

SUMMARY

The objective of this thesis is to gain insight in perioperative conditions and how these can be optimised by nutritional interventions. This is of high importance, since surgery has a major impact on the metabolism of the human body (CHAPTER 1). Reducing the stress of surgery can minimise catabolism, support anabolism throughout surgical treatment, and allow patients to recover substantially better and faster. Reducing malnutrition is an important strategy to minimize stress and to facilitate the recovery of physical function. Accordingly, there are various ways to feed surgical patients, including enteral and parenteral nutrition. Enteral nutrition is the preferred route of feeding over parenteral nutrition for the critically ill patients requiring nutritional support. The composition of enteral nutrition can however, influence the digestion and absorption of nutrients (CHAPTER 2). The tendency of a casein based enteral nutrition to coagulate in the stomach is increasingly acknowledged and new formulas may prevent solidification. The solidification of enteral nutrition by coagulation can cause serious complications, like gastrointestinal obstruction. In CHAPTER 3 literature on the solidification of enteral nutrition is reviewed. Predisposing factors for developing this severe complication are identified and the underlying mechanisms are discussed. Critically ill patients with an impaired digestion (e.g. Whipple surgery) should be considered for alternative enteral nutrition formulas with non-coagulating proteins or hydrolysed proteins. Awareness of risk factors in critically ill patients may help intensivists and surgeons to take appropriate measures to prevent this complication.

It has been suggested that enteral nutrition containing insoluble fibers plays a role in the

solidification and cases of bowel obstruction have been reported in literature. An in vitro study in CHAPTER 4 shows the effect of soluble and insoluble fibers on the coagulation of enteral nutrition. When high concentrations of soy polysaccharide and resistant starch are added to a 100 % casein-based enteral nutrition, the coagulate consists of more water and less proteins, which may lead to an increased protein digestion and absorption in a clinical setting. The suggestion that insoluble fibers increase the risk of gastrointestinal obstruction in critically ill patients is not supported by these data.

Dietary proteins are required to attenuate the loss of muscle mass and to support recovery after surgery. In addition, jejunal feeding is preferred over gastric feeding in patients who are intolerant for gastric feeding. However, the impact of gastric versus jejunal feeding on post-prandial dietary protein digestion and absorption kinetics in vivo in humans was largely unexplored. This was studied by utilizing a randomized cross-over study; eleven healthy young men (21 ± 2 y) were administered 25 g specifically produced intrinsically L-[1- ^{13}C] phenylalanine labeled intact casein via a nasogastric and a nasojejunal tube (CHAPTER 5). It was observed that, jejunal feeding of intact casein is followed by more rapid protein digestion and amino acid absorption when compared with gastric feeding in healthy young men. The greater post-prandial rise in circulating essential amino acids concentrations, may allow a more robust increase in muscle protein synthesis rate following jejunal as opposed to gastric casein feeding.

Surgical patients should be optimally fed before and after surgery to endure surgery and recover from their peak performance. CHAPTER 6 focuses on the endocrine response and how it can be influenced to optimise patient's conditions around surgery, to tolerate food intake as early as possible and to improve gastric emptying. Delayed gastric emptying limits the administration of enteral nutrition leading to severe malnutrition which is associated with higher mortality and morbidity. Currently available prokinetics have limitations in terms of sustained efficacy and side-effects. CHAPTER 7 reviews the available studies on the possible utility of gastrointestinal hormones to prevent or treat delayed gastric emptying in critically ill patients. Manipulation of endogenous secretion, physiological replacement and administration of gastrointestinal hormones in pharmacological doses is likely to have therapeutic potential in the treatment of delayed gastric emptying. We conclude that motilin receptor agonist with non-macrolide properties (ABT-229 and mitemincin GM-611) are currently the most advanced options. However, future clinical trials to evaluate their safety and long-term efficacy are required. Future challenges in this field will include the search for candidates with improved selectivity and favorable kinetic properties.

In CHAPTER 8 the impact of administering enteral nutrition either gastric or jejunal on the endocrine responses in vivo in humans is compared. In a randomized cross-over study, 12 healthy young males (21 ± 2 y) received continuous enteral nutrition containing proteins in a ratio in which it does not coagulate for 12 hours via a nasogastric tube or a nasojejunal tube. Enteral nutrition administered either gastric or jejunal in healthy young males resulted in similar post-prandial plasma amino acid and glucose concentrations. The endocrine response, however, differed substantially, with higher peak plasma CCK, PYY, GLP-1, and GLP-2 concentrations being attained following jejunal feeding. This may result in an improved anabolic response,

greater insulin sensitivity, and an improved intestinotropic effect. Nevertheless, it may also lead to delayed gastric emptying.

Although preoperative fasting is unwanted in all patients, fasting before surgery is still common practice in many Western countries. Presumably, the risk of vomiting and aspiration of acidic gastric content during induction of anaesthetics is the main cause of this omission. Supplementation of clear fluids such as water, tea and coffee, are safe up till 2 h before surgery and it does not increase gastric volume at time of surgery. Overnight fasting has serious consequences for patients' metabolism during and after surgery. It results in depletion of glycogen stores, dehydration, muscle wasting, a weakened immune response and unnecessary production of inflammatory mediators. A carbohydrate (CHO) drink given preoperatively can change the fasted state into a fed state. The ERAS guidelines for perioperative care include preoperative CHO loading and re-establishment of oral feeding as early as possible after surgery. CHAPTER 9 shows the results of an animal study in which an intestinal ischemia reperfusion model was used to investigate whether preoperative CHO loading increases spontaneous postoperative food intake, intestinal barrier function and the catabolic response. Preoperative CHO loading improves food intake, preserves the gastrointestinal function and reduces the catabolic response in an ischemia reperfusion animal model. These findings suggest that preoperative CHO loading preserves the intestinal function in order to accelerate recovery and food intake.

CHAPTER 10 summarises and discusses the main findings of this thesis; focusing on perioperative strategies in the surgical patient. The results of the present thesis show that the composition of enteral nutrition plays a major role in the digestion and absorption of nutrients. Standard enteral nutrition is well tolerated in the majority of patients. Nevertheless, when gastrointestinal function is compromised by surgery, or other trauma, nutritional support has to be provided tailored to patient's individual needs. To reach this goal, future studies are warranted to investigate what kind of protein will be best absorbed either gastric or jejunal and ultimately, will result in optimal muscle protein synthesis in critically ill patients.