IMPACT®

Family of Formulas

Clinical Study Reference

Evidence-Based Immunonutrition for Major Elective Surgery and Trauma Patients

NestléHealthScience

Overview of IMPACT® Formulas

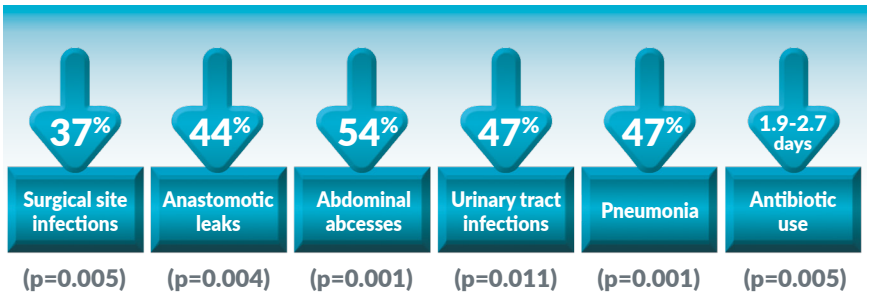
An Evidence-Based Choice: IMPACT® formulas have more evidence, in more patients, with more positive outcomes than any other immunonutrition formula.

IMPACT® formulas have consistently shown improved outcomes in major elective surgery, including: Upper GI, Lower GI, Cardiac, Head and Neck, Bladder Cancer, Gynecological Oncology, and Hip.

IMPACT® Formulas:

- Meet Surgical Nutrition Consensus Recommendations* for preoperative immunonutrition[1]
- Contain immune-modulating nutrients supported perioperatively by the 2016 Critical Care Nutrition Guidelines[2]**
- Meet Strong for Surgery® criteria for evidence-based immune modulating supplemental nutrition[3]
- Have been used successfully in conjunction with Enhanced Recovery Protocols (ERPs) [4–6]

Use of IMPACT® formulas in Major Elective Surgery Patients Clinical Outcomes[7,8] of IMPACT® formulas include reductions in risk of:



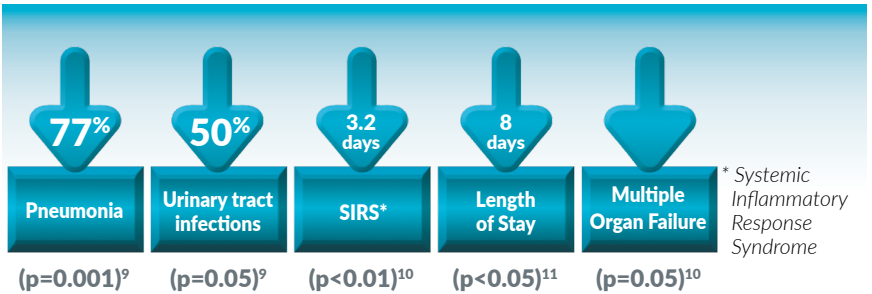
* Resulting from the North American Surgical Nutrition Summit, sponsored by Nestlé Health Science.

** The above statement does not constitute an endorsement of IMPACT® formula or any other Nestlé Health Science product by SCCM or A.S.P.E.N.

Strong for Surgery is a registered trademark of the American College of Surgeons

Use of IMPACT® Formulas in Trauma Patients

In clinical trials conducted on the early enteral use of IMPACT® formulas in trauma patients, results also include significant reductions in:

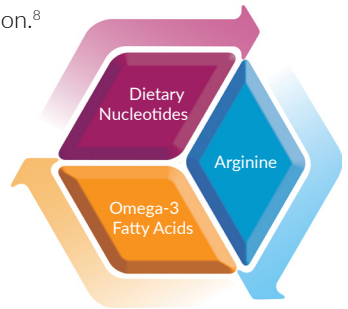


Mechanisms of Action

The IMPACT® family of enteral formulas contains a unique blend of three synergistic immunonutrients. This blend has documented outcomes in more than 80 publications, including several meta-analyses, which show these ingredients support the unique nutritional needs of the major elective surgery patient by helping support the immune and vascular systems to reduce the risk of postoperative complications.

Arginine:

- Enhances host immune response by promoting T-lymphocyte growth and replication, and nitrogen retention.[12–15]
- Increases levels of hydroxyproline, the main precursor for collagen, thereby playing a role during wound management.[12–16]
- Increases gut oxygenation and colonic microperfusion.[8]
- Stimulates synthesis of nucleotides in vitro.[17]



Dietary Nucleotides:

- Support replication of the rapidly dividing cells of the immune system, i.e., T-lymphocytes, by providing a source of purine and pyrimidine bases for DNA/RNA production.[17–19]

Omega-3 Fatty Acids from Fish Oil:

- Modulate cytokines to produce less inflammatory and less immunosuppressive mediators.[20]
- Produce less inflammatory prostaglandins (PGE3) to help to alleviate arginine deficiency by reducing induction of arginase 1.[21]

Changing Healthcare Environment

Inadequate nutrition intervention negatively affects outcomes,[22,23] impacting quality and safety scores, while placing significant healthcare dollars at risk.[24] This section provides information on Centers for Medicare and Medicaid (CMS)-related health care reform initiatives relevant to IMPACT® formulas.

Triple Aim

A national health quality strategy being utilized in healthcare organizations that is aligned with what IMPACT® formulas are designed to do:

- Better Care, Better Health, and Lower Cost[25]

Hospital Readmissions Reduction Program (HRRP)[26]

Hospitals will receive reduced payments from Medicare if they have excess readmissions within 30 days of discharge for certain diagnoses including coronary artery bypass graft (CABG) and hip replacement. IMPACT® formulas have been shown to improve clinical outcomes in both these surgeries.[5,27]

Complications after general surgery increase the risk of readmission by 4 times.[28] IMPACT® formulas reduce risk of infectious complications by 51%[23] and thereby support a reduction in readmissions following major elective surgery.

Hospital-Acquired Conditions Present on Admission (HAC POA)[29]

Hospitals will not receive additional Medicare payment for the following nutrition-related conditions if they were not present on admission: pressure injuries, urinary tract infections (UTIs), and surgical site infection (SSI) following CABG.

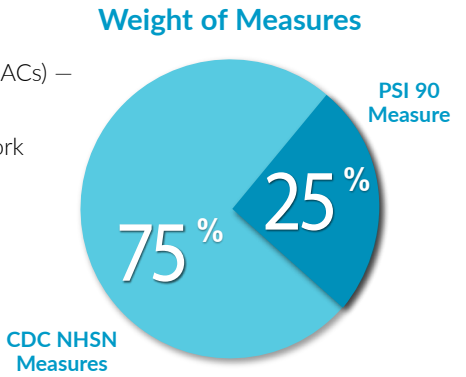
IMPACT® formulas have been found to reduce the risk of UTIs by 47% and SSIs by 37%[7]. In addition, IMPACT® PEPTIDE 1.5 contains increased levels of protein, supplementary arginine and micronutrients that support healing of Stage 3 and 4 pressure injuries.[30,31,32] IMPACT® formulas have been shown to reduce the risk of UTI after major elective surgery,[7] and reduce SSIs following gyn-onc[33] and colorectal surgeries.[34]

Hospital-Acquired Condition (HAC) Reduction Program[35]

Hospitals performing in the bottom 25% will have a reduced payment from CMS. Use of IMPACT® surgical protocols supports a reduction in wound complications, UTIs and SSIs in major elective surgery.[7,36]

Four measures:

1. Patient Safety Indicator (PSI)
   PSI 90 Composite Measure (15 HACs) — Includes wound dehiscence rate
2. National Healthcare Safety Network (NHSN) Measures (3 HACs)
   a. Central Line Associated Bloodstream Infections
   b. Catheter Associated UTIs
   c. SSIs — includes colonic surgeries and abdominal hysterectomies



IMPACT® formulas have been shown to reduce the risk of UTI after major elective surgery,[7] and reduce SSIs following gyn-onc[33] and colorectal surgeries.[34]

Comprehensive Care Joint Replacement (CJR) Bundled Payment Model[37,38]

CMS has implemented the CJR model in 67 Metropolitan Statistical Areas (MSAs), spanning 800 hospitals required to participate. As of October 1, 2016 an additional 100 MSAs were added.

The episode of care begins with an admission to a participant hospital and ends 90 days post-discharge in order to cover the complete period of recovery for beneficiaries.

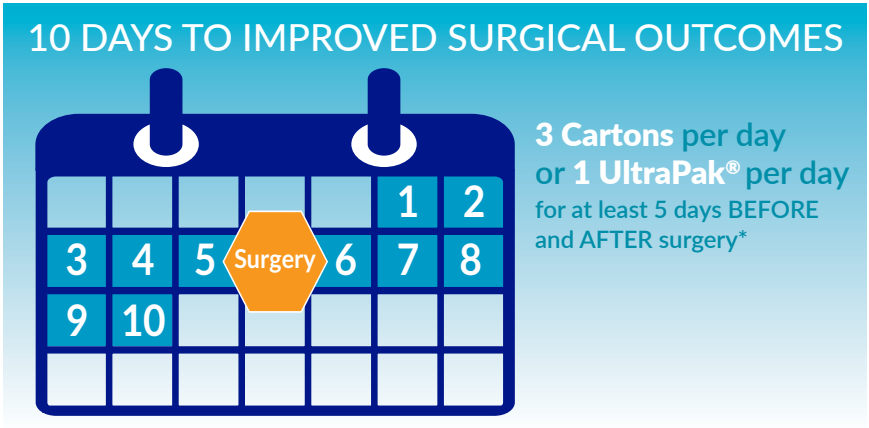
Use of preoperative immunonutrition (Oral IMPACT®)* was shown in a pilot study of hip replacement surgery patients to significantly decrease length of stay (LOS) ($p<0.01$).[5]

*IMPACT Advanced Recovery® Immunonutrition Drink is the oral form of IMPACT® formula offered in the United States.

Improving Surgical Outcomes with IMPACT® formulas

Perioperative IMPACT® protocols benefit patients undergoing major elective surgery, regardless of nutritional status.

It's a simple protocol:
Consume for 5 days before surgery and at least 5 days after surgery.



*Initiate IMPACT® tube feeding and advance to ≥ 1000 calories/day to meet nutritional needs for at least 5 days. Also available in open system.

Clinical Evidence of IMPACT® Formula by Surgery Type

Bladder Cancer Surgery

Hamilton-Reeves JM, Bechtel MD, Hand LK, Schleper A, Yankee TM, Chalise P, Lee EK, Mirza M, Wyre H, Griffin J and Holzbeierlein JM.

Effects of immunonutrition for cystectomy on immune response and infection rates: A pilot randomized controlled clinical trial. Eur Urol 2016;69(3):389-392.

A pilot randomized controlled clinical trial to compare immune response and post-operative complications between a group of bladder cancer surgery patients (n=29) that received perioperative immunonutrition (IMPACT Advanced Recovery® Drink) vs. a group that received isocaloric perioperative oral nutrition supplement (ONS). The immunonutrition and control groups had myeloid derived suppressor cell (MDSC) counts that were significantly different over time (p=0.005) and significantly lower in the immunonutrition group 2 days after surgery (p<0.001). Neutrophil:lymphocyte ratio was lower in the immunonutrition group vs ONS 3 hours after the first incision (p=0.039). Although not powered to detect outcome differences, the IMPACT Advanced Recovery® group had a 33% reduction in postop complication rate (p=0.060) and a 39% reduction in infection rate (p=0.027) during late phase recovery.

Perioperative

Bertrand J, Siegler N, Murez T, Poinas G, Segui B, Ayuso D, Gres P, Wagner L, Thuret R, Costa P, Droupy S. .

Impact of preoperative immunonutrition on morbidity following cystectomy for bladder cancer: A case-control pilot study. World J Urol 2014;32:233-237.

A prospective, multicenter, case-controlled pilot study to compare the rate of postoperative complications in patients with bladder cancer (n=60) who received preoperative immunonutrition (ORAL IMPACT®*) with those that did not prior to cystectomy. The immunonutrition group had a lower incidence of post-operative complications (40% vs. 77%; p=0.008) including paralytic ileus and infections than the control group. Mortality, pulmonary embolism, anastomotic fistula and wound dehiscence were similar between groups.

Preoperative

Cardiac Surgery

Iwase H, Kariyazono H, Arima J, Yamamoto H, Nakamura K.

Nutritional effect of oral supplement enriched in ω-3 fatty acids, arginine, RNA on immune response and leukocyte–platelet aggregate formation in patients undergoing cardiac surgery. *Nutr Met Ins*. 2014;7:39-46.

RCT completed to investigate if preoperative use of immunonutrition (Oral IMPACT®) vs. no supplementation would influence immune response and leukocyte platelet formation in patients (n=14) having cardiac surgery. HLA–DR expression, CD4/CD8 ratio and the production of IFN–γ by CD4–positive cells were increased in the immunonutrition group ($p<0.05$). Conversely, IL 10 level and the formation of leukocyte-platelet aggregates before and after surgery were suppressed to a greater extent in the immunonutrition group ($p<0.05$). These effects may decrease the incidence of complications after surgery.

Preoperative

Tepaske R, Velthuis HT, Oudemans-Van Straaten HM, Bossuyt PMM, Schultz JM, Eijsman L, Vroom M.

Glycine does not add to the beneficial effects of perioperative oral immune-enhancing nutrition supplements in high-risk cardiac surgery patients. *JPEN*. 2007; 31(3): 173-180.

A prospective, randomized study to measure outcomes from the addition of glycine to an oral immune-enhancing nutrition supplement (ORAL IMPACT®+ glycine) as compared to a standard oral immune-enhancing nutrition supplement (ORAL IMPACT®) and a control group receiving standard nutrition. Each nutrition supplement was administered for a minimum of 5 preoperative days. Patients (n=70) were 70+ years of age, had compromised left ventricular function or the need for mitral valve surgery. Outcomes of morbidity, organ function and postoperative recovery were analyzed. In both groups receiving the ORAL IMPACT® formula, infectious morbidity was decreased (23%/17% vs. 50%) as compared to the control ($p=0.02$). Conclusions of the study were that use of preoperative ORAL IMPACT® formula reduces the rate of infectious morbidity and results in more hemodynamic stability. The addition of glycine did not result in any additional benefit.

Preoperative

GI Cancer Surgery

Aida T, Furukawa K, Suzuki D, Shimizu H, Yoshidome H, Ohtsuka M, Kato A, Yoshitomi H, Miyazaki M.

Preoperative immunonutrition decreased postoperative complications by modulating prostaglandin E2 production and T-cell differentiation in patients undergoing pancreatoduodenectomy. *Surg* 2014;155:124-133.

RCT to investigate the effect of preoperative immunonutrition (ORAL IMPACT®) vs. early postop standard tube feeding on postop complications and immune response in patients having pancreatoduodenectomy (n=50). Infectious complications in the immunonutrition group were significantly lower than in the control group (28% vs. 60%, $p<0.05$), and the severity of complications were also lower ($p<0.05$). EPA, EPA:AA were higher and PGE2 levels lower in the immunonutrition vs control group ($p<0.05$). This preoperative modulation was associated with higher levels of T-Bet vs. GATA3 mRNA expression ($p<0.05$), showing favorable Th1/Th2 differentiation in the ORAL IMPACT® group. This demonstrates a decrease in stress-induced immunosuppression.

Preoperative

Marano L, Profidia R, Pezzella M, Grassia M, Petrillo M et al.

Clinical and immunological impact of early postoperative enteral immunonutrition after total gastrectomy in gastric cancer patients: A prospective randomized study. *Ann Surg Oncol* 2013; 20(12):3912-3918.

Randomized controlled trial done to investigate the effect of early post-op immunonutrition on outcomes in gastric cancer patients undergoing gastrectomy (n=109). Post-operative feedings were administered 6 hours post-op via jejunal tube and continued until post-op day 7. Formulas were isonitrogenous and isocaloric, however the study group tube feeding contained supplemental L-arginine, n-3 fatty acids and nucleotides (IMPACT®) and the control group received standard formula. Infectious complications in the study group were significantly lower than in the control group (7.4% vs. 20%, $p<0.05$), as was the rate of anastomotic leak (3.7% vs 7.3%, $p<0.05$). LOS for the intervention group was 3.2 days less than for the control group ($p=0.029$).

Postoperative

GI Cancer Surgery (continued)

Okamoto Y, Okano K, Izuishi K, Usuki H, Wakabayashi H, Suzuki Y.

Attenuation of the systemic inflammatory response and infectious complications after gastrectomy with preoperative oral arginine and omega-3 fatty acids supplemented immunonutrition. *World J Surg* 2009;33:1815-1821.

RCT designed to evaluate the effect of preoperative oral immunonutrition (ORAL IMPACT®) vs. postop isocaloric TPN on cellular immunity, duration of SIRS and postoperative complications after upper GI cancer surgery (n=60). Post-operative infectious complications in the intervention group were significantly lower than in the control group (6% vs. 28%, $p<0.05$), as was the duration of SIRS (0.77 vs. 1.34 days, $p<0.05$). Postoperative lymphocyte and CD4+T-cell counts decreased in both groups ($p<0.05$), however the CD4+T-cell counts on preop day 1 and post-op day 7 were higher in the interventional than control group ($p<0.05$).

Preoperative

Horie H, Okada M, Kojima M, Nagai H.

Favorable effects of preoperative enteral immunonutrition on a surgical site infection in patients with colorectal cancer without malnutrition. *Surg Today* 2006;36:1063-1068.

Prospective study to measure the effect of preoperative immunonutrition (ORAL IMPACT®) vs. no supplementation on surgical site infection (SSI) in patients with colorectal cancer (n=17) . Patients reported 100% compliance to the oral intervention. Frequency of SSI was reduced in the immunonutrition vs. the control group (0% vs. 14.7%, $p<0.05$). Superficial incision and organ/space SSI contributed to the data.

Preoperative

GI Cancer Surgery (continued)

Farreras N, Artigas V, Cardona D, Rius X, Trias M, Gonzalez JA.

Effect of early postoperative enteral immunonutrition on wound management in patients undergoing surgery for gastric cancer. *Clin Nutr.* 2005; 24: 55-65.

A prospective, randomized study to determine the effect of early postoperative enteral immunonutrition (IMPACT® formula) on wound management in patients undergoing surgery for gastric cancer. Sixty-six patients were randomized to receive IMPACT® formula or an isocaloric, isonitrogenous control formula. The wound management process was analyzed, as well as, development of surgical wound management complications in sixty patients. Those patients who received IMPACT® formula had significantly increased hydroxyproline levels (p=0.0018) and decreased incidence of wound management complications (p=0.005). Authors concluded that early provision of IMPACT® formula postoperatively improves wound management substrates and decreases wound complications.

Postoperative

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: 805-814.

A prospective, randomized, controlled trial of 200 patients with colorectal neoplasm requiring surgical resection. The 4 groups were randomized to: Group 1, perioperative supplementation with ORAL IMPACT® formula for 5 days preoperatively + ORAL IMPACT® or IMPACT® tube feeding postoperatively; Group 2, preoperative ORAL IMPACT® for 5 days; Group 3 (control), isonitrogenous/caloric oral supplement preoperatively for 5 days; and Group 4; no supplementation before or after surgery (conventional therapy). Immune response ($p<0.05$), gut oxygenation ($p<0.01$) and microperfusion ($p<0.02$) were found to be significantly better for Groups 1 and 2. Overall, Groups 1 and 2 fed IMPACT® formula both perioperatively and preoperatively had outcomes of decreased infectious complications ($p<0.02$ $p<0.04$); reductions in antibiotic therapy days ($p<0.005$, $p<0.004$) and length of hospital stay ($p<0.0005$), as compared to the control and conventional therapy groups.

Preoperative + Perioperative

GI Cancer Surgery (continued)

Braga M, Gianotti L, Nespoli L, Radaelli G, Di Carlo V.

Nutritional approach in malnourished surgical patients: A prospective randomized study. *Arch Surg*. 2002; 137: 174-180.

Prospective, randomized, controlled trial of 150 patients requiring major elective surgery of the GI tract for malignancy. All enrolled patients were malnourished with ≤10% body mass loss and randomized to 3 groups. Group 1 (Perioperative Treatment Group) was supplemented preoperatively with 1 liter per day ORAL IMPACT® formula for 7 consecutive days and tube fed with IMPACT® formula postoperatively. Group 2 (Preoperative Group) was supplemented with 1 liter per day of ORAL IMPACT® formula for 7 consecutive days preoperatively and standard formula post-op. Group 3 (Control Group) received standard tube feeding post-operatively. All formulas were isocaloric and isonitrogenous. ITT analysis reveals patients fed study formula preop and periop had decreased postop complications (28% and 18%, respectively) vs. the control group (42%, p=0.04, p=0.02, respectively). Reduction in LOS was observed in both intervention groups vs control: 2.1 days in the preop group (p=0.01), and 2.8 days in the periop group (p=0.001).

Preoperative + Perioperative

Gynecologic Oncology Surgery

Chapman JS, Roddy E, Westhoff G, Simons E, Brooks R, Ueda S, Chen L.

Post-operative enteral immunonutrition for gynecologic oncology patients undergoing laparotomy decreased wound complications. *Gyn Onc* 2015; 137:523-528.

Retrospective cohort study of postoperative immunonutrition (IMPACT Advanced Recovery® Drink) and no supplementation as a quality practice improvement for patients having laparotomy for gynecological malignancy (n=338). 75% patient compliance to postop intervention was noted. Fewer wound complications were observed in patients receiving immunonutrition (19.6% vs 33%; p=0.049). After controlling for variables associated with development of wound complications, patients receiving immunonutrition had a 78% reduction in CDC SSI class 2 and 3 infections (OR = 0.22, CI 0.05-0.95, p=0.044) in comparison to control.

Postoperative

Celik JB, Gezginc K, Ozcelik K, Celik C.

The role of immunonutrition in gynecologic oncologic surgery. *Eur J Gynaecol Oncol* 2009;30: 418-421.

RCT of perioperative immunonutrition (IMPACT®) and perioperative isocaloric standard formula in patients operated on with gynecological malignancies (n=50). WBC count, lymphocyte population and CRP levels were significantly higher in the intervention group ($p<0.05$). Post-op pulmonary and urinary infection rates were similar in both groups, but wound infection rate (4% vs 20%) and LOS (Δ 3.7 days) were significantly lower in the treatment group ($p<0.05$).

Perioperative

Head and Neck Cancer Surgery

Rowan NR, Johnson JT, Fratangelo CE, Smith BK, Kemerer PA, Ferris RL.

Utility of a perioperative nutrition intervention on postoperative outcomes in high-risk head and neck cancer patients. *Oral Onc* 2016;54:42-46.

Identify outcomes associated with implementing perioperative immunonutrition (IMPACT Advanced Recovery® Drink and IMPACT® Peptide 1.5 formula) vs. postop standard formula as part of a quality practice improvement (QPI) initiative with high-risk head and neck cancer surgical patients (n=195). 25.2% of the immunonutrition patients registered complications vs 47.5% in the standard of care group (p=0.0021). Pharyngeal leaks or fistulas were the most common complication in both groups, and more common in patients not receiving supplementation (p=0.007). Mean LOS was reduced by 2.8 days in those receiving immunonutrition (p=0.02). Readmission rates between the two groups were similar.

Perioperative

Felekis D, Eleftheriadou A, Papadakos G, Bosinakou I, Ferekidou E, Kandiloros D, Katsaragakis S et al.

Effect of perioperative immuno-enhanced enteral nutrition on inflammatory response, nutritional status, and outcomes in head and neck cancer patients undergoing major surgery. *Nutr and Cancer* 2010; 62(8): 1105-1112.

A randomized, double-blinded, prospective study done to evaluate that immunonutrition supplemented with arginine, RNA and n-3 fatty acids improves outcomes in head and neck cancer patients with squamous cell carcinoma undergoing surgery. The study group received ORAL IMPACT® 5 days prior to surgery and IMPACT® tube feeding post-surgery. The control group received no supplemental nutrition before surgery and isocaloric standard tube feeding post-surgery. Major complications included pneumonia, UTI, fistula and wound infection, and were followed until discharge (median = 12 days). Rate of major complications was significantly lower in the immunonutrition vs. the standard group (5% vs. 25%; $p<0.05$). Perioperative IMPACT® in head and neck cancer surgery patients may influence postoperative outcomes by reducing infections and wound complications.

Perioperative

Hip Surgery

Alito Aprelino M and
de Aguilar-Nascimento JE.

Multimodal perioperatrive care plus immunonutrition verses traditional care in total hip arthroplasty: A randomized pilot study. *Nutrition Journal* 2016;15:34.

Prospective, randomized pilot study to test the effect of adding preoperative immunonutrition (ORAL IMPACT®) to multimodal perioperative protocols vs. traditional care in patients having elective total hip arthroplasty (n=32). The median LOS was 3 days for study patients and 6 days for traditional care patients ($p<0.01$). Preoperative C-Reactive Protein (CRP) values were similar between groups, however levels on postoperative Day 2 were lower in the study than traditional group (66.5 mg/L vs. 80.6 mg/L; $p<0.01$).

Preoperative

Non-Small Cell Lung Cancer Surgery

Kaya SO, Akcam TI, Ceylan KC,
Samancılar O, Ozturk O, Usluer O.

Is preoperative protein-rich nutrition effective on postoperative outcome in non-small cell lung cancer surgery? A prospective randomized study. *J of Cardiothor Surg* 2016;11:14.

Prospective, randomized study to evaluate the benefit of a 10 day course of preoperative immunonutrition (Oral IMPACT®) vs. normal diet in well-nourished patients having anatomic resection for non-small cell lung cancer (n=58). Patients in the immunonutrition group reported fewer complications vs. the control group (19.4% vs. 44.4%; $p=0.049$). Study patients also reported a reduced chest tube drainage time vs. the control group, on average (4 days vs. 6 days; $p=0.019$).

Preoperative

Trauma

Rumberger L, Brantley S, Schumacher L, Lawson C.

Code Brown: Incidence of diarrhea in critically ill patients on defined enteral formulas. *JPEN*. Clinical Nutrition Week, Abstract 1835637.

Consecutive 3 month retrospective chart review to determine if there was a difference in the incidence of diarrhea between two formulas used in the SICU: Formula A = IMPACT® PEPTIDE 1.5 formula (n=52) and Formula B= Pivot® 1.5 Cal formula* (n=61). No statistical difference was noted in the following: number of C. difficile tests ordered or the number of antibiotics, laxatives or antimotility agents received. Use of IMPACT® Peptide 1.5 was associated with a significant reduction in the days of diarrhea (1.42 days vs. 4.25 days;p<0.001). The need for a rectal tube to manage diarrhea was also lower in the IMPACT® Peptide 1.5 group vs. the Pivot® 1.5 Cal group, respectively (12% vs. 30%).

Farber MS, Moses K, Korn M.

Reducing costs and patient morbidity in the enterally fed intensive care unit patient. *JPEN*. 2005; 29(1 Suppl): S62-S69.

Clinical trial of predominantly trauma patients prospectively identified to be enterally fed with IMPACT® 1.5 formula and compared with a historical cohort of similarly identified patients receiving standard nutrition. No differences in mean calories or protein received, days to feeding initiation or days to goal rate were observed between groups. A reduction in nosocomial pneumonia (12% in IMPACT® 1.5 formula patients vs. 52% in those on standard feeding, p=0.01) was shown. Although not statistically significant, the patients receiving IMPACT® 1.5 formula required 3 fewer days of ventilator support and had a 5 day shorter ICU stay, on average, than those receiving standard feeding. Using previously published costs of ICU care, cost of formulas and the difference in length of ICU stay, an economic analysis identified a savings of $11,374 for each patient receiving IMPACT® 1.5 formula.

*Pivot is a registered trademark of Abbott Laboratories

Meta-analyses Including IMPACT® Formulas

Mazaki T, Ishii Y, Murai I.

Immunoenhancing enteral and parenteral nutrition for gastrointestinal surgery: A multiple treatments meta-analysis. *Ann Surg* 2015;261(4):662-669.

Evaluate 74 RCTs (n=7572) of standard enteral (SEN), standard parenteral (SPN), immunoenhancing parenteral (IMPN) and immunoenhancing enteral (IMEN) nutrition to see which is best at reducing complications after GI surgery. IMEN formulas contained various combinations and amounts of supplemental arginine, glutamine, n-3 fatty acids (EPA + DHA) and nucleotides. 24/36 studies involving IMEN utilized formula containing supplemental arginine, n-3 and nucleotides (IMPACT®). IMPN formulas contained coconut oil/ MCT, olive oil, fish oil or various combinations and amounts of two or three of these oils. IMEN ranked first for reducing the incidence of 7 complications after GI surgery: any infection, overall complications, mortality, wound infection, intra-abdominal abscess, anastomotic leak and sepsis. IMEN was ranked second for reducing the incidence of pneumonia and UTI, whereas IMPN was ranked first for these complications. SPEN performed least well for almost all outcomes when compared to the other three types of nutrition. Authors conclude the results suggest IMEN outperformed other types of nutrition in the reduction of complications and should be considered the best available option for GI surgery.

Marimuthu K, Varadhan KK, Ljungquist 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;255:1060-1068.

Evaluate 26 RCTs on the effect immunonutrient combinations vs. isonitrogenous, isocaloric standard enteral formulas had on complications and LOS after open abdominal surgery. 15/26 trials utilized immunonutrition containing supplemental arginine, n-3 fatty acids and nucleotides (IMPACT® formulas). Immunonutrition was associated with strong evidence showing a significant reduction in LOS (-1.88,p=0.0004) and risk of postoperative complications (36%, p<0.00001). This reduction was statistically significant in all subgroups: preoperatively (52%; P=0.001), perioperatively (47%; P=0.0004), and postoperatively (32%; P<0.00001).A sub-analysis of perioperative studies showed a 47% reduction in risk of post-op complications (p<0.00001) and a difference in LOS of 2.71 days on average (p<0.00001). Immunonutrition was associated with an 18% reduction in non-infectious complications (p=0.007), however the quality of this evidence was low.

Meta-analyses (continued)

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): 385-399.

Thirty-five randomized controlled trials (n=3,438) of major elective surgical patients are reviewed in this meta-analysis to compare outcomes with enteral nutrition supplemented with arginine vs. standard formula. Twenty-five studies involved GI surgery patients and the other 10 studies represented other elective surgical procedures. Twenty-three of 35 studies utilized IMPACT® formula administered pre-, peri- or post-surgically. Although, no difference in mortality was noted, arginine-supplemented diets were associated with a 41% reduction in infectious complications ($p<0.00001$ and a 2.38 day reduction in length of stay (LOS) ($p<0.00001$), on average. Tests for heterogeneity were not significant in regards to reduced overall infectious complications ($p=0.11$), but were significant in regards to reduced LOS ($p<0.00001$). Sub-analyses found greater reductions in infectious complications and LOS associated with perioperative vs. pre- or post-operative use ($p=0.03$, $p=0.001$), and significant benefit associated with IMPACT® formula vs. other immunonutrition formulas ($p<0.0001$).

For example, IMPACT formula reduced risk of infectious complications by 51% ($p=0.00001$), whereas other arginine supplemented immunonutrition did not reduce the risk significantly. Authors support implementing use of perioperative nutritional therapy containing arginine and omega-3 fatty acids to support considerable reduction in morbidity for high-risk elective surgery patients and a substantial reduction in costs for the health care system.

Waitzberg DL, Saito H, Plank LD, Jamieson GG, Jagannath P, Tsann-Long H, Mijares JM, Bihari D.

Postsurgical infections are reduced with specialized nutrition support. *World J Surg*. 2006; 30:1592-1604.

This article reviewed 17 studies (n=2,305) where IMPACT® formula was used before and/or after major elective surgery and the clinical outcomes reported were included in this meta-analysis. Ten studies compared preoperative or perioperative IMPACT® formula provision vs. control and 7 studies looked at postoperative nutrition. Fourteen studies examined IMPACT® formula used with gastrointestinal (GI) cancer surgeries. IMPACT® formula supplementation was associated with significant reductions in postoperative infectious complications (39–61%) and a significant decrease in hospital stay by an average of 2 days. Anastomotic leaks were found to be less prevalent in gastrointestinal surgery patients who received IMPACT® formula perioperatively. Overall, 500 mL-1 L of IMPACT® formula 5–7 days preoperatively contributed to improved outcomes in GI, cardiac, and head/neck elective surgery patients.

Health Economics

Mauskopf JA, Candrilli SD,
Chevrou-Séverac H, Ochoa JB.

Immunonutrition for patients undergoing elective surgery for gastrointestinal cancer: Impact on hospital costs. *WJSO* 2012:10:136; doi:10.1186 1477-7819-10-136.

This study was completed to create a health economic model to determine the impact on hospital costs of immunonutrition (IMPACT® formulas) used in patients having major elective surgery for gastrointestinal (GI) cancer). United States (US) hospital costs were taken from the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (HCUP-NIP) database. These costs were used to estimate the effect of immunonutrition on hospital costs using reductions in length of stay (LOS) and risk of complications from a meta-analysis of 6 RCTs studying perioperative use of IMPACT® formulas in GI cancer surgery patients (n=889). Meta-analysis estimates show perioperative use of IMPACT® resulted in savings per patient of $6000 when costs were based on reduction in LOS, and a $3300 savings when costs were based on a reduction in infectious complications. The sensitivity analysis showed cost savings were present for baseline complication rates above 3.5%. When US baseline rates for LOS and infectious complications for upper and lower GI cancer surgery were inserted in the model, cost savings continued to present (range, $1200 to $6300). Use of immunonutrition for patients undergoing elective surgery for GI cancer was concluded an effective and cost-saving intervention.

NOTES:

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