

Original Article

Prolonged preoperative fasting and prognosis in critically ill gastrointestinal surgery patients

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Background and Objectives: This study aimed to assess the influence of prolonged preoperative fasting on prognosis in elective surgery. **Methods and Study Design:** A retrospective, controlled study involving patients admitted to our surgical intensive care unit who underwent a gastrointestinal operation under general anesthesia. Patients were divided into regular preoperative fasting time (n=57) and prolonged preoperative fasting time (n=73) groups. Clinical data were collected including patients' demographics, intraoperative and postoperative operation time, volume of blood loss, intensive care unit stay, hospital stay, postoperative complications and other factors. **Results:** Patients in the regular preoperative fasting time group had less duration of mechanical ventilation support after surgery [245 (177, 450) min vs 315 (210, 812) min ($p=0.021$)] and the postoperative myocardial injuries (myocardial injury 2 cases vs 11 cases, $p=0.038$) and reoperation percentages (reoperation 0 cases vs 7 cases, $p=0.044$) were lower compared to the prolonged preoperative fasting time group. In addition, patients in the regular preoperative fasting time group presented with a significantly shorter period of postoperative fasting time [6.0 (5.0, 8.0) vs 8.0 (6.0, 13.0), $p=0.005$]. **Conclusions:** Prolonged preoperative fasting time led to unfavorable outcomes after gastrointestinal operations. Thus, reducing preoperative fasting time is likely to accelerate postoperative recovery in gastrointestinal surgery patients.

Key Words: fasting, gastrointestinal surgery, elective surgery, myocardial injury, reoperation

INTRODUCTION

A prolonged preoperative fasting time is a very common phenomenon in surgical patients, due to the unpredictable nature of operating room scheduling and unavoidable delays.¹ However, prolonged periods of fasting are unnecessary and may cause postoperative complications in elective surgeries.² The metabolic response to long fasting times leads to intensification of the organic response occurring after trauma, which is mainly manifested as increased insulin resistance, an acute-phase response, and may contribute negatively to postoperative recovery.³ A prolonged fasting period increases inflammatory responses and exacerbates insulin resistance, muscle proteolysis and lipolysis,⁴⁻⁶ which are mediated by the release of cytokines and contra-regulatory hormones. Peripheral insulin resistance may produce hyperglycemia, which is highly associated with the length of hospital stay⁷⁻⁹ and postoperative complications.^{10,11} In the surgical intensive care unit (ICU), intensive insulin therapy to maintain blood glucose below 110 mg/dL and to inhibit the metabolic response can reduce morbidity and mortality among critically ill patients.¹¹

The American Society of Anesthesiologists (ASA) recommends a minimum fasting period of 2 h for clear liquids before surgery.² Many studies have demonstrated that it is safe to reduce the preoperative fasting time with

a carbohydrate-rich drink up to 2 h before surgery.¹² Benefits related to this shorter preoperative fasting include a reduction of postoperative gastrointestinal discomfort, insulin resistance and organic responses to surgical trauma.⁹ Additionally, this clinical practice reduces hospitalization time and accelerates postoperative recovery.^{8,13,14}

In this retrospective controlled study, we evaluated the influences of prolonged preoperative fasting time on surgical complications and intraoperative indexes such as postoperative infections, increased length of ICU stay, organ failure or injury, to determine whether prolonged preoperative fasting time increased mortality and morbidity among patients admitted to the ICU after gastrointestinal surgery.

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METHODS

Study population

All patients received elective surgery of the gastrointestinal tract and mechanical ventilation. They were admitted to our ICU between June 1, 2017 and December 31, 2017 to the Peking University People's Hospital. The patients were older than 18 years, and were divided into 2 groups. Patients in the regular preoperative fasting time (RPFT) group were subjected to regular fasting times starting at 10 pm of the previous night. Patients in the prolonged preoperative fasting time (PPFT) group received prolonged fasting times because the surgical procedures were performed at noon or the afternoon. For the patients with prolonged preoperative fasting, preoperative fluid could be substituted parenterally, but drinking was strictly prohibited. General anesthesia was used in both groups of patients. The study was approved by the ethical committee of the Peking University People's Hospital.

Data collection

Clinical data were collected from the medical records of all patients in the study. All surgeries were electively scheduled. Basic demographic and clinical information about the cohort of patients is summarized. Preoperative clinical data such as comorbidities (diabetes mellitus, hypertension and cardiovascular diseases), diagnosis (malignant or benign), previous gastrointestinal surgery, ASA level, surgical technique (conventional or laparoscopic) were collected. But emergency and palliative surgery was excluded from this study.

In addition, the volume of blood loss, surgery time were recorded during operation, and then postoperative complications associated surgery (surgical wound infection, anastomotic dehiscence, abdominal abscess, readmission into ICU, reoperation, Acute Kidney Injury (AKI), myocardial injury or others) after operation including ICU stay were also collected. Postoperative fasting time was quantified in days (postoperative day (POD)). POD was calculated from the day of surgery to the day received the first meal (oral or enteral). The hospital stay was calculated in days from the date of admission to hospital until patient discharge. The clinical result was classified as either patient discharge from the hospital or death. The duration of mechanical ventilation support was calculated in minutes from the time admitted

into ICU to the time weaned from mechanical ventilation. Acute Physiology And Chronic Health Evaluation (APACHE) II is a severity-of-disease classification system,¹⁵ which in this study was used to measure the patients disease status when patients were admitted into ICU after surgery.

Outcome measures

The primary outcome measure was the mortality from any cause during ICU or hospital. The secondary outcome measures included duration of ICU stay, number of readmission to ICU, duration of mechanical ventilation support, perioperative transfusion requirements, renal replacement therapy and complications after surgery.

Statistical analysis

SPSS 19.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Measurement data following a normal distribution is represented as mean \pm standard deviation. Inter-group comparisons were used with a t-test. Data not following a normal distribution are shown as the median (P25, P75), and a Wilcoxon rank sum test was employed to make inter-group comparisons. A χ^2 test was used for comparison between counting variables. While comparing groups for outcomes of interest, the differences in mean or median with the 95% CI around the differences. OR with the 95% CI around the risk ratio. A p -value <0.05 was considered as a significant result.

RESULTS

Basic characteristic and information of enrolled patients

A total of 130 patients were recruited into the present study and the main disease in both groups was malignancy, with most patients having a hypertension history (RPFT 50.9%, PPFT 43.8%). There was no significant difference in age, gender, preexisting cardiovascular disease, diabetes, benign and malignant disease, or surgery procedures as well as other disease history between the 2 groups (Table 1), which implied that these 2 groups were comparable.

Comparison of intraoperative data between two groups

Data collected during the surgery was not significantly difference, in terms of surgery time, blood loss and blood

Table 1. The demographic characteristics of patients

	RPFT group (n=57)	PPFT group (n=73)
Male [n (%)]	36 (63.2)	38 (52.1)
Age (year, mean \pm SD)	73 \pm 10	71 \pm 11
ASA level [n (%)]		
I	1 (1.8)	4 (5.5)
II	29 (50.9)	39 (53.4)
III	26 (45.6)	30 (41.1)
IV	1 (1.8)	0 (0)
History of hypertension [n (%)]	29 (50.9)	32 (43.8)
History of abdominal surgery [n (%)]	3 (5.3)	8 (11.0)
History of diabetes [n (%)]	18 (31.6)	21 (28.8)
History of cardiovascular diseases [n (%)]	22 (38.6)	17 (23.3)
Malignant [n (%)]	56 (98.2)	67 (91.8)
Laparoscopic procedure [n (%)]	19 (33.3)	28 (38.4)

ASA: American society of anesthesiologists; PPFT: prolonged preoperative fasting time; RPFT: regular preoperative fasting time.

transfusion during operation, between the two groups of patients (Table 2). The scores of APACHE were evaluated also similar in the two groups when patients were admitted into ICU after surgery, which suggest prolonged preoperative fasting time did not interfere the surgery time and blood losing volume and other acute physiology and chronic health patient indices.

Comparison of primary outcome between two groups

After surgery, 1 patient (1.8%) in the RPFT group and 1 patient (1.4%) in the PPFT group died, indicating no apparent difference between the 2 groups of patients.

Comparison of secondary outcomes and adverse events between two groups

In this study, the RPFT group presented with lower durations of mechanical ventilation support than the PPFT group, which was a statistically significant difference (245 (177, 450) min vs 315 (210, 812) ($p=0.021$)). The incidence of myocardial injury, reoperation and pulmonary infiltration after surgery were remarkably lower in the RPFT group compared to the PPFT group (myocardial injury, 3.5% vs 15.1%, $p=0.038$; reoperation, 0% vs 9.6%, $p=0.044$, pulmonary infiltration 7% vs 19.2%, $p=0.046$, respectively). In addition, compared to the PPFT group, a significant shortened period in postoperative fasting time was found in the RPFT group of patients ($p=0.005$).

However, the period of time spent in the ICU or hospital wards were not statistically difference between the 2 groups. The incidence of readmission to ICU, AKI, intestinal obstruction, pneumonia, intestinal leakage, bleeding/infection of abdominal cavity were not significantly different between the 2 groups (Table 3).

DISCUSSION

Surgery is inevitably a type of trauma to the human body and often produces changes in inflammatory cytokine formation and immune system responses. A prolonged fasting time before surgery is very common in surgical wards due to many unavoidable reasons, such as operating room schedule changes.¹ Recently, studies have shown that the extension of preoperative fasting time before surgery increases the inflammatory response and insulin resistance, contributing negatively to postoperative recovery.³⁻⁶ The underlying immunological mechanisms associated with trauma and major surgery infections were short-term hyperglycemia and hyperinsulinemia, which correlated well with complications due to infection and mortality.¹⁶ Hence, all these adverse effects during elective surgery should be avoided to decrease the mortality and morbidity of patients, although in this study, there is no significant difference on the mortality rate.

But the effect of preoperative fasting time on different types of surgery has been widely investigated during the last two decades (Table 4). Overnight fasting or pro-

Table 2. Clinical analyses during surgery

	RPFT group (n=57)	PPFT group (n=73)	U, χ^2	p-value	95% CI
Surgery time [min, M (P ₂₅ , P ₇₅)]	310 (267, 382)	320 (255, 405)	-0.031	0.976	(0.918, 0.990)
Volume of blood loss [mL, M (P ₂₅ , P ₇₅)]	100 (50, 200)	100 (50, 300)	-1.019	0.308	(0.214, 0.374)
APACHE II scores admitted to ICU after surgery	16 (15, 18)	17 (16, 17)	-1.374	0.169	(0.085, 0.207)

APACHE II: Acute Physiology and Chronic Health Evaluation; ICU: intensive care unit; PPFT: prolonged preoperative fasting time; RPFT: regular preoperative fasting time.

Table 3. Secondary outcome and adverse events evaluations of the two groups after surgery

	RPFT group (n=57)	PPFT group (n=73)	U, χ^2	p-value	OR	95% CI
ICU stay [d, M (P ₂₅ , P ₇₅)]	1.0 (1.0, 1.0)	1.0 (1.0, 1.0)	-0.359	0.719	-	(0.663, 0.814)
Duration of mechanical ventilation support [min, M (P ₂₅ , P ₇₅)]	245 (177, 450)	315 (210, 812)	-2.313	0.021	-	(0.000, 0.037)
Readmission to ICU [n, (%)]	1 (1.8)	7 (9.6)	2.181	0.14	0.168	(0.020, 1.410)
Hospital stay [d, M (P ₂₅ , P ₇₅)]	21 (17, 24)	21 (17, 30)	-0.729	0.466	-	(0.429, 0.601)
POD to first oral or enteral intake [d, M (P ₂₅ , P ₇₅)]	6.0 (5.0, 8.0)	8.0 (6.0, 13.0)	-2.798	0.005	-	(0.000, 0.023)
AKI [n (%)]	1 (1.8)	4 (5.5)	0.405	0.525	0.308	(0.033, 2.835)
Pneumonia [n (%)]	3 (4.1)	6 (8.1)	0.097	0.756	0.620	(0.148, 2.596)
Myocardial injury [n (%)]	2 (3.5)	11 (15.1)	3.555	0.038	0.205	(0.044, 0.965)
Reoperation [n (%)]	0 (0)	7 (9.6)	4.048	0.044	1.106	(1.026, 1.192)
Intestinal obstruction [n (%)]	2 (3.5)	8 (11.0)	1.563	0.211	0.295	(0.060, 1.450)
Intestinal leakage [n (%)]	1 (1.8)	6 (8.1)	1.510	0.219	0.199	(0.023, 1.706)
Infection of abdominal cavity [n (%)]	0 (0)	5 (6.8)	2.419	0.067	1.074	(1.009, 1.412)
Bleeding of abdominal cavity [n (%)]	0 (0)	3 (4.1)	0.921	0.337	1.043	(0.994, 1.094)
Pulmonary infiltration after surgery [n (%)]	4 (7.0)	14 (19.2)	3.968	0.046	0.318	(0.099, 1.026)

AKI: Acute Kidney Injury; ICU: intensive care unit; POD: postoperative day; PPFT: prolonged preoperative fasting time; RPFT: regular preoperative fasting time.

longed fasting before an operation has no benefit for patient prognosis, and can even induce a number of adverse effects such as vomiting, hunger, anxiety or more serious symptoms. Hence, the traditional guideline for overnight fasting before an operation has been challenged and a more rational procedure is about to be established, such as taking nutrition liquid solution 2 h before surgery.

Many studies sought to evaluate shortened preoperative fasting time on postoperative complications by taking carbohydrate and protein enriched solution prior to the operation.^{6,8} In our study, the adverse effects of a prolonged preoperative fasting period were assessed in 130 patients, which was a much larger cohort of patients than in previous clinical trials.^{6,8} In addition, the age and ASA level III or IV ratios in our investigation were much higher than reported in previous studies. With the upcoming aging society, it is a significant challenge to treat elderly patients who need surgery, especially those elderly patients with comorbidities who need to be admitted to ICU for intensive care after surgery. Our findings provide more evidence for priority treatment of these elderly patients.

Fasting time before surgery is directly related to the magnitude of the generation of inflammatory cytokines or cells released during the perioperative period, since organic responses to surgical trauma are enhanced by the prolonged fasting time.^{13,17,18} Some trials have shown that inflammatory cytokines or cells caused the tight junction collapse between pulmonary endothelial cells and the subsequent permeability of pulmonary microvascular endothelial cells (PMVECS).^{19,20} Results from this study demonstrated that the PPFT group exhibited an increased duration of mechanical ventilation after surgery during ICU care, which is possibly due to an increased inflammatory response. We also found a significantly higher postoperative unilateral or bilateral pulmonary infiltration in the PPFT group. Pulmonary edema may affect pulmonary function and consequently significantly increase the duration of mechanical ventilation support.

The mucosa of the intestine is known to play a major role in protecting the body against pathogens in the lumen. They also have a barrier function, protecting the body from endotoxin invasion via the wall of the intestine preventing them entering the bloodstream or abdominal cavity. A number of studies have presented evidence that intestinal tight junction barrier dysfunction is correlated with inflammatory cytokine generation and altered intestinal permeability.^{21,22} The increased metabolic response and inflammatory cytokines disrupt the intestinal epithelium integrity²¹ and contribute to the adverse clinical outcome. In this study, we also observed a tendency for higher postoperative intestinal leakage and abdominal cavity infection in the PPFT group of patients. Some se-

vere cases even needed a second operation, which was a significant difference in terms of reoperation cases in the two groups.

Metabolic stress as a result of surgery or trauma is a transitory phenomenon, which can last for 2-4 weeks postoperatively, was closely associated directly with the degree of surgical injury and also the fasting state of each patient.^{11,13,23} Patients who underwent minor surgery p.m. (afternoon) were in a greater fasting state than those who had morning (a.m.) surgery. It is noteworthy that hunger and thirst intensity also increased in the fasting period postoperatively in these patients and subsequently affected postoperative oral or gastric tube nutrition intake.⁶ Some studies have reported that postoperative enhanced metabolic stress leads to an increased risk of complications and morbidities (vital organ injury, abdominal infection).^{8,24} Some trials have also demonstrated that improved metabolic response to surgical trauma/injury can result in clinical benefits such as reduced nausea, vomiting and thirst, thus accelerating postoperative recovery.^{8,14,25} In the present study, we observed a significant difference in the postoperative fasting time between the two groups of patients. This finding may be attributable in part to the increased metabolic response due to the prolonged preoperative fasting state. On the other hand, regular preoperative fasting decreased stress and thus reduced the fasting time after surgery. One study was similar to our findings in that a reduction in the preoperative fasting time resulted in an earlier return to a normal diet postoperatively.⁶ Patients who had longer postoperative fasting periods presented with an increased incidence of complications.⁷ Figure 1 provides a conceptual diagram of the findings.

In our study, elderly patients were mainly involved in the gastrointestinal surgery. The findings are universally applicable in different surgeries, since any trauma or surgery can cause a metabolic response in the body. In addition, an increased metabolic response caused by the preoperative fasting status occurs in elderly as well as young patients.²⁶ Therefore, our results are valuable for most cases of elective surgery.

Conclusions

It has been demonstrated that a prolonged fasting time preoperatively increases the organic metabolic response and adverse events in patients who underwent elective gastrointestinal surgery. The compromised status in the perioperative period was associated with a higher incidence of postoperative complications. Therefore, reducing the preoperative fasting time is highly recommended to accelerate postoperative recovery for these patients (Figure 1).

Table 4. The effect of preoperative fasting time on different types of surgery

Surgery	Conclusion	References
Abdominal operation	Shortened time is better	3,8,12
Orthopedic surgery	Shortened time is better	27
Colorectal surgery	Peroral intake shortly before surgery was not associated with any risk	28
Gynecological surgery	Long fasting has higher incidence of nausea and vomiting	29
Different types of surgeries	Prolonged time is risky	30-35

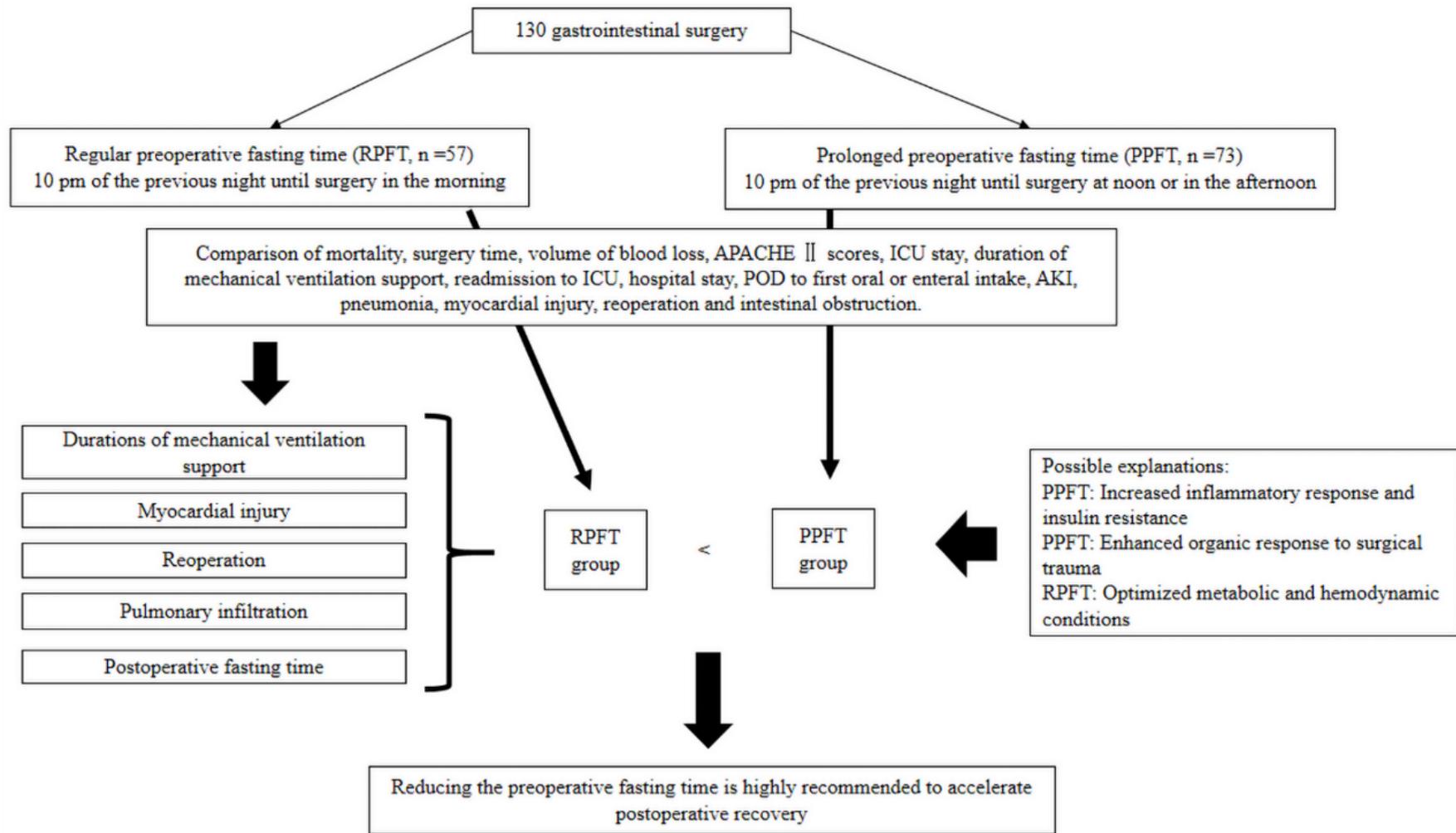


Figure 1. Conceptual diagram of the findings, mechanisms and clinical implications of prolonged preoperative fasting on prognosis in gastrointestinal surgery patients.

AUTHOR DISCLOSURES

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