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VOLUME STATUS OPTIMIZATION IN HEMODIALYSIS PATIENTS AND PULMONARY HYPERTENSION OUTCOMES

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Abstract: Achievement of optimal "dry weight" on program hemodialysis (HD) of patients with pulmonary hypertension. Hydration and "dry weight" were assessed by bioimpedanceometry, pulmonary artery pressure was investigated by Doppler-echocardiography. 52 patients (20 men, 32 women, mean age - 55±12 years) treated with HD were examined; 58% of patients had pulmonary hypertension. During the study, an association between regression of left ventricular hypertrophy and reduction of pulmonary hypertension was observed. Pulmonary artery pressure correlated with extracellular body water content according to bioimpedance data.

Keywords: hemodialysis, "dry weight", pulmonary hypertension.

Introduction

Pulmonary hypertension in hemodialysis patients is often multifactorial, arising from chronic volume overload, anemia, endothelial dysfunction, and arteriovenous access hemodynamics [1]. Repeated episodes of subclinical fluid retention may contribute to persistent elevation of pulmonary artery pressures, even in patients with stable interdialytic weight gain [2]. In this context, accurate determination of dry weight becomes not only a volumetric target but also a preventive measure against progressive right ventricular dysfunction and heart failure [3].

Recent studies have emphasized that bioimpedance spectroscopy allows for non-invasive and reproducible assessment of extracellular water (ECW) and total body water (TBW), enabling clinicians to detect subclinical overhydration [4]. In a prospective trial by Tanaka et al. (2023), targeting bioimpedance-guided dry weight adjustment led to significant improvements in LV mass index and arterial stiffness indicators [5]. Moreover, Doppler echocardiographic evaluation of pulmonary artery

pressure and left heart geometry provides complementary information to fluid status assessment [6].

Tsai et al. (2021) highlighted that PH was significantly associated with both increased ECW/ICW ratio and reduced hemoglobin levels, pointing to the complex interplay between volume status and anemia in this population [7]. Furthermore, vascular calcification and disturbances in phosphorus-calcium metabolism are thought to exacerbate vascular stiffness, further contributing to the pathophysiology of PH in chronic kidney disease (CKD) [8]. While some early data suggested that AV fistula flow could elevate cardiac output and PAP, more recent analyses demonstrate no consistent correlation between fistula blood flow and PH severity [9]. Therefore, the integration of echocardiography, bioimpedance, and laboratory markers is recommended for comprehensive cardiovascular risk stratification in HD patients [10].

Purpose of the Study:

The objective of this study is to evaluate the relationship between pulmonary artery pressure and hydration status in patients undergoing hemodialysis.

Materials and Methods:

A total of 52 patients (20 males and 32 females; mean age 55 ± 12 years) diagnosed with stage 5 chronic kidney disease (CKD) and undergoing maintenance hemodialysis (HD) were enrolled in the study. All patients were treated at the Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation. The predominant etiologies of CKD within the cohort were glomerulonephritis, diabetic nephropathy, and polycystic kidney disease.

Hemodialysis sessions were performed thrice weekly, each lasting approximately four hours, utilizing NephroPlus dialysis machines. The dialysis protocol included the

use of bicarbonate-based dialysis solutions and high-flux dialyzers (Elisio 17H and 21H) fitted with Polynephron membranes.

Comprehensive cardiac assessments were conducted using transthoracic echocardiography and Doppler-echocardiography in accordance with the guidelines of the American Society of Echocardiography, both at baseline and after 12 months of HD therapy. The following parameters were evaluated: interventricular septal and left ventricular posterior wall thickness in diastole, end-diastolic dimension (EDD), left atrial diameter, and left ventricular ejection fraction (EF). An EF exceeding 50% was considered indicative of preserved systolic function. The left ventricular mass index (LVMI) was calculated by indexing myocardial mass to body surface area, with left ventricular hypertrophy (LVH) defined as LVMI ≥115 g/m² in men and ≥95 g/m² in women. Relative wall thickness (RWT) was estimated using the formula RWT = 2 × LV posterior wall thickness / LV internal diameter at diastole. Hydration status was evaluated using multifrequency bioimpedance analysis (ABC-01 apparatus, "MEDAS," Sport-5 software), which provided data on total body water (TBW), extracellular water (ECW), and lean body mass. Blood flow through the arteriovenous (AV) fistula was assessed using Doppler ultrasonography. The diagnosis of pulmonary hypertension (PH) was established based on the diagnostic criteria of the European Society of Cardiology.

All statistical analyses were performed using Student's t-test and univariate correlation analysis. Quantitative data were expressed as mean ± standard deviation (SD) or as medians with interquartile ranges, depending on distribution type. A p-value less than 0.05 was considered statistically significant.

Results and Discussion.

A cohort of 52 patients (20 males and 32 females; mean age 55 ± 12 years) with stage 5 chronic kidney disease (CKD) receiving maintenance hemodialysis (HD) was

prospectively enrolled in the present study. All participants were managed at the Republican Specialized Scientific and Practical Medical Center of Nephrology and Kidney Transplantation. The principal underlying etiologies of CKD included glomerulonephritis, diabetic nephropathy, and autosomal dominant polycystic kidney disease.

Hemodialysis was administered three times per week, with each session lasting approximately four hours, using NephroPlus dialysis systems. The dialysis regimen incorporated bicarbonate-buffered dialysate and high-efficiency dialyzers (Elisio 17H and 21H) equipped with Polynephron synthetic membranes (Table 1).

Table 1. Baseline patient characteristics

Parameter	Value
Total patients	52
Male/Female	20 / 32
Mean age (years)	55 ± 12
Primary CKD etiologies	Glomerulonephritis, Diabetes, PKD
Dialysis frequency	3 sessions/week
Dialyzer type	Elisio 17H & 21H (Polynephron)
Duration per session	4 hours

Cardiac structure and function were evaluated via transthoracic and Doppler echocardiography, performed in accordance with the recommendations of the American Society of Echocardiography, at baseline and after 12 months of HD therapy. Measured echocardiographic parameters included diastolic interventricular septal and posterior wall thickness, end-diastolic dimension (EDD), left atrial diameter, and left ventricular ejection fraction (EF). Systolic function was classified as preserved if EF exceeded 50%. Left ventricular mass index (LVMI) was calculated by normalizing LV mass to body surface area. Left ventricular hypertrophy (LVH) was defined by an LVMI ≥115 g/m² in men and ≥95 g/m² in women. Relative wall thickness (RWT) was computed using the formula: RWT = 2 × posterior wall thickness / LV internal diameter at end-diastole (Table 2).

Table 2. Echocardiographic parameters before and after one year of hemodialysis

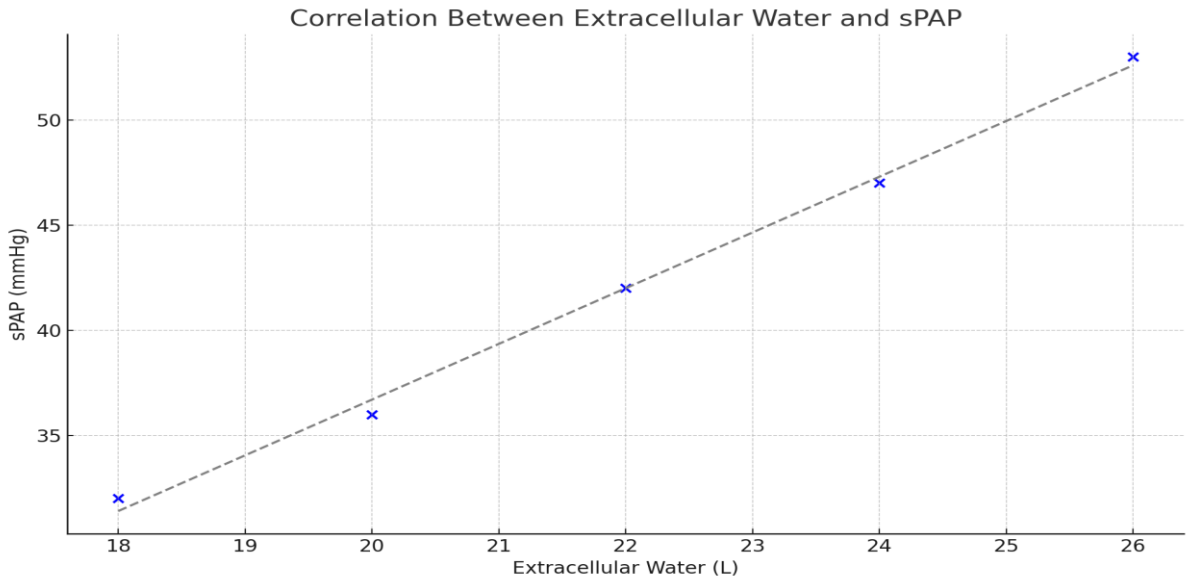
Parameter	Baseline	After 1 Year	p-value
EF (%)	57.4 ± 9.6	62.2 ± 8.0	<0.05
LVMI (g/m²)	159.1 ± 35.8	129.1 ± 42.2	<0.05
sPAP (mmHg)	46.3 ± 16.1	40.4 ± 11.7	<0.01
Hemoglobin (g/L)	106.5 ± 18.7	113.9 ± 11.5	<0.01
Pulse Arterial Pressure (mmHg)	50.6 ± 12.6	60.0 ± 15.2	<0.001

Hydration status was assessed by multifrequency bioimpedance spectroscopy (ABC-01 device, MEDAS, using Sport-5 software), providing estimates of total body water (TBW), extracellular water (ECW), and lean body mass. Blood flow through the arteriovenous (AV) fistula was quantified using Doppler ultrasound. The diagnosis of pulmonary hypertension (PH) was established based on the criteria of the European Society of Cardiology.

All statistical analyses were conducted using Student's t-test for paired samples and univariate correlation analysis. Data were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on the distribution pattern. A p-value <0.05 was considered to indicate statistical significance.

Total body water (TBW) is a crucial parameter in assessing fluid balance in patients undergoing hemodialysis (HD). In our study, the average TBW was 34.1±6.5 L, with extracellular water (ECW) comprising 21.5±4.4 L, and lean body mass averaging 12.5±2.1 kg**.** A statistically significant correlation was found between ECW content and systolic pulmonary artery pressure (sPAP) ($r=0.4$; $p<0.01$), indicating a possible role of fluid overload in the development of pulmonary hypertension in HD patients (Figure 1).

Figure 1. Correlation Between ECW and sPAP



One of the key findings of our study is the absence of a direct relationship between blood flow in the arteriovenous (AV) fistula and pulmonary artery pressure**.** Before initiation of dialysis**,** systolic left atrial pressure showed a significant correlation with left ventricular hypertrophy (LVH), left ventricular ejection fraction (LVEF), and anemia severity. After one year of HD treatment**,** a direct correlation emerged between ECW content and sPAP, suggesting that fluid retention and redistribution play a pivotal role in pulmonary hypertension in dialysis patients.

Existing literature supports these findings, indicating no significant changes in pulmonary hypertension before and 2-3 months after AV fistula formation. The reported prevalence of pulmonary hypertension in these studies was 34% before AV fistula creation and 38% after**,** reinforcing the notion that blood flow through the AV fistula does not independently contribute to pulmonary hypertension. Furthermore, postcapillary pulmonary hypertension is a common finding in HD patients**,** as confirmed by right heart catheterization. However, due to the invasive nature of this diagnostic method, routine clinical practice primarily relies on echocardiography and Doppler echocardiography for pulmonary hypertension assessment.

Our results suggest a high prevalence of pulmonary hypertension in the pre-dialysis stage**,** which appears to exhibit positive dynamics after one year of HD treatment. Notably, LVH severity was reduced**,** indicating a potential benefit of HD in mitigating cardiovascular complications. However, pulse arterial pressure (PAP) increased over the course of dialysis treatment, correlating significantly with body mass index (BMI)**.** It is well established that elevated PAP reflects increased vascular stiffness**,** which is strongly influenced by phosphorus-calcium metabolism**.** Several studies have demonstrated a direct relationship between vascular stiffness and disturbances in phosphorus-calcium homeostasis**,** particularly in patients with chronic hypertension.

In our cohort, parathyroid hormone (PTH) levels remained relatively stable, and no significant correlation was found between PTH, BMI, and systolic pulmonary artery pressure**.** Additionally, no direct relationship was observed between sPAP and pulse arterial pressure**.** Given these findings, we propose that the reduction in pulmonary artery pressure observed in some patients may be attributed to regression of chronic heart failure (CHF) and anemia correction**.** Future research should focus on preventing vascular stiffness**,** as this could contribute to further regression of LVH and potentially exert a positive impact on pulmonary artery pressure**.** Addressing these factors could improve cardiovascular outcomes in HD patients and reduce the burden of pulmonary hypertension in this vulnerable population.

Conclusions:

- Pulmonary hypertension in patients initiating hemodialysis therapy is closely associated with left ventricular hypertrophy (LVH), impaired left ventricular systolic function, and anemia. These interrelated cardiovascular alterations are commonly observed in end-stage renal disease and contribute to the elevated pulmonary artery pressures detected prior to dialysis initiation.
- Following one year of maintenance hemodialysis, a reduction in the severity of pulmonary hypertension is typically observed, likely due to improvements in

volume control, correction of anemia, and regression of LVH. However, complete normalization of pulmonary pressure is uncommon. Importantly, the presence and function of an arteriovenous fistula do not appear to exert a statistically significant influence on pulmonary artery pressure, suggesting that other hemodynamic and structural factors are more critical in PH pathophysiology.

- A significant positive correlation between extracellular water (ECW) and systolic pulmonary artery pressure (sPAP) was observed, indicating that fluid overload and redistribution play a central role in the development and persistence of pulmonary hypertension in the hemodialysis population. This underscores the importance of accurate hydration status monitoring, particularly using bioimpedance analysis, to optimize cardiovascular outcomes.

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