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Revisión

Surgical infection and malnutrition

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Abstract

Background: **Malnutrition in surgical patients is associated with delayed recovery, higher rates of morbidity and mortality, prolonged hospital stay, increased healthcare costs and a higher early re-admission rate.**

Methods: **Data synthesis after review of pertinent literature.**

Results: **The aetiology of malnutrition is multifactorial. In cancer patients, there is an abnormal peripheral glucose disposal, gluconeogenesis, and whole-body glucose turnover. Malnourished cancer patients undergoing major operations are at significant risk from perioperative complications such as infectious complications. Surgical aggression generates an inflammatory response which worsens intermediary metabolism.**

Conclusions: **Nutritional evaluation and nutritional support must be performed in all surgical patients, in order to minimize infectious complications. Enteral nutrition early in the postoperative period is effective and well tolerated reducing infectious complications, improving wound healing and reducing length of hospital stay. Pharmaconutrition is indicated in those patients, who benefit from enteral administration of arginine, omega 3 and RNA, as well as parenteral glutamine supplementation. When proximal sutures are used, tubes allowing early jejunal feeding should be used.**

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Key words: *Infection disease. Nutrition. Suergery.*

INFECCIÓN QUIRÚRGICA Y MALNUTRICIÓN

Resumen

Introducción: **La malnutrición en pacientes quirúrgicos está relacionada con un retraso en la recuperación, tasas más elevadas de morbilidad y mortalidad, estancia hospitalaria prolongada, mayores costes de atención sanitaria y una tasa más elevada de re-hospitalización temprana.**

Métodos: **Síntesis de datos tras la revisión de la bibliografía pertinente.**

Resultados: **La etiología de la malnutrición es multifactorial. En pacientes con cáncer, existe una alteración en la utilización de la glucosa periférica, en la gluconeogénesis, y en la producción de glucosa en todo el cuerpo. Los pacientes con cáncer que se someten a operaciones mayores tienen un riesgo significativo de complicaciones perioperativas, como es el caso de las complicaciones de tipo infeccioso. La agresión quirúrgica genera una respuesta inflamatoria que empeora el metabolismo intermediario.**

Conclusiones: **Es necesario realizar una evaluación nutricional y llevar a cabo un soporte nutricional en todos los pacientes quirúrgicos con el fin de minimizar las posibles complicaciones infecciosas. La nutrición enteral justo al inicio del periodo postoperatorio es bien tolerada y resulta eficaz a la hora de reducir complicaciones infecciosas, mejorando el proceso de curación de la herida y la duración de la estancia hospitalaria. La nutrición farmacológica está indicada en pacientes que reciben administración enteral de arginina, omega 3 y ARN, además de suplementación por vía parenteral. Cuando se utilizan suturas proximales, se deben emplear sondas que permitan una alimentación yeyunal temprana.**

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Palabras clave: *Complicación infecciosa. Nutrición. Cirugía.*

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Introduction

Malnutrition is associated with delayed recovery, higher rates of morbidity and mortality, prolonged hospital stay and both increased healthcare costs and a higher early re-admission rate. This fact has a negative effect upon hospitalized patients.[1,2,3].

The negative impact caused by malnutrition on a patient's outcome was long ago demonstrated. In 1936, Studley[4] showed that a 20% weight loss of usual body weight was correlated to a significant increase in the mortality rate of patients undergoing surgery for duodenal ulcer. On the other hand, infection after surgery is a central cause for increased morbidity and mortality, too. Alterations in both innate and adaptive immune function contribute significantly to increased susceptibility to infections[5]. Finally, patients undergoing major gastrointestinal or cancer surgery, are at increased risk of developing complications, such as infectious complications.

Malnutrition and Metabolic consequences of operative stress

Malnutrition is a pathologic depletion of the body's lean tissues caused by starvation, or a combination of starvation and catabolic stress. The aetiology of this syndrome is multifactorial and multiple factors contribute to it: reduced nutrient intake, changes in the ability to smell and taste; mechanical causes, such as dysphagia or bowel obstruction; and treatment-related factors, such as surgery, chemotherapy and radiation therapy. Although decreased nutrient intake is partly responsible, a major contribution comes from the well described abnormalities in the host intermediary metabolism of carbohydrate, protein and fat[6]. In the particular case of cancer patients, there is an abnormal peripheral glucose disposal, gluconeogenesis, and whole-body glucose turnover, which confirm alterations in the carbohydrate metabolism of these patients. Futile cycling of glucose carbons (Cori cycle) has been shown to be increased in cancer patients[7]. The cachectic cancer patient not only utilizes nutrients ineffectively, but he also seems unable to adapt to the malnourished state by conserving lean body mass[8], as healthy humans do. Malnourished cancer patients undergoing major operations are at significant risk from perioperative complications such as infectious complications (table I)[9].

Malnutrition is characterized by atrophy and weakness of the skeletal muscles (including the respiratory muscles), reduced heart muscle mass, impaired wound healing, skin thinning with a predisposition to decubitus ulcers, immune deficiency, fatigue, apathy and hypothermia (table II).

During the last years a large body of data and research has given a clear image of the process of catabolic stress and its relation to nutrition in surgical patients. Patients with severe tissue injury commonly develop a hypermetabolic response, termed the systemic inflammatory response syndrome (SIRS), which is defined by the presence of two or more of the following elements: fever (or profound hypothermia), tachypnea, tachycardia and leukocytosis. During the postoperative period the patient is in a catabolic state where energy and protein are utilized from the body's stores. Fat and protein stores become the primary reservoir, with an obligatory generation of the required glucose. Carbohydrate metabolism is altered during the uncomplicated postoperative period. Postoperative patients are typically hyperglycaemic and resistant to physiologic levels of insulin. Despite this finding, hepatic glucose production is elevated, with the principal source of the carbons being peripheral amino acids released from skeletal muscle. Protein wasting is believed to represent the metabolic cost of rapidly mo-

Table I
Incidence of infectious complications vs nutritional status

Infectious complications	*Well nourished %*	*Malnourished (Moderately and severely) %*
Pulmonary infection	4.1	5.9
Urinary infection	1.9	3.7
Wound infection	2.1	1.7
Sepsis	1.1	3.7
Intraabdominal abscess	0.4	2.1
Extraperitoneal abscess	0.2	0.8
Septic coagulopathy	0.2	0.4
Total	10.1	19.4

Table II
Clinical features of protein energy malnutrition

- Reduced body weight
- Reduced respiratory capacity
- Reduced cardiac capacity
- Muscle wasting
- Decreased strength
- Skin thinning
- Hair loss
- Decreased metabolic rate
- Hypothermia
- Apathy
- Edema
- Immunodeficiency

bilizing amino acids for wound healing and the synthesis of immune cells and proteins. Skeletal muscle is the primary source of the amino acids used during the postoperative state. These amino acids are utilized in the liver for conversion to glucose and for the protein necessary for the defence of the body's immune system, as well as for the maintenance of organ function. Alanine and glutamine are the primary amino acids released from the periphery, with uptake by the liver, gut and kidneys. Part of these changes are secondary to increasing levels of counterregulatory hormones (cortisol, glucagon, growth hormone)[10]. Moreover, surgical aggression generates an inflammatory response with changes in the concentration of acute-phase serum proteins (C-reactive protein, fibrinogen and ferritin), which worsens intermediary metabolism[11].

The stress of surgical intervention combined with the alterations of intermediary metabolism in severely ill patients produces significant risk, such as infectious complications. Both parenteral nutrition and enteral nutrition have been utilized in an effort to prevent and reverse these nutritional consequences in surgical patients.

Tools for diagnosis of protein energy malnutrition in surgical patients

In severe situations, diagnosis of malnutrition is evident from a physical examination, which reveals a combination of generalized fat and muscle loss typical of the disease, with a history of a weight loss and/or inadequate food intake. However, malnutrition is easiest to diagnose when fat stores are depleted, but it can occur without apparent fat loss in previously obese patients, in chronic protein deficiency without energy deficiency, and in high loss protein-catabolic states. The lean tissues are the fat-free, metabolically active tissues of the body, namely, the skeletal muscles, viscera, and the cells of the blood and immune system. They account for 35%–50% of the total weight of a healthy young adult. As the lean tissues are the largest body compartment, their rate of loss is the main determinant of total weight loss in most cases of malnutrition. For this reason, serial body weight measurements are very useful for assessing the evolution and severity of the disease (this is our first easy tool to assess malnutrition in surgical patients). A weight loss of 40%–50% is usually incompatible with survival, whereas milder lean tissue depletions induce important biochemical and functional abnormalities. These abnormalities, together with an immune system dysfunction, are evident after involuntary weight loss over 10% and they become highly physiologically obtrusive when weight loss exceeds about 15%.

Weight measurement, history of weight change and serial weight determinations are cheap and simple ways of measuring malnutrition. Although single weight determinations may be altered by abnormal body compartment distribution and water retention, body weight determination should always be registered. A way to classify the severity of malnutrition is simply by the degree of weight loss. For "normal" one can use the weight that would give a body mass index (BMI) of 23-24. In older adults, the lower end of the normal range for BMI is about 20, so one might consider malnutrition as mild or absent when the BMI is 20 or more (representing a weight deficit of 5%–15%), moderate when the BMI is over 16 but less than 20 (weight deficit of 16%–33%) and severe when the BMI is 16 or less (table III).

Biochemical parameters can be used to diagnose malnutrition, too. Serum albumin is an example. However some data must be taken to account. For example, serum albumin concentration is normal in successfully adapted malnutrition even when advanced, and it falls when adaptation fails. By contrast, serum levels of the hepatic secreted protein, prealbumin, are reduced in energy deficiency and adapted malnutrition, and may be used to screen for patients whose food intake is inadequate and who need a surgical intervention. Nevertheless, because albumin and prealbumin are negative acute-phase proteins, their serum levels fall in response to metabolic stress even in the absence of malnutrition. The rapid fall in serum albumin that occurs in acute severe inflammation is caused by its redistribution into an expanded extracellular fluid compartment. Despite its lack of specificity, hypoalbuminemia is an important finding in nutritional assessment. For example, a normal serum albumin concentration in a starving patient is a favourable prognostic finding. Hypoalbuminemia has an adverse prognostic implication, irrespective of whether it is due to metabolic stress or failed adaptation to malnutrition. As hypoalbuminemic patients are usually both catabolic and starving, the presence of hypoalbuminemia would mean that a careful nutritional assessment of these patients is necessary.

Finally, many formulae have been proposed for the classification of malnutrition but no fully satisfactory classification method currently exists[12] . Probably, the most universally accepted method for evaluating malnutrition is the so-called subjective global assessment (SGA)[13]. SGA involves the assessment of 7 clinical parameters, followed by a personal judgement as to whether the patient has (A) no malnutrition, (B) possible

Table III
Degree of Protein Energy Malnutrition according to BMI (Body mass index: Body weight/height^2 (Kg/cm^2))

Degree of PEM Body Mass Index
Normal, 24 or more
Mild, 20-24
Moderate, 16-20
Severe, 16 or less

or mild malnutrition, or (C) significant malnutrition (table IV).

Nutritional support in surgical patients:

The hypothesis that preventing or treating malnutrition will improve a surgical patient's clinical outcome, in particular infectious complications, is overwhelmingly biologically plausible, but in each case the anticipated benefit must be balanced against the risks of artificial feeding.

Oral nutrition is safest, cheapest and best. When nutritional needs cannot be met by modifications in the diet or its provision, forced feeding must be considered. When the alimentary tract cannot be used, the option of parenteral nutrition is available. In controlled clinical trials that involved this mode of nutrition therapy, the clinical outcome was improved in advanced malnutrition, but patients with only mild malnutrition fared worse when treated in this aggressive fashion[14]. However, enteric nutrition must be the main access route in surgical patients. The functional and structural integrity of the gastro intestinal tract depends on whether or not the gut is used for enteral feeding. Enteral feeding supports structural integrity and maintains mucosal mass, stimulates epithelial cell prolipheration, as well as maintaining villus height and promoting the production of brush border enzymes. It also stimulates the secretion of a sufficient volume of IgA and bile salts, both of which help coat bacteria within the GI tract, preventing adherence. Finally, enteral feeding stimulates the production of mucus and promotes good intestinal contractility, helping to wash away the bacteria in a caudal direction. Alimentary exclusion, in the setting of a major insult or injury, may significantly increase systemic or bacterial challenge to the host[15].

Table IV
Recognition of advanced protein energy malnutrition by subjective global assessment

- Unremitting weight loss greater than 10% in the previous 6 months, and especially in the last few weeks (failed adaptation)
- Food intake severely curtailed (objective evidence of starvation)
- Muscle wasting and fat loss
- Oedema or ascites
- Persistent gastrointestinal symptoms such as anorexia, nausea, vomiting or diarrhoea in the previous 2 weeks (strongly predicts inadequate food intake)
- Marked reduction in physical capacity (predicts poor intake and is evidence of its consequences)
- Presence of metabolic stress due to trauma, inflammation or infection (adaptation impossible)

In the last years, various nutritional formulas have been tested, using routines of access and administration schedules, to improve nutritional status in surgical patients and to decrease perioperative complications such as infectious complications. Diet containing supraphysiological quantities of glutamine, omega 3 fatty acids, arginine, nucleotides and antioxidants were developed more than 20 years ago[16] . These diets were called immune-enhancing diets, and these diets have been tested in multiple studies, mostly, in surgical and critically ill patients. Early reviews and meta-analyses suggested no change in mortality, but a decrease in postoperative infection rates and length of hospital stay with use of immunonutrition has been demonstrated (IN)[17,18,19]. In a recent metaanalysis, Cerantola et al[20] showed significantly reduced overall complications with immunonutrition when used before surgery, both before and after operation or after surgery. For these three timings of IN administration, odds ratios (Ors) of postoperative infection were 0.36 (0.24 to 0.56), 0.41 (0.28 to 0.58) and 0.53 (0.40 to 0.71) respectively. Use of IN led to a shorter hospital stay: mean difference −2.12 (95 per cent c.i. −2.97 to −1.26) days. Perioperative IN had no influence on mortality. Some systematic reviews have demonstrated significant reduction of infection and wound complications and the benefits of this IN required both arginine and fish oil in enteral formulas[21,22]. Specifically, in head and neck cancer surgery, formulas enhanced with arginine improved the infection rate[23,24]. In this topic area, some questions have been answered and other remained unclear. For example, the volume of this immunoenhaced formulas has been recommended around 50-1000 ml during 5-7 days containing omega 3 fatty acids, arginine and RNA[19]. The quantity of formula administered is also a matter of debate, A dose of 25 kcal per kg per day is about standard[18]. However, the timing of supplementation remains controversial. Perioperative administration could be better than postoperative alone.

Guidelines of some Nutritional Societies have remarked the importance of specialized nutrition in gastrointestinal surgery[25]. These recommendations can be summarized:

Administration of enteral nutrition early in the postoperative period is effective and well tolerated; reducing infectious complications, improving wound healing and reducing length of hospital stay.

Calorie-protein requirements do not differ from those in other critically-ill patients.

In patients intolerant to enteral nutrition, especially if the intolerance is due to increased gastric residual volume, prokinetic agents can be used to optimize calorie intake.

When proximal sutures are used, tubes allowing early jejunal feeding should be used.

Pharmaconutrition is indicated in those patients, who benefit from enteral administration of arginine, omega 3 and RNA, as well as parenteral glutamine supplementation.

Parenteral nutrition should be started in patients with absolute contraindication for use of the gastrointestinal tract or as complementary nutrition if adequate energy intake is not achieved through the enteral route.

However, the last item has been discussed recently, because Heidegger et al[26] have demonstrated that individually optimized energy supplementation with parenteral nutrition starting 4 days after ICU admission could reduce nosocomial infections and should be considered as a strategy to improve clinical outcome in surgical and medical patients in the intensive care units for whom enteral nutrition is insufficient.

In conclusion, nutritional evaluation and nutritional support must be two items to be performed in all surgical patients, in order to minimize infectious complications, in a heterogeneous group of subjects such as surgical patients[27,28,29,30].

Author Disclosure Statement

No competing financial interests exist.

References

1. de Luis DA, Aller R, Izaola O, Cuellar L, Terroba MC. Nutritional assessment: predictive variables at hospital admission related with length of stay. *Ann Nutr Metab* 2006:50:394-398.
2. Culebras JM. Malnutrition in the 21st century: an epidemic affecting surgical outcome. *Surgical Infections* 2013; 14(3): 237-243.
3. Fry DE. Fifty ways to cause Surgical site infections. Surgical *Infections* 2011;12(6):497-500.
4. Martin Pena G. Comments about the article by: Studley HO. Percentage of weight loss. A basic indicator of surgical risk in patients with chronic peptic ulcer. JAMA 1936. *Nutr Hosp* 2001; XVI:140-144.
5. Mannick JA, Rodrick ML, Lederer JA. The immunologic response to injury. *J Am Coll Surg* 2001;193:237-44.
6. Casimiro C, Garcia de Lorenzo A and Usan L: Nutricional and metabolic status and diet evaluation in institutionalized Spanish elderly patients with non insulin dependent diabetes mellitas. *Nutr Hosp* 2001; 16:104-111.
7. Heslin MJ and Brennan MF. Advances in perioperative nutrition: cancer. *World J Surg* 2000; 24:1477-1485.
8. Wolfe BM, Culebras JM, Sim AJW, Ball MR and Moore FD. Substrate interaction in intravenous feeding. Comparative effects of carbohydrates and fat in amino acids utilization in fasting man. *Ann Surg* 1977; 186:518-540.
9. Correia MIT and D Waitberg. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clinical Nutrition* 2003:22:235-239.
10. Wolfe BM, Culebras JM, Aoki TT, OConnor NE, Finney RJ, Kaczowka A and Moore FD. The effect of glucagon on protein metabolism in normal man. *SURGERY* 1979; 86:248-257.
11. Gabay C, Kushner I. Acute phase proteins and other systemic response to inflammation. N Engl J Med 1999;340:448-454.
12. Collins S, Yates R: The need to update the classification of acute malnutrition. *Lancet* 2003;362:249.
13. Baker JP, Detsky AS, Wesson DE, Colman SL, Stewart S, Whitewell J et al. A comparison of clinical judgement and objective measurements. *N Engl J Med* 1982;306:969-972.
14. Veterans Affairs Total Parenteral Nutrition Cooperative Study Group: Perioperative Total Parenteral Nutrition in Surgical Patients. *N Engl J Med* 1991; 325:525-532.
15. Jabbar A, Chang WK, Dryden GW and McClave SA. Gut immunology and the differential response to feeding and starvation. *Nutr in Clin Pract* 2003;18:461-482.
16. Beale RJ, Bryg DJ, Bihari DJ. Immunonutrition in the critically ill: a systematic review of clinical outcome. *Crit Care Med* 1999;27:2799-805.
17. Zheng Y, Li F, Qi B, Luo B, Sun H, Liu S et al. Application of perioperative immunonutrition for gastrointestinal surgery: a meta-analysis of randomized controlled trials. *Asia Pac J Clin Nutr* 2007; 16(Suppl 1): 253–257.
18. Akbarshahi H, Andersson B, Nord´en M, Andersson R. Perioperative nutrition in elective gastrointestinal surgery – potential for improvement? *Dig Surg* 2008; 25: 165–174.
19. Waitzberg DL, Saito H, Plank LD, Jamieson GG, Jagannath P, Hwang TL et al. Postsurgical infections are reduced with specialized nutrition support. *World J Surg* 2006; 30: 1592–1604.
20. Cerantola Y, Hübner M, Grass F, Demartines N, Schäfer M. Immunonutrition in gastrointestinal surgery. *Br J Surg* 2011 Jan;98(1):37-48.
21. Marik PE, Zaloga GP. Immunonutrition in high-risk surgical patients: a systematic review and analysis of the literature. *JPEN J Parenter Enteral Nutr* 2010 Jul-Aug;34(4):378-86.
22. Culebras-Fernández JM, de Paz-Arias R, Jorquera-Plaza F, García de Lorenzo A. Nutrition in the surgical patient: immunonutrition. *Nutr Hosp* 2001 May-Jun;16(3):67-77.
23. Casas-Rodera P, Gómez-Candela C, Benítez S, Mateo R, Armero M, Castillo R, Culebras JM. Immunoenhanced enteral nutrition formulas in head and neck cancer surgery: a prospective, randomized clinical trial. *Nutr Hosp* 2008;23:105-10.
24. Casas Rodera P, de Luis DA, Gómez Candela C, Culebras JM. Immunoenhanced enteral nutrition formulas in head and neck cancer surgery: a systematic review. *Nutr Hosp* 2012;27:681-90.
25. Sánchez Álvarez C, Zabarte Martínez de Aguirre M, Bordejé Laguna L; Metabolism and Nutrition Working Group of the Spanish Society of Intensive Care Medicine and Coronary units Guidelines for specialized nutritional and metabolic support in the critically-ill patient: update. Consensus SEMICYUC-SENPE: gastrointestinal surgery. *Nutr Hosp* 2011 ;26 Suppl 2:41-5
26. Heidegger CP, Berger MM, Graf S, Zingg W, Darmon P, Costanza MC, Thibault R, Pichard C. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. *Lancet* 2013;381(9864):385-93.
27. Zamora Elson M, Serón Arbeloa C, Labarta Monzón L, Garrido Ramírez de Arellano I, Lander Azcona A, Marquina Lacueva MI, López Claver JC, Escós Orta J. Nutritional support response in critically ill patients; differences between medical and surgical patients. *Nutr Hosp* 2012;27:1213-8.
28. Gerlach AT, Thomas S, Murphy CV, Stawicki PS, Whitmill ML, Pourzanjani L, Steinberg SM, Cook CH. Does delaying early intravenous fat emulsion during parenteral nutrition reduce infections during critical illness? *Surg Infect (Larchmt)* 2011;12(1):43-7.
29. Hermsen JL, Sano Y, Gomez FE, Maeshima Y, Kang W, Kudsk KA Parenteral nutrition inhibits tumor necrosis factor-alpha-mediated IgA response to injury. *Surg Infect (Larchmt)* 2008;9(1):33-40.
30. Gianotti L, M. Braga. Revising concepts of artificial nutrition in contemporary surgery: from energy and nitrogen to immuno-metabolic support. *Nutr Hosp* 2011;26(1):56-67.