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Provision of Enteral Nutrition During Vasopressor Therapy for Hemodynamic Instability: An Evidence-Based Review

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Abstract

Critical illness is associated with many complications that affect both medical and nutrition aspects of patient outcomes. Early enteral feeding is the preferred method of nutrition for patients in the intensive care unit due to apparent benefits in this patient population. However, these patients are also at risk for complications related to enteral nutrition (EN), which may be potentiated with the addition of vasopressors often used in the setting of hemodynamic instability. The clinician is often confronted with the decision of when to proceed with EN in critically ill patients who require vasopressors for hemodynamic support. This article reviews the effects of vasopressors on gastrointestinal blood flow, discusses complications associated with vasopressor use during EN, and proposes important considerations to determine the safety of EN in hemodynamically unstable patients requiring vasopressor support. (*Nutr Clin Pract.* 2012;27:521-526)

Keywords

critical illness; enteral nutrition; vasoconstrictor agents

Hemodynamic instability is often present in critically ill patients. Critical illness, which for the purpose of this review can be defined as any patient admitted to an intensive care unit (ICU), may adversely affect functionality of the gut. Impaired organ function can occur by way of decreased gastrointestinal (GI) motility secondary to sepsis and hypotension, placing patients at risk for the rare but serious complication of nonocclusive bowel ischemia.¹ For this reason, the guidelines for nutrition in critically ill patients set forth by the Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) recommend withholding enteral nutrition (EN) until the patient is fully resuscitated.² Early EN is the preferred route of caloric intake for the critically ill patient population as it has been shown to decrease infection rate, hospital length of stay, cost of nutrition support therapy, and mortality.³⁻⁵

Hypotension and sepsis in critically ill patients may warrant the use of vasopressors (eg, dopamine, epinephrine, phenylephrine, norepinephrine, vasopressin) to maintain adequate hemodynamic parameters (ie, mean arterial pressure [MAP] ≥ 65 mm Hg).⁶ Because splanchnic blood flow is highly dependent on cardiac output, hemodynamic changes and the redistribution of blood flow that occur during sepsis can significantly alter perfusion to this area of the body. Within the gut, the small intestine receives the most blood flow to supply enough O₂ (oxygen) to the mucosal region, which is highly vascularized due to the presence of microvilli. Here, in the dense capillary network responsible for absorption of nutrients and O₂ exchange, is where reduction of blood flow from sepsis or hypotension may lead to mucosal ischemia. Vasoconstriction from the addition of vasopressors may potentiate the changes

in splanchnic perfusion and oxygenation that occur during sepsis, potentially leading to further mucosal ischemia. Although in most circumstances, low-dose catecholamine infusions (eg, a dopamine infusion of 5 $\mu\text{g}/\text{kg}/\text{min}$) are thought to pose a relatively low risk of complications during enteral feeding, there has been little in the way of evidence to provide a definitive recommendation on how to safely manage this common clinical scenario. This article reviews the effects of vasopressors on GI blood flow, discusses complications associated with vasopressor use during EN, and proposes important considerations to determine the safety of EN in hemodynamically unstable patients requiring vasopressor support.

Effects of Vasopressors on GI Motility and Perfusion

All vasopressors produce vasoconstriction, and therefore each agent has the potential to affect GI motility and perfusion. The guidelines for severe sepsis and septic shock recommend norepinephrine or dopamine as first-line pressor agents in patients with septic shock.⁶ Although both agents increase MAP, due to its effects on dopaminergic and β -adrenergic

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receptors, dopamine has a greater propensity to increase heart rate, stroke volume, and cardiac output (eg, inotropic properties) than norepinephrine. Epinephrine is recommended for those patients who do not respond to either norepinephrine or dopamine, as its use is thought to be associated with tachycardia and decreased splanchnic perfusion due to effects on both α - and β -adrenergic receptors. Phenylephrine is recommended when pure α -adrenergic activity is warranted (eg, to minimize the effects on heart rate). Vasopressin is unique in that its vasoconstricting properties are due to effects on V1 receptors located in blood vessels, but it may also reduce gastric blood flow.^{6,7} Any effect on gut perfusion has the potential to decrease tolerance to EN and indeed becomes clinically relevant to nutrition support.

Dopamine

At low doses (<5 $\mu\text{g}/\text{kg}/\text{min}$), dopamine primarily increases mesenteric perfusion, whereas at higher doses, its vasoconstricting properties are enhanced through α -adrenergic activity. Several studies have demonstrated the GI effects of dopamine, albeit with varying degrees (Table 1).⁸⁻¹⁰ In 1 study, the effects of dopamine on jejunal mucosal perfusion in cardiac surgery (CS) patients were evaluated using laser Doppler flowmetry (LDF), a technique that uses Doppler technology to estimate microvascular perfusion.⁸ Dopamine was administered with doses titrated to achieve a 25% increase in cardiac output (CO) from baseline (mean dose \pm SD, $2.7 \pm 0.2 \mu\text{g}/\text{kg}/\text{min}$). Jejunal mucosal perfusion was increased by 27% in patients receiving dopamine. Another study assessed splanchnic blood flow and O_2 consumption in a mixed population of patients following cardiac surgery or with a diagnosis of sepsis.⁹ Splanchnic blood flow was estimated using the indocyanine green (ICG) dye technique whereby ICG is administered intravenously and subsequent levels of ICG present in arterial and hepatic venous blood samples are used to calculate splanchnic perfusion.¹¹ Oxygen consumption was measured by indirect calorimetry. Dopamine was titrated to achieve a 25% increase in CO from baseline (median dose [range], CS: $4.2 [1.4-8.5] \mu\text{g}/\text{kg}/\text{min}$; sepsis: $4 [2.1-9] \mu\text{g}/\text{kg}/\text{min}$). Investigators found that dopamine produced an increase in splanchnic blood flow in both groups of patients; however, splanchnic O_2 consumption was decreased in patients with sepsis only. The authors concluded that this decrease was due to an impairment of hepatosplanchnic metabolism in patients with sepsis that occurred despite an increase in regional perfusion. The effect of dopamine on gastric perfusion was studied in another group of ICU patients with sepsis.¹⁰ All patients received dopamine at $5 \mu\text{g}/\text{kg}/\text{min}$, and gastric perfusion was evaluated by measuring gastric intramucosal pH and LDF before and after dopamine administration. Oxygen transport was increased with the use of dopamine, but there was a decrease in gastric mucosal blood flow and no change in intramucosal pH. Gastrointestinal manometry was used to

assess the effects of dopamine on migrating motor complexes in a mixed ICU population of hemodynamically stable patients.¹² Dopamine was administered at $4 \mu\text{g}/\text{kg}/\text{min}$, and its effects on GI motility were assessed during fasting and nasogastric feeding conditions. Investigators found that dopamine decreased the number of antral contractions in both fasting and feeding states and concluded that gastroduodenal motility is adversely affected by dopamine in critically ill patients. Tolerance to EN was not a study end point. Although results have varied, it is reasonable to assume that dopamine does not consistently increase splanchnic blood flow, even at low doses.

Epinephrine, Norepinephrine, and Phenylephrine

A number of other studies have evaluated the effects of epinephrine, norepinephrine, and phenylephrine on splanchnic perfusion in critically ill patients (Table 1).¹³⁻¹⁶ Two studies compared epinephrine with the combination of dobutamine and norepinephrine in patients with septic shock.^{13,14} One group of authors measured gastric mucosal blood flow with LDF and hepatic function using ICG clearance.¹³ Eleven patients received epinephrine at 0.3 ± 0.2 (mean \pm SD) $\mu\text{g}/\text{kg}/\text{min}$ and 11 patients received fixed doses of dobutamine at $5 \mu\text{g}/\text{kg}/\text{min}$ plus norepinephrine at 0.9 ± 0.4 (mean \pm SD) $\mu\text{g}/\text{kg}/\text{min}$. In both groups, only the vasopressor agents were titrated to achieve a MAP of 70–80 mm Hg. Although there was no statistically significant difference in MAP, CI, or O_2 transport between groups, epinephrine increased gastric mucosal blood flow to a greater extent than dobutamine-norepinephrine (mean \pm SD, 662 ± 210 vs 546 ± 200 units; $P = .011$). The authors concluded that this difference was probably due to a higher CI induced by epinephrine. Although there was a trend toward higher values for CI in patients who received epinephrine vs dobutamine-norepinephrine (5 ± 1.6 vs $4.2 \pm 1.5 \text{ L}/\text{min}/\text{m}^2$; $P = .68$), the difference in CI was not statistically significant. A second group of authors evaluated splanchnic perfusion with ICG and O_2 transport in 8 patients with septic shock.¹⁴ Patients received either epinephrine (median dose [range], $0.36 [0.13-1] \mu\text{g}/\text{kg}/\text{min}$) or dobutamine plus norepinephrine (median dose [range], $14.7 [8.3-18.1]$ and $0.42 [0.08-0.68] \mu\text{g}/\text{kg}/\text{min}$, respectively). Compared with dobutamine-norepinephrine, epinephrine decreased splanchnic blood flow and O_2 uptake, and thus the authors concluded that epinephrine produced undesirable effects on splanchnic perfusion. In a study comparing the effects of dopamine, norepinephrine, and epinephrine on splanchnic circulation in patients with septic shock, ICG was used to determine hepatosplanchnic blood flow, and gas tonometry was used to measure gastric mucosal pCO_2 .¹⁵ Patients received dopamine during the first phase of the study. Dopamine was replaced by either norepinephrine and then epinephrine or vice versa during the second study phase. Vasopressor doses were titrated to maintain MAP ≥ 65 mm Hg. In patients with moderate shock,

Table 1. Clinical Trials of Vasopressor Effects on Gastric Perfusion in Critically Ill Patients

Study Design	No. of Patients	Diagnosis	Treatment Groups	Outcome
Prospective, randomized ⁸	10	CS	Dopamine vs dopexamine vs dobutamine ^a	↑ in jejunal mucosal perfusion by 27%, 20%, and 7%, respectively
Prospective, observational ⁹	20	Mixed: CS and sepsis	Dopamine	↑ in splanchnic blood flow by 34% and 23% in CS and septic patients, respectively; ↑ in splanchnic O ₂ consumption in CS and ↓ in septic patients
Prospective, randomized ¹¹	10	Sepsis	Dopamine vs dobutamine	↑ in O ₂ transport with both agents; ↓ in gastric mucosal blood flow but no change in gastric tonometered pCO ₂ , gastric-arterial pCO ₂ difference, and intramucosal pH for dopamine; ↑ in gastric mucosal blood flow, ↓ in gastric tonometered pCO ₂ and gastric-arterial pCO ₂ difference, and ↑ in intramucosal pH for dobutamine
Prospective, randomized ¹²	12	Mixed: trauma, surgery, medical	Dopamine vs placebo	↓ in number of antral contractions overall for dopamine; ↑ in phase III duodenal contractions during fasting and feeding for dopamine
Prospective, randomized ¹³	22	Septic shock	Epinephrine vs dobutamine + norepinephrine	↑ in gastric mucosal blood flow from epinephrine compared with dobutamine + norepinephrine
Prospective, controlled ¹⁴	8	Septic shock	Epinephrine vs dobutamine + norepinephrine	↓ in splanchnic blood flow, O ₂ uptake, mucosal pH and ↑ in hepatic vein lactate with epinephrine compared with dobutamine + norepinephrine
Prospective, randomized ¹⁵	20	Septic shock	Dopamine vs norepinephrine vs epinephrine	↑ in CI but ↓ in splanchnic blood flow with epinephrine in patients with severe septic shock
Prospective, randomized ¹⁶	10	CS	Norepinephrine vs phenylephrine	↑ in splanchnic O ₂ extraction and venous-hepatic vein O ₂ saturation with phenylephrine > norepinephrine; jejunal mucosal perfusion was not affected by either vasopressor
Prospective, open label ¹⁷	8	CS	Vasopressin	↓ in jejunal mucosal perfusion with increasing infusion rates of vasopressin
Prospective, open label ¹⁸	12	Severe sepsis	Vasopressin	No change in splanchnic blood flow; ↑ in gastric mucosal pCO ₂ gap

CI, cardiac index; CS, cardiac surgery, O₂, oxygen.

^aDopexamine and dobutamine are inotropic agents.

epinephrine produced a greater CI than dopamine or norepinephrine, but splanchnic blood flow was similar among all vasopressors. In severe shock, CI was higher with epinephrine vs norepinephrine, but splanchnic blood flow was lower, suggesting that epinephrine impairs splanchnic perfusion in severe septic shock. Other investigators compared the effects of norepinephrine with phenylephrine on intestinal mucosal perfusion in CS patients.¹⁶ LDF and gas tonometry were used to evaluate jejunal mucosal perfusion and the gastric-arterial pCO₂ gradient, respectively. Norepinephrine was infused at 0.052 ± 0.009 (mean \pm SD) $\mu\text{g}/\text{kg}/\text{min}$ or phenylephrine was infused at 0.5 ± 0.22 (mean \pm SD) $\mu\text{g}/\text{kg}/\text{min}$ to maintain MAP ≥ 90 mm Hg. Although both agents produced similar hemodynamic parameters, splanchnic oxygen extraction and increases in arterial lactate levels were greater with phenylephrine. However, jejunal mucosal perfusion was not significantly

affected by either agent. In summary, epinephrine has demonstrated inconsistent effects on splanchnic blood flow in patients with septic shock, but most studies suggest epinephrine reduces blood flow to the gut. Most available data evaluating the effects of norepinephrine on gastric perfusion are confounded by the use of dobutamine in the study population. The vasoconstricting effect of norepinephrine is likely counterbalanced by the increase in cardiac output, and therefore an increase in splanchnic blood flow, produced by dobutamine. Furthermore, the actual effects of norepinephrine on splanchnic blood flow compared with a control or placebo were not described in most studies. Very few data are available describing the effect of phenylephrine on splanchnic blood flow, but changes in O₂ extraction with the addition of phenylephrine suggest the presence of splanchnic vasoconstriction despite no measureable difference in mucosal perfusion.

Vasopressin

Two studies have evaluated the impact of vasopressin on gastric mucosal perfusion in critically ill patients.^{17,18} In a study of 8 patients post-CS, investigators evaluated intestinal mucosal perfusion using LDF while vasopressin was infused at 1.2, 2.4, and 4.8 U/h.¹⁷ In addition, all study patients received dopamine or milrinone plus norepinephrine to maintain MAP 70–80 mm Hg. Jejunal mucosal perfusion was significantly decreased and the arterial–gastric mucosal pCO₂ gradient was significantly increased with incremental doses of vasopressin. In a pilot study of 12 patients with severe sepsis, 0.04 U/kg/h vasopressin was infused while hepatosplanchnic blood flow was assessed using the ICG technique.¹⁸ All study patients received dobutamine at a constant rate of 2–6 µg/kg/min and norepinephrine titrated to maintain MAP ≥70 mm Hg. Hepatosplanchnic blood flow was unchanged, but the gastric mucosal P_{CO₂} gap increased significantly. Therefore, both of the studies available that have evaluated the effect of vasopressin on splanchnic blood flow in critically ill patients suggest its potential for impairment of gastric perfusion.

Ultimately, the effects of vasopressors on hemodynamics and GI perfusion vary widely among studies. Although these results do not provide definitive evidence that vasopressors adversely affect gastric blood flow, none of the aforementioned studies address the dilemma of whether it is safe to provide EN to patients receiving vasopressors.

Complications Associated With Concomitant EN and Vasopressors

One of the most serious complications from EN is nonocclusive bowel necrosis, which has been described in a number of case reports and retrospective reviews.^{19–28} Risk factors are somewhat unclear, but most documented cases have occurred with jejunal tube feedings at an incidence of 0.29%–1.14%.^{19,20,22–27} Two cases of bowel necrosis have been described with duodenal tube feedings, and 1 case of colonic ischemia and perforation has been described in a patient receiving EN through an ileal tube.^{21,28} Although it is suggested that providing EN during hemodynamic instability should be avoided as it may increase the likelihood of such complications, none of the authors reported hemodynamic instability or pressor use in these patients at the time EN was initiated.²

One group of investigators, however, has described intestinal obstruction with the concomitant use of EN and vasopressors in burn trauma patients.²⁹ Although 4 patients who experienced obstruction secondary to EN were identified in this retrospective review, 3 of the 4 patients actually received pressors for hemodynamic instability and sepsis at the same time EN was administered. All 3 patients were fed via nasogastric tube feedings with a fiber-supplemented enteral formula

after initial resuscitation was complete. Bowel necrosis occurred between posttrauma days 11–14 and was subsequently treated with laparotomy in all cases. The authors concluded that these cases of bowel necrosis resulted from delivery of fiber-containing EN in the presence of GI dysmotility due to critical illness and vasopressors. Thus, small bowel necrosis has been described during EN, particularly with jejunal tube feeding, but there is very little documentation regarding an association between concomitant use of vasopressors for hemodynamic instability and EN leading to such a complication.

More common and better documented is the risk for feeding intolerance associated with the use of vasopressors. In a prospective, observational study of a patients in a medical/surgical ICU receiving EN via nasogastric tube feedings, investigators evaluated intolerance to EN and associated complications.³⁰ Forty-six percent of patients experienced upper digestive intolerance, defined as 2 consecutive gastric aspirate volume (GAV) measurements between 150 and 500 mL, 1 GAV measurement >500 mL, or when vomiting occurred. Intolerance was usually present within the first 48 hours of EN initiation. Risk factors included GAV >20 mL before initiation of EN (odds ratio [confidence interval], 2.16 [1.11–4.18]; *P* = .02), sedation during EN (1.78 [1.17–2.71]; *P* = .007), and catecholamine administration during EN (1.81 [1.21–2.70]; *P* = .004). Patients who experienced upper digestive intolerance had a lower mean caloric intake vs those who did not experience intolerance (15 ± 8 vs 20 ± 8 kcal/kg/d; *P* = .0005). Feeding intolerance was associated with the development of pneumonia, longer length of stay in the ICU, and greater risk for ICU mortality. Another group of investigators performed a prospective study of critically ill patients receiving EN after cardiopulmonary bypass.³¹ During most of the study period, patients received EN via gastric tube feedings; however, patients were fed via jejunal feedings for a small percentage of the study duration (49% vs 13% artificial feeding days, respectively). Patients were fed orally or intravenously for the remaining study period. Most patients received inotropic agents (eg, dopamine or dobutamine) and vasopressors (eg, epinephrine or norepinephrine), with the majority of patients receiving a combination of dobutamine plus norepinephrine. Multiple linear regression analysis revealed that dopamine and norepinephrine were associated with a significantly lower amount of EN delivery per day than other vasoactive agents (*F* ratio = 4.69, *P* = .03 and 8.96, *P* = .003, respectively). Tolerance to EN was not a study end point and was not evaluated in relation to use of vasopressors. In a retrospective study of medical ICU patients who required vasopressors for hemodynamic instability, investigators compared outcomes between patients who received EN within 48 hours and those who did not.³² Lower ICU and hospital mortality were associated with early EN vs late EN (% of patients, 22.5% vs 28.3%, *P* = .03 and 33.8% vs 43.9%, *P* < .001, respectively). No data were provided regarding route of EN, specific vasopressor agents used, or markers for EN tolerance.

Although this study was not designed to assess complications associated with concomitant use of EN and vasopressors, it does provide some evidence that initiation of early EN may be beneficial in this patient population. Specifically, the results suggest that the mortality benefit of early EN may outweigh the risk of potential complications arising from the use of EN in the setting of vasopressor use in medical ICU patients.

Considerations for Initiation of EN in Patients Receiving Vasopressors

Type and Dose of Vasoactive Drug

The use of inotropic agents (eg, dobutamine, dopexamine, milrinone) should not dissuade the clinician from initiating EN in a patient with no other contraindications to enteral feeding. Because these agents increase CI, perfusion to the gut is increased, and complications with EN are unlikely as long as they are not used in combination with any vasopressors. Although dopamine should theoretically have little to no negative effects on gastric blood flow at low doses, study results have varied, and the dose-dependent effects of dopamine are inconsistent. For this reason, a conservative approach should be taken with dopamine, and it should be categorized with other vasopressors with regard to effects on GI perfusion. Although there is a theoretical difference in the effects of each vasopressor on splanchnic perfusion based on their varying mechanisms of action, study results are quite variable, and no firm differences among their effects can be concluded.

Route of EN

Most reports of bowel necrosis have been described in patients receiving EN via surgically placed jejunostomy tubes, regardless of hemodynamic stability or use of vasopressors. Although feeding into the small bowel is usually preferred due to a potentially lower risk of aspiration, alternative routes of administration (eg, gastric or nasogastric tube feedings) may need to be considered in patients at high risk for bowel ischemia. Critically ill patients receiving concomitant EN and vasopressor therapy should be closely monitored for intolerance to EN. An increase in nasogastric output or gastric residual volume (GRV) in addition to any other signs of intolerance with concomitant provision of EN and vasopressor may indicate early signs of gut ischemia.² Many patients in an ICU setting, however, may be fed into the small bowel, in which case routine monitoring of GRV is not recommended.² Because GRV would not be measured routinely in patients receiving postpyloric feeding and most case reports of bowel necrosis have been described in patients with surgically placed jejunostomy tubes, jejunal tube feedings should be avoided in patients requiring vasopressors. If small bowel feeding is provided concomitantly with vasopressors, patients should be

monitored closely for other signs of GI intolerance such as any increased nasogastric output, abdominal pain and/or distention, or constipation. Any signs of worsening hemodynamic instability or inflammatory processes in this scenario should warrant discontinuation of EN and surgical consultation for evaluation of possible small bowel necrosis.

Primary Diagnosis of the Patient

Most cases of bowel necrosis related to EN have been described in surgery, trauma, and burn patients. Special consideration should be given in these patients with regard to whether EN should be initiated in the presence of vasoactive drugs. No cases of bowel necrosis have been described in medical ICU patients without a history of GI surgery, and therefore, these critically ill patients are the least likely to develop this serious complication of EN, especially if gastric tube feeding is chosen. All critically ill patients, however, are at risk for intolerance to EN and a decrease in daily caloric intake, and this risk is increased in the presence of vasopressors.

Conclusion

Intolerance to EN is a common occurrence that warrants close monitoring in critically ill patients. Bowel necrosis is a rare complication that has been most often described in patients receiving EN via the jejunum. Although studies regarding the effects of vasopressors on gut perfusion yield inconsistent results, there have been very few documented cases of concomitant EN and vasopressor use leading to bowel necrosis. Therefore, in the majority of ICU patients, administration of EN into the stomach during the provision of low, stable doses of pressors with close monitoring for signs of intolerance or worsening hemodynamic stability poses very little risk for bowel necrosis. Further consideration should be made in surgical, trauma, or burn patients who require vasopressors for hemodynamic support, especially those with jejunal or nasojejunal access for EN, as these patients seem to be at higher risk for small bowel necrosis related to GI dysmotility and EN.

References

1. McClave SA, Chang WK. Feeding the hypotensive patient: does enteral feeding precipitate or protect against ischemic bowel? *Nutr Clin Pract.* 2003;18:279-284.
2. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult patient: Society for Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr.* 2009;33:277-316.
3. Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding: effects on septic morbidity after blunt and penetrating abdominal trauma. *Ann Surg.* 1992;215:503-513.

4. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P; Canadian Critical Care Clinical Practice Guidelines Committee. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *JPEN J Parenter Enteral Nutr.* 2003;27:355-373.
5. Artinian V, Krayem H, DiGiovine B. Effects of early enteral feeding on the outcome of critically ill mechanically ventilated medical patients. *Chest.* 2006;129:960-967.
6. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008 [published correction appears in *Crit Care Med.* 2008;36:1394-1396]. *Crit Care Med.* 2008;36:296-327.
7. Hollenberg SM. Vasopressor support in septic shock. *Chest.* 2007;132:1678-1687.
8. Thorén A, Elam M, Ricksten SE. Differential effects of dopamine, dopexamine, and dobutamine on jejunal mucosal perfusion early after cardiac surgery. *Crit Care Med.* 2000;28:2338-2343.
9. Jakob SM, Ruokonen E, Takala J. Effects of dopamine on systemic and regional blood flow and metabolism in septic and cardiac surgery patients. *Shock.* 2002;18:8-13.
10. Nevière R, Mathieu D, Chagnon JL, Lebleu N, Wattel F. The contrasting effects of dobutamine and dopamine on gastric mucosal perfusion in septic patients. *Am J Respir Crit Care Med.* 1996;154:1684-1688.
11. Uusaro A, Ruokonen E, Takala J. Estimation of splanchnic blood flow by the Fick principle in man and problems in the use of indocyanine green. *Cardiovasc Res.* 1995;30:106-112.
12. Dive A, Foret F, Jamart J, Bulpa P, Installé E. Effect of dopamine on gastrointestinal motility during critical illness. *Intensive Care Med.* 2000;26:901-907.
13. Seguin P, Bellissant E, Le Tulzo Y, et al. Effects of epinephrine compared with the combination of dobutamine and norepinephrine on gastric perfusion in septic shock. *Clin Pharmacol Ther.* 2002;71:381-388.
14. Meier-Hellmann A, Reinhart K, Bredle DL, Specht M, Spies CD, Hannemann L. Epinephrine impairs splanchnic perfusion in septic shock. *Crit Care Med.* 1997;25:399-404.
15. De Backer D, Creteur J, Silva E, Vincent JL. Effects of dopamine, norepinephrine, and epinephrine on the splanchnic circulation in septic shock: which is best? *Crit Care Med.* 2003;31:1659-1667.
16. Nygren A, Thorén A, Ricksten SE. Vasopressors and intestinal mucosal perfusion after cardiac surgery: norepinephrine vs. phenylephrine. *Crit Care Med.* 2006;34:722-729.
17. Nygren A, Thorén A, Ricksten SE. Vasopressin decreases intestinal mucosal perfusion: a clinical study on cardiac surgery patients in vasodilatory shock. *Acta Anaesthesiol Scand.* 2009;53:581-588.
18. Klinzing S, Simon M, Reinhart K, Meier-Hellman A, Sakr Y. Moderate-dose vasopressin therapy may impair gastric mucosal perfusion in severe sepsis. *Anesthesiology.* 2011;114:1396-1402.
19. Schunn CDG, Daly JM. Small bowel necrosis associated with postoperative jejunal tube feeding. *J Am Coll Surg.* 1995;180:410-416.
20. Lawlor DK, Inculet RI, Malthaner RA. Small-bowel necrosis associated with jejunal tube feeding. *Can J Surg.* 1998;41:459-462.
21. Marvin RG, McKinley BA, McQuiggan M, Cocanour CS, Moore FA. Nonocclusive bowel necrosis occurring in critically ill trauma patients receiving enteral nutrition manifests no reliable clinical signs for early detection. *Am J Surg.* 2000;179:7-12.
22. Munshi IA, Steingrub JS, Wolpert L. Small bowel necrosis associated with early postoperative jejunal tube feeding in a trauma patient. *J Trauma.* 2000;49:163-165.
23. Schloerb PR, Wood JG, Casillan AJ, Tawfik O, Udobi K. Bowel necrosis caused by water in jejunal feeding. *JPEN J Parenter Enteral Nutr.* 2004;28:27-29.
24. Messiner R, Griffen M, Crass R. Small bowel necrosis related to enteral nutrition after duodenal surgery. *Am Surg.* 2005;71:993-995.
25. Melis M, Fichera A, Ferguson MK. Bowel necrosis associated with early jejunal tube feeding: a complication of postoperative enteral nutrition. *Arch Surg.* 2006;141:701-704.
26. Spalding DRC, Behranwala KA, Straker P, Thompson JN, Williamson RCN. Non-occlusive small bowel necrosis in association with feeding jejunostomy after elective upper gastrointestinal surgery. *Ann R Coll Surg Engl.* 2009;91:477-482.
27. Sarap AN, Sarap MD, Childers J. Small bowel necrosis in association with jejunal tube feeding. *JAAPA.* 2010;23:28-32.
28. De Brabandere K, De Waele B, Delvaux G. Colonic ischemia and perforation associated with enteral feeding through an ileal tube. *Nutr Clin Pract.* 2010;25:301-303.
29. Scaife CL, Saffle JR, Morris SE. Intestinal obstruction secondary to enteral feedings in burn trauma patients. *J Trauma.* 1999;47:859-863.
30. Mentec H, Dupont H, Bocchetti M, Cani P, Pnche F, Bleichner G. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med.* 2001; 1955-1961.
31. Berger MM, Revelly JP, Cayeux MC, Chioloro RL. Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. *Clin Nutr.* 2005;24:124-132.
32. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. *Am J Crit Care.* 2010;19:261-268.