

Enteral nutrition for patients in septic shock: a retrospective cohort study

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Early enteral nutrition (EN) is considered best practice in critically ill patients.¹⁻⁴ However, EN is often limited by delayed gastric emptying, which is clinically evident from large gastric residual volumes.⁵ Studies consistently show that nasogastric nutrition delivers only about 60% of nutritional goals in critically ill patients.^{6,7} The aetiology of abnormal gastrointestinal motility in critical illness remains unclear, although factors such as admission diagnosis, inotropic support, opiate-based sedation,⁸ muscle relaxants, electrolyte abnormalities and inflammatory cytokines have all been implicated. Haemodynamic instability is also frequently considered a contraindication to enteral feeding.³ However, gastrointestinal function and the success of enteral feeding have never been formally examined in patients with shock. The aim of our study was to assess adequacy of EN in ventilated septic patients with and without shock.

Methods

We conducted a retrospective cohort study in the adult general intensive care unit of the Royal Adelaide Hospital. Institutional ethics committee approval was obtained. In view of the retrospective nature of the study, the ethics committee agreed to waive individual patient consent.

Patients were included in the study if they were admitted with sepsis of any cause requiring invasive ventilation on 3 or more days. The study period was over 12 months in 2006. Patients were identified with the aid of the Australasian Outcomes Research Tool for Intensive Care (AORTIC) database. All patients with the following diagnoses were considered to have the possibility of sepsis: non-urinary sepsis with or without shock, urinary sepsis with or without shock, bacterial pneumonia and intra-abdominal sepsis. Diagnosis was then confirmed by extensive review of case notes, ICU charts for systemic inflammatory response syndrome (SIRS) criteria,⁹ and ICU and hospital discharge summaries. Patient selection is shown in Figure 1.

ICU nursing charts were used to collect patient data for 7 days after initiation of enteral feeding. Data collection was ceased when the patient commenced an oral diet or was discharged from the ICU. Data collected included demographics, hospital and ICU outcomes, timing of initiation of feeds after ICU admission, SIRS criteria, type and cumulative daily dosage of inotropes and sedatives, type of feeds, net volume of feeds (enteral feeds administered minus gastric

ABSTRACT

Background: Haemodynamic instability is frequently considered a contraindication to enteral feeding. However, gastrointestinal function and the success of enteral feeding have never been formally examined in patients with shock.

Objective: To assess the adequacy of enteral nutrition in mechanically ventilated septic patients with and without shock.

Design, setting and participants: Retrospective cohort study of septic patients receiving enteral nutrition in the intensive care unit of the Royal Adelaide Hospital in 2006. Patient data were obtained from case notes, nursing charts and dietitian notes. Enteral feeding was reviewed over a 7-day period in septic patients who were ventilated on more than 3 days. Adequacy of nutrition was defined as net calories delivered (including propofol) as a percentage of goal calories prescribed.

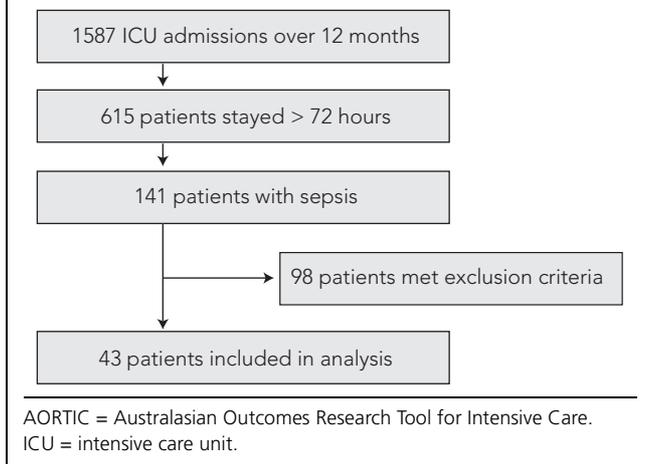
Mean outcome measures: Mean time to initiation of feeds; percentage of nutritional goals reached.

Results: 43 patients (mean age, 54 [SD, 20] years; mean APACHE II score, 20 [SD, 8]) were identified, of whom 33 had shock. The median length of ICU stay was 13 days (range, 3–55 days), and 32 patients (74%) survived hospital. Seventeen patients (40%) received <60% of goal nutrition over the 7 days. Overall calorie delivery improved over time and peaked at 86% of goal calories by Day 6. The mean time from ICU admission to start of feeding was 1.4 (range, 0–8) days. The mean time to initiation of feeding was not different in patients with or without shock: 1.3 (SD, 1.7) days v 1.7 (SD, 1.3) days ($P=0.16$). Patients with shock had higher mean daily gastric aspirate volumes than those without (113 [SD, 153] mL v 39 [SD, 47] mL; $P=0.02$), but no difference was found in the percentage of their nutritional goals reached (69% [SD, 23%] v 77% [SD, 16%]; $P=0.2$).

Conclusion: Despite delayed gastric emptying, protocol-directed enteral feeding can be considered in patients with septic shock.

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residual volumes not returned), total daily aspirate volumes, net calories and protein administered, and presence of concomitant parenteral nutrition. Dietitians' notes were then reviewed to confirm the type of feed prescribed, ideal body

Figure 1. Patient selection using AORTIC database and case note review

weight, goal calories and protein prescribed. Nutritional requirements for each patient were calculated using the Schofield equation. Goal calorie prescription did not take into account calories delivered as propofol. Adequacy of nutrition was defined as net calories delivered (including propofol) divided by goal calories prescribed (expressed as a percentage). Shock was defined a priori as any requirement for inotropes or vasopressors to maintain haemodynamic stability (ie, not adrenaline for asthma, etc) during the 7-day study period.

Major exclusions included patients who (i) were invasively ventilated for ≤ 3 days; (ii) received mask ventilation; (iii) did not commence enteral feeds; (iv) had surgical intra-abdominal pathology, precluding successful enteral feed administration (eg, gastrointestinal perforation, intestinal obstruction, laparotomy); or (v) had missing records.

Statistical analysis

Data are shown as mean (SD) or median (range), as appropriate. Demographic groups were compared on overall success of feeding via a two-sample *t*-test, assuming unequal variances. Continuous demographic characteristics were related to overall success of feeding via Pearson correlation coefficients. Relationships between drugs (inotropes, sedatives and opioids) and overall success of feeding were compared via a two-sample *t*-test, assuming unequal variances. Within-subject correlations between daily measurements of feeding success and clinical characteristics were calculated using the method of Bland and Altman.¹⁰ The effect of shock on feeding success was tested using analysis of covariance, controlling for APACHE II (Acute Physiology and Chronic Health Evaluation II) score. The χ^2 test was used to test for independence between prokinetic usage on any day and presence of shock. SPSS software, version 17 (SPSS Inc, Chicago, Ill, USA) was used for statistical analysis.

Results

Forty-three patients were included in the analysis. Patient characteristics are shown in Table 1 and patient diagnostic groups in Table 2. Thirty-three patients had shock, 41 received EN via the nasogastric route, and two were fed through a pre-existing gastrostomy. Only one patient with infected pancreatic necrosis received parenteral nutrition in addition to EN. Among the 98 patients excluded, 44 (45%) were excluded for not meeting the ventilatory criteria, 29 (30%) for surgical intra-abdominal pathology precluding successful enteral feed administration, and 5 (5%) for non-commencement of feeds. The rest were excluded for wrong diagnosis and/or missing records.

The time from ICU admission to start of enteral feeding ranged from 0 to 8 days, with a mean (SD) of 1.4 (1.7) days.

Table 1. Patient demographics

Characteristic	Total (n = 43)	Shock (n = 33)	No shock (n = 10)	P
Mean age (years) (SD; range)	54 (20; 21–81)	56 (16; 27–81)	47 (21; 21–77)	0.237
Sex, n (%)				0.120
Male	30 (70%)	8 (24%)	5 (50%)	
Female	13 (30%)	25 (76%)	5 (50%)	
Median stay in ICU (days) (range)	13 (3–55)	14 (3–55)	11 (5–21)	0.073
Median stay in hospital (days) (range)	28 (3–217)	42 (15–217)	17 (7–46)	0.012
Mean APACHE II score (SD)	20 (8)	21 (7)	17 (9)	0.184
Mean weight (kg) (SD)	76 (22)	75 (21)	80 (24)	0.581
Mean calories prescribed (kcal/day) (SD)	1995 (260)	1994 (262)	1995 (268)	0.966
Mean protein prescribed (g/day) (SD)	87 (15)	87 (15)	87 (13)	0.854
ICU mortality, n (%)	7 (16%)	6 (18%)	1 (10%)	0.539
Hospital mortality, n (%)	11 (26%)	9 (27%)	2 (20%)	0.644

APACHE = Acute Physiology and Chronic Health Evaluation. ICU = intensive care unit.

Over the 7-day study period, patients received a mean (SD) of 65% (22%) of daily nutritional goals from the enteral route alone. Seventeen patients (40%) received less than 60% of prescribed goals. When calories from propofol and parenteral nutrition were included in the analysis, patients received a mean (SD) of 71% (22%) of nutritional goals. Overall calorie delivery improved over time and peaked at 86% of goal calories by Day 6 in the ICU (Figure 2). Thirty-eight patients received propofol at some time over the 7-day period. Daily calories provided from propofol ranged from 0 to 426kcal (median, 79kcal); percentage goal feeds ranged from 0 to 18% (median, 4%). Twenty-one patients exceeded their nutritional goals (101%–126%) on at least 1 day of the week as a result of concurrent administration of propofol.

There was no relationship between age, hospital or ICU outcome, APACHE II score, and any parameter of success of feeding (all $P > 0.10$). Pre-existing comorbidities (diabetes, head trauma, previous abdominal surgery, and high alcohol intake) did not appear to affect the success of feeding (all $P > 0.05$). There was no relationship between the amount of nutrition received and any clinical outcomes, including mortality, length of ICU stay and length of hospital stay (all $P > 0.10$). Morphine use was inversely associated with nutritional goals ($r = -0.2$; $P = 0.03$).

There was no within-patient correlation between daily SIRS criteria and delivery of nutrition (all $P > 0.10$). The presence of shock had no effect on the time of initiation of feeding: mean, 1.3 (SD, 1.7) days with shock versus mean, 1.7 (SD, 1.3) days without shock ($P = 0.16$) (Figure 3). Patients with shock had significantly higher mean (SD) daily gastric aspirate volumes than those without shock: 113 (155) mL versus 39 (47) mL ($P = 0.02$) (Figure 4). There was no difference in unadjusted average nutritional goals between shocked and haemodynamically stable patients: 69% (23%) versus 77% (16%) kcal delivered/prescribed ($P = 0.2$) (Figure 5), and this remained the case after adjusting for APACHE II score ($P = 0.4$). Additional adjustment for the number of days in hospital did not alter the above results.

Twenty-three patients received prokinetics on at least 1 day during the study. There was no difference in prokinetic use

Figure 2. Goal calories received over 7 days (mean [SE])

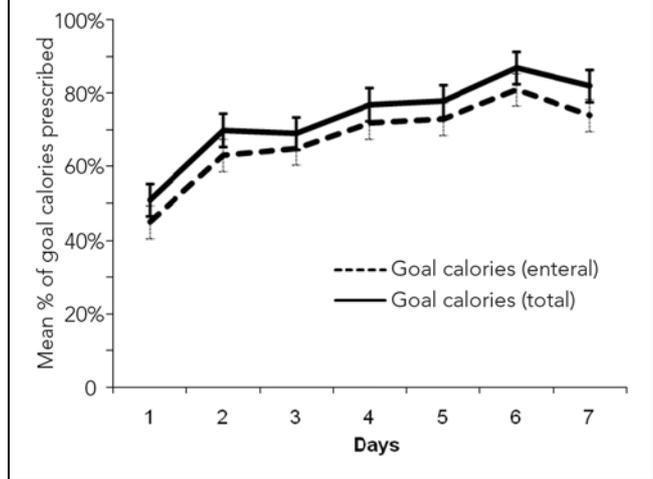


Figure 3. Time to initiation of feeding in patients

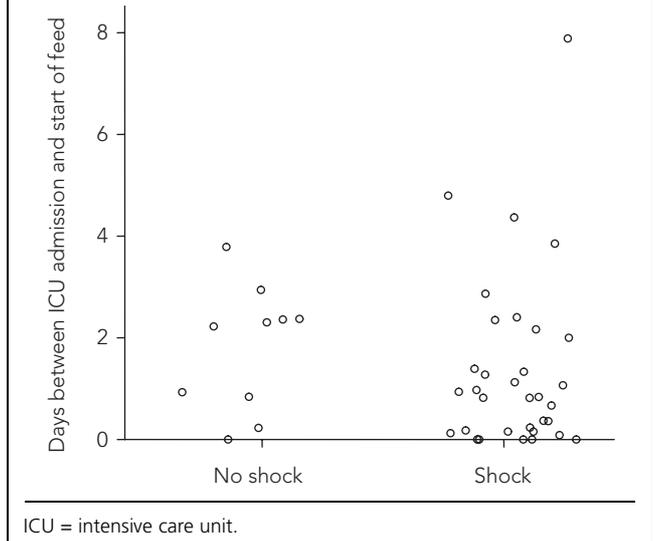


Figure 4. Aspirate volumes over 7 days (mean [SE])

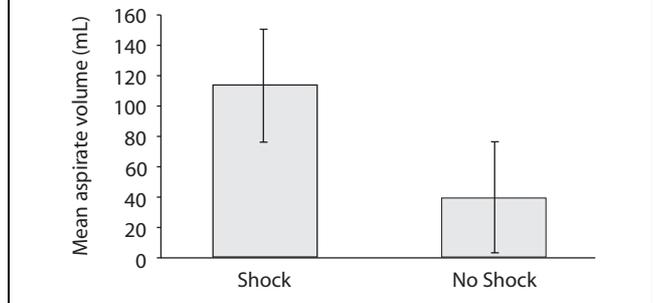
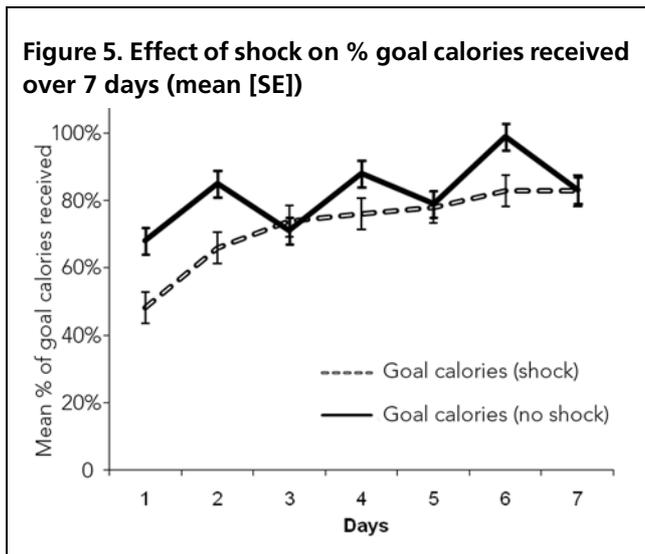


Table 2. Patient diagnostic groups

Diagnosis	Number (%) of patients (n = 43)
Pneumonia	23 (54%)
Skin and soft tissue infection	7 (16%)
Urosepsis	6 (14%)
Other*	7 (16%)

* Included one patient each with meningitis, septic arthritis, biliary sepsis, infected pancreatic necrosis, febrile neutropenia, bacteraemia, disseminated varicella.



between patients with shock and those without shock ($P=0.8$). Within patients, prokinetic use was weakly associated with improved enteral nutritional goals ($r=0.15$; $P=0.02$).

Noradrenaline was the most commonly used inotrope/vasopressor, with a mean (SD) requirement of 8.1 (3.3) mg per 24 hours. Adrenaline use was only noted in the first 48 hours, with a mean (SD) requirement of 1.4 (0.6) mg per 24 hours. Patients who had a higher percentage of days on inotropes had a tendency to have larger aspirate volumes ($r=0.26$; $P=0.09$) and reduced total kcal goals ($r=-0.29$; $P=0.06$).

Discussion

Our results suggest that septic shock is associated with delayed gastric emptying, as indicated by larger gastric residual volumes. However, it appears that EN can be administered to patients with or without shock.

Several factors related to critical illness have been reported to be associated with gastric dysmotility and feed intolerance, including mechanical ventilation, sedatives, opioids,⁸ cytokine release, and splanchnic hypoperfusion due to shock and sepsis.^{5,11-13} Admission diagnoses, including sepsis, are believed to influence the incidence of delayed gastric emptying and subsequent feed intolerance.¹⁴ Cellular mechanisms of sepsis-induced gastrointestinal dysfunction remain enigmatic. Animal studies suggest that cytokines (IL1, TNF- α),¹⁵ inducible nitric oxide synthase¹⁶ and septic mediators such as lipopolysaccharide^{17,18} may be responsible for delayed intestinal transit. High concentrations of circulating catecholamines, either endogenous or exogenous, are common in critically ill patients and may adversely affect gastroduodenal motility in this population.¹⁹⁻²¹

EN is often cautiously prescribed to patients with shock, in the belief that EN increases splanchnic metabolic demands,

which may lead to oxygen and/or energy mismatch when the gut is hypoperfused. It is thought that the presence of luminal contents increases gut blood flow, a phenomenon termed postprandial hyperaemia.²² Absorptive processes in the hypoperfused gut may overwhelm the limits of cellular metabolism and cause cellular ischaemia. Feeding guidelines are unclear about the timing of initiation of EN in patients with shock. American and European guidelines suggest that in the setting of haemodynamic compromise, EN should be withheld until the patient is fully resuscitated and/or stable.^{3,23} Recent Australian and New Zealand guidelines do not mention haemodynamic instability as a contraindication to early enteral feeding.¹ There is no doubt that, in shock, resuscitation takes precedence over other intensive care issues. However, the early initiation of EN may preserve mechanical and immunological gut barrier function, stimulating intestinal trophism and reducing bacterial translocation and the incidence of sepsis and multisystem failure.²⁴ Few studies have evaluated the safety of EN in patients with septic shock. Previous studies have shown that, while EN is possible for most patients with cardiogenic shock and severe haemodynamic failure, nutritional goals are rarely attained.^{25,26}

Current sepsis guidelines support aggressive resuscitation in patients with septic shock. Aggressive resuscitation to achieve near-normal haemodynamic goals may be associated with better splanchnic perfusion and feed tolerance. Early and successful resuscitation may explain the success of early feeding of the patients with shock reported in our study, despite the known effects of catecholamines on gastrointestinal motility. Interestingly, although shocked patients had significantly larger aspirate volumes in our study, this was not associated with increased prokinetic use or decreased success of feeding. Our results suggest that gastrointestinal motility is not affected by haemodynamic state alone and that reduced motility may be multifactorial. Our results also suggest that it is safe to initiate protocol-based EN in patients with shock after adequate resuscitation, even if they continue to require inotropic/vasoactive support.

An important finding of our study was the amount of calories provided by propofol and the attendant overfeeding in certain patients. Propofol provides around 1.1 kcal/mL as lipid.²⁷ Hypocaloric feeding has been proposed as beneficial to critically ill patients.²⁸ Although there is a lack of data from well designed, large, randomised controlled trials to support hypocaloric feeding, overfeeding critically ill patients certainly has been shown to worsen clinical outcomes.²⁹ Propofol doses need to be considered in the calculation of daily nutritional goals, especially when high doses are being given. Failure to do so creates significant risk of overfeeding patients.

Our study is limited by shortcomings that are often associated with retrospective studies. It is possible that some patients with sepsis were not included in the study because of

the method of patient identification. In addition, the study population was small and quite specific and hence the results cannot be generalised to all critically ill patients. Also, the best method of clinically identifying delayed gastric emptying and feed intolerance is uncertain. In view of the retrospective nature of the study, we were limited to using gastric residual volume as a surrogate marker for gastric emptying. An appropriately powered, prospective study randomising patients with septic shock to early or delayed initiation of enteral feeding is needed to confirm the safety of this practice in haemodynamically unstable ventilated patients.

Conclusion

Despite delayed gastric emptying, protocol-directed enteral feeding can be considered in patients with septic shock.

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References

- Doig G, Simpson F, Finfer S, et al. Effect of evidence-based feeding guidelines on mortality in critically ill adults – a cluster randomized controlled trial. *JAMA* 2008; 300: 2731-41.
- Doig G, Heighes P, Simpson F, et al. Early enteral nutrition, provided within 24h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomized controlled trials. *Intensive Care Med* 2009; 35: 2018-27.
- McClave S, Martindale R, Vanek V, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *JPEN* 2009; 33: 277-316.
- Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. *Crit Care Med* 2001; 29: 2264-70.
- Mentec H, Dupont H, Bocchetti M, et al. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med* 2001; 29: 1955-61.
- Deane A, Fraser R, Chapman M. Prokinetic drugs for feed intolerance in critical illness: current and potential therapies. *Crit Care Resusc* 2009; 11: 132-43.
- Cahill NE, Dhaliwal R, Day A, et al. Nutritional therapy in the critical care setting: what is "best achievable" practice? An international multicenter observational study. *Crit Care Med* 2010; 38: 395-401.
- Nguyen NQ, Chapman MJ, Holloway RH, et al. The effects of sedation on gastric emptying and intra-gastric meal distribution in critical illness. *Intensive Care Med* 2008; 34: 454-60.
- American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Crit Care Med* 1992; 20: 864-74.
- Bland MJ, Altman DG. Calculating correlation coefficients with repeated observations. Part 1 – correlation within subjects. *BMJ* 1995; 310: 446.
- Multu G, Multu E, Factor P. Gastrointestinal complications in patients receiving mechanical ventilation. *Chest* 2001; 119: 1222-41.
- Heyland DK, Tougas G, King D, Cook DJ. Impaired gastric emptying in mechanically ventilated, critically ill patients. *Intensive Care Med* 1996; 22: 1339-44.
- Glatzle J, Leutenegger CM, Mueller MH, et al. Mesenteric lymph collected during peritonitis or sepsis potentially inhibits gastric motility in rats. *J Gastrointest Surg* 2004; 8: 645-52.
- Nguyen NQ, Ng MP, Chapman M, et al. The impact of admission diagnosis on gastric emptying in critically ill patients. *Crit Care* 2007; 11: R16.
- Lodato R, Khan A, Zembowicz M, et al. Roles of IL-1 and TNF in the decreased ileal muscle contractility induced by lipopolysaccharide. *Am J Physiol* 1999; 276: G1356-62.
- Cullen JJ, Mercer D, Hinkhouse M, et al. Effects of endotoxin on regulation of intestinal smooth muscle nitric oxide synthase and intestinal transit. *Surgery* 1999; 125: 339-44.
- Eskandari MK, Kalff JC, Billiar TR, et al. LPS-induced muscularis macrophage nitric oxide suppresses rat jejunal circular muscle activity. *Am J Physiol Gastrointest Liver Physiol* 1999; 277: G478-86.
- Hurwitz A, Furtado D, Low RR. The effects of endotoxemia and bacteremia on gastrointestinal drug absorption in mice and rats. *J Pharmacol Exp Ther* 1975; 192: 236-41.
- Levein NG, Thörn SE, Wattwil M. Dopamine delays gastric emptying and prolongs oro-caecal transit time in volunteers. *Eur J Anaesthesiol* 1999; 16: 246-50.
- Stanghellini V, Malagelada JR, Zinsmeister AR, et al. Stress-induced gastroduodenal motor disturbances in humans: possible humoral mechanisms. *Gastroenterology* 1983; 85: 83-91.
- Barnert J, Goebel J, Neeser G, et al. High doses of catecholamines diminish the effect of erythromycin on antral motility and gastric emptying in intensive care unit patients. In: Herbert MK, Holzer P, Roewer N, editors. Problems of the gastrointestinal tract in anesthesia, the perioperative period, and intensive care. New York: Springer Verlag, 1999: 83-7.
- Jeays A, Lawford P, Gillott R, et al. A framework for the modeling of gut blood flow regulation and postprandial hyperaemia. *World J Gastroenterol* 2007; 13: 1393-8.
- Kreymann K, Berger M, Deutz N, et al. ESPEN guidelines on enteral nutrition: intensive care. *Clin Nutr* 2006; 25: 210-23.
- Hadfield RJ, Sinclair DG, Houldsworth PE, Evans TW. Effects of enteral and parenteral nutrition on gut mucosal permeability in the critically ill. *Am J Respir Crit Care Med* 1995; 152: 1545-8.
- Revelly JP, Tappy L, Berger MM, et al. Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. *Intensive Care Med* 2001; 27: 540-7.
- Berger MM, Revelly JP, Cayeux MC, Chioloro RL. Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. *Clin Nutr* 2005; 24: 124-32.
- DeChicco R, Matarese L, Hummel AC, et al. Contribution of calories from propofol to total energy intake. *J Am Diet Assoc* 1995; 95 (9 Suppl): A25.
- Casadei E, Scolletta S, Franchi F, et al. Effects of hypocaloric feeding on clinical outcome in ICU patients. *Crit Care* 2006; 10 Suppl 1: P217.
- Krishnan J, Parce P, Martinez A, et al. Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes. *Chest* 2003; 124: 297-305. □