

Effects of Preoperative Oral Carbohydrate on Cirrhotic Patients Under Endoscopic Therapy with Anesthesia: A Randomized Controlled Trial

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Abstract

Background: Preoperative fasting is a major cause of perioperative discomfort in patients. Addressing this problem by preoperative oral carbohydrate (POC) has been recommended as an important element of the enhanced recovery after surgery (ERAS) protocol, but its effect on cirrhotic patients who tend to show abnormalities in gastric emptying function has not yet been clarified. Our study aims to investigate the influence of POC on gastric emptying and preoperative well-being in cirrhotic patients.

Methods: A prospective, randomized and controlled study of cirrhotic patients with gastroesophageal varices scheduled for elective endoscopic therapy under intravenous anesthesia was conducted. 180 patients were enrolled in this study. Patients were divided into three groups: those not supplemented with carbohydrate for 8h prior to endoscopic therapy (Control group), those given a carbohydrate beverage 2h (2h group) or 4h (4h group) prior to endoscopy. Gastric emptying was evaluated by gastric sonography score and collecting gastric content aspirated endoscopically before anesthesia. Stresses caused by examination associated fasting were evaluated by visual analogue scale (VAS) scores for six parameters (thirst, hunger, mouth dryness, nausea, vomit and weakness) preoperatively. Hemodynamic changes, peristole and postoperative complications were also recorded.

Results: Before anesthesia, gastric sonography score was similar among three groups. In addition, no patient had residual gastric volume more than 1.5ml/kg in control and 4h group, but six patients (11%) reached a residual gastric volume of more than 1.5ml/kg in 2h group. Moreover, compared with control fasting, VAS scores for six parameters (thirst, hunger, mouth dryness, nausea, vomiting and fatigue) in 2h group and for three parameters (thirst, hunger and mouth dryness) in 4h group were both significantly lower. Gastric peristaltic score and operation score before operation, postoperative complication, lengths of hospital stay and in-hospital expense were not significantly different among three groups.

Conclusions: For the first time, we demonstrate that avoiding preoperative fasting with oral carbohydrates given 4h prior to anesthesia can improve preoperative well-being feelings, without enhancing the risk of aspiration and regurgitation in cirrhotic patients. Our study adds knowledge for preoperative fasting guidelines in anesthesia for cirrhotic patients.

Trial registration: This trial was registered at Clinicaltrials.gov under the number ChiCTR2000032394.

Background

Liver cirrhosis is the end stage of chronic liver diseases and characterized by accumulation of fibrotic tissue and abnormal regenerative nodules (1, 2). Portal hypersensitive gastropathy and its devastating complication, variceal hemorrhage, are common in cirrhotic patients (3). Variceal hemorrhage poses the most life-threatening complication of liver cirrhosis associated with increased mortality, particularly in those with hepatic decompensation (4). Endoscopic therapy including endoscopic sclerotherapy (ES), endoscopic band ligation (EBL) and endoscopic tissue adhesives (ETA) is the recommended standard of care for the treatment and prevention of gastroesophageal variceal bleeding due to hepatic cirrhosis that

requires preoperative fasting (5, 6). However, given a more rapid rate of catabolic state of starvation in patients with liver cirrhosis, avoiding long-term fasting is an essential element for these patients (7). Furthermore, patients with liver cirrhosis often show decreased gastric motility and prolonged gastric emptying closely related with abnormalities in autonomic functions and portal hemodynamics (8). Therefore, in clinical preoperative management, the need for determining a specific time period of fasting before anesthesia for cirrhotic patients is urgent (9, 10).

The Enhanced recovery after surgery (ERAS) has been widely investigated and shown to be associated with improved postoperative outcomes in patients undergoing elective surgery (11, 12). Based mainly on recommendations issued by ERAS societies, the current guideline for preoperative fasting is 6 h for solid foods and 2 h for clear fluids (13). Preoperative oral carbohydrates (POC), avoiding preoperative fasting by oral intake of a carbohydrate fluid is widely adopted as part of ERAS protocol that has shown beneficial effect on improving perioperative well-beings and clinical outcomes of patients (14). Although several studies have reported POC, with high energy content, does not pose any threat from vomiting or aspiration when taken 2 h before anesthesia in patients undergoing elective surgery (15, 16), there is lack of evidence about the effect of POC on some individual constituents with a propensity for delayed gastric emptying, including cirrhotic patients (17). We therefore designed a randomized controlled trial to assess the effect of POC, compared with preoperative fasting, on gastric emptying, preoperative well-being, hemodynamic changes and clinical outcomes in cirrhotic patients subjected to endoscopic therapy with anesthesia. This study further gets an insight into the application of POC for cirrhotic patients.

Methods

Patients

This investigation was designed as prospective, randomized controlled trial. Trial was conducted in The First Affiliated Hospital, College of Medicine, Zhejiang University, China. A total of 196 adult cirrhotic patients with gastroesophageal varices hospitalized for elective endoscopic therapy under anesthesia between Feb 2019 and Sep 2019 were assessed for eligibility. This study was limited to participants with an American Society of Anesthesiologists (ASA) grade of I to III. We excluded patients who were with gastrointestinal hemorrhage in acute stage, with severe anemia (hemoglobin less than 70 g /L), with known or predicted difficult airway, with moderate or severe heart and lung function impairment, with asthma, or with hepatic encephalopathy. 180 patients were selected for randomization. Informed consent for participation was obtained from each patient or their immediate relatives. This trial was approved by the Ethics Committee of The First Affiliated Hospital, College of Medicine, Zhejiang University and registered at Clinicaltrials.gov under the number ChiCTR2000032394.

Types Of Intervention

Enrolled patients were randomly assigned to one of three groups: control group, 2 h group and 4 h group (n = 60) according to random number table method provided by an independent statistician. The control group was managed by receiving nothing for 8 h prior to gastroscopy. The intervention group included participants who were given carbohydrate by oral beverage (3% energy, 5% carbohydrate and 2% sodium) 355 mL 2 h or 4 h prior to the scheduled endoscopic procedure. On operation day, anesthesiologists were blinded after assignment to interventions. 63 patients were excluded due to long operation time (> 2 h), cancelled operation, sent to Intensive Care Unit or transferred to open operation. Consequently, 117 patients were eligible for inclusion among whom 39 patients belonged to control group, 54 patients belonged to 2 h group and 24 patients belonged to 4 h group.

Anesthesia Methods

On arrival in the operation room, patients were regularly monitored heart rate (HR), blood pressure and SpO₂. All patients were given 3L/min oxygen administration through nasal tube in operation room. After patients were positioned in the left lateral position, intravenous injection of propofol (1.5-2 mg/kg) and sufentanil 0.1 ug/kg were administered. A stable depth of anesthesia in which patients were unconscious and unresponsive to painful stimulation was targeted by maintaining with propofol at the rate of 3–9 mg·kg⁻¹·h⁻¹ during endoscopic therapy. HR, blood pressure and SpO₂ were continually recorded. 0.2–0.5 mg of atropine was given once heart rate was lower than 50 per min. Ephedrine/phenylephrine was injected when blood pressure was lower than 90/60 mmHg or decreased 30% of the basic value. If blood pressure was higher than 160/100 mmHg and the effects of anesthesia depth and surgical complications were excluded firstly, urapidil was injected.

Outcome Measurements

The primary outcome measures were gastric emptying assessment by gastric sonography and gastric content aspirated by gastroscopy, and general well-being measured by visual analogue scales (VAS) for six parameters (thirst, hunger, mouth dryness, nausea, vomit and weakness). Secondary outcomes included hemodynamic changes, peristole, postoperative complications and length of hospital stay (LOS).

Gastric Emptying Assessment Before Intravenous Anesthesia

Gastric ultrasound is a reliable diagnostic tool to assess gastric content and volume (18). A standardized gastric scanning protocol was applied before anesthesia. We proposed a 3-point grading system based on qualitative sonographic assessment of the antrum in the supine and right lateral positions that correlates well with predicted gastric volume. Patients were classified as followings: Grade 0 means

empty antrum on both supine and right lateral positions, corresponding to a completely empty stomach; Grade 1 means minimal fluid volume detected only in the right lateral position, suggesting a negligible fluid volumes mostly less than 100 mL; Grade 2 means antrum clearly distended with fluid visible in both supine and right lateral positions, correlating with significantly higher fluid volumes (> 100 mL) and higher risk of regurgitation of gastric contents on anesthesia induction (19). In addition, all patients were performed gastric endoscope to collect residual volume through a collection bottle before anesthesia. The entire gastric volume is compatible with the risk of gastric aspiration. The relation of gastric volume to weight, whose value above 1.5 ml/kg was considered a risk for bronchoaspiration (20). Lidocaine gel and midazolam 0.03 mg/kg were given prior to gastroscopy to ensure the adaptation of patient to the procedure and to decrease anxiety and discomfort during the procedure.

Vas Score

Patients' general well-being (thirst, hunger, mouth dryness, nausea, vomit and fatigue) was measured by VAS in this study. VAS scores 0–10 were assessed before intravenous anesthesia (21). Score 0 means patients have no discomfort at all and score 10 presents patients have the most severe discomfort. Higher score means more severe discomfort. All VAS-scores were guided by a blinded investigator.

Hemodynamic Changes

Hemodynamic stability was assessed by measurements of mean arterial pressure (MAP), SpO₂ and HR at the following time intervals: just before intravenous anesthesia (T₀), 1 minute after injection of propofol (T₁), and 5 minutes after injection of propofol (T₂).

Gastric Peristaltic Score And Operation Score Before Operation

Gastric peristalsis was evaluated using a 4-grade scale according to the following scale: Grade 1 = No peristalsis; Grade 2 = Mild peristalsis that peristaltic wave is formed without reaching the pyloric ring; Grade 3 = Moderate peristalsis that a pronounced peristaltic wave is formed and reaches the pyloric ring; Grade 4 = Vigorous peristalsis that peristaltic wave is deep and strangulating the antrum (22). Operation score was also a 4-grade scale based on our previous study and evaluated by endoscopic operator. When operation score is more than 2, intravenous injection of antispasmodic agents is required.

Follow-up

Follow-up of patients was done at 1st, 2nd and 5th day after endoscopic therapy. Postoperative complications (fever and bleeding), LOS and in-hospital expense were recorded.

Statistical analysis

Based on our pilot study, the means and standard deviations (SD) of VAS score were 2.75 ± 1.15 (control group), 1.45 ± 1.22 (2 h group) and 1.9 ± 1.51 (4 h group). Thus, a minimal sample size of 63 participants (21 per group) was required with a 2-tailed $\alpha = 0.05$ and a power of 90% to guarantee such results. Assuming 10% of participants would drop out, a minimum sample size of 69 participants was established. SPSS (V.20.0) statistical software was used to analyze data. Continuous variables were presented as mean \pm SD or medians and interquartile ranges (IQR; 25th-75th percentiles), as appropriate. Categorical variables were shown as number (n) and percentage (%). Between-groups differences were evaluated by the X^2 test or an analysis of variance (ANOVA) for continuous variables. Chi-square test or Fisher exact test were used for comparison of categorical variables. The variables in each group were compared using ANOVA with Bonferroni's correction. Differences were considered significant at $p < 0.017$ in ANOVA with Bonferroni's correction and at $p < 0.05$ in the other analyses.

Results

Basic characteristics of patients

As shown in Table 1, age, gender, BMI, ASA classification, duration of endoscopic therapy and the number of patients receiving ephedrine or phenylephrine had no statistical significance among three groups.

Table 1
Basic characteristics of patients

	Control	2 h	4 h	p	
Age	54.87 \pm 10.25	55.85 \pm 9.43	58.54 \pm 11.09	0.366	
Female/male sex	11/28	17/37	4/20	0.395	
BMI	22.97 \pm 3.08	7/32	22.40 \pm 2.53	22.68 \pm 1.92	0.593
ASA (II/III)		10/44	2/22	0.546	
Duration of surgery (min)	27.15 \pm 13.98	34.57 \pm 21.65	34.96 \pm 15.71	0.113	
Receiving ephedrine					
/phenylephrine(No/Yes)	23/16	29/25	16/8	0.559	
Note: BMI = body mass index; ASA = American Society of Anesthesiology					

Evaluation Of Residual Fluid In The Stomach Before Anesthesia

Table 2 shows a summary of evaluation of residual fluid in the stomach by gastric sonography grade and gastric content volume aspirated by gastroscopy before anesthesia. There were no significant differences among the groups with regard to gastric sonography score. No patient had residual gastric volume more than 1.5 ml/kg in control and 4 h group, but six patients (11%) reached a residual volume of more than 1.5 ml/kg in 2 h group. No patient in either control group, 2 h group or 4 h group had an episode of regurgitation of gastric content at the time of anesthesia.

Table 2
Evaluation of residual fluid in the stomach before anesthesia

	Control	2 h	4 h	<i>p</i>
Gastric sonography score	0.586			
0	37/39	48/54	22/24	
1	2/39	5/54	2/24	
2	0/39	1/54	0/24	
Sucked fluid by gastroscopy	0.043			
< 1.5 ml/kg	39/39	48/54	24/24	
≥ 1.5 ml/kg	0/39	6/54	0/24	

Vas Scores Assessed Before Anesthesia

Subjective feelings of discomfort were measured during preoperative period for six parameters using VAS scores (thirst, hunger, mouth dryness, nausea, vomit and fatigue). We found that the 2 h group experienced significantly less thirst, hunger, mouth dryness, nausea, vomit and fatigue compared with control group. In addition, VAS scores for thirst, hunger and mouth dryness were significantly lower in 4 h group compared to control group, whereas no change was found in nausea, vomit and fatigue (Table 3).

Table 3
Well-being by VAS score before anesthesia

	Control	2 h	4 h	<i>p</i>
Thirst	3.69 ± 1.58	1.83 ± 1.20	2.94 ± 1.32	∅0.05 ^{a,b}
Hunger	4.21 ± 1.74	2.94 ± 1.50	2.54 ± 1.67	∅0.05 ^{a,b}
Mouth dryness	4.41 ± 1.77	3.44 ± 1.76	2.50 ± 1.32	∅0.05 ^{a,b}
Nausea	1.13 ± 2.18	0.09 ± 0.68	0.75 ± 0.99	∅0.05 ^a
Vomit	1.13 ± 2.18	0.09 ± 0.68	0.75 ± 0.99	∅0.05 ^a
Fatigue	4.26 ± 2.00	2.42 ± 0.97	3.52 ± 1.55	∅0.05 ^b
Note: <i>p</i> < 0.05 ^a : control group vs 2 h group; <i>p</i> < 0.05 ^b : control group vs 4 h group				

Changes In Haemodynamics

SpO₂ remained unchanged throughout the observation period in all three groups (Table 4). HR was significantly lower at T1 than at T0 (*p* < 0.001), but did not change significantly between T1 and T2 in the control group. HR remained unchanged throughout the observation period in 2 h and 4 h group (Fig. 1A). MAP decreased significantly at T1 than at T0 in all three groups (*p* < 0.001). MAP changed significantly between T1 and T2 in control group (*p* < 0.05), but did not reach significant difference between T1 and T2 in 2 h and 4 h group (Fig. 1B).

Table 4
SpO₂ changes at three time intervals

	Control	2 h	4 h	<i>p</i>
T0	99(98,100)	100∅99∅100∅	99∅98∅100∅	0.194
T1	100(99,100)	100∅98∅100∅	99∅98∅100∅	0.302
T2	100(99,100)	100∅99∅100∅	100∅98∅100∅	0.479
Note: T0: just before intravenous anesthesia; T1: 1 minute after injection of propofol; T2: 5 minutes after injection of propofol.				

Gastric peristaltic score and operation score assessment before operation

We calculated gastric peristaltic score and found that there was no significance in the difference among each group. In addition, the operation score of subjects in 2 h and 4 h group was similar with that in control group (Table 5).

Table 5
Evaluation of gastric peristaltic score and operation score

	Control	2 h	4 h	<i>p</i>
Gastric peristaltic score	1.85 ± 0.54	1.65 ± 0.48	1.87 ± 0.68	0.172
Operation score	1.90 ± 0.60	1.65 ± 0.48	1.87 ± 0.68	0.114

Convalescence

Summary of postoperative rehabilitation was shown in Table 6. In total, nine patients experienced postoperative adverse events. Bleeding complication after endoscopy therapy was observed in two and two patients in the control and 4 h group, respectively. Fever complication after endoscopy therapy was observed in three, one and one patients in the control, 2 h and 4 h group, respectively. Postoperative bleeding rate and fever rate did not reach significant difference among three group patients. The LOS for control group was 9.15 ± 4.37 days, for 2 h group was 8.26 ± 4.34 days and for 4 h group was 8.13 ± 5.24 days. No significant difference was detected in the LOS among three groups. Hospitalization expenses appeared to be similar among three groups.

Table 6
Postoperative complication and LOS

	Control	2 h	4 h	<i>p</i>
Postoperative bleeding rate (No/Yes)	37/2	54/0	22/2	0.066
Postoperative fever rate (No/Yes)	36/3	53/1	23/1	0.356
LOS time (day)	9.15 ± 4.37	8.26 ± 4.34	8.13 ± 5.24	0.319
Hospitalization expenses (RMB)	29147 ± 19365	31810 ± 30962	20643 ± 9585	0.220
Note: LOS = Length of hospital stay				
Figure legends: Changes in (A) heart rate and (B) mean arterial pressure. Data are expressed as means ± SD. Bold solid line, control group (n = 39); thin solid line, 2 h group (n = 54); broken line, 4 h group (n = 24). * <i>p</i> < 0.001 compared with level at T0; ** <i>p</i> < 0.05 compared with level at T1; T0, just before intravenous anesthesia; T1, 1 minute after injection of propofol; T2, 5 minutes after injection of propofol; HR, heart rate; MAP, mean arterial pressure.				

Discussion

The current study shows that preoperative carbohydrate given 4 h prior to anesthesia could improve well-being feelings of cirrhotic patients without increasing gastro-oesophageal reflux and aspiration pneumonia risk, suggesting the safety and promising role of POC applied in cirrhotic patients. This study also suggests that the intake of POC had beneficial effects on hemodynamic stability. Other aspects studied showed no significant differences regardless of gastric peristalsis and postoperative complication.

Preoperative fasting strategies have undergone various modifications over the past few decades. Guidelines for sedation and anesthesia in gastrointestinal endoscopy indicate that patients without a propensity for delayed gastric emptying should fast a minimum of 2 hours after ingestion of clear liquids and 6 hours after ingestion of light meals before anesthesia (9). However, patients with liver cirrhosis often show gastric dysmotility associated with prolonged gastric emptying and decreased gastric wall compliance. Previous studies suggest that parasympathetic hypofunction, sympathetic hyperfunction, portal blood flow and gastrointestinal hormones are closely related with gastric motility in cirrhotic patients (23). Delayed gastric emptying also appears to cause disturbance in postprandial glucose, insulin and ghrelin levels, and further results in low energy intake contributing to malnutrition and increased morbidity (24, 25). Up to now, there is no data to support a direct relationship between duration of fasting and the risk of pulmonary aspiration in cirrhotic patients. And there is also no practice standard for pre-procedural fasting that has been universally accepted for cirrhotic patients. Initial promising reports using preoperative carbohydrate intake have been published to reduce perioperative discomfort, but it has not been a well-defined approach in cirrhotic patients. The best timing for the use of preoperative carbohydrate in this population has been a topic of discussion that has recently been revitalized with the availability of carbohydrate beverages. Thus, understanding the evidence-based preoperative carbohydrate recommendations that might impact on well-being feelings and clinical outcomes of cirrhotic patient is utmost importance.

For the first time, we conducted randomized controlled trial to recommend the timing for oral intake before anesthesia in cirrhotic patients. This study was designed to test whether preoperative carbohydrate application, when performed 2 h or 4 h before endoscopic therapy, could improve the well-being feelings of patients without increasing risk of reflux and aspiration. In situations where gastric emptying is impaired such as in cirrhotic patients, the potential for pulmonary aspiration of gastric contents must be considered in determining a specific time period of fasting before anesthesia (10). Therefore, in this study, to confirm the safety of preoperative carbohydrate in cirrhotic patients, endoscopic examiner would perform gastroscopy to suck stomach content before anesthesia. We then measured and analysed, as primary outcome parameter, the volume of gastric content, which is an important factor in estimating the severity of aspiration and regurgitation. Interestingly, we found no patient had residual fluid more than 1.5 ml/kg in control and 4 h group. It is, however, definitely worth pointing out that six patients (11%) reached a residual volume of more than 1.5 ml/kg in 2 h group, indicating at high risk of regurgitation. Based on these findings, we suggest that preoperative carbohydrate administered 4 h rather than 2 h prior to anesthesia may be safely applied for cirrhotic patients. Our study adds knowledge for preoperative fasting guidelines in anesthesia for cirrhotic patients.

Malnutrition is common in cirrhotic patients with a reported prevalence as high as 80%. Low energy intake and poor nutritional status have been reported to facilitate the development of hepatic encephalopathy, which is associated with a poor prognosis in cirrhotic patients (26). Hypermetabolism is a characteristic of patients with liver cirrhosis who should ensure energy intake is adequate. (27). Thus, avoiding long-term fasting is fundamental for appropriate management in these patients (28, 29).

However, for examination and treatment of complications including gastric esophageal varices among cirrhotic patients, endoscopy intervention is commonly used that requires preoperative fasting. Determining a specific time period of fasting before anesthesia is thereby considered to be of central importance in perioperative management of patients with liver cirrhosis. Based on our findings, we recommend that preoperative fasting time for cirrhotic patients could reduce to 4 h instead of standard 8 h. The concept that reducing fasting time to 4 h may have long-term beneficial effect on cirrhotic patients is an interesting one and should prompt further research.

On the other hand, previous study has demonstrated that 200 kcal supplement could reduce both self-assessment of physical and mental stresses that exist for examination associated fasting in cirrhotic patients requiring contrast-enhanced CT or contrast-enhanced MRI (26). In this study, we further examine the effect of preoperative carbohydrate supplement on stresses caused by endoscopy examination associated fasting in cirrhotic patients. Our second significant finding was that lower preoperative VAS scores for thirst, hunger, mouth dryness, nausea, vomit and fatigue were reported in the carbohydrate group than in control group, which suggests that preoperative carbohydrate loading is better accepted. This is in accordance with previous reports that found patients had effectively reduced thirst, hunger, nausea and vomiting, as main components in preoperative discomfort, when taking carbohydrate before surgery (30, 31).

To date, esophageal and gastric variceal bleedings have been considered the major cause of upper gastrointestinal hemorrhage in cirrhotic patients, with a high risk of mortality and poor prognosis. It is therefore essential that patients who are with liver cirrhosis should not only receive intervention to survive from acute variceal hemorrhage, but also undergo secondary prophylaxis (32). The advancements in multidisciplinary approaches that include pharmacological therapy, endoscopic intervention, transjugular intrahepatic portosystemic shunt and surgery have improved outcomes of cirrhotic patients. Endoscopic intervention has great clinical value in achieving hemostasis and preventing first as well as recurrent bleeding from esophageal and isolated gastric varices for cirrhotic patients (33–35). Although endoscopy intervention is at rapid development, the choice of sedation and anesthesia selected for cirrhotic patients continues to be a controversial issue. In our study, we used propofol in combination with opioids to keep patients in moderate or deep sedation during endoscopic operation. Among 117 patients, no gastro-oesophageal reflux and aspiration pneumonia was caused, indicating propofol-based sedation with appropriate monitoring seems to be a safe procedure during endoscopy therapy in cirrhotic patients. This is in accordance with previous reports that found during colonoscopy and ERCP, the use of propofol for sedation was safe in patients with liver cirrhosis (36).

There are some limitations in this study. Firstly, the effect of preoperative carbohydrate on long term is unclear in patients with liver cirrhosis. Large multicenter RCTs will be needed to further strengthen whether propofol-based sedation is the best choice for this subgroup of patients.

Conclusions

In summary, the results of this study suggest that avoiding preoperative fasting with intake of carbohydrates 4 h prior to anesthesia, cirrhotic patients undergoing endoscopy treatment for gastroesophageal varices have improvement on preoperative feelings without increasing risk of regurgitation. Our data add new insights to be considered in future evidence-based guidelines for preoperative fasting in anesthesia for cirrhotic patients.

Abbreviations

American Society of Anesthesiologists

ASA

Analysis of variance

ANOVA

Endoscopic band ligation

EBL

Enhanced recovery after surgery

ERAS

Endoscopic sclerotherapy

ES

Endoscopic tissue adhesives

ETA

Heart rate

HR

Length of hospital stay

LOS

Declarations

Ethics approval and consent to participate: This randomized controlled study was approved by the local ethics committee of The First Affiliated Hospital, College of Medicine, Zhejiang University and registered on ClinicalTrials.org.cn (ChiCTR2000032394). Written informed consents were obtained from all patients or their legal representatives.

Consent for publication: The manuscript has been read and approved by all authors for publication.

Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' Contributions: Y Wang, Y Tu and B Cheng designed the study; Z Liu and H Li collected the data; Y Wang, Y Tu, H Li and B Cheng in analyze and interpretation the data. All authors read and approved the final manuscript.

References

1. Ibrahim M, El-Mikkawy A, Hamid MA, et al. Early application of haemostatic powder added to standard management for oesophagogastric variceal bleeding: a randomised trial. *Gut*. 2019;68:844.
2. Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. *Lancet*. 2014;383:1749.
3. Tripathi D, Stanley AJ, Hayes PC, et al. UK guidelines on the management of variceal haemorrhage in cirrhotic patients. *Gut*. 2015;64:1680.
4. Sarin SK, Kumar A, Angus PW, et al. Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations. *Hepatol Int*. 2011;5:607.
5. Mallet M, Rudler M, Thabut D. Variceal bleeding in cirrhotic patients. *Gastroenterology Report*. 2017;5:185.
6. Ljubicic N, Biscanin A, Nikolic M, et al. A randomized-controlled trial of endoscopic treatment of acute esophageal variceal hemorrhage: N-butyl-2-cyanoacrylate injection vs. variceal ligation. *Hepatogastroenterology*. 2011;58:438.
7. Nakaya Y, Shimohata T, Haraguchi S, et al. Severe catabolic state after an overnight fast in patients with chronic renal failure. *Nutrition*. 2011;27:329.
8. Furgala A, Thir PJ, Maccallum DS, et al. Terlipressin facilitates gastric and autonomic system dysfunctions in liver cirrhosis. *Hepatogastroenterology*. 2011;58:2041.
9. Early DS, Lightdale JR, Vargo JJ, et al. Guidelines for sedation and anesthesia in GI endoscopy. *Gastrointest Endosc*. 2018;87:327.
10. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924.
11. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: A Review. *JAMA Surg*. 2017;152:292.
12. Low DE, Allum W, De MG, et al. Guidelines for perioperative care in esophagectomy: enhanced recovery after surgery society recommendations. *World J Surg*. 2019;43:299.
13. Weimann A, Braga M, Carli F, et al. ESPEN guideline: clinical nutrition in surgery. *Clin Nutr*. 2017;36:623.
14. Williams JB, McConnell G, Allender JE, et al. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS Cardiac) program. *J Thorac Cardiovasc Surg*. 2019;157:1881.
15. Beamish AJ, Chan DS, Blake PA, et al. Systematic review and meta-analysis of enhanced recovery programmes in gastric cancer surgery. *Int J Surg*. 2015;19:46.
16. Mathur S, Plank LD, McCall JL, et al. Randomized controlled trial of preoperative oral carbohydrate treatment in major abdominal surgery. *Br J Surg*. 2010;97:485.

17. Kiamanesh D, Rumley J, Moitra VK. Monitoring and managing hepatic disease in anaesthesia. *Br J Anaesth.* 2013;111:i50.
18. Putte PV, Perlas A. Ultrasound assessment of gastric content and volume. *Br J Anaesth.* 2014;113:12.
19. Perlas A, Mitsakakis N, Liu L, et al. Validation of a mathematical model for ultrasound assessment of gastric volume by gastroscopic examination. *Anesth Analg.* 2013;116:357.
20. Bisinotto FM, Silveira LA, Rossi TC, et al. Comparative ultrasound study of gastric emptying between an isotonic solution and a nutritional supplement. *Rev Bras Anesthesiol.* 2019;69:115.
21. Tudor-Drobjewski BA, Marhofer P, Kimberger O, et al. Randomised controlled trial comparing preoperative carbohydrate loading with standard fasting in paediatric anaesthesia. *Br J Anaesth.* 2018;121:656.
22. Hiki N, Kaminishi M, Yasuda K, et al. Antiperistaltic effect and safety of L-menthol sprayed on the gastric mucosa for upper GI endoscopy: a phase III, multicenter, randomized, double-blind, placebo-controlled study. *Gastrointest Endosc.* 2011;73:932.
23. Ohta M, Yamaguchi S, Gotoh N, et al. Pathogenesis of portal hypertensive gastropathy: A clinical and experimental review. *Surgery.* 2002;131:165.
24. Kalaitzakis E, Lipponen P, Olsson R, et al. Increased prevalence of gastrointestinal symptoms in patients with liver cirrhosis. Association with health-related quality of life. *Gastroenterology.* 2005;128:W1702.
25. Kalaitzakis E, Sadik R, Holst JJ, et al. Gut transit is associated with gastrointestinal symptoms and gut hormone profile in patients with cirrhosis. *Clin Gastroenterol Hepatol.* 2009;7:346.
26. Kalaitzakis E, Olsson R, Henfridsson P, et al. Malnutrition and diabetes mellitus are related to hepatic encephalopathy in patients with liver cirrhosis. *Liver international.* 2007;27:1194.
27. Kawaguchi T, Taniguchi E, Itou M, et al. Supplement improves nutrition and stresses caused by examination-associated fasting in patients with liver cirrhosis. *Hepatol Res.* 2008;38:1178.
28. Plauth M, Schuetz T. Hepatology-guidelines on parenteral nutrition. *Chap 16 Ger Med Sci.* 2009;7:Doc12.
29. Plauth M, Cabre E, Campillo B, et al. ESPEN guidelines on parenteral nutrition: hepatology. *Clin Nutr.* 2009;28:436.
30. Dilmen OK, Yentur E, Tunali Y, et al. Does preoperative oral carbohydrate treatment reduce the postoperative surgical stress response in lumbar disc surgery? *Clin Neurol Neurosurg.* 2017;153:82.
31. Makuuchi R, Sugisawa N, Kaji S, et al. Enhanced recovery after surgery for gastric cancer and an assessment of preoperative carbohydrate loading. *Eur J Surg Oncol.* 2017;43:210.
32. Kong DR, Wang JG, Chen C, et al. Effect of intravariceal sclerotherapy combined with esophageal mucosal sclerotherapy using small-volume sclerosant for cirrhotic patients with high variceal pressure. *World J Gastroenterol.* 2015;21:2800.

33. Hsu YC, Chung CS, Wang HP. Application of endoscopy in improving survival of cirrhotic patients with acute variceal hemorrhage. *Int J Hepatol*. 2011;2011:893973.
34. Malik SM, deVera ME, Fontes P, et al. Outcome after liver transplantation for NASH cirrhosis. *Am J Transplant*. 2009;9:782.
35. Al-Khazraji A, Curry MP. The current knowledge about the therapeutic use of endoscopic sclerotherapy and endoscopic tissue adhesives in variceal bleeding. *Expert Rev Gastroenterol Hepatol*. 2019;13:893.
36. Faga E, Cento MD, Giordanino C, et al. Safety of propofol in cirrhotic patients undergoing colonoscopy and endoscopic retrograde cholangiography: results of a prospective controlled study. *Eur J Gastroenterol Hepatol*. 2012;24:70.

Figures

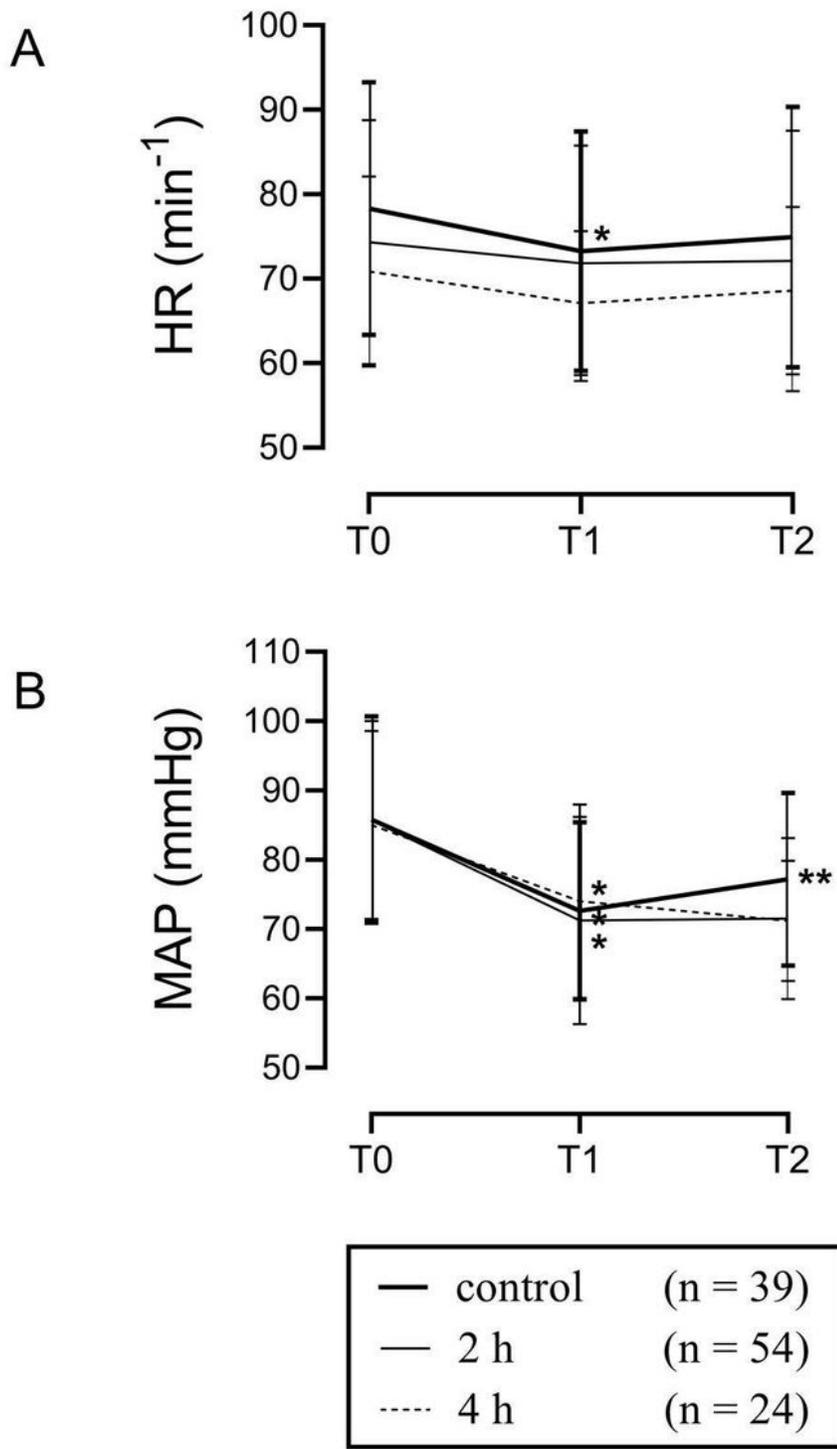


Figure 1

Hemodynamic changes Changes in (A) heart rate and (B) mean arterial pressure. Data are expressed as means \pm SD. Bold solid line, control group (n=39); thin solid line, 2h group (n=54); broken line, 4h group (n=24). * $p < 0.001$ compared with level at T0; ** $p < 0.05$ compared with level at T1; T0, just before intravenous anesthesia; T1, 1 minute after injection of propofol; T2, 5 minutes after injection of propofol; HR, heart rate; MAP, mean arterial pressure.

Supplementary Files

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