5.39	0.025
Pre-dialysis BP Systolic, mmHg	155.5 (130–172.7)	155 (141.5–160.5)	148.5 (126.5–158)	146 (136.5–153.7)	145 (131–166.5)	140.5 (132.5–166.5)	Non-significant
Diastolic, mmHg	72.5 (68.5–79.7)	73 (68–95)	77 (64.7–81.7)	66.5 (59.5–77.0)	78 (72–85)	73 (64–88)	Non-significant
kT/V	1.05 (0.96–1.24)	1.41 (0.94–1.57)	1.1 (0.94–1.27)	1.03 (0.88–1.27)	1.18 (1.05–1.38)	0.96 (0.9–1.12)	Non-significant

HF – heart failure; rEF – reduced ejection fraction; pEF – preserved ejection fraction; HD – hemodialysis; HTA – hypertension; CVI – cardiovascular insult; DM2 – diabetes mellitus type 2; PVD – peripheral vascular disease; COPB – chronic obstructive pulmonary disease; IM – myocardial infarction; PCI – percutaneous coronary intervention; CABG – coronary artery by-pass grafting; NYHA – New York Heart Association classification of heart failure;
Median (IQR), X ± SE, N – patients number;
Statistically significant differences:
age: group 2 survivors *vs.* deceased; sex: survivors group 1 *vs.* group 2; group 2 survivors *vs.* deceased; HD vintage: deceased group 1: group 2, group 2 *vs.* group 3; renal anemia: deceased group 2 *vs.* group 3; NYHA class 3: group 2 survived *vs.* deceased; EF: deceased group 1 *vs.* group 3

Table 2. Laboratory parameters of examined patients

Parameters	Group 1 (HFrEF + HFmrEF)		Group 2 (HFpEF)		Group 3 (no HF)		p-value
	Survivors (N = 12 pts)	Deceased (N = 9 pts)	Survivors (N = 20 pts)	Deceased (N = 22 pts)	Survivors (N = 13 pts)	Deceased (N = 20 pts)	
Leukocytes, $\times 10^9$/l	6.68 (5.75–8.81)	5.01 (3.62–7.23)	6.72 (5.28–8.16)	5.92 (5.20–7.58)	5.64 (5.28–7.37)	7.37 (5.99–8.73)	< 0.042
Hemoglobin, g/l	98 (93–103)	94 (86–120)	107 (89–121)	98 (84.2–110.5)	107 (94–120)	108 (97–125)	0.047
Platelets, $\times 10^9$/l	190 (176–203)	122.5 (106.7–182.2)	202 (162–222)	215 (176.7–255.2)	208 (127–229)	189 (156–247)	< 0.036
Sodium, mmol/l	139 (138–141.5)	137 (132–142)	138 (138–140)	138.5 (137–141)	138 (137–139.5	139 (138–141)	Non-significant
Calcium, mmol/l	2.15 (1.89–2.22)	2 (1.79–2.2)	2.16 (2.10–2.27)	2.13 (2.04–2.25)	2.15 (2–2.32)	2.16 (2.14–2.26)	Non-significant
Phosphate, mmol/l	1.31 (1.11–1.65)	1.17 (0.77–1.61)	1.76 (1.23–2.12)	1.38 (1.17–1.8)	1.31 (1.11–1.79)	1.35 (1.07–1.59)	Non-significant
iPTH, ng/ml	158.4 (51–404.8	133.4 (21.9–687.5)	418.3 (151.8–774.4)	163.3 (132–294.6)	438.4 (81.9–948.4)	319.2 (148.2–889.7)	Non-significant
CRP, mg/l	3.85 (1.36–7.57)	4.59 (1.72–15.94)	2.86 (1.37–5.40)	4.26 (3.14–16.61)	2.31 (1.11–5.88)	4.17 (2.76–21.63)	Non-significant
Total cholesterol, mmol/l	4.6 (3.85–5.66)	3.8 (3.74–5.62)	4.56 (3.96–5.27)	3.96 (3.52–5.24)	4.51 (3.92–5.009)	3.89 (3.61–5.28)	Non-significant
HDL-c, mmol/l	1.02 (0.84–1.33)	1.17 (0.92–1.47)	1.04 (0.84–1.65)	1.38 (0.94–1.92)	1.56 (1.25–2.01)	1.01 (0.63–1.54)	< 0.012
LDL-c, mmol/l	2.59 (2–2.93)	2.17 (1.96–3.43	2.41 (2.03–3)	1.89 (1.46–2.7)	2.06 (1.68–2.62)	2.35 (2.05–3.14)	Non-significant
HDL/LDL ratio	2.31 (1.7–3.23)	2.11 (1.6–2.39)	2.16 (1.91–2.75)	1.53 (0.98–2.29)	1.17 (0.65–1.94)	2.38 (2.06–3.55)	< 0.006
TG, mmol/l	1.65 (1.15–3.89)	1.39 (1.12–2.36)	1.96 (1.22–2.48)	1.2 (0.85–2.25)	1.09 (0.87–1.9)	1.72 (1.24–2.76)	Non-significant

PTH – parathyroid hormone, TG – triglyceride, HDL-c – high-density lipoprotein (LDL) cholesterol particles, LDL-c – low-density lipoprotein (LDL) cholesterol particles;
Median (IQR); statistically significant differences: leukocytes: deceased: group 1 *vs.* group 3, group 3: survived *vs.* deceased; hemoglobin deceased group 2 *vs.* group 3; platelets: group 1: survived *vs.* deceased, deceased: group 1 *vs.* group 2; group 1 *vs.* group 3; HDL-c: survived: group 1 *vs.* group 3; group 2 *vs.* group 3; group 3 survived *vs.* deceased; HDL/LDL ration: survived: group 1 *vs.* group 3, group 2 *vs.* group 3, deceased: group 2 *vs.* group 3; group 3: survived *vs.* deceased

Table 3. Number and causes of hospitalization and patients' death during the study period

Parameter	Group 1 (HFrEF + HFmrEF)		Group 2 (HFpEF)		Group 3 (no HF)		p
	Survivors (N = 12 pts)	Deceased (N = 9 pts)	Survivors (N = 20 pts)	Deceased (N = 22 pts)	Survivors (N = 13 pts)	Deceased (N = 20 pts)	
Hospitalization							Non-significant
0 1 2 ≥ 3	4 4 3 1	6 1 1 1	6 12 1 1	10 6 4 3	5 2 4 2	8 6 2 6	
Causes							Non-significant
Infection CVD others	6 1 1	1 2 0	10 3 1	5 4 2	5 3 0	7 5 0	
Death		9		22		20	
Causes							Non-significant
COVID-19 CVD Others		4 5		19 3		13 5 2	

CVD – cardiovascular diseases

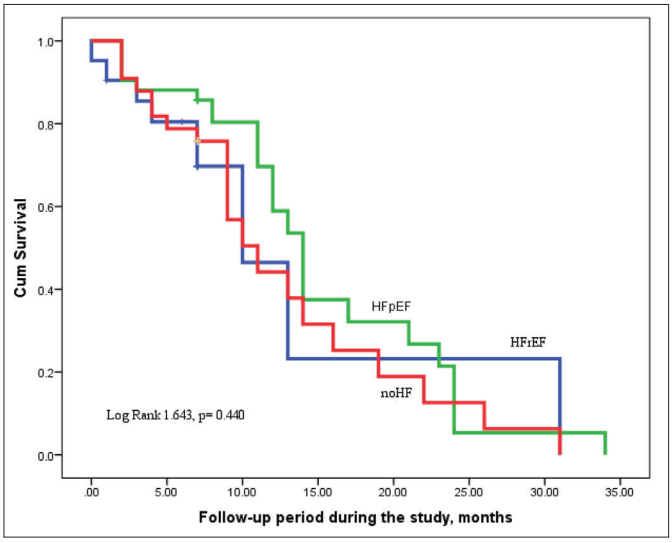

Figure 1. Survival plots for prevalent hemodialysis patients with heart failure (Kaplan–Meier analysis)

the lowest mean EF compared to the other two groups of patients. No other difference was found among subgroups regarding demographic, clinical, treatment, and ultrasound heart parameters except for the EF, which was the basis for patient grouping (data are not presented).

Laboratory analyses and lipid profile

Table 2 presents the results of laboratory analyses. When comparing survivors and deceased patients, those with HFrEF had higher platelet counts, while those without HF had lower leukocytes and serum sodium (both within normal limits). Minor differences, not statistically significant in iPTH and CRP were noted in both HFpEF and no HF subgroups. Also, deceased patients with HFrEF had the lowest leukocyte, hemoglobin, and platelet counts in comparison to other subgroups. Among survivors, patients with HFrEF had slightly lower phosphate and PTH compared to group 2 with HFpEF, but this difference was not statistically significant. Looking at lipids, in comparisons between survivors and deceased patients, group 3 had higher HDL-c levels, but a lower HDL/LDL ratio. On the other hand, survivors from group 2 showed a higher HDL/LDL ratio than deceased from the same subgroup.

Clinical outcome and survival analysis

No difference was found in the frequency and cause of hospitalizations between the examined groups of patients (Table 3). Throughout the 36 months of follow-up, 51 patients died. The frequency of COVID-19 infection being the cause of death (Table 3) was notably higher in comparison to cardiovascular diseases (CVD) across all groups of patients studied, i.e. 36 *vs*. 13 patients ($\chi^2 = 35.41$, $p < 0.001$).

No difference in patients' survival curves among the studied groups was found, as shown by Kaplan–Meier analysis (Figure 1). The medians for survival time – representing the point at which half of the patients were anticipated to remain alive – were as follows: 10 months (IQR 4.9–15.1) for HFrEF, 14 months (IQR 12.0–15.9) for HFpEF, and 11 months (IQR 7.39–14.61) for the no-HF group.

Mortality predictors were separately analyzed in each group using Cox regression analysis. Univariate Cox logistic regression analysis in patients with HFrEF identified the following mortality predictors: cardiovascular insult (CVI), pulse rate, and interventricular septum (IVS) thickness. However, multivariate analysis revealed only pulse rate and IVS thickness as independent predictors after adjusting for other variables in the model (Table 4). Each unit increase in the pulse rate correlated with a 187.47 times higher risk of mortality, though with considerable uncertainty due to a wide confidence interval. Similarly, IVS thickness showed a substantial risk increase, but with significant uncertainty.

For HFpEF patients, diabetes mellitus type 2 (DM2) and nephroangiosclerosis (as an underlying kidney disease), myocardial infarction, coronary artery bypass grafting, the use of diuretics, and the number of hospitalizations were identified by univariate analysis as significant predictors of mortality. Multivariate analysis retained only DM2, nephroangiosclerosis, and diuretic use as independent positive mortality predictors (Table 5). Although the wide confidence interval indicates some uncertainty in the estimate, the point estimate suggests a strong association between DM2, nephroangiosclerosis, and use of diuretics and mortality in patients with HFpEF.

Table 4. Mortality predictors selected with multivariable Cox regression analysis for patients from group 1 with heart failure with reduced ejection fraction

Parameter	Exp (B)	Sig	95% CI for Exp(B)	
			Lower	Upper
Pulse rate	187.470	0.027	1.839	19,110.495
IVS	8864.416	0.023	3.482	22,566,646.151

IVS – interventricular septum thickness

Table 5. Mortality predictors selected with multivariable Cox regression analysis for patients from group 2 with heart failure with preserved ejection fraction

Parameter	Exp (B)	Sig	95.0% CI for Exp(B)	
			Lower	Upper
DM2	15.366	0.007	2.091	112.930
Nscl	5.657	0.049	1.011	31.664
Diuretics, yes	4.043	0.044	1.036	15.777

DM2 – diabetes mellitus type 2; Nscl – nephroangiosclerosis

Table 6. Mortality predictors selected with multivariable Cox regression analysis for patients from group 3 with no heart failure

Parameter	Exp (B)	Sig	95% CI for Exp (B)	
			Lower	Upper
NYHA	2.055	0.031	2.055	3.953
Posterior wall	0.002	0.001	0.002	0.080
BMI, kg/m^2	1.271	0.006	1.271	1.511
Adipose tissue mass, kg	0.882	0.011	0.882	0.971

NYHA – New York Heart Association classification of heart failure; BMI – body mass index

In the case of patients with no HF, univariate Cox logistic regression analysis identified CVI, chronic obstructive pulmonary disease, IVS and posterior wall thickness, BMI, fat tissue, adipose tissue mass, sodium, HDL/LDL ratio, and number of hospitalizations as significant predictors of mortality. Multivariate analysis highlighted independent predictors for mortality to be NYHA class, BMI, posterior wall thickness, and adipose tissue mass after adjusting for other variables in the model (Table 6). Higher NYHA class correlated with a 2.05 times higher mortality risk, while each unit increase in BMI was associated with a 1.271 times higher risk. Conversely, each unit increase in adipose tissue mass is associated with a 0.882 times lower risk of mortality. Additionally, each unit increase in posterior wall thickness is associated with lower risk of mortality. However, the extremely small hazard ratio and wide CI indicate caution in interpreting this result.

DISCUSSION

In this single-center study, we aimed to examine the factors influencing the survival of prevalent HD patients with different HF phenotypes over a 36-month follow-up period. The key findings can be summarized as follows: 1) mortality rate among prevalent HD patients was high, with 53% of patients dying; 2) the survival rates of patients with two distinct HF phenotypes and those without HF were similar throughout the study; 3) COVID-19 infections emerged as a significantly greater risk factor for mortality compared to CVD; 4) *de novo* cardiovascular events contributed to a quarter of the recorded deaths, reaffirming the enduring significance of CVD as a mortality cause even during the pandemic; 5) analysis of laboratory and clinical parameters revealed noteworthy predictive associations with mortality: elevated pulse rate and specific cardiac structural parameters in patients with HFrEF, while primary kidney diseases, and diuretic usage in patients with HFpEF.

Our findings corroborate the elevated mortality observed in the studied population, aligning with conclusions drawn by other researchers. Comparing survival rates over two years, notable differences emerge when HF is present, with rates of 80% for patients without HF, and 33% for those with HF [12]. Regarding HF phenotypes, survival disparities have been reported. Among patients with HFpEF, a longer survival of 73% was noted, contrasting with HFrEF patients at 55% [12, 13, 14]. In the present study, mortality rates were 42.9% for HFrEF, 52.4% for HFpEF, and 60.6% for the no-HF patients. These outcomes, divergent from mortality analyses published so far, prompted us to investigate the underlying causes.

We conducted this study during the COVID-19 pandemic, and 70% of patients died due to COVID-19 infection equally distributed in all three groups of patients, compared to 25% who died due to *de novo* CVD (acute myocardial infarction, cerebrovascular insult). It is well known that COVID-19 infection has caused a substantial increase in mortality rates among the general population, and various patient populations, including those with cardiovascular diseases and patients with chronic kidney disease and on renal replacement therapy [15]. High mortality after the diagnosis of COVID-19 in HD patients was reported: the 28-day probability of death was 25%, but during the 90 days after diagnosis it reached 40.5%, emphasizing the increased vulnerability of HD patients due to a compromised immune system and the presence of numerous comorbidities [16, 17]. Our results led us to suspect that COVID-19 infection might have masked the impact of HF phenotype on patients' survival.

Our findings emphasize the ongoing significance of CVD in mortality, even beyond the context of the pandemic. Notably, 25% of the studied patients died of new cardiovascular events. Some differences in demographics and laboratory values between surviving and deceased patient subgroups could have influenced mortality. A higher prevalence of anemia was observed among deceased patients with HFpEF. This suggests a potential link between anemia, HF, and unfavorable outcomes, consistent with prior research [7]. Analyzing subgroups within HFrEF and HFpEF, deceased patients were older and with a higher proportion of males. Additionally, deceased patients with HFpEF had a shorter HD vintage. Patient age has consistently emerged as a mortality risk factor across studies, reflecting increasing mortality with age [5, 18]. Our observation of higher mortality among male patients with shorter HD vintage contrasts with findings by Sumida et al. [19]. They reported an inverse relationship between patient mortality and prolonged HD duration in a Japanese registry cohort. These disparities underscore the intricate

and multifaceted nature of factors contributing to patient outcomes, influenced in part by the size of the analyzed sample.

The observed associations between laboratory and clinical parameters with survival outcomes align with prior research. For instance, regardless of the limitations in interpretation and the uncertainty of the results, elevated pulse rate and cardiac structural parameters in HFrEF patients as positive predictors of mortality highlight the potential significance of both cardiac and hemodynamic factors in this cohort which is well-known from previous studies [14, 20]. The impact of underlying kidney disease (diabetic kidney disease and nephroangiosclerosis, to be more precise), and the use of diuretics (which reduce the risk of death) in patients with HFpEF on survival outcomes is consistent with the complex interaction between kidney function, cardiovascular health, and survival observed by other authors [14, 21, 22]. Additionally, the impact of metabolic parameters, serum sodium level, and lipid ratios on survival outcomes among patients with no HF offers further insights into the intricate finding of determinants in this cohort.

It is essential to acknowledge the limitations of our study, including the small sample size and the single-center design, which may limit the generalizability of our findings. Nevertheless, our analysis provides valuable insights into the complex of factors influencing survival outcomes in prevalent HD patients with different HF phenotypes. These findings pave the way for further research, potentially in multicenter studies, to validate and expand upon our observations, ultimately leading to a more comprehensive understanding of the predictors driving survival in this complex clinical scenario.

CONCLUSION

In this study of prevalent hemodialysis patients with diverse HF phenotypes, we analyzed survival dynamics. During the pandemic, COVID-19 emerged as a prominent cause of mortality, potentially obscuring expected differences in HF subtypes. While survival rates between the HFrEF, HFpEF, and no-HF subgroups showed no significant disparities, multivariable Cox regression unveiled independent predictors specific to each group that included pulse rate and cardiac parameters in HFrEF, kidney diseases in HFpEF, and metabolic factors in no-HF patients. As we interpret these results in the pandemic context, we emphasize the significance of ongoing research in the interplay of HF, dialysis, COVID-19, and survival, to guide enhanced patient care strategies. By combining personalized treatment plans, multidisciplinary collaboration, patient education, and ongoing research, healthcare providers can strive to improve outcomes and enhance the quality of life for these patients.

Conflict of interest: None declared.

REFERENCES

1. Rangaswami J, McCullough PA. Heart Failure in End-Stage Kidney Disease: Pathophysiology, Diagnosis, and Therapeutic Strategies. Semin Nephrol. 2018;38(6):600–17. [DOI: 10.1016/j. semnephrol.2018.08.005] [PMID: 30413254]
2. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al; Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18(8):891–975. [DOI: 10.1002/ejhf.592] [PMID: 27207191]
3. Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. Nephrol Dial Transplant. 2018;33(suppl_3):iii28–iii34. [DOI: 10.1093/ndt/gfy174] [PMID: 30281132]
4. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(18):e895–e1032. [DOI: 10.1161/CIR.0000000000001063] [PMID: 35363499]
5. Raja A, Warming PE, Nielsen TL, Plesner LL, Ersbøll M, Dalsgaard M, et al. Left-sided heart disease and risk of death in patients with end-stage kidney disease receiving hemodialysis: an observational study. BMC Nephrol. 2020;21(1):413. [DOI: 10.1186/s12882-020-02074-3] [PMID: 32977752]
6. De Lima JJG, Macedo TA, Gowdak LHW, David-Neto E, Bortolotto LA. Diastolic and systolic left ventricular dysfunction and mortality in chronic kidney disease patients on hemodialysis. Nephrology (Carlton). 2022;27(1):66–73. [DOI: 10.1111/nep.13960] [PMID: 34378284]
7. Babitt JL, Eisenga MF, Haase VH, Kshirsagar AV, Levin A, Locatelli F, et al; Conference Participants. Controversies in optimal anemia management: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Conference. Kidney Int. 2021;99(6):1280–95. [DOI: 10.1016/j.kint.2021.03.020] [PMID: 33839163]
8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl (2011). 2017;7(1):1–59. [DOI: 10.1016/j.kisu.2017.04.001] Erratum in: Kidney Int Suppl (2011). 2017;7(3):e1. [DOI: 10.1016/j.kisu.2017.10.001] [PMID: 30675420]
9. Association NYH, Fox AC, Gorlin R, Levin RI; New York Heart Association. Criteria Committee. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Lippincott Williams and Wilkins; 1994. p. 352.
10. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. J Am Soc Nephrol. 1993;4(5):1205–13. [DOI: 10.1681/ASN.V451205] [PMID: 8305648]
11. Dobricic M, Pakic V, Arsenovic A, Pejovic V, Kuzmanovic A, Milic M, et al. Chronic heart failure phenotypes in prevalent patients treated with hemodialysis- a single-center experience. Srp Arch Celok Lek. 2022;150(11–12):660–6. [DOI: 10.2298/SARH220509096D]
12. Derthoo D, Belmans A, Claes K, Bammens B, Ciarka A, Droogné W, et al. Survival and heart failure therapy in chronic dialysis patients with heart failure and reduced left ventricular ejection fraction: an observational retrospective study. Acta Cardiol. 2013;68(1):51–7. [DOI: 10.1080/ac.68.1.2959632] [PMID: 23457910]
13. Wang AY, Wang M, Lam CW, Chan IH, Lui SF, Sanderson JE. Heart failure with preserved or reduced ejection fraction in patients treated with peritoneal dialysis. Am J Kidney Dis. 2013;61(6):975–83. [DOI: 10.1053/j.ajkd.2012.12.030] [PMID: 23474006]

14. Antlanger M, Aschauer S, Kopecky C, Hecking M, Kovarik JJ, Werzowa J, et al. Heart Failure with Preserved and Reduced Ejection Fraction in Hemodialysis Patients: Prevalence, Disease Prediction and Prognosis. Kidney Blood Press Res. 2017;42(1):165–76. [DOI: 10.1159/000473868] [PMID: 28395286]
15. Speranza M, López-López JD, Schwartzmann P, Morr I, Rodríguez-González MJ, Buitrago A, et al. Cardiovascular Complications in Patients with Heart Failure and COVID-19: CARDIO COVID 19-20 Registry. J Cardiovasc Dev Dis. 2024;11(2):34. [DOI: 10.3390/jcdd11020034] [PMID: 38392248]
16. Hilbrands LB, Duivenvoorden R, Vart P, Franssen CFM, Hemmelder MH, Jager KJ, et al; ERACODA Collaborators. COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. Nephrol Dial Transplant. 2020;35(11):1973–83. [DOI: 10.1093/ndt/gfaa261]. Erratum in: Nephrol Dial Transplant. 2021;36(10):1962. [DOI: 10.1093/ndt/gfab028] [PMID: 33151337]
17. Johansen KL, Chertow GM, Gilbertson DT, Ishani A, Israni A, Ku E, et al. US Renal Data System 2022 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2023;81(3 Suppl1):A8–A11. [DOI: 10.1053/j.ajkd.2022.12.001] [PMID: 36822739]
18. Escoli R, Carvalho MJ, Cabrita A, Rodrigues A. Diastolic Dysfunction, an Underestimated New Challenge in Dialysis. Ther Apher Dial. 2019;23(2):108–17. [DOI: 10.1111/1744-9987.12756] [PMID: 30255628]
19. Sumida K, Yamagata K, Iseki K, Tsubakihara Y. Different impact of hemodialysis vintage on cause-specific mortality in long-term hemodialysis patients. Nephrol Dial Transplant. 2016;31(2):298–305. [DOI: 10.1093/ndt/gfv402] [PMID: 26666499]
20. Tschöpe C, Kherad B, Klein O, Lipp A, Blaschke F, Gutterman D, et al. Cardiac contractility modulation: mechanisms of action in heart failure with reduced ejection fraction and beyond. Eur J Heart Fail. 2019;21(1):14–22. [DOI: 10.1002/ejhf.1349] [PMID: 30485591]
21. Mark PB, Mangion K, Rankin AJ, Rutherford E, Lang NN, Petrie MC, et al. Left ventricular dysfunction with preserved ejection fraction: the most common left ventricular disorder in chronic kidney disease patients. Clin Kidney J. 2022;15(12):2186–99. [DOI: 10.1093/ckj/sfac146] [PMID: 36381379]
22. Wu J, Li X, Zhang H, Lin L, Li M, Chen G, et al. Development and validation of a prediction model for all-cause mortality in maintenance dialysis patients: a multicenter retrospective cohort study. Ren Fail. 2024;46(1):2322039. [DOI: 10.1080/0886022X.2024.2322039] [PMID: 38415296]

Фактори који утичу на смртност код превалентних болесника лечених хемодијализом са различитим типовима срчане инсуфицијенције – искуство једног центра

Марија Добричић[1], Весна Пакић[1], Весна Пејовић[1], Александра Кузмановић[1], Миодраг Милић[1], Јелена Маринковић[2], Вишња Лежаић[2]

[1]Специјална болница за интерне болести, Лазаревац, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија

САЖЕТАК

Увод/Циљ Ова ретроспективна студија са дужим праћењем имала је за циљ да анализира факторе преживљавања код превалентних болесника лечених хемодијализом са различитим фенотиповима срчане инсуфицијенције (СИ).

Методе Током 36 месеци, праћено је 96 болесника, а забележен је 51 смртни случај. Према типу СИ болесници су подељени у групе: СИ са смањеном ејекционом фракцијом (СИрЕФ), СИ са очуваном ејекционом фракцијом (СИоЕФ) и без СИ. Анализирани су демографски, клинички и лабораторијски параметри како би се идентификовали предиктори преживљавања унутар сваке подгрупе.

Резултати Криве преживљавања нису се значајно разликовале међу испитаним групама, а број умрлих је био следећи: 42,9% за СИрЕФ, 52,4% за СИоЕФ и 60,6% за болеснике без СИ. Главни узроци смрти били су инфекција ковидом 19 (70%), а затим *de novo* кардиоваскуларне болести (инфаркт миокарда и цереброваскуларни инсулт) (25%). Подгрупе преживелих и умрлих болесника разликују се по старости, полу, трајању хемодијализе и анемији и профилу липида. Мултиваријантна анализа идентификовала је предикторе преживљавања: код СИрЕФ брзину пулса и дебљину интервентрикуларног септума; код СИпЕФ примарно обољење бубрега, претходне срчане болести и употребу диуретика; код групе без СИ индекс телесне масе, натријум у серуму и однос *HDL*/*LDL* липида.

Закључак Добијени налази доприносе разумевању СИ код превалентних болесника лечених хемодијализом у ери пандемије. Како се СИ, дијализа и ковид 19 преплићу, даље истраживање је кључно за објашњење ове замршене интеракције и оптимизацију бриге о болесницима.

Кључне речи: срчана инсуфицијенција; хемодијализа; морталитет; фактори ризика