

Immunonutrition in High-Risk Surgical Patients: A Systematic Review and Analysis of the Literature

Marik PE and Zaloga GP

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Objective

To determine the impact of immunomodulating diets (IMDs) on the clinical outcomes of high-risk patients undergoing elective surgery.

Methods

Meta-analysis included prospective, controlled, clinical trials that compared clinical outcomes of elective surgical patients who were randomized to receive an IMD or control enteral formula. Studies were included if they reported one or more of the following clinical outcomes (1) number of patients with hospital acquired infections (2) wound complications (3) hospital length of stay, and (4) mortality. Outcomes were recorded according to intention-to-treat analysis. Studies were stratified according to type of IMD (arginine and fish oil either alone or in combination) and timing of initiation of the IMD (preoperative only, postoperatively only, and perioperatively).

Study Characteristics

- 21 relevant studies were identified with 1918 patients. 18 studies used an IMD with added arginine and fish oil, 2 studies used arginine alone, 1 study used fish oil alone:
 - IMPACT[®], which contains added arginine, fish oil, RNA, and selenium, was used in 16 studies
 - Stresson[®], which contains added arginine, fish oil, and selenium, was used in 2 studies
- IMDs were given postoperatively in 15 studies, whereas 5 studies used IMDs during the perioperative (both pre- and post-operative) period, and 1 study used preoperative immunonutrition alone.
- 15 studies enrolled patients undergoing abdominal surgery for GI malignancy, 2 studies evaluated patients undergoing general abdominal surgery, 3 studies evaluated head/neck (H&N) surgery patients undergoing resection for malignancy, and 1 study enrolled high-risk cardiac surgery patients.

Summary of Studies Included in Meta-Analysis						
Timing of Immunonutrition	Author	Year	Setting	Type	Blind	Number of Patients
Pre-op (n=1)	Xu	2006	GI malignancy	IMPACT [®]	N	60
	Daly	1992	GI malignancy	IMPACT [®]	N	85
Post-op (n=15)	Daly	1995	GI malignancy	IMPACT [®]	Y	60
	Kenler	1996	GI malignancy	Fish Oil	Y	35
	Braga	1996	GI malignancy	IMPACT [®]	Y	40
	Schilling	1996	GI malignancy	IMPACT [®]	N	28
	Gianotti	1997	GI malignancy	IMPACT [®]	N	174
	Senkal	1997	GI malignancy	IMPACT [®]	Y	154
	Braga	1998	GI malignancy	IMPACT [®]	Y	110
	Snyderman	1999	H&N malignancy	IMPACT [®]	Y	129
	Di Carlo	1999	GI malignancy	IMPACT [®]	N	68
	De Luis	2002	H&N malignancy	Arginine	Y	47
	Jiang	2004	GI surgery	Stresson [™]	Y	120
	Farreras	2005	GI malignancy	IMPACT [®]	Y	60
	Lobo	2006	GI malignancy	Stresson [™]	Y	108
	Casas-Rodera	2008	H&N malignancy	Arginine	Y	30
	Peri-op (n=5)	Braga	1999	GI malignancy	IMPACT [®]	Y
Senkal		1999	GI malignancy	IMPACT [®]	Y	154
Tepaske		2001	Cardiac surgery	IMPACT [®]	Y	50
Braga		2002	GI malignancy	IMPACT [®]	Y	100
Helminen		2007	GI surgery	IMPACT [®]	Y	100

Results

- Immunonutrition significantly reduced the risk of acquired infections (OR 0.49; 95% CI, 0.39-0.62, $P<.0001$) in high risk patients undergoing elective surgery.
 - This benefit was noted in the post-op and peri-op subgroups that received an IMD with both arginine and fish oil.
 - Similarly, the risk of infection was lower in those studies that enrolled patients with GI malignancy (OR 0.44; 95% CI, 0.34-0.59) as well as those without GI malignancy (OR 0.50; 95% CI, 0.32-0.77).
- Wound complications were significantly reduced in patients who received an IMD (OR 0.60; 95% CI, 0.40-0.91 $P=0.02$) compared to control formula
- Hospital length of stay (LOS) was significantly reduced in patients who received an IMD, on average by 3 days (-3.03 days; 95% CI, -3.43 to -2.64 days, $P<0.0001$) compared to control formula
- The treatment effect was similar for perioperative and postoperative use of the IMD.
- The benefits of immunonutrition required use of formulas containing both arginine and fish oil.
- A difference in mortality across groups was not noted.

Conclusion

- This meta-analysis demonstrates that immunonutrition formulas with added arginine and fish oil may work synergistically to reduce the risk of hospital acquired infections (HAI), reduce wound complications, and shorten hospital LOS in both malnourished and non-malnourished high-risk patients undergoing elective surgery.
- As the majority of studies utilized IMPACT formula containing added nucleotides and antioxidants, it's unclear whether the effects can be extrapolated to other IMDs differing in composition.
- Although optimal IMD timing cannot be determined from this meta-analysis, it is suggested that immunonutrition be initiated at least 5 days preoperatively, and continued into the postoperative period, when feasible.

Summary prepared by Nestlé Healthcare Nutrition. The complete study can be accessed online at:

<http://pen.sagepub.com/content/34/4/378.full>

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