Effect of vitamin K on improving post-kidney transplant outcomes: a meta-analysis

ZHOU SUN, KEJING ZHU, GUOFU LIANG, FU YAN, SHENG CHAO, LEI JIA and YULIN NIU

Department of Organ Transplantation, The Affiliated Hospital of Guizhou Medical University, Guiyang, Guizhou 550004, P.R. China

Received April 11, 2023; Accepted August 18, 2023

DOI: 10.3892/etm.2023.12318

Abstract. The effect of vitamin K on clinical outcomes in patients receiving kidney transplantation is contested according to previous studies. This meta-analysis aimed to summarize the impact of vitamin K on all-cause mortality, renal function, inflammation, and vascular/bone health in patients receiving kidney transplantation. EMBASE, PubMed, and Cochrane were searched for literature concerning the effect of vitamin K on clinical outcomes of patients receiving kidney transplantation until December 2022. Normal vitamin K status/vitamin K supplementation was considered as the experimental group; while vitamin K deficiency/no vitamin K supplementation was considered as the control group. All-cause mortality, renal function indexes, C-reactive protein (CRP), and vascular/bone health indexes were extracted and analyzed. A total of seven studies with 1,101 patients in the experimental group and 651 patients in the control group were included. All-cause mortality was decreased in the experimental group vs. the control group [relative risk (95% confidence interval (CI)]: 0.72 (0.60-0.86), P<0.001]. Regarding renal function indexes, the estimated glomerular filtration rate was increased in the experimental group vs. the control group [mean difference (95% CI): 9.87 (1.48-18.26), P=0.021]; while creatinine and albumin remained unchanged between the two groups (both P>0.05). Moreover, CRP, systolic blood pressure, diastolic blood pressure, triglycerides, hemoglobin, calcium, and 25-hydroxyvitamin D were unchanged between the two groups (all P>0.05). Publication bias was low, and the robustness assessed by sensitivity analysis was generally acceptable. Thus vitamin K exerted a potential implication in reducing all-cause mortality and improving renal function in patients receiving kidney transplantation.

Correspondence to: Dr Yulin Niu, Department of Organ Transplantation, The Affiliated Hospital of Guizhou Medical University, 28 Guiyi Street, Guiyang, Guizhou 550004, P.R. China
E-mail: nddnyl@126.com

Key words: kidney transplantation, vitamin K, all-cause mortality, renal function, vascular and bone health

Introduction

Kidney transplantation is a treatment option for end-stage renal disease patients, which has several benefits for the patients, such as a higher quality of life, lower costs, and fewer dietary restrictions, amongst others (1-3). However, this surgery carries the risks of post-transplant complications, including delayed graft function, vascular calcification, bone fractures, diabetes, and infection, amongst other issues (4-8). These complications threaten the success of a graft and may further lead to the death of patients who received kidney transplantation (9-11). Therefore, exploring therapeutic approaches that reduce the occurrence of these post-transplant complications is crucial to improve the clinical outcomes of patients receiving kidney transplantation.

Vitamin K is a hydrophobic vitamin that serves as a cofactor of the enzyme γ-glutamyl carboxylase to activate several vitamin K-dependent proteins, thereby improving vascular and bone health (12). Recently, several studies have explored the effect of vitamin K on improving clinical outcomes (such as renal function, vascular calcification, and all-cause mortality) in patients receiving kidney transplantation (13-20); however, these findings are contested. For example, one previous study found that a higher vitamin K status was related to increased renal function in patients receiving kidney transplantation (20). Additionally, vitamin K sufficiency is correlated with lower all-cause mortality in these patients (15). However, another study found that vitamin K supplementation did not reduce vascular stiffness, vascular calcification, or renal function in patients receiving kidney transplantation, which indicated that vitamin K supplementation had no influence on improving the clinical outcomes of these patients (19). As a result, whether vitamin K improves clinical outcomes in patients receiving kidney transplantation should be further explored.

Accordingly, this meta-analysis was performed to explore the correlation of vitamin K status with all-cause mortality, renal function, inflammation, as well as vascular and bone health in patients receiving kidney transplantation.

Materials and methods

Search strategy. Electronic databases (EMBASE, PubMed, and Cochrane) were used to screen the papers relating to the effects of vitamin K status on clinical outcomes of patients

who received kidney transplantation from conception to December 2022. Key words and medical subject headings were applied, including 'vitamin K', 'VK', 'vitamin-K', 'V-K', 'kidney transplant', 'renal transplant', 'kidney transplantation', 'renal transplantation', 'kidney graft', and 'renal graft'.

Eligibility criteria. Inclusion criteria for study screening were: i) Patients >18 years old; ii) patients received a kidney transplant; iii) studies assessed the impact of vitamin K status or vitamin K supplementation on clinical outcomes after kidney transplantation; iv) studies involved at least one clinical outcomes of interest to the present study; and v) published in English. The exclusion criteria were: i) Reviews, case reports, or letters; or ii) had no available data for extraction.

The clinical outcomes of interest in the present study were: i) All-cause mortality; ii) renal function indexes; iii) and C-reactive protein (CRP).

Study selection. In the present meta-analysis, two reviewers independently completed the study screening. In brief, the titles and abstracts were assessed for preliminary screening. Then, the full texts which met the inclusion criteria were downloaded and assessed. The studies which met the exclusion criteria were ineligible for inclusion, and the excluded cause was recorded. Additionally, the relevant publications lists were also identified. Any disagreements were resolved by conversation and reaching a consensus. For studies with overlapping populations, those with a larger population or a longer follow-up period were included.

Data collection and risk of bias. Two reviewers independently finished the data collection and assessment of bias risk. The disagreements were resolved by consensus. The extracted data included authors' names, publication year, study design, demographic information of patients, and outcomes. The Newcastle-Ottawa Scale criteria were utilized to assess the risk of bias, involving 3 domains: Selection, comparability, and outcome (21). The risk of bias in the included studies was classified as low risk (score, >8), medium risk (score, 5-7), or high risk (score, ≤4).

Statistical analysis. The analyses were completed per the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) using Stata (version 14.0, StataCorp LP). In the present meta-analysis, normal vitamin K status or vitamin K supplementation was considered as the experimental group; while vitamin K deficiency or no vitamin K supplementation was considered as the control group. Relative risk (RR) with 95% confidence intervals (CIs) was used for dichotomous outcomes, and mean difference (MD) with 95% CI was used for continuous outcomes. The heterogeneity was determined using I^2 statistics: If $I^2 \leq 50.0\%$ and/or $P \geq 0.05$, the heterogeneity was considered insignificant, and the fixed effects model was used; otherwise, the random effects model was used (22). The sensitivity analysis was performed by omitting each study and then repeating the analysis. Egger's and Begg's tests were utilized to evaluate publication bias and $P<0.05$ was considered to indicate a statistically significant difference. R version 3.6 and R studio version 4.2.2 were utilized for analyses (23,24).

Results

Study screening procedure. A total of 393 records were identified through searching of databases, including 161 records from EMBASE, 187 records from PubMed, and 45 records from Cochrane, of which 108 records were excluded as duplicates, leaving 285 records to be screened. A further 264 records were excluded after screening of the titles and abstracts, including 172 reviews or meta-analyses, 89 irrelevant studies, and 3 case reports. Subsequently, 21 full-text records were assessed for eligibility, and 14 records with no relevant data reported were further excluded. Ultimately, 7 records were included in the present meta-analysis (Fig. 1).

Characteristics of the included studies. The included studies were published between 2012 and 2021 in various countries, including the Netherlands, Lebanon, the Kingdom of Belgium, and the United Kingdom (14-20). Regarding study design, there were 5 cohort studies (14,15,17,18,20), 1 subgroup analysis of a single-arm trial (16), and 1 randomized controlled trial (19). Notably, 1,752 patients receiving kidney transplantation were involved, including 1,101 patients in the experimental group and 651 patients in the control group. The detailed information on the included studies is listed in Table I.

Quality assessment. The included studies were assessed using the Newcastle-Ottawa Scale criteria, which suggested that 1 study was ranked as low risk of bias with a total score of 8 (18). Additionally, 5 studies were ranked as medium risk of bias with a range of total scores from 5 to 7 (14,15,17,19,20). Notably, 1 study was ranked as a high risk of bias with a total score of 4 (16); in detail, the scores of the selection bias, comparability bias, and outcome bias were evaluated as 1, 2 and 1, respectively (Table II).

All-cause mortality. A total of 3 studies reported all-cause mortality. The fixed effects model revealed that all-cause mortality was reduced in the experimental group compared to the control group [RR (95% CI): 0.72 (0.60-0.86), $P<0.001$]. Heterogeneity did not exist among studies ($I^2=45\%$, $P=0.160$; Fig. 2).

Renal function indexes. A total of 3 studies reported the estimated glomerular filtration rate (eGFR). The random effects model suggested that eGFR was increased in the experimental group compared with the control group [MD (95% CI): 9.87 (1.48-18.26), $P=0.021$). Heterogeneity existed among these studies ($I^2=81\%$, $P=0.005$) (Fig. 3A). Additionally, five studies reported creatinine. After the random effects model was applied, it was found that creatinine did not differ between the two groups (MD (95% CI): -1.24 (-3.27-0.79), $P=0.231$). Heterogeneity existed among these studies ($I^2=100\%$, $P<0.001$; Fig. 3B). Moreover, five studies reported albumin. The random effects model revealed that albumin was not different between the two groups [MD (95% CI): 0.07 (-1.35-1.49), $P=0.923$]. Heterogeneity existed among these studies ($I^2=90\%$, $P<0.001$; Fig. 3C).

CRP. CRP was reported in four studies. Notably, the random effects model showed that CRP did not differ between the experimental group and the control group [MD (95% CI):

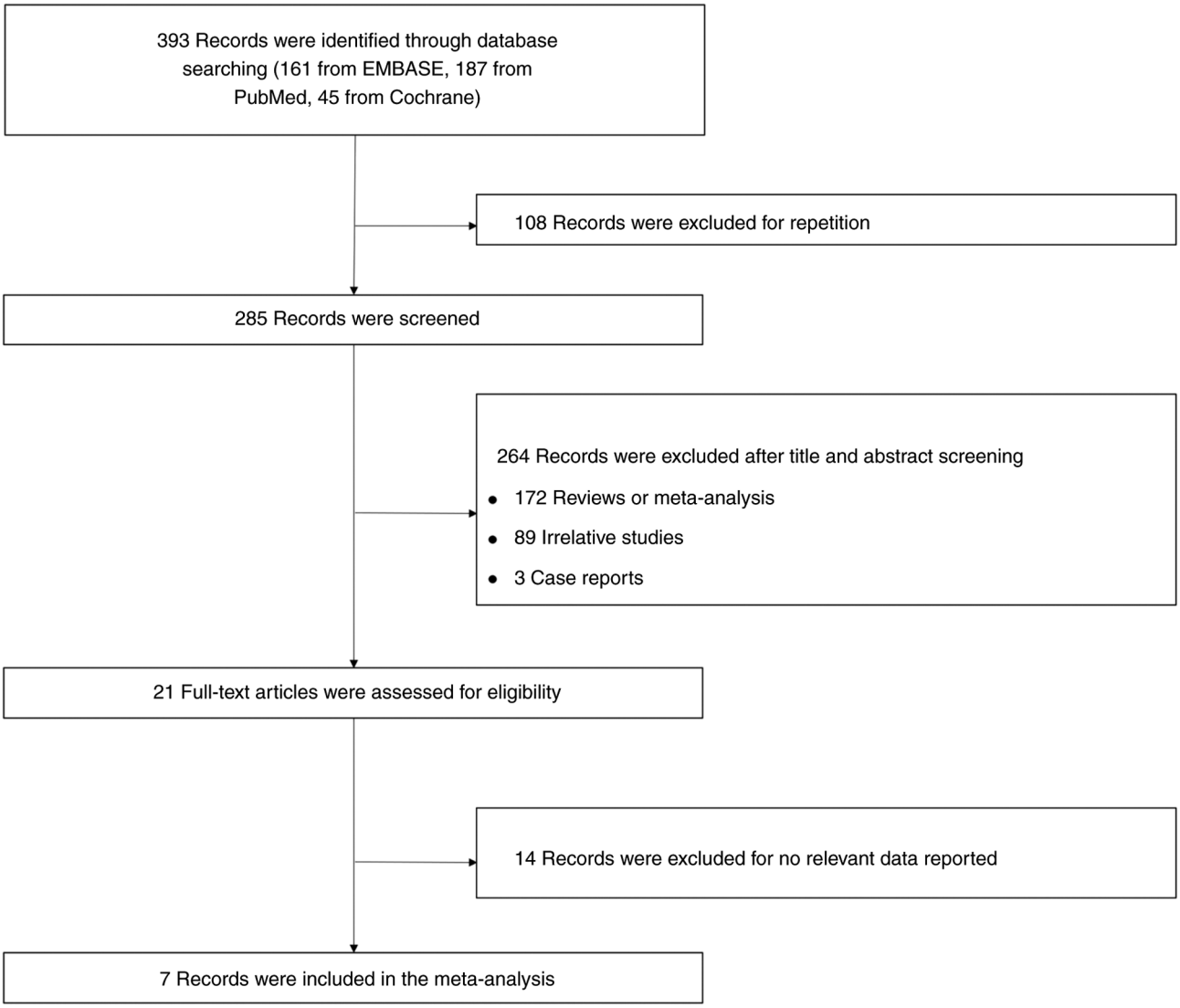

Figure 1. Flow diagram of the search criteria and inclusion of the selected articles.

-2.25 (-5.47-0.97), P=0.171]. Heterogeneity existed among these studies (I^2=97%, P<0.001; Fig. 4).

Cardiovascular and bone health indexes. There were 5 studies that reported systolic blood pressure. After the random effects model was applied, it was found that systolic blood pressure did not differ between the experimental group and the control group [MD (95% CI): -1.55 (-5.34-2.25), P=0.424]. Heterogeneity existed among these studies (I^2=76%, P=0.003; Fig. 5A). Additionally, 3 studies reported diastolic blood pressure. The fixed effects model showed that diastolic blood pressure remained unchanged between the two groups [MD (95% CI): -1.30 (-3.24-0.64), P=0.188]. Heterogeneity did not exist among these studies (I^2=42%, P=0.181; Fig. 5B). There were 4 studies that reported triglycerides. The random effects model suggested that triglycerides did not differ between the two groups [MD (95% CI): -16.61 (-59.16-25.94), P=0.444] with heterogeneity among these studies (I^2=96%, P<0.001; Fig. 5C). Moreover, 5 studies reported hemoglobin. The random effects model showed that no difference in hemoglobin was found between the two groups [MD (95% CI): 5.12 (-0.88-11.12), P=0.094] with heterogeneity among these studies (I^2=90%, P<0.001; Fig. 5D).

A total of 3 studies reported calcium. The fixed effects model found that calcium remained unchanged between the two groups [MD (95% CI): 0.04 (-0.06-0.14), P=0.468) without heterogeneity among these studies (I^2=0%, P=0.649; Fig. 5E). There were 4 studies reported on 25-hydroxyvitamin D levels. The random effects model suggested that 25-hydroxyvitamin D did not differ between the two groups [MD (95% CI): -3.16 (-7.03-0.72); P=0.110] with heterogeneity among these studies (I^2=71%, P=0.015; Fig. 5F).

Publication bias and sensitivity analysis. Begg's test and Egger's test were performed to estimate the potential publication bias, which indicated that no publication bias existed for all-cause mortality, eGFR, creatinine, albumin, CRP, systolic blood pressure, diastolic blood pressure, triglycerides, hemoglobin, calcium, and 25-hydroxyvitamin D (all P>0.05; Table III).

The sensitivity analysis showed that omitting Keyzer *et al* (15) or van Ballegooijen *et al* (18) resulted in eGFR

Table I. Details of the included studies.

First author, year	Country	Study design	Sample size of cohorts, n	Age in years, mean ± SD	Male, n (%)	Outcomes	(Ref.)
Boxma *et al*, 2012	Netherlands	Cohort	Experimental, 30; Control, 30	Experimental, 55.0±NK; Control, 57.0±NK	Experimental: 15 (50.0) Control: 15 (50.0)	Creatinine, CRP, systolic blood pressure	(14)
Keyzer *et al*, 2015	Netherlands	Cohort	Experimental, 130; Control, 129	Experimental, 48.1±12.6; Control, 54.6±10.8	Experimental: 70 (54.0) Control: 70 (54.0)	All-cause mortality, eGFR, albumin, CRP, triglycerides, hemoglobin, calcium	(15)
Mansour *et al*, 2017	Lebanese	Subgroup analysis of the single-arm trial	Experimental, 56; Control, 56	NK	NK	Creatinine, albumin, systolic blood pressure, diastolic blood pressure, hemoglobin, 25-hydroxyvitamin D	(16)
Evenepoel *et al*, 2018	The Kingdom of Belgium	Cohort	Experimental, 155; Control, 159	Experimental, 51.6±14.4; Control, 57.6±11.0	NK	Creatinine, CRP triglycerides, calcium, 25-hydroxyvitamin D	(17)
van Ballegooijen *et al*, 2020	Netherlands	Cohort	Experimental, 107; Control, 108	Experimental, 50.3±12.1; Control, 51.6±11.2	Experimental: 59 (55.0) Control: 68 (63.0)	All-cause mortality, eGFR, albumin, CRP, systolic blood pressure, diastolic blood pressure, triglycerides, hemoglobin	(18)
Lees *et al*, 2021	United Kingdom	Randomized controlled trial	Experimental, 45; Control, 45	Experimental, 5 6.3±11.1; Control, 58.9±7.8	Experimental, 32 (71.7) Control: 31 (68.9)	All-cause mortality, eGFR, creatinine, albumin, systolic blood pressure, diastolic blood pressure, triglycerides, hemoglobin, calcium, 25-hydroxyvitamin D	(19)
Kremer *et al*, 2021	Netherlands	Cohort	Experimental, 578; Control, 124	Experimental, 56.0±13.0; Control, 53.0±14.0	Experimental, 341 (59.0); Control, 79 (64.0)	Creatinine, systolic blood pressure, hemoglobin, 2 5-hydroxyvitamin D	(20)

CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; NK, unknown.

Table II. Assessment of the risk of bias using the Newcastle-Ottawa Scale criteria.

First author, year	Selection	Comparability	Outcome	Total score	(Ref.)
Boxma *et al*, 2012	2	1	2	5	(14)
Keyzer *et al*, 2015	3	1	2	6	(15)
Mansour *et al*, 2017	1	2	1	4	(16)
Evenepoel *et al*, 2018	2	2	1	5	(17)
van Ballegooijen *et al*, 2020	4	1	3	8	(18)
Lees *et al*, 2021	4	1	2	7	(19)
Kremer *et al*, 2021	3	1	3	7	(20)

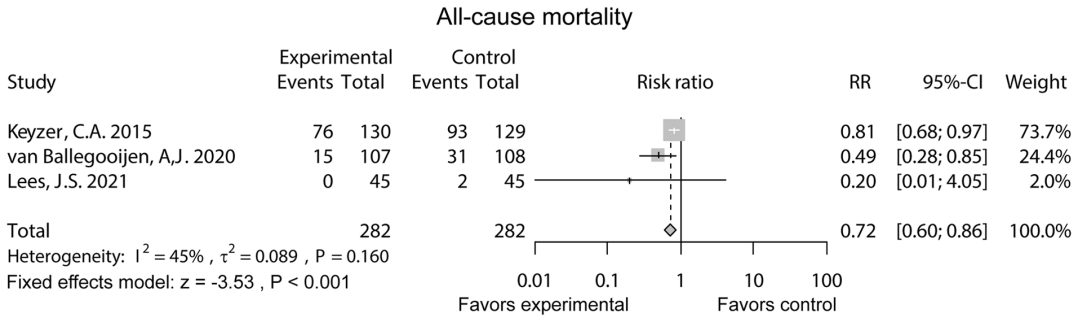

Figure 2. Comparison of all-cause mortality between the experimental group and the control group. RR, relative risk; CI, confidence interval.

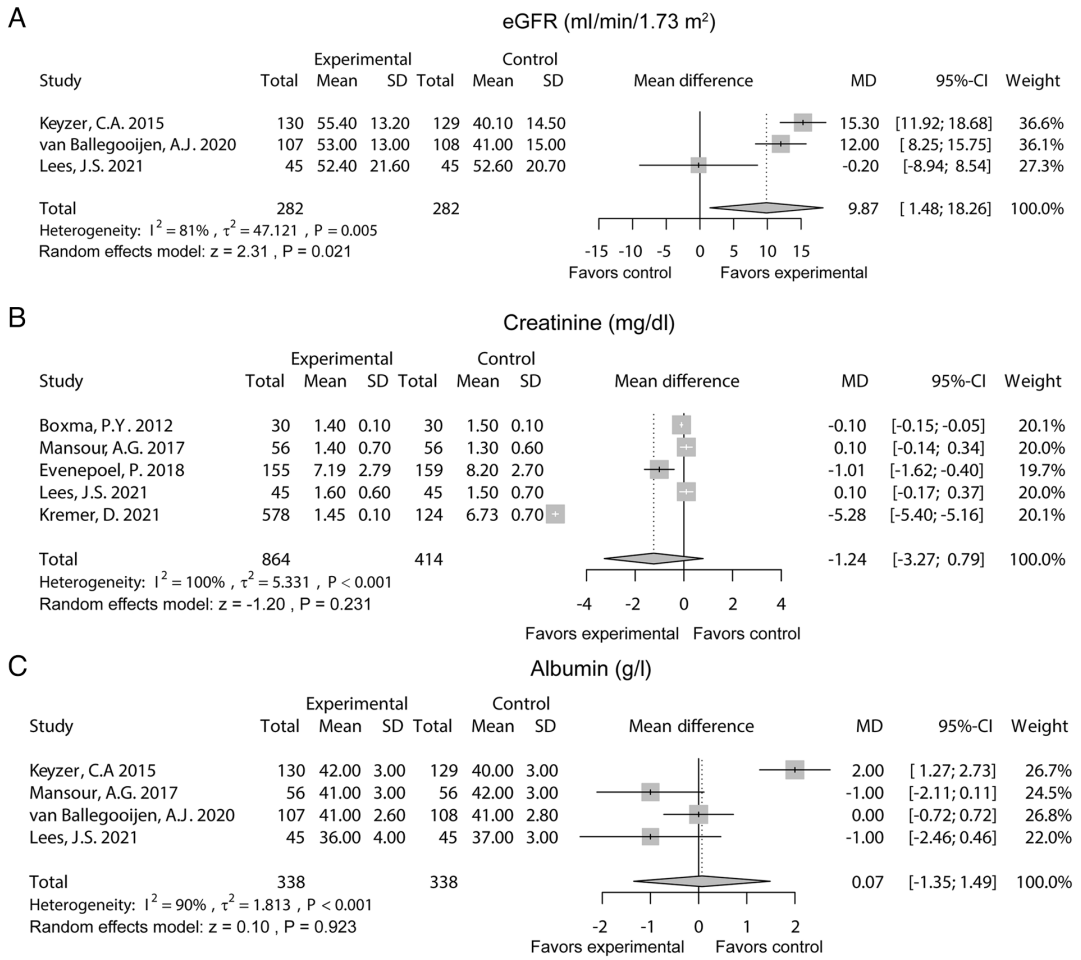

Figure 3. Comparison of renal function indexes between the experimental group and the control group. Pooled analysis of (A) eGFR, (B) creatine, and (C) albumin. MD, mean difference; eGFR, estimated glomerular filtration rate.

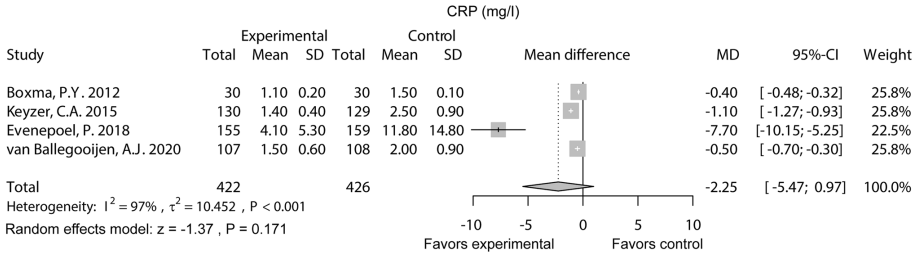

Figure 4. Comparison of CRP between the experimental group and the control group. CRP, c-reactive protein.

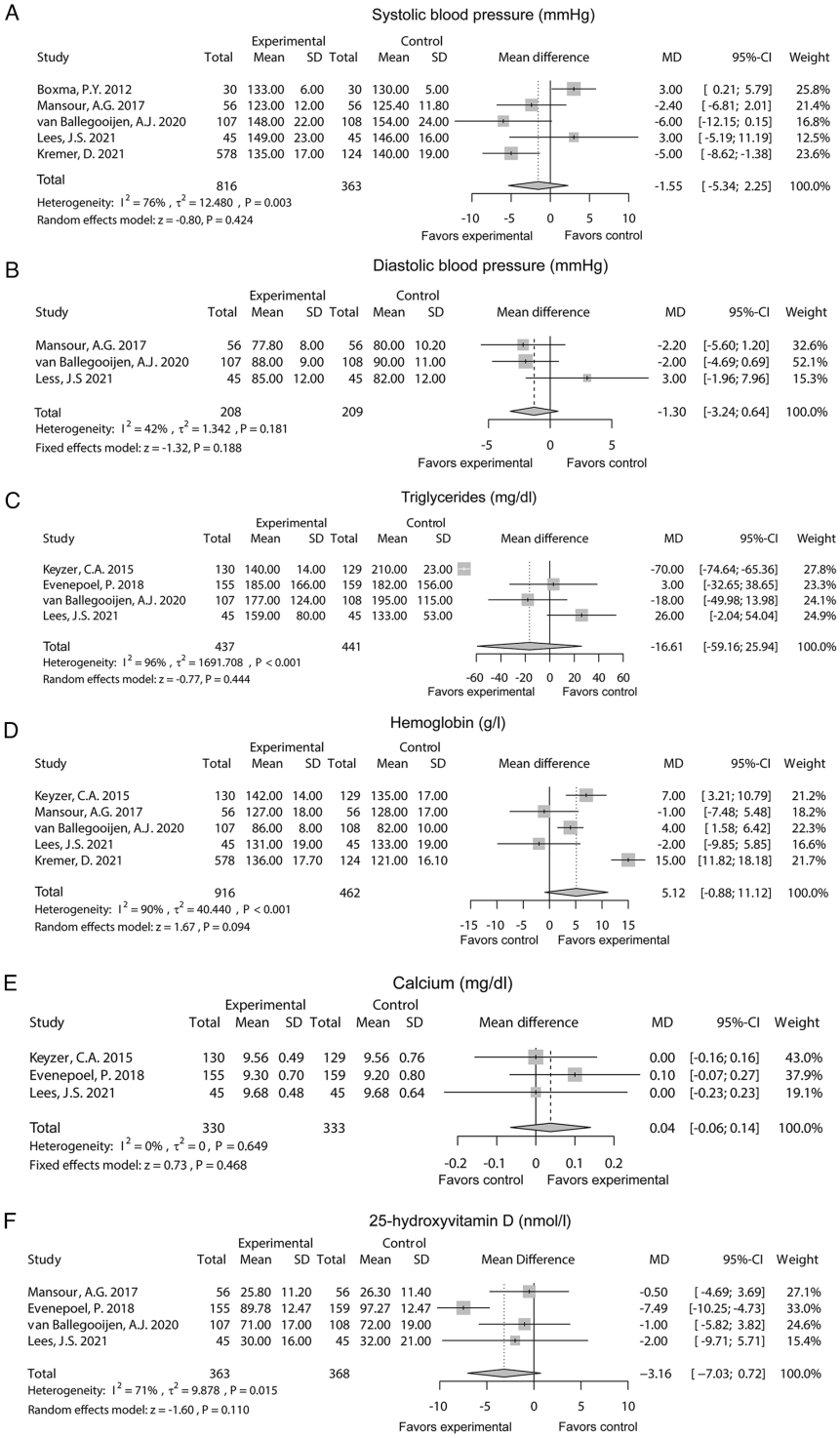

Figure 5. Comparison of vascular and bone health indexes between the experimental group and the control group. Pooled analysis of systolic (A) blood pressure, (B) diastolic blood pressure, (C) triglycerides, (D) hemoglobin, (E) calcium, and (F) 25-hydroxyvitamin D.

Table III. Publication bias.

Outcomes	Number of included studies	P-value, Begg's test	P-value, Egger's test
All-cause mortality	3	0.602	0.310
eGFR	3	0.117	0.173
Creatinine	5	0.327	0.644
Albumin	4	0.497	0.351
CRP	4	0.497	0.192
Systolic blood pressure	5	1.000	0.560
Diastolic blood pressure	3	0.120	0.300
Triglycerides	4	0.500	0.060
Hemoglobin	5	1.000	0.592
Calcium	3	0.602	0.854
25-hydroxyvitamin D	4	1.000	0.265

eGFR, estimated glomerular filtration rate; CRP, C-reactive protein.

Table IV. Sensitivity analysis.

Omitted study	Estimate	95% Confidence interval	
		Lower	Upper
All-cause mortality, relative risk			
Keyzer *et al*, 2015	0.47	0.27	0.81
van Ballegooijen *et al*, 2020	0.80	0.66	0.95
Lees *et al*, 2021	0.73	0.61	0.88
Combined	0.72	0.60	0.86
eGFR, ml/min/1.73 m^2, MD			
Keyzer *et al*, 2015	6.57	-5.32	18.45
van Ballegooijen *et al*, 2020	8.10	-7.06	23.25
Lees *et al*, 2021	13.75	10.53	16.98
Combined	9.87	1.48	18.26
Creatinine, mg/dl, MD			
Boxma *et al*, 2012	-1.53	-4.04	0.99
Mansour *et al*, 2017	-1.58	-4.05	0.90
Evenepoel *et al*, 2018	-1.30	-3.90	1.31
Lees *et al*, 2021	-1.58	-4.05	0.90
Kremer *et al*, 2021	-0.16	-0.57	0.26
Combined	-1.24	-3.27	0.79
Albumin, g/l, MD			
Keyzer *et al*, 2015	-0.51	-1.27	0.25
Mansour *et al*, 2017	0.41	-1.30	2.12
van Ballegooijen *et al*, 2020	0.06	-1.96	2.08
Lees *et al*, 2021	0.37	-1.35	2.09
Combined	0.07	-1.35	1.49
CRP, mg/l, MD			
Boxma *et al*, 2012	-2.95	-7.31	1.42
Keyzer *et al*, 2015	-2.72	-7.31	1.87
Evenepoel *et al*, 2018	-0.66	-1.09	-0.23
van Ballegooijen *et al*, 2020	-2.91	-7.32	1.49
Combined	-2.25	-5.47	0.97

Table IV. Continued.

Omitted study	Estimate	95% Confidence interval	
		Lower	Upper
Systolic blood pressure, mmHg, MD			
Boxma *et al*, 2012	-3.66	-6.09	-1.23
Mansour *et al*, 2017	-1.33	-6.23	3.56
van Ballegooijen *et al*, 2020	-0.65	-4.80	3.50
Lees *et al*, 2021	-2.22	-6.43	1.98
Kremer *et al*, 2021	-0.47	-4.73	3.79
Combined	-1.55	-5.34	2.25
Diastolic blood pressure, mmHg, MD			
Mansour *et al*, 2017	-0.87	-3.23	1.50
van Ballegooijen *et al*, 2020	-0.54	-3.34	2.26
Lees *et al*, 2021	-2.08	-4.18	0.03
Combined	-1.30	-3.24	0.64
Triglycerides, mg/dl, MD			
Keyzer *et al*, 2015	4.63	-21.71	30.97
Evenepoel *et al*, 2018	-22.10	-77.78	33.58
van Ballegooijen *et al*, 2020	-15.38	-74.05	43.29
Lees *et al*, 2021	-31.25	-75.69	13.20
Combined	-16.61	-59.16	25.94
Hemoglobin, g/l, MD			
Keyzer *et al*, 2015	4.47	-3.30	12.24
Mansour *et al*, 2017	6.48	-0.15	13.12
van Ballegooijen *et al*, 2020	5.27	-2.60	13.14
Lees *et al*, 2021	6.55	0.13	12.96
Kremer *et al*, 2021	3.06	-0.71	6.82
Combined	5.12	-0.88	11.12
Calcium, mg/dl, MD			
Keyzer *et al*, 2015	0.07	-0.07	0.20
Evenepoel *et al*, 2018	0.00	-0.13	0.13
Lees *et al*, 2021	0.05	-0.07	0.16
Combined	0.04	-0.06	0.14
25-hydroxyvitamin D, nmol/l, MD			
Mansour *et al*, 2017	-4.12	-8.76	0.53
Evenepoel *et al*, 2018	-0.90	-3.82	2.02
van Ballegooijen *et al*, 2020	-3.78	-8.65	1.09
Lees *et al*, 2021	-3.29	-7.99	1.40
Combined	-3.16	-7.03	0.72

MD, mean difference; CI, confidence interval; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein.

remaining unchanged between the experimental group and the control group. Meanwhile, omitting Evenepoel *et al* (17) resulted in a decrease in CRP in the experimental group compared to the control group. Omitting Boxma *et al* (14) may have contributed to systolic blood pressure reduction in the experimental group vs. the control group. Additionally, hemoglobin was increased in the experimental group compared to the control group after omitting Lees *et al* (19). Apart from these, the RR of all-cause mortality, as well as the MD of creatinine, albumin, diastolic blood pressure, triglycerides, calcium, and 25-hydroxyvitamin D did not significantly change by omitting any single study, which suggested the stability of this meta-analysis (Table IV).

Discussion

Vitamin K deficiency is very common in patients receiving kidney transplantation, which may ultimately contribute to

an increase in all-cause mortality (15). Therefore, several studies have explored the effect of vitamin K sufficiency on all-cause mortality in patients receiving kidney transplantation (15,18,19). A previous study found that higher vitamin K status is related to reduced all-cause mortality in patients receiving kidney transplantation (15). Additionally, another study also showed that vitamin K sufficiency estimates decreased premature mortality in patients receiving kidney transplantation (18). The present meta-analysis discovered that higher vitamin K status or supplementation of vitamin K was related to decreased all-cause mortality in patients receiving kidney transplantation. The possible reasons may be: i) Vitamin K may inhibit the progression of vascular calcification by increasing the activity of matrix Gla protein (MGP) by accelerating γ-carboxylation (25,26); ii) vitamin K may also improve bone health by regulating osteocalcin (27,28). Notably, vascular calcification and bone damage were two major causes of mortality in patients receiving kidney transplantation (29), and vitamin K can improve these situations as discussed above. As a result, vitamin K may reduce all-cause mortality in these patients.

This meta-analysis also explored the effect of vitamin K on improving renal function in patients receiving kidney transplantation, and it was found that a higher vitamin K status or supplementation of vitamin K was related to increased eGFR in patients receiving kidney transplantation. A possible reason would be that vitamin K may activate MGP through carboxylation to improve renal function, which further led to the increase of eGFR (30). Thus, a positive correlation was found between vitamin K status or supplementation and eGFR in patients receiving kidney transplantation. Notably, heterogeneity existed among the analyzed 3 studies; meanwhile, sensitivity analysis displayed that omitting Keyzer *et al* (15) or van Ballegooijen *et al* (18) affected the results of eGFR, which indicated the notable weight these two articles had on the outcomes. Thus, these findings still require additional studies to verify these results. In addition, the present meta-analysis also observed that higher vitamin K status or supplementation of vitamin K was slightly associated with reduced CRP in patients receiving kidney transplantation, but this was statistically significant. A possible interpretation may be that vitamin K may reduce inflammation by regulating the nuclear factor κB pathway, a Gla-rich protein (31,32). However, heterogeneity existed among the four analyzed studies. Omitting Evenepoel *et al* (17) affected the results of CRP, highlighting the notable weight of this study on the results. Thus, this finding still requires further exploration.

The effect of vitamin K on improving vascular and bone health is contested based on previous studies (15,16,18-20). The present meta-analysis found that vitamin K status or supplementation of vitamin K was not related to systolic blood pressure, diastolic blood pressure, triglycerides, hemoglobin, calcium, or 25-hydroxyvitamin D in patients receiving kidney transplantation. A possible reason may be that the disease conditions were complicated in patients after kidney transplantation, and the change of a single factor (vitamin K) does not greatly influence these vascular and bone health indexes; thus, the benefits of vitamin K alone in improving vascular and bone health would not be notable (27,33,34). Heterogeneity of systolic blood pressure, triglycerides, hemoglobin, calcium, and 25-hydroxyvitamin D existed among the analyzed studies; meanwhile, sensitivity analysis found that omitting Boxma *et al* (14) and Lees *et al* (19) affected the results of systolic blood pressure and hemoglobin, respectively. this highlighted the notable weight of these two studies on the corresponding results. Therefore, these findings require further studies to confirm the results.

Although several interesting findings were discovered in the present meta-analysis, some limitations should be noted: i) Although robustness assessed by sensitivity analysis was acceptable, omitting certain articles did affect the corresponding results; thus, additional studies are required to further improve the reliability of the results; ii) most of the included studies were cohort studies; thus, the findings of this meta-analysis should be further validated; and iii) one included study was ranked as high risk of bias according to the Newcastle-Ottawa Scale criteria, which may have interfered with the results.

In conclusion, vitamin K may improve all-cause mortality and renal function in patients receiving kidney transplantation. Clinically, the intake of vitamin K after kidney transplantation may improve the clinical outcomes of these patients. However, additional large-scale studies are required to validate these findings.

Acknowledgements

Not applicable.

Funding

This study was supported by the Basic Research Program of Guizhou Province (Guizhou Science and Technology Combination Foundation) [grant no. ZK (2023) General 380].

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ZS and YN contributed to the research design, data analysis, writing the paper, and critical review of the paper. KZ, GL, and FY collected the data and wrote the paper. SC and LJ contributed to the data analysis and critical review of the paper. ZS and YN confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Wouk N: End-stage renal disease: Medical management. Am Fam Physician 104: 493-499, 2021.
2. Wang Y, Hemmelder MH, Bos WJW, Snoep JD, de Vries APJ, Dekker FW and Meuleman Y: Mapping health-related quality of life after kidney transplantation by group comparisons: A systematic review. Nephrol Dial Transplant 36: 2327-2339, 2021.
3. Axelrod DA, Schnitzler MA, Xiao H, Irish W, Tuttle-Newhall E, Chang SH, Kasiske BL, Alhamad T and Lentine KL: An economic assessment of contemporary kidney transplant practice. Am J Transplant 18: 1168-1176, 2018.
4. Agrawal A, Ison MG and Danziger-Isakov L: Long-term infectious complications of kidney transplantation. Clin J Am Soc Nephrol 17: 286-295, 2022.
5. Sotomayor CG, Benjamens S, Gomes-Neto AW, Pol RA, Groothof D, Te Velde-Keyzer CA, Chong G, Glaudemans AWJM, Berger SP, Bakker SJL and Slart RHJA: Bone mineral density and aortic calcification: evidence for a bone-vascular axis after kidney transplantation. Transplantation 105: 231-239, 2021.
6. Ponticelli C, Favi E and Ferraresso M: New-onset diabetes after kidney transplantation. Medicina (Kaunas) 57: 250, 2021.
7. Ponticelli C, Reggiani F and Moroni G: Delayed graft function in kidney transplant: Risk factors, Consequences and prevention strategies. J Pers Med 12, 2022.
8. Bahl D, Haddad Z, Datoo A and Qazi YA: Delayed graft function in kidney transplantation. Curr Opin Organ Transplant 24: 82-86, 2019.
9. Haberal M, Boyvat F, Akdur A, Kirnap M, Ozcelik U and Yarbug Karakayali F: Surgical complications after kidney transplantation. Exp Clin Transplant 14: 587-595, 2016.
10. Ammi M, Daligault M, Sayegh J, Abraham P, Papon X, Enon B and Picquet J: Evaluation of the vascular surgical complications of renal transplantation. Ann Vasc Surg 33: 23-30, 2016.
11. Ghadiani MH, Peyrovi S, Mousavinasab SN and Jalalzadeh M: Delayed graft function, allograft and patient srvival in kidney transplantation. Arab J Nephrol Transplant 5: 19-24, 2012.
12. Cozzolino M, Mangano M, Galassi A, Ciceri P, Messa P and Nigwekar S: Vitamin K in chronic kidney disease. Nutrients 11: 168, 2019.
13. Eelderink C, Kremer D, Riphagen IJ, Knobbe TJ, Schurgers LJ, Pasch A, Mulder DJ, Corpeleijn E, Navis G, Bakker SJL, *et al*: Effect of vitamin K supplementation on serum calcification propensity and arterial stiffness in vitamin K-deficient kidney transplant recipients: A double-blind, randomized, placebo-controlled clinical trial. Am J Transplant 23: 520-530, 2023.
14. Boxma PY, van den Berg E, Geleijnse JM, Laverman GD, Schurgers LJ, Vermeer C, Kema IP, Muskiet FA, Navis G, Bakker SJ and de Borst MH: Vitamin K intake and plasma desphospho-uncarboxylated matrix Gla-protein levels in kidney transplant recipients. PLoS One 7: e47991, 2012.
15. Keyzer CA, Vermeer C, Joosten MM, Knapen MH, Drummen NE, Navis G, Bakker SJ and de Borst MH: Vitamin K status and mortality after kidney transplantation: A cohort study. Am J Kidney Dis 65: 474-483, 2015.
16. Mansour AG, Hariri E, Daaboul Y, Korjian S, El Alam A, Protogerou AD, Kilany H, Karam A, Stephan A and Bahous SA: Vitamin K2 supplementation and arterial stiffness among renal transplant recipients-a single-arm, single-center clinical trial. J Am Soc Hypertens 11: 589-597, 2017.
17. Evenepoel P, Claes K, Meijers B, Laurent M, Bammens B, Naesens M, Sprangers B, Pottel H, Cavalier E and Kuypers D: Poor vitamin K status is associated with low bone mineral density and increased fracture risk in end-stage renal disease. J Bone Miner Res 34: 262-269, 2019.
18. van Ballegooijen AJ, Beulens JWJ, Keyzer CA, Navis GJ, Berger SP, de Borst MH, Vervloet MG and Bakker SJL: Joint association of vitamins D and K status with long-term outcomes in stable kidney transplant recipients. Nephrol Dial Transplant 35: 706-714, 2020.
19. Lees JS, Rankin AJ, Gillis KA, Zhu LY, Mangion K, Rutherford E, Roditi GH, Witham MD, Chantler D, Panarelli M, *et al*: The ViKTORIES trial: A randomized, double-blind, placebo-controlled trial of vitamin K supplementation to improve vascular health in kidney transplant recipients. Am J Transplant 21: 3356-3368, 2021.
20. Kremer D, Groothof D, Keyzer CA, Eelderink C, Knobbe TJ, Post A, van Londen M, Eisenga MF, TransplantLines Investigators, Schurgers LJ, *et al*: Kidney function-dependence of vitamin K-status parameters: Results from the transplantlines biobank and cohort studies. Nutrients 13: 3069, 2021.
21. Wells GA, Shea B, O'Connell D, je Peterson, Welch V, Losos M and Tugwell P: The newcastle-ottawa scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Ottawa Hospital Research Institute, Ottawa, ON, 2015.
22. Higgins JP, Thompson SG, Deeks JJ and Altman DG: Measuring inconsistency in meta-analyses. BMJ 327: 557-560, 2003.
23. R Core Team: A language and environment for statistical computing. R foundation for statistical computing, Vienna, 2013. http://www.R-project.org/.
24. RStudio Team: RStudio: Integrated development for R. RStudio, Inc., Boston, MA. 2015. http://www.rstudio.com/.
25. Shioi A, Morioka T, Shoji T and Emoto M: The inhibitory roles of vitamin K in progression of vascular calcification. Nutrients 12: 583, 2020.
26. Roumeliotis S, Duni A, Vaios V, Kitsos A, Liakopoulos V and Dounousi E: Vitamin K supplementation for prevention of vascular calcification in chronic kidney disease patients: Are we there yet? Nutrients 14: 925, 2022.
27. Alonso N, Meinitzer A, Fritz-Petrin E, Enko D and Herrmann M: Role of vitamin K in bone and muscle metabolism. Calcif Tissue Int 112: 178-196, 2023.
28. Fusaro M, Cianciolo G, Brandi ML, Ferrari S, Nickolas TL, Tripepi G, Plebani M, Zaninotto M, Iervasi G, La Manna G, *et al*: Vitamin K and osteoporosis. Nutrients 12: 3625, 2020.
29. Bellone F, Cinquegrani M, Nicotera R, Carullo N, Casarella A, Presta P, Andreucci M, Squadrito G, Mandraffino G, Prunestì M, *et al*: Role of vitamin K in chronic kidney disease: A focus on bone and cardiovascular health. Int J Mol Sci 23: 5282, 2022.
30. Wei FF, Drummen NE, Thijs L, Jacobs L, Herfs M, Van't Hoofd C, Vermeer C and Staessen JA: Vitamin-K-dependent protection of the renal microvasculature: Histopathological studies in normal and diseased kidneys. Pulse (Basel) 4: 85-91, 2016.
31. Ohsaki Y, Shirakawa H, Miura A, Giriwono PE, Sato S, Ohashi A, Iribe M, Goto T and Komai M: Vitamin K suppresses the lipopolysaccharide-induced expression of inflammatory cytokines in cultured macrophage-like cells via the inhibition of the activation of nuclear factor κB through the repression of IKKα/β phosphorylation. J Nutr Biochem 21: 1120-1126, 2010.
32. Bordoloi J, Dihingia A, Kalita J and Manna P: Implication of a novel vitamin K dependent protein, GRP/Ucma in the pathophysiological conditions associated with vascular and soft tissue calcification, osteoarthritis, inflammation, and carcinoma. Int J Biol Macromol 113: 309-316, 2018.
33. Vermeer C, Shearer MJ, Zittermann A, Bolton-Smith C, Szulc P, Hodges S, Walter P, Rambeck W, Stöcklin E and Weber P: Beyond deficiency: Potential benefits of increased intakes of vitamin K for bone and vascular health. Eur J Nutr 43: 325-335, 2004.
34. Kluch M, Bednarkiewicz P, Orzechowska M, Grzelak P and Kurnatowska I: Vitamin K1 and K2 in the diet of patients in the long term after kidney transplantation. Nutrients 14: 5070, 2022.