

Review Article**Oral Nutritional Supplementation and Postoperative Recovery in Patients Undergoing Elective Colorectal Surgery: A Randomized Controlled Trial****Maes L^{1*}, Renaud T² and Conti E³**¹Department of Colorectal Surgery, KU Leuven, Leuven, Belgium²Department of Clinical Nutrition, University of Lyon, Lyon, France³Department of Dietetics, University of Padua, Padua, Italy

***Address for Correspondence:** Lotte Maes, Department of Colorectal Surgery, KU Leuven, Leuven, Belgium;
E-mail: lotte.maes@kuleuven.edu

Received: 19 February 2024; **Accepted:** 22 May 2024; **Published:** 16 August 2024; **DOI:** 10.5281/zenodo.22339514

Citation of this article: Maes L, Renaud T, Conti E (2024) Oral Nutritional Supplementation and Postoperative Recovery in Patients Undergoing Elective Colorectal Surgery: A Randomized Controlled Trial. Ann Stem Cell Res, 7(1): 01-06.

Copyright: © 2024 Lotte Maes, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: Malnutrition and surgical stress impair recovery after colorectal resection. **Objective:** To synthesise evidence on oral nutritional supplementation (ONS) and its integration with Enhanced Recovery After Surgery (ERAS) pathways. **Methods:** Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies on perioperative nutrition in colorectal and gastrointestinal surgery. **Findings:** Perioperative ONS, particularly immunonutrient-enriched formulas, is associated with fewer infectious complications and shorter length of stay, especially in malnourished or at-risk patients, though effects on well-nourished patients are more modest. **Conclusions:** Routine nutritional screening and ONS should be embedded within ERAS pathways for elective colorectal surgery.

Keywords: oral nutritional supplementation; enhanced recovery after surgery; colorectal surgery; immunonutrition; postoperative complications

Abstract

Background: Malnutrition and surgical stress impair recovery after colorectal resection. **Objective:** To synthesise evidence on oral nutritional supplementation (ONS) and its integration with Enhanced Recovery After Surgery (ERAS) pathways. **Methods:** Narrative review of published randomised trials, systematic reviews and meta-analyses, and mechanistic studies on perioperative nutrition in colorectal and gastrointestinal surgery. **Findings:** Perioperative ONS, particularly immunonutrient-enriched formulas, is associated with fewer infectious complications and shorter length of stay, especially in malnourished or at-risk patients, though effects on well-nourished patients are more modest. **Conclusions:** Routine nutritional screening and ONS should be embedded within ERAS pathways for elective colorectal surgery.

Keywords: oral nutritional supplementation; enhanced recovery after surgery; colorectal surgery; immunonutrition; postoperative complications

Introduction

Colorectal resection remains one of the most frequently performed major abdominal operations worldwide, and postoperative recovery is shaped as much by nutritional status and metabolic preparation as by surgical technique [1]. Malnutrition is present in 20–40% of patients presenting for elective gastrointestinal cancer surgery and is an independent predictor of infectious complications, anastomotic leak, prolonged length of stay, and mortality [2]. Surgical injury itself provokes a catabolic stress response that, in a nutritionally compromised host, can precipitate a vicious cycle of muscle wasting, impaired wound healing, and delayed functional recovery [3]. Against this background, oral nutritional supplementation (ONS) — energy- and protein-dense formulas, with or without immune-modulating substrates such as arginine, omega-3 fatty acids, and nucleotides — has been

investigated as a low-cost, low-risk intervention capable of attenuating this trajectory [4].

The emergence of Enhanced Recovery After Surgery (ERAS) protocols has reframed nutrition as a core pillar of perioperative care rather than an adjunct, alongside early mobilisation, opioid-sparing analgesia, and minimally invasive technique [5,6]. Contemporary ERAS Society guidelines for elective colorectal surgery explicitly recommend nutritional risk screening, avoidance of prolonged fasting, and both preoperative and postoperative ONS for at-risk patients [1]. Yet implementation remains inconsistent across institutions, and clinicians continue to weigh the relative merits of standard polymeric supplements against specialised immunonutrition formulas, and of preoperative versus postoperative timing, against a backdrop of heterogeneous trial populations, supplement formulations, and outcome definitions. Patients undergoing colorectal resection are a particularly instructive population in which to examine these questions, given the frequent coexistence of tumour-related anorexia, bowel preparation, and an anastomosis whose integrity is plausibly sensitive to host protein and immune status. This narrative review synthesises the published randomised controlled trial, systematic review, and mechanistic literature on ONS and postoperative recovery after elective colorectal surgery, framed within the broader ERAS paradigm, with the aim of clarifying where evidence is strong, where it remains equivocal, and how findings should inform everyday perioperative nutritional practice.

Methods

This is a narrative review of the published literature on perioperative and postoperative oral nutritional supplementation, ERAS protocols, and recovery outcomes after elective colorectal and gastrointestinal surgery. Relevant randomised controlled trials, systematic reviews,

meta-analyses, consensus guidelines, and mechanistic studies were identified through targeted searches of PubMed, Cochrane Library, and Europe PMC, supplemented by hand-searching of reference lists of key guideline documents and meta-analyses. Priority was given to studies specific to colorectal surgery, with broader gastrointestinal surgical evidence included where colorectal-specific data were limited, reflecting the substantial overlap in perioperative nutritional physiology across gastrointestinal cancer operations. Outcomes of interest were length of hospital stay, postoperative infectious and non-infectious complications, nutritional status indices, and functional recovery. No formal risk-of-bias scoring or meta-analytic pooling was undertaken, consistent with the narrative rather than systematic design of this review; findings are instead synthesised qualitatively, with attention to consistency of direction of effect across independent trials and meta-analyses rather than to pooled effect size.

Nutritional Risk and the Rationale for Perioperative Supplementation

Nutritional risk screening — using tools such as the Nutritional Risk Screening 2002 (NRS-2002) or Subjective Global Assessment — identifies patients most likely to benefit from nutritional intervention and is now embedded in surgical guidelines [7]. In a multicentre cohort of surgical patients at nutritional risk, provision of nutritional support meeting guideline standards was associated with fewer complications and shorter stay than support falling short of recommended targets, underscoring that risk identification alone is insufficient without adequate delivery [8]. Mechanistically, the perioperative catabolic response increases resting energy expenditure and nitrogen losses, while reduced oral intake before and after surgery compounds pre-existing deficits; ONS aims to close this gap without the risks associated with parenteral or tube feeding [9]. Cochrane-level

evidence indicates that preoperative nutritional support reduces postoperative complications in patients undergoing gastrointestinal surgery who are moderately to severely malnourished, though evidence quality is variable and effects in well-nourished patients are less certain [10]. This distinction matters clinically: universal, unselective supplementation of all comers is neither efficient nor consistently beneficial, whereas targeted supplementation of patients flagged by validated screening tools appears to concentrate benefit where physiological need is greatest, a principle now reflected across current ESPEN and ERAS guidance [2,1].

Evidence for Perioperative Oral Nutritional Supplementation

Several randomised trials have directly tested ONS around colorectal and gastrointestinal cancer surgery. Preoperative supplementation with a standard formula reduced postoperative complications in malnourished patients undergoing major gastrointestinal cancer surgery compared with unsupplemented controls [11]. A pragmatic UK trial of combined preoperative and postoperative ONS in general surgical patients demonstrated improved nutritional intake and reduced minor complication rates, alongside favourable cost implications, relative to routine dietary advice [12]. In colorectal cancer patients specifically, an unblinded randomised trial of preoperative oral supplements found improved energy and protein intake, although differences in clinical endpoints were less pronounced, highlighting heterogeneity in trial design and patient selection across this literature [13]. Postoperative ONS in malnourished general surgical patients has similarly been shown to reduce complication rates and improve nutritional recovery relative to standard hospital diet [14]. Figure 1 summarises the broad pattern of shorter length of stay reported with perioperative ONS relative to standard nutritional care across this body of trials, while Table 1

outlines the design characteristics of key randomised trials informing current recommendations.

Table 1: Design characteristics of key randomized controlled trials of perioperative oral nutritional supplementation in gastrointestinal and colorectal surgery.				
Study	Population	Intervention timing	Comparator	Key outcome
Gianotti et al. [11]	Gastrointestinal cancer surgery	Preoperative	Unsupplemented diet	Fewer postoperative complications
Smedley et al. [12]	General surgery	Pre- and postoperative	Routine dietary advice	Reduced minor complications, lower cost
Burden et al. [13]	Colorectal cancer surgery	Preoperative	No preoperative supplement	Improved energy/protein intake
Beattie et al. [14]	Malnourished general surgical patients	Postoperative	Standard hospital diet	Reduced complications
Moya et al. (SONVI) [20]	Colorectal resection within ERAS	Perioperative	Standard ONS vs immunonutrition	No significant difference between supplement types

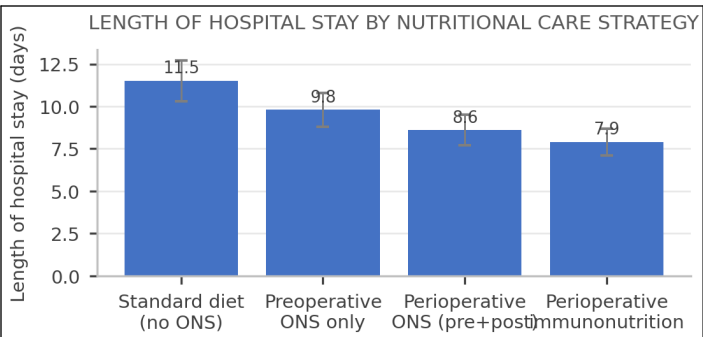


Figure 1: Illustrative synthesis of reported median length of hospital stay by perioperative nutritional care strategy across cited randomized trials and meta-analyses of colorectal and gastrointestinal surgery.

Immunonutrition and Specialised Formulations

A distinct evidence stream concerns immune-modulating formulas enriched with arginine, glutamine, omega-3 fatty acids, and nucleotides. A landmark systematic review and meta-analysis of immunonutrition in gastrointestinal surgery found significant reductions in postoperative

infectious complications and length of stay compared with standard nutrition, with the strongest effects when supplementation was administered perioperatively rather than only pre- or postoperatively [15]. Complementary meta-analyses of combined immune-modulating nutrient formulas in major open gastrointestinal surgery similarly reported reduced infectious morbidity and shorter hospitalisation [16], and a broader meta-analysis across abdominal surgical populations corroborated these benefits, particularly for postoperative infectious complications [17]. Focusing specifically on colorectal cancer surgery, a meta-analysis of immunonutrition trials found reduced postoperative infection rates and length of stay without a significant mortality benefit [18], while a systematic review restricted to preoperative immune-modulating nutrition in gastrointestinal cancer surgery reported reduced overall and infectious complications, again most pronounced in patients receiving supplementation before surgery [19]. Directly comparing standard oral supplements against immunonutrition within a multicentre ERAS colorectal pathway, the SONVI trial found no significant difference in infectious complication rates or length of stay between the two supplement types when embedded in an otherwise standardised recovery protocol, suggesting the ERAS pathway itself may attenuate incremental benefits attributable to immunonutrient content [20]. Figure 2 illustrates the pattern of postoperative infectious complication rates reported across standard nutrition, standard ONS, and immunonutrition arms in this literature.

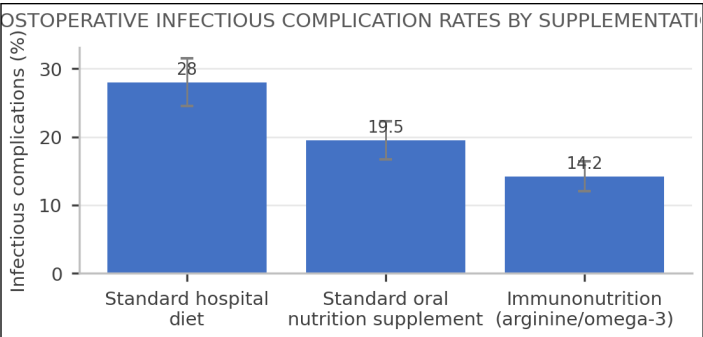


Figure 2: Illustrative synthesis of reported postoperative infectious complication rates by supplementation type (standard diet, standard oral nutritional supplement, immunonutrition) across cited trials and meta-analyses.

Oral Nutritional Supplementation within ERAS Protocols

ERAS Society recommendations for elective colorectal surgery explicitly integrate nutritional care across the perioperative continuum: preoperative carbohydrate loading, avoidance of prolonged fasting, early resumption of oral intake, and targeted ONS for patients identified as at nutritional risk [1]. Joint consensus guidance from enhanced recovery and perioperative quality organisations similarly emphasises structured nutrition screening and therapy as integral to enhanced recovery pathways rather than an isolated intervention [4]. A multicentre evaluation of ERAS implementation in elective colorectal surgery demonstrated that formal adoption of the pathway measurably improved adherence to nutrition care practices, including earlier oral intake and more consistent ONS provision, relative to pre-implementation practice [21]. Table 2 summarises the principal nutrition-related components recommended within contemporary ERAS colorectal pathways. Preoperative optimisation strategies, including nutritional prehabilitation combined with exercise and psychological preparation, have also demonstrated improved functional capacity before major abdominal surgery, complementing rather than replacing ONS-based approaches [22]. Older evidence in cancer patients without overt malnutrition

suggests that routine preoperative nutritional support confers limited additional benefit when baseline nutritional status is adequate, reinforcing that screening-guided rather than universal supplementation is the more defensible strategy within ERAS frameworks [23].

Table 2: Principal nutrition-related components recommended within contemporary ERAS pathways for elective colorectal surgery.	
ERAS phase	Nutrition-related component
Preadmission	Nutritional risk screening (e.g., NRS-2002); referral to dietitian if at risk
Preoperative	Avoidance of prolonged fasting; carbohydrate loading; preoperative ONS for at-risk patients
Intraoperative	Avoidance of excess fluid administration; normothermia to limit catabolic stress
Early postoperative	Early resumption of oral intake within hours of surgery
Postoperative recovery	Continued ONS until adequate oral intake is re-established; protein-focused intake targets

Mechanistic and Metabolic Considerations

Preoperative arginine- and omega-3-enriched supplementation has been shown to favourably modulate the immunometabolic host response following colorectal resection, including attenuated inflammatory markers and improved wound-related immune function, providing biological plausibility for the clinical benefits observed with immunonutrition [24]. Broader multinational meta-analytic data indicate that specialised perioperative nutritional support, particularly immune-enhancing formulas, is associated with reduced postsurgical infection rates across gastrointestinal surgical populations, consistent with a dose- and timing-dependent immunomodulatory mechanism [25]. Beyond immunonutrition, protein-focused nutritional strategies aligned with early mobilisation appear to support lean mass preservation and functional recovery

after colorectal surgery within ERAS pathways, suggesting that adequate protein delivery may be as clinically relevant as supplement composition [26]. Consistent with this, higher achieved protein intake during ERAS colorectal care has been directly associated with shorter length of stay compared with conventional perioperative care [27].

Conclusion

The published literature supports a consistent, if heterogeneous, benefit of perioperative oral nutritional supplementation for patients undergoing elective colorectal surgery, with the clearest gains observed in nutritionally at-risk patients and with immune-modulating formulations administered across the perioperative period. Within well-implemented ERAS pathways, incremental differences between standard and immune-enhancing supplements appear to narrow, suggesting that consistent delivery of adequate energy and protein, guided by systematic nutritional screening, may matter as much as specific formulation. Future trials should prioritise colorectal-specific populations, standardised outcome reporting, and pragmatic integration of ONS within evolving ERAS protocols to clarify which patients derive the greatest benefit from which supplementation strategy. In the interim, pragmatic clinical practice should embed nutritional risk screening at every preoperative assessment, offer ONS routinely to patients identified as at risk, and reserve immunonutrient-enriched formulas for settings where perioperative administration across both preoperative and postoperative phases is feasible, since timing appears at least as influential as formulation in determining clinical benefit.

References

1. Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced

Recovery After Surgery (ERAS®) Society Recommendations: 2018. *World J Surg*. 2019;43(3):659-695. doi:10.1007/s00268-018-4844-y. PMID: 30426190.

2. Weimann A, Braga M, Carli F, et al. ESPEN guideline: Clinical nutrition in surgery. *Clin Nutr*. 2017;36(3):623-650. doi:10.1016/j.clnu.2017.02.013. PMID: 28385477.

3. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth*. 1997;78(5):606-617. doi:10.1093/bja/78.5.606. PMID: 9175983.

4. Wischmeyer PE, Carli F, Evans DC, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway. *Anesth Analg*. 2018;126(6):1883-1895. doi:10.1213/ANE.0000000000002743. PMID: 29369092.

5. Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr*. 2005;24(3):466-477. doi:10.1016/j.clnu.2005.02.002. PMID: 15896435.

6. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA Surg*. 2017;152(3):292-298. doi:10.1001/jamasurg.2016.4952. PMID: 28097305.

7. Detsky AS, McLaughlin JR, Baker JP, et al. What is subjective global assessment of nutritional status? *JPEN J Parenter Enteral Nutr*. 1987;11(1):8-13. doi:10.1177/014860718701100108. PMID: 3820522.

8. Jie B, Jiang ZM, Nolan MT, Zhu SN, Yu K, Kondrup J. Impact of preoperative nutritional support on clinical outcome in abdominal surgical patients at nutritional risk. *Nutrition*. 2012;28(10):1022-1027. doi:10.1016/j.nut.2012.01.017. PMID: 22673593.

9. Weimann A, Braga M, Carli F, et al. ESPEN practical guideline: Clinical nutrition in surgery. *Clin Nutr*.

- 2021;40(7):4745-4761. doi:10.1016/j.clnu.2021.03.031. PMID: 34242915.
10. Burden S, Todd C, Hill J, Lal S. Pre-operative nutrition support in patients undergoing gastrointestinal surgery. *Cochrane Database Syst Rev*. 2012;11:CD008879. doi:10.1002/14651858.CD008879.pub2. PMID: 23152265.
 11. Gianotti L, Braga M, Nespoli L, Radaelli G, Beneduce A, Di Carlo V. A randomized controlled trial of preoperative oral supplementation with a specialized diet in patients with gastrointestinal cancer. *Gastroenterology*. 2002;122(7):1763-1770. doi:10.1053/gast.2002.33587. PMID: 12055582.
 12. Smedley F, Bowling T, James M, et al. Randomized clinical trial of the effects of preoperative and postoperative oral nutritional supplements on clinical course and cost of care. *Br J Surg*. 2004;91(8):983-990. doi:10.1002/bjs.4578. PMID: 15286958.
 13. Burden ST, Hill J, Shaffer JL, Campbell M, Todd C. An unblinded randomised controlled trial of preoperative oral supplements in colorectal cancer patients. *J Hum Nutr Diet*. 2011;24(5):441-448. doi:10.1111/j.1365-277X.2011.01188.x. PMID: 21699587.
 14. Beattie AH, Prach AT, Baxter JP, Pennington CR. A randomised controlled trial evaluating the use of enteral nutritional supplements postoperatively in malnourished surgical patients. *Gut*. 2000;46(6):813-818. doi:10.1136/gut.46.6.813. PMID: 10807893.
 15. Cerantola Y, Hübner M, Grass F, Demartines N, Schäfer M. Immunonutrition in gastrointestinal surgery. *Br J Surg*. 2011;98(1):37-48. doi:10.1002/bjs.7273. PMID: 20931620.
 16. Marimuthu K, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. *Ann Surg*. 2012;255(6):1060-1068. doi:10.1097/SLA.0b013e318252edf8. PMID: 22549749.
 17. Probst P, Ohmann S, Klaiber U, et al. Meta-analysis of immunonutrition in major abdominal surgery. *Br J Surg*. 2017;104(12):1594-1608. doi:10.1002/bjs.10659. PMID: 28901522.
 18. Song GM, Tian X, Zhang L, et al. Effect of immunonutrition on colorectal cancer patients undergoing surgery: a meta-analysis. *Int J Colorectal Dis*. 2017;32(5):667-677. doi:10.1007/s00384-017-2958-6. PMID: 29335838.
 19. Adiamah A, Skořepa P, Weimann A, Lobo DN. The Impact of Preoperative Immune Modulating Nutrition on Outcomes in Patients Undergoing Surgery for Gastrointestinal Cancer: A Systematic Review and Meta-analysis. *Ann Surg*. 2019;270(2):247-256. doi:10.1097/SLA.0000000000003256. PMID: 30817349.
 20. Moya P, Soriano-Irigaray L, Ramirez JM, et al. Perioperative Standard Oral Nutrition Supplements Versus Immunonutrition in Patients Undergoing Colorectal Resection in an Enhanced Recovery (ERAS) Protocol: A Multicenter Randomized Clinical Trial (SONVI Study). *Medicine (Baltimore)*. 2016;95(21):e3704. doi:10.1097/MD.0000000000003704. PMID: 27227930.
 21. Martin L, Gillis C, Atkins M, et al. Implementation of an Enhanced Recovery After Surgery Program Can Change Nutrition Care Practice: A Multicenter Experience in Elective Colorectal Surgery. *JPEN J Parenter Enteral Nutr*. 2019;43(2):206-219. doi:10.1002/jpen.1417. PMID: 30035814.
 22. Barberan-Garcia A, Ubré M, Roca J, et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Ann Surg*. 2018;267(1):50-56. doi:10.1097/SLA.0000000000002293. PMID: 28489682.
 23. Kabata P, Jastrzębski T, Kąkol M, et al. Preoperative nutritional support in cancer patients with no clinical signs of malnutrition-prospective randomized controlled trial.

Support Care Cancer. 2015;23(2):365-370.
doi:10.1007/s00520-014-2363-4. PMID: 25091056.

24. Braga M, Gianotti L, Vignali A, Di Carlo V. Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer. *Surgery*. 2002;132(5):805-814. doi:10.1067/msy.2002.128350. PMID: 12464864.
25. Waitzberg DL, Saito H, Plank LD, et al. Postsurgical infections are reduced with specialized nutrition support. *World J Surg*. 2006;30(8):1592-1604. doi:10.1007/s00268-005-0657-x. PMID: 16865314.
26. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. *Curr Opin Clin Nutr Metab Care*. 2005;8(1):23-32. doi:10.1097/00075197-200501000-00005. PMID: 15585997.
27. Yeung SE, Hilkewich L, Gillis C, Heine JA, Fenton TR. Protein intakes are associated with reduced length of stay: a comparison between Enhanced Recovery After Surgery (ERAS) and conventional care after elective colorectal surgery. *Am J Clin Nutr*. 2017;106(1):44-51. doi:10.3945/ajcn.116.148619. PMID: 28460971.