**G20 - Is there a role for nutritional supplementation for prevention of surgical site infection (SSI) in patients undergoing major orthopedic surgery?**

Carlo L Romano, Wael K Barsoum, Muhammad A Chinoy, Serban Dragosloveanu, Gérard C Giordano, Takeshi Morii, Wayne E Moschetti, Cristian Scheau, Takeaki Yamamoto

**Response/Recommendation:** Protein-based nutritional supplementation reduces the occurrence of early surgical site infection (SSI) in major orthopedic surgery, particularly in patients who are at poor nutritional status.

**Level of evidence:** Limited

**Delegate Vote:**

**Rationale:**

Malnutrition or suboptimal nutrition, commonly found in orthopedic and trauma patients, can impair immune response, delay wound healing, and increase susceptibility to infections, including surgical site infections (SSIs) after major orthopedic and trauma surgical procedures [1, 2, 3, 4, 5]. Moreover, hypoalbuminemia, a proxy of malnutrition, has been identified as a risk factor for failure of surgical treatment of periprosthetic joint infection (PJI), including debridement and retention as well as one- or two-stage revision surgery [6, 7, 8].

Nutritional supplementation has been increasingly investigated in the last decade [9, 10] and recently recognized by some authors as an important aspect of preventing SSIs in orthopedic patients [11].

In particular, protein supplementation with or without other nutritional supplements, including amino-acids and vitamins, has been shown to reduce the incidence of early SSIs in patients undergoing major orthopedic surgical procedures. Goncalves and co-workers [12] reported on a retrospective study on patients aged ≥60 years, undergoing elective orthopedic-cemented or uncemented total hip or knee replacement, divided into 2 groups: control and immunonutrition (a mix of proteins, arginine, omega 3 and nucleotides). The immunonutrition group was instructed to start oral intake of the nutritional supplement 5 days before and to resume it 5 days after arthroplasty. Logistic regression analysis showed that patients in the immunonutrition group had a 55% reduction in infectious complications (odds ratio [OR], 0.45; 95% CI, 0.30–0.68; $P < 0.001$). Chen et al. [13] conducted a recent systematic review and meta-analysis on the role of high protein-based diet strategies containing (or not containing) carbohydrates, fat, vitamins, and minerals. Randomized trials in older patients with hip fracture (aged ≥ 50 years) were included. Overall, 18 studies involving 1,522 patients met the inclusion criteria, providing substantial data for analysis. High protein-based diet strategies were found to be associated with significantly elevated albumin levels as well as a significant risk reduction in infective complications (odds ratio 0.54, 95% CI 0.39 to 0.76), reduced incidence of pressure ulcers and total complications. Length of hospital stay was also significantly reduced, with a tendency towards a lower mortality risk and readmission rate, although not statistically significant. The overall compliance with the high protein diet ranged from 64.7% to 100%.

More recently, a retrospective study on patients undergoing spinal fusion surgery [14] disclosed that patients receiving the supplemental diet (n=229) demonstrated fewer wound complications

(7% vs. 21%, p=0.004) and reoperations (3% vs. 11%, P=0.016) compared to those without supplementation (n=56). Patients with normal preoperative pre-albumin levels experienced more wound complications without the supplemental diet (5% vs. 18%, p=0.025). A similar trend was seen in patients with low preoperative pre-albumin (12% vs. 26%, p=0.12). The postoperative nutritional program was designed by a registered dietitian to supplement but not replace regular meals and increase the nitrogen balance. Components of the diet consisted of a mix of proteins, collagen, specific amino-acids, vitamins, zinc and other components. This study confirmed findings of a prior study by Saleh et al., whose prospective randomized controlled trial of 103 patients undergoing elective primary spine surgery demonstrated significantly lower rates of perioperative wound healing complications (3.4% vs. 17.9%, p< 0.05). The trial also showed that patients receiving supplementation had 10 times lower rates of in-hospital minor complications (2.1% vs. 23.2%, P<0.01), while subgroup analysis demonstrated that malnourished patients who received perioperative nutritional supplementation had lower rates of minor complications during admission (0.0% vs. 34.4%, P= 0.01) and return to the operating room within 90 days (0.0% vs. 12.4%, p=0.04). Intervention group received nutritional supplementation (protein shake) twice daily from postoperative day 0 to two weeks post-discharge.

Scientific evidence concerning other nutritional supplements and their impact on post-surgical infection is limited. Arginine and glutamine alone have been reported to enhance wound healing, even if not specifically in orthopedic surgery [15] and a four oral probiotics regime has been suggested to reduce the occurrence of post-surgical infection in an heterogenous series of trauma patients [16].

Recent systematic reviews and meta-analysis do not support a statistically significant role to prevent post-surgical infection complications in orthopedic and trauma patients for vitamin C [17], vitamin D [18] or zinc [19], when used alone.

Concerning the methodological aspects of the available literature, it is worth noting that SSIs and wound complications are often endpoints included among others, with only isolated studies specifically addressing septic complications only. Furthermore, a univocal definition of these two endpoints is lacking across the studies, while the observational period is restricted to a maximum of 12 weeks after index surgery, with no information regarding the impact of nutritional supplementation on longer term implant-related infection rate, cost-effectiveness and possible side effects.

Conclusion:

There is limited evidence supporting the role of protein-based nutritional supplementation in reducing SSIs, particularly in malnourished patients or nutritionally at-risk patients undergoing major orthopedic surgery. Nevertheless, the assessment and correction of patients' nutritional status must be considered in infection management algorithms in orthopedics, particularly with regard to the prevention of SSIs, even if the effectiveness of supplementation may vary based on the individual patient factors, and further studies are needed to refine guidelines on nutrient dosages, timing and the comparative efficacy of different supplements.

## References


1. Yi PH, Frank RM, Vann E, Sonn KA, Moric M, Della Valle CJ. Is potential malnutrition associated with septic failure and acute infection after revision total joint arthroplasty? Clin Orthop Relat Res. 2015 Jan;473(1):175-82.

2. Tsantes AG, Papadopoulos DV, Lytras T, Tsantes AE, Mavrogenis AF, Korompilias AV, Gelalis ID, Tsantes CG, Bonovas S. Association of malnutrition with periprosthetic joint and surgical site infections after total joint arthroplasty: a systematic review and meta-analysis. J Hosp Infect. 2019 Sep;103(1):69-77.
3. Handcox JE, Gutierrez-Naranjo JM, Salazar LM, Bullock TS, Griffin LP, Zelle BA. Nutrition and Vitamin Deficiencies Are Common in Orthopaedic Trauma Patients. J Clin Med. 2021 Oct 28;10(21):5012.
4. Chen Y, Chen W. Association between malnutrition status and total joint arthroplasty periprosthetic joint infection and surgical site infection: a systematic review meta-analysis. J Orthop Surg Res. 2024 Oct 15;19(1):660. doi: 10.1186/s13018-024-05165-1.
5. Wang C, Lv S. Association between malnutrition and surgical site and periprosthetic joint infections following joint arthroplasty: A systematic review and meta-analysis. Int Wound J. 2024 Mar;21(3):e14520.
6. Scarcella NR, Mills FB 4th, Seidelman JL, Jiranek WA. The Effect of Nutritional Status in the Treatment of Periprosthetic Joint Infections in Total Hip Arthroplasty. J Arthroplasty. 2024 Sep;39(9S1):S225-S228.
7. Traverso G, Núñez JH, Gehrke T, Citak M. Hypoalbuminemia increases the risk of failure following one-stage septic revision for periprosthetic joint infection. Arch Orthop Trauma Surg. 2023 Sep;143(9):5641-5648.
8. Green CC, Valenzuela MM, Odum SM, Rowe TM, Springer BD, Fehring TK, Otero JE. Hypoalbuminemia Predicts Failure of Two-Stage Exchange for Chronic Periprosthetic Joint Infection of the Hip and Knee. J Arthroplasty. 2023 Jul;38(7):1363-1368.
9. Tedesco A, Sharma AK, Acharya N, Rublev G, Hashmi S, Wu HH, Lee YP, Scolaro J, Bhatia N. The Role of Perioperative Nutritional Status and Supplementation in Orthopaedic Surgery: A Review of Postoperative Outcomes. JBJS Rev. 2024 Apr 12;12(4).
10. Zink TM, Kent SE, Choudhary AN, Kavolus JJ. Nutrition in Surgery: An Orthopaedic Perspective. J Bone Joint Surg Am. 2023 Dec 6;105(23):1897-1906.
11. Gregori P, Franceschetti E, Basciani S, Impieri L, Zampogna B, Matano A, Manzi C, Carbone L, Marano L, Papalia R. Immunonutrition in Orthopedic and Traumatic Patients. Nutrients. 2023 Jan 19;15(3):537.
12. Gonçalves TJM, Gonçalves SEAB, Nava N, Jorge VC, Okawa AM, Rocha VA, Forato LCH, Furuya VAO, Martins SS, Oksman D. Perioperative Immunonutrition in Elderly Patients Undergoing Total Hip and Knee Arthroplasty: Impact on Postoperative Outcomes. JPEN J Parenter Enteral Nutr. 2021 Sep;45(7):1559-1566.
13. Chen B, Zhang JH, Duckworth AD, Clement ND. Effect of oral nutritional supplementation on outcomes in older adults with hip fractures and factors influencing compliance. Bone Joint J. 2023 Nov 1;105-B(11):1149-1158.
14. Como CJ, Setliff JC, Dalton JF, Tang YM, Oyekan AA, Hua K, Byrne K, Sadhwani S, Spitnale M, Russell KL, Wawrose R, Lee JY, Shaw JD. Focused Perioperative Nutritional Supplementation Reduces Wound Complications in Patients Undergoing Spinal Fusion Surgery. Spine (Phila Pa 1976). 2024 Aug 29.
15. Arribas-López E, Zand N, Ojo O, Snowden MJ, Kochhar T. The Effect of Amino Acids on Wound Healing: A Systematic Review and Meta-Analysis on Arginine and Glutamine. Nutrients. 2021 Jul 22;13(8):2498
16. Tzikos G, Tsalkatidou D, Stavrou G, Thoma G, Chorti A, Tsilika M, Michalopoulos A,

Papavramidis T, Giamarellos-Bourboulis EJ, Kotzampassi K. A Four-Probiotic Regime to Reduce Surgical Site Infections in Multi-Trauma Patients. Nutrients. 2022 Jun 24;14(13):2620.
17. Suter M, Bollen Pinto B, Belletti A, Putzu A. Efficacy and safety of perioperative vitamin C in patients undergoing noncardiac surgery: a systematic review and meta-analysis of randomised trials. Br J Anaesth. 2022 Apr;128(4):664-678.
18. Patel A, Caruana EJ, Hodson J, Morrison R, Khor B, Gysling S, Trevis J, Mangel T, Benson R, Zakeri R, Manders J, Vaja R, Rogers L, Baker P, Pournaras DJ, Thickett D, Hewison M, Naidu B, Lim E. Role of vitamin D supplementation in modifying outcomes after surgery: a systematic review of randomised controlled trials. BMJ Open. 2024 Jan 17;14(1):e073431.
19. Lin PH, Sermersheim M, Li H, Lee PHU, Steinberg SM, Ma J. Zinc in Wound Healing Modulation. Nutrients. 2017 Dec 24;10(1):16.