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RESEARCH LETTER

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Association of mildly elevated pulmonary vascular resistance with major cardiovascular events in pulmonary hypertension and chronic kidney disease: A retrospective cohort analysis

Jose M. Martinez Manzano[1] | **Alexander Prendergast**[1] | **Tara John**[1] | **Raul Leguizamon**[1] | **Ian McLaren**[1] | **Rasha Khan**[1] | **Andrew Geller**[1] | **Phuuwadith Wattanachayakul**[1] | **John Malin**[1] | **Simone A. Jarrett**[1] | **Kevin Bryan Lo**[1] | **Sadia Benzaquen**[2] | **Christian Witzke**[3]

[1]Department of Medicine, Jefferson Einstein Hospital, Philadelphia, Pennsylvania, USA

[2]Department of Pulmonary and Critical Care, Jefferson Einstein Hospital, Philadelphia, Pennsylvania, USA

[3]Department of Cardiology, Jefferson Einstein Hospital, Philadelphia, Pennsylvania, USA

Correspondence
Jose M. Martinez Manzano, MD, Jefferson Einstein Hospital, 5501 Old York Rd, Philadelphia, PA 19141, USA.
Email: jose.martinezmanzano@jefferson.edu

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Abstract

Pulmonary hypertension (PH) is associated with adverse outcomes in chronic kidney disease (CKD) patients. Our study suggests mildly elevated pulmonary vascular resistance (> 2 to ≤ 3) is independently associated with major adverse cardiovascular events at 1-year follow-up. Early diagnosis of precapillary PH in CKD patients can potentially improve clinical outcomes.

KEYWORDS

hypertensive vascular renal disease, pulmonary hypertension, renal hemodynamics

INTRODUCTION

Recent pulmonary hypertension (PH) guidelines established a new pulmonary vascular resistance (PVR) cutoff of 2 Wood units (WU) to diagnose precapillary PH.[1] This adjustment was based on evidence that mildly elevated PVR is also associated with adverse clinical outcomes.[2]

Among chronic kidney disease (CKD) patients, PH is a prevalent complication associated with adverse clinical outcomes, particularly in those with precapillary or combined PH.[3–5] Thus, recognition of mildly elevated PVR in CKD patients is paramount and, to our knowledge, has not been studied before. This study aims to assess if mildly elevated PVR (> 2 to ≤ 3 WU) is associated with adverse clinical outcomes among patients with advanced CKD.

METHODS AND STATISTICAL ANALYSIS

This was a single-center retrospective cohort study of patients with CKD stage 3b–5 who received right heart catheterization (RHC) between August 2018 and June 2023. We identified patients who underwent (RHC) using

Jose M. Martinez Manzano, Alexander Prendergast, and Tara John contributed equally to this work.

current procedural terminology (CPT) codes.[6] The diagnosis of CKD3b, CKD4, and CKD5 were based on a baseline estimated glomerular filtration rate (eGFR) of 44–30, 15–29, and <15 mL/min or dialysis requirement, respectively.[7] The eGFR was calculated using the 2021 CKD-EPI creatinine equation.[8] For inpatients, the baseline eGFR was obtained from the most recent prior admission or outpatient visit. We used the eGFR at discharge as the baseline if no prior records were available. For patients on dialysis or who underwent elective (outpatient) RHC, the baseline eGFR was the closest to the RHC date, either before or after the procedure.

Following recent guidelines proposing the use of a lower PVR cutoff to diagnose precapillary and combined PH, we stratified data according to PVR values into three groups: ≤2 Wood units (WU), >2 to ≤3 WU, and >3 WU.[1] Cardiac output (CO) was measured using Fick's equation.[9] PVR was calculated by applying the formula (mean pulmonary artery pressure [mPAP] – pulmonary artery wedge pressure [PAWP])/CO. We defined PH as mPAP of > 20 mmHg; isolated precapillary PH was defined as mPAP of > 20 mmHg associated with a PVR of > 2 WU and PAWP of <15 mmHg, isolated postcapillary PH as mPAP of > 20 mmHg, PAWP of > 15 mmHg, and PVR ≤ 2 WU, and combined PH as mPAP of > 20 mmHg, PAWP of > 15 mmHg, and PVR of > 2 WU.[10]

The adverse outcomes of interest were major cardiovascular events (MACE) and all-cause mortality within a year after the RHC date. We defined MACE as cardiovascular (CV) death or hospitalizations for heart failure (HF), acute coronary syndrome (ACS), stroke, and peripheral artery disease (PAD).[11]

The demographic, clinical, and outcome data were obtained through chart review from electronic medical records and recorded in Jefferson's REDCap electronic database. Echocardiographic interpretation, including the presence of right ventricular (RV) strain and dilation, was done by board-certified cardiologists as part of the routine clinical care and according to established guidelines.[12] The RV systolic function assessment was variable between echocardiographers; qualitative visual inspection along with an objective parameter, such as tricuspid annular plane systolic excursion (TAPSE) of < 1.6 cm or tricuspid annular velocity (S') of <9.5 cm/s, were the most commonly used methods.[13] We defined RV dilation as an RV to LV ratio of ≥ 1:1, IVC dilation as an IVC diameter of > 2.1 cm, and noncollapsible IVC as an inspiratory collapse of <50%. Our project was approved by Jefferson's institutional review board (iRISID-2023-2277).

We presented categorical data using frequencies and percentages and continuous variables using median and interquartile ranges (IQR). We used the Kruskal–Wallis Rank test to compare continuous variables and Chi-square tests for categorical variables. Kaplan–Meier curves with log-rank tests were used to compare PVR groups for MACE outcomes and all-cause mortality within a year after the RHC date. Univariable and multivariable Cox regression analyses were done to generate hazard ratios (HR) with 95% confidence intervals (CI) for MACE outcomes. We adjusted the data for potential confounders associated with MACE outcomes, including demographics (age, sex, and body mass index), comorbidities (hypertension, diabetes mellitus, and hyperlipidemia), and surrogates of left ventricular function, PH severity, and kidney disease severity (PAWP, mPAP, right atrial pressure, and eGFR). A p-value of < 0.05 was considered statistically significant. The statistical analyses were done using Stata (StataCorp. 2023. Stata Statistical Software: Release 18; StataCorp LLC).

RESULTS

We included 649 patients in the analysis, including 5% ($n = 32$) with CKD stage 3b, 39% ($n = 250$) with CKD stage 4, and 57% ($n = 367$) with CKD stage 5. Eighty-three percent ($n = 536$) of patients had evidence of PH; 20% ($n = 129$) had isolated precapillary PH, 28% ($n = 182$) had isolated postcapillary PH, and 25% ($n = 164$) had combined PH. Nine percent ($n = 61$) of patients had elevated mPAP but were unclassifiable based on normal PVR and PAWP.

Furthermore, 52% ($n = 340$) of patients had normal PVR (≤ 2 WU), 21% ($n = 137$) had mildly elevated PVR (> 2 to ≤ 3 WU), and 27% ($n = 172$) had PVR > 3 WU. Their median mPAP was 26 mmHg (IQR 20–34), 35 mmHg (IQR 28–39), and 40 mmHg (IQR 33–47), respectively.

- *Baseline characteristics of mildly elevated PVR (> 2– ≤ 3 WU) group*

  Their median age was 67 years (IQR 57–74), they had a balanced gender distribution (49% females), and were predominantly African American (80%, $n = 110$). Fifty-six percent ($n = 77$) had CKD5, and 42% ($n = 58$) were on hemodialysis. Their most prevalent comorbidities were hypertension (96%, $n = 132$), hyperlipidemia (80%, $n = 110$), and diabetes mellitus (63%, $n = 86$). Further demographic characteristics and comorbidities of other groups are shown in Table 1.
- *Group comparisons*

  The median right atrial pressure, mPAP, and transpulmonary gradient were all directly proportional to PVR severity, whereas CO and cardiac index were

TABLE 1 Data stratified by PVR groups.

Variable	Group with PVR ≤ 2 WU $n = 340$	Group with PVR > 2–≤ 3 WU $n = 137$	Group with PVR > 3 WU $n = 172$	p-Value
Median age (IQR)	64 (55–72)	67 (57–74)	66 (59–75)	0.007
Female gender - n (%)	136 (40)	67 (49)	90 (52)	0.018
Race – n (%)				
African American	191 (56)	110 (80)	136 (79)	<0.0001
Non-African American	149 (44)	27 (20)	36 (21)	
Body mass index in kg/m^2 – median (IQR)	29 (25–35)	29 (25–38)	28 (23–34)	0.047
RHC data – median (IQR)				
RAP (mmHg)	9 (5–15)	10 (6–16)	12 (7–18)	<0.0001
mPAP (mmHg)	26 (20–34)	35 (28–39)	40 (33–47)	<0.0001
PAWP (mmHg)	16 (11–23)	17 (11–23)	16 (10–24)	0.891
TPG (mmHg)	9 (7–12)	16 (13–20)	22 (17–27)	<0.0001
PVR (Wood units)	1.2 (0.8–1.6)	2.5 (2.3–2.7)	4.1 (3.6–5.4)	<0.0001
Cardiac output (L/min)	8.1 (6.2–10.3)	6.4 (4.9–8)	4.8 (3.7–6)	<0.0001
Cardiac index (L/min/m^2)	4.1 (3.1–5.2)	3.2 (2.7–4.1)	2.5 (2–3.3)	<0.0001
Pulmonary hypertension (mPAP > 20 mmHg)	243 (71)	124 (91)	169 (98)	<0.0001
Kidney disease features - n (%)				
CKD 3b	14 (4)	11 (8)	7 (4)	0.193
CKD 4	134 (39)	49 (36)	67 (39)	0.753
CKD 5	192 (56)	77 (56)	98 (57)	0.990
Median eGFR in mL/min (IQR)	15 (9–23)	15 (9–22)	15 (10–23)	0.943
Median creatinine in mg/dl (IQR)	3.7 (2.6–6.4)	3.5 (2.5–5.7)	3.4 (2.7–5.4)	0.401
On dialysis	117 (34)	58 (42)	67 (39)	0.235
Hemodialysis	113 (33)	58 (42)	65 (38)	0.373
• Arteriovenous fistula	60 (18)	38 (28)	45 (26)	0.017
• Arteriovenous graft	3 (1)	1 (1)	4 (2)	0.400
• Permanent hemodialysis line	52 (15)	19 (14)	17 (10)	0.239
Peritoneal dialysis	4 (3)	None	2 (3)	0.486
Echocardiography features – n (%)				
Median left ventricular ejection fraction (%)	55 (35–60)	55 (30–55)	40 (25–55)	0.0001
Right ventricle strain	81 (24)	44 (32)	95 (55)	<0.0001
Right ventricle dilation	104 (31)	51 (37)	84 (49)	<0.0001
Right atrium dilation	103 (30)	62 (45)	91 (53)	<0.0001
IVC dilation	102 (30)	56 (41)	90 (52)	<0.0001
IVC noncollapsible	108 (32)	64 (47)	97 (56)	<0.0001
Comorbidities – n (%)				
Hypertension	297 (87)	132 (96)	168 (98)	<0.0001

(Continues)

TABLE 1 (Continued)

Variable	Group with PVR ≤ 2 WU $n = 340$	Group with PVR > 2–≤ 3 WU $n = 137$	Group with PVR > 3 WU $n = 172$	p-Value
Diabetes mellitus	201 (59)	86 (63)	106 (62)	0.719
Hyperlipidemia	244 (72)	110 (80)	140 (81)	0.024
Chronic lung disease	58 (17)	39 (28)	62 (36)	<0.0001
• Chronic obstructive pulmonary disease	36 (11)	30 (22)	40 (23)	<0.0001
• Asthma	22 (6)	5 (4)	18 (10)	0.063
• Interstitial lung disease	1 (0)	4 (3)	6 (3)	0.007
• Others	2 (1)	4 (3)	3 (2)	0.103
Hypoventilation syndrome	46 (14)	16 (12)	36 (21)	0.039
History of venous thromboembolism	38 (11)	14 (10)	18 (10)	0.943
Adverse clinical outcomes at 1-year follow-up – n (%)				
Composite MACE + all-cause mortality	137 (40)	67 (49)	94 (55)	0.006
MACE	75 (22)	44 (32)	59 (34)	0.005
Cardiovascular death	10 (3)	9 (6)	5 (3)	-
Heart failure exacerbation	53 (16)	30 (22)	48 (28)	-
Acute coronary syndrome	20 (6)	10 (7)	7 (4)	-
Stroke	3 (1)	2 (1)	1 (1)	-
Peripheral artery disease	2 (1)	1 (1)	3 (2)	-
All-cause mortality	78 (23)	37 (27)	48 (28)	0.401

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IVC, inferior vena cava; MACE, major adverse cardiovascular events; RAP, right atrial pressure; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RHC, right heart catheterization; TPG: transpulmonary gradient.

inversely proportional. The median PAWP was comparable between groups ($p = 0.891$). We observed multiple similarities in between PVR > 2–≤ 3 WU and PVR > 3 groups; both groups were older ($p = 0.007$), more likely females ($p = 0.018$), and more likely to have hypertension, chronic lung disease, and RV abnormalities on echocardiography, including RV strain and dilation ($p < 0.0001$).

- *Clinical outcomes*

  Forty-nine percent ($n = 67$) of patients with PVR > 2–≤ 3 WU had adverse composite outcomes within a year of follow-up; 32% ($n = 44$) had MACE outcomes, predominantly HF hospitalizations in 22% ($n = 30$), whereas 27% ($n = 37$) died within a year. Their median time from the RHC date to the first adverse clinical outcome was 71 days (IQR 20–170).

In comparison, we observed that MACE outcomes were more prevalent among patients with PVR > 2–≤ 3 WU and PVR > 3 ($p = 0.005$). Kaplan–Meier curves and log-rank test showed more MACE outcomes among patients with PVR > 2–≤ 3 WU and PVR > 3 ($p = 0.004$) (Figure 1a). A similar analysis showed no difference in all-cause mortality between PVR groups ($p = 0.477$) (Figure 1b).

On univariable Cox regression analysis, PVR > 2–≤ 3 was associated with MACE outcomes (HR 1.52, CI 1.05–2.22, $p = 0.026$). On multivariable Cox regression analysis, after adjusting for multiple covariables, PVR > 2-≤ 3 remained independently associated with MACE outcomes (HR 1.53, CI 1.00–2.34, $p = 0.047$) (Table 2).

DISCUSSION

Our study described a large, single-center, retrospective cohort analysis of patients with CKD 3b-5 who underwent invasive hemodynamic assessments. We observed that patients with advanced CKD and mildly elevated

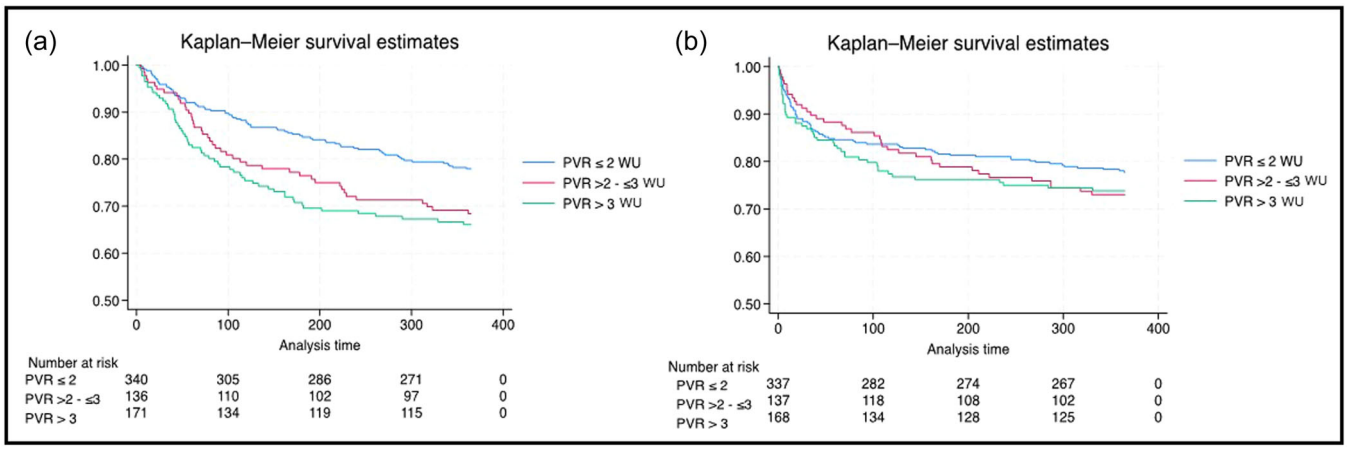

FIGURE 1 (a and b). Unadjusted Kaplan–Meier curves of (a) MACE outcomes within a year after RHC date. ($p = 0.004$) and (b) all-cause mortality within a year after RHC date. ($p = 0.401$). MACE, major cardiovascular events; PVR, pulmonary vascular resistance; RHC, right heart catheterization; WU, Wood units.

TABLE 2 Cox regression univariable and multivariable analysis of factors associated with MACE outcomes within a year of follow-up.

Variable	Hazards ratio	95% Confidence interval	*p*-Value
Unadjusted			
PVR < 2 WU	Ref		
PVR 2–3 WU	1.52	1.05–2.22	0.026
PVR > 3 WU	1.71	1.21–2.42	0.002
Adjusted*			
PVR < 2 WU	Ref		
PVR 2–3 WU	1.53	1.00–2.34	0.047
PVR > 3 WU	1.95	1.21–3.15	0.006

Abbreviations: eGFR, estimated glomerular filtration rate; MACE, major cardiovascular events; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; WU, Wood units.

*Covariables included demographics (age, sex, and body mass index), comorbidities (hypertension, diabetes mellitus, hyperlipidemia), PAWP, mPAP, RAP, and eGFR.

PVR (> 2– ≤ 3 WU) had an adjusted 53% greater risk of developing MACE outcomes within a year of follow-up when compared with patients with normal PVR.

The PVR cutoff to diagnose precapillary PH was lowered based on existing data showing a PVR of 2 WU to be the upper limit of normal in healthy individuals.[14] Furthermore, a recent study demonstrated an increased risk of all-cause mortality and HF events among patients with PVR ~ 2.2 WU compared with PVR of 1 WU.[2]

Early precapillary PH diagnosis has proven beneficial in certain groups of patients, such as in systemic sclerosis, in whom lowering the PVR threshold captures patients at risk of PH progression.[15] Similarly, among patients with chronic liver disease, early precapillary PH diagnosis has shown better response to pulmonary vasodilators as opposed to severe precapillary PH, an established contraindication for orthotopic liver transplantation.[16] To our knowledge, this is the first study to validate the clinical relevance of mildly elevated PVR among patients with advanced CKD.

In our study, the increased risk of MACE observed in the mildly elevated PVR group was primarily driven by HF hospitalizations, consistent with findings from prior CKD-PH studies.[4] Furthermore, in the present study, echocardiographic patterns of RV strain and RV dilation were more prevalent in the mildly elevated PVR group compared to the normal PVR group. Indeed, even a subtle increase in RV afterload at baseline can potentially compromise the RV function in CKD patients, among whom the RV commonly deals with heightened RV preload due to volume overload and neurohormonal dysregulation, likely precipitating RV failure and HF hospitalizations.[17]

To improve clinical outcomes in CKD patients with mildly elevated PVR, early management of risk factors associated with precapillary PH, such as chronic lung disease, obstructive sleep apnea, and secondary hyperparathyroidism (associated with metastatic calcifications in the pulmonary vessel walls), is a reasonable approach.[18,19] Likewise, maintaining a lower dry weight can optimize the RV function with better volume control.[20]

Furthermore, our findings highlight the importance of RHC in risk stratification and prognostication among CKD patients. While RHC is an invasive procedure, its ability to provide hemodynamic data, including PVR, helps in identifying patients at increased risk of adverse outcomes and may facilitate early intervention.

Despite the strengths of our study, including a large cohort of CKD patients undergoing RHC, our study had multiple limitations, including its retrospective and single-center design. The clinical indications for RHC were non-standardized potentially introducing selection bias to our study. Similarly, we were unable to standardize the timing of RHC and hemodialysis. Hence, we cannot rule out that a few patients were misclassified based on hemodynamic data. Future prospective studies with standardized protocols and long-term follow-up are warranted to validate our findings. Similarly, we used the available serum creatinine concentration, as detailed in the methods section, to calculate the baseline eGFR. Therefore, we acknowledge this could have led to misclassification of CKD staging. Most of our patients were African American, and we only included patients with CKD 3b–5, which may limit the generalizability of our results. While we cannot rule out the presence of residual confounders associated with MACE outcomes, we adjusted the data for pre-established CV risk factors, as explained in the methods section. As this project only included patients with advanced CKD, including 37% ($n = 242$) on dialysis, we did not collect data on urine albumin-creatinine ratio.

CONCLUSION

Among patients with advanced CKD referred for RHC, mildly elevated PVR was independently associated with major cardiovascular events within a year of follow-up. Early diagnosis of precapillary PH in CKD patients can potentially improve clinical outcomes.

AUTHOR CONTRIBUTIONS

Project conceptualization and design: Jose M. Martinez Manzano, Alex Prendergast, and Tara John. *Acquisition, analysis, or interpretation of the data*: Jose M. Martinez Manzano, Alex Prendergast, Tara John, Raul Leguizamon, Ian McLaren, Rasha Khan, Andrew Geller, Phuuwadith Wattanachayakul, John Malin, Simone A. Jarrett, Kevin Bryan Lo, Sadia Benzaquen, and Christian Witzke. *Manuscript writing—original draft*: Jose M. Martinez Manzano, Alex Prendergast, and Tara John. *Critical revision of the manuscript for intellectual content*: Jose M. Martinez Manzano, Alex Prendergast, Tara John, Raul Leguizamon, Ian McLaren, Rasha Khan, Andrew Geller, Phuuwadith Wattanachayakul, John Malin, Simone A. Jarrett, Kevin Bryan Lo, Sadia Benzaquen, and Christian Witzke. *Statistical analysis*: Jose M. Martinez Manzano.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

This research was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective study design, the requirement for written informed consent was waived.

ORCID

Jose M. Martinez Manzano https://orcid.org/0000-0002-5688-9692

REFERENCES

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M, Rosenkranz S, Schwerzmann M, Dinh-Xuan AT, Bush A, Abdelhamid M, Aboyans V, Arbustini E, Asteggiano R, Barberà JA, Beghetti M, Čelutkienė J, Cikes M, Condliffe R, de Man F, Falk V, Fauchier L, Gaine S, Galié N, Gin-Sing W, Granton J, Grünig E, Hassoun PM, Hellemons M, Jaarsma T, Kjellström B, Klok FA, Konradi A, Koskinas KC, Kotecha D, Lang I, Lewis BS, Linhart A, Lip GYH, Løchen ML, Mathioudakis AG, Mindham R, Moledina S, Naeije R, Nielsen JC, Olschewski H, Opitz I, Petersen SE, Prescott E, Rakisheva A, Reis A, Ristić AD, Roche N, Rodrigues R, Selton-Suty C, Souza R, Swift AJ, Touyz RM, Ulrich S, Wilkins MR, Wort SJ. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43(38):3618–731. https://doi.org/10.1093/eurheartj/ehac237
2. Maron BA, Brittain EL, Hess E, Waldo SW, Barón AE, Huang S, Goldstein RH, Assad T, Wertheim BM, Alba GA, Leopold JA, Olschewski H, Galiè N, Simonneau G, Kovacs G, Tedford RJ, Humbert M, Choudhary G. Pulmonary vascular resistance and clinical outcomes in patients with pulmonary hypertension: a retrospective cohort study. Lancet Respir Med. 2020;8(9):873–84. https://doi.org/10.1016/S2213-2600(20)30317-9

3. Kawar B, Ellam T, Jackson C, Kiely DG. Pulmonary hypertension in renal disease: epidemiology, potential mechanisms and implications. Am J Nephrol. 2013;37(3):281–90. https://doi.org/10.1159/000348804
4. Navaneethan SD, Roy J, Tao K, Brecklin CS, Chen J, Deo R, Flack JM, Ojo AO, Plappert TJ, Raj DS, Saydain G, Sondheimer JH, Sood R, Steigerwalt SP, Townsend RR, Dweik RA, Rahman M. Prevalence, predictors, and outcomes of pulmonary hypertension in CKD. J Am Soc Nephrol. 2016;27(3):877–86. https://journals.lww.com/jasn/fulltext/2016/03000/prevalence,_predictors,_and_outcomes_of_pulmonary.24.aspx
5. Edmonston DL, Parikh KS, Rajagopal S, Shaw LK, Abraham D, Grabner A, Sparks MA, Wolf M. Pulmonary hypertension subtypes and mortality in CKD. Am J Kidney Dis. 2020;75(5):713–24. https://doi.org/10.1053/j.ajkd.2019.08.027
6. CPT® overview and code approval | American Medical Association. Accessed March 24, 2024. https://www.ama-assn.org/practice-management/cpt/cpt-overview-and-code-approval
7. Stevens PE. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013;158(11):825–30. https://doi.org/10.7326/0003-4819-158-11-201306040-00007
8. Inker, LA, Eneanya, ND, Coresh J, Tighiouart H, Wang D, Sang Y, Crews DC, Doria A, Estrella MM, Froissart M, Grams ME, Greene T, Grubb A, Gudnason V, Gutiérrez OM, Kalil R, Karger AB, Mauer M, Navis G, Nelson RG, Poggio ED, Rodby R, Rossing P, Rule AD, Selvin E, Seegmiller JC, Shlipak MG, Torres VE, Yang W, Ballew SH, Couture SJ, Powe NR, Levey AS. New creatinine- and cystatin C–based equations to estimate GFR without race. N Engl J Med. 2021;385(19):1737–49. https://doi.org/10.1056/NEJMoa2102953
9. Saddawi-Konefka D, Charnin JE. Chapter 6 - Hemodynamic monitoring. In: Parsons PE, Wiener-Kronish JPBT-CCS, editors. Critical Care Secrets. Mosby; 2013. p. 39–46. https://doi.org/10.1016/B978-0-323-08500-7.00007-2
10. Maron BA. Revised definition of pulmonary hypertension and approach to management: a clinical primer. J Am Heart Assoc. 2023;12(8):e029024. https://doi.org/10.1161/JAHA.122.029024
11. Hicks KA, Mahaffey KW, Mehran R, Nissen SE, Wiviott SD, Dunn B, Solomon SD, Marler JR, Teerlink JR, Farb A, Morrow DA, Targum SL, Sila CA, Hai MTT, Jaff MR, Joffe HV, Cutlip DE, Desai AS, Lewis EF, Gibson CM, Landray MJ, Lincoff AM, White CJ, Brooks SS, Rosenfield K, Domanski MJ, Lansky AJ, McMurray JJV, Tcheng JE, Steinhubl SR, Burton P, Mauri L, O'Connor CM, Pfeffer MA, Hung HMJ, Stockbridge NL, Chaitman BR, Temple RJ. 2017 cardiovascular and stroke endpoint definitions for clinical trials. Circulation. 2018;137(9):961–72. https://doi.org/10.1161/CIRCULATIONAHA.117.033502
12. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr. 2010;23(7):685–713. https://doi.org/10.1016/j.echo.2010.05.010
13. Schneider M, Aschauer S, Mascherbauer J, Ran H, Binder C, Lang I, Goliasch G, Binder T. Echocardiographic assessment of right ventricular function: current clinical practice. Int J Cardiovasc Imaging. 2019;35(1):49–56. https://doi.org/10.1007/s10554-018-1428-8
14. Kovacs G, Olschewski A, Berghold A, Olschewski H. Pulmonary vascular resistances during exercise in normal subjects: a systematic review. Eur Respir J. 2012;39(2):319–28. https://doi.org/10.1183/09031936.00008611
15. Puigrenier S, Giovannelli J, Lamblin N, De Groote P, Fertin M, Bervar JF, Lamer A, Edmé JL, Balquet MH, Sobanski V, Launay D, Hachulla É, Sanges S. Mild pulmonary hemodynamic alterations in patients with systemic sclerosis: relevance of the new 2022 ESC/ERS definition of pulmonary hypertension and impact on mortality. Respir Res. 2022;23(1):284. https://doi.org/10.1186/s12931-022-02205-4
16. Jasso-Baltazar EA, Peña-Arellano GA, Aguirre-Valadez J, Ruiz I, Papacristofilou-Riebeling B, Jimenez JV, García-Carrera CJ, Rivera-López FE, Rodriguez-Andoney J, Lima-Lopez FC, Hernández-Oropeza JL, Díaz JAT, Kauffman-Ortega E, Ruiz-Manriquez J, Hernández-Reyes P, Zamudio-Bautista J, Rodriguez-Osorio CA, Pulido T, Muñoz-Martínez S, García-Juárez I. Portopulmonary hypertension: an updated review. Transplant Direct. 2023;9(8):e1517. https://journals.lww.com/transplantationdirect/fulltext/2023/08000/portopulmonary_hypertension__an_updated_review.8.aspx
17. Dini FL, Demmer RT, Simioniuc A, Morrone D, Donati F, Guarini G, Orsini E, Caravelli P, Marzilli M, Colombo PC. Right ventricular dysfunction is associated with chronic kidney disease and predicts survival in patients with chronic systolic heart failure. Eur J Heart Fail. 2012;14(3):287–94. https://doi.org/10.1093/eurjhf/hfr176
18. Abuyassin B, Sharma K, Ayas, NT, Laher I. Obstructive sleep apnea and kidney disease: a potential bidirectional relationship? J Clin Sleep Med. 2015;11(08):915–24. https://doi.org/10.5664/jcsm.4946
19. Amin M, Fawzy A, Hamid MA, Elhendy A. Pulmonary hypertension in patients with chronic renal failure. Chest. 2003;124(6):2093–7. https://doi.org/10.1378/chest.124.6.2093
20. Sinha AD, Agarwal R. Setting the dry weight and its cardiovascular implications. Sem Dialysis. 2017;30(6):481–8. https://doi.org/10.1111/sdi.12624

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