# Meta-analysis of the correlation between pulmonary hypertension and echocardiographic parameters in patients with chronic kidney disease

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## ABSTRACT

**Objective:** To investigate the correlation between pulmonary hypertension (PH) and echocardiographic parameters in patients with chronic kidney disease (CKD).

**Methods:** PubMed, Embase, Web of Science, Cochrane, VIP, CNKI, and Wanfang databases were systematically searched for articles published from inception to 19 May 2023. Study quality was estimated using the Quality Assessment of Case-Control Studies tool. Forest plots were drawn using R language software. The "metacor" function in the "meta" package was utilized for meta-analysis of the $r$-values and their standard errors. Heterogeneity and sensitivity analyses were carried out, with the main outcomes as $r$-value, $p$-value, and $I^2$ value.

**Results:** Eleven studies were included, with 1,809 CKD patients. The correlations between 12 echocardiographic parameters and PH were analyzed. Except for FS and LVEF which were negatively correlated with CKD-PH, the other 10 parameters were positively correlated with CKD-PH. Among them, LA was highly correlated with CKD-PH ($0.70 < r < 0.89$); LVDD, RA, RV, LVMI, and LVDS were moderately correlated with CKD-PH ($0.40 < r < 0.69$); while PA, IVS, LVPW, SV, FS, and LVEF were lowly correlated with CKD-PH ($0.20 < r < 0.39$). The synthesized estimates were stable against heterogeneity.

**Conclusion:** CKD-PH patients may have large cardiac chambers, thickened septal tissue on both sides of the chambers, reduced pulmonary artery flow rates, and decreased left ventricular function.

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## INTRODUCTION

By the year 2040, chronic kidney disease (CKD) is anticipated to be the fifth leading cause of death globally. In adults aged ≥20 years, the prevalence of CKD is expected to reach as high as 11.1% (*Kuro-o et al., 1997*). It is considered one of the major public health concerns worldwide due to its substantial impact on society, including high treatment costs, multiple complications, and poor prognosis (*Jager et al., 2019*). Cardiovascular complications are more prevalent and serious in CKD patients than in the general

population (*Thomas et al., 2017*). These complications are the leading factors contributing to mortality in patients with end-stage renal disease (ESRD) (*Walther et al., 2020*). CKD patients are most commonly afflicted by cardiovascular disease (CVD), which is identified as the most prevalent cause of morbidity and mortality in this population (*Heine et al., 2020*). Pulmonary hypertension (PH), a prevalent and serious complication in CKD patients, is known to affect up to 50% of ESRD patients (*Devasahayam et al., 2020*). The incidence of PH increases with disease progression, ranging from 9–39% in CKD patients at stage 5, which is 2–3 times higher than that in patients at stage 2–3. Additionally, the incidence of PH in patients undergoing hemodialysis is as high as 58.9% (*Bai, Cui & Liu, 2022*). In ESRD patients, PH has been established as an independent predictor of all-cause mortality and CVD (*Bai, Cui & Liu, 2022*). Moreover, the presence of PH is associated with an increased incidence of cardiovascular complications. A recent meta-analysis revealed that PH was associated with a higher risk of death and CVD in patients with CKD and ESRD (*Tang et al., 2018*). Nevertheless, the connection between PH and CKD remains unclear, and the presence of traditional risk factors such as hypertension, hyperlipidemia, and diabetes mellitus does not fully explain this association. Therefore, CKD-PH perhaps has a unique pathogenesis (*Page et al., 2021*).

According to the latest ERS/ESC classification in 2022, CKD-induced PH is classified as type V (PH due to unknown mechanisms) (*Humbert et al., 2022*). Currently, the gold standard for PH diagnosis is the right heart catheterization using floating catheters (*Meinel et al., 2020*). However, the extensive application of this diagnostic procedure in clinical practice is challenging due to its high cost, invasive nature, potential risks, and the requirement for technical support from experienced clinicians. Echocardiography is commonly considered the primary method for screening PH due to its affordability and non-invasive nature, despite its limitations in accurately estimating parameters (*Tiengo, Fadini & Avogaro, 2008*). PH is assessed based on tricuspid regurgitant velocity (TRV) and right atrial pressures (RAP) through echocardiography using the simplified Bernoulli's equation formula: $PH = 4 \times (TRV)^2 + RAP$ (*Poch & Mandel, 2021*).

The influence of CKD and PH on cardiac morphology is profound and has been extensively investigated. Nevertheless, the relationship between echocardiographic parameters and CKD-PH has not yet been summarized. Therefore, this article synthesizes the available evidence to unveil the relationship between PH and echocardiographic indices in CKD patients.

## METHODS

### Registration

We mistakenly filled in the "time period" for May 4th during registration, and the correct time should be May 19th. However, when we later discovered it, we were no longer able to modify it on PROSPERO. Please refer to the search time in the article for accuracy. Moreover, to check if there are some new eligible articles, we updated the literature search on 1 December 2023, and nothing new was found. This update was described in our

revised manuscript, too. This article followed the PRISMA statement (*Mills et al., 2015*). The review program and records were available online through PROSPERO (#CRD42023407420) (*Jin, Xie & Hao, 2023*).

## Article retrieval

PubMed, Embase, Web of Science, Cochrane, VIP, CNKI, and Wanfang databases were searched using the main search terms "chronic kidney disease" and "pulmonary hypertension". The search strategy was developed under the guidance of an experienced researcher (Wen Hao) and detailed in the Supplemental Materials. The searches were conducted firstly on 19 May 2023 and updated to 1 December 2023 before submission, with no language or other restrictions. References in the included articles were further manually searched.

## Article screening criteria

Article screening was carried out independently by two researchers (Jiahui Jin, Deqiong Xie) and any disagreements were resolved by a third experienced researcher (Wen Hao). After eliminating duplicates, the titles and abstracts of the remaining articles were reviewed to determine the initial article inclusion, and then the final inclusion was determined by reading the full text. Inclusion criteria were as follows: (1) patients with CKD; (2) receiving echocardiography and with extractable data; (3) conducting correlation analysis between PH and other echocardiographic parameters. The articles were excluded for the following reasons: (1) reviews, case reports, conference proceedings, animal and cellular experiments, and unrelated literature; (2) for different studies on the same study population, only the latest study was included, and others were excluded; (3) unclear diagnostic criteria for cases; (4) duplicate articles; and (5) unavailability of data for statistical analysis.

## Risk of bias assessment

The risk of bias was assessed independently by two researchers using the NIH Quality Assessment of Case-Control Studies (*National Heart, Lung, and Blood Institute, 2021*), and the results were combined by a third researcher. The tool consisted of 12 aspects: (1) Definition of study purpose; (2) definition of the population; (3) sample size justification; (4) consistency of included population; (5) strict implementation of standards for all participants; (6) clear definition of disease; (7) case and control groups were randomly selected; (8) with a control group; (9) researchers know exposure and occurrence risks in advance; (10) the factors associated with exposure/risk measurement of participants are strictly implemented; (11) researchers do not know the disease status of the participants; (12) accurate calculation of numerical variables. The assessment results of each aspect included YES, NO, and NR (including three options: CD: cannot determine, NA: not applicable, NR: not report), with YES scored as 1 point and NO and NR scored 0. Based on the total scores, 0–4 represented poor (low quality), 5–8 fair (medium quality), and 9–12 good (high quality).

## Data extraction

Data were extracted independently by two researchers according to the data table prepared in advance and merged by the third one. The extracted data included (1) basic study information: first author, year of publication, and region or country; (2) patient characteristics: sample size, age, gender, and creatinine value; and (3) outcome index: correlation between each echocardiographic parameter and PH.

## Statistical analyses

Forest plots were drawn using R language software 4.2.3 (*R Core Team, 2023*). The "metacor" function in the "meta" package was utilized for meta-analysis of the *r*-values and their standard errors. First, heterogeneity tests were performed. If $I^2 > 50\%$ and $p < 0.05$, the random-effect models (REM) were used, otherwise, the fixed-effect models (FEM) were used. Sensitivity analysis was performed for REM, including subgroup analysis and leave-one-out method The result was statistically different with $p < 0.05$, otherwise, it was not statistically different. If there were more than 10 studies, the publication bias was assessed using Egger's tests, with $p \geq 0.05$ indicating there was no significant publication bias, otherwise, there was significant publication bias. The results of the meta-analyses were presented using forest plots.

# RESULTS

## Literature retrieval results

In 3,327 articles were initially searched, of which 368 duplicates were excluded; 2,083 articles that did not meet the inclusion criteria were excluded after reading the abstracts; 73 animal studies, 116 conference proceedings, 424 registrations or protocols, 96 reviews, and 42 meta-analyses were also excluded. After reading the full text, articles on other related factors of PH such as inflammatory indicators, parathyroid hormone, creatinine, glomerular filtration rate, and other renal function indicators were excluded. Additionally, articles with unavailable full text and without correlation analyses were excluded. Articles that did not list the detailed correlation between echocardiographic parameters and PH in CKD patients were excluded due to unavailable data. Finally, 11 articles were included, with 1,809 patients. 12 parameters were evaluated in the echocardiography, including LA (left atrium), LVDD (left ventricular end-diastolic diameter), RA (right atrium), RV (right ventricle), PA (pulmonary artery diameter), IVS (interventricular septal thickness), LVPW (left ventricular posterior wall thickness), FS (left ventricular short axis systole rate), LVEF (left ventricular ejection fraction), SV (left ventricular per beat volume), LVMI (left ventricular mass index), and LVDS (left ventricular end-systolic diameter). The literature acquisition process is shown in Fig. 1.

## Risk of bias

The risk of bias was evaluated in 11 articles and was all rated as good, indicating that the overall risk of bias was low, possibly because researchers knew the disease status of the participants. None of the studies blinded the researchers to the disease status of the
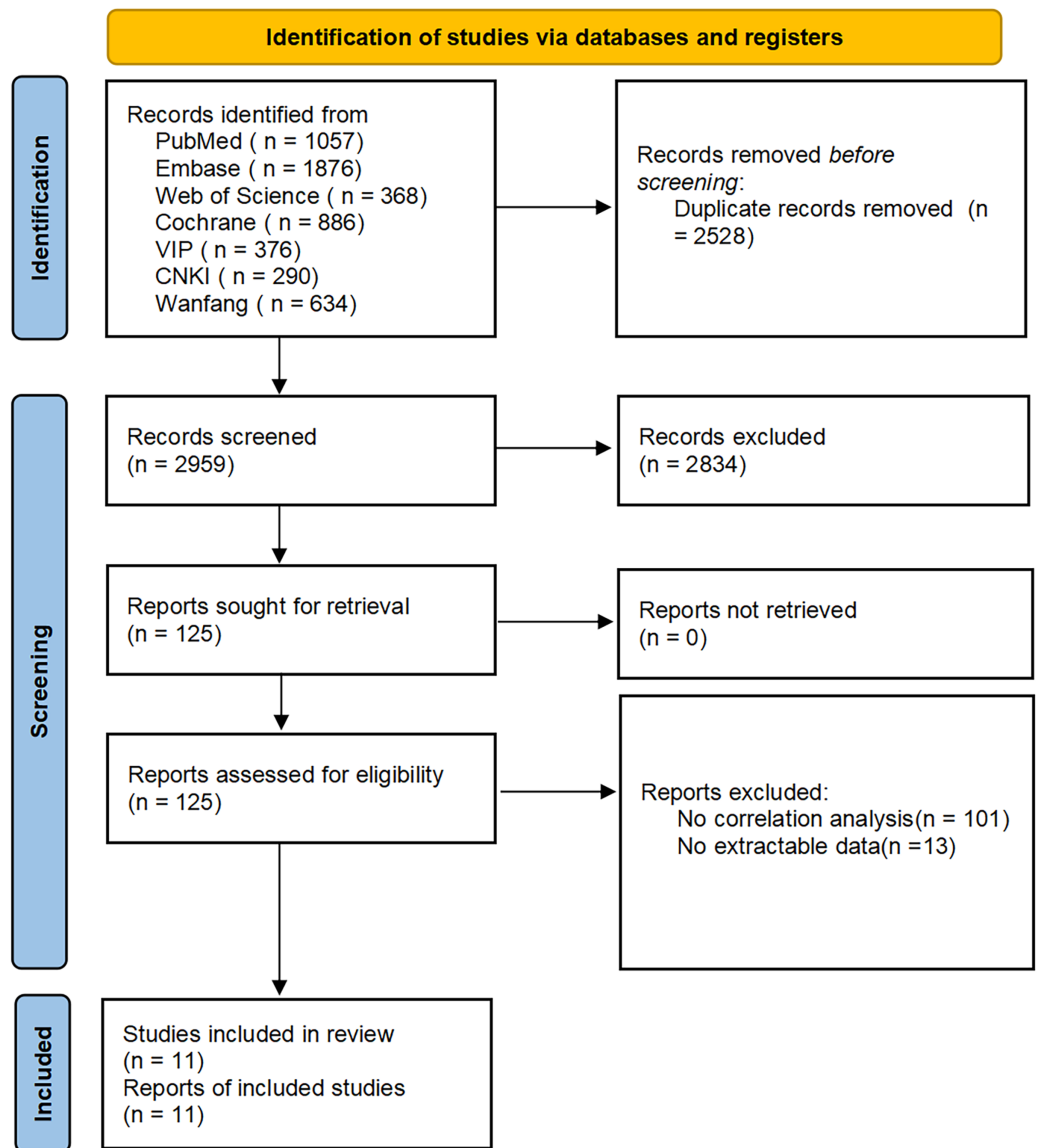
**Figure 1  Flowchart of article retrieval and screening.**

patients. All other aspects met the NIH-QAT requirements for a well-designed case-control study. Table S1 displays the details of the evaluation results.

## Characteristics of the included studies

The 11 studies (including 1,809 CKD patients, with both males and females) were all conducted in Asian countries and published between 2009 and 2022. The inclusion indicator for all participants was creatinine value >178 umol/L or glomerular filtration rate <60 ml/min. Information on the basic characteristics of the included studies is presented in Table 1. Among them, nine articles investigated the relationship between LA and PH in CKD patients, five articles on LVDD, four articles on RA, four articles on RV, three articles on PA, five articles on IVS, three articles on LVPW, four articles on FS, nine articles on

**Table 1 Basic feature information included in the study.**

| Study | Population | Age (mean, SD) | Gender (female, male) | Creatinine (mean, SD) | GFR (mean, SD) | LVEF (mean, SD) | sPAP (mean, SD) | TRV (mean, SD) | ΔP (mean, SD) | Quality rating |
|---|---|---|---|---|---|---|---|---|---|---|
| Ding et al. (2022) | 163 | 67.35, 10.42 | 86, 70 | 759.61, 303.42 | NR | 0.62, 0.09 | 27.46, 3.97 | 235.58, 22.72 | 22.54, 4.23 | Good |
| Yang & Bao (2014) | 128 | 53.59, 17.52 | 66, 62 | NR | 66.49, 32.60 | 0.64, 0.06 | 32.37, 8.55 | NR | NR | Good |
| He et al. (2015) | 136 | 52.00, 16.38 | 56, 80 | NR | NR | 0.63, 0.10 | NR | NR | NR | Good |
| Zhang et al. (2020) | 283 | 52.63, 14.28 | 107, 176 | 818.90, 295.18 | NR | 0.60, 0.10 | NR | 276.31, 53.67 | 31.24, 13.17 | Good |
| Yang & Bao (2012) | 397 | 52.17, 18.56 | 189, 208 | NR | 68.32, 32.47 | 0.63, 0.06 | 31.65, 7.56 | NR | NR | Good |
| Lv et al. (2019) | 94 | 60.65, 13.16 | 42, 52 | 266.56, 162.21 | 25.00, 12.08 | 0.59, 0.07 | 35.27, 13.26 | NR | NR | Good |
| Feng & Ren (2020) | 144 | 52.70, 14.60 | 61, 83 | 703.71, 78.49 | NR | 0.65, 0.08 | 38.72, 12.41 | NR | NR | Good |
| Wang et al. (2014a) | 76 | 45.90, 11.90 | 35, 41 | NR | NR | 0.61, 0.12 | NR | 651.32, 185.83 | NR | Good |
| Wang et al. (2014b) | 136 | NR | NR | NR | NR | 0.63, 0.10 | NR | NR | NR | Good |
| Shen et al. (2021) | 219 | 60.62, 14.66 | 99, 120 | 663.25, 220.63 | NR | 0.60, 0.10 | 38.27, 11.94 | NR | NR | Good |
| Gao et al. (2021) | 33 | 46.00, 14.61 | 14, 19 | 859.06, 260.85 | NR | 0.64, 0.12 | 24.76, 20.63 | NR | NR | Good |

**Note:**
mean, average value; SD, standard deviation; NR, not mentioned; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; sPAP, pulmonary artery pressure; TRV, tricuspid regurgitation velocity; ΔP, tricuspid valve pressure difference.

LVEF, two articles on SV, four articles on LVMI, and three articles on LVDS. The number of articles involved in each echocardiographic parameter is shown in Fig. 2.

## Results of statistical analysis

In the 11 articles, 12 parameters associated with PH in CKD patients were involved, including three categories: left heart parameters (LA, LVDD, LVPW, FS, LVEF, SV, LVMI, and LVDS), right heart parameters (RA and RV), and other parameters (IVS and PA). Except for FS and LVEF, which were negatively correlated with PH in CKD patients, the other 10 parameters were positively correlated. The parameters that were highly correlated with PH in CKD patients were LA, those moderately correlated with PH in CKD patients were LVDD, RA, RV, LVMI, and LVDS, and those lowly correlated with PH in CKD patients were PA, IVS, LVPW, SV, FS, and LVEF. Detailed information on each of the 12
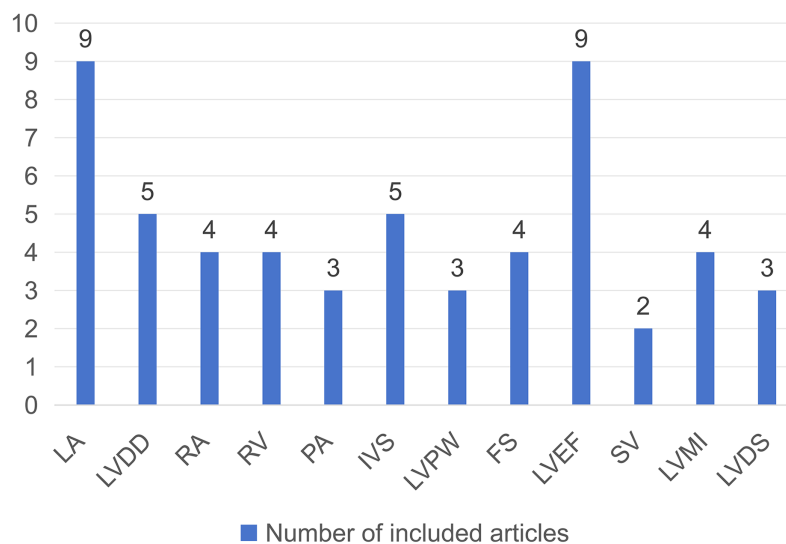
**Figure 2  Bar chart incorporating echocardiographic parameters and number of related articles.**

parameters is provided in Table 2. The forest plots of correlation analysis are displayed in the Supplemental Materials.

Among left heart parameters, LA was highly correlated with PH [9 studies, 1,496 patients; $I^2 = 98\%$, $p < 0.01$; REM; $r$ (95% CI) = 0.74 [0.47–0.88], $p < 0.01$]. LVDD [five studies, 862 patients; $I^2 = 76\%$, $p < 0.01$; REM; $r$ (95% CI) = 0.45 [0.34–0.55], $p < 0.01$], LVMI [four studies, 846 patients; $I^2 = 93\%$, $p < 0.01$; REM; $r$ (95% CI) = 0.45 [0.18–0.66], $p < 0.01$], and LVDS [three studies, 263 patients; $I^2 = 53\%$, $p < 0.01$; FEM; $r$ (95% CI) = 0.40 [0.30–0.50], $p = 0.12$] were moderately correlated with PH. LVPW [3 studies, 843 patients; $I^2 = 72\%$, $p < 0.01$; REM; $r$ (95% CI) = 0.24 [0.11–0.36], $p = 0.03$], FS [four studies, 676 patients; $I^2 = 39\%$, $p < 0.01$; FEM; $r$ (95% CI) = −0.30 [−0.36 to −0.23], $p = 0.18$], LVEF [nine studies, 1,284 patients, $I^2 = 64\%$, $p < 0.01$; REM; $r$ (95% CI) = −0.31[−0.39 to −0.22], $p = 0.05$], and SV [two studies, 446 patients; $I^2 = 29\%$, $p < 0.01$; FEM; $r$ (95% CI) = 0.20 [0.11–0.29], $p = 0.23$] were lowly associated with PH.

Among right heart parameters, RA [four studies, 718 patients; $I^2 = 40\%$, $p < 0.01$; FEM; $r$ (95% CI) = 0.51 [0.45–0.56], $p = 0.17$] and RV [4 studies, 718 patients; $I^2 = 87\%$, $p < 0.01$; REM; $r$ (95% CI) = 0.65 [0.51–0.76], $p < 0.01$] were moderately associated with PH.

As for other parameters, IVS [five studies, 1115 patients; $I^2 = 97\%$, $p = 0.03$; REM; $r$ (95% CI) = 0.33 [0.04–0.56], $p < 0.01$] and PA parameters [three studies, 582 patients; $I^2 = 0\%$, $p < 0.01$; FEM; $r$ (95% CI) = 0.36 [0.29–0.43], $p = 0.39$] were lowly associated with PH.

Due to significant heterogeneity ($I^2 > 50\%$, $p < 0.05$) in the results of LA, LVDD, RV, IVS, LVPW, LVMI, and LVEF, sensitivity analyses were performed using the leave-one-out method, which revealed that all synthesized estimates were stable against heterogeneity. The forest plot of sensitivity analysis is exhibited in the Supplemental Materials.

Finally, funnel plots were made for each of the 12 parameters associated with PH in CKD patients in the 11 included articles. The results of these funnel plots indicated no

**Table 2 Statistical analysis of echocardiographic parameters related to PH in CKD patients.**

| Group | Index | Sample size | Heterogeneity | Pooled estimation | Sensitivity analysis | Forest plot |
|---|---|---|---|---|---|---|
| Left heart | LA | nine studies, 1,496 patients | $I^2 = 98\%$, $p < 0.01$ | $r$ (95% CI) = 0.74 [0.47–0.88], $p < 0.01$ | Stable | Figs. S1, S13 |
| | LVDD | five studies, 862 patients | $I^2 = 76\%$, $p < 0.01$ | $r$ (95% CI) = 0.45 [0.34–0.55], $p < 0.01$ | Stable | Figs. S2, S14 |
| | LVPW | three studies, 843 patients | $I^2 = 72\%$, $p < 0.01$ | $r$ (95% CI) = 0.24 [0.16–0.36], $p = 0.03$ | Stable | Figs. S3, S17 |
| | FS | four studies, 676 patients | $I^2 = 39\%$, $p < 0.01$ | $r$ (95% CI) = −0.30 [−0.36 to −0.23], $p = 0.18$ | – | Fig. S4 |
| | LVEF | nine studies, 1,284 patients | $I^2 = 64\%$, $p < 0.01$ | $r$ (95% CI) = −0.31 [−0.39 to −0.22], $p = 0.05$ | Stable | Figs. S5, S19 |
| | SV | two studies, 446 patients | $I^2 = 29\%$, $p < 0.01$ | $r$ (95% CI) = 0.20 [0.11–0.29], $p = 0.23$ | – | Fig. S6 |
| | LVMI | four studies, 846 patients | $I^2 = 93\%$, $p < 0.01$ | $r$ (95% CI) = 0.45 [0.18–0.66], $p < 0.01$ | Stable | Figs. S7, S18 |
| | LVDS | three studies, 263 patients | $I^2 = 53\%$, $p < 0.01$ | $r$ (95% CI) = 0.40 [0.30–0.50], $p = 0.12$ | – | Fig. S8 |
| Right heart | RA | four studies, 718 patients | $I^2 = 40\%$, $p < 0.01$ | $r$ (95% CI) = 0.51 [0.45–0.56], $p = 0.17$ | – | Fig. S9 |
| | RV | four studies, 718 patients | $I^2 = 87\%$, $p < 0.01$ | $r$ (95% CI) = 0.65 [0.51–0.76], $p < 0.01$ | Stable | Figs. S10, S15 |
| Other | IVS | five studies, 1,115 patients | $I^2 = 97\%$, $p = 0.03$ | $r$ (95% CI) = 0.33 [0.04–0.56], $p < 0.01$ | Stable | Figs. S11, S16 |
| | PA | three studies, 582 patients | $I^2 = 0\%$, $p < 0.01$ | $r$ (95% CI) = 0.36 [0.29–0.43], $p = 0.39$ | – | Fig. S12 |

Note:
LA, left atrium; LVDD, left ventricular end diastolic diameter; LVPW, thickness of the posterior wall of the left ventricle; FS, left ventricular short axis systolic rate; LVEF, left ventricular ejection fraction; SV, left ventricular stroke volume; LVMI, left ventricular mass index; LVDS, left ventricular end systolic diameter; RA, right atrium; RV, right ventricle; IVS, thickness of the interventricular septum; PA, inner diameter of the pulmonary artery.

significant publication bias. However, because the number of relevant studies included for each parameter was less than 10, the results of Egger's test were unreliable under such conditions. Therefore, we did not perform the test. The funnel plots of the correlation analyses are shown in the attachment.

## DISCUSSION

This study discovered that CKD-PH may be associated with large cardiac chambers, thickened septal tissue on both sides of the chambers, reduced pulmonary artery flow rates, and LV dysfunction. CKD-PH is characterized by a complex interplay of factors that affect the heart. The unique therapeutic approaches for CKD, comorbidities, and shared factors with PH collectively affect the cardiac structure and functions, leading to the distinct echocardiographic manifestations of CKD-PH. Taken together, the enlarged left heart cavity may be attributed to increased blood pressure, fluid retention, and arteriovenous fistula (AVF). The enlarged right heart cavity is an intrinsic feature of PH, and it may share certain mechanisms with the changes in the left heart cavity. The thickened interventricular septum may be related to the increase in blood pressure.

CKD patients may have abnormalities of some substances including fibroblast growth factor23 (FGF23)-klotho protein (KLOTHO), asymmetric dimethylarginine (ADMA), and inflammatory factors due to renal failure. These abnormalities profoundly affect the circulatory system, leading to cardiac remodeling and PH. Abnormalities in the FGF23-KLOTHO axis, characterized by increased FGF23 and diminished KLOTHO levels, can lead to LV hypertrophy and increased mass (*National Heart, Lung, and Blood Institute, 2021*). Animal studies similarly substantiated the aforementioned results and confirmed the presence of cardiotoxicity (*Faul et al., 2011*). Both the FGF23-KLOTHO axis and parathyroid hormone are strongly associated with PH severity, but their roles in CKD-PH

are not fully understood (*Zhang et al., 2018*). Plasma ADMA impairs the vasoprotective function of high-density lipoprotein, thereby enhancing the risk of coronary artery disease (*Zewinger et al., 2017*). Moreover, ADMA acts as an inhibitor of endogenous nitric oxide synthesis and is synthesized in significant amounts in CKD, resulting in its accumulation in the lungs (*Devasahayam et al., 2020*). ADMA has been suggested to be potentially correlated with CKD-PH (*Bolignano et al., 2013*). Levels of several inflammatory biomarkers such as interleukin-6 (IL-6) and tumor necrosis factor (TNF) are elevated in the context of CKD (*Gilligan & Raphael, 2017*; *Yu et al., 2009*). CKD-induced inflammation can initiate endothelial dysfunction, which disrupts the balance of vasomotor function and leads to abnormal pulmonary vasoconstriction and fibrosis (*Edmonston & Sparks, 2020*). Chronic inflammation is a key player in the pathogenesis of various cardiac structural changes, such as cardiomyopathy (*Kakraba et al., 2023*). It is implicated in the inflammatory state due to other diseases and in the microinflammatory state in CKD, thus exacerbating cardiac remodeling and promoting PH progression (*von Siebenthal et al., 2016*). Since the renal excretory function is gradually decompensated, CKD patients suffer from abnormalities in the internal environment, such as disturbances in calcium and phosphorus metabolism. The microinflammatory state of the body can lead to gradual myocardial fibrosis and even myocardial hypertrophy or other structural changes (*Bonacina et al., 2016*; *Doni et al., 2015*). The large accumulation of uremic toxins in the internal environment, including large molecules such as parathyroid hormone, and medium molecules such as peptides produced due to cellular metabolism disorders, acts on the heart and lead to cardiac damage (*Valkenburg, Glorieux & Vanholder, 2021*). Accumulation of small molecule substances guanidines and amines can inhibit platelet function and lead to pulmonary edema, increasing the burden on the cardiovascular system (*Evans, Reddan & Szczech, 2004*). These changes, in turn, contribute to PH.

The complications of fluid retention, obstructive sleep apnoea/hypopnoea syndrome (OSAHS), anemia, and hyperparathyroidism in CKD patients lead to both cardiac structural changes and PH. Echocardiography has revealed that patients with high heart disease frequently display different levels of thickening of the interventricular septum (*Li & Jiamarideng, 2014*). CKD patients commonly experience fluid retention and subsequent hypertension. Consequently, it is reasonable that CKD-PH patients exhibit similar manifestations in the septum as those observed in individuals with high heart disease (*He & MacGregor, 2011*). On the other hand, mechanisms such as uremic toxin-induced neuropathy or myopathy, altered chemosensitivity, and hypervolemia in CKD or ESRD increase the risk of developing sleep apnoea (*Lin, Lurie & Lyons, 2020*). As a result, OSAHS is common in patients with CKD and ESRD (*Nicholl et al., 2012*), potentially leading to recurrent hypoxemia and an imbalance of the sympathovagal system. Hypoxemia aggravates PH by directly promoting pulmonary vasoconstriction (*Edmonston & Sparks, 2020*) and causes concentric LV hypertrophy (*Zoccali et al., 2001*). In addition, CKD can give rise to anemia, and prolonged anemia leads to a sustained increase in cardiac output, which in turn results in cardiac remodeling (*Eckardt, 2005*) and hypoxia. Similar to OSAHS-induced PH, anemia can aggravate PH by indirectly inducing pulmonary vasoconstriction (*Budhiraja, Tuder & Hassoun, 2004*). Uremic toxins can trigger chronic

hemolysis, release free hemoglobin, and promote PH by scavenging nitric oxide (*Billings et al., 2011*). Finally, hyperparathyroidism is frequently complicated with hypercalcemia and coronary vascular calcification, thus stimulating the development of coronary artery disease, myocardial hypertrophy, and fibrosis (*Amann et al., 2003*; *Ketteler et al., 2011*). Autopsies of ESRD patients have indicated that vascular calcification is present in 40–80% of those patients (*Devasahayam et al., 2020*). The improvement in pulmonary vascular compliance and vascular calcification after removal of the parathyroid glands suggests that hyperparathyroidism may be a potential etiological factor for CKD-PH (*Sise, Courtwright & Channick, 2013*).

The therapeutic measures for CKD also bring about structural changes in the cardiovascular system and the development of PH. In CKD patients undergoing long-term hemodialysis, the creation of an AVF is a common procedure. After that, these patients show a trend towards LV dilatation and an increase in LV mass, which is positively correlated with systemic inflammation (*Sahinoz et al., 2020*). Specifically, they present with increases in the LV internal diameter and LV end-diastolic and end-systolic volumes, as well as cardiac dysfunction (*Meinel et al., 2020*). The creation of an AVF accelerates the development of left heart failure and PH, which is more likely to occur in patients complicated with heart disease or large aneurysmal AVF (*Nakhoul et al., 2005*). The venous shower of microbubbles from the tubing or dialyzer is unavoidable during dialysis in CKD patients. These microbubbles can obstruct the microvascular system of pulmonary arteries, potentially leading to inflammation, complement activation, ischemia, and sclerosis, thus exacerbating PH (*Kosmadakis et al., 2013*). A study compared PH before and after dialysis with cellulose membranes *vs*. biocompatible high-flux polysulfone dialyzers and showed a greater reduction in PH treated with biocompatible high-flux dialyzers (*Kawar et al., 2013*). PH was not significantly altered post-dialysis using cellulose acetate membrane, whereas synthetic and modified cellulose membranes attenuated but did not eliminate it. High-flux polysulfone filters showed a pronounced reduction in post-dialysis PH compared to cellulose acetate filters. Hence, the correlation between PH and dialysis membranes is also crucial (*Kiykim et al., 2010*).

In summary, factors such as substance abnormalities, comorbidities, and treatment methods of CKD are implicated in the pathogenesis or progression of PH, resulting in changes in cardiac structure and function (*Yu et al., 2017*). Cardiac insufficiency due to myocardial hypertrophy and fibrosis in turn contributes to the onset and worsening of PH (*O'Byrne et al., 2015*). CKD-PH and cardiac remodeling share common pathogenic factors and are causative of each other. Therefore, echocardiography helps to provide better clinical screening for PH in CKD patients and to monitor and manage CKD patients more comprehensively in the future. Currently, there are fewer studies on the progression of cardiac structural changes and PH in CKD patients. More studies are needed to further elucidate the specific mechanisms underlying the correlation between CKD-PH and echocardiographic parameters. In this study, we systematically integrated previous findings on the correlation between echocardiographic parameters and PH and revealed the presence of significant cardiac structural and functional alterations in CKD-PH patients, including an increase in the total volume of the cardiac chambers, thickening of

the interventricular septum and interatrial septal tissues, and LV dysfunction. However, the sample of included studies is small and there are no reports of echocardiographic databases for CKD-PH patients. Currently, several representative disease-specific echocardiographic databases have been established in the field of cardiology. Given the high incidence of CKD-PH and its widespread effects on the heart, we believe that there is an urgent need to build a set of echocardiographic databases specifically for CKD-PH patients. This will enable clinicians and researchers to explore the pathophysiological mechanisms and clinical diagnosis and treatment strategies in a more in-depth and comprehensive manner, thus realizing the close connection and two-way promotion between basic research and clinical application. Based on this, we advocate that future research should focus on the establishment and utilization of echocardiographic databases of CKD-PH patients, to attract more attention and practical application. Such databases will greatly enrich our data on large samples of CKD-PH patients and thus enhance the reliability and validity of research results. Our findings could also provide practical evidence and deepen concepts in such cutting-edge areas as 'translational clinical implications' or 'therapeutic echocardiographic integration'.

This study has some limitations: 24 studies were finally included, but the correlation between various echocardiographic parameters and CKD-PH was documented in only 11 studies. The number of included study samples is limited, and the echocardiographic database for CKD-PH patients has not been reported in the literature. Few of the existing articles have used either 'multivariable logistic regression analysis' or 'propensity score matching'. It is expected that future studies will make greater use of these two methods to ensure that intergroup comparability and assessed relationships are not affected by other confounding factors (*Ding et al., 2022*; *Feng & Ren, 2020*; *Gao et al., 2021*; *He et al., 2015*; *Lv et al., 2019*; *Shen et al., 2021*; *Wang et al., 2014a*, *2014b*; *Yang & Bao, 2012*; *Yang & Bao, 2014*; *Zhang et al., 2020*) (all the included articles are shown in 44–54 in the references).

## CONCLUSION

Statistical results unveil that CKD-PH is associated with left atrial enlargement, right atrial chamber enlargement, increases in LVDD and LVDS, and increased cardiac work. In CKD, increased fluid and pressure loads in the circulation may be the main reason for PH. Ultimately, the cardiac workload exacerbates decompensation until heart failure. Therefore, reducing fluid loads and increasing cardiac compensation of CKD patients may be the key therapeutic and preventive methods for reducing PH incidence. The present study incorporated many echocardiographic parameters and a substantial number of patients, so the conclusions were relatively reliable. Additional clinical studies with more patients are still needed to further support and refine the conclusions.

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## Competing Interests

The authors declare that there are no conflicts of interest.

## Author Contributions

- Jiahui Jin conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Wen Hao conceived and designed the experiments, performed the experiments, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Deqiong Xie conceived and designed the experiments, performed the experiments, authored or reviewed drafts of the article, and approved the final draft.

## Data Availability

This is a systematic review/meta-analysis.

## Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.17245#supplemental-information.

## REFERENCES

**Amann K, Törnig J, Kugel B, Gross M-L, Tyralla K, El-Shakmak A, Szabo A, Ritz E. 2003.** Hyperphosphatemia aggravates cardiac fibrosis and microvascular disease in experimental uremia. *Kidney International* **63(4)**:1296–1301 DOI 10.1046/j.1523-1755.2003.00864.x.

**Bai B, Cui J, Liu H. 2022.** Mechanism and influencing factors of pulmonary hypertension in end-stage renal disease patients. *International Journal of Transplantation and Hemopurification* **20(2)**:10–12 DOI 10.3760/cma.j.cn115399-20220225-02003.

**Billings FT IV, Ball SK, Roberts LJ II, Pretorius M. 2011.** Postoperative acute kidney injury is associated with hemoglobinemia and an enhanced oxidative stress response. *Free Radical Biology and Medicine* **50(11)**:1480–1487 DOI 10.1016/j.freeradbiomed.2011.02.011.

**Bolignano D, Rastelli S, Agarwal R, Fliser D, Massy Z, Ortiz A, Wiecek A, Martinez-Castelao A, Covic A, Goldsmith D, Suleymanlar G, Lindholm B, Parati G, Sicari R, Gargani L, Mallamaci F, London G, Zoccali C. 2013.** Pulmonary hypertension in CKD. *American Journal of Kidney Diseases* **61(4)**:612–622 DOI 10.1053/j.ajkd.2012.07.029.

**Bonacina F, Barbieri SS, Cutuli L, Amadio P, Doni A, Sironi M, Tartari S, Mantovani A, Bottazzi B, Garlanda C, Tremoli E, Catapano AL, Norata GD. 2016.** Vascular pentraxin 3 controls arterial thrombosis by targeting collagen and fibrinogen induced platelets aggregation. *Biochimica Et Biophysica Acta* **1862(6)**:1182–1190 DOI 10.1016/j.bbadis.2016.03.007.

**Budhiraja R, Tuder RM, Hassoun PM. 2004.** Endothelial dysfunction in pulmonary hypertension. *Circulation* **109(2)**:159–165 DOI 10.1161/01.CIR.0000102381.57477.50.

**Devasahayam J, Oliver T, Joseph V, Nambiar S, Gunasekaran K. 2020.** Pulmonary hypertension in end-stage renal disease. *Respiratory Medicine* **164(Suppl 1)**:105905 DOI 10.1016/j.rmed.2020.105905.

**Ding XH, Chai X, Zheng J, Chang H, Zheng W, Bian SZ, Ye P. 2022.** Baseline ratio of soluble Fas/FasL predicts onset of pulmonary hypertension in elder patients undergoing maintenance

hemodialysis: a prospective cohort study. *Frontiers in Physiology* **13**:847172
DOI 10.3389/fphys.2022.847172.

**Doni A, Musso T, Morone D, Bastone A, Zambelli V, Sironi M, Castagnoli C, Cambieri I, Stravalaci M, Pasqualini F, Laface I, Valentino S, Tartari S, Ponzetta A, Maina V, Barbieri SS, Tremoli E, Catapano AL, Norata GD, Bottazzi B, Garlanda C, Mantovani A. 2015.** An acidic microenvironment sets the humoral pattern recognition molecule PTX3 in a tissue repair mode. *Journal of Experimental Medicine* **212(6)**:905–925
DOI 10.1084/jem.20141268.

**Eckardt KU. 2005.** Managing a fateful alliance: anaemia and cardiovascular outcomes. *Nephrology Dialysis Transplantation* **20(Suppl 6)**:vi16–vi20 DOI 10.1093/ndt/gfh1097.

**Edmonston DL, Sparks MA. 2020.** Therapeutic options for chronic kidney disease-associated pulmonary hypertension. *Current Opinion in Nephrology & Hypertension* **29(5)**:497–507
DOI 10.1097/MNH.0000000000000624.

**Evans K, Reddan DN, Szczech LA. 2004.** Nondialytic management of hyperkalemia and pulmonary edema among end-stage renal disease patients: an evaluation of the evidence. *Seminars in Dialysis* **17(1)**:22–29 DOI 10.1111/j.1525-139X.2004.17110.x.

**Faul C, Amaral AP, Oskouei B, Hu M-C, Sloan A, Isakova T, Gutiérrez OM, Aguillon-Prada R, Lincoln J, Hare JM, Mundel P, Morales A, Scialla J, Fischer M, Soliman EZ, Chen J, Go AS, Rosas SE, Nessel L, Townsend RR, Feldman HI, St. John Sutton M, Ojo A, Gadegbeku C, Di Marco GS, Reuter S, Kentrup D, Tiemann K, Brand M, Hill JA, Moe OW, Kuro-o M, Kusek JW, Keane MG, Wolf M. 2011.** FGF23 induces left ventricular hypertrophy. *Journal of Clinical Investigation* **121(11)**:4393–4408 DOI 10.1172/JCI46122.

**Feng S, Ren W. 2020.** A study on the correlation between neutrophil/lymphocyte ratio and pulmonary arterial hypertension in stage 5 non dialysis patients with chronic kidney disease. *Journal of Clinical Nephrology* **20(10)**:807–812.

**Gao C, Zhang R, Yang S, Chen X, Yang S. 2021.** Clinical characteristics and risk factors analysis of pulmonary hypertension in single center maintenance hemodialysis patients in Yunnan Province. *Medicine and Pharmacy of Yunnan* **42(4)**:317–321.

**Gilligan S, Raphael KL. 2017.** Hyperkalemia and Hypokalemia in CKD: prevalence, risk factors, and clinical outcomes. *Advances in Chronic Kidney Disease* **24(5)**:315–318
DOI 10.1053/j.ackd.2017.06.004.

**He FJ, MacGregor GA. 2011.** Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *The Lancet* **378(9789)**:380–382 DOI 10.1016/S0140-6736(11)61174-4.

**He Y, Wang Y, Luo X, Ke J, Du Y, Li M. 2015.** Risk factors for pulmonary hypertension in maintenance hemodialysis patients: a cross-sectional study. *International Urology and Nephrology* **47(11)**:1889–1897 DOI 10.1007/s11255-015-1119-5.

**Heine GH, Eller K, Stadler JT, Rogacev KS, Marsche G. 2020.** Lipid-modifying therapy in chronic kidney disease: pathophysiological and clinical considerations. *Pharmacology & Therapeutics* **207(47)**:107459 DOI 10.1016/j.pharmthera.2019.107459.

**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, 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. *European Heart Journal* **43(38)**:3618–3731 DOI 10.1093/eurheartj/ehac237.

Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. 2019. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Nephrology Dialysis Transplantation* **34(11)**:1803–1805 DOI 10.1093/ndt/gfz174.

Jin J, Xie D, Hao W. 2023. The correlation between echocardiography parameters and pulmonary arterial systolic pressure: a systematic review and meta-analysis. *Available at https://www.crd. york.ac.uk/prospero/display_record.php?ID=CRD42023407420.*

Kakraba S, Ayyadevara S, Mainali N, Balasubramaniam M, Bowroju S, Penthala NR, Atluri R, Barger SW, Griffin ST, Crooks PA, Shmookler Reis RJ. 2023. Thiadiazolidinone (TDZD) analogs inhibit aggregation-mediated pathology in diverse neurodegeneration models, and extend c. elegans life- and healthspan. *Pharmaceuticals* **16(10)**:1498 DOI 10.3390/ph16101498.

Kawar B, Ellam T, Jackson C, Kiely DG. 2013. Pulmonary hypertension in renal disease: epidemiology, potential mechanisms and implications. *American Journal of Nephrology* **37(3)**:281–290 DOI 10.1159/000348804.

Ketteler M, Rothe H, Krüger T, Biggar PH, Schlieper G. 2011. Mechanisms and treatment of extraosseous calcification in chronic kidney disease. *Nature Reviews Nephrology* **7(9)**:509–516 DOI 10.1038/nrneph.2011.91.

Kiykim AA, Horoz M, Ozcan T, Yildiz I, Sari S, Genctoy G. 2010. Pulmonary hypertension in hemodialysis patients without arteriovenous fistula: the effect of dialyzer composition. *Renal Failure* **32(10)**:1148–1152 DOI 10.3109/0886022X.2010.516854.

Kosmadakis G, Aguilera D, Carceles O, Da Costa Correia E, Boletis I. 2013. Pulmonary hypertension in dialysis patients. *Renal Failure* **35(4)**:514–520 DOI 10.3109/0886022X.2013.766559.

Kuro-o M, Matsumura Y, Aizawa H, Kawaguchi H, Suga T, Utsugi T, Ohyama Y, Kurabayashi M, Kaname T, Kume E, Iwasaki H, Iida A, Shiraki-Iida T, Nishikawa S, Nagai R, Nabeshima Y-I. 1997. Mutation of the mouse klotho gene leads to a syndrome resembling ageing. *Nature* **390(6655)**:45–51 DOI 10.1038/36285.

Li T, Jiamarideng. 2014. Clinical analysis of ventricular septal thickening in patients with high heart disease using Doppler ultrasound. *Chinese Journal of Trauma and Disability Medicine* **22(09)**:201 DOI 10.13214/j.cnki.cjotadm.2014.09.170.

Lin CH, Lurie RC, Lyons OD. 2020. Sleep apnea and chronic kidney disease: a state-of-the-art review. *Chest* **157(3)**:673–685 DOI 10.1016/j.chest.2019.09.004.

Lv L, Sun H, Huang H, Huang P. 2019. Changes in left ventricular structure and function in patients with chronic kidney disease stages 3 to 5 with combined pulmonary hypertension. *International Medicine and Health Herald* **25(8)**:1177–1181 DOI 10.3760/cma.j.issn.1007-1245.2019.08.001.

Meinel K, Koestenberger M, Sallmon H, Hansmann G, Pieles GE. 2020. Echocardiography for the assessment of pulmonary hypertension and congenital heart disease in the young. *Diagnostics* **11(1)**:49 DOI 10.3390/diagnostics11010049.

Mills KT, Xu Y, Zhang W, Bundy JD, Chen C-S, Kelly TN, Chen J, He J. 2015. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney International* **88(5)**:950–957 DOI 10.1038/ki.2015.230.

**Nakhoul F, Yigla M, Gilman R, Reisner SA, Abassi Z. 2005.** The pathogenesis of pulmonary hypertension in haemodialysis patients via arterio-venous access. *Nephrology Dialysis Transplantation* **20(8)**:1686–1692 DOI 10.1093/ndt/gfh840.

**National Heart, Lung, and Blood Institute. 2021.** Quality assessment of case-control studies. *Available at* https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.

**Nicholl DDM, Ahmed SB, Loewen AHS, Hemmelgarn BR, Sola DY, Beecroft JM, Turin TC, Hanly PJ. 2012.** Declining kidney function increases the prevalence of sleep apnea and nocturnal hypoxia. *Chest* **141(6)**:1422–1430 DOI 10.1378/chest.11-1809.

**O'Byrne ML, Glatz AC, Mercer-Rosa L, Gillespie MJ, Dori Y, Goldmuntz E, Kawut S, Rome JJ. 2015.** Trends in pulmonary valve replacement in children and adults with tetralogy of fallot. *American Journal of Cardiology* **115(1)**:118–124 DOI 10.1016/j.amjcard.2014.09.054.

**Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. 2021.** The PRISMA, 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* **372**:n71 DOI 10.1136/bmj.n71.

**Poch D, Mandel J. 2021.** Pulmonary hypertension. *Annals of Internal Medicine* **174(4)**:Itc49–Itc64 DOI 10.7326/AITC202104200.

**R Core Team. 2023.** *R: A language and environment for statistical computing*. Version 4.2.3. Vienna: R Foundation for Statistical Computing. *Available at* https://www.r-project.org.

**Sahinoz M, Tintara S, Deger SM, Alsouqi A, Crescenzi RL, Mambungu C, Vincz A, Mason OJ, Prigmore HL, Guide A, Stewart TG, Harrison DG, Luft FC, Titze J, Ikizler TA. 2020.** Tissue sodium stores in peritoneal dialysis and hemodialysis patients determined by 23-sodium magnetic resonance imaging. *Nephrology Dialysis Transplantation* **36(7)**:1307–1317 DOI 10.1093/ndt/gfaa350.

**Shen Y, Yao Y, Huang H, Shen L. 2021.** The correlation between red blood cell distribution width and pulmonary arterial hypertension in maintenance hemodialysis patients. *Journal of Clinical Nephrology* **21(8)**:660–665.

**Sise ME, Courtwright AM, Channick RN. 2013.** Pulmonary hypertension in patients with chronic and end-stage kidney disease. *Kidney International* **84(4)**:682–692 DOI 10.1038/ki.2013.186.

**Tang M, Batty JA, Lin C, Fan X, Chan KE, Kalim S. 2018.** Pulmonary hypertension, mortality, and cardiovascular disease in CKD and ESRD patients: a systematic review and meta-analysis. *American Journal of Kidney Diseases* **72(1)**:75–83 DOI 10.1053/j.ajkd.2017.11.018.

**Thomas B, Matsushita K, Abate KH, Al-Aly Z, Ärnlöv J, Asayama K, Atkins R, Badawi A, Ballew SH, Banerjee A, Barregård L, Barrett-Connor E, Basu S, Bello AK, Bensenor I, Bergstrom J, Bikbov B, Blosser C, Brenner H, Carrero J-J, Chadban S, Cirillo M, Cortinovis M, Courville K, Dandona L, Dandona R, Estep K, Fernandes Jão, Fischer F, Fox C, Gansevoort RT, Gona PN, Gutierrez OM, Hamidi S, Hanson SW, Himmelfarb J, Jassal SK, Jee SH, Jha V, Jimenez-Corona A, Jonas JB, Kengne AP, Khader Y, Khang Y-H, Kim YJ, Klein B, Klein R, Kokubo Y, Kolte D, Lee K, Levey AS, Li Y, Lotufo P, El Razek HMA, Mendoza W, Metoki H, Mok Y, Muraki I, Muntner PM, Noda H, Ohkubo T, Ortiz A, Perico N, Polkinghorne K, Al-Radaddi R, Remuzzi G, Roth G, Rothenbacher D, Satoh M, Saum K-U, Sawhney M, Schöttker B, Shankar A, Shlipak M, Silva DAS, Toyoshima H, Ukwaja K, Umesawa M, Vollset SE, Warnock DG, Werdecker A, Yamagishi K, Yano Y, Yonemoto N, Zaki MES, Naghavi M, Forouzanfar MH, Murray CJL, Coresh J, Vos T, On behalf of the Global Burden of Disease 2013 GFR Collaborators. 2017.** CKD Prognosis Consortium. 2017. Global Burden of Disease Genitourinary Expert Group. 2017.

Global cardiovascular and renal outcomes of reduced GFR. *Journal of the American Society of Nephrology* **28(7)**:2167–2179 DOI 10.1681/ASN.2016050562.

Tiengo A, Fadini GP, Avogaro A. 2008. The metabolic syndrome, diabetes and lung dysfunction. *Diabetes & Metabolism* **34(5)**:447–454 DOI 10.1016/j.diabet.2008.08.001.

Valkenburg S, Glorieux G, Vanholder R. 2021. Uremic toxins and cardiovascular system. *Cardiology Clinics* **39(3)**:307–318 DOI 10.1016/j.ccl.2021.04.002.

von Siebenthal C, Aubert JD, Mitsakis P, Yerly P, Prior JO, Nicod LP. 2016. Pulmonary hypertension and indicators of right ventricular function. *Frontiers in Medicine* **3(5)**:23 DOI 10.3389/fmed.2016.00023.

Walther CP, Nambi V, Hanania NA, Navaneethan SD. 2020. Diagnosis and management of pulmonary hypertension in patients with CKD. *American Journal of Kidney Diseases* **75(6)**:935–945 DOI 10.1053/j.ajkd.2019.12.005.

Wang Y, He Y, Luo X, Ke J, Du Y, Li M. 2014a. Analysis of the correlation between echocardiography parameters and pulmonary artery pressure in 136 patients undergoing maintenance hemodialysis. *Chinese Journal of Clinicians* **8(1)**:27–30.

Wang Y, Zhao N, Liu Y, Song Y, Qin L, Xiao Y, Yao L. 2014b. Analysis of changes in pulmonary arterial pressure and related factors in patients with refractory secondary hyperparathyroidism in uremia. *Journal of Lanzhou University(Medical Sciences)* **40(03)**:17–21 DOI 10.13885/j.issn.1000-2812.2014.03.004.

Yang Q, Bao X. 2012. Changes in pulmonary artery pressure and its correlation with cardiac morphology and function in non dialysis chronic kidney disease patients. *Chinese Journal of Respiratory and Critical Care Medicine* **11(2)**:138–141.

Yang QM, Bao XR. 2014. Pulmonary hypertension in patients with stage 1–3 chronic kidney disease. *Genetics and Molecular Research* **13(3)**:5695–5703 DOI 10.4238/2014.July.25.25.

Yu T-M, Chen Y-H, Hsu J-Y, Sun C-S, Chuang Y-W, Chen C-H, Wu M-J, Cheng C-H, Shu K-H. 2009. Systemic inflammation is associated with pulmonary hypertension in patients undergoing haemodialysis. *Nephrology Dialysis Transplantation* **24(6)**:1946–1951 DOI 10.1093/ndt/gfn751.

Yu CK, Wong WH, Li VW, Cheung YF. 2017. Left ventricular stiffness in adolescents and young adults with repaired tetralogy of fallot. *Scientific Reports* **7**:1252 DOI 10.1038/s41598-017-01448-2.

Zewinger S, Kleber ME, Rohrer L, Lehmann M, Triem S, Jennings RT, Petrakis I, Dressel A, Lepper PM, Scharnagl H, Ritsch A, Thorand B, Heier M, Meisinger C, de las Heras Gala T, Koenig W, Wagenpfeil S, Schwedhelm E, Böger RH, Laufs U, von Eckardstein A, Landmesser U, Lüscher TF, Fliser D, März W, Meinitzer A, Speer T. 2017. Symmetric dimethylarginine, high-density lipoproteins and cardiovascular disease. *European Heart Journal* **38(20)**:1597–1607 DOI 10.1093/eurheartj/ehx118.

Zhang Y, Ding X-H, Rao R, Wang Y, Pang F, Tang S, Nie L, Bian S-Z. 2020. The prevalence of pulmonary hypertension among maintenance dialysis patients with ESRD and its associated factors: a retrospective study. *Frontiers in Medicine* **7**:570874 DOI 10.3389/fmed.2020.570874.

Zhang Q, Wang L, Zeng H, Lv Y, Huang Y. 2018. Epidemiology and risk factors in CKD patients with pulmonary hypertension: a retrospective study. *BMC Nephrology* **19**:70 DOI 10.1186/s12882-018-0866-9.

Zoccali C, Benedetto FA, Mallamaci F, Tripepi G, Candela V, Labate C, Tassone F. 2001. Left ventricular hypertrophy and nocturnal hypoxemia in hemodialysis patients. *Journal of Hypertension* **19(2)**:287–293 DOI 10.1097/00004872-200102000-00016.