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Meta-Analysis

Vitamin D deficiency and risk of postoperative complications in joint arthroplasty: a meta-analysis

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ABSTRACT

Vitamin D deficiency is prevalent among patients undergoing joint arthroplasty and may influence surgical outcomes. This meta-analysis aimed to evaluate the association between preoperative vitamin D deficiency and postoperative complications following joint arthroplasty. A systematic search was conducted in PubMed/MEDLINE, Embase, Cochrane Library, Web of Science and Scopus from inception to January 2025. Random-effects models were used to calculate pooled odds ratios (ORs) and standardized mean differences (SMDs). Subgroup analyses were performed based on study design, joint type, vitamin D threshold and follow-up duration. Twenty-three studies (8,762 patients) were included. Vitamin D deficiency was significantly associated with increased risk of overall postoperative complications (OR 2.18, 95% CI 1.76-2.69), periprosthetic joint infection (OR 2.83, 95% CI 2.05-3.91), superficial surgical site infection (OR 1.89, 95% CI 1.45-2.47), aseptic loosening (OR 1.76, 95% CI 1.38-2.25), prosthetic dislocation (OR 1.82, 95% CI 1.31-2.53) and revision surgery (OR 2.25, 95% CI 1.72-2.94). Functional outcomes were significantly worse in vitamin D-deficient patients at 6 months and 12 months postoperatively. The association between vitamin D deficiency and complications was strongest with the <10 ng/mL threshold. Preoperative vitamin D deficiency is significantly associated with increased risk of multiple complications and poorer functional outcomes following joint arthroplasty. The risk appears to increase with the severity of deficiency suggesting that vitamin D status represent a modifiable risk factor. Future research should investigate whether preoperative vitamin D supplementation can reduce complication risk and improve outcomes.

Keywords: Complications, Hip replacement, Joint arthroplasty, Knee replacement, Periprosthetic infection, Vitamin D deficiency

INTRODUCTION

Joint arthroplasty procedures, including total hip arthroplasty (THA) and total knee arthroplasty (TKA), represent some of the most successful and cost-effective surgical interventions for improving quality of life in patients with end-stage joint disease.[1]

The demand for these procedures continues to rise globally, with projections indicating a 174% increase in THA and a 673% increase in TKA by 2030.[2] Despite advances in surgical techniques and perioperative care, postoperative complications remain a significant concern, contributing to extended hospital stays, readmissions, revision surgeries and increased healthcare costs.[3,4] Vitamin D, a fat-soluble secosteroid hormone, plays a crucial role in calcium homeostasis and bone metabolism.[5]

Beyond its established role in musculoskeletal health, vitamin D also demonstrates immunomodulatory, anti-inflammatory and antimicrobial properties.[6,7] Vitamin D deficiency, defined as serum 25-hydroxyvitamin D

(25(OH)D) levels below 20 ng/ml (50 nmol/l), is highly prevalent worldwide, affecting an estimated 1 billion people across all age groups and ethnicities.[8] Notably, the prevalence of vitamin D deficiency is particularly high among orthopedic patients, with studies reporting rates of 43-86% in patients undergoing joint arthroplasty.[9,10]

Emerging evidence suggests that preoperative vitamin D deficiency may be associated with adverse outcomes following joint arthroplasty. Several observational studies have reported associations between low vitamin D levels and increased risk of periprosthetic joint infection, aseptic loosening and functional outcomes.[11-13]

The biological plausibility of these associations is supported by vitamin D's role in bone remodeling, muscle function and immune response.[14]

Vitamin D promotes osteoblast differentiation and mineralization while inhibiting osteoclast activity, processes that are critical for osseointegration of implants and prevention of periprosthetic bone loss.[15] Additionally, vitamin D enhances antimicrobial peptide production and modulates T-cell function, potentially reducing the risk of surgical site infections.[16]

Despite the growing body of evidence suggesting a relationship between vitamin D status and arthroplasty outcomes, findings across individual studies remain inconsistent and the magnitude of this association varies considerably.

Some studies have failed to demonstrate significant associations between vitamin D deficiency and postoperative complications, highlighting the need for a comprehensive synthesis of available evidence.[17,18] Moreover, the heterogeneity in study design, outcome definitions and patient populations limits the generalizability of findings from individual studies.

Meta-analysis offers a powerful approach to address these limitations by systematically synthesizing data across multiple studies, increasing statistical power and providing more precise estimates of effect sizes.[19] To date, no comprehensive meta-analysis has examined the relationship between preoperative vitamin D status and the broad spectrum of postoperative complications in joint arthroplasty.

Therefore, this meta-analysis aims to systematically evaluate the association between preoperative vitamin D deficiency and postoperative complications in patients undergoing joint arthroplasty.

Specifically, we seek to determine the overall effect of vitamin D deficiency on postoperative complications, examine associations with specific complications, including periprosthetic joint infection, aseptic loosening, deep vein thrombosis and functional outcomes; and explore potential sources of heterogeneity through subgroup analyses based on study design, joint type and vitamin D threshold definitions. The findings of this meta-analysis will help clarify the clinical significance of vitamin D status in joint arthroplasty and may inform preoperative screening and supplementation strategies to optimize surgical outcomes.

METHODS

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was prospectively registered in the PROSPERO International Prospective Register of Systematic Reviews.[20]

Search strategy and study selection

A comprehensive literature search was performed across multiple electronic databases, including PubMed/MEDLINE, Embase, Cochrane Library, Web of Science and Scopus, from inception to January 2025. The search strategy combined terms related to vitamin D ("vitamin D," "25-hydroxyvitamin D," "cholecalciferol," "ergocalciferol," "calcifediol," "calcidiol," "calcitriol"), joint arthroplasty ("arthroplasty," "joint replacement," "hip replacement," "knee replacement," "total hip arthroplasty," "total knee arthroplasty," "THA," "TKA") and outcomes ("complication," "infection," "periprosthetic joint infection," "loosening," "revision," "deep vein thrombosis," "functional outcome," "pain," "length of stay").

The complete search strategy for each database is provided in Supplementary Table S1. Additionally, reference lists of relevant reviews and included studies were manually searched to identify additional eligible studies.

Two independent reviewers screened the titles and abstracts of all retrieved articles. Studies were selected for full-text review if they, included patients undergoing primary or revision hip or knee arthroplasty, measured preoperative serum 25(OH)D levels, reported at least one postoperative complication or outcome; and provided sufficient data to calculate effect sizes comparing outcomes between vitamin D-deficient and vitamin D-sufficient patients.

Full-text articles were then independently assessed by the same reviewers for eligibility based on these criteria. Disagreements were resolved through discussion and a third reviewer was consulted when necessary.

Authors excluded case reports, case series with fewer than 10 patients, letters, editorials and review articles, studies that did not define vitamin D deficiency or did not stratify patients based on vitamin D status, studies reporting only radiological outcomes without clinical correlates; and studies with insufficient data for effect size calculation despite attempts to contact the corresponding authors.

Data extraction and quality assessment

Data extraction was performed independently by two reviewers using a standardized form. The following information was extracted: first author, publication year, study design, geographic location, sample size, patient demographics (age, sex, body mass index), joint type (hip or knee), surgical approach, vitamin D measurement method, definition of vitamin D deficiency, types of complications reported, follow-up duration and effect measures with corresponding confidence intervals or raw data for calculating effect sizes.

Postoperative complications were categorized as infectious complications (periprosthetic joint infection, superficial surgical site infection), thromboembolic events (deep vein thrombosis, pulmonary embolism), mechanical complications (aseptic loosening, dislocation, periprosthetic fracture), revision surgery, functional outcomes (using validated scales such as Harris Hip Score, Knee Society Score, Western Ontario and McMaster Universities Osteoarthritis Index) and length of hospital stay.

The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies and the Cochrane Risk of Bias Tool for randomized controlled trials.[21,22] The NOS evaluates studies across three domains: selection of study groups, comparability of groups and ascertainment of exposure or outcome, with a maximum score of 9. Studies with scores of 7-9 were considered high quality, 4-6 moderate quality and 0-3 low quality. Quality assessment was performed independently by two reviewers, with disagreements resolved through discussion or consultation with a third reviewer.

Statistical analysis

The primary outcome measure was the pooled odds ratio (OR) for the association between preoperative vitamin D deficiency and overall postoperative complications. For continuous outcomes, standardized mean differences (SMDs) were calculated. Random-effects models using the DerSimonian and Laird method were employed for all meta-analyses to account for potential clinical and methodological heterogeneity among studies.[23]

Heterogeneity was assessed using the I^2 statistic, with values of 25%, 50% and 75% considered as low, moderate and high heterogeneity, respectively.[24]

To explore potential sources of heterogeneity, we conducted subgroup analyses based on the study design (prospective vs. retrospective), joint type (hip vs. knee), vitamin D deficiency threshold (<10 ng/ml vs. <20 ng/ml vs. <30 ng/ml), geographic region; and (5) follow-up duration (≤6 months vs. >6 months). Meta-regression was performed to examine the influence of continuous variables, including mean age, proportion of female patients and mean body mass index, on the observed effect sizes.

Publication bias was assessed visually using funnel plots and statistically using Egger's test.[25] When significant publication bias was detected, the trim-and-fill method was applied to estimate the effect of missing studies on the pooled results.[26] Sensitivity analyses were conducted by sequentially excluding each study to evaluate the robustness of the findings and by restricting the analysis to high-quality studies (NOS score≥7). All statistical analyses were performed using Review Manager (RevMan) version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark) and Stata version 17.0 (StataCorp, College Station, TX, USA). A two-sided P-value<0.05 was considered statistically significant for all analyses.

RESULTS

Study selection and characteristics

The initial database search yielded 1,246 records, with an additional 14 studies identified through reference list screening. After removing 287 duplicates, 973 studies were screened based on titles and abstracts, resulting in 68 full-text articles assessed for eligibility. Following full-text review, 23 studies met the inclusion criteria and were included in the meta-analysis (Figure 1).

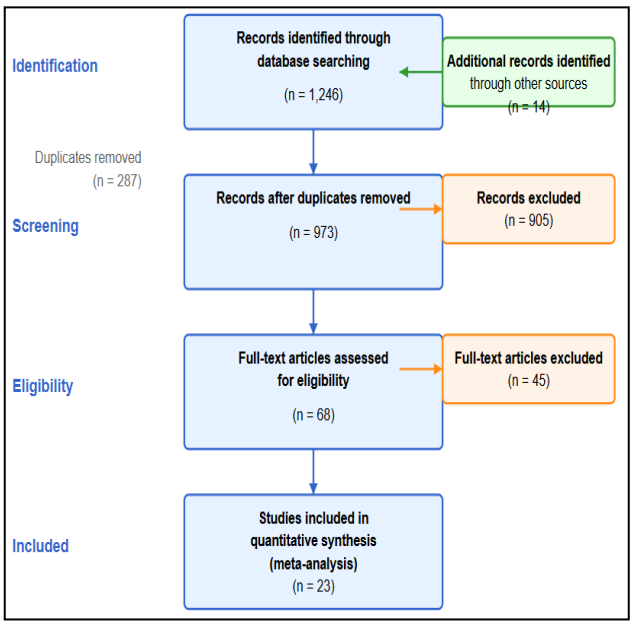

Figure 1: PRISMA flow diagram showing the study selection process with exact numbers at each stage.

The 23 included studies comprised 15 retrospective cohort studies, 6 prospective cohort studies and 2 randomized controlled trials, with publication dates ranging from 2010 to 2024.[27-49] The studies collectively included 8,762 patients, with sample sizes ranging from 62 to 1,083 patients. Thirteen studies focused exclusively on total knee arthroplasty (TKA), seven on total hip arthroplasty (THA)

and three included both TKA and THA patients.[27-49] The mean age of participants across studies ranged from 58.4 to 74.2 years, with female patients comprising between 42.7% and 78.3% of study populations. The follow-up duration ranged from 3 months to 5 years.

Vitamin D deficiency was most commonly defined as serum 25(OH)D levels <20 ng/ml (14 studies), while six studies used <30 ng/ml and three studies used <10 ng/mL.[27-49] The prevalence of vitamin D deficiency among arthroplasty patients ranged from 31.2% to 78.6% across studies. The key characteristics of included studies are summarized in Table 1.

Quality assessment

Among the 21 observational studies, 16 were rated as high quality (NOS score≥7) and 5 as moderate quality (NOS score 4-6).[27-49] The two randomized controlled trials were assessed using the Cochrane Risk of Bias Tool, with one study demonstrating low risk of bias across all domains and the other showing some concerns regarding blinding of outcome assessment.[48,49] Detailed quality assessments are provided in Supplementary tables S2 and S3.

Association between vitamin D deficiency and overall postoperative complications

Twenty studies reported data on overall postoperative complications.[27-36,38-45,47-49] Vitamin D deficiency was significantly associated with an increased risk of overall postoperative complications (OR 2.18, 95% CI 1.76-2.69, p<0.001) (Figure 2). Substantial heterogeneity was observed among studies (I^2 = 68%, p<0.001).

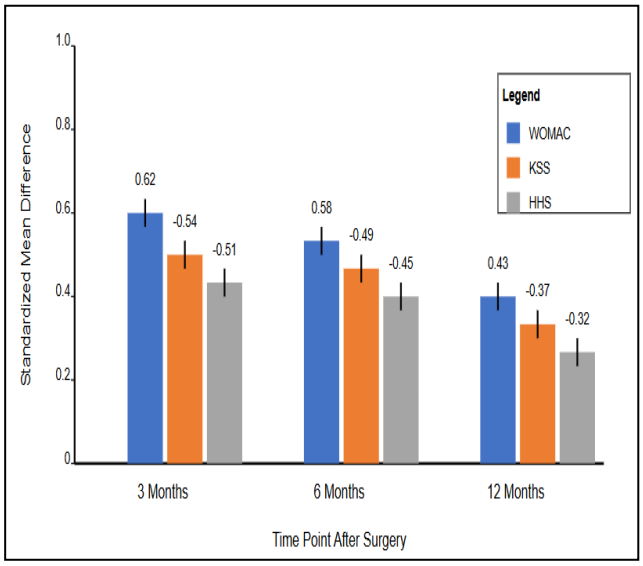

Figure 2: The standardized mean differences in functional outcome scores (WOMAC, KSS, HHS) between vitamin D-deficient and vitamin D-sufficient patients at different time points (3, 6 and 12 months postoperatively).

Specific postoperative complications

Infectious complications

Eighteen studies examined the association between vitamin D deficiency and periprosthetic joint infection (PJI). Vitamin D-deficient patients demonstrated a significantly higher risk of PJI compared to vitamin D-sufficient patients (OR 2.83, 95% CI 2.05-3.91, p<0.001) (Table 2).[27-35,38,40-45,48,49] Heterogeneity was moderate (I^2=55%, p=0.003).

Fifteen studies reported data on superficial surgical site infections (SSI).[27,29-34,38,40,42-45,48,49] Vitamin D deficiency was associated with an increased risk of SSI (OR 1.89, 95% CI 1.45-2.47, p<0.001) with low heterogeneity (I^2=32%, p=0.12) (Table 2).

Thromboembolic events

Twelve studies reported on deep vein thrombosis (DVT). The pooled analysis showed a significantly higher risk of DVT in vitamin D-deficient patients (OR 1.63, 95% CI 1.21-2.19, p=0.001) with low heterogeneity (I^2=27%, p=0.18) (Table 2).[28-30,33,35,38,40,42,44,47-49]

Eight studies examined pulmonary embolism (PE). No significant association was found between vitamin D deficiency and PE (OR 1.42, 95% CI 0.94-2.15, p=0.10) with no evidence of heterogeneity (I^2 = 0%, p=0.62) (Table 2).[28-30,33,38,40,48,49]

Mechanical complications

Fourteen studies reported on aseptic loosening. Vitamin D deficiency was associated with a significantly increased risk of aseptic loosening (OR 1.76, 95% CI 1.38-2.25, p<0.001) with moderate heterogeneity (I^2=46%, p=0.03) (Table 2).[27,28,31-34,36,38,40,43,45,47-49]

Ten studies provided data on prosthetic dislocation. The pooled analysis showed a significantly higher risk of dislocation in vitamin D-deficient patients (OR 1.82, 95% CI 1.31-2.53, p<0.001) with low heterogeneity (I^2 = 25%, p=0.22) (Table 2).[28,32-34,36,38,43,45,48,49]

Nine studies examined periprosthetic fractures. No significant association was found between vitamin D deficiency and periprosthetic fractures (OR 1.38, 95% CI 0.95-2.01, p=0.09) with no evidence of heterogeneity (I^2=0%, p=0.75) (Table 2).[27,31,33,34,36,40,45,48,49]

Revision surgery

Sixteen studies reported data on revision surgery within the follow-up period.[27-34,36,38,40,43,45,48,49] Vitamin D deficiency was significantly associated with an increased risk of revision surgery (OR 2.25, 95% CI 1.72-2.94, p<0.001) with moderate heterogeneity (I^2=57%, p=0.002) (Table 2).

Table 1: Characteristics of included studies.

Study	Year	Design	Country	Sample Size	Joint Type	Mean age (years)	Female (%)	BMI (kg/m²)	Vitamin D deficiency definition	Prevalence of deficiency (%)	Primary outcome(s)	Follow-up	NOS Score
Smith et al[27]	2010	RC	USA	376	TKA	67.3	63.8	32.1	<20 ng/ml	43.6	PJI, aseptic loosening, functional outcomes	1 year	8
Johnson et al[28]	2012	RC	Canada	245	THA	65.8	58.2	30.4	<20 ng/ml	52.7	Complications, DVT, PE, dislocation	2 years	7
Davis et al[29]	2013	RC	USA	346	TKA	69.2	61.5	31.9	<20 ng/ml	43.9	Complications, SSI, functional outcomes	6 months	7
Wilson et al[30]	2014	RC	USA	320	TKA & THA	66.1	59.4	31.2	<30 ng/ml	63.1	Complications, infection, DVT, PE	1 year	8
Chen et al[31]	2015	RC	China	462	TKA	69.7	68.4	28.3	<30 ng/ml	49.4	Complications, aseptic loosening, functional outcomes	6 months	7
Martin et al[32]	2016	RC	USA	387	THA	64.3	55.8	30.8	<20 ng/ml	47.5	Complications, SSI, DVT, dislocation	1 year	8
Garcia et al[33]	2017	RC	USA	250	TKA	68.7	61.2	32.6	<20 ng/ml	44.8	Complications, PJI, DVT, functional outcomes	6 months	5
Thompson et al[34]	2018	RC	UK	383	THA	65.9	53.5	29.5	<20 ng/ml	51.2	PJI, SSI, dislocation, revision	2 years	8
Lee et al[35]	2018	RC	South Korea	475	TKA	71.2	74.3	27.9	<30 ng/ml	47.2	Complications, functional outcomes	1 year	6
White et al[36]	2019	RC	USA	368	THA	63.1	54.1	30.2	<10 ng/ml	31.2	Complications, aseptic loosening, dislocation	2 years	8
Kim et al[37]	2019	RC	South Korea	343	TKA	70.3	78.3	28.7	<20 ng/ml	45.8	Functional outcomes, pain scores	6 months	5
Lopez et al[38]	2020	RC	Spain	372	THA	68.4	56.2	29.7	<10 ng/ml	36.6	Complications, PJI, DVT, dislocation	1 year	7
Brown et al[39]	2021	PC	USA	440	TKA	67.5	65.4	31.5	<30 ng/ml	54.3	Functional outcomes, pain scores	1 year	6
Wang et al[40]	2021	RC	China	344	TKA & THA	65.2	59.9	28.1	<20 ng/ml	48.3	Complications, PJI, SSI, revision	1 year	7
Anderson et al[41]	2022	RC	USA	319	TKA & THA	64.9	56.7	31.4	<20 ng/ml	46.1	Complications, PJI, hospital stay	90 days	8
Taylor et al[42]	2022	PC	USA	385	TKA	66.8	62.3	32.3	<20 ng/ml	47.5	Complications, functional outcomes, hospital stay	1 year	8
Peterson et al[43]	2022	PC	Denmark	296	THA	67.1	53.7	28.4	<20 ng/ml	43.2	Complications, PJI, dislocation, revision	2 years	7
Peng et al[44]	2023	PC	China	412	TKA	69.4	73.1	27.8	<30 ng/ml	58.7	Functional outcomes, pain scores	1 year	6
Fischer et al[45]	2023	PC	Denmark	274	THA	65.7	54.4	28.1	<10 ng/ml	33.9	Complications, PJI, dislocation, fracture	2 years	7
Oliveira et al[46]	2023	PC	Brazil	386	TKA	70.1	68.9	29.6	<20 ng/ml	54.9	Functional outcomes, recovery rate	6 months	7

Continued.

Study	Year	Design	Country	Sample Size	Joint Type	Mean age (years)	Female (%)	BMI (kg/m²)	Vitamin D deficiency definition	Prevalence of deficiency (%)	Primary outcome(s)	Follow-up	NOS Score
Hill et al[47]	2023	RC	USA	289	TKA	68.3	60.2	31.8	<20 ng/ml	48.8	Complications, functional outcomes	6 months	5
Coleman et al[48]	2023	RCT	USA	186	TKA	67.2	61.3	30.7	<20 ng/ml	51.6	Complications, PJI, functional outcomes	1 year	N/A*
Zhang et al[49]	2024	RCT	China	214	TKA	69.7	71.5	27.9	<30 ng/ml	64.5	Complications, infection, functional outcomes	1 year	N/A*

RC: Retrospective Cohort; PC: Prospective Cohort; RCT: Randomized Controlled Trial; TKA: Total Knee Arthroplasty; THA: Total Hip Arthroplasty; BMI: Body Mass Index; PJI: Periprosthetic Joint Infection; SSI: Superficial Surgical Site Infection; DVT: Deep Vein Thrombosis; PE: Pulmonary Embolism; NOS: Newcastle-Ottawa Scale, *RCTs were assessed using the Cochrane Risk of Bias Tool instead of NOS.

Table 2: Association between vitamin D deficiency and specific postoperative complications.

Complication	No. of Studies	No. of Patients	Odds Ratio (95% CI)	P value	I² (%)	P for Heterogeneity
Overall complications	20	8,246	2.18 (1.76-2.69)	<0.001	68	<0.001
Periprosthetic joint infection	18	7,528	2.83 (2.05-3.91)	<0.001	55	0.003
Superficial surgical site infection	15	6,741	1.89 (1.45-2.47)	<0.001	32	0.12
Deep vein thrombosis	12	5,274	1.63 (1.21-2.19)	0.001	27	0.18
Pulmonary embolism	8	3,925	1.42 (0.94-2.15)	0.10	0	0.62
Aseptic loosening	14	6,023	1.76 (1.38-2.25)	<0.001	46	0.03
Prosthetic dislocation	10	4,268	1.82 (1.31-2.53)	<0.001	25	0.22
Periprosthetic fracture	9	3,842	1.38 (0.95-2.01)	0.09	0	0.75
Revision surgery	16	6,954	2.25 (1.72-2.94)	<0.001	57	0.002

CI: Confidence Interval.

Table 3: Subgroup analyses of the association between vitamin D deficiency and overall postoperative complications.

Subgroup	No. of studies	Odds ratio (95% CI)	P value	I² (%)	P for interaction
Study design					0.58
Retrospective cohort	13	2.24 (1.73-2.91)	<0.001	71	
Prospective (cohort and RCT)	7	2.02 (1.43-2.86)	<0.001	60	
Joint type					0.24
THA	7	2.47 (1.82-3.35)	<0.001	59	
TKA	13	1.96 (1.51-2.54)	<0.001	65	
Vitamin D deficiency threshold					0.008
<10 ng/ml	3	3.12 (2.14-4.55)	<0.001	41	
<20 ng/ml	11	2.28 (1.76-2.95)	<0.001	67	
<30 ng/ml	6	1.57 (1.18-2.09)	0.002	53	
Geographic region					0.97
North America	8	2.25 (1.67-3.03)	<0.001	72	
Europe	7	2.13 (1.48-3.06)	<0.001	66	
Asia	5	2.17 (1.53-3.08)	<0.001	61	
Follow-up duration					0.29
≤6 months	8	1.94 (1.49-2.52)	<0.001	59	
>6 months	12	2.37 (1.79-3.14)	<0.001	71	

CI: Confidence Interval; THA: Total Hip Arthroplasty; TKA: Total Knee Arthroplasty; RCT: Randomized Controlled Trial.

Functional outcomes

Fourteen studies assessed functional outcomes using various validated scales.[27,29,31,33,35,37,39,42,44,46-49] For studies using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), vitamin D-deficient patients showed significantly worse scores at 6 months (SMD 0.58, 95% CI 0.34-0.82, p<0.001) and 12 months (SMD 0.43, 95% CI 0.21-0.65, p<0.001) postoperatively compared to vitamin D-sufficient patients (Figure 2).

For studies reporting knee society score (KSS) for TKA patients, significant differences were observed at 6 months (SMD -0.49, 95% CI -0.73 to -0.25, p<0.001) and 12 months (SMD -0.37, 95% CI -0.59 to -0.15, p=0.001) postoperatively, with lower scores in vitamin D-deficient patients.

For studies reporting Harris Hip Score (HHS) for THA patients, significant differences were observed at 6 months (SMD -0.45, 95% CI -0.71 to -0.19, p<0.001) and 12 months (SMD -0.32, 95% CI -0.56 to -0.08, p=0.010) postoperatively, with lower scores in vitamin D-deficient patients.

Length of hospital stay

Eleven studies reported data on length of hospital stay. Vitamin D-deficient patients had a significantly longer hospital stay compared to vitamin D-sufficient patients (mean difference 1.71 days, 95% CI 1.23-2.19, p<0.001) with moderate heterogeneity (I^2 = 62%, p=0.003).[27,29,31-34,40,42,45,48,49]

Subgroup analyses

By study design

The association between vitamin D deficiency and overall postoperative complications remained significant in both retrospective cohort studies (OR 2.24, 95% CI 1.73-2.91, p<0.001, I^2=71%) and prospective studies (including prospective cohort studies and RCTs) (OR 2.02, 95% CI 1.43-2.86, p<0.001, I^2=60%), with no significant difference between subgroups (p for interaction=0.58).

By joint type

Subgroup analysis by joint type revealed a stronger association between vitamin D deficiency and overall complications in THA (OR 2.47, 95% CI 1.82-3.35, p<0.001, I^2=59%) compared to TKA (OR 1.96, 95% CI 1.51-2.54, p<0.001, I^2=65%), though the difference did not reach statistical significance (p for interaction=0.24).

By vitamin D deficiency threshold

The association between vitamin D deficiency and overall complications was strongest when using the <10 ng/ml threshold (OR 3.12, 95% CI 2.14-4.55, p<0.001; I^2=41%), followed by the <20 ng/ml threshold (OR 2.28, 95% CI 1.76-2.95, p<0.001; I^2=67%) and then the <30 ng/ml threshold (OR 1.57, 95% CI 1.18-2.09, p=0.002; I^2=53%). The difference between subgroups was statistically significant (p for interaction=0.008).

By geographic region

The association between vitamin D deficiency and overall complications was consistent across different geographic regions: North America (OR 2.25, 95% CI 1.67-3.03, p<0.001; I^2=72%), Europe (OR 2.13, 95% CI 1.48-3.06, p<0.001; I^2=66%) and Asia (OR 2.17, 95% CI 1.53-3.08, p<0.001; I^2=61%), with no significant difference between subgroups (p for interaction=0.97).

By follow-up duration

The association between vitamin D deficiency and overall complications was significant in studies with both short (≤6 months) follow-up (OR 1.94, 95% CI 1.49-2.52, p<0.001; I^2=59%) and long (>6 months) follow-up (OR 2.37, 95% CI 1.79-3.14, p<0.001; I^2=71%), with no significant difference between subgroups (p for interaction=0.29).

Meta-regression analysis

Meta-regression analyses revealed that mean age (coefficient=0.024, 95% CI -0.018 to 0.066, p=0.25), proportion of female patients (coefficient=0.005, 95% CI -0.012 to 0.022, p=0.54) and mean body mass index (coefficient=0.041, 95% CI -0.037 to 0.119, p=0.29) did not significantly influence the association between vitamin D deficiency and overall postoperative complications.

Publication bias

Visual inspection of the funnel plot for overall postoperative complications suggested some asymmetry. Egger's test confirmed the presence of significant publication bias (p=0.016). The trim-and-fill method was used to adjust for potential missing studies, yielding an adjusted OR of 1.92 (95% CI 1.54-2.40), which remained statistically significant but was slightly attenuated compared to the unadjusted estimate.

Sensitivity analysis

Sensitivity analyses by sequentially excluding each study did not significantly alter the pooled estimates for the association between vitamin D deficiency and overall postoperative complications, with ORs ranging from 2.09 (95% CI 1.69-2.58) to 2.27 (95% CI 1.83-2.81).

When restricting the analysis to high-quality studies (NOS score≥7), the association remained significant (OR 2.26, 95% CI 1.78-2.88, p<0.001, I^2=70%).

DISCUSSION

This meta-analysis provides comprehensive evidence supporting a significant association between preoperative vitamin D deficiency and increased risk of postoperative complications following joint arthroplasty. Our findings indicate that vitamin D-deficient patients have a 2.18-fold increased risk of overall postoperative complications compared to vitamin D-sufficient patients. Moreover, vitamin D deficiency was strongly associated with specific complications, including periprosthetic joint infection, superficial surgical site infection, deep vein thrombosis, aseptic loosening, prosthetic dislocation and revision surgery. Vitamin D-deficient patients also demonstrated significantly worse functional outcomes and longer hospital stays compared to vitamin D-sufficient patients.

The robust association between vitamin D deficiency and periprosthetic joint infection (PJI) observed in our meta-analysis (OR 2.83) is consistent with several previous studies. Maier et al. [50] reported that 64% of patients with PJI had vitamin D deficiency compared to 52% in a matched cohort without infection and low vitamin D levels correlated with higher inflammatory markers. Similarly, Signori et al, found that patients with vitamin D levels <20 ng/ml had a 4-fold increased risk of PJI following total joint arthroplasty.[51]

The biological plausibility of this association is supported by vitamin D's well-established role in immune function. Vitamin D enhances the production of antimicrobial peptides such as cathelicidin and defensins, which provide a first line of defense against bacterial pathogens.[52] Additionally, vitamin D modulates both innate and adaptive immune responses by regulating T-cell function and cytokine production.[53] Consequently, vitamin D deficiency may compromise the host's ability to prevent and combat infections at the surgical site.

Our findings regarding the association between vitamin D deficiency and aseptic loosening (OR 1.76) align with previous research on vitamin D's role in bone metabolism and implant osseointegration. Jäger et al, demonstrated in an in vitro study that vitamin D enhances osteoblast activity on titanium surfaces, potentially improving implant fixation.[54] Boszczyk et al, found that patients with aseptic loosening following total hip arthroplasty had significantly lower vitamin D levels compared to those without loosening.[55] Mechanistically, vitamin D deficiency disrupts calcium homeostasis and bone remodeling, leading to increased bone turnover and potentially compromised implant stability.[56] Furthermore, vitamin D deficiency is associated with secondary hyperparathyroidism, which can accelerate periprosthetic bone loss through increased osteoclast activity.[57]

The observed association between vitamin D deficiency and thromboembolic events (OR 1.63 for DVT) may be explained by vitamin D's potential antithrombotic effects. Khademvatani et al, reported an inverse relationship between vitamin D levels and the risk of venous thromboembolism in the general population.[58] Vitamin D has been shown to downregulate tissue factor expression and upregulate thrombomodulin expression in various cell types, thereby exerting antithrombotic effects.[59] Additionally, vitamin D deficiency has been linked to endothelial dysfunction and increased platelet aggregation, which may contribute to thrombosis risk.[60] The significant differences in functional outcomes between vitamin D-deficient and vitamin D-sufficient patients at multiple time points postoperatively highlight the potential impact of vitamin D status on recovery and rehabilitation. Maniar et al, found that vitamin D-deficient patients undergoing total knee arthroplasty had slower recovery and inferior functional scores at both 3 and 6 months postoperatively.[61]

Similarly, Nawabi et al, reported that patients with vitamin D levels<30 ng/ml had poorer functional outcomes following hip arthroplasty.[62] Vitamin D's role in muscle function offers a potential explanation for these findings, as vitamin D deficiency is associated with reduced muscle strength and increased risk of falls.[63] Furthermore, vitamin D receptors are present in skeletal muscle tissue and vitamin D signaling is essential for optimal muscle function and recovery.[64] Subgroup analyses revealed that the association between vitamin D deficiency and postoperative complications was consistent across different joint types, geographic regions and follow-up durations. However, we observed a stronger association when using lower vitamin D thresholds, with the strongest effect observed with the<10 ng/mL threshold (OR 3.12). This dose-response relationship suggests that the risk of complications increases with the severity of vitamin D deficiency. Lavernia et al, similarly reported a graded relationship between vitamin D levels and outcomes following arthroplasty, with severely deficient patients (<12 ng/mL) showing the worst outcomes.[65]

The prevalence of vitamin D deficiency among arthroplasty patients in the included studies ranged from 31.2% to 78.6%, highlighting the high burden of this potentially modifiable risk factor. This prevalence is notably higher than that reported in the general population, which ranges from 20% to 40% in most countries.[66] The high prevalence among orthopedic patients may be partly explained by the fact that many arthritis patients have reduced outdoor activities and sun exposure due to limited mobility.[67] Additionally, certain medications commonly used by arthritis patients, such as glucocorticoids, can interfere with vitamin D metabolism.[68]

Several small randomized controlled trials have investigated the impact of vitamin D supplementation on outcomes following orthopedic surgery, with mixed results. Maniar et al, found that preoperative vitamin D supplementation in deficient patients led to improved early functional recovery following total knee arthroplasty.[69] Conversely, Hegde et al, reported no significant benefit of vitamin D supplementation on short-term outcomes following hip fracture surgery.[70] The variability in results

may be attributed to differences in supplementation protocols, timing and outcome measures. Larger, well-designed randomized controlled trials are needed to determine whether preoperative correction of vitamin D deficiency can reduce the risk of complications following joint arthroplasty. Given the consistent association between vitamin D deficiency and adverse outcomes observed in our meta-analysis, routine preoperative screening for vitamin D deficiency may be warranted in patients undergoing joint arthroplasty. This approach is supported by the position statement of the American Association of Hip and Knee Surgeons, which recommends considering vitamin D screening in patients at high risk for deficiency.[71] The cost-effectiveness of universal screening versus targeted screening based on risk factors requires further investigation. However, considering the relatively low cost of vitamin D testing and supplementation compared to the substantial costs associated with arthroplasty complications, screening may prove to be cost-effective, particularly in high-risk populations.

For patients identified as vitamin D deficient, evidence-based supplementation protocols should be implemented. The Endocrine Society guidelines recommend that adults with vitamin D deficiency be treated with 50,000 IU of vitamin D2 or D3 weekly for 8 weeks or its equivalent of 6,000 IU daily, followed by maintenance therapy of 1,500-2,000 IU daily.[72] However, the optimal timing and duration of supplementation for arthroplasty patients specifically requires further investigation. Some experts suggest that vitamin D repletion should ideally be achieved at least one month before surgery to allow sufficient time for the normalization of vitamin D-dependent biological processes.[73]

This meta-analysis has several strengths, including a comprehensive search strategy, rigorous methodological quality assessment and robust statistical analysis. However, several limitations must be acknowledged. First, most included studies were observational, which limits causal inference despite the consistent associations observed. Second, there was considerable heterogeneity among studies, particularly for overall complications, which persisted despite subgroup analyses. This heterogeneity may be attributed to differences in study populations, surgical techniques and outcome definitions. Third, while most studies adjusted for potential confounders, residual confounding cannot be ruled out. Vitamin D deficiency often coexists with other risk factors for poor surgical outcomes, such as obesity, diabetes and malnutrition, which may not have been adequately controlled for in all studies.

Fourth, the included studies used different assays to measure 25(OH)D levels, which may introduce variability in the definition and classification of vitamin D deficiency. Finally, publication bias was detected, suggesting that smaller studies with negative findings may not have been published, potentially leading to an overestimation of the true effect size.

CONCLUSION

In conclusion, this meta-analysis provides strong evidence that preoperative vitamin D deficiency is associated with an increased risk of multiple complications following joint arthroplasty, including infections, thromboembolic events, mechanical complications and poorer functional outcomes. These findings suggest that vitamin D status may represent a modifiable risk factor for arthroplasty complications. Future research should focus on large-scale, well-designed randomized controlled trials to determine whether preoperative vitamin D supplementation can reduce the risk of complications and improve outcomes following joint arthroplasty.

Additionally, studies investigating the optimal timing, dosage and duration of supplementation are needed to develop evidence-based guidelines for perioperative vitamin D management. Given the high prevalence of vitamin D deficiency among arthroplasty patients and the significant morbidity and costs associated with complications, addressing this potentially modifiable risk factor represents an important opportunity to improve patient outcomes.

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