

G-21 – Does the level of preoperative vitamin D have an influence on the incidence of Surgical Site Infection (SSI)/Periprosthetic Joint Infection (PJI) in patients undergoing major orthopedic surgery?

Armin Arshi, John K. Cordero, David Novikov, Atsuhiko Fujie, Aydin Gahramanov, Lucian Bogdan Solomon, Ariel E Saldana, Nicolas S. Piuze, Boopalan Ramasamy, James Kigera

Response/Recommendation: Yes. There is consistent evidence demonstrating that vitamin D deficiency is associated with increased risk of subsequent SSIs and/or PJIs in patients undergoing orthopaedic procedures, particularly in lower extremity arthroplasty.

Strength of recommendation: Limited

Delegate Vote:

Rationale:

Vitamin D is critical in modulating the human body's calcium axis, maintaining bone mineral density, and regulating the immune system [1]. Given its essential role in innate immunity, determining the influence of vitamin D deficiency (VDD) on the rates of surgical site infection (SSI) and periprosthetic joint infection (PJI) is a focus by researchers and clinicians. This is critical given the high prevalence of VDD, cited as 41.6% in the general United States population and up to 75% of patients undergoing arthroplasty [2, 3]. Most of the relevant literature on VDD in arthroplasty pertains to hip and knee total joint arthroplasty (TJA). Generally, it is accepted that serum 25-hydroxyvitamin D levels below 20 ng/mL are associated with a higher incidence of postoperative complications, including PJI, and may be a modifiable risk factor in TJA [4]. However, the majority of studies are observational rather than interventional and thus cannot infer causation [5].

An observational study by Maeir et al. published in 2014 highlighted the significance of this topic, identifying a VDD prevalence rate of 64% in those undergoing primary hip and knee TJA. Additionally, they found a 52% prevalence in those undergoing aseptic revision and 86% in those undergoing septic revision ($p < 0.001$) [6]. Due to this association, these authors and others recommended vitamin D supplementation as a potential intervention to reduce the risk of PJI. A similar study was published by Signori et al. in 2015, which included patients with PJI and surgically treated osteoarticular infections. In their cohort, both aseptic and infection-related cases had serum vitamin D levels below reference values. Conversely, they observed that the average vitamin D values of patients who had aseptic failure were significantly lower than those with infection (18.5 ± 6.5 ng/mL vs. 13.6 ± 9.4 ng/mL, $p < 0.05$) [7].

Perhaps the most promising study was an *in vivo* mouse model by Hegde et al. Researchers implanted a stainless steel implant in vitamin D deficient mice, sufficient, and “rescued” mice who received parenteral supplementation three days prior to surgery. They concluded that VDD results in increased bacterial burden and neutrophil infiltration and that this effect can be reversed with preoperative repletion of vitamin D [8]. The same group followed up in 2018 with a retrospective study that included 6,593 patients, 868 of whom had VDD. They showed that the

cohort with VDD had a higher risk of SSI necessitating irrigation and debridement (OR 1.76, $p = 0.001$) as well as prosthesis removal (OR 2.97, $p < 0.001$), at the one-year follow-up. Notably, no assessment of whether vitamin D repletion could mitigate risk was performed in this study [4]. Traven et al. had similar results in their retrospective case control study that included 126 TJA patients. They found that VDD, while controlling for nutritional parameters such as albumin and transferrin, was associated with an increased risk of 90-day complications including PJI as a reason for revision surgery [9]. Furthermore, they showed that revised PJI patients were more likely to have VDD as compared to aseptically revised patients (72.7% vs. 48.4%, $p = 0.016$). The researchers concluded that VDD should be considered a modifiable risk factor for complications following revision arthroplasty.

Recently, in a prospective database study published in 2024, Birinci et al. compared patients who received a single oral dose of 7.5 mg two weeks prior to index surgery ($n = 488$) with a group whose preoperative vitamin D levels were unknown and who did not receive vitamin D supplementation ($n = 592$). The total number of complications (8.6% vs. 4.3%; respectively; $P = 0.005$), superficial wound infection (2.5% vs. 0.2%, respectively; $P < 0.001$), and postoperative cellulitis (2.2% vs. 0% respectively; $P < 0.001$) were statistically higher in the patient group who did not receive vitamin D supplementation. They concluded that preoperative vitamin D supplementation in deficient TJA patients may reduce postoperative complications, including superficial wound infection and postoperative cellulitis. Furthermore, they specifically recommend a single preoperative oral dosage of 300,000 U to correct VDD and improve TJA outcomes [10].

Conclusion:

There is supportive evidence that VDD in the early postoperative period following primary arthroplasty is a risk factor for complications, including PJI, SSI, and wound problems [11]. More specifically, several observational studies correlate serum vitamin D concentrations to a reduced incidence of orthopaedic infection, consistent with studies in other specialties that demonstrate VDD as a risk factor for infection [12, 13]. This suggests that supplementation may improve outcomes. However, most studies are inconsistent regarding when vitamin D levels were measured, with some studies evaluating levels at the point of infection diagnosis, while others reporting baseline levels [14]. Additionally, there is limited data on the optimal route of administration and dosing of vitamin D. In summary, further large-scale, prospective studies are needed to establish clear causation of complications and infection from VDD and standardize recommendations for vitamin D optimization in orthopedic surgery patients.

References

1. Hassan-Smith ZK, Hewison M, Gittoes NJ. Effect of vitamin D deficiency in developed countries. *Br Med Bull*. 2017 Jun 1;122(1):79-89. doi: 10.1093/bmb/ldx005. PMID: 28334220.
2. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res*. 2011 Jan;31(1):48-54. doi: 10.1016/j.nutres.2010.12.001. PMID: 21310306.
3. Jeon YD, Cho SD, Youm YS, Song JY, Lee KJ, Park KB. The Prevalence of Vitamin D Deficiency in Patients Undergoing Total Knee Arthroplasty: A Propensity Score Matching Analysis. *Arch Osteoporos*. 2022 Mar 23;17(1):53. doi: 10.1007/s11657-022-01097-7. PMID:

35320426; PMCID: PMC8942953.

4. Hegde V, Arshi A, Wang C, Buser Z, Wang JC, Jensen AR, Adams JS, Zeegen EN, Bernthal NM. Preoperative Vitamin D Deficiency Is Associated With Higher Postoperative Complication Rates in Total Knee Arthroplasty. *Orthopedics*. 2018 Jul 1;41(4):e489-e495. doi: 10.3928/01477447-20180424-04. Epub 2018 Apr 30. PMID: 29708568.
5. Zargarán A, Zargarán D, Trompeter AJ. The role of Vitamin D in orthopaedic infection: a systematic literature review. *Bone Jt Open*. 2021 Sep;2(9):721-727. doi: 10.1302/2633-1462.29.BJO-2020-0192.R1. PMID: 34488428; PMCID: PMC8479837.
6. Maier GS, Horas K, Seeger JB, Roth KE, Kurth AA, Maus U. Is there an association between periprosthetic joint infection and low vitamin D levels? *Int Orthop*. 2014 Jul;38(7):1499-504. doi: 10.1007/s00264-014-2338-6. Epub 2014 Apr 16. PMID: 24737149; PMCID: PMC4071483.
7. Signori V, Romanò CL, De Vecchi E, Mattina R, Drago L. May osteoarticular infections be influenced by vitamin D status? An observational study on selected patients. *BMC Musculoskelet Disord*. 2015 Aug 5;16:183. doi: 10.1186/s12891-015-0648-5. PMID: 26242985; PMCID: PMC4526280.
8. Hegde V, Dworsky EM, Stavrakis AI, Loftin AH, Zoller SD, Park HY, Richman S, Johansen D, Hu Y, Taylor JA, Hamad CD, Chun RF, Xi W, Adams JS, Bernthal NM. Single-Dose, Preoperative Vitamin-D Supplementation Decreases Infection in a Mouse Model of Periprosthetic Joint Infection. *J Bone Joint Surg Am*. 2017 Oct 18;99(20):1737-1744. doi: 10.2106/JBJS.16.01598. PMID: 29040128; PMCID: PMC6948832.
9. Traven SA, Chiaramonti AM, Barfield WR, Kirkland PA, Demos HA, Schutte HD, Drew JM. Fewer Complications Following Revision Hip and Knee Arthroplasty in Patients With Normal Vitamin D Levels. *J Arthroplasty*. 2017 Sep;32(9S):S193-S196. doi: 10.1016/j.arth.2017.02.038. Epub 2017 Mar 8. PMID: 28372917.
10. Birinci M, Hakyemez ÖS, Geçkalan MA, Mutlu M, Yildiz F, Bilgen ÖF, Azboy İ. Effect of Vitamin D Deficiency on Periprosthetic Joint Infection and Complications After Primary Total Joint Arthroplasty. *J Arthroplasty*. 2024 Sep;39(9S2):S151-S157. doi: 10.1016/j.arth.2024.05.012. Epub 2024 May 10. PMID: 38734328.
11. Kenanidis E, Kakoulidis P, Karponis D, Tsiridis E. The Effect of Perioperative Vitamin D Levels on the Functional, Patient-Related Outcome Measures and the Risk of Infection Following Hip and Knee Arthroplasty: A Systematic Review. *Patient Relat Outcome Meas*. 2020 Sep 8;11:161-171. doi: 10.2147/PROM.S261251. PMID: 32982524; PMCID: PMC7490061.
12. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, Dubnov-Raz G, Esposito S, Ganmaa D, Ginde AA, Goodall EC, Grant CC, Griffiths CJ, Janssens W, Laaksi I, Manaseki-Holland S, Mauger D, Murdoch DR, Neale R, Rees JR, Simpson S Jr, Stelmach I, Kumar GT, Urashima M, Camargo CA Jr. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*. 2017 Feb 15;356:i6583. doi: 10.1136/bmj.i6583. PMID: 28202713; PMCID: PMC5310969.
13. Yamshchikov AV, Desai NS, Blumberg HM, Ziegler TR, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. *Endocr Pract*. 2009 Jul-Aug;15(5):438-49. doi: 10.4158/EP09101.ORR. PMID: 19491064; PMCID: PMC2855046.
14. Zargarán A, Zargarán D, Trompeter AJ. The role of Vitamin D in orthopaedic infection: a systematic literature review. *Bone Jt Open*. 2021 Sep;2(9):721-727. doi: 10.1302/2633-1462.29.BJO-2020-0192.R1. PMID: 34488428; PMCID: PMC8479837.