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Right ventricular-pulmonary arterial coupling and pulmonary hypertension in hemodialysis: insights into structural cardiac changes and clinical implications

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ABSTRACT

Objectives: This cross-sectional analysis from the CZecking Heart Failure in patients with advanced Chronic Kidney Disease trial (ISRCTN18275480) examined pulmonary hypertension and right ventricular-pulmonary arterial coupling in patients on chronic hemodialysis. The aims of this analysis were: 1. To analyze relations between pulmonary hypertension and right ventricular-pulmonary arterial coupling with dialysis access flow and current hydration; 2. To analyze structural heart changes associated with right ventricular-pulmonary arterial uncoupling; 3. To reveal the prevalence, etiology and severity of pulmonary hypertension in the Czech hemodialysis population.

Methods: We performed expert echocardiography, vascular access flow measurements, bioimpedance analysis, and laboratory testing in 336 hemodialysis patients.

Results: Pulmonary hypertension was present in 34% (114/336) patients and right ventricular-pulmonary arterial uncoupling was present in 25% of patients with pulmonary hypertension. Only weak associations between the flow of the dialysis arteriovenous access and estimated pulmonary arterial systolic pressure and right ventricular-pulmonary arterial coupling was proved. There was a strong association between hydration status assessed by estimated central venous pressure with pulmonary arterial systolic pressure (Rho 0.6, $p<0.0001$) and right ventricular-pulmonary arterial coupling (Rho −0.52, $p<0.0001$) and association between overhydration to extracellular water ratio with pulmonary arterial systolic pressure (Rho 0.31, $p=0.0001$) and right ventricular-pulmonary arterial coupling (Rho −0.29, $p=0.002$). The prevalence of heart failure was significantly higher in patients with right ventricular-pulmonary arterial uncoupling (88% vs. 52%, $p=0.0003$).

Conclusion: These findings suggest that optimizing volume status and treating heart failure should be prioritized in hemodialysis patients to prevent pulmonary hypertension progression and right ventricular-pulmonary arterial uncoupling.

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Introduction

Chronic kidney disease (CKD) affects more than 13% of worldwide population and its prevalence in both developed and developing countries is rising, especially due to comorbidities such as diabetes mellitus and arterial hypertension [1]. CKD may gradually progress to end stage kidney disease (ESKD) with the need of renal replacement therapy, either dialysis or kidney transplantation [2]. The most common type of kidney replacement therapy is hemodialysis, either *via* a catheter or *via* a surgically created arteriovenous access (fistula or graft).

The morbidity and mortality of ESKD patients on hemodialysis remains high, especially due to cardiovascular complications [3]. Pulmonary hypertension (PH) is frequent in patients with ESKD and is associated with poor outcome. Several studies proved different causes of PH in ESKD patients: heart failure (HF), especially the type with preserved ejection fraction (HFpEF) [4], high arteriovenous access flow (Qa) [5], but also uremic toxins [6], vascular calcifications [7,8], attenuated basal and induced nitric oxide levels after hemodialysis [9] etc. Some studies showed higher prevalence of PH in patients with high Qa, (>1500–2000 mL/min) [5,10,11]. However, most of the aforementioned studies were small and/or included

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only patients with a particular abnormality (such as those with high Qa). Therefore, we initiated a prospective cohort trial of prevalent hemodialysis patients - CZecking Heart Failure in Chronic Kidney Disease [12]. We already published analysis of the distribution of different heart failure phenotypes [13], but PH was not analyzed in detail.

The efficiency with which right ventricular (RV) stroke work is transferred into the pulmonary artery (PA) is called RV-PA coupling [14,15]. In compensated states, RV contractile function increases gradually with the rise in afterload (pulmonary arterial pressure) to maintain steady RV-PA coupling ratios – an example of adaptation. On the contrary, in decompensated states, RV contractile function is no more able to increase in response to higher afterload – RV-PA uncoupling. By echocardiography, RV-PA coupling is calculated as a ratio of the tricuspid annular plane systolic excursion (TAPSE) and estimated pulmonary arterial systolic pressure (PASP). The most commonly used pathological value is <0.36 [16], marked as RV-PA uncoupling predicting worse outcome [17,18]. Although the high prevalence of PH among patients on chronic hemodialysis is known, data about the RV-PA relations is sparse.

Therefore, we analyzed patients on chronic hemodialysis using a combination of detailed echocardiography, arteriovenous fistula flow calculation and bio-impedance to reveal relations between PH and RV-PA coupling with hydration and structural heart changes. Specifically, the aims of this study were the following ones: (1) To analyze the relations between PH and RV-PA coupling with Qa and current hydration; (2) To analyze structural heart changes associated with RV-PA uncoupling; (3) To reveal the prevalence, etiology and severity of PH in the Czech hemodialysis population.

Materials and methods

We analyzed selection visit data of the subjects included into the CZecking Heart Failure in CKD study (ISRCTN No. 18275480) since April 2019 till March 2024. This study includes all prevalent patients that come for hemodialysis to any of the 6 collaborating hemodialysis units and fulfill the broad inclusion criteria. In brief, the criteria include willingness to participate, lack of a living kidney transplant donor and life expectation >6 months at inclusion. All examinations (details below) were done within an hour and at least 24 h after the previous hemodialysis [12]. The diagnosis of heart failure was based on the guidelines of the European Society of Cardiology and KDIGO (Kidney disease: improving global outcomes) and is described in detail in our previous publication [19].

The following data were recorded: basic medical history data, full blood count, levels of albumin, total blood protein and of N-terminal prohormone of brain natriuretic peptide (NTproBNP), expert echocardiography, volume status estimation, heart rhythm analysis, and Qa calculation.

Expert echocardiography

Expert echocardiography was performed using a matrix echocardiography probe of Vivid E95 device (General Electric, Vingmed, Norway), as well as detailed analysis of the volumes of heart cavities, quantification of valvular disease, diastolic dysfunction according to the recent guidelines [19], and cardiac output (CO) calculation (using the left ventricular outflow tract diameter and velocity time interval). Examinations were performed by one of 3 examiners experienced in cardio-nephrology (K.B.S., A.V., and J.M.). Interindividual variability of heart chamber diameters was 5% and in volumes 8%. There was no variation in the assessment of the peak gradient of tricuspid regurgitation because this value depends on the changed (Doppler) frequency and on device factory setting. PH was defined by the PASP >35 mmHg (calculated by the peak gradient of the tricuspid regurgitation plus estimated central venous pressure (CVP) in mmHg) or by the presence of indirect signs of PH such as presence of right ventricular hypertrophy, D-shape of left ventricle or dilation of truncus pulmonalis. Right ventricular area was measured in adjusted apical four chamber view (A4C) and fractional area change was calculated as ((end-diastolic area (EDA)—end-systolic area (ESA))/EDA. Right atrial area and volume and TAPSE were measured in A4C projection.

Pulmonary artery pressure evaluation

PASP was calculated according to the current recommendations as tricuspid regurgitation peak gradient plus estimated CVP [4]. CVP was estimated from the inferior vena cava diameter and collapsibility [20]. The cutoff for pulmonary hypertension was PASP >35 mmHg as the most widely accepted value [21–23]. Patients were further subdivided into four groups: no PH (PASP < 36 mmHg), mild PH (PASP 36–45 mmHg), moderate PH (PASP 46–60 mmHg) and severe PH (PASP > 60 mmHg) [24]. In patients without tricuspid regurgitation, we searched for indirect PH signs as presence of right ventricular hypertrophy, D-shape of right ventricle or dilation of truncus pulmonalis. However, no patients with indirect signs of PH but without tricuspid regurgitation were found.

Right ventricular-pulmonary arterial coupling

TAPSE/PASP ratio was calculated as a surrogate of RV-PA coupling as recommended [14]. We applied the cutoff value 0.36 as suggested by the recent metanalysis of Anastasiou et al. [25]. RV-PA coupling was analyzed only in patients with PH.

Arteriovenous access flow quantification

Qa measurement was performed by ultrasonography, using a linear high-frequency probe of Vivid E95 device (General Electric, Vingmed, Norway). Qa was calculated as an average of at least three flow volume measurements in a straight segment of the brachial artery feeding the fistula or ascending loop in arteriovenous graft as described earlier [26].

Hemodynamic calculations

Effective cardiac output (COef) was measured as the difference between the total CO and Qa. Total vascular resistance

(TVR) was calculated as follows: TVR = (MAP-CVP)/CO where MAP = mean arterial pressure (MAP = 2/3 of diastolic pressure + 1/3 of systolic pressure). Moreover, the systemic vascular resistance (SVR) that does not consider Qa was calculated: SVR = (MAP-CVP)/COef.

Hydration assessment

Bioelectrical impedance analysis (BIA), using Body composition monitor (FMC, Germany) gave the level of overhydration in liters, but this value is not indexed for the body size. Therefore, we also used overhydration adjusted to extracellular water as a more accurate assessment of hydration status [27].

Statistical analysis

The statistical software STATISTICA (StatSoft Inc. ISA) was used for statistical analysis. Variables were tested by Shapiro-Wilk test for the data distribution (Gaussian vs. non-Gaussian). Missing data were treated by pairwise deletion. In non-Gaussian data distribution Mann-Whitney U-test was used. Unpaired t-test was used in data with Gaussian distribution. According to the test used, results were expressed as either mean ± standard deviation in unpaired t-test or median (quartile range) for Mann-Whitney U-test. Further Spearman's rank correlation and regression analysis were used. Chi-square test (X2) was used for comparison of categorical values and was reported as X^2 = chi-square value, $p = p$ value. The odds ratio (OR) was obtained as a measurement of association between variables and the 95% confidence interval (CI) was used. P values < 0.05 were considered significant. Multivariate regression analysis was used to determine the dependence of the observed dependent quantitative variables on chosen independent quantitative variables. Suitable regression model was used and the significance was considered according to F-test.

Results

Study population

Out of 362 screened patients, 10 were excluded because of having a living kidney donor, 14 were excluded because the hemodialysis center team estimated their prognosis as shorter than 6 months and 2 patients did not agree with the inclusion into this study. Therefore, we included 336 consecutive patients into the analysis, aged 69.5 (19.6) years, of which 63% were males and 98.5% of included patients were Caucasian race. The mean dialysis vintage was 47 months (median 24 months), the mean interval between the end of hemodialysis session and the examination was 32.7 h (median 24 h). The most frequent causes of CKD were diabetes mellitus (29%), arterial hypertension (25%), and chronic tubulointerstitial nephritis (9%). Hemodialysis vascular access was native arteriovenous fistula in 73%, arteriovenous graft in 19%, or catheter in 8%. For the use of this analysis, we considered Qa = 0 mL/min in patients dialyzed *via* a catheter. Baseline data of the included patients are presented in Table 1.

Table 1. Baseline data of analyzed patients.

Age (years)	69.5 (19.6)
Heart rate (min^{-1})	72 (16)
Systolic blood pressure (mmHg)	134 ± 26.4
Diastolic blood pressure (mmHg)	74.5 (19)
Mean arterial pressure (mmHg)	94 (21.33)
Body mass index (kg/m^2)	25.9 (7.5)
Body surface area (BSA) (m^2)	1.9 (0.31)
Estimated pulmonary arterial systolic pressure (mmHg)[a]	35 (20)
Ejection fraction (%)	59 (13)
Cardiac output (CO) (L/min)	5.89 (2.26)
Effective cardiac output (L/min)	4.81 (1.91)
Dialysis access flow (Qa) (mL/min)	1021 (725)
Qa/CO (%)	17 (16)
Left ventricular mass indexed to BSA (g/m^2)	92 (58)
Left atrial volume indexed to BSA (mL/m^2)	40 (21.5)
End diastolic area of right ventricle (cm^2)	19 (7.3)
Fractional area change (%)	43.8 ± 11.8
End-diastolic volume of right atrium indexed to BSA (mL/m^2)	30.53 (20.35)
Tricuspid annular plane systolic excursion (mm)	23 (7)
Central venous pressure (mmHg)	5 (6)
Right ventricular-pulmonary arterial coupling (mm/mmHg)$^{+)}$	0.63 (0.42)
Overhydration (OH) (L)	1.3 (2.6)
OH/extracellular water (%)	0.07 (0.15)
Total vascular resistance (Wood units)	18.51 (9.15)
Access resistance (Wood units)	100.33 (64.37)
Systemic vascular resistance (Wood units)	15.27 (6.35)
N-terminal pro-brain natriuretic peptide (ng/L)	4859 (12064)
Hemoglobin (g/L)	110 (16.5)
Total blood protein (g/L)	66 (8)
Albumin (g/L)	39 (5)

Data are reported as mean ± standard deviation in variables with Gaussian distribution or as median (quartile range) in variables with non-Gaussian distribution.
[a]Data are based on 190 patients with tricuspid regurgitation.

Prevalence of PH and RV-PA uncoupling

PH was present in 114 (34%) analyzed patients. Among those patients, mild PH was present in 54 (47%) patients, moderate in 43 (38%) patients and severe in 17 (15%) patients. RV-PA uncoupling was present in 25% of patients with PH.

Differences of patients with and without PH and RV-PA coupling and uncoupling

Patients with PH were significantly older, had longer dialysis vintage, and had worse echocardiographic parameters of all four heart chambers (see Table 2 for the details). There was a significant correlation of PASP with left atrial volume index (LAVi), left ventricular mass indexed to body surface area (LVMi) and N-terminal pro-brain natriuretic peptide (NTproBNP) (Table 3). The prevalence of PH did not significantly differ in patients with or without lung disease (X^2= 2.33, $p = 0.127$), neither did the PASP value (34 (19) vs. 40 (23.5), $p = 0.097$).

Patients with RV-PA uncoupling were more overhydrated, had worse LV EF and lower CO, worse systolic function of the

Table 2. Differences in patients with and without pulmonary hypertension.

	No PH	PH	*p*-Value
Dialysis access flow (mL/min)	935 (700)	1000 (890)	0.584
Age (years)	68.25 (21.2)	70.75 (15.1)	**0.025**
Dialysis vintage (months)	20.5 (54)	37 (74)	**0.015**
NTproBNP (ng/L)	3289 (7835.5)	13017 (30054)	**<0.0001**
Central venous pressure (mmHg)	4 (4)	9 (10)	**<0.0001**
Overhydration (OH) (L)	1 (2.3)	1.8 (2.65)	**0.007**
OH/extracellular water (%)	0.05 (0.13)	0.1 (0.15)	**0.003**
LAVi (mL/m^2)	35 (21)	48 (19)	**<0.0001**
LVEDVi (mL/m^2)	52.32 (23.95)	60.25 (28.96)	**0.001**
LVMi (g/m^2)	88 (55)	99 (66)	0.198
Cardiac output (L/min)	5.97 (1.99)	5.66 (2.65)	**0.015**
Effective cardiac output (L/min)	5.07 (1.8)	4.34 (2.29)	**0.001**
Qa/CO (%)	16 (14)	18 (18)	0.090
LVEF (%)	60 (11)	56 (19)	**0.002**
End-diastolic area (mm^2)	18 (6.1)	20.15 (9.3)	**0.006**
End-systolic area (mm^2)	9.6 (5.6)	12.6 (8)	**0.001**
RAEDV (mL)	44.5 (33)	71 (48)	**<0.0001**
RV-PA coupling (mm/mmHg)	0.88 (0.41)	0.48 (0.27)	**<0.0001**
Fractional area change (%)	46.38 ± 11.04	40.22 ± 12	**0.001**
TVR (Wood units)	17.65 (8.45)	19.89 (11.25)	**0.01**
SVR (Wood units)	15.04 (6.31)	15.96 (7.16)	**0.03**
Albumin (g/L)	39 (4.6)	38 (5)	**0.02**
Hemoglobin (g/L)	110 (16.5)	109 (19)	0.181

Data are reported as mean ± SD in variables with Gaussian distribution or as median (quartile range) in variables with non-Gaussian distribution; NTproBNP: N-terminal pro-brain natriuretic peptide, LAVi: Left atrial volume indexed to BSA, LVEDVi: Left ventricular end-diastolic volume indexed to BSA, LVMi: Left ventricular mass indexed to BSA, LVEF: Ejection fraction of left ventricle, Qa/CO; Arteriovenous access flow to cardiac output ratio, RAEDV: Right atrial end-diastolic volume, RV-PA coupling: Right ventricular-pulmonary arterial coupling, TVR: Total vascular resistance, SVR: Systemic vascular resistance.

Table 3. Univariate correlation of the peak systolic pulmonary arterial pressure with echocardiographic and hemodynamic variables.

	Rho	*P*
Left atrial volume indexed to BSA	**0.49**	**<0.0001**
Left ventricular mass indexed to BSA	**0.13**	**0.047**
Central venous pressure	**0.60**	**<0.0001**
N-terminal pro-brain natriuretic peptide	**0.50**	**<0.0001**
Overhydration (OH)	**0.31**	**<0.0001**
OH/extracellular water	**0.31**	**0.0001**
Cardiac output (CO)	**−0.15**	**0.027**
Effective cardiac output	**−0.15**	**0.022**
Dialysis access flow/CO	0.03	0.712
Albumin	**−0.18**	**0.008**
Hemoglobin	−0.06	0.359
Systemic vascular resistance	**0.16**	**0.028**
Total vascular resistance	**0.14**	**0.050**

Table 4. Univariate correlation of TAPSE/PASP with echocardiographic and hemodynamic variables.

	Rho	*p*
LAVi	**−0.46**	**<0.0001**
LVMi	−0.11	0.127
CVP	**−0.52**	**<0.0001**
NTproBNP	**−0.55**	**<0.0001**
Overhydration (OH)	**−0.28**	**0.003**
OH/ extracellular water	**−0.29**	**0.002**
CO	**0.34**	**<0.0001**
LVEF	**0.35**	**<0.0001**
EDA	**−0.30**	**0.0001**
ESA	**−0.39**	**<0.0001**
FAC	**0.30**	**0.022**
RAEDV	−0.23	0.065
TVR	−0.19	0.089

LAVi: Left atrial volume indexed to BSA; LVMi: Left ventricular mass indexed to BSA; CVP: Central venous pressure; NTproBNP: N-terminal pro-brain natriuretic peptide; CO: Cardiac output; EF LV: Ejection fraction of the left ventricle; EDA: End diastolic area of the right ventricle; ESA: End systolic area of the right ventricle; FAC: Fractional area change; RAEDV: Right atrial end-diastolic volume; TVR: Total vascular resistance.

right ventricle and both ventricles were dilated (see Table 5 for details). The TAPSE/PASP value was positively related to LAVi, systolic function of both ventricles and NTproBNP (Table 4).

There were no significant differences in Qa in patients with or without PH (see Table 2 for details) as well as there was no significant difference in the presence of PH in patients with a catheter or arteriovenous fistula ($X^2 = 0.083$, $p = 0.773$). The only statistically significant contribution of higher Qa to PH was present in the odds ratio analysis using upper and lower quartile (Qa 1400 mL/min v.s. 510 mL/min) (OR 1.27, CI 1.10–1.46). There was no difference of Qa in patients with RV-PA coupling and uncoupling (see Table 5 for details).

The effects of heart failure on PH and RV-PA coupling

HF was significantly more frequent in patients with PH (79% vs. 37.5%, X^2 = 50.477, $p < 0.0001$) and, among them, also in patients with RV-PA uncoupling (88% vs. 52%, X^2= 12.827, $p = 0.0003$). The presence of HF increased the probability of PH (OR, 6.3, 95% CI, 3.7–10.3, $p < 0.0001$). Patients without diastolic dysfunction (DD) or with DD grade I had significantly lower PASP than those with DD grade II-III (26 (8) vs. 40 (19.5), $p < 0.0001$).

The effects of hydration on PH and RV-PA uncoupling

Patients with PH were significantly more overhydrated when assessed by CVP and BIA (see Tables 2 and 3 for more details). Patients with RV-PA uncoupling had higher CVP, overhydration to extracellular water ratio; however overhydration assessed by BIA alone did not differ significantly (see Tables 4 and 5 for more details).

Multivariate regression analysis

We performed multivariate regression analysis separately for patients with and without PH and for patients with RV-PA coupling and uncoupling. Covariates of PH that remained statistically significant were albumin, right atrial end diastolic volume and total vascular resistance. Covariates of RV-PA uncoupling were the following: albumin, overhydration,

Table 5. PH—positive patients: differences in right ventricular-pulmonary arterial coupling.

	PA coupling; $N=70$	PA uncoupling; $N=24$	p-Value
Arteriovenous access flow (mL/min)	1020 (900)	765 (1050)	0.235
Age (years)	72 .6 (13.4)	73.35 (24.7)	0.689
Dialysis vintage (months)	40.5 (65)	30 (75)	0.805
NTproBNP (ng/L)	10264 (17802)	35000 (20348)	**<0.0001**
CVP (mmHg)	8 (8)	18 (5)	**<0.0001**
Overhydration (OH) (L)	1.7 (2.8)	2.9 (1.6)	0.095
OH/extracellular water	0.07 (0.16)	0.15 (0.2)	**0.006**
LAVi (mL/m^2)	47 (20)	52.5 (27)	0.052
LVEDVi (mL/m^2)	56.14 (23.1)	76.33 (43.32)	**0.009**
LVMi (g/m^2)	103.5 (69)	77 (63.5)	0.894
CO (L/min)	5.78 (2.43)	4.21 (2.56)	**0.001**
COef (L/min)	4.60 (2.16)	3.44 (1.67)	**0.0003**
Qa/CO	0.17 (0.18)	0.19 (0.23)	0.666
LVEF (%)	59 (13)	42 (20.5)	**0.001**
EDA (mm^2)	20 (7.65)	27.5 (9)	**0.002**
ESA (mm^2)	11.55 (5)	19.5 (13)	**0.001**
RAEDV (mL)	69 (41.5)	74 (46)	0.162
FAC (%)	45.3 ± 11.1	33.4 ± 13.2	**0.001**
TVR (Wood units)	19.88 (9.14)	21.97 (14.1)	0.059
SVR (Wood units)	16.12 (6.55)	19.04 (7.84)	0.218
Albumin (g/L)	38 (5)	38 (5.6)	0.884
Hemoglobin (g/L)	109.5 (15)	108.5 (18.5)	0.853

NTproBNP: N-terminal pro-brain natriuretic peptide; CVP: Central venous pressure; LAVi: Left atrial volume indexed to BSA; EDVi: End-diastolic left ventricular volume indexed to BSA; CO: Cardiac output; COef: Effective cardiac output; Qa/CO: Arteriovenous fistula flow to cardiac output ratio; EF LV: Ejection fraction of the left ventricle; EDA: End diastolic area of the right ventricle; ESA: End systolic area of the right ventricle; RAEDV: Right atrial end-diastolic volume; FAC: Fractional area change; TVR: Total vascular resistance; SVR: Systemic vascular resistance.

overhydration to extracellular water ratio, cardiac output, ejection fraction of left ventricle, right atrial end diastolic volume and total vascular resistance (Suppl. 1 and Suppl. 2).

Discussion

Lack of stronger relation between Qa and PH in this study representing a real-world hemodialysis population is surprising. In patients with PH, previous studies documented decreased PASP during a short manual compression of the fistula [6,28]. Previous studies also documented a decrease of PASP in patients with high Qa after a surgical reduction of Qa, but were limited to that specific patient population [29,30]. In a swine model of high Qa, the PASP increased significantly after opening of an arteriovenous access [29].

Overhydration assessed either by CVP estimation or by BIA was a significant contributing factor to both PH and RV-PA uncoupling. Chronic overhydration is a known risk factor of higher mortality [31], and also another study found its link to PH [32]. In non-ESKD population, management of HF with the help of implantable hemodynamic system measuring pulmonary arterial pressure, decreased significantly the hospitalizations for HF decompensations. We can therefore speculate that more appropriate (lower) dry weight setting would improve PASP and RV-PA coupling, and, more importantly, that such improvement would lead to better patients' prognosis. On the other hand, overhydration may be the expression of the need for a higher filling pressure of the RV and its reduction is not possible in some patients because of systemic hypotension. Further analysis of these association in needed.

The presence of HF was associated with higher probability of PH, but also of RV-PA uncoupling. Analogously, NTproBNP levels were higher in the latter two subgroups. According to these findings, the postcapillary element of PH (HF) is the most commonly present one in the hemodialysis population. Similar findings were previously presented in other studies [14,33–36]. Interestingly, subjects with PH and especially those with RV-PA uncoupling had lower CO and especially COef. In other words, systemic arteriolar constriction directed higher proportion of the total CO into the arteriovenous shunt used as a vascular access.

In accordance with previous studies [37,38], patients with PH had a significantly longer duration of dialysis therapy (but no difference with regards to RV-PA coupling). These observations support the contribution of non-hemodynamic mechanisms, such as uremic toxins [5], vascular calcifications [6,7], attenuated basal and induced nitric oxide levels after hemodialysis [8]. Both PH and RV-PA uncoupling were associated with dilation and worse systolic function of both ventricles. The size of atria was significantly greater in PH patients, however only slightly greater in those with RV-PA uncoupling. RV-PA uncoupling was associated with adverse outcomes in acute decompensated patients with HFpEF [39] and a similar finding was reported in a smaller recent study in patients on chronic (maintenance) hemodialysis [40].

According to our analysis, the prevalence of PH was 34% among the Czech patients on hemodialysis, which is a mean of other reported prevalences (17%–56%) [5,28,41] RV-PA uncoupling affected a quarter of PH patients [36].

The main limitation of this analysis is its cross-sectional character. On the contrary, the strength of this study are that the patients were examined prospectively by a team experienced in cardio-nephrology and all examinations occurred within one hour.

Conclusion

The main findings of this study were: 1. The relation between arteriovenous access flow and the diagnosis of PH or RV-PA uncoupling is weak, both parameters are more strongly related to fluid overload; 2. RV-PA uncoupling is associated with more advanced structural heart changes in patients with PH; 3. PH is present in about one-third of Czech hemodialysis population and among them, one quarter of patients suffered from RV-PA uncoupling. HF was the strongest contributor of PH in hemodialysis population. The main associations of PH and RV-PA uncoupling are summarized in Figure 1.

Based on our experience prevention of overhydration and HF treatment are important to avoid pulmonary hypertension and RV-PA uncoupling in hemodialysis population.

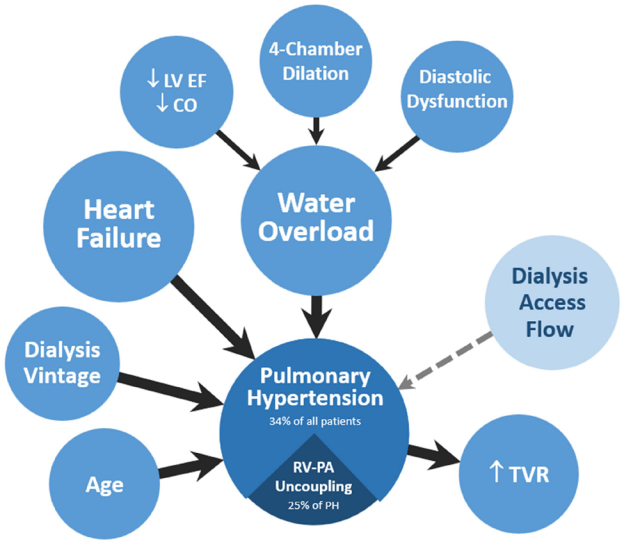

Figure 1. Key relationships between pulmonary hypertension, RV-PA uncoupling, and clinical factors in chronic hemodialysis patients. RV-PA: Right ventricular-pulmonary arterial; LV EF: Ejection fraction of the left ventricle; CO: Cardiac output; TVR: Total vascular resistance

Disclosure statement

The authors declare that they have no competing interest

Ethics approval and consent to participate

Approved 23/05/2019, protocol amendment approved 23/05/2020, title amendment approved 18/02/2021, Institutional ethics committee of the General University Hospital in Prague (Na Bojisti 1, 128 08 Prague 2, Czech Republic; +420 224 964 131; eticka.komise@vfn.cz), ref: 789/19, protocol amendment ref: 30/20.

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Data availability statement

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

References

[1] Lv JC, Zhang LX. Prevalence and disease burden of chronic kidney disease. Adv Exp Med Biol. 2019;1165:3–15. doi: 10.1007/978-981-13-8871-2_1.

[2] Gusev E, et al. The pathogenesis of end-stage renal disease from the standpoint of the theory of general pathological processes of inflammation. Int J Mol Sci. 2021;22(21):11453.

[3] Msaad R, Essadik R, Mohtadi K, et al. Predictors of mortality in hemodialysis patients. Pan Afr Med J. 2019;33:61. doi: 10.11604/pamj.2019.33.61.18083.

[4] Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J. 2023;61(1):2200879. doi: 10.1183/13993003.00879-2022.

[5] Malik J, Valerianova A, Tuka V, et al. The effect of high-flow arteriovenous fistulas on systemic haemodynamics and brain oxygenation. ESC Heart Fail. 2021;8(3):2165–2171. doi: 10.1002/ehf2.13305.

[6] Yigla M, Nakhoul F, Sabag A, et al. Pulmonary hypertension in patients with end-stage renal disease. Chest. 2003;123(5):1577–1582. doi: 10.1378/chest.123.5.1577.

[7] Block GA, Hulbert-Shearon TE, Levin NW, et al. Association of serum phosphorus and calcium x phosphate product with mortality risk in chronic hemodialysis patients: a national study. Am J Kidney Dis. 1998;31(4):607–617. doi: 10.1053/ajkd.1998.v31.pm9531176.

[8] Floege J, Kim J, Ireland E, et al. Serum iPTH, calcium and phosphate, and the risk of mortality in a European haemodialysis population. Nephrol Dial Transplant. 2011;26(6):1948–1955. doi: 10.1093/ndt/gfq219.

[9] Nakhoul F, Yigla M, Gilman R, et al. The pathogenesis of pulmonary hypertension in haemodialysis patients via arterio-venous access. Nephrol Dial Transplant. 2005;20(8):1686–1692. doi: 10.1093/ndt/gfh840.

[10] Saleh MA, El Kilany WM, Keddis VW, et al. Effect of high flow arteriovenous fistula on cardiac function in hemodialysis patients. Egypt Heart J. 2018;70(4):337–341. doi: 10.1016/j.ehj.2018.10.007.

[11] Sequeira A, Tan TW. Complications of a high-flow access and its management. Semin Dial. 2015;28(5):533–543. doi: 10.1111/sdi.12366.

[12] Malik J, Valerianova A, Pesickova SS, et al. CZecking heart failure in patients with advanced chronic kidney disease (Czech HF-CKD): study protocol. J Vasc Access. 2024;25(1):294–302. doi: 10.1177/11297298221099843.

[13] Malik J, Valerianova A, Pesickova SS, et al. Heart failure with preserved ejection fraction is the most frequent but commonly overlooked phenotype in patients on chronic hemodialysis. Front Cardiovasc Med. 2023;10:1130618. doi: 10.3389/fcvm.2023.1130618.

[14] Houston BA, Brittain EL, Tedford RJ. Right ventricular failure. N Engl J Med. 2023;388(12):1111–1125. doi: 10.1056/NEJMra2207410.

[15] Fourie PR, Coetzee AR, Bolliger CT. Pulmonary artery compliance: its role in right ventricular-arterial coupling. Cardiovasc Res. 1992;26(9):839–844. doi: 10.1093/cvr/26.9.839.

[16] He Q, Lin Y, Zhu Y, et al. Clinical usefulness of right ventricle-pulmonary artery coupling in cardiovascular disease. J Clin Med. 2023;12(7):2526. doi: 10.3390/jcm12072526.

[17] Srdanović I, Stefanović M, Milovančev A, et al. Relevance of the TAS'/PASP ratio as a predictor of outcomes in patients with heart failure with a reduced ejection fraction. Life (Basel). 2024;14(7). doi: 10.3390/life14070863.

[18] Inciardi RM, Abanda M, Shah AM, et al. Right ventricular function and pulmonary coupling in patients with heart failure and preserved ejection fraction. J Am Coll Cardiol. 2023;82(6):489–499. doi: 10.1016/j.jacc.2023.05.010.

[19] McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599–3726. doi: 10.1093/eurheartj/ehab368.
[20] Kircher BJ, Himelman RB, Schiller NB. Noninvasive estimation of right atrial pressure from the inspiratory collapse of the inferior vena cava. Am J Cardiol. 1990;66(4):493–496. doi: 10.1016/0002-9149(90)90711-9.
[21] Agarwal R. Prevalence, determinants and prognosis of pulmonary hypertension among hemodialysis patients. Nephrol Dial Transplant. 2012;27(10):3908–3914. doi: 10.1093/ndt/gfr661.
[22] Bolignano D, Rastelli S, Agarwal R, et al. Pulmonary hypertension in CKD. Am J Kidney Dis. 2013;61(4):612–622. doi: 10.1053/j.ajkd.2012.07.029.
[23] McQuillan BM, Picard MH, Leavitt M, et al. Clinical correlates and reference intervals for pulmonary artery systolic pressure among echocardiographically normal subjects. Circulation. 2001;104(23):2797–2802. doi: 10.1161/hc4801.100076.
[24] Galiè N, Humbert M, Vachiery J-L, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Rev Esp Cardiol (Engl Ed). 2016;69(2):177. doi: 10.1016/j.rec.2016.01.002.
[25] Anastasiou V, Papazoglou AS, Moysidis DV, et al. The prognostic impact of right ventricular-pulmonary arterial coupling in heart failure: a systematic review and meta-analysis. Heart Fail Rev. 2024;29(1):13–26. doi: 10.1007/s10741-023-10341-2.
[26] Kudlicka J, Kavan J, Tuka V, et al. More precise diagnosis of access stenosis: ultrasonography versus angiography. J Vasc Access. 2012;13(3):310–314. doi: 10.5301/jva.5000047.
[27] Vega A, Abad S, Macías N, et al. Any grade of relative overhydration is associated with long-term mortality in patients with Stages 4 and 5 non-dialysis chronic kidney disease. Clin Kidney J. 2018;11(3):372–376. doi: 10.1093/ckj/sfy018.
[28] Havlucu Y, Kursat S, Ekmekci C, et al. Pulmonary hypertension in patients with chronic renal failure. Respiration. 2007;74(5):503–510. doi: 10.1159/000102953.
[29] Valerianova A, Mlcek M, Grus T, et al. New porcine model of arteriovenous fistula documents increased coronary blood flow at the cost of brain perfusion. Front Physiol. 2022;13:881658. doi: 10.3389/fphys.2022.881658.
[30] Huang X-M, Yu F, Wang Y, et al. Effect of proximal artery restriction on flow reduction and cardiac function in hemodialysis patients with high-flow arteriovenous fistulas. J Vasc Surg. 2023;78(2):526–533. doi: 10.1016/j.jvs.2023.04.017.
[31] Zoccali C, Moissl U, Chazot C, et al. Chronic fluid overload and mortality in ESRD. J Am Soc Nephrol. 2017;28(8):2491–2497. doi: 10.1681/ASN.2016121341.
[32] Yılmaz S, Yildirim Y, Yilmaz Z, et al. Pulmonary function in patients with end-stage renal disease: effects of hemodialysis and fluid overload. Med Sci Monit. 2016;22:2779–2784. doi: 10.12659/msm.897480.
[33] Ortwein J, Feustel A, Reichenberger F. Prevalence of pulmonary hypertension in dialysis patients with end-stage renal disease. Pneumologie. 2020;74(4):210–216. doi: 10.1055/a-1069-0691.
[34] Alhwiesh AK, Abdul-Rahman IS, Alshehri A, et al. The problem of pulmonary arterial hypertension in end-stage renal disease: can peritoneal dialysis be the solution. BMC Nephrol. 2022;23(1):386. doi: 10.1186/s12882-022-02998-y.
[35] Ramasubbu K, et al. A prospective echocardiographic evaluation of pulmonary hypertension in chronic hemodialysis patients in the United States: prevalence and clinical significance. Int J Gen Med. 2010;3:279–286.
[36] Warner ED, Corsi DR, Jimenez D, et al. Determinants of pulmonary hypertension in patients with end-stage kidney disease and arteriovenous access. Curr Probl Cardiol. 2024;49(4):102406. doi: 10.1016/j.cpcardiol.2024.102406.
[37] Mukhtar KN, Mohkumuddin S, Mahmood SN. Frequency of pulmonary hypertension in hemodialysis patients. Pak J Med Sci. 2014;30(6):1319–1322. doi: 10.12669/pjms.306.5525.
[38] Fabbian F, Cantelli S, Molino C, et al. Pulmonary hypertension in dialysis patients: a cross-sectional Italian study. Int J Nephrol. 2010;2011:283475. doi: 10.4061/2011/283475.
[39] Nakagawa Y, Nishikimi T, Kuwahara K. Atrial and brain natriuretic peptides: hormones secreted from the heart. Peptides. 2019;111:18–25. doi: 10.1016/j.peptides.2018.05.012.
[40] Wang L, Xu X, Zhang M, et al. Prevalence of Chronic Kidney Disease in China: results From the Sixth China chronic disease and risk factor surveillance. JAMA Intern Med. 2023;183(4):298–310. doi: 10.1001/jamainternmed.2022.6817.
[41] Song L, Quan Z-L, Zhao L-Y, et al. Impact of pulmonary hypertension on arteriovenous fistula failure of hemodialysis patients: a 10years follow-up cohort study. J Vasc Access. 2023;24(2):261–270. doi: 10.1177/11297298211027408.