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Research Article

Impact of timing of elective abdominal surgery on postoperative liver function

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ABSTRACT

Background: The objective of the study was to investigate the impact of timing of surgery on liver function in a cohort of patients undergoing elective abdominal surgery.
Methods: We retrospectively analysed 14584 patients who underwent elective abdominal surgery at the First Affiliated Hospital, College of Medicine, Zhejiang University, from January to June, 2014. The patients were divided into three groups according to the start time of their surgery: CT1 (06:00 to 12:00), CT2 (12:01 to 18:00), and CT3 (18:01 to 05:59). The liver function of all subjects was assessed at 24 h post-surgery, using biomarkers.
Results: The blood glucose level at 24 h post-surgery was significantly increased in CT3 group. Notably, the total and indirect bilirubin and alkaline phosphate (ALP) were all increased in CT3 group control to the other groups (one-way ANOVA, $P < 0.05$).
Conclusions: We observed that the Child-Pugh score did not differ significantly among the three study groups. However, total and indirect bilirubin, glucose and ALP levels were significantly higher in subjects who underwent surgery between 18:01 and 05:59 hours of the day, implying that biomarkers of liver function varied with the time of surgery.

Keywords: Time, Surgery, Liver function tests, Biochemical marker

INTRODUCTION

Liver failure is one of the most serious and life-threatening post-operative complications, especially in patients with previous liver disease or toxicity secondary to modern chemotherapy, in whom mortality rates are as high as 32%.[1,2] Despite recent advances in surgical techniques and intensive care management, liver function damage is still a challenging problem after elective surgery.

The liver is innervated by both sympathetic as well as parasympathetic systems.[3] It is well known that the autonomic nervous system displays a circadian profile.[4] Additionally, liver function varies according to the circadian rhythm.[5] Studies have also demonstrated that the time of the day when elective surgery and

hemodialysis (HD) are performed has a bearing on the survival of the patient.[6]

Clinical scoring systems, such as Child-Pugh can roughly evaluate the risks of operation. Among other techniques for the assessment of liver injuries, biochemical testing of liver enzymes is a common clinical practice. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are generally considered a measure of hepatocellular function. Other biomarkers include gamma-glutamyl transferase (GGT), alkaline phosphates (ALP), bilirubin, glucose, creatinine, urea etc.

We therefore undertook this study to determine the impact of time at which surgery was performed on postoperative liver function, in patients who underwent elective abdominal surgery.

METHODS

Ethics statement

The study was approved by the Ethics Committee, the First Affiliated Hospital, College of Medicine, Zhejiang University. All subjects signed a written informed consent before the start of the study. Related trials for this intervention were registered in Chinese clinical trial registry: ChiCTR-EOC-15006514

Subject characteristics

Patients, who underwent abdominal surgery from January to June, 2014 were included in the study. They were divided into three groups according to the start time of surgery: CT1 (06:00 to 12:00), CT2 (12:01 to 17:59) and CT3 (18:00 to 05:59). Will take into account starvation will alter the concentration of some liver markers, fasting for 8 hours, fordif drinking for 4 hours preoperation.

The patients were excluded if they,

1. Underwent emergency surgery
2. Were younger than 18 years of age
3. Were mentally incompetent or unwilling to give informed consent
4. Died within four-weeks.

Data collection

Venous blood samples (10 mL) were drawn from each of the patients preoperatively and 24 h after the surgery, and sent immediately to the clinical laboratory for examination. All tests on samples were performed in duplicate per manufacturer instructions. Child-Pugh scoring was done at 24 h post-surgery in all the patients. Each patients' clinical and biochemical status was monitored in the morning of the day before surgery and at 24 h postoperatively.

Statistical analysis

Quantitative variables were expressed as mean (standard error of mean) or median (range). One-way ANOVA was used for comparison among groups. Qualitative variables were expressed as the number (percentage), and mean values were compared using Chi square test or Fisher exact test. The chosen significance threshold for statistical comparisons was $P < 0.05$ in a one-sided test. All statistical analysis was performed using SPSS 17.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 14584 patients were included in the study. The baseline and demographic characteristics of patients in all the three groups were similar (Table 1).

Table 1: Baseline characteristics of the study population.

	Group		
Variable	CT1 (n=5054)	CT2 (n=5787)	CT3 (n=3743)
Men (Women)	3068 (1986)	3453 (2334)	2364 (1379)
Age, mean (range), years	63 (25-91)	62 (27-88)	59 (22-91)
ASA classification (I/II/III/IV)	1235/2356/1405/58	1138/3221/1349/79	1075/1739/921/8
Duration of surgery, mean (SEM), min	162.5 (6.57)	152.5 (5.97)	178.2 (7.16)
Cirrhosis	101(94)	164(131)	103(87)
Diabetes mellitus	385 (1739)	231 (212)	193 (107)
Renal insufficiency	157 (53)	120 (62)	128 (45)
alcohol use	1466 (18)	1697 (15)	1333 (13)

ASA: American Society of Anesthesiologists
SEM: Standard error of mean

Table 2: Child-Pugh score 24h after surgery.

	Group		
Variable	CT1 (n=5054)	CT2 (n=5787)	CT3 (n=3743)
Child-pugh score (A/B/C)	4625/371/58	5259/449/79	3496/239/8

At 24 h postoperatively, totally 1204 patients had a Child-Pugh score of less than B. Of these 429, 528 and 247 patients were in the CT1, CT2 and CT3 groups respectively (Table 2). However, there was no significant difference in this score among the three groups ($P = 0.57$). The laboratory values of liver function markers are

described in Figure 1. The serum glucose level at 24 h post-surgery showed significant differences among three groups and was significantly increased in the CT3 group ($P < 0.01$). Additionally, there was a significant increase in the total and indirect bilirubin, and ALP levels in the CT3 group compared to the other two groups ($P < 0.05$). However, the serum ALT, AST, GGT, creatinine and urea were not significantly different among the three groups (all $P > 0.05$).

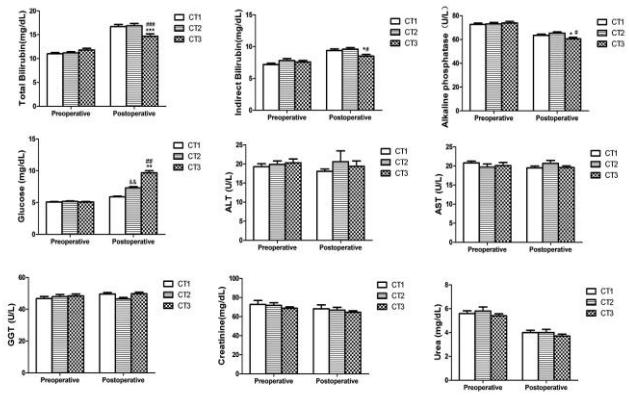

Figure 1: The laboratory values of liver function markers.

DISCUSSION

Our study demonstrated that there was a significant change in the biomarkers of liver function (serum total and indirect bilirubin, ALP and glucose) in the CT3 group compared to the other two groups.

Several factors are known to regulate the circadian rhythm. For example, the circadian rhythm observed in glucocorticoid hormones have been found to be linked with the magnitude of pulmonary inflammation.[7] In addition, the periodic variations in levels of melatonin indirectly affects inflammatory reaction.[8] Mattana et al. reported that patients who underwent HD late in the day had relatively higher levels of potassium and phosphorus than those dialyzed earlier in the day.[6] The possibility exists that some impairment of biochemical clearance might increase the expression of certain biomarkers in patients that started surgery in the later part of the day.

It has been previously demonstrated that circadian rhythm affects the autonomic nervous system and in turn, the glucose metabolism.[9] Further, according to published literature, the total, direct and indirect levels of bilirubin vary according to the circadian in healthy men[10] and ALT activity is greater in the afternoons than in the early morning hours,[11] which was consistent with our studies. However, significant differences were found between daytime and nighttime excretion of creatinine and urea.[12] Several factors may affect the ALT levels apart from the time of surgery, of which the most important is the direct effect of the surgery itself. In our study, we observed significant changes in the total and indirect bilirubin, ALP and glucose levels; however, there was no significant variation in the ALT, AST, GGT, creatinine and urea levels, based on the time of surgery. To our knowledge, this is the first study to evaluate the association between the operation timing and liver function.

One of the limitations of our study was that the start time of surgery was not chosen randomly. Additionally, a multicentre study would have yielded more robust data.

CONCLUSION

In conclusion, our study findings demonstrated that there was no significant variation in the Child-Pugh score with respect to time of surgery. However, total and indirect bilirubin, glucose and ALP levels were significantly higher in subjects who underwent surgery between 6:01 PM in the evening, to 05:59 AM in the morning, implying that biomarkers of liver function varied with the time of surgery.

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Ethical approval: The study was approved by the institutional ethics committee

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