CLINICAL STUDY

Prevalence and risk factors for pulmonary arterial hypertension in end-stage renal disease patients undergoing continuous ambulatory peritoneal dialysis

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Abstract

Background: Pulmonary arterial hypertension (PAH) is a major complication in renal failure patients, but very little information is available on the cardiovascular parameters in these patients. The prevalence and risk factors for PAH were systematically evaluated in patients with end-stage renal diseases (ESRD) undergoing continuous ambulatory peritoneal dialysis (CAPD).

Methods: Between January 2010 and January 2014, 177 ESRD patients (85 males and 92 females) undergoing CAPD therapy were recruited. General data, biochemical parameters and echocardiographic findings were collected and PAH risk factors studied. Results: Study participants consisted of 65 patients (36.52%) with PAH (PAH group) and 112 patients without PAH (non-PAH group). The interdialytic weight gain, systolic blood pressure and diastolic blood pressure (DBP), mean arterial pressure and hypertensive nephropathy incidence in the PAH group were significantly higher than the non-PAH group (all p<0.05). There were significant differences between PAH group and non-PAH group in C-reactive protein-positive rate, N-terminal pro-brain natriuretic peptide (NT-proBNP), hemoglobin, prealbumin and serum albumin levels (all p<0.05). Compared with non-PAH group, PAH group showed significant increases in right ventricular internal diameter (RVID), right ventricular outflow tract diameter (RVOTD), main pulmonary artery diameter, left atrial diameter (LAD), left ventricular end-diastolic diameter, interventricular septal thickness, left ventricular mass index, early diastolic mitral annulus velocity and valve calcification incidence (all p<0.05), and decreased left ventricular ejection fraction (LVEF), tricuspid annulus plane systolic excursion (TAPSE) and early diastolic blood flow peak and mitral annulus velocity (E/E’)(all p<0.05). Logistic regression analysis revealed that DBP, NT-proBNP, LAD, RVID, RVOTD, LVEF, TAPSE and E/E’ are major risk factors for PAH. Conclusion: We observed a high incidence of PAH in ESRD patients undergoing CAPD. Logistic regression analysis revealed that DBP, NT-proBNP, LAD, RVID, RVOTD, LVEF, TAPSE and E/E’ are high-risk factors for PAH in ESRD patients undergoing CAPD.

Keywords

Biochemical parameters, continuous ambulatory peritoneal dialysis, echocardiographic findings, end-stage renal disease, pulmonary arterial hypertension, prevalence, risk factors

History

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Introduction

Chronic kidney disease (CKD) is characterized by gradual loss of renal function over time. CKD prevalence is estimated between 10% and 16% globally and CKD-associated worldwide annual death rate in 2013 was at 16.3 per 100,000 and increasing at a rate of 6–7% per year, representing a significant global healthcare burden.¹,² Kidney diseases are generally evaluated based on overall kidney function and presence of kidney damage. CKD is classified into stages 1–5 according to disease severity, with stage-5 CKD known as the end-stage renal disease (ESRD), which affects 2 million adults worldwide and is associated with extremely poor outcomes if timely intervention is not provided.³⁻⁵ ESRD necessitates renal replacement therapies, such as dialysis and kidney transplant. Such therapies can be maintained indefinitely to prolong patients’ lives. However, only about 20% of the world’s ESRD patients have access to such therapies and these therapies are still associated with severely reduced quality of life, high healthcare costs and high rates of sudden-death.⁶⁻⁸ Hemodialysis (HD) is associated with higher adjusted mortality (12.7%) compared to peritoneal dialysis (PD). Further, the annual payer cost for PD is also lower than HD and PD exhibits survival advantages over HD in short-, medium- and long-term outcomes.⁹⁻¹¹ Treatment choice for ESRD is further complicated by the presence of serious comorbidities. ESRD patients exhibit significantly elevated risk for cardiovascular diseases and, in most cases, succumb to cardiac arrest well before kidney failure. Hypertension is the most common comorbidity in CKD patients and cardiovascular complications, such as pulmonary arterial hypertension (PAH), which are the major cause of mortality in ESRD patients undergoing PD.¹²⁻¹⁴
PAH is defined as an abnormally high blood pressure in the pulmonary artery (carries blood from the heart to the lungs), pulmonary vein or pulmonary capillaries, and is a chronic and progressive disease that results in right heart failure and sudden-death if left untreated. PAH occurs when blood vessels within the lungs and the vessels connected to the lungs narrow in diameter, increasing resistance to blood flow and impeding blood circulation in the lungs. PAH may be caused by diverse mechanisms, such as certain heart diseases, lung conditions (emphysema, tumors and chronic obstructive pulmonary disease), thromboembolic diseases and other systemic diseases like rheumatic disorders and liver diseases. Importantly, 30–50% of CKD and ESRD patients have PAH and the risk factors for ESRD-associated PAH include altered endothelial function, increased cardiac output (CO), myocardial defects and left heart dysfunction. In the USA, PAH is diagnosed in 50% of PD patients and is associated with very high mortality. High prevalence of PAH is observed in ESRD patients undergoing chronic HD or conservative treatment, and PAH in these patients is associated with enlarged left atrium, altered arteriovenous fistula (AVF) flow, elevated thromboxane B2 and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and abnormal left ventricular diastolic diameter. Although the precise mechanisms remain unknown, it is proposed that PAH in ESRD is caused by diastolic dysfunction, volume overload, left ventricular disorders, AVF, sleep disorder, dialysis membrane exposure, endothelial dysfunction and vascular calcification. Nevertheless, few studies investigated the incidence of PAH in ESRD patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or examined the risk factors promoting PAH in these patients. To address this, we investigated the prevalence of PAH in ESRD patients undergoing CAPD by collecting detailed information on general data, biochemical parameters and echocardiographic findings. Further, risk factors for PAH were assessed from the collected data to provide the theoretical basis for future studies aimed at early prevention of PAH in ESRD patients undergoing CAPD.

Materials and methods

Study subjects

Between January 2010 and January 2014, 177 ESRD patients undergoing CAPD therapy were recruited to this study at the Dialysis Center of the People’s Hospital of Linyi. The 177 patients include 85 males and 92 females (mean age, 54.94 ± 14.42 years; age range, 18–80 years; mean dialysis time, 36.22 ± 13.52 months). After obtaining study-related approvals from the Ethics committee of the People’s Hospital of Linyi, written informed consents was also obtained from all patients and their legal guardians. Study protocols conformed to the ethical principles of medical research involving human subjects based on the Helsinki Declaration.

Inclusion and exclusion criteria

Study inclusion criteria were (1) patients undergoing CAPD with a daily cumulative dialysate dose of 6–8 L, (2) age > 18 years, (3) patients receiving renal replacement therapy for more than 6 months with stable disease, and (4) patients with complete clinical data on laboratory tests and echocardiography results. Exclusion criteria (1) patients with congenital heart diseases, rheumatic heart disease, valvular heart disease (valvular regurgitation or severe valvular stenosis), severe left ventricular dysfunction (New York Heart Association class III/IV heart failure or left ventricular ejection fraction (LVEF) <40%), respiratory diseases (chronic obstructive pulmonary disease, chest wall or lung parenchymal disease and pulmonary embolism) or autoimmune diseases (systemic lupus erythematosus, choriitis and polyangitis) and (2) patients who previously received HD.

PAH evaluation

PAH was confirmed by established diagnostic criteria using ultrasound, echocardiography and measurement of systolic pulmonary artery pressure (PASP, resting states) ≥35 mmHg (1 mm Hg = 0.133 kPa), based on Echocardiographic Assessment of Right Heart Guidelines published by American Society of Echocardiography in 2010. Systolic tricuspid regurgitant jet velocity (V) was measured directly by Doppler echocardiography and PASP was calculated according to Bernoulli equations: PASP = 4 × V² + right atrial pressure (estimated according to respiratory motion of the inferior vena cava and respiratory variations). Patients were categorized into PAH group and non-PAH group based on the PASP values.

Echocardiographic examination

All the patients were followed-up bimonthly for an echocardiographic examination and general evaluation. The follow-up endpoint was defined as escalating PAH complications and all follow-ups ended on 31 January 2015. Echocardiographic examinations in all subjects were performed by Vivid E9 (GE Healthcare, Milwaukee, WI) by the same physician. Echocardiographic data recorded included right ventricular internal diameter (RVID), right ventricular outflow tract diameter (RVOTD), main pulmonary artery diameter (MPAD), left atrial diameter (LAD), left ventricular outflow tract diameter (LVOTD), aortic root diameter (ARD), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-systolic volume (LVESV), left ventricular end-diastolic volume (LVEDV), stroke volume (SV), CO, cardiac index (CI), LVEF, pericardial effusion (PE), interventricular septal thickness (IVST), left ventricular mass index (LVMI), tricuspid annulus plane systolic excursion (TAPSE), the ratio of early diastolic transmitral inflow velocity to early diastolic mitral annulus velocity (E/A), the ratio of mitral early diastolic blood flow peak and mitral annulus velocity (E/E’), and valve calcification.

Data collection

The patient general data and biochemical indicators collected included: age, gender, body mass index (BMI), dialysis time, interdialytic weight gain (IDWG), erythropoietin (EPO) dosage, pre-dialysis systolic blood pressure (SBP), pre-dialysis diastolic blood pressure (DBP), mean arterial
pressure (MAP), ESRD propathy, hemoglobin (Hb), hematocrit (Hct), serum albumin (ALB), prealbumin (PA), serum creatinine (SCr), blood urea nitrogen (BUN), blood calcium (Ca), serum phosphorus (P), parathyroid hormone (PTH), C-reactive protein (CRP), alkaline phosphatase (ALP), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), NT-proBNP and urea clearance index (KT/V) per week.

**Statistical analysis**

Continuous variables are presented as mean ± SD; categorical variables were presented as frequencies and percentages. Comparisons between continuous variables were conducted by analysis of variance and t-test. Chi-square test was used to compare categorical variables. Related risk factors of PAH were analyzed by logistic regression analysis. p-Values of <0.05 were considered as statistically significant.

**Results**

**Experiment grouping**

Based on the results of the echocardiographic examination, PAH complication was confirmed in 65 ESRD patients (36.52%) undergoing CAPD, with PASP value of 44.45 ± 6.39 mmHg. The PAH patient group included 31 males and 34 females, with a mean age of 56.29 ± 15.27 and mean dialysis time of 36.92 ± 14.55 months. The remaining 112 non-PAH patients showed a PASP of 26.35 ± 4.37 mmHg. The non-PAH patient group consisted of 54 males and 58 females, with a mean age of 54.15 ± 13.91 and mean dialysis time of 35.81 ± 12.94 months.

**Comparisons in general data**

The IDWG, pre-dialysis SBP, pre-dialysis DBP, MAP and hypertensive nephropathy incidence in the PAH group were higher compared to the non-PAH group (all \( p < 0.05 \)). However, no differences in age, gender, BMI, dialysis time, EPO and incidences of propathy (diabetic nephropathy, chronic glomerulonephritis and other diseases) were detected between the PAH group and non-PAH group (all \( p > 0.05 \)) (Table 1).

**Comparisons in biochemical indicators**

CRP-positive rate and NT-proBNP in the PAH group were significantly higher than the non-PAH group (all \( p < 0.05 \)). On the other hand, Hb, PA and serum ALB levels in the PAH group were significantly lower than the non-PAH group (all \( p < 0.05 \)). No significant differences were found between the PAH group and the non-PAH group in SCr, BUN, Hct, ALP, TC, TG, LDL-C, HDL-C, KT/V per week, Ca, P or PTH (all \( p > 0.05 \)) (Table 2).

**Comparisons in echocardiographic parameters**

Compared to non-PAH group, the PAH group showed a significant increase in RVID, RVOTD, MPAD, LAD, LVEDD, IVST, LVMI, E/A and valve calcification incidence (all \( p < 0.05 \)), and LVEF, TAPSE and E/E’ decreased significantly in the PAH group in comparison with the non-PAH group (all \( p < 0.05 \)). No significant changes in LVOTD, ARD, LVEDSD, LVESV, LVEDV, SV, CO, CI or PE were observed between the PAH group and non-PAH group (all \( p > 0.05 \)) (Table 3).

**Logistic regression analysis**

The following risk factors were analyzed by univariate logistic regression analysis: IDWG, SBP, DBP, MAP, hypertensive nephropathy incidence, Hb, ALB, PA, CRP-positive rate, NT-proBNP, RVID, RVOTD, MPAD, LAD, LVEDD, LVEF, IVST, LVMI, TAPSE, E/A, E/E’ and valve calcification incidence. The logistic regression analysis revealed that pre-dialysis DBP, ALB, NT-proBNP, LAD, RVID, RVOTD, LVEF, TAPSE and E/E’ are the highest risk factors for PAH in ESRD patients undergoing CAPD (Table 4).

**Discussion**

PAH is a major complication in several systemic disorders. In this study, we found a high prevalence of PAH (36.52%) in ESRD patients undergoing CAPD. Since early symptoms of PAH are generally mild and often difficult to diagnose without employing invasive diagnostic approaches, our results indicate the need for improved clinical monitoring in ESRD patients undergoing CAPD, for early detection of PAH. PAH prevalence in dialysis patients varies between 17% and 49.53%, depending on the dialysis mode and other comorbidities in individual patients.\(^{24}\) Our study results are consistent with previous studies that reported high PAH incidence rates ranging between 9–39% in general in ESRD patients and 12–42% PAH rates for patients undergoing PD.\(^{25–27}\)

Increased CO induced by AVF, endothelial dysfunction in pulmonary vasculature resulting in plexiform lesions, changes in vascular tone caused by abnormal production of vasoactive mediators, local and systemic inflammation, vasoconstriction and vascular sclerosis triggered by microbubbles from the dialysis circuit, have all been associated with PAH pathogenesis.\(^{16–18,24}\) CAPD is safe and is widely used in ESRD patients. However, the long-term effectiveness of CAPD is limited by complications because peritonitis is a significant risk and continuous absorption of glucose from the dialysate causes weight gain (generally fat), dyslipidemia, hyperleptinemia and atherosclerosis.\(^{28–30}\) IDWG is related to sodium (DNA) and fluid overload,\(^{31,32}\) but the benefits of reducing IDWG by decreasing DNA prescriptions for electrolyte balance must be carefully weighed against a higher risk of adverse outcomes.\(^{33,34}\) Partly consistent with our study, a previous study showed that PAH was diagnosed in 18.5% of PD patients and 58.6% of HD patients, and PAH patients exhibited higher IDWG.\(^{35}\) We propose that elevated IDWG may increase volume overload and promote PAH in CAPD patients.

Systolic and mean pulmonary arterial pressure are the two main echocardiographic parameters used to evaluate PAH,\(^{36,37}\) while MAP is an index of overall blood pressure. We found that pre-dialysis DBP, SBP and MAP is associated with PAH onset. Elevated systolic pressure is a valuable measure for evaluating hypertension.\(^{38,39}\) DBP positively correlates with the severity of aortic and mitral regurgitation.
in patients with heart valve regurgitation. However, no obvious differences in SBP and DBP were observed between PAH patients and non-PAH patients. Interestingly, lower DBP level is observed in dialysis patients with PAH, compared to dialysis patients without PAH, contrary to our findings. The incidence of PAH in hypertensive nephropathy patients was found to be significantly higher than non-hypertensive nephropathy patients. Hypertensive nephropathy associated with progressive decline in glomerular filtration rate despite reduced blood pressure is the second leading cause of total kidney failure and is associated with significant morbidity and mortality.

Some of the routine biochemical parameters, reflecting anemia, hypocarbia, elevated uric acid and increased CRP levels, are non-specific indicators of disease severity. However, BNP and NT-proBNP are recommended in the current guidelines for diagnosis of PAH. Nevertheless, increased plasma CRP levels are found in chronic obstructive pulmonary disease patients associated with PAH (COPD-PAH) as opposed to COPD without PAH, suggesting a possible link between CRP and PAH in COPD patients. In addition, Scognamiglio et al. reported that serum CRP levels predict higher mortality in PAH patients associated with congenital heart disease. NT-proBNP is an important biomarker to assess the severity of PAH disease and baseline NT-proBNP correlates with changes in 6-min walking distance in PAH patients, a measure of clinical and hemodynamic severity.

Table 1. Comparison in general data between the PAH group and the non-PAH group.

| General data                     | PAH (n = 65) | Non-PAH (n = 112) | t/χ² | p     |
|----------------------------------|-------------|-------------------|------|-------|
| Age (years)                      | 56.29 ± 15.27 | 54.15 ± 13.91 | 0.952 | 0.343 |
| Gender (male/female)             | 31/34       | 54/58             | 0.004 | 0.947 |
| Dialysis time (month)            | 36.92 ± 14.55 | 35.81 ± 12.94 | 0.523 | 0.660 |
| BMI (kg/m²)                      | 21.43 ± 2.26 | 21.28 ± 2.85     | 0.397 | 0.708 |
| IDWG (kg)                        | 2.43 ± 0.75  | 2.14 ± 0.97      | 2.075 | 0.039 |
| Pre-dialysis SBP (mmHg)          | 142.12 ± 10.56 | 138.24 ± 6.35 | 3.055 | 0.003 |
| Pre-dialysis DBP (mmHg)          | 92.20 ± 13.34 | 84.25 ± 13.17   | 3.853 | <0.001 |
| MAP (mmHg)                       | 108.84 ± 8.72 | 102.25 ± 9.22   | 4.678 | <0.001 |
| Erythropoietin dosage (10,000 u/week) | 1.02 ± 0.31  | 0.96 ± 0.29     | 1.277 | 0.203 |
| ESRD protopathy (n, %)           |              |                   |      |       |
| Chronic glomerulonephritis       | 20 (11.30%)  | 45 (25.42%)      | 0.226 | 0.635 |
| Diabetic nephropathy             | 12 (29.23%)  | 23 (14.29)       | 0.112 | 0.738 |
| Hypertensive nephropathy         | 28 (43.08%)  | 30 (26.79%)      | 4.955 | 0.026 |
| Other diseases                   | 5 (9.23%)    | 14 (11.61%)      | 0.992 | 0.319 |
| PASP                             | 44.45 ± 6.39 | 26.35 ± 4.37     | 22.32 | <0.001 |

Notes: PAH, pulmonary arterial hypertension; BMI, body mass index; IDWG, interdialytic weight gain; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; ESRD, end-stage renal disease; PASP, pulmonary arterial systolic pressure.

Table 2. Comparison in biochemical indicators between the PAH group and the non-PAH group.

| Biochemical indicators          | PAH (n = 65) | Non-PAH (n = 112) | t/χ² | p     |
|---------------------------------|-------------|-------------------|------|-------|
| Scr (umol/L)                    | 603.51 ± 113.12 | 626.39 ± 141.32 | 1.114 | 0.267 |
| BUN (mmol/L)                    | 24.26 ± 7.25  | 25.15 ± 8.04      | 0.736 | 0.463 |
| Hb (g/L)                        | 110.34 ± 10.47 | 116.82 ± 17.25   | 2.747 | 0.007 |
| Hct (%)                         | 34.97 ± 9.23  | 36.25 ± 3.57      | 1.310 | 0.192 |
| ALB (g/L)                       | 29.16 ± 14.28 | 35.77 ± 17.23    | 2.535 | 0.012 |
| PA (g/L)                        | 0.30 ± 0.06   | 0.32 ± 0.05       | 2.401 | 0.017 |
| ALP (mmol/L)                    | 127.60 ± 19.55 | 122.42 ± 48.13 | 0.828 | 0.409 |
| TC (mmol/L)                     | 3.80 ± 1.12   | 3.58 ± 1.09       | 1.282 | 0.202 |
| TG (mmol/L)                     | 1.49 ± 0.76   | 1.65 ± 0.34       | 1.766 | 0.080 |
| LDL-C (mmol/L)                  | 2.26 ± 0.75   | 2.07 ± 0.63       | 1.807 | 0.073 |
| HDL-C (mmol/L)                  | 1.16 ± 0.61   | 1.07 ± 0.07       | 1.551 | 0.123 |
| KT/V                            | 1.45 ± 0.42   | 1.38 ± 0.31       | 1.277 | 0.203 |
| CRP-positive rate (n, %)        | 27 (41.54%)   | 45 (25.42%)       | 0.226 | 0.635 |
| Ca (mmol/L)                     | 2.19 ± 0.38   | 2.27 ± 0.24       | 1.720 | 0.087 |
| P (mmol/L)                      | 2.03 ± 0.28   | 1.97 ± 0.32       | 1.259 | 0.210 |
| iPTH (ng/mL)                    | 325.23 ± 113.05 | 315.14 ± 121.45 | 0.546 | 0.586 |
| NT-proBNP (ng/L)                | 348.03 ± 24.15 | 322.12 ± 32.51  | 5.590 | <0.001 |

Notes: PAH, pulmonary arterial hypertension; SCR, serum creatinine; BUN, blood urea nitrogen; Hb, hemoglobin; Hct, hematocrit; ALB, serum albumin; PA, prealbumin; ALP, alkaline phosphatase; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; KT/V, urea clearance index; CRP, C-reactive protein; Ca, blood calcium; P, serum phosphorus; PTH, parathyroid hormone; NT-proBNP, N-terminal pro-brain natriuretic peptide.
Unal et al. reported no differences in high-sensitivity-CRP levels between CAPD patients with PAH and without PAH. On the other hand, the levels of important indicators of nutritional status, Hb, PA and serum ALB, were significantly lower in PAH group compared to the non-PAH group in patients receiving dialysis. PASP inversely correlates with serum ALB level and Hb level. The Hb level was significantly lower in patients with PAH, compared with normal PAH group. When patients with and without PAH were compared, the Hb and serum ALB levels were found to be significantly higher in patients with PAH than those without PAH.

Echocardiography allows measurement of multiple parameters in ESRD patients to estimate cardiovascular complication risks, such as LVMi, LVEF and LV chamber volume, and aids patient stratification into a high-risk group for closer monitoring. In this regard, vascular and valvular calcification also contributes to the increased mortality in PD patients and are important indicators of disease outcomes. Our echocardiographic findings showed significant increases in RVID, RVOTD, MPAD, LAD, LVEDD, IVST, LVMI, E/A and valve calcification incidence in PAH group compared with non-PAH group, while LVEF, TAPSE and E/E’ decreased significantly in the PAH group in comparison to

### Table 3. Comparison in echocardiographic parameters between the PAH group and the non-PAH group.

| Echocardiographic parameters | PAH (n = 65) | Non-PAH (n = 112) | t/χ² | p       |
|-----------------------------|-------------|-------------------|------|---------|
| RVID (mm)                   | 21.21 ± 2.45| 20.25 ± 2.07      | 2.778| 0.006   |
| RVOOTD (mm)                 | 32.54 ± 4.15| 30.45 ± 3.02      | 3.855| <0.001  |
| MPAD (mm)                   | 24.43 ± 3.07| 23.27 ± 2.32      | 3.951| 0.005   |
| LAD (mm)                    | 41.86 ± 4.06| 40.07 ± 3.75      | 2.970| 0.003   |
| LVOTD (mm)                  | 27.14 ± 3.12| 26.21 ± 3.41      | 1.803| 0.073   |
| ARD (mm)                    | 31.08 ± 3.32| 30.15 ± 3.21      | 1.834| 0.068   |
| LVEDD (mm)                  | 49.41 ± 9.94| 43.23 ± 5.24      | 2.101| 0.037   |
| LVESD (mm)                  | 34.02 ± 4.12| 32.35 ± 7.13      | 0.901| 0.369   |
| LVESV (mL)                  | 99.02 ± 17.27| 93.13 ± 22.57    | 1.817| 0.071   |
| LVEDV (mL)                  | 37.42 ± 13.14| 34.47 ± 12.63    | 1.476| 0.142   |
| SV (mL)                     | 57.01 ± 8.42| 55.76 ± 6.46      | 1.108| 0.270   |
| CO (L)                      | 4.53 ± 1.64 | 4.33 ± 1.30       | 0.894| 0.373   |
| CI (L/m²)                   | 2.45 ± 0.79 | 2.32 ± 0.43       | 1.415| 0.159   |
| LVEF (%)                    | 52.59 ± 5.93| 61.36 ± 7.84      | 7.810| <0.001  |
| PE (%)                      | 8.01 ± 1.19 | 7.90 ± 0.70       | 0.782| 0.435   |
| IVST (mm)                   | 12.09 ± 2.76| 11.19 ± 1.37      | 2.896| 0.004   |
| LVMI                        | 162.78 ± 61.16| 135.30 ± 53.41  | 3.126| 0.002   |
| TAPSE                       | 13.56 ± 3.81| 17.10 ± 2.70      | 7.207| <0.001  |
| E/A (n, %)                  | 27 (15.25%) | 25 (14.12%)       | 0.007| 0.988   |
| >1                          | 38 (21.47%) | 87 (49.15%)       | 0.001| 0.978   |
| Valve calcification (n, %)  | 34 (20.90%) | 37 (19.21%)       | 0.001| 0.977   |
| Calcification               | 31 (17.51%) | 75 (42.37%)       | 0.012| 0.907   |
| Non-calcification           |             |                   |      |         |

Notes: PAH, pulmonary arterial hypertension; RVID, right ventricular internal diameter; RVOTD, right ventricular outflow tract diameter; MPAD, main pulmonary artery diameter; LAD, left atrial diameter; LVOTD, left ventricular outflow tract diameter; ARD, aortic root diameter; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end systolic volume; LVEDV, left ventricular end-diastolic volume; SV, stroke volume; CO, cardiac output; CI, cardiac index; LVEF, left ventricular ejection fraction; PE, pericardial effusion; IVST, interventricular septal thickness; LVMi, left ventricular mass index; TAPSE, tricuspid annulus plane systolic excursion; E/A, the ratio of early diastolic transmitral inflow velocity to early diastolic mitral annulus velocity; E/E’, the ratio of mitral early diastolic blood flow peak and mitral annulus velocity.

### Table 4. Logistic regression analysis of risk factors associated with PAH in ESRD patients undergoing CAPD.

| Variables                  | Regression coefficient | Standard error | Wald    | p   | OR  | 95%CI    |
|----------------------------|------------------------|---------------|---------|-----|-----|----------|
| DBP                        | 0.075                  | 0.036         | 4.219   | 0.040| 1.078| 1.003    |
| ALB                        | −0.096                 | 0.037         | 6.777   | 0.009| 0.908| 0.845    |
| NT-proBNP                  | 0.063                  | 0.018         | 4.016   | 0.045| 1.066| 1.028    |
| RVID                       | 0.572                  | 0.237         | 5.837   | 0.016| 1.771| 1.114    |
| RVOTD                      | 0.322                  | 0.139         | 5.384   | 0.020| 1.380| 1.051    |
| LAD                        | 0.560                  | 0.167         | 11.184  | 0.001| 1.751| 1.261    |
| LVEF                       | −0.326                 | 0.102         | 10.227  | 0.001| 0.722| 0.591    |
| TAPSE                      | −7.355                 | 0.229         | 10.278  | 0.001| 0.479| 0.306    |
| E/E’                       | −2.895                 | 0.120         | 8.584   | 0.016| 0.749| 0.592    |

Notes: PAH, pulmonary arterial hypertension; ESRD, end-stage renal disease; CAPD, continuous ambulatory peritoneal dialysis; DBP, diastolic blood pressure; ALB, serum albumin; NT-proBNP, N-terminal of pro-hormone brain natriuretic peptide; RVID, right ventricular internal diameter; RVOTD, right ventricular outflow tract diameter; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annulus plane systolic excursion; E/A, the ratio of mitral early diastolic blood flow peak and mitral annulus velocity.
non-PAH group. PAH is associated with right ventricular (RV) dysfunction and left ventricular (LV) systolic dysfunction, and left-sided valvular disease leading to a chronic elevation in LV filling pressures.\textsuperscript{35,36} TAPSE is an indicator of RV function and predicts survival in idiopathic PAH and in patients with systemic sclerosis-associated PAH.\textsuperscript{37} E/E’ is a non-invasive biomarker to assess left ventricular filling pressure and indicates hypertrophy.\textsuperscript{58} In agreement with our findings, a study examining the prevalence and characteristics of PAH in PD patients revealed that patients with PAH had lower LVEF compared to patients without PAH.\textsuperscript{59} Ventricular hypertrophy increases ventricular diameter and occurs in PAH in response to pressure overload.\textsuperscript{60} In addition, a previous study suggested that LVMI is a major risk factor for PAH in CAPD patients.\textsuperscript{41} The results of logistic regression analysis further confirmed that DBP, ALB, NT-proBNP, LAD, RVOTD, LVEF, TAPSE and E/E’ are the highest risk factors for PAH in ESRD patients undergoing CAPD.

In conclusion, our results provided valuable clinical reference data to assess the risk of PAH in ESRD patients undergoing CAPD. Further studies are required to confirm our findings in a larger patient population and test the effectiveness of early diagnostic and treatment methods in ESRD patients undergoing CAPD. Our results also provide important clues to the underlying mechanisms of PAH development in ESRD patients undergoing CAPD.

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Declaration of interest

All the authors in our study have no conflict of interest.

References

1. Levey AS, Coresh J. Chronic kidney disease. \textit{Lancet}. 2012;379:165–180.
2. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. \textit{Lancet}. 2015;385:117–171.
3. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. \textit{Ann Intern Med}. 2003;139:137–147.
4. Fox CS, Matsushita K, Woodward M, et al. Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: A meta-analysis. \textit{Lancet}. 2012;380:1662–1673.
5. Levey AS, Becker C, Inker LA. Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: A systematic review. \textit{JAMA}. 2015;313:837–846.
6. Heidenheim AP, Kooistra MP, Lindsay RM. Quality of life in chronic kidney disease. \textit{Contrib Nephrol}. 2004;145:99–105.
7. Yong DS, Kwok AO, Wong DM, et al. Symptom burden and quality of life in end-stage renal disease: A study of 179 patients on dialysis and palliative care. \textit{Palliat Med}. 2009;23:111–119.
8. Villar E, McDonald SP, Couchoud C. Incidence of treatment for end-stage renal disease among individuals with diabetes in the U.S. continues to decline: Response to Barrow, Li, and Geiss. \textit{Diabetes Care}. 2010;33:e69 (author reply e70).
9. Sanabria M, Muñoz J, Trillos C, et al. Dialysis outcomes in Colombia (DOC) study: A comparison of patient survival on peritoneal dialysis vs hemodialysis in Colombia. \textit{Kidney Int Suppl}. 2008;108:S165–S172.
10. Mehrotra R, Chiu YW, Kalantar-Zadeh K, et al. Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. \textit{Arch Intern Med}. 2011;171:110–118.
11. Rufino JM, García C, Vega N, et al. [Current peritoneal dialysis compared with hemodialysis: Medium-term survival analysis of incident dialysis patients in the Canary Islands in recent years]. \textit{Nefrologia}. 2011;31:174–184.
12. Crowe E, Halpin D, Stevens P. Guideline Development Group. Early identification and management of chronic kidney disease: Summary of NICE guidance. \textit{Bmj}. 2008;337:a1530.
13. Abdelwhab S, Elshinnawy S. Pulmonary hypertension in chronic renal failure patients. \textit{Am J Nephrol}. 2008;28:990–997.
14. Alhamad EH, Al-Ghonaime M, Alfaleh HF, et al. Pulmonary hypertension in end-stage renal disease and post renal transplantation patients. \textit{J Thorac Dis}. 2014;6:606–616.
15. Hooper MM. Definition, classification, and epidemiology of pulmonary arterial hypertension. \textit{Semin Respir Crit Care Med}. 2009;30:369–375.
16. Montani D, Günther S, Dorfmüller P, et al. Pulmonary arterial hypertension. \textit{Orphanet J Rare Dis}. 2013;8:97.
17. Zhao LJ, Huang SM, Liang T, Tang H. Pulmonary hypertension and right ventricular dysfunction in hemodialysis patients. \textit{Eur Rev Med Pharmacol Sci}. 2014;18:3267–3273.
18. Sise ME, Courtwright AM, Channick RN. Pulmonary hypertension in patients with chronic and end-stage kidney disease. \textit{Kidney Int}. 2013;84:682–692.
19. Agarwal R. Prevalence, determinants and prognosis of pulmonary hypertension among hemodialysis patients. \textit{Nephrol Dial Transplant}. 2012;27:3908–3914.
20. Ramaasubbu K, Deswal A, Herdejürgen C, et al. A prospective echocardiographic evaluation of pulmonary hypertension in chronic hemodialysis patients in the United States: Prevalence and clinical significance. \textit{Int J Gen Med}. 2010;3:279–286.
21. Li Z, Liang X, Liu S, et al. Pulmonary hypertension: Epidemiology in different CKD stages and its association with cardiovascular morbidity. \textit{PloS One}. 2014;9:e114392.
22. Glas J, Seiderer J, Bues S, et al. IRGM variants and susceptibility to inflammatory bowel disease in the German population. \textit{PloS One}. 2013;8:e54338.
23. Mansour IN, Lang RM, Aburuwaida WM, et al. Evaluation of the clinical application of the ACCF/ASE appropriateness criteria for stress echocardiography. \textit{J Am Soc Echocardiogr}. 2010;23:1199–1204.
24. Kosmadakis G, Aguilera D, Carceles O, et al. Pulmonary hypertension in dialysis patients. \textit{Ren Fail}. 2013;35:514–520.
25. Etemadi J, Zolfaghari H, Firoozi R, et al. Unexplained pulmonary hypertension in peritoneal dialysis and hemodialysis patients. \textit{Rev Port Pneumol}. 2012;18:10–14.
26. Oygar DD, Zekican G. Pulmonary hypertension in dialysis patients. \textit{Ren Fail}. 2012;34:840–844.
27. Nasri H. Unexplained pulmonary hypertension in peritoneal dialysis and hemodialysis patients. \textit{Rev Port Pneumol}. 2013;19:238–239.
28. Cho KH, Do JY, Park JW, Yoon KW. Effect of icodextrin dialysis solution on body weight and fat accumulation over time in CAPD patients. \textit{Nephrol Dial Transplant}. 2010;25:593–599.
29. Kurella M, Booth TC, Cash CJ, et al. Complications of ambulatory peritoneal dialysis. \textit{Radiographics}. 2009;29:441–460.
30. Zanger R. Hyponatremia and hypokalemia in patients on peritoneal dialysis. \textit{Semin Dial}. 2010;23:575–580.
31. Bots CP, Brand HS, Veerman EC, et al. Interdialytic weight gain in patients on hemodialysis is associated with dry mouth and thirst. \textit{Kidney Int}. 2004;66:1662–1668.
32. Bruzda-Zwiew A, Szczepańska J, Zwiech R. Sodium gradient, xerostomia, thirst and inter-dialytic excessive weight gain: A possible relationship with hyposalivation in patients on maintenance hemodialysis. \textit{Int Urol Nephrol}. 2014;46:1411–1417.
33. López-Gómez JM, Villalvende M, Jofre R, et al. Interdialytic weight gain as a marker of blood pressure, nutrition, and survival in hemodialysis patients. \textit{Kidney Int Suppl}. 2005;93:S63–S68.
34. Hecking M, Karaboyas A, Saran R, et al. Dialysate sodium concentration and the association with interdialytic weight gain, hospitalization, and mortality. \textit{Clin J Am Soc Nephrol}. 2012;7:92–100.
35. Fabbian F, Cantielli S, Molino C, et al. Pulmonary hypertension in dialysis patients: A cross-sectional Italian study. *Int J Nephrol*. 2011;2011:283475.

36. Pyxaras SA, Pinamonti B, Barbati G, et al. Echocardiographic evaluation of systolic and mean pulmonary artery pressure in the follow-up of patients with pulmonary hypertension. *Eur J Echocardiogr*. 2011;12:696–701.

37. Chemla D, Humbert M, Sitbon O, et al. Systolic and mean pulmonary arterial pressures: Are they interchangeable in patients with pulmonary hypertension? *Chest*. 2015;147:943–950.

38. Kannel WB. Elevated systolic blood pressure as a cardiovascular risk factor. *Am J Cardiol*. 2000;85:251–255.

39. Glynn RJ, L’Italien GJ, Sesso HD, et al. Development of predictive models for long-term cardiovascular risk associated with systolic and diastolic blood pressure. *Hypertension*. 2002;39:105–110.

40. Gottdiener JS, Panza JA, St John Sutton M, et al. Testing the test: The reliability of echocardiography in the sequential assessment of valvular regurgitation. *Am Heart J*. 2002;144:115–121.

41. Unal A, Sipahioglu M, Oguz F, et al. Pulmonary hypertension in peritoneal dialysis patients: Prevalence and risk factors. *Perit Dial Int*. 2009;29:191–198.

42. Mahajan A, Simoni J, Sheather SJ, et al. Daily oral sodium bicarbonate preserves glomerular filtration rate by slowing its decline in early hypertensive nephropathy. *Kidney Int*. 2010;78:303–309.

43. Hart PD, Bakris GL. Hypertensive nephropathy: Prevention and treatment recommendations. *Expert Opin Pharmacother*. 2010;11:2675–2686.

44. Foris V, Kovacs G, Tscherner M, et al. Biomarkers in pulmonary hypertension: What do we know? *Chest*. 2013;144:274–283.

45. Kwon YS, Chi SY, Shin HJ, et al. Plasma C-reactive protein and endothelin-1 level in patients with chronic obstructive pulmonary disease and pulmonary hypertension. *J Korean Med Sci*. 2010;25:1487–1491.

46. Scognamiglio G, Kempny A, Price LC, et al. Creative protein in adults with pulmonary arterial hypertension associated with congenital heart disease and its prognostic value. *Heart*. 2014;100:1335–1341.

47. Frantz RP, McDevitt S, Walker S. Baseline NT-proBNP correlates with change in 6-minute walk distance in patients with pulmonary arterial hypertension in the pivotal inhaled treprostinil study TRIUMPH-1. *J Heart Lung Transplant*. 2012;31:811–816.

48. Soon E, Doughty NJ, Treacy CM, et al. Log-transformation improves the prognostic value of serial NT-proBNP levels in apparently stable pulmonary arterial hypertension. *Palm Circ*. 2011;1:244–249.

49. Obineche EN, Pathan JY, Fisher S, et al. Natriuretic peptide and adrenomedullin levels in chronic renal failure and effects of peritoneal dialysis. *Kidney Int*. 2006;69:152–156.

50. David S, Kümpers P, Seidler V, et al. Diagnostic value of N-terminal pro-B-type natriuretic peptide (NT-proBNP) for left ventricular dysfunction in patients with chronic kidney disease stage 5 on hemodialysis. *Nephrol Dial Transplant*. 2008;23:1370–1377.

51. K/DOQI Workgroup. *K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients*. *Am J Kidney Dis*. 2005;45:S1–S153.

52. London GM, Pannier B, Guerin AP, et al. Alterations of left ventricular hypertrophy in and survival of patients receiving hemodialysis: Follow-up of an interventional study. *J Am Soc Nephrol*. 2001;12:2759–2767.

53. Wang AY, Wang M, Woo J, et al. Cardiac valve calcification as an important predictor for all-cause mortality and cardiovascular mortality in long-term peritoneal dialysis patients: A prospective study. *J Am Soc Nephrol*. 2003;14:159–168.

54. Wang AY. Vascular and valvular calcification in chronic peritoneal dialysis patients. *Int J Nephrol*. 2011;2011:Article ID 198045.

55. Agarwal R, Shah SJ, Foreman AJ, et al. Risk assessment in pulmonary hypertension associated with heart failure and preserved ejection fraction. *J Heart Lung Transplant*. 2012;31:467–477.

56. Adir Y, Amir O. Pulmonary hypertension associated with left heart disease. *Semin Respir Crit Care Med*. 2013;34:665–680.

57. Mathai SC, Sibley CT, Forfia PR, et al. Tricuspid annular plane systolic excursion is a robust outcome measure in systemic sclerosis-associated pulmonary arterial hypertension. *J Rheumatol*. 2011;38:2410–2418.

58. De Sutter J, De Backer J, Van de Veire N, et al. Effects of age, gender, and left ventricular mass on septal mitral annulus velocity (E′) and the ratio of transmitral early peak velocity to E′ (E/E′). *Am J Cardiol*. 2005;95:1020–1023.

59. Kumbar L, Fein PA, Rafiq MA, et al. Pulmonary hypertension in peritoneal dialysis patients. *Adv Perit Dial*. 2007;23:127–131.

60. Piao L, Fang YH, Parikh KS, et al. GRK2-mediated inhibition of adrenergic and dopaminergic signaling in right ventricular hypertrophy: Therapeutic implications in pulmonary hypertension. *Circulation*. 2012;126:2859–2869.