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## ИНФЕКЦИОННЫЙ ЭНДОКАРДИТ У ПАЦИЕНТОВ НА ПРОГРАММНОМ ГЕМОДИАЛИЗЕ

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## Infective Endocarditis in Patients on Maintenance Hemodialysis

### Резюме

**Аннотация.** Актуальность проблемы определяется увеличением распространенности заместительной почечной терапии (ЗПТ) и связанных с ней инфекционных осложнений, в том числе инфекционного эндокардита (ИЭ) — заболевания с высокой смертностью и неблагоприятным прогнозом. **Цель исследования.** Изучить особенности течения, клинические характеристики, лабораторно-инструментальные параметры и исходы ИЭ у пациентов, получающих лечение программным гемодиализом (ПГД). **Материал и методы.** Обследованы 371 пациент с определенным ИЭ (модифицированные DUKE-критерии), госпитализированные с 2000 по 2024 г. Из них 23 (6,2%) пациента получали ПГД в амбулаторных диализных центрах Саратовской области. Группу сравнения составили 348 пациентов с ИЭ, не нуждающихся в ЗПТ. **Результаты.** Медиана возраста пациентов с ИЭ на ПГД составила 51 [38; 56] год. Диализный стаж 13 [2; 58,5] мес. Частота встречаемости ИЭ в исследуемой когорте составила 6,2% (23 из 371 пациента с ИЭ). Положительная гемокультура получена у 14 (60,8%) пациентов с ИЭ на ПГД, золотистый стафилококк выделен у 9 (39%) и энтерококк — у 5 (21,7%). У большинства пациентов на ПГД отмечена левосторонняя локализация ИЭ (17 (73,9%)), как и в группе сравнения. В группе пациентов с ИЭ на ПГД оказались значимо выше частота острого течения заболевания, сахарного диабета, неврологических осложнений ( $p < 0,05$ ), а также более высокие количественные значения маркеров системного воспаления: С-реактивного протеина, прокальцитонина ( $p < 0,05$ ). Индекс коморбидности Charlson был выше, анемия и тромбоцитопения более выражены у пациентов с ИЭ на ПГД ( $p < 0,05$ ). Госпитальная летальность при ИЭ на ПГД составила 52,17% против 17,8% в группе сравнения (OR 4,228, 95% ДИ: 1,784 — 10,02; ( $p < 0,05$ )). **Заключение.** ИЭ у пациентов на ПГД — инфекционное заболевание, ассоциированное с медицинским вмешательством, вызываемое, главным образом, золотистым стафилококком. ИЭ на ПГД характеризуется острым течением, выраженностью воспалительной реакции, высокой летальностью. В связи с повышенным риском развития ИЭ у пациентов на ПГД из-за эксплуатации сосудистого доступа и неблагоприятным прогнозом, пациентам показаны строгие меры асептики, эхокардиографическое исследование при клиническом подозрении на ИЭ (необъяснимой лихорадке). В ведении пациентов с ИЭ на ПГД существуют особенности антибактериальной терапии, диализной терапии и профилактики с целью минимизации факторов риска и т.п., что требует мультидисциплинарного взаимодействия специалистов.

**Ключевые слова:** инфекционный эндокардит, сердечно-сосудистые заболевания, программный гемодиализ

### Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

### Источники финансирования

Авторы заявляют об отсутствии финансирования при проведении исследования

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## Abstract

**Background.** The relevance of the problem is determined by the increasing prevalence of renal replacement therapy and associated infectious complications, including infective endocarditis (IE) — a disease with high mortality and poor prognosis. **Aim.** To study the clinical characteristics, laboratory and instrumental parameters, and outcomes of IE in patients undergoing maintenance hemodialysis (HD). **Materials and methods.** A total of 371 patients with definite IE (modified DUKE criteria) hospitalized between 2000 and 2024 were examined. Of these, 23 patients received maintenance HD at outpatient dialysis centers in the Saratov region. The control group consisted of 348 patients with IE who did not require renal replacement therapy. **Results.** The mean age of dialysis patients with IE was 51 [38; 56] years, with a dialysis duration of 13 [2; 58.5] months. The prevalence of IE in the studied cohort was 6.2% (23 out of 371 patients with IE). Positive blood cultures were obtained in 14 (60.8%) of patients with IE on maintenance HD, with *Staphylococcus aureus* isolated in 9 (39%) and *Enterococcus* in 5 (21.7%) cases. Left-sided IE localization was observed in the majority of maintenance HD patients (17 (73.9%)), similar to the comparison group. Patients with IE on maintenance HD exhibited a significantly higher frequency of acute disease progression, diabetes mellitus, and neurological complications ( $p < 0.05$ ), along with elevated quantitative levels of systemic inflammation markers, such as C-reactive protein and procalcitonin ( $p < 0.05$ ). The Charlson comorbidity index was higher, and anemia and thrombocytopenia were more severe in patients with IE on maintenance HD ( $p < 0.05$ ). Hospital mortality in IE patients on maintenance HD was 52.17%, compared to 17.8% in the comparison group (OR 4.228, 95% CI: 1.784–10.02;  $p < 0.05$ ). **Conclusion.** IE in patients on maintenance HD is a healthcare-associated infection primarily caused by *Staphylococcus aureus*. IE in maintenance HD patients is characterized by an acute course, severe inflammatory response, and high mortality. Due to the increased risk of IE in maintenance HD patients related to vascular access use and poor prognosis, strict aseptic measures and echocardiographic evaluation in cases of clinical suspicion of IE (e.g., unexplained fever) are recommended. The management of IE in maintenance HD patients requires specific approaches to antibiotic therapy, dialysis treatment, and prevention to minimize risk factors, necessitating multidisciplinary collaboration among specialists.

**Key words:** *infective endocarditis, cardiovascular disease, maintenance hemodialysis*

## Conflict of interests

The authors declare no conflict of interests

## Sources of funding

The authors declare no funding for this study

## Conformity with the principles of ethics

The study protocol was approved by the local ethics committee of the Saratov State Medical University named after V.I. Razumovsky (Protocol № 8, dated 04.02.2025). All patients provided written informed consent.

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AV prosthesis — arteriovenous prosthesis, AVF — arteriovenous fistula, RRT — renal replacement therapy, IE — infective endocarditis, PHD — program hemodialysis, CKD — chronic kidney disease, CKD-5D — chronic kidney disease, Stage 5 (dialysis-dependent stage), EchoCG — echocardiography

## Introduction

Infectious endocarditis (IE) is a disease with unfavorable prognosis and high mortality [1]. Modern IE is characterized by the trend to increased incidence and clinical variability, with several IE forms associated with medical care specifically contributing to it [2]. One example is IE in patients with chronic kidney disease (CKD) Stage 5 administered renal replacement therapy (RRT) with program hemodialysis (PHD). The prevalence of IE in patients administered PHD is 2.9%, which is 50–180 fold higher than in the general population [3]. This is due to the following risk factors of IE reported among patients with CKD-5D: relapsing bacteremia due to constant vascular access, heart valve calcification due to impaired phosphorus-calcium metabolism, immunosuppression in patients with uremia, comorbidity [4].

Hospital and annual mortality in “dialysis” IE exceeds those parameters in the “non-dialysis” population [3, 4]. Poor prognosis and high mortality level underscore the need for early IE diagnosis in PHD, detection of high-risk patients, and development of treatment and prevention strategies [3, 5]. The effective management of such patients requires multidisciplinary approach and coordinated operations of various specialists [6].

The Department of Hospital Therapy of Saratov State Medical University (SMU) has been studying the IE issue for many years, with the multidisciplinary inpatient department as the main clinical base — this includes three cardiological departments, nephrology and renal replacement therapy departments. The department and inpatient employees have an experience in managing patients with IE in PHD.

**Study objective:** analyzing features of the course, clinical-laboratory characteristics, and outcomes of inpatient IE treatment in patients with CKD Stage 5 administered PHD.

## Materials and Methods

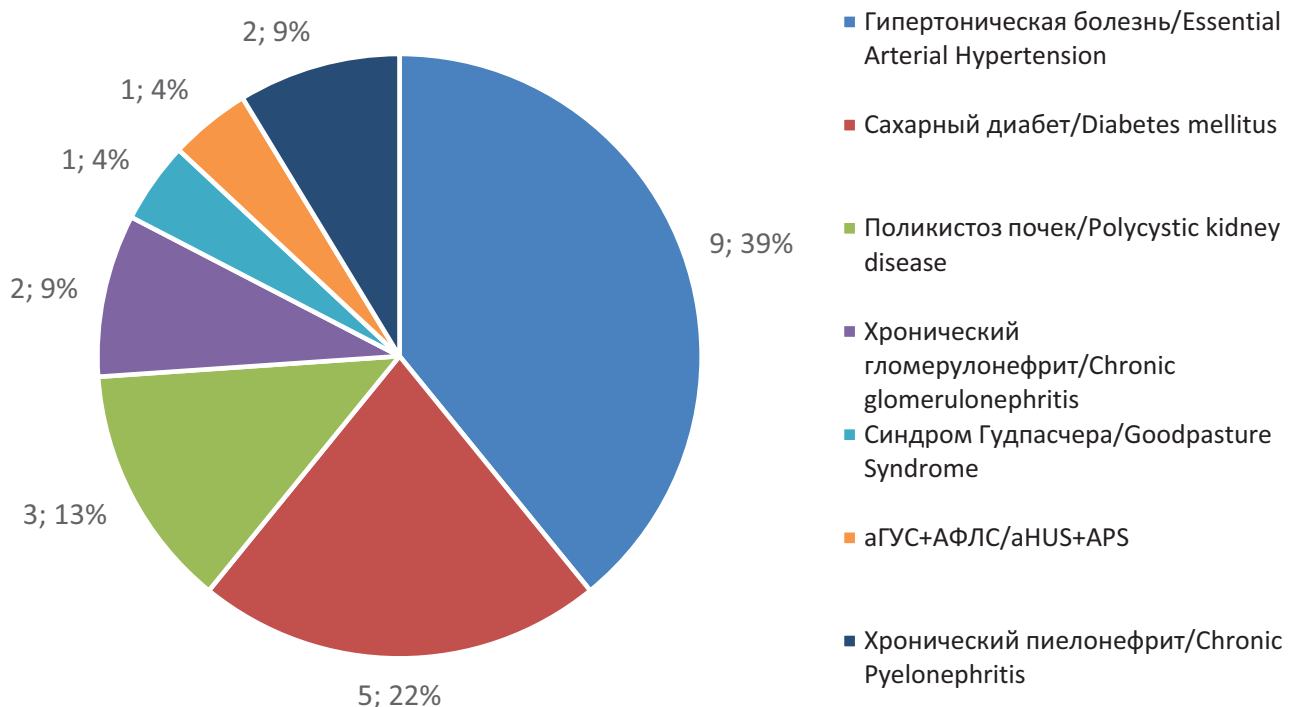
371 patients with definite IE (according to the modified Duke criteria) [2] were examined during their treatment in SBI Regional Clinical Hospital of Saratov City within the period from 2000 until 2024. 23 patients received PHD due to CKD Stage 5 in outpatient dialysis centers of Saratov City and the Saratov Region. Apart from the standard examination, all patients underwent transthoracic echocardiography (EchoCG) (transesophageal EchoCG was arranged in 7 patients) with three blood cultures sampled to verify IE. The results obtained in patients with IE in PHD were compared to those in 348 patients that did not require treatment with dialysis. All examined patients were included into the IE patient database (Rospatent Certificate on State Database Authorization No. 2024625267 dated November 18, 2024).

Materials were statistically processed using StatTech 4.6.1 software (developed by ©StatTech LLC, Russia). Quantitative parameters were assessed regarding normal distribution using the Shapiro–Wilk test (for < 50 subjects) or the Kolmogorov–Smirnov test (for > 50 subjects). Normally distributed quantitative parameters

were described using mean arithmetics (M) and standard deviations (SD), 95 % confidence interval (95 % CI) limits. Concerning non-normal distribution, quantitative signs were presented as medians (Me) [lower and upper quartiles (Q1; Q3)]. Two groups were compared in quantitative parameters with the normal distribution (provided variance was equal) using the Student’s test, for unequal variance — using the Welch’s t-test, and for non-normal distribution — using the Mann–Whitney U-test. Binary categorical signs in two groups were compared in the confusion matrix analysis using the Pearson’s chi-square test (with the expected event values > 10) or the exact Fischer’s test (with those values < 10). The odds ratio (OR) with 95 % confidence intervals (CIs) were calculated to assess the association between the analyzed risk factor and the primary outcome. Statistically significant differences were considered with  $p < 0.05$ .

## Results

The median patient’s age with IE in PHD was 51 [38; 56] years, with the PHD duration of 13 [2; 58.5] months. Classic hemodialysis was used as a PHD method in 19 (82.6%) of 23 patients, hemodiafiltration — in 4 (17.4%) patients. The incidence of “dialysis” endocarditis in the analyzed cohort was 6.2 % (23 of 371 patients with IE). The character of primary nephropathy patients with “dialysis” IE is presented in Figure 1.



**Figure 1.** Types of nephropathy leading to renal replacement therapy in patients with infective endocarditis on maintenance hemodialysis (n=23)

Note: aHUS — atypical hemolytic-uremic syndrome, APS — antiphospholipid syndrome

The following bacteremia sources were detected in patients with IE in PHD: arteriovenous fistula (AVF) (in 6 (26.1%) patients), vascular prosthesis (1 (4.3%)), permanent dialysis catheter/central venous catheter (16 (69.6%)). Positive blood cultures were obtained in 14 (60.8%) patients with IE in PHD. *Staphylococcus aureus* was isolated in 9 (39%), *Enterococcus* — in 5 (21.7%) patients.

The left-sided endocarditis was detected in 17 (73.9%) patients with IE in PHD, right-sided — in 6 (26.1%) patients. In 20 (91.3%) patients IE affected one heart valve; two valves were affected in 3 (8.7%) patients. Aortic valve IE was observed in 11 (47.8%), mitral valve IE — in 9 (39.1%), and tricuspid valve IE — in 5 (22%) patients. Simultaneous lesions of two valves were detected in 2 (8.7%) (mitral + aortic) and in 1 (4.3%) (aortic + tricuspid) patients, respectively (Fig. 2). No significant differences in valvular lesion rates were detected in the control group.

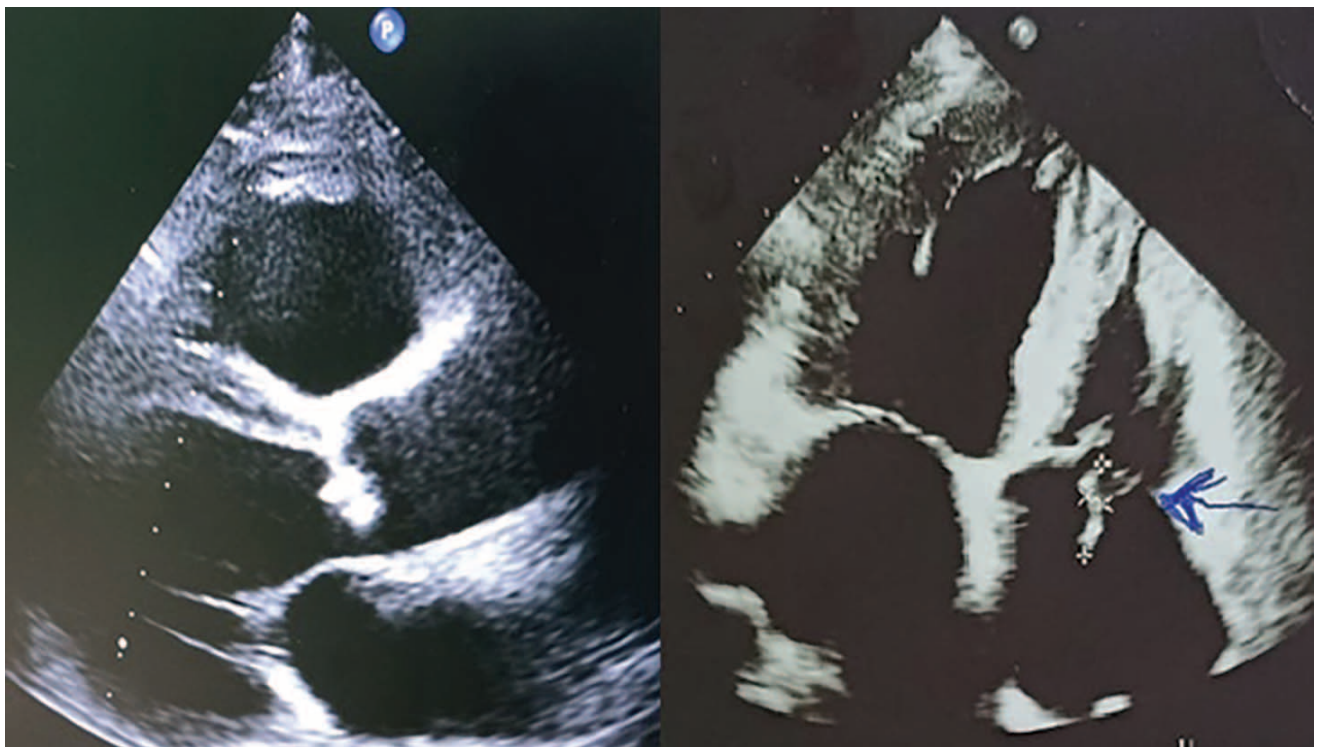
All examined patients with IE were administered antibiotics in accordance with recommendations on the treatment of this disease [1, 2]. Cardiac surgery was arranged in 5 (21.7%) patients with IE in PHD and 82 (26%) in the control group ( $p > 0.05$ ).

Features of several demographic, clinical, and laboratory parameters of examined patients with IE are presented in Table 1.

Febrile undulating fever with chills was the most common sign in both groups of patients with IE (in all patients with IE in PHD and in 321 (92%) patients in the non-dialysis group). No significant differences were detected between groups concerning the rate of large vegetations, peripheral symptoms, cutaneous hemorrhagic vasculitis, emboli, myocardial and hepatic lesions ( $p > 0.05$ ). At the same time the rate of acute disease course, diabetes mellitus, neurological complications was significantly higher in the group of patients with IE in PHD (Table 1;  $p < 0.05$ ). Hospital mortality in IE in PHD was 52.17% vs. 17.8% in the control group (OR 4.228 (95% CI: 1.784–10.02;  $p = 0.0012$ ).

Table 2 defines several parameters of patients with “dialysis-associated” IE ( $n = 23$ ) depending on the inpatient treatment outcome (deceased and survived patients).

Significant differences were observed between the survived and deceased patients with IE in PHD (Table 2): deceased ones had higher peripheral white blood cell counts ( $p = 0.005$ ), fibrinogen levels ( $p = 0.027$ ), erythrocyte sedimentation rate ( $p = 0.01$ ), and lower systolic BP levels ( $p = 0.017$ ). At the same time, left ventricular hypertrophy parameters (myocardial weight and myocardial mass index) were higher in the group of survived patients ( $p = 0.017$  and  $p = 0.039$ , respectively).



**Figure 2.** Subacute staphylococcal infective endocarditis of the native aortic and tricuspid valves in a 37-year-old female (left — parasternal long-axis view, PLAX; right — apical 4-chamber view, A4C).

**Details.** A hyperchoic, round, fixed structure measuring 0.6 cm is observed on the non-coronary cusp. A hyperchoic, mobile structure measuring 1.0 × 0.4 cm is present on the anterior coronary cusp. A hyperchoic, mobile structure measuring 2.0 × 0.5 cm is noted on the anterior leaflet of the tricuspid valve

**Table 1.** Clinical and laboratory characteristics of patients with infective endocarditis (n=371) receiving and not receiving maintenance hemodialysis

Parameters		Non-dialysis IE patients (n=348)	Maintenance hemodialysis patients (n=23)	p-value
Age (years)		42,50 [33,75; 54,00]	51,00 [38,50; 56,00]	0,128
Gender, n (%)	Male	241 (69,3 %)	17 (73,9 %)	0,638
	Female	107 (30,7 %)	6 (26,1 %)	
Course of infective endocarditis, n (%)	Acute IE	96 (27,6 %)	16 (70 %)	p < 0,001*
	Subacute IE	252 (72,4 %)	7 (30 %)	
Diabetes mellitus, n (%)	No Diabetes	328 (94,3 %)	18 (78,3 %)	0,003*
	Diabetes	20 (5,7 %)	5 (21,7 %)	
In-hospital mortality, n (%)	Deceased	62 (17,8 %)	12 (52,17 %)	0,0012
	Survived	286 (82,2 %)	11 (47,82 %)	
Neurological complications, n (%)	Yes	94 (27,5 %)	13 (72,2 %)	p=0,000*
	No	248 (72,5 %)	5 (27,8 %)	
Charlson comorbidity index (points)		2,00 [1,00; 3,00]	4,00 [3,00; 5,00]	< 0,001*
Red blood cells (*10 <sup>12</sup> /L)		3,70 [3,20; 4,20]	2,75 [2,54; 3,08]	< 0,001*
Hemoglobin (g/L)		108,00 [92,50; 125,00]	96,00 [79,50; 100,00]	0,004*
Platelets (×10 <sup>9</sup> /L)		203,00 [154,50; 265,00]	176,00 [129,50; 232,50]	0,465
Erythrocyte sedimentation rate (mm/h)		29,00 [14,00; 39,00]	40,00 [28,00; 53,00]	0,011*
Fibrinogen (g/L)		4,50 [3,90; 6,00]	6,00 [5,03; 6,92]	0,053
Albumin (g/L)		35,00 [30,00; 40,00]	34,15 [29,75; 36,02]	0,399
Total cholesterol (mmol/L)		4,00 [3,45; 4,90]	3,50 [3,00; 3,98]	0,037*
Total bilirubin (µmol/L)		15,00 [12,00; 18,05]	11,20 [7,95; 15,50]	0,016*
C-reactive protein (mg/L)		36,00 [12,00; 96,00]	96,00 [71,00; 180,00]	< 0,001*
Procalcitonin (ng/mL)		0,40 [0,10; 1,00]	11,00 [1,05; 13,38]	0,004*
Natriuretic peptide (pg/mL)		2850,00 [905,25; 3375,00]	2204,00 [2203,50; 2204,50]	0,398
Systolic blood pressure (mmHg)		110,00 [110,00; 120,00]	130,00 [125,00; 140,00]	0,002*
Diastolic blood pressure (mmHg)		70,00 [60,00; 70,00]	80,00 [70,00; 80,00]	0,049*
Left ventricular posterior wall (cm)		1,10 [1,00; 1,22]	1,25 [1,16; 1,39]	0,041*

Note: \* — p<0.05. For p<0.05, the exact significance value of the test is provided. Non-normally distributed data are presented as Me [Q1; Q3].

## Discussion

Patients with IE in PHD did not differ from the “non-dialysis” group with IE in demographics (gender, age). A younger age than the mean age of patients with IE described in the literature is a feature of patients examined by us [2]. The trend to increasing age is observed among patients with IE, including that associated with medical care [2]. The same trend is observed by us, but mainly in the latest decade, while the database of examined patients covers a rather large time period. The predominance of males among patients with IE confirms

global, European, and Russian data, regardless of whether patients are on dialysis or not [1, 2].

The risk of IE in PHD rises when using a central and permanent dialysis catheter, while it is lower with AVF and arteriovenous (AV) prosthesis as a vascular access method for dialysis. The least risk of bloodstream infections and IE is associated with AVF [7]. Due to this, preventive AVF before the start of permanent RRT is recommended in patients in PHD for the prophylaxis of IE and its relapses [5]. AVF is considered a safer option compared to the central venous catheter, as it demonstrates a lower rate of bacteremia.

**Table 2.** Comparative characteristics of patients with dialysis-associated infective endocarditis (n=23) based on the outcome of inpatient treatment

Parameters	Outcome		p-value
	Survivors (n=12)	Non-survivors (n=11)	
Age (years)	48,80 (8,11)	48,09 (16,45)	0,903
Dialysis duration (months)	20,5 [3,5; 101]	9,5 [2; 43,5]	0,414
Charlson comorbidity index (points)	3,50 [3,00; 4,75]	4,00 [3,00; 5,00]	0,642
Systolic pulmonary artery pressure (mmHg)	47,00 [43,00; 71,00]	52,00 [51,50; 61,50]	0,354
Left ventricular ejection fraction (%)	61,81 (5,84)	57,50 (7,42)	0,294
Left ventricular myocardial mass (g)	367,75 (36,04)	272,33 (34,65)	0,017*
Left ventricular mass index (g/m <sup>2</sup> )	209,40 (34,22)	148,00 (26,51)	0,039*
Fibrinogen (g/L)	4,88 (0,94)	7,30 (1,13)	0,027*
Albumin (g/L)	36,00 [30,50; 36,80]	30,00 [29,50; 30,00]	0,298
C-reactive protein (mg/L)	71,00 [49,00; 79,05]	96,00 [96,00; 126,50]	0,120
Procalcitonin (ng/mL)	5,55 [1,05; 10,50]	8,04 [4,05; 12,02]	1,000
Hemoglobin (g/L)	98,00 [96,00; 103,75]	86,00 [79,50; 93,00]	0,362
Leukocytes (×10 <sup>9</sup> /L)	8,33 (3,78)	14,24 (2,20)	0,005*
Band Neutrophils (%)	7,29 (4,23)	13,86 (3,24)	0,007*
Platelets (×10 <sup>9</sup> /L)	207,83 (113,73)	175,00 (67,22)	0,665
Erythrocyte sedimentation rate (mm/h)	27,00 [23,25; 28,50]	56,00 [45,00; 60,00]	0,01*
Systolic blood pressure (mmHg)	138,33 (7,53)	120,00 (10,00)	0,017*
Diastolic blood pressure (mmHg)	80,00 (8,94)	63,33 (15,28)	0,072

Note: \* — p < 0.05. For p < 0.05, the exact significance value of the test is provided. Data are presented as mean ± SD for normally distributed variables and median [IQR] for non-normally distributed variables.

However, a high blood flow rate via AVF ( $\geq 1500$  mL/min) may create a turbulent flow that can potentially damage the endocardium, especially in patients with pre-existing valvular diseases. This proposal requires additional research, as currently no direct evidence concerning this issue is published in the literature. It is considered important to control the “discharge” rate via the fistula to prevent this endocardial injury.

It is evident that the vascular access, which is a source of bacteremia in IE, should be removed/replaced. Some authors conclude that transferring the patient with IE to peritoneal dialysis is an efficient strategy [7].

Blood culture results presented by us completely correspond to literature data about the etiology of IE in patients in PHD. *Staphylococcus aureus* (most often MSSA, although the role of MRSA increases) is the main cause of bacteremia in patients in PHD [7]. With the vascular access, skin becomes the main source of causative agents that enters the bloodstream, although the role of nasal carriage cannot be excluded. Enterococci are second in the list [3, 5]. Staphylococcal etiology predominantly explains the acute IE course in patients in

PHD, as it is typical for this highly virulent pathogen. This may also explain the systemic inflammation severity and higher levels of such markers as C-reactive protein, procalcitonin, erythrocyte sedimentation rate ( $p < 0.05$ ). High inflammatory reaction activity is also important regarding poor outcomes of inpatient treatment in patients with IE on PHD (Table 2).

An issue of vascular access in IE in patients in PHD requires an individual approach in each case: not enough controlled studies have been conducted regarding this problem [7]. However, one should follow international guidelines, including those concerning the management of patients with vascular access infections/catheter-associated bloodstream infections. They are associated with biofilms, which are often resistant to systemic antibiotics. In cases of fever lasting over 48–72 hours, bacteremia, sepsis it is recommended to immediately remove the dialysis catheter [8].

Left-sided IE lesions were predominant among examined patients in PHD. One should also not a sufficiently high rate of right-sided lesions, especially concerning the absence of injection drug users among our patients

in PHD. A variable rate of left- and right-sided cardiac lesions in IE in PHD is described in the literature. Left-sided lesions are most common, although enough attention is also paid to right-sided and tricuspid valve lesions. Left-sided IE lesions in patients in PHD are caused by high pressures in left cardiac chambers, hemodynamic risk factors in IE also include pulmonary hypertension and hypervolemia [9]. Infected blood flow from the vascular access devices, injury of endothelium in major veins, atrial endocardium, and the tricuspid valve by implantable dialysis catheters, endocardial micro-injuries by air bubbles due to turbulent blood flow in the tubing system and the dialyzer play a role in the pathogenesis of right-sided IE lesions [9, 10].

When analyzing EchoCG data, left ventricular posterior wall thickness was significantly higher in the dialysis group compared to the group of patients not administered PHD ( $p = 0.041$ ) (Table 1), which may be associated with a higher level and prolonged hypertension in these patients. The same parameters were higher in survived patients, while the BP level was lower in deceased patients when comparing two subgroups of patients with IE in PHD with different outcomes ( $p < 0.05$ ) (Table 2). Lower BP is an indirect feature of the activity of the infectious process affecting the endothelium. Thus, the bacterial infection may promote or worsen the pre-existing intra-dialysis hypotension. Otherwise, no significant differences in echocardiographic parameters were detected in groups of patients with IE administered or not administered PHD (Table 1). The majority of EchoCG parameters are probably determined predominantly by the location of valvular lesions, which was detected with similar rates in both groups.

One should account for several features of using echocardiography and interpreting its results in patients administered PHD. Excessive fluid removal during the dialysis procedure may decrease the cardiac chamber volumes, affecting the myocardial contractility. This reflects on several EchoCG parameters (e.g., end-diastolic volume, end-systolic volume, left ventricular ejection fraction) [11]. Hypervolemia correction and decreased pressures in cardiac chambers decrease the functional valvular regurgitation degree, although the latter one is not affected in organic valvular lesions. Thus, specific EchoCG parameters may differ before and after hemodialysis/hemodiafiltration [11]. The character of changes depends on the baseline condition of the cardiovascular system, volume of the fluid removed, and ultrafiltration time/rate during dialysis. Thus, it is feasible to arrange EchoCG with the normal hydration status (preferably during the first day after the procedure), or if it is impossible (e.g., in urgent examinations), considering the time elapsed from the previous dialysis in order to assess several intracardiac hemodynamics parameters correctly.

It was expected to observe the differences of the dialysis IE patient cohort from those not administered PHD in the comorbidity index and severity of anemia, with the latter one specific for terminal renal failure. The diabetes mellitus rate was significantly higher in the group of patients in PHD compared to others — 21.7 % and 5.8 %, respectively ( $p = 0.003$ ). It is interesting to note that all 5 (21.7 %) dialysis patients with IE had Type 1 DM.

Antibiotic IE therapy in patients in PHD is administered based on general regulations and principles of IE treatment, with antibiotics active against staphylococci/enterococci recommended during the initial treatment (before isolating the pathogen). However, it is important to adjust dosages of antibiotics accounting for clearance and pharmacodynamics features in patients with CKD Stage 5D during hemodialysis/hemodiafiltration. It is recommended to administer antibiotics immediately after dialysis to maintain efficient therapeutic levels. The low rate of binding with plasma proteins and a low molecular weight of the antibiotic promote adequate drug elimination during hemodialysis/hemodiafiltration. On the contrary, the high rate of binding with proteins significantly limits drug elimination by all dialysis methods. Using high-flow membranes during hemodiafiltration promotes efficient removal of antibiotics (e.g., daptomycin) despite their high molecular weights. It is recommended to monitor blood levels and account for nephrotoxicity of antibiotics with a narrow therapeutic index (vancomycin, aminoglycosides) in the setting of preserved residual renal function [2, 10, 12].

We did not detect significant differences in the rate of cardiac surgeries in patients with IE in PHD or without it ( $p = 0.626$ ). Cardiac surgeries in patients with IE in PHD are indicated in acute heart failure, uncontrollable infections, and high risk of embolic complications [1, 2]. Patients with IE in PHD have a higher risk of adverse cardiac surgery outcomes. Nevertheless, refusal or delays in indicated surgeries worsen IE outcomes in patients in PHD [7, 13].

Optimal strategies of preventing IE and its relapses in patients in PHD have not been developed yet. Nevertheless, general and local measures of IE prevention in these patients are discussed in the literature [14]. General measures of IE prevention include adequate RRT use (achieving the required “dialysis dose”, timely “dry weight” adjustment, maintenance of normal nutritional status, correction of anemia and phosphorus-calcium disorders/prevention of valvular calcification, etc.) [10], minimizing the rate of using temporary dialysis catheters, elimination of chronic infectious foci, regular bacteriological tests of the nasopharyngeal flora, staphylococcal vaccinations, quality control of dialyzing solutions. Local measures for the prevention of IE and its relapses

in patients in PHD presume the preventive formation of a permanent (AVF, AV-prosthesis) vascular access, skin treatment and strict adherence to aseptics during procedures [14].

## Conclusion

Thus, IE in patients in PHD is an infectious disease associated with the medical intervention, mainly caused by *Staphylococcus aureus*, commonly — by *Enterococcus*. Our results confirm the literature data about the high mortality among patients with IE in PHD exceeding values in the general population. Patients administered PHD should belong to the high-risk IE group, while the vascular access should be primarily considered as a source of bacteremia. IE features in dialysis patients include a predominantly acute course, comorbidity, high risk of poor outcomes. Early IE detection is required in such patients (with special attention to the vascular access condition and EchoCG in cases of any unexplained fever). In general, patients with IE in PHD are managed based on general regulations, accounting for features of antibiotic therapy in dialysis patients, vascular access procedures and possible replacement, cardiac surgeries (as indicated). Preventive IE measures in patients in PHD may be aimed at decreasing risk factors via the preventive formation of a permanent vascular access (AVF, AV-prosthesis), adequate selection of the RRT method, achievement of target “dialysis dose” parameters, timely correction of phosphorus-calcium disorders, etc. Nephrologist (specializing in renal replacement therapy) should always be a part of a multidisciplinary “endocarditis team when diagnosing IE in PHD to determine the patient management in this disease.

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All authors made significant contributions to the preparation of the work, read and approved the final version of the article before publication

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