Impact of Early Postoperative Oral Nutritional Supplement Utilization on Clinical Outcomes in Colorectal Surgery

David G.A. Williams
Duke University School of Medicine
Tetsu Ohnuma
Duke University School of Medicine
Vijay Krishnamoorthy
Duke University School of Medicine
Karthik Raghunathan
Duke University School of Medicine
Suela Sulo
Abbott Nutrition
Bridget A. Cassady
Abbott Nutrition
Refaat Hegazi
Abbott Nutrition
Paul E. Wischmeyer (paul.wischmeyer@duke.edu)
Duke University School of Medicine https://orcid.org/0000-0002-3369-7911

Research

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Abstract

Background: Small randomized trials of early postoperative oral nutritional supplementation (ONS) suggest various health benefits following colorectal surgery (CRS). However, real-world evidence of the impact of early ONS on clinical outcomes in CRS is lacking.

Methods: Using a nationwide administrative-financial database (Premier Healthcare Database), we examined the association between early ONS use and postoperative clinical outcomes in patients undergoing elective open or laparoscopic CRS between 2008–2014. Early ONS was defined as the presence of charges for ONS before postoperative day (POD) 3. The primary outcome was composite infectious complications. Key secondary efficacy (intensive care unit (ICU) admission and gastrointestinal complications) and falsification (blood transfusion and myocardial infarction) outcomes were also examined. Propensity score matching was used to assemble patient groups that were comparable at baseline and differences in outcomes were examined.

Results: Overall, patients receiving early ONS were older with greater comorbidities, and more likely to be Medicare beneficiaries with malnutrition. In a well-matched sample of early-ONS recipients (n=267) versus non-recipients (n= 534), infectious complications were significantly lower in early-ONS recipients (6.7% vs. 11.8%, P<0.03). Early-ONS use was also associated with significantly reduced rates of pneumonia (P<0.04), ICU admissions (P<0.04), and gastrointestinal complications (P<0.05). There were no significant differences in falsification outcomes.

Conclusions: Although early postoperative ONS after CRS was more likely to be utilized in elderly patients with greater comorbidities, use of early ONS was associated with reduced infectious complications, pneumonia, ICU admission, and gastrointestinal complications. This propensity-score matched study using real-world data suggests that clinical outcomes are improved with early ONS use, a simple and inexpensive intervention in CRS patients.

Introduction

Perioperative malnutrition is a widely prevalent and potentially modifiable risk factor in patients undergoing colorectal surgery (CRS). Recent data indicate as many as 2 out of 3 patients are malnourished at time of presentation for major gastrointestinal surgery, including CRS.(1),(2) Further, perioperative malnutrition is a clinical predictor of postoperative mortality and morbidity in CRS. Malnutrition has been associated with increased hospital length of stay (LOS)(3), readmissions, costs of care(4), and especially increased risk of postoperative infection.(5, 6) Postoperative infection remains among the major complications following CRS(7) and quality improvement initiatives aimed at reducing surgical infections focus on appropriate administration of prophylactic antibiotics, perioperative hair clipping, normothermia,(8, 9) and early perioperative nutritional support.(2)

Postoperative nutritional support is vital in maintaining nutritional status during the catabolic postoperative period and underscored by evidence for early oral intake following surgery as a routine part

of ERAS protocols.[10-12] In fact, early oral intake has been identified as a key independent factor of improved outcomes following CRS.(10) Oral feeding is the preferred mode of nutrition for post-surgical patients.(11) Recovering postoperative patients, especially older adults, are challenged by decreased appetites, persistent nausea, opioid induced constipation, and lack of education about how to optimize their diet.(12) Thus, nutritional therapy, often via oral nutritional supplements (ONS), may be required during the postoperative period following major surgery to avoid significant risk for occurrence of postoperative malnutrition.(2, 13) To address this, recent guidelines suggest that ONS should be routinely included in the postoperative care of gastrointestinal (GI) surgery patients to meet their nutritional needs.(2) However, research evidence on clinical outcomes data to support this recommendation are currently limited.(14)

ONS use in general hospitalized populations is variable between hospitals and it's use early during the postoperative period is currently not routine standard of care. Prior small randomized controlled trials and older meta-analysis of such trials show initial benefits of early oral feeding (on postoperative day (POD) 1)(14) versus delayed feeding, on outcomes for patients undergoing GI surgery. The more recent Cochrane review of early post-operative nutrition in lower GI surgery continues to indicate promise of early nutrition delivery for improved clinical outcomes, but indicates additional data is urgently needed.(14) Additional meta-analysis data has examined the specific use of perioperative immunonutrition (arginine-containing ONS). These data from have consistently shown benefit of perioperative immunonutrition primarily on infectious outcomes.(15) Further, recent surgical nutrition guidelines emphasize the key role of high-protein delivery to improve recovery post-major abdominal surgery, such as CRS.(2) Despite this, quite limited data exists from only few trials of solely high-protein ONS (non-immunonutrition) and this data show promise for improved outcomes from early postoperative high-protein ONS use.(16, 17) However, large-scale real-world evidence is lacking to support the hypothesis that early postoperative ONS is associated with improved outcomes and is urgently needed to help support or refute the existing guideline reccomendations.(2) Thus, we examined the impact of early ONS (within 3 days of surgery) on post-operative infection and other clinical outcomes for patients undergoing CRS using a large administrative U.S. healthcare database.

Materials And Methods

Data Source

The Premier Healthcare Database (PHD) contains cumulative data from over 970 contributing teaching and nonteaching hospitals/healthcare system hospitals across the U.S. (see https://products.premierinc.com/downloads/PremierHealthcareDatabaseWhitepaper.pdf for details). These hospitals vary in bed capacity and provide care to a largely urban population from all four geographic regions and their respective divisions as defined by the U.S. Census. The PHD contains data on patient demographics, payer status, International Classification of Diseases (ICD) Diagnosis Codes, day-stamped Current Procedural Terminology (CPT) codes, and day-stamped hospital charge codes for every patient encounter for over 208 million unique patients.

Population and Study Design

This was a retrospective cohort study among patients aged ≥ 18 years who underwent elective open or laparoscopic CRS between October 2008 and September 2014. Exclusion criteria included nonsurgical and outpatient surgical encounters (i.e., ambulatory surgeries and encounters with hospital LOS < 1-day, non-elective, non-colorectal surgeries, and encounters with missing ONS charges, or patients who experienced in-hospital death or required mechanical ventilation within the first three POD. This created an eligible study population of 61,031 patient encounters from 172 hospitals. The final study cohort was divided into groups of patients exposed and not-exposed to early ONS following CRS.

Exposures, Outcomes, and Covariates

Exposure to early ONS within the PHD was analyzed for inpatient encounters following CRS to determine the association between receiving ONS early during the postoperative period and subsequent clinical outcomes. The study exposure was early ONS, defined as receipt by POD 3 following colorectal surgery. To ensure that each encounter in the study cohort had the potential for exposure to ONS early during the postoperative period, we used tight exclusion criteria as previously described. Because there are not specific ICD-9/10 or CPT codes identifying ONS use, we relied on the PHD definition of “complete nutritional supplement, oral”. Product information under this definition were manually checked for accuracy. Enteral nutrition or tube feeding products were excluded, as were modular nutrient supplements (i.e. sole protein alone supplements or glutamine alone). The primary outcome was a composite of infectious complications, which was identified using ICD-9 codes [*See Supplement 1 for full infectious outcome details*]. Secondary efficacy outcomes included ICU admission and GI complications as well as falsification outcomes such as red blood cell (RBC) transfusion and myocardial infarction. The falsification outcomes were assessed to examine non-biologically plausible outcomes that are highly unlikely to be related to an early post-operative ONS.(18) A confirmed falsification test —in this case, an association between early ONS use and risks of these conditions—would suggest that perhaps residual confounding exists. Covariates considered in our analyses included malnutrition diagnosis, age, gender, race/ethnicity, insurance type (i.e., Medicare, Medicaid, and Managed Care Organizations (MCO), and other), hospital teaching status, hospital bed size, cancer, chronic obstructive pulmonary disease (COPD), chronic renal failure, vasopressor use, the van Walraven (VW) score, and data year. Comorbidity scores are validated and utilized in healthcare to classify a patient’s disease burden and predict mortality based on the type and number of patient comorbidities present.(19, 20) The VW score condenses the Elixhauser comorbidity system to a single numeric score that summarizes disease burden and is adequately discriminative for death in hospital.(21)

Statistical Analysis

Patients exposed to early ONS were identified and matched with greedy propensity score techniques (in a 1:2 fashion),(22) to match exposed patients to unexposed patients to early ONS. A propensity score was built with the following variables: malnutrition, sex, age, VW score, payor category, race/ethnicity, cancer, renal failure, COPD, elective surgery, open surgery, vasopressor, hospital bed size, teaching hospital, and

rural hospital. After matching, the standardized mean difference (SMD) were used to test the balance of covariates. A univariable logistic regression for binary outcomes was used to determine the association between early ONS exposure and clinical outcomes in the fully matched cohort. All analyses were performed via SAS version 9.4 (SAS Institute), and a *P*-value of < 0.05 was considered statistically significant.

Results

Beginning with all patient encounters from 655 participating hospitals, the applied exclusion criteria resulted in 61,031 eligible patients [Figure 1]. ONS was provided in 267 (0.4%) of these patients. Of all patients eligible for ONS by POD 3, 5% had the diagnosis of malnutrition, 60% were aged ≥ 60 year, 48% were Medicare beneficiaries, 74% were Caucasian, 43% were from teaching hospitals, and 53% received care at mid-sized hospitals [Table 1]. Outcome analysis in the overall cohort revealed 4% of patients required ICU admission after POD 3, 15% required RBC transfusion, 5% experienced infectious complications, 2% experienced pneumonia, 15% experienced GI complications, and the median hospital cost was $24,954 [Table 2].

Propensity Score Matching

Propensity-score matching produced a sample of 801 hospitalizations that was more balanced than the pre-matched sample in terms of observed characteristics such as age, sex, race/ethnicity, and comorbidities [Table 3]. After matching, the two groups were comparable in terms of baseline characteristics (-0.1 < SMD < 0.1) [Figure 2].

Association Between Early ONS Exposure and Reduced Infectious Complications

Early ONS exposure was associated with significantly fewer infectious complications (6.7% vs 11.7%, P < 0.03) and pneumonia rates (2.6% vs 6.2%, P < 0.04) in the matched sample [Table 4]. Early ONS use was also associated with fewer ICU admissions (6% vs. 10%, P < 0.04) and fewer GI complications (16.5% vs 22.5%, P < 0.05). The matched sample did not, however, show a statistically significant difference in LOS and hospital costs associated with early ONS use.

Falsification Variable Analysis:

Falsification variable analysis was used as described previously to assess for residual confounding in health outcome research(23). As described in a recent JAMA publication, pre-specified falsification end points, when confirmed, assist in validating true observational associations(23). We believe that it is highly unlikely for red blood cell transfusions and myocardial infarction to be causally related to early ONS use, (i.e. we do not see an obvious causal pathway between early ONS use and these outcomes). Finding an association therefore would suggest possible residual confounding. We did not observe a statistically significant difference in RBC transfusion and myocardial infarction in the matched sample.

This assists in supporting the validity of the biologically plausible finding that ONS was associated with decreased infectious complications.

Table 1. Baseline characteristics of colorectal surgery patients receiving oral nutritional supplement prior to matching.

Characteristics	Before matching	
	Overall Cohort (n=61,031)	Column Percentage
Malnutrition	*3103*	*5%*
Male	*28047*	*46%*
Age Group		
<30	*1142*	*2%*
30 - 39	*2783*	*5%*
40 - 49	*6734*	*11%*
50 - 59	*14042*	*23%*
60 - 69	*16507*	*27%*
70 - 79	*13248*	*22%*
>=80	*6575*	*11%*
VW Score Category		
<-5	*897*	*1%*
-5 to -1	*7563*	*12%*
-1 to 1	*29018*	*48%*
1 to 5	*9133*	*15%*
>5	*14420*	*24%*
Co-morbidities		
Cancer	*12333*	*20%*
Renal failure	*2444*	*4%*
Chronic pulmonary disease	*8440*	*14%*
Payor Category		
Managed care organization	*21682*	*36%*
Medicaid	*2353*	*4%*
Medicare	*29018*	*48%*
Other	*7978*	*13%*
Race		
Black	*4953*	*8%*
Hispanic	*1030*	*2%*
Other	*9808*	*16%*
White	*45240*	*74%*
Open Colorectal Surgery	*36371*	*60%*
Hospital Bedsize		
<200	*5446*	*9%*
200-499	*32410*	*53%*
≥500	*23175*	*38%*
Teaching hospital	*26037*	*43%*
Rural Hospital	*5644*	*9%*
Vasopressor	*17381*	*28%*

Table 2. Outcomes of colorectal sugery patient cohort receiving oral nutritional supplement prior to matching.

Outcome	Before matching	
	Overall Cohort (n=61,031)	Column Percentage
ICU admission after POD 3	*2670*	*4%*
In-hospital mortality	*287*	*0%*
Myocardial Infarction	*872*	*1%*
RBC Transfusion	*9373*	*15%*
Thrombosis (DVT, PE)	*29*	*0%*
Pneumonia	*1501*	*2%*
Infection	*3133*	*5%*
GI complication	*9389*	*15%*
30-day readmission	*6797*	*11%*
90-day readmission	*10123*	*17%*
	Median	*IQR*
LOS	*4*	*(3, 6)*
Hospital Cost	*$24,953.88*	*($7,472.57, $20,422.25)*

ICU, intensive care unit; POD, postoperative day; RBC, red blood cell; DVT, deep vein thrombosis; PE, pulmonary embolism; GI, gastrointestinal; LOS, length of stay; IQR, interquartile range

Table 3. Baseline characteristics of colorectal surgery patient cohorts analyzed for ONS and non-ONS use after matching.

Characteristics	After Matching				
	ONS	Percentage	Non-ONS	Percentage	SMD
	(n=267)		(n=534)		
Malnutrition	*57*	*21.3*	109	20.4	0.02
Male	*125*	*46.8*	247	46.3	0.01
Age Group					0.13
<30	*11*	*4.1*	21	3.9	
30 - 39	*10*	*3.7*	15	2.8	
40 - 49	*10*	*3.7*	18	3.4	
50 - 59	*50*	*18.7*	90	16.9	
60 - 69	*60*	*22.5*	130	24.3	
70 - 79	*67*	*25.1*	125	23.4	
>=80	*59*	*22.1*	135	25.3	
VW Score Category					0.17
<-5	*3*	*1.1*			
5 to -1	*32*	*12*	57	10.7	
-1 to 1	*95*	*35.6*	214	40.1	
1 to 5	*35*	*13.1*	58	10.9	
>5	*102*	*38.2*	205	38.4	
Co-morbidities					0.00
Cancer	*71*	*26.6*	142	26.6	0.02
Renal failure	*14*	*5.2*	26	4.9	0.11
Chronic pulmonary disease	*46*	*17.2*	71	13.3	
Payor Category					0.11
Managed care organization	*61*	*22.8*	114	21.3	
Medicaid	*15*	*5.6*	23	4.3	
Medicare	*169*	*63.3*	351	65.7	
Other	*22*	*8.2*	46	8.6	
Race					0.08
Black	*25*	*9.4*	38	7.1	
Hispanic	*2*	*0.7*	3	0.6	
Other	*21*	*7.9*	46	8.6	
White	*219*	*82*	447	83.7	
Open Colorectal Surgery	*193*	*72.3*	402	75.3	0.11
Hospital Bedsize					0.02
<200	*76*	*28.5*	157	29.4	
200-499	*132*	*49.4*	255	47.8	
≥500	*59*	*22.1*	122	22.8	
Teaching hospital	*69*	*25.8*	138	25.8	0.00
Rural Hospital	*50*	*18.7*	99	18.5	0.00
Vasopressor	*108*	*40.4*	216	40.4	0.00

Table 4. Outcomes of colorectal surgery patient cohorts analyzed for ONS and non-ONS use after matching.

Outcome	After Matching				
	ONS (n=267)	Percentage	Non-ONS (n=534)	Percentage	p-value*
ICU after POD3	*16*	*6*	56	10.5	0.0384
In-hospital mortality	*3*	*1.1*	14	2.6	0.18
Myocardial Infarction	*5*	*1.9*	18	3.4	0.24
RBC Transfusion	*87*	*32.6*	147	27.5	0.14
Thrombosis (DVT, PE)	*0*	*0*	0	0	None
Pneumonia	*7*	*2.6*	33	6.2	0.034
Infection	*18*	*6.7*	63	11.8	0.027
GI complication	*44*	*16.5*	120	22.5	0.049
30-day readmission	*34*	*12.7*	68	12.7	1
90-day readmission	*52*	*19.5*	97	18.2	0.65
	Median	*IQR*	Median	IQR	
LOS	*7*	*(4, 10)*	6	(4, 9)	0.3471
Hospital Cost	*16132.94*	*(11472.1, 22448.69)*	14279.46	(10102.68, 19844.54)	0.3454

ICU, intensive care unit; POD, postoperative day; RBC, red blood cell; DVT, deep vein thrombosis; PE, pulmonary embolism; GI, gastrointestinal; LOS, length of stay; IQR, interquartile range.

* Univariable logistic regression for binary outcomes or paired t-test for continuous outcomes.

Discussion

Our real-world practice data shows, despite surgical guidelines encouraging early ONS utilization, ONS remains highly underutilized following CRS. Early ONS use was more frequently utilized in older CRS surgery patients with higher numbers of comorbid conditions. Our key finding was exposure to early ONS was associated with reduced infectious complications including pneumonia. Further, early ONS utilization led to fewer ICU admissions and reduced GI complications. These real-world findings support the results from existing limited randomized controlled trial data in the postoperative CRS patients.(15-17)

Surgery exerts a significant catabolic stress characterized by the presence of an inflammatory response associated with mobilization of muscle amino acid stores and potentially conditionally essential nutrients, which is associated with a dysregulated immune response that increases risk for postoperative complications, especially infectious complications.(24) Both innate and adaptive immunity undergo

change in response to the physiologic stress of surgery.(25) The severity of immune dysfunction is proportional to the extent of surgical trauma and depends on a number of factors, including the underlying disease requiring surgical treatment (e.g., cancer), coexisting infections, and impaired nutritional status. It is generally believed that major surgery is accompanied by sustained postoperative immunosuppression, which potentially increases the risk for infectious complications particularly in patients undergoing surgery for cancer.(26) These data suggest that early ONS, administered by POD 3, may modulate the immune response to surgery and lead to reduced infectious complications.

These data provide key support to previous studies showing a signal of reduced infectious as a result of the use of postoperative ONS, primarily immunonutrition (IMN).(15) A few recent studies demonstrated that IMN continues to show benefit, even in the context of modern enhanced recovery after surgery (ERAS) pathways. Moya et. al demonstrated a reduction in infectious complications (23.8% vs 10.7%; P = 0.0007), especially wound infections (16.4% vs 5.7%; P = 0.0008) with the use of IMN ONS when compared to standard high-calorie ONS.(27) This trial delivered IMN ONS both pre- and postoperatively, whereas our data demonstrate an outcome benefit of postoperative ONS delivery alone on infectious complications. Our data reports the composite effect of all types of early ONS therapy and does not distinguish between IMN and standard ONS (including high protein ONS). As previously described, very limited data exists for standard and high protein ONS in CRS surgery. To our knowledge, only one recent trial was conducted examining postoperative standard ONS in CRS and demonstrated that postoperative high protein ONS reduced LOS.(17) These data is among the first to demonstrate early ONS use, regardless of the specific formulation, improved infectious outcomes compared to patients not receiving ONS.

Early post-operative feeding in CRS has traditionally been challenged by perceived concerns for dysmotility, ileus, and postoperative gastrointestinal dysfunction.(2, 28, 29) Traditionally, postoperative oral intake is delayed until clinical signs of the return of bowel function are present. Current ERAS practice, emphasizing immediate post-operative initiation of oral nutrition challenges this dogma(30). Early oral feeding after CRS has been shown to be a key factor in improving bowel motility after surgery, and reduces the incidence of postoperative paralytic ileus.(31) Finally, early oral intake (on POD 1) after GI surgery has been shown in meta-analysis of multiple studies to significantly reduce mortality after GI surgery (when compared with patients who receive delayed feeding). In fact, surgical oncology patients who receive care with at least 70% of recommended ERAS pathways (including feeding on POD 1) have 42% improved 5-year survival versus patients not receiving ERAS care.(32) Early postoperative feeding along with appropriate fluid management were shown to be the key ERAS components essential to improving postoperative outcomes in this study. Thus, the current scientific literature supports that oral intake should be resumed as soon as possible after CRS.

The reduction in overall infection rates observed in this study potentially bears a financial consequence for hospitals as healthcare reimbursement progresses to a fee-for-value based system.(33) The Centers for Medicare and Medicaid Services (CMS) linked payment to specific quality measures through both the Hospital-Acquired Condition (HAC) Reduction Program and the Hospital Value-Based Purchasing (VBP)

Program.(34, 35) These two programs put hospitals at risk of losing over $1.9 billion in annual revenue through a reduction in payment to those deemed to be providing lower quality of care and a redistribution of payment to others deemed to be providing higher quality care. Surgical site infection (SSI) rates are one of the major hospital quality metrics tracked by these programs, which is key as SSI following CRS remains a significant challenge.(7) Our data implies early ONS use following CRS as a feasible, practical clinical measure to improve this surgical outcome and provide financial savings to hospitals through cost avoidance.

This study has several limitations. First, it was not possible to discern how much of the prescribed ONS was consumed by patients. Next, it was also not possible to address whether certain ONS formulations were more advantageous than others since we relied on the PHD definition of “complete nutritional supplement, oral.” Also, while PHD is a representation of the broad surgical patient population and hospital systems that provide perioperative care, its generalizability may be limited. Propensity score methods can help address confounding by observable characteristics through balancing the exposure and treatment groups according to those observable characteristics. However, unobservable characteristics, which may be associated with the propensity to receive ONS and influence clinical outcomes (i.e., unmeasured health status and socioeconomic status) are not addressed by propensity score methods. Lastly, as this study is a retrospective cohort study, it allows only for causal inferences that are hypothesis generating for further prospective investigation.

Conclusion

This large-scale study of real-world practice demonstrate benefits of providing early postoperative ONS in CRS patients. Our data show early postoperative ONS was more likely to be utilized in elderly patients, with greater comorbidities following CRS. Our key finding is that infectious complications were significantly reduced when early ONS was delivered in a well-matched sample of CRS patients. In addition, rates of pneumonia, ICU admission and GI complications were decreased with early ONS use. Despite the observed benefits in this study, and surgical guidelines suggesting early post-operative ONS use in abdominal surgery, we observed limited ONS use in this high-risk group of surgical patients. These data suggest improved clinical outcomes and potential healthcare cost savings can be achieved from this simple and inexpensive clinical intervention. These findings also provide key initial data for future surgical nutrition clinical outcomes work and much needed randomized clinical trials and quality improvement studies in post-operative ONS use to improve patient health and economic outcomes.

Declarations

- Ethics approval and consent to participate- Not applicable/required as only anonymous healthcare database data with no personal health information (PHI) utilized
- Consent for publication- Not applicable

- Availability of data and materials- The data that support the findings of this study are available from Premier Health Inc but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Premier Health Inc.
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References

1. Bruns ERJ, Argillander TE, Van Den Heuvel B, Buskens CJ, Van Duijvendijk P, Winkels RM, et al. Oral Nutrition as a Form of Pre-Operative Enhancement in Patients Undergoing Surgery for Colorectal Cancer: A Systematic Review. Surg Infect (Larchmt). 2018;19(1):1-10.
2. Wischmeyer PE, Carli F, Evans DC, Guilbert S, Kozar R, Pryor A, 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):1883-95.
3. Garth AK, Newsome CM, Simmance N, Crowe TC. Nutritional status, nutrition practices and post-operative complications in patients with gastrointestinal cancer. J Hum Nutr Diet. 2010;23(4):393-401.
4. Bliss LA, Maguire LH, Chau Z, Yang CJ, Nagle DA, Chan AT, et al. Readmission After Resections of the Colon and Rectum: Predictors of a Costly and Common Outcome. Dis Colon Rectum. 2015;58(12):1164-73.
5. Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbuminemia Independently Predicts Surgical Site Infection, Pneumonia, Length of Stay, and Readmission After Total Joint Arthroplasty. The Journal of arthroplasty. 2016;31(1):15-21.

6. Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Maeda S, Haraguchi N, et al. Prevalence of Malnutrition Among Gastric Cancer Patients Undergoing Gastrectomy and Optimal Preoperative Nutritional Support for Preventing Surgical Site Infections. Annals of surgical oncology. 2015;22 Suppl 3:S778-85.
7. Smith RL, Bohl JK, McElearney ST, Friel CM, Barclay MM, Sawyer RG, et al. Wound infection after elective colorectal resection. Annals of surgery. 2004;239(5):599-607.
8. Arriaga AF, Lancaster RT, Berry WR, Regenbogen SE, Lipsitz SR, Kaafarani HMA, et al. The Better Colectomy Project: Association of Evidence-Based Best-Practice Adherence Rates to Outcomes in Colorectal Surgery. Annals of surgery. 2009;250(4):507-13.
9. Berenguer CM, Ochsner MG, Jr., Lord SA, Senkowski CK. Improving Surgical Site Infections: Using National Surgical Quality Improvement Program Data to Institute Surgical Care Improvement Project Protocols in Improving Surgical Outcomes. Journal of the American College of Surgeons. 2010;210(5):737-41.
10. Vlug MS, Bartels SA, Wind J, Ubbink DT, Hollmann MW, Bemelman WA. Which fast track elements predict early recovery after colon cancer surgery? Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2012;14(8):1001-8.
11. Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. Clin Nutr. 2006;25(2):224-44.
12. Wischmeyer PE. Are we creating survivors...or victims in critical care? Delivering targeted nutrition to improve outcomes. Curr Opin Crit Care. 2016;22(4):279-84.
13. Weimann A, Braga M, Carli F, Higashiguchi T, Hubner M, Klek S, et al. ESPEN guideline: Clinical nutrition in surgery. Clinical nutrition (Edinburgh, Scotland). 2017;36(3):623-50.
14. Herbert G, Perry R, Andersen HK, Atkinson C, Penfold C, Lewis SJ, et al. Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications. Cochrane Database Syst Rev. 2019;7:CD004080.
15. Drover JW, Dhaliwal R, Weitzel L, Wischmeyer PE, Ochoa JB, Heyland DK. Perioperative use of arginine-supplemented diets: a systematic review of the evidence. J Am Coll Surg. 2011;212(3):385-99, 99 e1.
16. Keele AM, Bray MJ, Emery PW, Duncan HD, Silk DB. Two phase randomised controlled clinical trial of postoperative oral dietary supplements in surgical patients. Gut. 1997;40(3):393-9.
17. 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. The American journal of clinical nutrition. 2017.
18. Pizer SD. Falsification Testing of Instrumental Variables Methods for Comparative Effectiveness Research. Health Serv Res. 2016;51(2):790-811.
19. Thompson NR, Fan Y, Dalton JE, Jehi L, Rosenbaum BP, Vadera S, et al. A new Elixhauser-based comorbidity summary measure to predict in-hospital mortality. Med Care. 2015;53(4):374-9.

20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases. 1987;40(5):373-83.
21. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A Modification of the Elixhauser Comorbidity Measures Into a Point System for Hospital Death Using Administrative Data. Med Care. 2009;47(6):626-33.
22. Austin PC. A comparison of 12 algorithms for matching on the propensity score. Stat Med. 2014;33(6):1057-69.
23. Prasad V, Jena AB. Prespecified Falsification End Points: Can They Validate True Observational Associations? Jama. 2013;309(3):241-2.
24. Hegazi RA, Hustead DS, Evans DC. Preoperative standard oral nutrition supplements vs immunonutrition: results of a systematic review and meta-analysis. J Am Coll Surg. 2014;219(5):1078-87.
25. Maung AA, Davis KA. Perioperative Nutritional Support: Immunonutrition, Probiotics, and Anabolic Steroids. Surgical Clinics of North America. 2012;92(2):273-83.
26. Dąbrowska AM, Słotwiński R. The immune response to surgery and infection. Cent Eur J Immunol. 2014;39(4):532-7.
27. Moya P, Soriano-Irigaray L, Ramirez JM, Garcea A, Blasco O, Blanco FJ, 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.
28. Petrini J. Colon and Rectal Surgery. Corman ML Diet and drugs in colorectal surgery 6th Ed New York: Lippincott Williams & Wilkins. 2005:50.
29. Artinyan A, Nunoo-Mensah JW, Balasubramaniam S, Gauderman J, Essani R, Gonzalez-Ruiz C, et al. Prolonged Postoperative Ileus—Definition, Risk Factors, and Predictors after Surgery. World journal of surgery. 2008;32(7):1495-500.
30. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. JAMA Surg. 2017;152(3):292-8.
31. Ng WQ, Neill J. Evidence for early oral feeding of patients after elective open colorectal surgery: a literature review. Journal of Clinical Nursing. 2006;15(6):696-709.
32. Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O. Adherence to the ERAS protocol is Associated with 5-Year Survival After Colorectal Cancer Surgery: A Retrospective Cohort Study. World J Surg. 2016;40(7):1741-7.
33. Aronson S, Westover J, Guinn N, Setji T, Wischmeyer P, Gulur P, et al. A Perioperative Medicine Model for Population Health: An Integrated Approach for an Evolving Clinical Science. Anesth Analg. 2018;126(2):682-90.
34. VanLare JM, Conway PH. Value-Based Purchasing — National Programs to Move from Volume to Value. New England Journal of Medicine. 2012;367(4):292-5.

35. Calderwood MS, Kleinman K, Huang SS, Murphy MV, Yokoe DS, Platt R. Surgical Site Infections: Volume-Outcome Relationship and Year-to-Year Stability of Performance Rankings. Med Care. 2017;55(1):79-85.

Figures

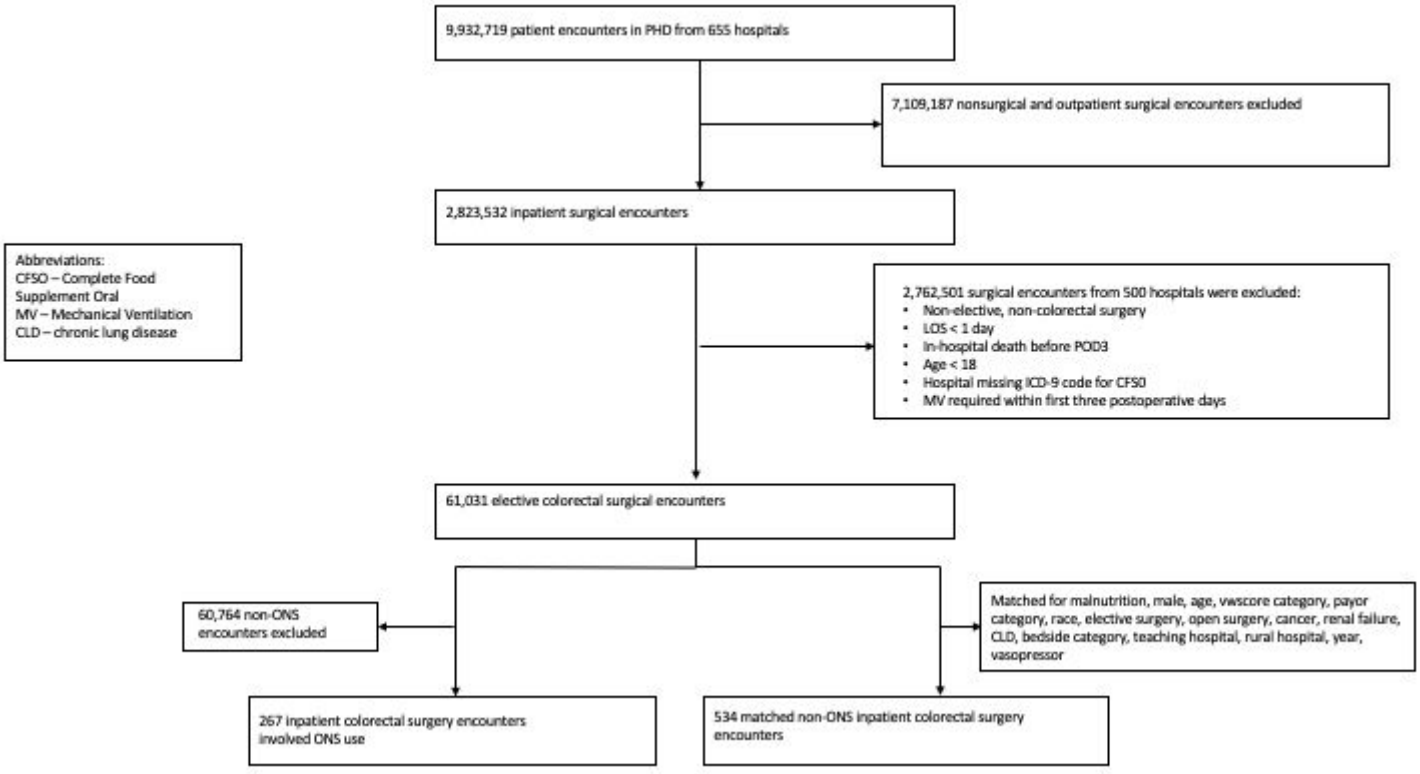

Figure 1

Patient Flow and Availability Chart

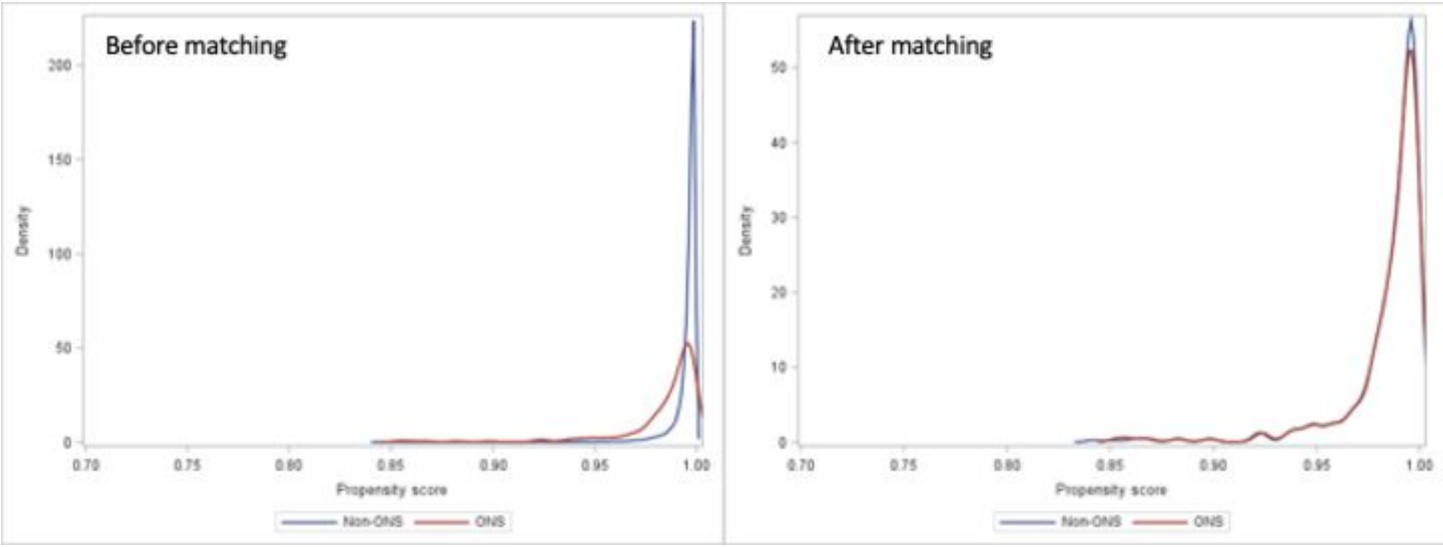

Figure 2

Kernel density plot with comparison of Non-ONS group (blue line) and ONS group (red line) before (left panel) and after (right panel) propensity score matching.