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Impact of vitamin D deficiency on postoperative outcomes in patients with chronic kidney disease undergoing surgery: a retrospective study

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Although both chronic kidney disease (CKD) and vitamin D deficiency (VDD) are associated with increased surgical risk, their combined impact remains unclear. Using the TriNetX Analytics Network, we conducted a matched cohort study comparing postoperative outcomes in CKD patients with preoperative VDD (≤ 20 ng/mL) to those with normal vitamin D levels (≥ 30 ng/mL). The primary outcome was 30-day mortality; secondary outcomes included acute kidney injury (AKI), pneumonia, acute myocardial infarction (AMI), and atrial fibrillation/flutter (AF). After propensity score matching (21,033 patients per group), results showed that VDD was associated with higher 30-day mortality (Odds ratio[OR]: 2.33, 95% confidence interval [CI] 1.91–2.85, $p < 0.0001$), AKI (OR:1.94, 95% CI1.80–2.10, $p < 0.0001$), and pneumonia (OR:1.76, 95% CI 1.15–2.70, $p = 0.0087$), with no significant difference in AMI and AF. These associations persisted for 90 days. The impact of VDD on mortality and AKI was consistent across sex and CKD stages. Vitamin D insufficiency (21–29 ng/mL) showed attenuated but significant associations, suggesting a dose-dependent effect. In conclusion, preoperative VDD in patients with CKD is associated with increased risks of mortality, AKI, and pneumonia. These findings suggest the potential value of preoperative vitamin D screening and correction in patients with CKD.

Keywords Chronic kidney disease, Vitamin D deficiency, Surgery, Acute kidney injury, Mortality

Chronic kidney disease (CKD) poses a substantial burden on global health, not only as a direct contributor to worldwide morbidity and mortality but also as a significant risk factor for cardiovascular diseases[1,2]. In 2017, an estimated 697.5 million individuals were living with CKD at various stages, representing a global prevalence of 9.1%[1]. This underscores the widespread nature of CKD and highlights the urgency of addressing its health impact, given its association with increased risks of other major health issues. In surgical patients, preoperative CKD has been reported to significantly affect prognosis, including an elevated risk of all-cause mortality, surgical site infection, and postoperative acute kidney injury (AKI)[3–6]. Among the various metabolic derangements observed in patients with CKD, vitamin D deficiency (VDD) is especially prevalent, affecting up to 85.7% of patients with CKD Stage 5[7]. This high prevalence is often attributed to decreased sun exposure and poor nutritional status commonly observed in patients with CKD[8].

Evidence suggests that vitamin D has important immunomodulatory, anti-inflammatory, cardioprotective, and anticancer actions[9–12]. Consistently, low vitamin D status has been associated with an increased risk of autoimmune disorders, various types of cancer, diabetes mellitus, cardiovascular disease, and susceptibility to infections[13–18]. The diverse biological actions of vitamin D are particularly significant in the surgical context, where patients are subjected to considerable physiological stress and are vulnerable to numerous complications. Evidence has indicated an association between low vitamin D concentration and postoperative complications,

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including infections, cardiovascular complications, postoperative delirium, and renal function decline[19–21]. Notably, VDD is also highly prevalent, affecting up to 62% of both surgical and non-surgical patients[20,22], which raises concerns about its potential impact on surgical recovery and complication rates.

Although both CKD and VDD are associated with an increased risk of postoperative complications, the impact of VDD in surgical patients with CKD remains largely unexplored. Unlike CKD, preoperative VDD is a modifiable factor that presents an opportunity for intervention to potentially improve surgical outcomes. Understanding the relationship between vitamin D status and postoperative outcomes could help identify potentially modifiable risk factors for adverse events in this vulnerable population. Therefore, we conducted a large-scale matched cohort study using real-world data to investigate the association between preoperative VDD and postoperative outcomes in patients with CKD.

Methods

Data sources

This retrospective study was conducted using the TriNetX Analytics Network, which is a federated research network operating under a waiver of informed consent. This waiver has been granted by the Western Institutional Review Board (WIRB), as TriNetX only provides de-identified counts and statistical summaries without any direct human contact or interventions. Additionally, the data used were anonymized in compliance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, Section § 164.514(a), ensuring that no personal identifiers are accessible. The platform contains de-identified data from over 157 million unique patients, including demographics, diagnoses (using International Classification of Diseases [ICD] codes), procedures (using Current Procedural Terminology [CPT] codes), medications, laboratory results, and clinical observations. The TriNetX platform enables real-time access to patient data, while maintaining robust data privacy protection. This platform provides built-in analytical tools for cohort selection, comparison, and outcome analysis. While individual patient-level data cannot be directly accessed, the platform allows researchers to analyze aggregated patient populations and their outcomes.

The study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of Chi Mei Medical Center (Approval No. 11310-E04). This cohort study is in line with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Inclusion and exclusion criteria

Using the CPT codes in the TriNetX database, we identified patients who underwent any surgical procedure between January 2010 and December 2019. Eligible patients met the following criteria: (1) age ≥ 50 years, (2) documented CKD history, (3) multiple healthcare facility visits (≥ 2), and (4) serum 25-hydroxyvitamin D measurement within one month before surgery. Surgical procedures were not restricted to specific types to maintain adequate statistical power, given the requirement for preoperative vitamin D measurements. We selected the one-month window for vitamin D measurement based on evidence regarding the biological half-life and stability of vitamin D. The half-life of serum 25-hydroxyvitamin D is approximately 2–3 weeks[23], and its levels remain relatively stable over a one-month period in the absence of significant interventions or seasonal changes. This timeframe provides a reliable representation of patients' vitamin D status while allowing sufficient time for preoperative laboratory testing and surgical planning.

Patients were excluded if they had (1) a history of heart failure; (2) end-stage renal disease requiring dialysis; (3) a recent history (within 1 month) of pneumonia, acute myocardial infarction (AMI), or intensive care unit admission prior to surgery; (4) a previous history of renal transplantation, heart surgery, atrial fibrillation/flutter (AF), or ventricular arrhythmias; and (5) missing data on key variables.

Study design

The study population was divided into two groups based on vitamin D status measured within one month prior to surgery. Patients with serum 25-hydroxyvitamin D levels ≤ 20 ng/mL were categorized as the VDD group, while those with vitamin D levels ≥ 30 ng/mL were classified as the control group. In addition, we also examined the potential association of vitamin D insufficiency (VDI)(25-hydroxyvitamin D levels: 21–29 ng/mL) with on postoperative outcomes.

To minimize potential confounding factors, we employed 1:1 propensity score matching among the groups before the analysis. The propensity scores were calculated using logistic regression, incorporating demographic variables (age at index date, sex, race, and body mass index), baseline comorbidities (e.g., essential hypertension, diabetes mellitus, neoplasms, overweight and obesity, ischemic heart diseases, nicotine dependence, liver diseases, cerebrovascular diseases, malnutrition, and alcohol-related disorders), and laboratory data (i.e., potassium, hemoglobin, and albumin). The quality of matching was assessed using standardized mean differences, with values < 0.1 considered indicative of good balance between groups.

Primary and secondary outcomes

The primary outcome was all-cause mortality within 30 days after surgery, as it represents the most definitive adverse outcome and has been consistently linked to VDD in various clinical settings. The study's outcome measurement was limited to all-cause mortality, as cause-specific mortality data were not available in the TriNetX database. The secondary outcomes included the incidence of pneumonia, AKI, AMI, and AF. Secondary outcomes were selected based on their potential mechanistic relationship with vitamin D status. For example, pneumonia was selected as the primary infectious outcome based on the established role of vitamin D in respiratory immunity and barrier function[24,25]. While other infections are relevant, including multiple infection types would have required excluding patients with pre-existing infections, potentially compromising the statistical power for our primary outcomes.

Subgroup analysis

To evaluate the consistency of the impact of VDD across different patient populations and investigate potential effect modifications, we conducted three pre-specified subgroup analyses. First, we performed sex-stratified analysis by separately analyzing the male and female subgroups to assess potential sex-specific differences in the association between VDD and postoperative outcomes. Second, we conducted CKD stage-stratified analysis by dividing patients into early stage (stages 1–3) and advanced-stage (stages 4–5) CKD groups to examine whether the impact of VDD varies with disease severity.

Sensitivity analysis

We performed two sensitivity analyses. First, we extended the follow-up period to 90 days to capture any delayed effects of VDD on postoperative outcomes. Second, to validate our findings, we conducted a sensitivity analysis incorporating additional laboratory parameters in propensity score matching. Beyond the original matching variables, we included CKD stage, estimated glomerular filtration rate (eGFR), serum calcium, serum sodium, serum phosphate, and parathyroid hormone (PTH) levels. Primary and secondary outcomes were reassessed in this matched subcohort using the same statistical approach as in the main analysis.

Impact of vitamin D insufficiency on postoperative outcomes

We conducted an analysis by creating an additional matched cohort to compare patients with VDI (21–29 ng/mL) with those with normal vitamin D levels, aiming to explore the potential effects of VDI on postoperative outcomes. For this analysis, we maintained the same outcome definitions and statistical approaches as those used in the primary analysis.

Data collection

Patient data were extracted from the TriNetX Analytics Network using standardized diagnostic codes, procedure codes, and laboratory values. Comorbidities were identified using the following ICD-10 codes: essential hypertension (I10), diabetes mellitus (E08-E13), neoplasms (C00-D49), overweight and obesity (E66), nicotine dependence (F17), ischemic heart disease (I20-I25), alcohol-related disorders (F10), cerebrovascular disease (I60-I69), malnutrition (E40-E46), and liver disease (K76).

The study outcomes were identified using the following ICD-10 codes: AMI (I21, I21.3, I21.4, I21.09, I21.29, I21.11, and I22), pneumonia (J18), and AKI (N17 and Z99.2). Mortality was determined using the 'deceased"s status in the demographic records. For incident AF cases, we used comprehensive ICD-10 coding that captured all AF subtypes, including paroxysmal (I48.0), persistent (I48.1, I48.19), chronic (I48.2, I48.20), permanent (I48.21), and unspecified (I48.91) subtypes.

Statistical analyses

Statistical analyses were performed using the built-in analytics tools of the TriNetX platform. Baseline characteristics were compared between groups using standardized mean differences (SMD), with values < 0.1 considered indicative of good balance. Continuous variables are presented as mean ± standard deviation, while categorical variables are expressed as numbers (percentages). For 30-day outcomes, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression, with statistical significance defined as $p < 0.05$ for two-sided tests. For 90-day outcomes, hazard ratios (HRs) with 95% CIs were estimated using a Cox proportional hazards regression model.

Results

Patient selection

From 157,386,562 patients in the TriNetX database, 35, 076, 809 adult patients aged ≥ 50 years with multiple healthcare visits were identified. Among them, 1,406,355 had a documented history of CKD prior to surgery. After applying the exclusion criteria, the initial analysis identified 21,641 patients with VDD (≤ 20 ng/mL; VDD group) and 71,240 patients with vitamin D levels ≥ 30 ng/mL (control group). Propensity score matching was performed in a 1:1 ratio, considering age at index date, sex, race, and comorbidities. The final matched cohort comprised 21,033 patients in each group (Fig. 1).

Patient characteristics before and after matching

Before propensity score matching, notable differences were observed between the VDD and control groups: the VDD group was younger (64.5 ± 18.9 vs. 68.7 ± 9.0 years), had a higher proportion of males (44.7% vs. 36.2%), and a lower proportion of white patients (58.9% vs. 73.1%) (Table 1). After 1:1 propensity score matching ($n = 21,033$ per group), baseline characteristics were well balanced between the groups, with all standardized differences below 0.025. The matched cohorts had a mean age of approximately 64.7 years, with 43.7% being male, and the majority of patients were White (59%). Health factors, such as conditions affecting health status and contact with health services, were similar between the groups, with a prevalence of 85.8%. The most common comorbidities in both matched groups were essential hypertension (77.1% in VDD vs. 78.0% in control group), diabetes mellitus (48.6% vs. 48.9%), neoplasms (41.2% vs. 41.0%), and overweight/obesity (31.0% vs. 31.3%).

Primary outcome and secondary outcome at 30-day follow-up

In the analysis of 30-day postoperative outcomes among patients with CKD, preoperative VDD was associated with substantially higher mortality compared to those with normal vitamin D levels (1.52% vs. 0.66%; OR 2.33, 95% CI 1.91–2.85, $p < 0.0001$), suggesting more than twice the odds of postoperative mortality in the VDD group (Table 2). Among secondary outcomes, AKI emerged as the most frequent complication, with a significantly higher occurrence in the VDD group (9.27% vs. 4.99%; OR 1.94, 95% CI 1.80–2.10, $p < 0.0001$), representing

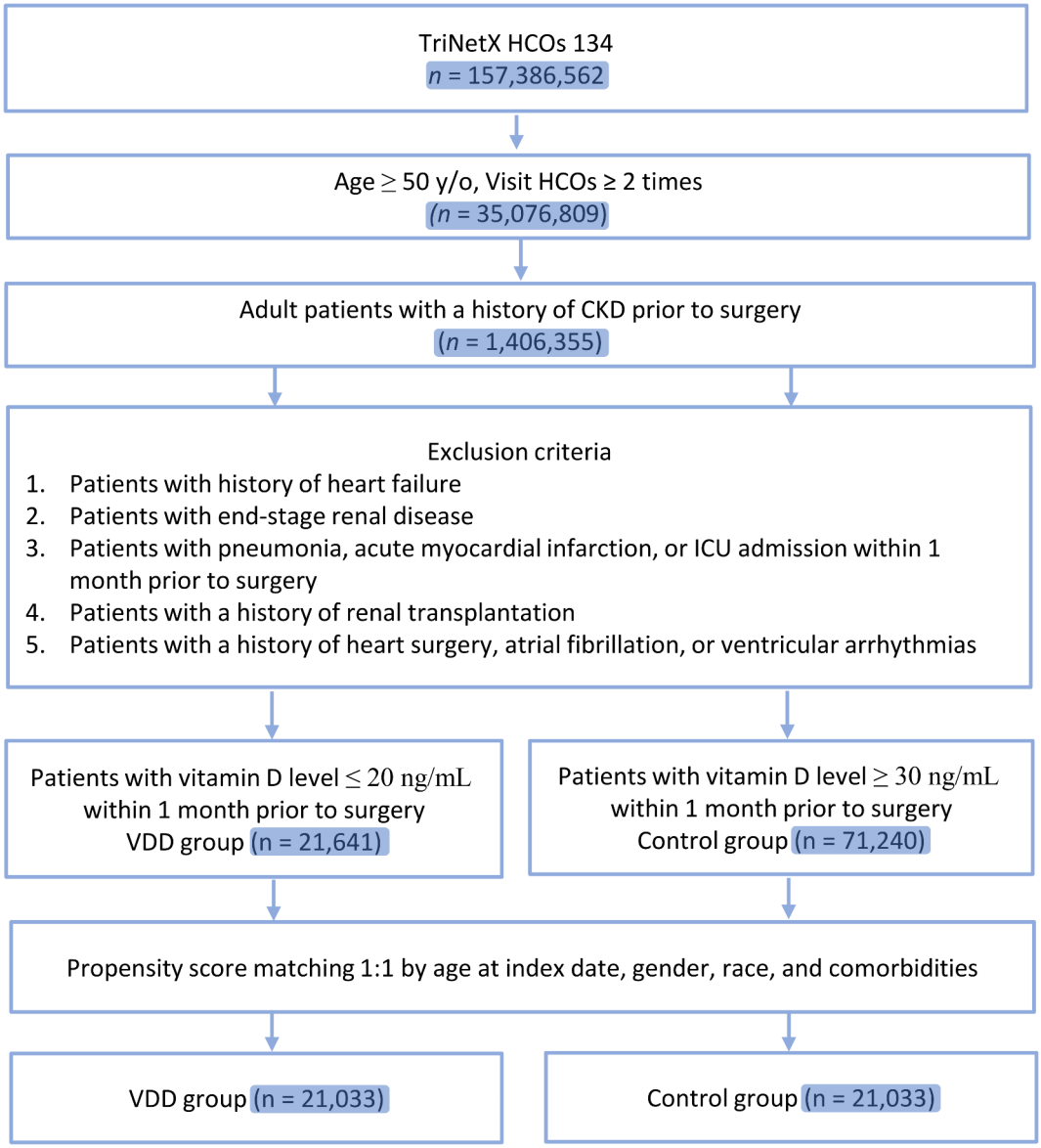

Fig. 1. Patient selection from the Trinetx database.

nearly double the risk compared to controls. Similarly, postoperative pneumonia was observed more frequently in VDD patients (0.28% vs. 0.16%; OR 1.76, 95% CI 1.15–2.70, $p = 0.0087$), although the absolute event rates were relatively low in both groups. Other complications, including AMI (0.12% vs. 0.08%; OR 1.53, 95% CI 0.83–2.82, $p = 0.1697$) and AF (0.05% in both groups; OR 1.00, 95% CI 0.42–2.40, $p = 1.00$), showed no statistically significant differences between the groups.

Sensitivity analysis

In our sensitivity analysis, extending the follow-up period to 90 days postoperatively, the adverse impact of VDD on postoperative outcomes remained consistent (Table 3). The 90-day mortality rate was significantly higher in the VDD group than in the control group (2.97% vs. 1.37%; HR 2.19, 95% CI 1.92–2.52, $p < 0.0001$) (Fig. 2), maintaining a similar magnitude of association to that observed at 30 days. This pattern of increased risk in the VDD group persisted for AKI (13.83% vs. 7.87%; HR 1.83, 95% CI 1.72–1.94, $p < 0.0001$) (Fig. 3) and pneumonia (0.58% vs. 0.35%; HR 1.66, 95% CI 1.25–2.22, $p = 0.0005$). As with the 30-day outcomes, no significant differences were observed in the incidence of AMI or AF at 90 days. These findings reinforce the robustness of our primary analysis and suggest that the negative impact of VDD extends beyond the immediate postoperative period.

After incorporating additional laboratory parameters and CKD stage in the propensity score matching, 19,912 pairs of patients were available for sensitivity analysis (Supplemental Table 1). The association between VDD and adverse outcomes remained consistent with our primary analysis. The 30-day mortality rate was significantly higher in the VDD group (1.43% vs. 0.69%; OR 2.08, 95% CI 1.70–2.55, $p < 0.0001$) (Supplemental Table 2).

Variables	Before matching			After matching		
	VDD group ($n=21,641$)	Control group ($n=71,240$)	Std diff	VDD group ($n=21,033$)	Control group ($n=21,033$)	Std diff
Patient characteristics						
Age at Index (years)	64.5 ± 8.9	68.7 ± 9.0	0.468	64.8 ± 8.9	64.7 ± 8.8	0.013
Body mass index (kg/m^2)	30.8 ± 7.8	29.8 ± 6.9	0.042	30.9 ± 7.8	30.5 ± 7.2	0.008
Male	9679 (44.7%)	25,773 (36.2%)	0.175	9247 (44.0%)	9130 (43.4%)	0.011
White	12,552 (58.0%)	52,093 (73.1%)	0.322	12,424 (59.1%)	12,268 (58.3%)	0.015
Factors influencing health status and contact with health services	18,524 (85.6%)	63,200 (88.7%)	0.093	18,046 (85.8%)	18,013 (85.6%)	0.004
Comorbidities						
Essential (primary) hypertension	16,668 (77.0%)	55,185 (77.5%)	0.011	16,225 (77.1%)	16,411 (78.0%)	0.021
Diabetes mellitus	10,598 (49.0%)	28,336 (39.8%)	0.186	10,211 (48.6%)	10,294 (48.9%)	0.008
Neoplasms	8826 (40.8%)	32,913 (46.2%)	0.109	8663 (41.2%)	8613 (41.0%)	0.005
Overweight and obesity	6678 (30.9%)	19,708 (27.7%)	0.070	6510 (31.0%)	6578 (31.3%)	0.007
Ischemic heart diseases	3527 (16.3%)	11,785 (16.5%)	0.007	3434 (16.3%)	3346 (15.9%)	0.011
Nicotine dependence	3549 (16.4%)	6661 (9.4%)	0.212	3260 (15.5%)	3253 (15.5%)	0.001
Liver diseases	3089 (14.3%)	7517 (10.6%)	0.113	2882 (13.7%)	2768 (13.2%)	0.016
Cerebrovascular diseases	2676 (12.4%)	8396 (11.8%)	0.018	2574 (12.2%)	2442 (11.6%)	0.019
Malnutrition	1877 (8.7%)	2772 (3.9%)	0.198	1623 (7.7%)	1559 (7.4%)	0.012
Alcohol related disorders	1453 (6.7%)	2250 (3.2%)	0.165	1258 (6.0%)	1195 (5.7%)	0.013
Hyperparathyroidism and other disorders of parathyroid gland	1217 (5.6%)	5370 (7.5%)	0.077	1211 (5.8%)	1113 (5.3%)	0.020
Laboratory data						
Potassium (3.5–5.3 mmol/L)	20,968 (96.9%)	69,274 (97.2%)	0.021	20,382 (96.9%)	20,438 (97.2%)	0.016
Hemoglobin (≥ 12 g/dL)	19,841 (91.7%)	66,753 (93.7%)	0.078	19,357 (92.0%)	19,491 (92.7%)	0.024
Albumin (≥ 3.5 g/dL)	18,351 (84.8%)	65,939 (92.6%)	0.247	18,130 (86.2%)	18,309 (87.1%)	0.025

Table 1. Baseline characteristics of patients before and after matching. Data are presented as mean ± standard deviation (SD) or as number (percentage).

Outcomes	VDD group ($n=21,033$)	Control group ($n=21,033$)	OR (95% CI)‡	*p*-value
	Events (%)	Events (%)		
Mortality	319 (1.52%)	138 (0.66%)	2.33 (1.91, 2.85)	< 0.0001
Pneumonia	58 (0.28%)	33 (0.16%)	1.76 (1.15, 2.70)	0.0087
AKI	1,949 (9.27%)	1,050 (4.99%)	1.94 (1.80, 2.10)	< 0.0001
AMI	26 (0.12%)	17 (0.08%)	1.53 (0.83, 2.82)	0.1697
AF	10* (0.05%)	10* (0.05%)	1 (0.42, 2.40)	1

Table 2. Postoperative 30-day outcomes in surgical patients with chronic kidney disease: comparison of patients with and without vitamin D deficiency. *AKI* acute kidney injury, *AMI* acute myocardial infarction, *OR* odds ratio, *VDD* vitamin D deficiency, *AF* atrial fibrillation and flutter. ‡Control group as reference. *To protect patient privacy, numbers are rounded up to 10.

Outcomes	VDD group ($n=21,033$)	Control group ($n=21,033$)	HR (95% CI)‡	*p*-value¶
	Events (%)	Events (%)		
Mortality	625 (2.97%)	288 (1.37%)	2.19 (1.91, 2.52)	< 0.0001
Pneumonia	122 (0.58%)	74 (0.35%)	1.66 (1.25, 2.22)	0.0005
AKI	2,909 (13.83%)	1,655 (7.87%)	1.83 (1.72, 1.94)	< 0.0001
AMI	51 (0.24%)	34 (0.16%)	1.51 (0.98, 2.33)	0.06
AF	21 (0.10%)	13 (0.06%)	1.63 (0.82, 3.25)	0.163

Table 3. Sensitivity analysis: postoperative 90-day outcomes in surgical patients with chronic kidney disease: comparison of patients with and without vitamin D deficiency. *AKI* acute kidney injury, *AMI* acute myocardial infarction, *HR* hazard ratio, *VDD* vitamin D deficiency, *AF* atrial fibrillation and flutter. ‡Control group as reference; ¶Log-rank test.

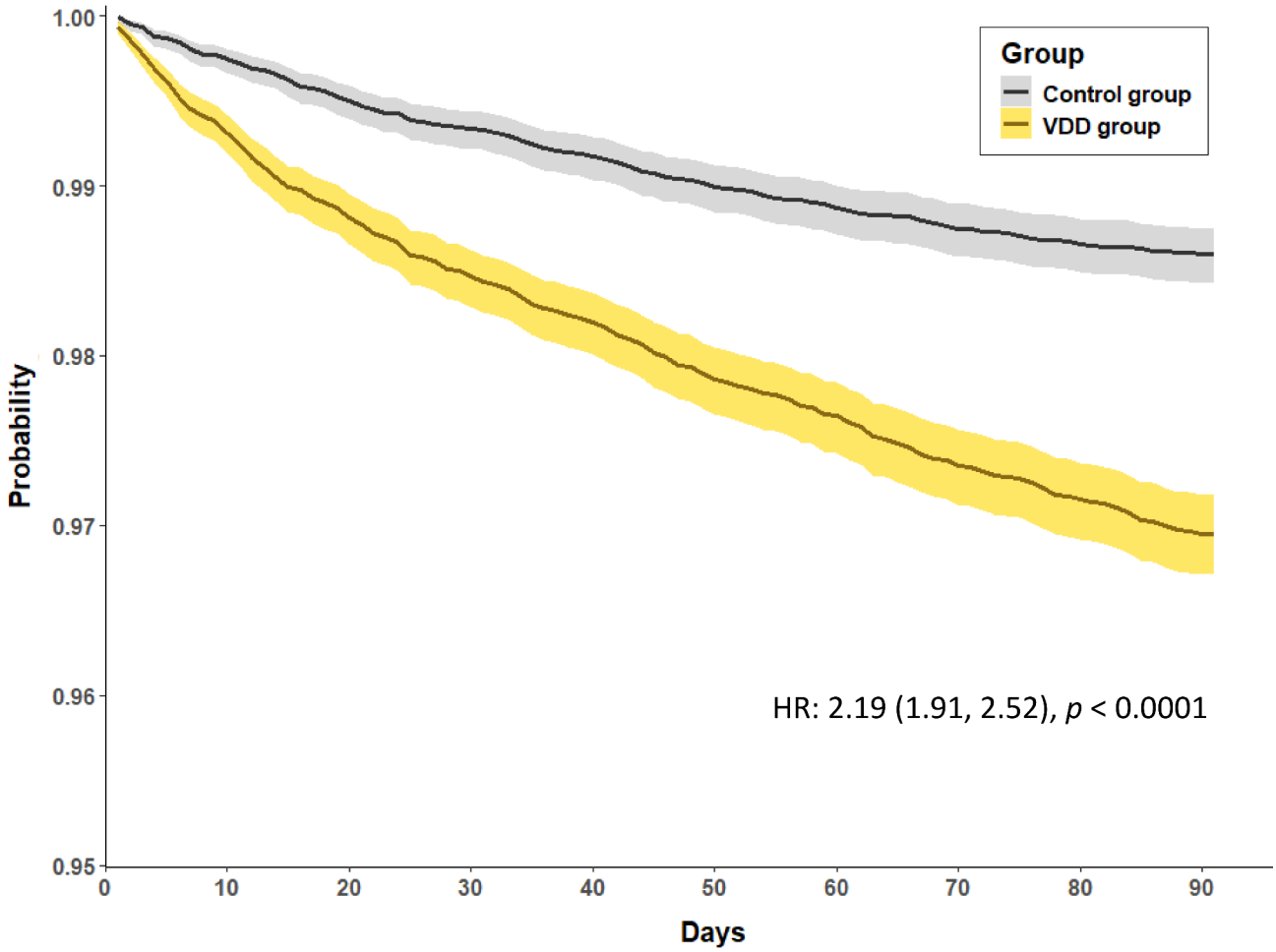

Fig. 2. Kaplan-Meier survival curves comparing 90-day mortality between vitamin D deficient (VDD) and control groups in patients with chronic kidney disease (CKD) undergoing surgery. The VDD group (yellow line) showed significantly higher mortality compared to the control group (gray line) with a hazard ratio (HR) of 2.19 (95% CI1.91–2.52, $p < 0.0001$). Shaded areas represent 95% confidence intervals. Control group represents patients with vitamin D levels ≥ 30 ng/mL, while the VDD group includes patients with vitamin D levels ≤ 20 ng/mL.

Similarly, VDD remained associated with increased risks of AKI (9.37% vs. 5.77%; OR 1.69, 95% CI 1.57–1.82, $p < 0.0001$) and pneumonia (0.30% vs. 0.17%; OR 1.74, 95% CI 1.14–2.65, $p = 0.0094$) (Supplemental Table 2). Consistent with our main analysis, no significant associations were found for AMI or AF (Supplemental Table 2).

Subgroup analysis

In sex-stratified subgroup analyses of 30-day outcomes, VDD was associated with increased mortality risk in both males (OR 2.26, 95% CI 1.72–2.97, $p < 0.0001$) and females (OR 1.98, 95% CI 1.48–2.66, $p < 0.0001$), with males showing a slightly stronger association (Table 4). Similarly, the risk of AKI was significantly elevated in both male (OR 2.05, 95% CI 1.84–2.29, $p < 0.0001$) and female (OR 1.84, 95% CI 1.65–2.06, $p < 0.0001$) VDD patients. While the primary analysis showed significant associations for pneumonia, the sex-stratified analysis revealed no statistically significant differences in either males or females, possibly due to reduced statistical power in the subgroups. Consistent with the overall analysis, neither AMI nor AF showed significant associations with VDD in either sex (all $p > 0.05$).

Subgroup analysis stratified by CKD stage revealed consistent associations between VDD and adverse outcomes across different stages of kidney disease (Table 5). In early stage CKD (stages 1–3, $n = 16{,}954$), VDD was significantly associated with increased mortality (OR 1.90, 95% CI 1.49–2.43, $p < 0.0001$) and AKI (OR 1.88, 95% CI 1.72–2.05, $p < 0.0001$). Similarly, in advanced-stage CKD (stages 4–5, $n = 4{,}956$), VDD remained significantly associated with both mortality (OR 1.84, 95% CI 1.22–2.78, $p = 0.0034$) and AKI (OR 3.45, 95% CI 2.96–4.01, $p < 0.0001$), with a notably stronger association for AKI in this subgroup. The association between VDD and other complications, including pneumonia and AMI, was not statistically significant in either group. The incidence of AF was similar between the VDD and control groups in early stage CKD (OR 1.00, 95% CI 0.42–2.40, $p = 1$), while the analysis was not feasible in advanced-stage CKD due to the absence of events in the control group.

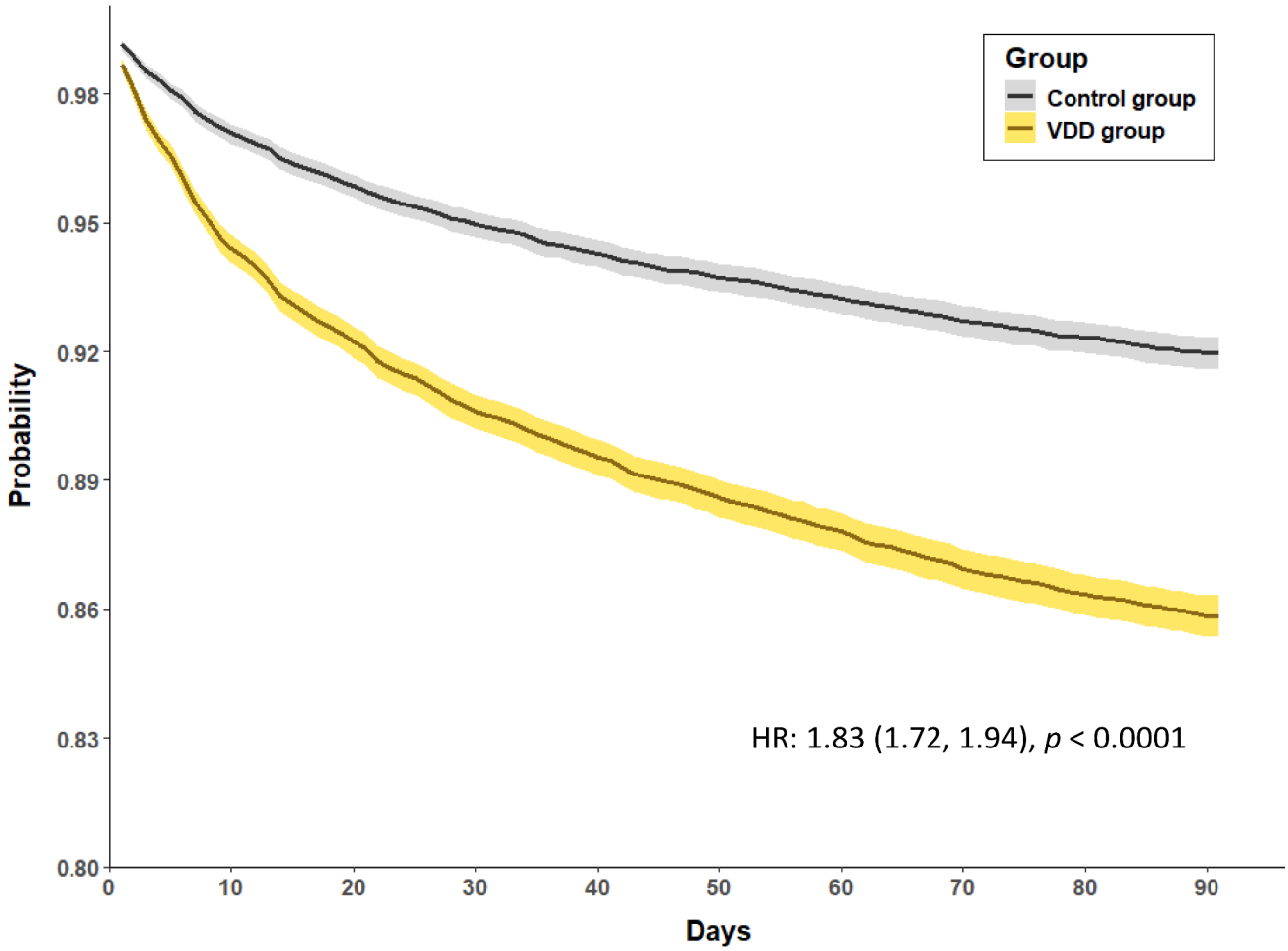

Fig. 3. Kaplan-Meier curves showing the cumulative incidence of acute kidney injury (AKI) over 90 days in vitamin D deficient (VDD) and control groups among patients with chronic kidney disease (CKD) undergoing surgery. The VDD group (yellow line) demonstrated a significantly higher risk of developing AKI compared to the control group (gray line), with a hazard ratio (HR) of 1.83 (95% CI1.72–1.94, $p < 0.0001$). Shaded areas represent 95% confidence intervals. Control group represents patients with vitamin D levels ≥ 30 ng/mL, while the VDD group includes patients with vitamin D levels ≤ 20 ng/mL.

	Male subgroup ($n = 9174$)‡		Female subgroup ($n = 11,275$)‡		
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	Interaction *P* values
Mortality	2.26 (1.72, 2.97)	< 0.0001	1.98 (1.48, 2.66)	< 0.0001	0.52
Pneumonia	1.77 (0.97, 3.21)	0.0576	1.24 (0.65, 2.34)	0.5161	0.46
AKI	2.05 (1.84, 2.29)	< 0.0001	1.84 (1.65, 2.06)	< 0.0001	0.18
AMI	1.10 (0.47, 2.59)	0.8272	1.4 (0.62, 3.15)	0.414	0.72
AF	1.00 (0.42, 2.40)	1	1 (0.42, 2.40)	1	1

Table 4. Subgroup analysis of 30-day postoperative outcomes by sex in surgical patients with chronic kidney disease: comparison of patients with and without vitamin D deficiency. *AKI* acute kidney injury, *AMI* acute myocardial infarction, *OR* odds ratio, *VDD* vitamin D deficiency, *AF* atrial fibrillation and flutter. ‡Control group as reference.

Impact of vitamin D insufficiency on postoperative outcomes

To assess the impact of VDI on postoperative outcomes, we analyzed a matched cohort of 31,331 pairs comparing patients with VDI to those with normal vitamin D levels. While mortality risk remained elevated in the VDI group (0.86% vs. 0.63%; OR 1.36, 95% CI 1.13–1.63, $p = 0.0011$) (Table 6), the magnitude was lower than that in VDD patients. Similarly, AKI showed a significant but attenuated association (5.97% vs. 4.60%; OR 1.32, 95% CI

	CKD stage 1–3 ($n=16,954$)‡		CKD stage 4–5 ($n=4956$)‡		
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	Interaction *P* values
Mortality	1.90 (1.49, 2.43)	< 0.0001	1.84 (1.22, 2.78)	0.0034	0.90
Pneumonia	1.30 (0.79, 2.14)	0.3092	1.70 (0.78, 3.72)	0.1773	0.63
AKI	1.88 (1.72, 2.05)	< 0.0001	3.45(2.96, 4.01)	< 0.0001	< 0.0001
AMI	1.00 (0.51, 1.96)	1	1.00 (0.42, 2.41)	1	1
AF	1.00 (0.42, 2.40)	1	NA¶	NA¶	–

Table 5. Subgroup analysis of 30-day postoperative outcomes by chronic kidney disease stage in surgical patients with and without vitamin D deficiency. *AKI* acute kidney injury, *AMI* acute myocardial infarction, *OR* odds ratio, *VDD* vitamin D deficiency, *AF* atrial fibrillation and flutter, *CKD* Chronic kidney disease. ‡Control group as reference. ¶no event was noted in control group; NA: not available.

Outcomes	VDI group ($n=31,331$)	Control group ($n=31,331$)		
	Events (%)	Events (%)	OR (95% CI)‡	*p*-value
Mortality	268 (0.86%)	198 (0.63%)	1.36 (1.13, 1.63)	0.0011
Pneumonia	43 (0.14%)	45 (0.14%)	0.96 (0.63, 1.45)	0.8311
AKI	1870 (5.97%)	1441 (4.60%)	1.32 (1.23, 1.41)	< 0.0001
AMI	21 (0.07%)	26 (0.08%)	0.81(0.45, 1.44)	0.4656
AF	11 (0.04%)	10* (0.03%)	1.1 (0.47, 2.59)	0.8272

Table 6. Postoperative 30-day outcomes in surgical patients with chronic kidney disease: comparison of patients with and without vitamin D insufficiency. *AKI* acute kidney injury, *AMI* acute myocardial infarction, *OR* odds ratio, *VDI* vitamin D insufficiency, *AF* atrial fibrillation and flutter. ‡Control group as reference. *To protect patient privacy, numbers are rounded up to 10.

1.23–1.41, $p < 0.0001$) (Table 6). Unlike VDD, VDI showed no significant association with pneumonia (0.14% vs. 0.14%; OR 0.96, 95% CI 0.63–1.45, $p = 0.8311$), AMI, or AF.

Discussion

In this large-scale matched cohort study of 42,066 patients with CKD undergoing surgery, preoperative VDD (≤ 20 ng/mL) was associated with a significantly increased risk of mortality, pneumonia, and AKI. The 30-day risks of mortality (OR 2.33) and AKI (OR 1.94) were more than twice as high in vitamin D-deficient patients than in those with normal vitamin D levels. These associations remained consistent at the 90-day follow-up. Subgroup analyses revealed that the adverse effects of VDD on mortality and AKI were consistent in both males and females, although slightly more pronounced in males. This effect was consistent across CKD stages, with particularly strong associations with AKI in advanced-stage CKD (OR, 3.45). Notably, patients with VDI showed attenuated but significant associations with the risk of mortality and AKI, suggesting a dose-dependent effect of vitamin D status on postoperative complications.

Our study demonstrates that preoperative VDD is strongly associated with increased postoperative mortality in patients with CKD, with vitamin D-deficient individuals having more than twice the risk of 30-day mortality and a persistently elevated risk at 90 days, indicating the prolonged impact of VDD beyond the perioperative period. The observed mortality risk was consistent across both sexes, though slightly more pronounced in males (OR 2.26 vs. 1.98 in females). This sex-based difference might reflect underlying biological variations in vitamin D metabolism or differences in comorbidity profiles between male and female patients with CKD. Importantly, our analysis revealed that VDI was associated with an increased mortality risk, albeit with a lower magnitude (OR 1.36) than frank deficiency, suggesting a potential gradient effect of vitamin D status on survival outcomes. The pathophysiological mechanism underlying this increased mortality risk appears to be primarily mediated by AKI rather than cardiovascular complications. This interpretation is supported by our observation of significantly higher rates of AKI in vitamin D-deficient patients, while finding no significant differences in the incidence of AMI or AF. The well-documented high mortality rates associated with postoperative AKI[26,27] suggest that AKI may be the primary driver of the increased mortality in this population. While our large sample size and matched cohort design strengthened our findings, the high prevalence of neoplasms in our study population may affect generalizability. Patients with cancer often have unique risk factors and complications that could influence surgical outcomes independently of vitamin D status. However, our propensity score matching balanced neoplasm prevalence between groups (41.2% vs. 41.0%), minimizing this as a confounder for our primary analyses.

CKD has been well established as a significant risk factor for AKI[28–30], which can significantly increase the risk of postoperative mortality[26]. Our findings revealed that VDD significantly compounds this risk of AKI after surgery, with vitamin D-deficient CKD patients experiencing nearly double the rate of AKI compared to those with normal vitamin D levels. This association was particularly pronounced in patients with advanced-stage CKD

(OR, 3.45), suggesting that VDD may have an amplified detrimental effect in patients with more severe renal dysfunction. The biological plausibility of this relationship is supported by the renoprotective effects of vitamin D, including suppression of the renin-angiotensin system, reduction of inflammatory responses, and direct antiproteinuric effects[31,32]. Our analysis showed an attenuated but still significant risk in vitamin D-insufficient patients, further strengthening the evidence for a causal relationship. These findings have important clinical implications, suggesting that preoperative vitamin D screening and correction might be particularly crucial for preventing AKI in patients with CKD undergoing surgery, especially in those with advanced disease stages where the impact appears most significant.

The association between VDD and increased risk of postoperative pneumonia in our study aligns with previous research demonstrating the role of vitamin D in respiratory health[24,33]. Previous studies have shown that vitamin D enhances innate immune responses to respiratory pathogens, modulates inflammatory responses[34], and maintains pulmonary barrier function[35], with low vitamin D levels linked to increased susceptibility to respiratory infections in both surgical and non-surgical populations[36–38]. Consistently, a prior meta-analysis involving data from 48,488 participants indicated that vitamin D supplementation had protective effects against acute respiratory infections[39]. Our findings demonstrated a consistent pattern at both the 30- and 90-day follow-up, suggesting a sustained impact of vitamin D status on respiratory complications. However, when we conducted sex-stratified subgroup analyses, the association between VDD and pneumonia did not reach statistical significance in either the male or female subgroups, despite showing similar trends. This loss of statistical significance in subgroup analyses likely reflects reduced statistical power due to the relatively low absolute incidence of postoperative pneumonia in our cohort rather than the true absence of an effect, highlighting the need for larger studies specifically powered to evaluate this outcome in different patient subgroups.

Given the well-established relationship between vitamin D and cardiovascular health in previous literature, including its roles in endothelial function, inflammation regulation, and cardiac remodeling[18,40–43], we specifically examined postoperative AMI and AF in our CKD population. However, contrary to expectations, we found no significant association between VDD and either AMI or AF at 30 days post-surgery, with similar null findings persisting at the 90-day follow-up. This lack of association remained consistent across sex and CKD stage subgroups, suggesting a robust finding rather than a limitation of statistical power. The absence of a significant relationship may reflect the dominant role of CKD in cardiovascular complications, as the underlying renal dysfunction, associated metabolic derangements, and vascular calcification in patients with CKD[44,45] might overshadow any potential cardiovascular effects of VDD. These findings suggest that while vitamin D status assessment and correction remain important for overall perioperative risk management in patients with CKD, focusing on other modifiable risk factors might be more crucial for preventing postoperative cardiovascular complications in this specific population.

Our study has several advantages that enhance the strength of our findings. First, the observed associations remained consistent across multiple analytical approaches, including extended follow-up periods and subgroup analyses. Second, the demonstration of a relationship with VDI, showing attenuated but significant associations, suggests a biological plausibility. Third, the large sample size and consistency of our findings across different patient subgroups (sex and CKD stage) suggest broad applicability within the CKD population. However, our exclusion of patients with certain comorbidities (e.g., heart failure) meant that the results may not be generalizable to these specific high-risk groups.

Several important limitations of this study should be considered when interpreting the findings. First, we lacked data on important variables, such as physical activity levels, dietary habits, sun exposure, and vitamin D supplementation, all of which could influence both vitamin D status and surgical outcomes. Additionally, while our matching included healthcare utilization patterns (i.e., factors influencing health status and contact with health services), the TriNetX database lacked direct information on education level, income, and health literacy. These unmeasured confounders could have biased our results. Second, coding practices and documentation quality may vary across participating institutions, potentially affecting our ability to accurately identify all relevant comorbidities and complications. For example, we lacked data on whether CKD diagnoses were based on eGFR, proteinuria, or structural abnormalities, and whether AKI was diagnosed using standardized criteria. This variation in diagnostic approaches across institutions could have affected case identification accuracy. Third, our study did not capture data on surgical complexity, operative time, or perioperative care protocols, which could significantly influence the outcomes. The heterogeneity in the surgical procedures included in our analysis may mask procedure-specific associations between vitamin D status and outcomes. Fourth, we lacked information on seasonal variation in vitamin D measurements and the geographic location of patients, which could affect vitamin D status independently of underlying health conditions. This may introduce some degree of measurement bias, although the large sample size and year-round recruitment likely minimize this effect. Finally, while our study demonstrated associations between VDD and adverse outcomes, we cannot establish causality. The observed relationships may reflect that VDD serves as a marker of overall poor health status rather than a direct causal factor.

Conclusions

In this large matched cohort study of patients with CKD undergoing surgery, preoperative VDD was independently associated with significantly increased risks of 30-day mortality, AKI, and pneumonia. These associations between VDD and the risks of mortality and AKI remained consistent at the 90-day follow-up and across the sex and CKD stage subgroups. While causality cannot be established, these findings suggest that vitamin D status may be an important modifiable risk factor in the preoperative assessment of patients with CKD and warrant future randomized trials investigating whether vitamin D supplementation could improve surgical outcomes in this population.

Data availability

The data that support the findings of this study are available from TriNetX Research Network, but restrictions apply to the availability of these data, which were used under a collaboration agreement for the current study and so are not publicly available. Data are however available from the corresponding author (I-Wen Chen) upon reasonable request and with permission of TriNetX. Access to the de-identified data requires either TriNetX network membership or establishment of a collaborative agreement with TriNetX.

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Author contributions

Author Contributions: K.-C.H. and T.-S.Y.: conceptualization. I.-Y.H., J.-Y.W. and M.Y.: methodology and software. K.-C.H. and J.-Y.W.: validation. K.-C.H and M.Y.: formal analysis. K-C.H. and I.-W.C.: investigation. K-C.H. and I.-W.C.: resources. K-C.H. and I.-Y.H.: data curation. K-C.H. and J.-Y.W.: writing—original draft preparation. K-C.H. and I.-W.C.: writing—review and editing. K-C.H. and I.-W.C.: visualization and supervision. All authors have read and agreed to the published version of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Human ethics and consent to participate declarations

This study was approved by the Institutional Review Board of Chi Mei Medical Center (No. 11310-E04). Our study utilizes data obtained from TriNetX, which is a federated research network operating under a waiver of informed consent.

Additional information

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