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Review

Enteral immunonutrition versus standard enteral nutrition for patients undergoing oesophagogastric resection for cancer

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ABSTRACT

A best evidence topic in surgery was written according to a structured protocol. The question addressed was "In cancer patients undergoing oesophageal or gastric resection for cancer and requiring postoperative nutritional support, does enteral immunonutrition confer additional clinical benefits as compared to standard enteral nutrition? Two hundred and fifty-eight papers were identified by a search of the MEDLINE and EMBASE databases, of which six randomized controlled trials represented the best evidence to answer this clinical question. The authors, journal, date and country of publication, patient group, study group, relevant outcomes and results of these papers were tabulated. All six of these randomised controlled trials compared the clinical benefits of standard enteral nutrition with those of enteral nutrition supplemented with a variety of immune-modulating substances. The studies failed to demonstrate consistent differences in patients' postoperative clinical course, complications, length of hospital stay and inflammatory marker levels. Hence although there is reasonable evidence to suggest that immunonutrition improves humoral immunity as opposed to cellular immunity, this improvement does not result in reductions in infection rates or reduced hospital stay. There is currently not enough evidence to recommend routine immunonutrition in all patients undergoing oesophageal or gastric resection for cancer.

1. Introduction

A best evidence topic was constructed according to a structured protocol as described in a previous publication.[1]

2. Clinical scenario

You are in an upper gastrointestinal malignancy multidisciplinary clinic discussing a patient scheduled to undergo resection for a gastro-oesophageal junctional tumour. It has been decided that following surgery he will receive enteral nutritional support. The dietician suggests that instead of standard enteral feed, he should be given enteral immunonutrition (EIN). You resolve to check the literature to determine whether or not postoperative enteral immunonutrition (EIN) confers any additional clinical benefit as compared to standard enteral nutrition (SEN).

3. Three-part question

In patients undergoing oesophagogastric resection for cancer does postoperative enteral immunonutrition as compared to standard enteral nutrition confer additional clinical benefits?

4. Search strategy

The following string was run using the PubMed and EMBASE interfaces:

[((gastr* OR stomach OR resection).ti,ab OR (esophag* OR oesophag*).ti,ab) AND (immunonutr*.ti,ab OR (immune AND nutr*)) AND enteral.ti,ab].

The search was limited to English and duplicate filtered. In addition, the reference lists of relevant papers were searched. The search was current as of April 2012.

5. Search outcome

Two hundred and fifty-eight papers were found using the reported search, of which 228 were irrelevant to the clinical question. Of the 30 remaining potentially relevant papers, 5 were literature reviews and 17 papers analysed patients with malignancies other

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than oesophagogastric. These were excluded. The remaining eight studies compared EIN with SEN in patients with oesophagogastric cancers. Two of these were retrospective case analyses and the remaining six were randomized controlled trials. These six randomized controlled trials (RCTs) were identified as representing the best evidence to answer this clinical question.

6. Results

The results of the RCTs are summarised in Table 1.

7. Discussion

Oesophagogastric cancers have long been known to be associated with impairment of nutritional status. As a consequence of this, it has been suggested that some of these patients may benefit from enteral feeding immediately following resectional surgery.[2] In addition, the impaired immune response associated with cancer has led some to suggest that, these patients may benefit from the addition of immunomodulating compounds in their enteral feeds. The immune-modulating substances most commonly added to enteral feeds to form enteral immunonutrition (EIN) are arginine, ribose nucleic acid (RNA) and omega-3-fatty acids (O-3FA). Arginine, a precursor to nitric oxide synthesis, is a conditionally essential amino acid that becomes essential during growth and recovery after injury.[2] RNA nucleotide-deficient diets have resulted in the decreased production of interleukin (IL)-2 and diminished T-cell responses, suggesting that nucleotides may play role in the immune response.[2] Similarly high level of high O-3FA has been shown to associated with immunological benefits.[2] Although the addition of these compounds may have theoretical benefits, the actual clinical efficacy of EIN versus standard enteral nutrition (SEN) for patients undergoing oesophagogastric resection for cancer has only been formally assessed in six randomised controlled trials.

Sakurai et al.[3] randomised 30 patients undergoing oesophagectomy to receive either SEN ($n = 14$) or EIN ($n = 16$). The patients EIN group received perioperative Impact® regime (Ajinomoto Pharma Tokyo, Japan), which contains arginine, RNA, and -3 polyunsaturated fatty acids, whereas the SEN patients received perioperative regular polymeric enteral formula. No difference was seen in the length of time patients suffered from systemic inflammatory response syndrome (SIRS), the time they took to resume oral intake and the length of hospital stay. In terms of biochemical outcomes, there were no significant difference in the levels of C-reactive protein (CRP) and interleukin (IL)-6. Postoperatively, serum ornithine and eicosapentoic acid (EPA) levels were the only amino- and fatty acids, respectively, higher in the EIN group. However, as these marginal differences were only from 3 to 7 days after surgery, the authors questioned their significance. However, this trial suggested that perioperative EIN was beneficial in maintaining humoral immunity rather than cellular immunity because the EIN group had a significantly higher B-cell fraction on postoperative days (PODs) 5, 7 and 14, serum IgG on POD 3, CD4/CD8 ratio on POD 7 but a lower T-cell fraction. This trial was underpowered to enable firm conclusions to be drawn on the effect of EIN on postoperative clinical outcomes. Although all complications were proportionally lower in the EIN group, the differences were not statistically significant. This study was limited by low power, non-disclosure of the randomisation method, the absence of any blinding and no CONSORT diagram.

Ryan et al.[4] randomised 53 patients undergoing oesophagectomy to receive either SEN ($n = 25$) or EIN ($n = 28$). The EIN group received 5 days of preoperative supplementation of an EPA enriched (2.2 g EPA/d) enteral feed whilst the SEN group receive an isocalorific and isonitrogenous standard nutritional feed without EPA. There was no significance difference in the rates of any complications between the groups. The SEN group lost a mean of 1.8 kg weight and 1.9 kg lean mass which was significantly more than the EIN group who did not lose any weight or lean mass. Analysis of inflammatory and immunological marker profiles revealed no significant difference in the levels of CRP, serum amyloid A, prothrombin time, D-dimer, platelets, IL-6 and -10 and TNF-α between the groups, however the EIN group had significantly lower IL-8 levels. Although this was an RCT, it should be noted that groups were heterogeneous with respect to gender distribution and disease with the EIN have significantly more advanced disease. The study was underpowered for an analysis of postoperative complications and did not examine the full spectrum of cytokine changes related to nutritional immunomodulation, therefore no firm conclusions can be drawn from the cytokine data. However, the study provides proof of concept that EIN is associated with preservation of lean body mass post-oesophagectomy compared with SEN.

Sultan et al.[5] randomised 195 patients undergoing surgery for gastric or oesophageal cancer to three groups: SEN ($n = 63$) and omega-3-fatty acid supplemented enteral nutrition (EIN) ($n = 66$) and a control group ($n = 66$). The SEN and EIN groups both received their feeding regimens 7 days before surgery and also for 7 days after surgery. The control group only received supplementation with Osmolite® (Abbott Nutrition) postoperatively. The SEN group received Oxepa® containing 0.73 g of O-3FAs per 100 mL, 1.5 kcal/mL with 6.25 g per 100 mL protein and no free arginine or glutamine. The SEN group received Ensure Plus® containing 1.5 kcal/mL with 6.25 g per 100 mL protein. There was no significant difference in the rates of any complications or the length of critical care stay, hospital stay, morbidity and mortality rates. Unlike Ryan et al.[4] no difference was seen in body weight between groups. However, like Ryan et al.[4] and Sakurai et al.,[3] there was no significant difference in the levels of CRP. There was also no significant difference between the groups in monocyte and lymphocyte HLA-DR expression. Although there was homogeneity between the study groups, only 47% of the patients reached the maximum planned feeding rate owing to problems with tolerance and/or complications. Overall this study demonstrated that EIN conferred no advantage in overall clinical or immunological outcome compared with SEN.

Farreras et al.[6] randomised 66 patients undergoing gastrectomy postoperatively to receive either SEN ($n = 30$) or EIN ($n = 30$) immediately after surgery. The EIN group received Impact® (Novartis Consumer Health, Spain) which contained (per 100 mL) 1.2 g of arginine, 0.12 g of RNA and 3.5 units of O-3FA. The SEN group received Isosource Proteins® (Novartis Consumer Health, Spain) which contained (per 100 mL) 1.7 units of O-3FA and no arginine and RNA. Three patients in both arms discontinued the interventions. The EIN group stayed in hospital for a mean of 13 days, two less than the SEN group ($p < 0.05$). The SEN group had a significantly higher rate of wound healing complications, suture failure, infectious and global complications and a lower hydroxyproline level ($p < 0.05$). However, there was no significance difference in the rates of abdominal abscess, dehiscence, sepsis, UTI, surgical wound and lung infection and mortality. The EIN group showed both a lower decrease and a faster recovery of lymphocyte count, total proteins, albumin and pre-albumin levels. Although this study suggested that EIN may improve surgical wound healing, it had several limitations. The analysis was not on an intention-to-treat basis. The groups were heterogeneous i.e. the EIN group was younger, weighed more and had a higher basal metabolic rate. The study group also had significantly higher basal caloric requirements than the control group. In addition, it should be noted that the study was funded by supplier of the immunonutrition formula.

Chen et al.[7] randomised 40 patients undergoing gastrectomy into EIN ($n = 20$) and SEN ($n = 20$) groups postoperatively. The EIN

Table 1
Best evidence papers.

Author, date and country	Study type and level of evidence	Patient group (EIN = enteral immunonutrition; SEN = standard enteral nutrition)	Outcomes	Key results	Comments
Sakurai et al.,[3] 2007, Japan	Prospective, randomized trial, Level 2	30 patients undergoing oesophagectomy to receive either SEN ($n = 14$) or EIN ($n = 16$). The patients EIN group received perioperative Impact® (Ajinomoto Pharmaceutical Company, Tokyo, Japan) whereas the SEN patients received perioperative regular polymeric enteral formula (Ensure, Abbott Japan Company Ltd., Tokyo, Japan)	Postoperative complications (EIN vs. SEN)	**Pulmonary complication**: 2 (12.5%) vs. 3 (21.4%) **Pneumonia**: 2 (12.5%) 3 (21.4%) **Gastrointestinal complications**: 3 (19.6%) vs. 4 (28.5%) **Anastomotic dehiscence**: 2 (13.3%) vs. 3 (21.4%) **Intestinal obstruction**: 1 (6.3%) vs. 1 (6.3%) **Surgical site infection**: 1 (6.3%) vs. 3 (21.4%) Although all complications were lower in the EIN arm, none of these differences were statistically significant.	This trial was underpowered to enable firm conclusions to be drawn on the effect of EIN on postoperative clinical outcomes. Although all complications were proportionally lower in the EIN group, the differences were not statistically significant.This study was limited by low power, non-disclosure of the randomisation method, no blinding and no CONSORT diagram.
			Postoperative clinical course	No difference in length of SIRS, start of oral intake postoperative and length of hospital stay ($p > 0.05$)	
			Inflammatory and immunological marker profiles	**CRP and IL-6**: No difference but data not presented **WBC count**: EIN > SEN ($p < 0.05$ POD7) **% lymphocyte fraction:** EIN > SEN ($p < 0.05$ POD 1 and 3) **B-cell fraction**: EIN > SEN ($p < 0.05$, POD 5,7 and 14) **T-cell fraction**: EIN < SEN ($p < 0.05$, POD 5,7 and 14) **Serum IgG**: EIN > SEN ($p < 0.05$ POD 3) **CD4:CD8**: EIN > SEN ($p < 0.05$ POD 7)	
			Other outcomes		
			Serum amino acid profiles	**Ornithine**: EIN > SEN POD5 ($p < 0.05$)	
			Serum fatty acid profiles	**EPA**: EIN > SEN ($p < 0.05$ POD7) ***n* − 3/*n* − 6 ratio**: EIN > SEN ($p < 0.05$, POD7)	
Ryan et al.,[4] 2009 Ireland	Prospective, double-blinded, randomised trial Level II	53 patients undergoing oesophagectomy were randomised to receive either SEN ($n = 25$) or EIN ($n = 28$). The EIN group received 5 days of preoperative supplementation of an EPA enriched (2.2 g EPA/d) enteral feed (ProSure®, Abbott Laboratories, Ireland) whilst the SEN group receives an isocalorific and isonitrogenous standard nutritional feed (Ensure Plus®, Abbott Laboratories, Ireland) without EPA.	Postoperative complications (EIN vs. SEN)	No significance difference in any complications: **Sepsis**: 5 (18%) vs. 2 (8%) **Anastomotic leak**: 1 (4%) vs. 1 (4%) **Renal failure**: 1 (4%) vs. 3 (12%) **Wound infection**: 0 (0%) vs.2 (8%) **Pneumonia**: 7 (25%) vs. 5 (20%) **ARDS**: 1 (4%) 0 (0%) 1.000 **SIRS >3 d**: 3 (18%) 7 (41%) 0.259 **SIRS >5 d**: 1 (6%) 4 (24%) 0.335	This study had several limitations. The EIN group had significantly more males than females and more positive nodes, making the groups heterogeneous. Analysis was not done on an intention-to-treat basis. The study was underpowered for an analysis of postoperative complications and of the full spectrum of cytokine changes relating to nutritional immunomodulation, therefore no firm conclusions can be drawn from the cytokine data.However, the study provides proof of concept that EIN is associated with preservation of lean body mass post-oesophagectomy compared with SEN.
			Postoperative clinical course	Not reported	
			Inflammatory and immunological marker profiles	No significant difference in CRP, IL-6 and SAA between groups ($p > 0.05$) No significant difference in PT, D-dimer and platelets between groups ($p > 0.05$) **IL-8**: EIN < SEN ($p < 0.05$ POD7, 14) **IL-10 and TNF-α**: $p > 0.05$	
			Other outcomes		

			Plasma and cell membrane fatty acid composition	In EIN group, eicosapentoic acid significantly increased in serum ($p < 0.05$) but remained constant in the SEN group ($p > 0.05$).	
			Body composition analysis	The SEN group lost a significant amount of weigh and lean mass whereas the EIN group remained constant	
Sultan et al.,[5] 2012 UK	Prospective, double-blinded, randomised trial Level II	195 patients undergoing respective surgery for gastric or oesophageal cancer were randomised to receive either SEN ($n = 63$), omega-3-fatty acid supplemented enteral nutrition (EIN) ($n = 66$) 7 days before and after surgery, or to postoperative supplementation alone (control) ($n = 66$).The SEN group received Oxepa® (Abbott Nutrition, Maidenhead, UK) which contains 0.73 g of O-3FAs per 100 mL, 1.5 kcal/mL with 6.25 g per 100 mL protein and no free arginine or glutamine. The SEN group received Ensure Plus® (Abbott Nutrition), containing 1.5 kcal/mL with 6.25 g per 100 mL protein. The control group received enteral Osmolite® (Abbott Nutrition) postoperatively only.	Postoperative complications (EIN vs. SEN)	**Wound infection**: 9 vs. 9 **Urinary tract infection**: 12 vs. 7 **Respiratory tract infection**: 20 vs. 23 **Intra-abdominal abscess**: 0 vs. 0 **Feeding tube infection**: 2 vs. 1 **Infective diarrhoea**: 3 vs. 2 **Septicaemia**: 3 vs. 2 **Anastomotic leak**: 4 vs. 7 **Total no. of infections**: 54 vs. 51 **No. of patients with an infective complication**: 33 (50) vs. 34 (54) There was no statistically significant difference in any of the complications.	Although there was homogeneity between the study groups, only 46.7% of the patients reached the maximum planned feeding rate owing to problems with tolerance and/or complications and anthropometric data may be limited by inter-rater variability, limiting the strength of conclusions. In this study, EIN conferred no advantage in overall clinical or immunological outcome compared with SEN. Therefore, this study failed to elucidate the optimal quantity and combination of nutrients, the timing of their delivery and the patient group(s) most likely to benefit from immunonutrition.
			Postoperative clinical course	**Critical care stay (days)**: 2 (0–75) vs. 4 (0–34) **Hospital stay (days)**: 18 (4–141) 16 (11–116) **Overall morbidity**: 43 (65) vs. 37 (59) **Death**: 2 (3) vs. 2 (3) None of these differences were statistically significant.	
			Inflammatory and immunological marker profiles	**CRP**: no significant difference although EIN group had lower levels than the SEN group on all days of the study ($p > 0.05$) **HLA-DR expression**: No significant difference between the groups in monocyte and lymphocyte HLA-DR expression ($p > 0.05$)	
			Other outcomes		
			Serum fatty acid profiles	**Arachidonate**: EIN > SEN ($p < 0.05$) **Eicosapentoate**: EIN > SEN ($p < 0.05$) **DHA**: EIN > SEN ($p < 0.05$) **O-6FA/O-3FA ratio**: EIN < SEN ($p < 0.05$)	
Farreras et al.,[6] 2004 Spain	Prospective, double-blinded, randomised trial Level II	66 patients undergoing gastrectomy were randomised postoperatively to receive either SEN ($n = 30$) or EIN ($n = 30$) immediately after surgery. The EIN group received Impact® (Novartis Consumer Health, Spain) which contained, for every 100 mL, 1.2 g of arginine, 0.12 g of RNA and 3.5 (unknown units) of O-3FA. The SEN group received Isosource Proteins® (Novartis Consumer Health, Spain) which contained, for every 100 mL, 1.7 (unknown units) of O-3FA and no arginine and RNA	Postoperative complications	The SEN group had a significantly higher rate of wound healing complications, suture failure, infectious and global complications ($p < 0.05$). No significance difference in: abdominal abscess, wound dehiscence, sepsis, UTI, surgical wound and lung infection, and mortality.	Although this study suggested that EIN may improve surgical wound healing, it had several limitations. The analysis was not on an intention-to-treat basis. The groups were heterogeneous: the EIN group was younger, weighed more and had a higher BMR and calorific intake. It was not clear whether all operations were carried out by one or more surgeons. Also, the study was funded by supplier of the immunonutrition formula.
			Postoperative clinical course	**Length of hospital stay**: EIN mean 13 days vs. SEN mean 15 days ($p < 0.05$)	
			Inflammatory and immunological marker profiles	EIN patients show both a lower decrease and a faster recovery of lymphocyte count, total proteins, albumin and pre-albumin levels ($p < 0.05$). **Hydroxyproline levels**: EIN 59.7 nmol vs.SEN 28 nmol ($p < 0.05$)	
		40 patients undergoing gastrectomy were randomised to receive either EIN	Postoperative complications	Not reported	The limitations of this study include that the demographics of the groups were not

(*continued on next page*)

Table 1 (*continued*)

Author, date and country	Study type and level of evidence	Patient group (EIN = enteral immunonutrition; SEN = standard enteral nutrition)	Outcomes	Key results	Comments
Chen et al.[7] 2005 China	Prospective, randomised trial Level II	($n = 20$) and SEN ($n = 20$) groups postoperatively. The EIN group received (Stresson®, Nutricia China, Shanghai, China), a feed enriched with 0.89 g of arginine, 1.3 g of glutamine and an O-3FA:O-6FA ratio of 3.45:1 for every 100 mL. The SEN grouped received Nutrison® (Nutricia), a feed containing with 0.16 g of arginine, 0.4 g of glutamine and an O-3FA:O-6FA ratio of 5:1 for every 100 mL.	Postoperative clinical course Inflammatory and immunological marker profiles	Not reported **Albumin**: $p > 0.05$ **Pre-albumin**: on POD9, EIN > SEN ($p < 0.05$) **Transferrin:** on POD9, EIN > SEN ($p < 0.01$) **IgG, IgM, IgA**: on POD9, EIN > SEN ($p < 0.05$) **CD4/CD8 ratio**: on POD9, EIN > SEN ($p < 0.05$) **IL-2**: on POD9, EIN > SEN ($p < 0.05$) **IL-6** and **TNF-α**: on POD9, EIN > SEN ($p < 0.05$)	detailed and statistically analysed to assess comparability. The method of randomisation was also not detailed and the study poorly adhered to the CONSORT standards of reporting.
Fujitani et al.,[8] 2012 Japan	Prospective, randomised trial Level II	244 patients undergoing gastrectomy were randomised to receive either EIN ($n = 127$) or SEN ($n = 117$). Preoperatively, the EIN group received 1000 mL/day of oral Impact® (Ajinomoto Pharmaceutical Company) containing 1.28 g of arginine and 0.13 g of RNA per 100 mL. The O-3FA:O-6FA ratio was 4:5. The SEN group received a regular diet with no supplements	Postoperative complications (EIN vs. SEN) Postoperative clinical course (EIN vs. SEN) Inflammatory and immunological marker profiles	**Abdominal abscess**: 11 (9.2) vs. 7 (6.3) **Pancreatic fistula**: 8 (6.7) vs. 7 (6.3) **Anastomotic leakage**: 3 (2.5) 3 (2.7) 1·000 **Wound infection or dehiscence**: 13 (10.8) vs. 8 (7.2) **Drain infection**: 3 (2.5) vs. 1 (0.9) **Pneumonia**: 5 (4.2) vs. 0 (0) **Venous catheter infection**: 2 (1.7) vs. 1 (0.9) **Pleural effusion**: 1 (0.8) vs. 1 (0.9) **Postoperative bleeding**: 3 (2.5) vs. 0 (0) **Ileus**: 2 (1.7) vs. 1 (0.9) No significance difference in any of the complications above. **SIRS**: 38.3% vs. 30.6% ($p > 0.05$) **Morbidity rate**: 30.8% vs. 26.1% [RR 1.18 (0.78,1.78)] **Reoperation**: 0 vs. 0 ($p > 0.05$) **Hospital death**: 0 vs. 0 ($p > 0.05$) **Hospital stay (days)**: 18 (9–85) vs. 17 (10–88) ($p > 0.05$) **CRP value on day 3 or 4 (mg/dl)**: 11 · 8 (2 · 3–38 · 1) vs. 9 · 2 (1 · 1–38 · 9) ($p > 0.05$)	This well-designed study concluded that routine preoperative use of immunonutrition in well-nourished patients having gastric cancer resections could not be recommended.

group received Stresson® (Nutricia China, Shanghai, China)- a feed containing (per 100 mL) 0.89 g of arginine, 1.3 g of glutamine and an O-3FA:O-6FA ratio of 3.45:1. The SEN grouped received Nutrison® (Nutricia), a feed containing (per 100 mL) 0.16 g of arginine, 0.4 g of glutamine and an O-3FA:O-6FA ratio of 5:1. On POD 9, serum levels of pre-albumin and transferrin were higher in the immunonutrition group. On POD 7, the EIN group also had significantly higher levels of IgG, IgM, IgA, CD4 cell counts, CD4:CD8 ratio and IL-2 than the SEN group. However, IL-6 and TNF-α levels were significantly lower in the immunonutrition group on POD 7. Overall these findings suggest that EIN can improve immune mechanisms and modulate inflammatory responses after gastrectomy. The limitations of this study include that the demographics of the groups were not detailed and statistically analysed to assess comparability. The method of randomisation was also not detailed and the study poorly adhered to the CONSORT standards of reporting.

Fujitani et al.,[8] randomised 244 patients undergoing gastrectomy to receive either EIN ($n = 127$) or SEN ($n = 117$). Preoperatively, the EIN group received 1000 mL/day of oral Impact® (Ajinomoto Pharmaceutical Company) containing (per 100 mL) 1.28 g of arginine and 0.13 g of RNA per 100 mL. The O-3FA:O-6FA ratio was 4:5. The SEN group received a regular diet with no supplements. No significance difference was seen in the rates of postoperative morbidity or infectious complications. This well-designed study concluded that routine preoperative use of immunonutrition in well-nourished patients having gastric cancer resections could not be recommended.

On reviewing all of these studies, there is heterogeneity with respect to the types of operations undertaken (two studied patients undergoing oesophagectomy, three studied patients undergoing gastrectomy and one had patients undergoing both operations). In addition the RCTs all used different formulations of EIN and SEN, limiting comparability of the studies. Moreover not all studies reported the same outcomes and in particular, not all studies investigated similar inflammatory and immunological marker profiles limiting the conclusions that can be drawn from these studies. Finally the quality of the reporting of the RCTs was variable with some studies not conforming to the CONSORT principles. Nonetheless the results of most of the studies demonstrate no definitive clinical differences in outcomes with EIN.

8. Clinical bottom line

Although postoperative enteral immunonutrition seems to improve humoral immunity in patients undergoing oesophagogastric resection, this improvement does not lead to a reduced hospital stay, nor does it reduce the rate of infections. There is no convincing evidence in support of routine immunonutrition in patients undergoing oesophageal or gastric resection for cancer.

Ethical approval

Not applicable.

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Author contribution

N Mabvuure – Literature search, analysis, writing.
A Roman – Analysis and editing of manuscript.
Omar Khan – Analysis and editing of manuscript.

Conflict of interest

None.

References

1. Khan OA, Dunning J, Parvaiz AC, Agha R, Rosin D, Mackway-Jones K. Towards evidence-based medicine in surgical practice: best BETs. *Int J Surg* 2011;**9**(8):585–8.
2. Sax HC. Immunonutrition and upper gastrointestinal surgery: what really matters. *Nutr Clin Pract* 2005;**20**(5):540–3.
3. Sakurai Y, Masui T, Yoshida I, Tonomura S, Shoji M, Nakamura Y, et al. Randomized clinical trial of the effects of perioperative use of immune-enhancing enteral formula on metabolic and immunological status in patients undergoing esophagectomy. *World J Surg* 2007 Nov;**31**(11):2150–7. discussion 8–9.
4. Ryan AM, Reynolds JV, Healy L, Byrne M, Moore J, Brannelly N, et al. Enteral nutrition enriched with eicosapentaenoic acid (EPA) preserves lean body mass following esophageal cancer surgery: results of a double-blinded randomized controlled trial. *Ann Surg* 2009 Mar;**249**(3):355–63.
5. Sultan J, Griffin SM, Di F, Kirby JA, Shenton BK, Seal CJ, et al. Randomized clinical trial of omega-3 fatty acid-supplemented enteral nutrition versus standard enteral nutrition in patients undergoing oesophagogastric cancer surgery. *Br J Surg* 2012;**99**(3):346–55.
6. Farreras N, Artigas V, Cardona D, Rius X, Trias M, Gonzalez JA. Effect of early postoperative enteral immunonutrition on wound healing in patients undergoing surgery for gastric cancer. *Clin Nutr* 2005;**24**(1):55–65.
7. Chen DW, Fei ZW, Zhang YC, Ou JM, Xu J. Role of enteral immunonutrition in patients with gastric carcinoma undergoing major surgery. *Asian J Surg* 2005;**28**(2):121–4.
8. Fujitani K, Tsujinaka T, Fujita J, Miyashiro I, Imamura H, Kimura Y, et al. Prospective randomized trial of preoperative enteral immunonutrition followed by elective total gastrectomy for gastric cancer. *Br J Surg* 2012 May;**99**(5):621–9.