RESEARCH PAPER

Parathyroid Hormone and Cardiac Remodeling in Hemodialysis Patients: A Systematic Review of LVH and LVMI Outcomes

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ABSTRACT

Introduction: Left ventricular hypertrophy (LVH) is highly prevalent in patients with end-stage renal disease (ESRD) and is a major predictor of cardiovascular morbidity and mortality. Secondary hyperparathyroidism has been proposed as a contributing factor, but its relationship with cardiac remodeling remains inconsistent.

Objective: To evaluate the association between parathyroid hormone (PTH) levels and left ventricular hypertrophy, as measured by left ventricular mass index (LVMI) or LVH prevalence, in patients undergoing dialysis.

Methods: A systematic review was conducted following PRISMA guidelines. Literature searches were performed in PubMed, Cochrane Library, and ScienceDirect. Seven observational studies involving 373 hemodialysis patients were included. Data on PTH levels, LVMI, LVH prevalence, and echocardiographic parameters were extracted and analyzed qualitatively.

Results: Most studies demonstrated a positive association between PTH and LVMI, with reported correlations ranging from r = 0.31 to 0.44, and up to r = 0.71 in patients with established LVH. Elevated PTH levels were consistently higher in patients with LVH compared to those without. A threshold effect was observed, with significant associations primarily at higher PTH levels (>300–500 pg/mL). Additionally, PTH was linked to diastolic dysfunction and interacted with calcium–phosphorus metabolism and anemia in influencing cardiac remodeling.

Discussion: PTH appears to act as a disease amplifier in uremic cardiomyopathy, contributing to both structural and functional cardiac changes. Its effects are non-linear and modulated by metabolic and hemodynamic factors, which may explain variability across studies.

Conclusion: Elevated PTH is associated with LVH in dialysis patients, particularly at higher levels, supporting its role in cardiovascular remodeling. Targeted management of secondary hyperparathyroidism may help mitigate cardiovascular risk in this population.

Keywords: *parathyroid hormone; left ventricular hypertrophy; hemodialysis; left ventricular mass index; secondary hyperparathyroidism*

How to cite this article: Etik Mertianti, Nur Samsu, Atma Gunawan, Achmad Rifai, Eden Suryoiman Winoto. Parathyroid Hormone and Cardiac Remodeling in Hemodialysis Patients: A Systematic Review of LVH and LVMI Outcomes. Int J Drug Deliv Technol. 2026;16(79s):838-842 DOI: 10.25258/ijddt.16.79s.150.

INTRODUCTION

Cardiovascular disease remains the leading cause of morbidity and mortality in patients with end-stage renal disease (ESRD), accounting for a disproportionately high burden of adverse outcomes compared to the general population.[1] Among the spectrum of cardiovascular complications, left ventricular hypertrophy (LVH) is particularly prevalent, affecting up to 70–80% of patients undergoing maintenance hemodialysis and serving as a strong independent predictor of cardiovascular events and all-cause mortality.[2,3] The development of LVH in this population is multifactorial, involving traditional risk factors such as hypertension and volume overload, as well as non-traditional uremia-related mechanisms.

In recent years, increasing attention has been directed toward the role of mineral and bone disorder in chronic kidney disease (CKD-MBD), particularly secondary hyperparathyroidism, as a potential contributor to cardiovascular remodeling.[4] Parathyroid hormone (PTH), beyond its classical role in calcium–phosphorus homeostasis, has been implicated in the pathogenesis of myocardial hypertrophy through direct and indirect mechanisms. Experimental and clinical studies suggest that elevated PTH promotes cardiomyocyte hypertrophy, interstitial fibrosis, and disturbances in intracellular calcium handling, ultimately leading to

structural and functional alterations of the left ventricle.[5,6]

Additionally, abnormalities in calcium–phosphorus metabolism frequently coexist with elevated PTH levels and may further exacerbate cardiovascular injury. Hyperphosphatemia and increased calcium–phosphorus product have been associated with vascular calcification, arterial stiffness, and adverse cardiac remodeling, thereby amplifying the cardiovascular risk profile of dialysis patients.[7,8] These metabolic disturbances often interact synergistically, making it difficult to isolate the independent contribution of PTH to LVH.

Despite growing evidence, the clinical relationship between PTH levels and LVH in patients undergoing dialysis remains inconsistent. Some studies have demonstrated a clear positive association between elevated PTH and increased left ventricular mass, while others have reported weak, non-significant, or even paradoxical relationships, particularly when accounting for confounding factors such as blood pressure, anemia, and dialysis duration.[9] Furthermore, emerging data suggest that the effect of PTH on cardiac remodeling may not be linear, but rather dependent on threshold levels and the underlying myocardial adaptation state.[10]

This variability highlights an important gap in the current understanding of uremic cardiomyopathy. Specifically, it remains unclear whether PTH acts as an independent driver of LVH, a cofactor that amplifies existing cardiovascular stressors, or a marker of broader metabolic dysregulation. Clarifying this relationship is clinically relevant, as targeted management of secondary hyperparathyroidism may offer a potential strategy to mitigate cardiovascular risk in ESRD patients.

Therefore, this systematic review aims to evaluate the association between parathyroid hormone levels and left ventricular hypertrophy, as measured by left ventricular mass index (LVMI) or LVH prevalence, in patients undergoing dialysis. In addition, this study seeks to explore the interplay between PTH, mineral metabolism, and other clinical factors in shaping cardiac remodeling patterns in this high-risk population.

METHODS

Study Design and Reporting

This study was conducted as a systematic review to evaluate the association between parathyroid hormone (PTH) levels and left ventricular hypertrophy (LVH) in patients undergoing dialysis. The review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring transparency and reproducibility throughout the study selection and reporting process.

Search Strategy

A comprehensive literature search was conducted across three electronic databases: PubMed, Cochrane Library, and ScienceDirect. The search strategy combined keywords related to parathyroid hormone, cardiac structural outcomes, and dialysis populations. The following Boolean structure was applied:

("parathyroid hormone" OR PTH OR hyperparathyroidism) AND ("left ventricular hypertrophy" OR LVH OR "left ventricular mass" OR LVMI) AND ("hemodialysis" OR dialysis OR ESRD).

The search was designed to capture studies reporting both hypertrophic (LVH prevalence) and morphometric (LVMI) cardiac outcomes. No field restrictions were applied, and the search was limited to studies published in English. The final search results yielded a total of 1,075 records across all databases.

Eligibility Criteria

Studies were included if they met the following criteria:

(1) involved adult patients with end-stage renal disease undergoing dialysis;

(2) evaluated parathyroid hormone (PTH) levels as an exposure variable;

(3) reported left ventricular hypertrophy (LVH) or left ventricular mass index (LVMI) assessed by echocardiography; and

(4) used observational or comparative study designs, including cross-sectional, cohort, or case–control studies.

Studies were excluded if they involved non-dialysis populations, pediatric patients, or lacked extractable data on PTH and cardiac outcomes. Studies focusing on unrelated interventions or with inappropriate participant characteristics were also excluded.

Study Selection

All identified records were screened independently based on title and abstract. A total of 1,075 records were initially screened, of which 1,066 were excluded due to irrelevance. Nine duplicate records were identified and removed. The remaining eight articles underwent full-text assessment for eligibility. One study was excluded at this stage due to inappropriate participant characteristics and intervention regimen. Ultimately, seven studies met the inclusion criteria and were included in the qualitative synthesis.

Data Extraction

Data were extracted using a standardized table as per the predefined format. Extracted variables included: first author and publication year, country, study design, sample size, patient characteristics, dialysis modality, PTH measurement method, LVH assessment criteria, LVMI values, LVH prevalence, key statistical findings, and adjusted variables where available.

Both continuous outcomes (LVMI) and dichotomous outcomes (LVH prevalence) were recorded. When available, correlation coefficients, regression results, and group comparisons were extracted to facilitate comprehensive synthesis.

Outcome Measures

The primary outcomes were:

(1) left ventricular hypertrophy (LVH), defined based on echocardiographic criteria; and

(2) left ventricular mass index (LVMI), expressed in g/m².

Secondary outcomes included measures of cardiac function, such as ejection fraction (EF) and diastolic function parameters, when reported. Additional variables related to mineral metabolism, including calcium and phosphorus levels, were also considered in the qualitative synthesis.

Risk of Bias Assessment

The methodological quality of included studies was assessed using a design-appropriate approach, focusing on selection bias, measurement validity, and control of confounding variables. Given that most included studies were observational in nature, particular attention was paid to the presence of adjusted analyses and the consistency of outcome definitions.

In accordance with the predefined criteria of this review, the overall risk of bias for included studies was categorized as low to moderate, with no studies classified as high risk of bias.

Data Synthesis

Due to heterogeneity in study design, PTH categorization, and outcome reporting, a quantitative meta-analysis was not performed. Instead, a narrative synthesis approach was used to summarize findings across studies.

The qualitative synthesis focused on identifying patterns in the relationship between PTH and cardiac remodeling, including correlation strength, threshold effects, interaction with clinical variables, and differences in structural versus functional outcomes. Particular attention was given to consistency of findings and potential sources of heterogeneity across studies.

Table 1. Characteristics and results of the included studies

First Author (Year)	Country	Study Design	Population (n)	Mean Age (years)	Dialysis Modality (HD/PD)	PTH Assessment (method / categorization)	LVH Assessment (Echo criteria / LVMI cut-off)	LVMI (g/m²) (mean ± SD or median)	LVH Prevalence (%)	Key Findings (Association between PTH & LVH/LVMI)	Adjusted Variables	Summary of Findings	Risk of Bias
Rasic et al. (2004)	Bosnia and Herzegovina	Prospective comparative cohort	50 ESRD patients	~41–49 (varies by group)	Hemodialysis only	Serum PTH measured serially over 12 months (continuous values, pg/mL; no cat	Echocardiography; LVH defined as LVMI >131 g/m² (male), >100 g/m² (fe	Not directly reported overall; higher in LV dysfunction groups	72% at baseline	Higher PTH levels significantly associated with LVH (p ≈0.0	Age, sex, Hb, SBP, DBP, MAP, PTH (multivariable regress	Elevated PTH contributes to LV remodeling and LVMI increase in HD patients; sup	Low

						egorical cut-off)	male)			43) and LV dysfunction; PTH independently predicted increase	ion)	ports role of hyperparathyroidism as cardiovascular risk factor	
										in LVMI (β=0.537, p=0.002)			
Shaltout et al. (2021)	Egypt	Cross-sectional comparative	40 ESKD patients (20 LVH vs	44.6 ± 14.8	Hemodialysis only	Serum PTH measured (pg/mL); continuous	Echocardiography; LVH defined as LVMI	LVMI correlated with PTH (r=0.3	Not directly reported overall (grou	PTH significantly higher in LV	None (correlation analysis only; no	Elevated PTH is associated with increased LV	Moderate

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										c function (↑HR, ↓LVET)			
Stróżecki et al. (2001)	Poland	Cross-sectional study	22 normotensive HD + 43 hypertensive HD	46.2 ± 11.1 (normotensive)	Hemodialysis	Serum intact PTH (continuous variable; correlation analysis)	Echocardiography (ASE M-mode; LVMI indexed; LVH: >100 g/m^2 women, >131 g/m^2 men)	Normotensive: 128.3 ± 46.2; Hypertensive: 165.8 ± 46.7	55% (normotensive), 86% (hypertensive)	Positive correlation between PTH and LVMI ($r = 0.44$; $p < 0.05$); stronger in LVH subgroup (r	Unadjusted (correlation-based; no multivariable model)	Elevated PTH associated with increased LV mass, especially in patients already exhibiting LVH; also linked with diastolic dysfunction via Ca–P met	Moderate

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RESULTS

Study Selection

A total of 1,075 records were identified through database searching, including 334 from PubMed, 50 from the Cochrane Library, and 691 from ScienceDirect. After title and abstract screening, 1,066 records were excluded due to irrelevance. Nine duplicate records were identified and removed. Eight full-text articles were assessed for eligibility, of which one study was excluded due to inappropriate participant characteristics and intervention regimen. Ultimately, seven studies were included in the qualitative synthesis.

Characteristics of Included Studies

The seven included studies were published between 1987 and 2021 and comprised a total of 373 patients undergoing maintenance hemodialysis. All studies employed observational designs, predominantly cross-sectional analyses, with one prospective cohort study.

Geographically, the studies were conducted across diverse regions, including Europe (Bosnia, Poland, France), the Middle East (Iran), Asia (Japan), and Africa (Egypt), reflecting a broad representation of dialysis populations.

All studies focused exclusively on patients receiving hemodialysis, with no eligible studies directly comparing peritoneal dialysis populations. Sample sizes ranged from 22 to 81 participants, with mean ages generally between 40 and 60 years.

Parathyroid hormone (PTH) levels were assessed using standard biochemical assays and analyzed either as continuous variables or stratified into categorical groups based on predefined thresholds. Left ventricular hypertrophy (LVH) was evaluated using echocardiography in all studies, with left ventricular mass index (LVMI) as the primary quantitative parameter. Diagnostic thresholds for LVH were largely consistent across studies, typically defined as LVMI >100 g/m² in women and >131 g/m² in men.

Association Between PTH and Left Ventricular Hypertrophy

Across the included studies, a consistent relationship between elevated PTH levels and left ventricular structural changes was observed, although the strength and nature of this association varied.

Several studies demonstrated a significant positive correlation between PTH and LVMI, indicating that higher PTH levels are associated with increased left ventricular mass. For instance, moderate correlations were reported in multiple cohorts ($r \approx 0.31–0.44$), with stronger associations observed in subgroups of patients already exhibiting LVH. In one study, the correlation between PTH and LVMI was markedly higher among patients with established hypertrophy ($r \approx 0.71$), suggesting that PTH may act as a potentiating factor in advanced cardiac remodeling rather than as an initial trigger.

In addition, studies employing categorical comparisons consistently showed higher PTH levels in patients with LVH compared to those without, reinforcing the association between secondary hyperparathyroidism and myocardial hypertrophy.

Threshold and Dose-Dependent Effects of PTH

Notably, the relationship between PTH and LVH appeared to be non-linear and dose-dependent. Evidence from subgroup analyses indicated that the impact of PTH becomes more pronounced at higher concentrations.

One study reported no significant association between PTH and LVMI in the overall population; however, when patients with markedly elevated PTH levels (>500 pg/mL) were analyzed separately, a significant increase in LVMI and interventricular septal thickness was observed. Similarly, another study demonstrated that correlations between PTH and LVMI were significant only in patients with high PTH levels, while no association was found in those with lower concentrations. These findings suggest the presence of a threshold effect, whereby PTH contributes to cardiac remodeling primarily when levels exceed a certain pathological range.

Independent Predictive Role of PTH

Beyond simple correlation, one study demonstrated that PTH remained an independent predictor of LVMI after adjustment for potential confounders, including age, hemoglobin, body mass index, and blood pressure. This finding supports a more direct role of PTH in the pathogenesis of left ventricular hypertrophy, independent of traditional cardiovascular risk factors.

However, not all studies confirmed this independence. In some cohorts, the association between PTH and LVH diminished after accounting for hemodynamic variables such as hypertension and volume status, highlighting the multifactorial nature of cardiac remodeling in dialysis patients.

Interaction with Other Risk Factors

The qualitative synthesis revealed that PTH does not act in isolation but interacts with multiple metabolic and clinical factors. Anemia emerged as a consistent co-contributor, with inverse correlations observed between hemoglobin levels and LVMI. This suggests that reduced oxygen-carrying capacity may synergistically exacerbate myocardial hypertrophy alongside elevated PTH.

Disturbances in calcium–phosphorus metabolism also played a significant role. Several studies demonstrated associations between serum phosphorus levels and LVMI, as well as between calcium–phosphorus product and impaired diastolic

function. These findings indicate that secondary hyperparathyroidism, hyperphosphatemia, and mineral imbalance collectively contribute to adverse cardiac remodeling.

Structural Versus Functional Cardiac Effects

In addition to structural changes, several studies evaluated the impact of PTH on cardiac function. Elevated PTH levels were associated with impaired left ventricular performance, particularly reduced ejection fraction and diastolic dysfunction.

Significant correlations were observed between PTH and parameters of diastolic function, including the E/A ratio, suggesting that PTH-mediated myocardial fibrosis and calcium overload may impair ventricular relaxation. Moreover, inverse relationships between PTH and ejection fraction were reported in specific subgroups, indicating potential effects on systolic function.

Heterogeneity of Cardiac Remodeling Patterns

An important finding from the qualitative synthesis was the heterogeneity in cardiac remodeling patterns associated with PTH. While most studies supported a hypertrophic effect of elevated PTH, one study demonstrated an alternative pattern characterized by inadequate or maladaptive hypertrophy, where patients with severe secondary hyperparathyroidism exhibited reduced left ventricular mass relative to hemodynamic load. This suggests that excessive PTH may impair normal compensatory myocardial adaptation, leading to structurally inefficient remodeling.

This variability highlights the complexity of PTH-related cardiac effects and may explain inconsistencies across studies.

Summary of Qualitative Synthesis

Overall, the evidence indicates that elevated PTH levels are associated with left ventricular hypertrophy and altered cardiac structure in patients undergoing hemodialysis. The relationship appears to be:

- Positive and clinically significant, particularly at higher PTH levels
- Dose-dependent, with stronger effects observed beyond pathological thresholds
- Multifactorial, influenced by anemia, mineral metabolism, and hemodynamic factors
- Heterogeneous, encompassing both adaptive hypertrophy and maladaptive remodeling patterns

These findings support a central role of secondary hyperparathyroidism in the pathophysiology of uremic cardiomyopathy, while also emphasizing the need to consider interacting metabolic and clinical variables.

DISCUSSION

Interpretation of Findings

This systematic review demonstrates that elevated parathyroid hormone (PTH) levels are consistently associated with alterations in left ventricular structure in patients undergoing hemodialysis, although the magnitude and direction of this relationship vary across studies. Most included studies reported a positive association between PTH and left ventricular mass index (LVMI), supporting the hypothesis that secondary hyperparathyroidism contributes to myocardial hypertrophy. However, the strength of this relationship appeared to be context-dependent, with stronger correlations observed in patients with established left ventricular hypertrophy (LVH) or markedly elevated PTH levels.

Importantly, the findings suggest that PTH may function more as a disease amplifier rather than a primary initiator of LVH. In several cohorts, PTH–LVMI correlations were absent in patients with normal cardiac structure but became significant in those with pre-existing hypertrophy. This indicates that PTH likely exacerbates ongoing myocardial remodeling rather than independently triggering its onset.

Comparison with Previous Studies

The relationship between PTH and cardiovascular remodeling in chronic kidney disease has been increasingly recognized, yet remains incompletely defined. Previous large-scale analyses have demonstrated that CKD-related mineral and bone disorder (CKD-MBD) plays a central role in cardiovascular pathology, particularly through mechanisms involving vascular calcification and myocardial fibrosis.[4,8] The findings of this review are consistent with these broader observations, reinforcing the role of PTH as part of a complex metabolic axis influencing cardiac structure.

However, the heterogeneity observed across included studies aligns with prior reports suggesting that the association between PTH and LVH is not uniformly linear.[9] While some studies support a direct hypertrophic effect of PTH, others indicate that its impact is modulated by coexisting clinical factors such as hypertension, anemia, and volume status. This variability underscores the multifactorial nature of uremic cardiomyopathy.

Dose-Dependent and Threshold Effects

A key finding of this review is the presence of a dose-dependent and threshold-dependent relationship between PTH and LVH. Evidence from subgroup analyses indicates that the association becomes clinically significant primarily at higher PTH concentrations. Patients with markedly elevated PTH levels demonstrated significantly increased LVMI and myocardial wall thickness, whereas those with lower levels showed weaker or absent associations.

This non-linear pattern may explain inconsistencies in prior studies and suggests that PTH-related cardiotoxicity manifests predominantly in advanced secondary hyperparathyroidism. Such findings are supported by previous research indicating that severe disturbances in CKD-MBD are required to produce measurable structural cardiac changes.[5]

Pathophysiological Mechanisms

The mechanisms linking PTH to left ventricular remodeling are likely multifactorial. Experimental studies have demonstrated that PTH exerts direct trophic effects on cardiomyocytes, promoting hypertrophy and increasing intracellular calcium influx, which may disrupt excitation–contraction coupling.[6] In addition, PTH stimulates cardiac fibroblast activation, leading to interstitial fibrosis and increased myocardial stiffness.

Furthermore, elevated PTH levels are closely associated with abnormalities in calcium–phosphorus metabolism, which themselves contribute to cardiovascular injury. Hyperphosphatemia and increased calcium–phosphorus product have been linked to vascular calcification, arterial stiffness, and increased cardiac afterload.[7,8] These factors may act synergistically with PTH to accelerate cardiac remodeling.

Recent evidence also highlights the interplay between PTH and other hormonal mediators, such as fibroblast growth factor-23 (FGF-23), which has been independently associated with LVH and adverse cardiovascular outcomes in CKD patients.[5] Together, these findings suggest that PTH operates within a broader endocrine network influencing cardiovascular structure.

Structural Versus Functional Cardiac Effects

Beyond structural remodeling, several studies included in this review demonstrated associations between PTH and impaired cardiac function, particularly diastolic dysfunction. Correlations between PTH and parameters such as the E/A ratio suggest that elevated PTH contributes to reduced ventricular compliance, likely mediated by myocardial fibrosis and calcium overload.

However, the relationship between PTH and systolic function appears less consistent. While some studies reported inverse associations between PTH and ejection fraction, others found no significant relationship after adjusting for confounders. This discrepancy may reflect differences in patient populations, disease severity, and methodological approaches.

Heterogeneity and Maladaptive Remodeling

An important observation from this review is the heterogeneity in cardiac remodeling patterns associated with PTH. While most studies support a hypertrophic effect, some evidence suggests that excessive PTH may lead to maladaptive or inadequate hypertrophy, characterized by impaired myocardial adaptation relative to hemodynamic load.

This concept of maladaptive remodeling has been described in uremic cardiomyopathy and may reflect advanced myocardial injury, where structural changes no longer confer functional benefit.[11,12] Such findings highlight the complexity of PTH-related cardiac effects and suggest that its role may evolve across different stages of disease progression.

Clinical Implications

The findings of this review have important clinical implications. Given the association between elevated PTH and adverse cardiac remodeling, effective management of secondary hyperparathyroidism may represent a potential strategy to reduce cardiovascular risk in dialysis patients. Current therapeutic approaches, including vitamin D analogs and calcimimetics, have been shown to modulate PTH levels and may influence cardiac outcomes.[11,13]

However, the non-linear and context-dependent nature of the PTH–LVH relationship suggests that treatment strategies should be individualized, taking into account the severity of hyperparathyroidism and the presence of coexisting risk factors. Early intervention before the development of advanced myocardial remodeling may be particularly beneficial.[13–15]

Limitations

Several limitations should be acknowledged. First, all included studies were observational in design, limiting the ability to infer causality. Second, substantial heterogeneity existed in PTH measurement methods, categorization thresholds, and outcome definitions, which precluded quantitative meta-analysis. Third, many studies lacked adjustment for key confounders, including blood pressure, volume status, and anemia.

Additionally, the absence of studies involving peritoneal dialysis limits the generalizability of findings across different dialysis modalities. Finally, the relatively small sample sizes in several studies may have reduced statistical power.

Future Directions

Future research should focus on large-scale prospective studies to clarify the causal role of PTH in cardiac remodeling. Standardization of PTH measurement and LVH assessment is also needed to improve comparability across studies. Moreover, interventional trials evaluating the impact of PTH-lowering therapies on cardiac structure and function would provide valuable insights into potential therapeutic benefits. Exploration of the interaction between PTH and other hormonal mediators, such as

FGF-23, may further enhance understanding of the complex pathophysiology of uremic cardiomyopathy.

CONCLUSION

Elevated parathyroid hormone (PTH) levels are associated with left ventricular hypertrophy (LVH) and increased left ventricular mass index (LVMI) in patients undergoing hemodialysis. The relationship appears to be dose-dependent and more pronounced in patients with advanced secondary hyperparathyroidism or established cardiac remodeling. PTH likely contributes to myocardial hypertrophy through multifactorial mechanisms involving calcium–phosphorus imbalance, myocardial fibrosis, and intracellular calcium dysregulation. However, the effect is heterogeneous and influenced by coexisting factors such as hypertension and anemia. These findings support the role of secondary hyperparathyroidism as an important contributor to uremic cardiomyopathy and highlight the potential value of targeted PTH control in reducing cardiovascular risk in dialysis patients.

REFERENCES

1. Afsar B, Turkmen K, Covic A, Kanbay M. An update on coronary artery disease and chronic kidney disease. Int J Nephrol. 2014;2014:767424. doi:10.1155/2014/767424 PubMed PMID: 24734178; PubMed Central PMCID: PMC3964836.
2. Lassen MCH, Qasim A, Webber A, Gao Y, Biering-Sørensen T, Park M. The effect of kidney transplantation on left ventricular remodeling and global diastolic strain rate in end-stage renal disease. Echocardiography. 2021 Nov;38(11):1879–86. doi:10.1111/echo.15226 PubMed PMID: 34713484.
3. Xu C, Tsihlis G, Chau K, Trinh K, Rogers NM, Julovi SM. Novel Perspectives in Chronic Kidney Disease-Specific Cardiovascular Disease. IJMS. 2024 Feb 24;25(5):2658. doi:10.3390/ijms25052658
4. Evenepoel P, Cunningham J, Ferrari S, Haarhaus M, Javaid MK, Lafage-Proust MH, et al. European Consensus Statement on the diagnosis and management of osteoporosis in chronic kidney disease stages G4-G5D. Nephrol Dial Transplant. 2021 Jan 1;36(1):42–59. doi:10.1093/ndt/gfaa192 PubMed PMID: 33098421.
5. Kim A, Parikh MA, Khalid H, Frishman WH, Peterson SJ. Fibroblast Growth Factor-23 and Cardiovascular Disease in Patients With Chronic Kidney Disease. Cardiol Rev. 2026 Feb 13. doi:10.1097/CRD.0000000000001203 PubMed PMID: 41680987.
6. Moe SM, Chen NX. Pathophysiology of Vascular Calcification in Chronic Kidney Disease. Circulation Research. 2004 Sep 17;95(6):560–7. doi:10.1161/01.RES.0000141775.67189.98
7. Vervloet MG, Sezer S, Massy ZA, Johansson L, Cozzolino M, Fouque D, et al. The role of phosphate in kidney disease. Nat Rev Nephrol. 2017 Jan;13(1):27–38. doi:10.1038/nrneph.2016.164 PubMed PMID: 27867189.
8. Turner ME, Beck L, Hill Gallant KM, Chen Y, Moe OW, Kuro-O M, et al. Phosphate in Cardiovascular Disease: From New Insights Into Molecular Mechanisms to Clinical Implications. Arterioscler Thromb Vasc Biol. 2024 Mar;44(3):584–602. doi:10.1161/ATVBAHA.123.319198 PubMed PMID: 38205639; PubMed Central PMCID: PMC10922848.
9. Fujii H. Association between Parathyroid Hormone and Cardiovascular Disease. Ther Apher Dial. 2018 Jun;22(3):236–41. doi:10.1111/1744-9987.12679 PubMed PMID: 29707916.
10. Di Lullo L, House A, Gorini A, Santoboni A, Russo D, Ronco C. Chronic kidney disease and cardiovascular complications. Heart Fail Rev. 2015 May;20(3):259–72. doi:10.1007/s10741-014-9460-9 PubMed PMID: 25344016.
11. Packer M, Testani J, Butler J, Zannad F, Lam CSP, Vaduganathan M, et al. Chronic Kidney Disease in Patients With Heart Failure With a Preserved Ejection Fraction. JACC. 2025 Nov;86(20):1900–16. doi:10.1016/j.jacc.2025.08.086
12. Richardson T, Gardner M, Salani M. Cardiovascular Disease and Dialysis: A Review of the Underlying Mechanisms, Methods of Risk Stratification, and Impact of Dialysis Modality Selection on Cardiovascular Outcomes. Kidney and Dialysis. 2025 Jan 23;5(1):5. doi:10.3390/kidneydial5010005
13. Liu Y, Yang Q, Chen G, Zhou T. A Systematic Review and Meta-analysis of Efficacy and Safety of Calcimimetic Agents in the Treatment of Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease. Curr Pharm Des. 2022;28(40):3289–304. doi:10.2174/1381612829666221027110656 PubMed PMID: 36305135.
14. Kurpas A, Supel K, Wieczorkiewicz P, Bodalska Duleba J, Zielinska M. Fibroblast Growth Factor 23 and Cardiovascular Risk in Diabetes Patients-Cardiologists Be Aware. Metabolites. 2022 May 30;12(6):498. doi:10.3390/metabo12060498 PubMed PMID: 35736431; PubMed Central PMCID: PMC9254740.

15. Thadhani R, Appelbaum E, Pritchett Y, Chang Y, Wenger J, Tamez H, et al. Vitamin D therapy and cardiac structure and function in patients with chronic kidney disease: the PRIMO randomized controlled trial. JAMA. 2012 Feb 15;307(7):674–84. doi:10.1001/jama.2012.120 PubMed PMID: 22337679.