The effect and clinical significance of using nathanson liver retractor on liver function tests in laparoscopic gastric cancer surgery

Afig Gojayev1, Cemil Yüksel2, Ümit Mercan3, Mehmet Ali Çaparlar1, Özhan Çetindağ1, Serkan Akbulut1, Ali Ekrem Ünal1, Salim Demirci1, Sancar Bayar4

1Clinic of Surgical Oncology, Department of General Surgery, Faculty of Medicine, Ankara University, Ankara, Turkey
2Department of Surgical Oncology, University of Health Science, Ankara Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey
3Department of Surgical Oncology, Sanliurfa Mehmet Akif Inan Training and Research Hospital, Sanliurfa, Turkey

ABSTRACT:

Aim: There are very few studies in the literature investigating the changes caused by the Nathanson retractors in liver function tests (LFT) after LG and their clinical significance. The present study investigated the changes made by the Nathanson retractor used during laparoscopic gastrectomy (LG) in LFT and their clinical significance.

Material and methods: The data of 236 patients who underwent radical gastrectomy for primary gastric cancer at Surgical Oncology Unit in the period between January 2015 and January 2020 were retrospectively studied. The patients were divided into two groups: laparoscopic gastrectomy (LG; 136 cases) and open gastrectomy (OG; 106 cases). Patients after cholecystectomy, with primary or secondary liver tumors, with chronic hepatic disease, with high preoperative ALT, AST and bilirubin values were excluded from the study. LFT were measured preoperatively and on postoperative day 1 (LFT1), LFT3, LFT5 and LFT7. LFT: ALT, AST and Total bilirubin (BIL).

Results: ALT1, ALT3, ALT5, ALT7 ALT values and AST1, AST3, AST5 AST values of patients in the LG group were found to be significantly higher (P < 0.001). Mean total bilirubin values of the groups were similar (P > 0.05). In order to evaluate how the increase in LFT due to the use of the Nathanson retractors reflected on the patients’ clinic, we divided the patients who underwent LG into two groups based on ALT increase in ALT1: Normal and Elevated. The in-hospital mortality rates (P = 0.080) and oral nutrition time (P = 0.913) of the groups were similar. No liver infarction developed in any of the groups. The duration of stay in the ICU was significantly longer in individuals with elevated LFT (P = 0.019).

Conclusion: Although the use of the Nathanson retractor during LG causes an increase in liver function test results, this does not cause major clinical problems in patients.

KEYWORDS: gastrectomy, gastric cancer, laparoscopy, liver enzymes, liver dysfunction

ABBREVIATIONS

ALHA – aberrant left hepatic artery
ALT – alanine aminotransferase
ASA – American Society of Anesthesiologists
AST – aspartate aminotransferase
BMI – body mass index
LC – laparoscopic colectomy
LFT – liver function tests
LG – laparoscopic gastrectomy
OC – open colectomy
SD – standard deviation

INTRODUCTION

Despite the development of new surgical and medical treatment methods, gastric cancer continues to be a life-threatening type of cancer. After its first use by Kitano et al. [1] in 1994, laparoscopic method has become a feasible technique for operating early gastric cancers and an increasingly preferred technique for advanced gastric cancers [2–9]. Previous studies have described some superior aspects of laparoscopic gastrectomy (LG) such as minimal postoperative pain, shorter hospital stays, rapid normalization of bowel movements and early initiation of oral nutrition [10–15]. Among the disadvantages of the laparoscopic method there are factors such as longer operation time and disruption of the circulatory and respiratory system by carbon dioxide pneumoperitoneum.

Although LG does not increase overall morbidity, previous studies have reported a temporary increase in liver enzymes after LG [16–18]. Some studies indicate that the formation of the pneumoperitoneum leads to increased intra-abdominal pressure and transient liver damage by disrupting hepatic venous flow [16, 18]. In addition, as described before, the causes of LFT impairment after LG include patient position, anesthetic drugs, ligation of the aberrant left hepatic artery (ALHA), and rough handling of the liver tissue too [6]. Nathanson liver retractors are increasingly used in LG. There are very few studies in the literature investigating the changes caused by the Nathanson retractors in LFT after LG and their clinical significance [16–18].

We aimed to investigate the impact of changes made by the Nathanson retractor used during LG on liver function tests and their clinical significance.
MATERIALS AND METHODS

Present research was approved by the ethics committee of our clinic. The data of 236 patients who underwent radical gastrectomy for histologically proven primary gastric cancer in our clinic in the period between January 2015 and January 2020 were retrospectively studied. The individuals were categorized into two groups considering the operation approach: laparoscopic gastrectomy (LG; 136 cases) and open gastrectomy (OG; 106 cases). The criteria for exclusion in the study were as follows: patients after cholecystectomy; with primary or secondary liver tumors; with chronic hepatic disease (those with positive hepatitis B virus or hepatitis C virus test); those with preoperative grade ≥2 increase of LFT markers [16]. On the other hand, the inclusion criteria were as follows: previous laparoscopic or open radical gastrectomy for pre-operatively pathologically proven gastric adenocarcinoma; using the Nathanson retractor in laparoscopic gastrectomy; complete medical record. The clinicopathological findings, operation outcomes and postoperative LFT findings of the patients were compared between the two groups. Clinicopathological findings included demographic data, American Society of Anesthesiologists (ASA) scores, pathological stage, neoadjuvant treatment status. The following operative findings were assessed: extent of resection (proximal or total), operation time, blood loss, inhospital mortality, hospital stay (day), intensive care unit (ICU) stay, oral intake time (day) and postoperative complications. Postoperative morbidity was classified under the following four categories: surgical complications, cardiovascular complications, pulmonary complications, and liver infarction. As laboratory findings, preoperative and postoperative ALT, AST and total bilirubin values on the 1st, 3rd, 5th and 7th day were retrospectively obtained from the hospital database.

In our institution, the normal reference ranges for ALT, AST, and bilirubin values were 0–50 IU/L, 0–50 IU/L, and 0.3–1.2 mg/dL, respectively. Findings obtained were compared between groups.

The technical summary of LG is stated in the previous study [19]. D2 lymphadenectomy was performed in all patients, whether open or laparoscopic. In all laparoscopic cases, Nathanson liver retractor (G03123; Cook-Medical, Bloomington) (Fig. 1.) was used for easy lymph node dissection, especially along the small curvature. In OG cases, blade type Roschard retractor was used for the same purpose.

Statistical analysis

IBM SPSS Statistics for Windows, Version 23.0 was used for statistical analysis. The normality assumptions were controlled by the Shapiro-Wilk test. Descriptive analyses were presented using mean ± standard deviation (SD), median (min-max) or n (%), where appropriate. Categorical data were compared with Pearson chi-square and Fisher’s Exact test. Mann-Whitney U test and independent t-test were used for analysis of non-normally and normally distributed numerical data, respectively. Paired t-test was performed for comparison of repeated measurements. Statistical significance was denoted by P < 0.05.

RESULTS

Findings such as demographic data, body mass index (BMI) (P = 0.656) and ASA score distributions (P = 0.990) were statistically similar between the groups. The rate of local advanced
patients in the OG group was higher (P = 0.005). The rate of individuals receiving neoadjuvant therapy was higher in the LG group (P = 0.002). These characteristics are described in Tab. I.

Operation time was longer in the LG group (P < 0.001). Postoperative complication rates (P = 0.972) and types of complications (P > 0.05) of the groups were found to be similar. Hospital stay was higher in the OG group (P < 0.001). In-hospital mortality rate (P = 0.757) and ICU stay (P = 0.306) were similar. The operation findings are shown in Tab. II.

Laboratory findings of LFT are shown in Tab. III. and Fig. 1. While the preoperative mean ALT values of the groups were found to be similar (P = 0.537), the ALT1, ALT3, ALT5 and ALT7 ALT values of the patients in the LG group were found to be significantly higher than in the OG group (P < 0.001). Mean total bilirubin values were similar between the groups (P > 0.05). It was observed that postoperative ALT and AST values on the 1st, 3rd and 5th day in the OG group were significantly higher than preoperative values (P < 0.05). ALT and AST values measured at all postoperative times in the LG group were significantly higher than preoperative values (P < 0.05). In the OG group, only BIL1 bilirubin values were significantly higher than preoperative values (P < 0.05).

In order to evaluate how the increase in liver function tests due to the use of the Nathanson retractors reflected on the patients’ clinic, we divided the patients who underwent LG into two groups based on ALT increase in ALT1: Normal and Elevated. Patients with grade 2 increase in ALT were included in the elevated group [19]. ICU stay was significantly longer in the elevated group (P = 0.019). The in-hospital mortality rates (P = 0.080) and oral nutrition time (P = 0.913) of the groups were similar. No liver infarction developed in any of the groups. These findings are shown in Tab. IV.
In LG operations, in order to perform D2 dissection around the station 3a and 3b lymph nodes, the left lobe of the liver must be retracted from the area with a special retractor [16, 20–22]. Therefore, the Nathanson liver retractor (G03123; Cook-Medical, Bloomington) has been used in our clinic since 2014 (Fig. 2.). It has now been suggested that liver injury after LG may be attributed to the use of the Nathanson retractors. Sometimes, rough use of the Nathanson retractor can even lead to intraoperative liver parenchyma damage (Fig. 3.). Changes in LFT due to liver damage caused by the Nathanson retractor and their clinical significance are still controversial.

In present study, ALT and AST values increased significantly in both groups in the postoperative period. ALT and AST peak value was reached on postoperative day 1 in both groups. ALT and AST values in the OG group returned to baseline on postoperative day 7. In the LG group, ALT and AST values did not return to baseline values even on postoperative day 7. When the groups were compared, ALT and AST values were found to be significantly higher in the LG group during the entire postoperative period (P < 0.001). Mean total bilirubin values were similar in OG and LG groups (P > 0.05). These results are similar with the Kinjo et al. [16] study in many aspects. In both studies, the ALT recovery was delayed. In contrast, Kinjo et al. reported that there was a significant increase in total bilirubin values in the LG group. In their study, to analyze the alone effect of insufflated carbon dioxide on LFT, they examined patients who underwent laparoscopic colectomy (LC) too. LFT changes were similar in open colectomy (OC) and LC patients. At the same time, the change in patient position did not affect liver enzymes in patients who underwent LC in Kinjo et al.’s study [16]. These data show that pneumoperitoneum and patient
position do not cause liver function test changes in patients after laparoscopic surgery. Therefore, we did not include LC and OC cases in our study. In order for LG to be the only factor affecting postoperative liver enzymes we excluded cases such as primary or secondary liver tumor or chronic liver disorder, patients after cholecystectomy, or patients with LFT impairment on laboratory tests before surgery. After excluding these cases, LG remained the sole factor affecting liver enzymes.

Temporary liver enzyme changes after LG have been associated with many reasons such as anesthetic drugs, patient position, rough behavior with the liver, ligation of an aberrant left hepatic artery (ALHA) and pneumoperitoneum in the literature [16, 18, 23, 24]. In some studies on laparoscopic surgery, the pneumoperitoneum has been discussed as the main cause for postoperative liver dysfunction [25, 26, 27].

It is thought that pneumoperitoneum, which is one of the main parts of laparoscopic surgery, reduces blood flow to the liver by making pressure on blood vessels. In contrast, Meierhenrich et al. reported that insufflated carbon dioxide does not decrease liver blood flow during laparoscopic operations, but it increases liver blood flow. In their study they used transesophageal echocardiography [28].

Transient elevation in liver enzymes is also seen in open gastric cancer operations. Some studies have reported that ALHA ligation during lymph node dissection may affect liver enzymes after gastrectomy [28, 29, 30]. To perform a complete D2 lymphadenectomy, many studies routinely recommend to divide the left gastric artery at its origin, regardless of whether it is an open or a laparoscopic method, even when ALHA is recognized during the operation [28, 29]. In our study, the effect of ALHA division on LFT was not investigated.

Jeong et al. reported that frequent and rough contact with liver tissue may be another reason for elevated liver enzymes after LG [19]. Liver retraction is important for the dissection of station 3a and 3b lymph nodes [30]. We use the Nathanson liver retractors in laparoscopic gastric cancer surgery. Although this retractor enables the operator to easily perform lymphadenectomy in station 3a and 3b, some studies have reported that this retractor causes LFT elevation [15, 20, 31, 32]. Among them there were studies by Shinohara et al. [21], Kinjo et al. [16], and Kitajima et al. [18] in which Nathanson retractor was used. In the study by Shinohara...
et al. and Kinjo et al., peak ALT values were 213 and 153 respectively. In our study, the peak ALT value was 889, which was higher than in the previous studies. These investigations show that heavier retraction by a Nathanson retractor can damage the liver more than any other method. But, in the present study, although the peak value of liver enzymes was high, none of the groups developed liver infarction.

The clinical significance of the increase in LFTs due to the use of the Nathanson retractors has not been examined in the previous studies. In our study, contrary to other studies, it was investigated how the increase in LFT affects the clinical condition of the patients. For this, we divided the patients who underwent LG into two groups based on ALT increase in ALT1: Normal and Elevated (details are given in the Results section). As a result of the analysis, it was found that the increase in liver enzymes prolonged hospital stay (P = 0.052) and ICU (P = 0.019) stay. On the other hand, the effect of LFT increase on oral intake time, in hospital mortality and liver infarction development was not detected.

The limitations of this study are its retrospective and single-center nature.

CONCLUSION

In conclusion, performing LG with the Nathanson retractors leads to a significant increase in liver enzymes. Although this increase in LFT prolongs the stay at the ICU, it does not cause major problems such as increased mortality and liver infarction in the patient’s clinic. In our opinion, the Nathanson retractor can be safely used during LG if the liver is gently retracted.

REFERENCES

Afig Gojayev MD; Ankara Üniversitesi Tıp Fakültesi Cebeci Araştırma ve Uygulama Hastanesi; Balkiraz Mahallesi, Tıp Fakültesi Cd. No: 23, 06620 Mamak/Ankara, Turkey; Phone: +90 552 385 33 69; E-mail: afiggojayev@gmail.com