ABSTRACT

Background: Retracting the lateral liver segment during laparoscopic distal gastrectomy is important to achieve an optimal surgical field. However, excessive force may injure the liver, causing temporary abnormalities in liver function tests after laparoscopic surgery. Since we developed a new liver retraction method, we verified and assessed its safety and usefulness.

Patients and Methods:

This is a retrospective analysis using prospectively compiled records in our surgical database in our institute. Consecutive surgical patients...
who underwent laparoscopic distal gastrectomy (LDG) for 229 early gastric cancer, were extracted from the database, and the perioperative data were obtained. We divided the 229 patients into two groups depending on whether our liver retraction technique (the Flexible Liver method) was used, either flexible liver retraction method with Clipping and Suturing techniques (FLICS group) or Nathanson’s retractor (NR group) was used. After that, one-to-one propensity score matching was performed to align patient backgrounds, and match patients, resulting in the records of 53 pairs of cases were extracted. Serum AST, ALT, CRP and T-Bil were measured at from the database.

Operative and postoperative days 1, 3, 5, 7 and outcomes were assessed, including following the values of serum liver enzymes, total bilirubin, and C-reactive protein until postoperative day 30.

Results: There were no significant differences in patient background and characteristics or preoperative examination data after PSM. There was no addition or change of Liver retractor data in the two groups. No serious complications associated with liver retraction were observed in both groups. No postoperative liver failure was observed in all patients.

Conclusions: Our new liver retraction technique provided an optimal surgical field without inducing post-operative liver dysfunction. It is a simple, safe, protective new, and effective liver retraction technique.

(301 words)

Key words: Laparoscopic gastrectomy, Gastric cancer, Liver retraction, Internal Organ Retractor, Nathanson’s retractor, propensity score-matched analysis.
INTRODUCTION

Laparoscopic distal gastrectomy (LDG) has been widely used for treating patients within Japan since 1991 to treat gastric cancer since 1991 in Japan [1].

Therefore, we have devised and enforced a liver retraction method combining Internal Organ use of an internal retractor with sutures to help lift up the organ, which we designated flexible liver retraction with clipping and suturing (FLICS).

MATERIALS AND METHODS

Patients and characteristics

This is a retrospective analysis using prospectively analyzed patient records compiled in our institution's surgical database. All patients were given sufficient explanations and written informed consents. Consecutive records of consecutive surgical patients who underwent laparoscopic distal gastrectomy (LDG) for gastric cancer were extracted from the database, and the following data were collected: patient characteristics (age, sex, performance status, American Society of Anesthesiologists Physical Status Classification [ASA-PS], height, weight, body mass index [BMI, calculated as kg/m²], tumor size, and histology), body weight, body mass index (BMI, weight in kg divided by height in meters squared [kg/m²]), preoperative tumor data (clinical T status, clinical N status, clinical stage, Lauren classification, presence or absence of preoperative and preoperative with endoscopic submucosal dissection), preoperative laboratory data (hemoglobin, total bilirubin, ALB, BUN, creatinine, PT, INR, CRP, GTP, C-reactive protein, gamma-glutamyl transpeptidase, T-Bil).
Bilirubin), surgical outcomes including intraoperative events (surgical approach, operative time and, and immediate intraoperative immediate complications (if any)), postoperative course and laboratory tests of liver function, and mid-term and long-term outcomes. TNM staging was based on the Japanese Classification of Gastric Carcinoma, 3rd English Edition [18].

Finally, patients who satisfied inclusion criteria were divided into the FLICS group and the NR group. The clinical characteristics and perioperative outcomes were compared between the two groups after propensity score matched (PSM) – (A, B, or C).

Liver retraction method during LG at our hospital 

Nathanson retractor 

In use of Nathanson Liver Retractor, the liver retractor is inserted close to the xiphoid process and then placed near the hepatic hilum under the lateral segment of the liver. Basically, Retractor The retractor was fixed during surgery, and fixation was changed when or repositioned as necessary to provide an adequate surgical field deployment. accompanying Liver retraction was necessary. In addition, when, If the pressure applied was strong, enough to cause congestion and ischemic findings were observed, weakened or signs of ischemia, the pressure on the liver was weakened.

Flexible liver-retraction method with clipping and suturing techniques (FLICS) technique 

Details of the FLICS procedure are shown in Figure 2. When using Along with the Internal Organ Retractor, 48mm Straight needle PLOLENE prolene sutures (Ethicon Endo-Surgery, Cincinnati, OH, USA) was used for traction.

UnderDuring pneumoperitoneum, puncture-the right hypochondrium was punctured and lift the hepatic crown lifted to the right temporal side with using 2-0 PLOLENE the suture. After
dissection of the lesser omentum, Internal Organ Retractor was inserted into one of the 12-mm trocars, and clipped to the cut edge of lesser omentum was grasped by the retractor. Liver retraction was accomplished by towing from outside external traction on the body sutures.

It was performed using a logistic regression model and with the following covariates: Age, Sex, ASA-PS, BMI, histology, preoperative laboratory data (ALB, PT, CRP, AST, ALT, T-Bil, bilirubin, and ALP), preoperative treatment, Location, with endoscopic submucosal dissection, Lauren classification, and preoperative clinical stage.

Elevations of serum liver enzymes in blood test were evaluated based on CTCAE and on the basis of the Common Terminology Criteria for Adverse Events Version [22], with an abnormal value was defined as ≥3 times the upper limit of normal value [22].

Statistical analysis

All statistical calculations were performed with JMP® PRO software (JMP version 13.1.0, SAS Institute, Cary, NC, USA). All values were two-tailed, and P-values <0.05 were considered significant. We used a caliper width of 0.2 of the pooled standard deviation of the logit of the propensity score for PSM.

RESULTS

patient characteristics after PSM analysis

The Figure 3 depicts the study flow chart is described in Figure 3. Between 2012 January 2012 and 2012 December 2016, a total of 1,432 patients with gastric cancer...
were admitted to our institution, of whom 334 patients who underwent laparoscopic gastrectomy (LDG) for clinical early-stage gastric cancer (cT1N0M0, clinical stage I) were identified in a retrospectively maintained database. The reasons for exclusion criteria before PSM analysis were as follows: multiple of records from the study included other organ resections \((n = 65)\), a higher clinical stage \((n = 67)\), use of other liver retraction techniques \((n = 85)\). In addition to the above, the patients with, or the presence of chronic liver damage and/or a history of alcohol abuse or liver disease such as of hepatitis B virus, hepatitis C virus, and acute viral hepatitis were excluded from the study. Finally, 160 LDG with A, B, or C.

After PSM, the FLICS and 69 with the NR patients were enrolled in this study.

The clinical characteristics and short-term and long-term outcomes were compared between the two groups after PSM analysis. A total of 106 patients with laparoscopic distal gastrectomy who had undergone LDG for early gastric cancer were included in the study, 53 patients (50%) were included in the FLICS group, and the remaining 53 patients were included in the NR group.

The surgical outcomes of patients undergoing the FLICS group and NR group are detailed in Table 2. In the comparison of surgical characteristics, the demonstrated a significantly shorter median operation time was shorter in the FLICS group than in the NR group (224 min [140-300 min] vs. 262 min [191-336 min], \(P < 0.001\)). Both techniques provided a satisfactory view of the working field(surgical field) during laparoscopic distal gastrectomy and LDG. There were no intraoperative complications required any treatments relating to retraction of the liver. Curative resection (R0) was achieved in all patients. The number of lymph nodes retrieved did not differ significantly between the two groups \((P = 0.185)\).
Surgical complications classified as **Clavien–Dindo grade II or higher** are described in Table 2. Concerning early postoperative complications, more cases (7 cases, 13.2%) were observed in the NR group than in the FLICS group (7 cases, 13.2% vs 3 cases, 5.7%), but the difference was not statistically significant (p = P = 0.097) (Table 2). One patient in the NR group (1.9%) had a Clavien–Dindo class III or higher complication, whereas no patients in the FLICS group. In the NR group, one case of complication (anastomotic leakage required reoperation) compared with none in the FLICS group. No liver dysfunction was found in both groups. Curative resection (R0) was performed in all patients. No significant difference in number of retrieved lymph node was observed between the two groups (p = 0.185). There was no 30 day mortality or postoperative liver failure in either group.

**Parameters of liver damage and inflammatory status**

After PSM analysis, there was no significant difference between two groups in the patient’s baseline levels of each liver function tests. Circulating at baseline between the two groups, ALT and AST levels increased significantly from baseline within 24 hours following surgery in each group. The levels of serum ALT on both groups. On postoperative day (POD) days 3, 5, and 7, both serum ALT (Fig. 4a) and AST (Fig. 4b) levels were statistically significantly higher in the NR group than in the FLICS group (Fig. 4a). Furthermore, levels of serum AST on POD 3, 5 and 7 were significantly higher in the NR group than in the FLICS group (Fig. 4b). Peak of On the other hand, the total bilirubin levels became the highest on POD 1 and gradually decreased thereafter were also elevated in the first few days, but the levels did not differ significantly between groups (Fig. 4d). The CRP showed the same trend as has a
trajectory similar to that of the AST and ALT—values, with the elevation in the FLICS group remaining significantly lower than that in the NR group ($P = 0.0038$, 0.004) (Fig. 4d).

**DISCUSSION**

The present study demonstrated that FLICS, our new flexible liver retraction method without, was associated with only minimal transient elevation of liver enzymes and did not cause liver injury. During laparoscopic gastrectomy (LG), it is important to establish a good operative field and ensure an adequate working space.

Furthermore, investigation of hepatic injury on postoperative CT caused by use of Nathanson Liver Retractor during In a study using computed tomography, liver abnormalities were seen after use of the NR in 14 of 52 (27%) patients who had undergone laparoscopic gastrectomy for cancer and 2 of 11 (18%) who had had laparoscopic upper gastrointestinal surgery revealed some liver abnormality in 27% of LG performed cases and 18% of bariatric surgery [28]. Such damage to the liver is caused by the persistent strong exclusion of the liver, occurring without noticing can result in damage that goes unnoticed intraoperatively [8]. To date, various liver retraction methods have been done and reported to reduce the damage to the liver [12, 17, 29, 30]. Kitajima et al. [17] suggested that reducing liver damage could be prevented when using the NR by limiting the duration of liver retraction and moving the position of periodically repositioning the retractor, or releasing it intermittently could avoid physical pressure by Nathanson Liver Retractor. Although they demonstrated that their technique was safe and useful, it is technically difficult to arrange, and it is necessary to set up the hepatic relief again during surgery. Our retraction FLICS method can be continuously carry...
out steady operative field deployment in order deployed to mobilize the liver to the patient's upper right side of the patient, but allowing a clear surgical field. It is adaptable by changing the traction on the sutures, allowing adjustment as needed of fixation of the liver is done with leeway so adaptability is high enough that as well as normal respiratory variation remains.

[Other text deleted]

The absence of elevation of fact that increases in liver enzyme and CRP levels were less marked in the FLICS than the NR group confirms that FLICS is a proof that our safer retraction method is a compulsive excretion method against the liver.

We believe that the overall reliability of our results is enhanced by the one-to-one matching of this the study are very accurate by groups using PSM to adjust the background factors as much as possible. Moreover, since this method is simple, stable and safe, it is considered to be very useful, which should have reduced the influence of unknown confounders.

Acknowledgments

Table 1 Baseline characteristics of one-to-one propensity score-matched patients who underwent laparoscopic distal gastrectomy for gastric cancer

<table>
<thead>
<tr>
<th></th>
<th>FLICS group (n = 53)</th>
<th>NR group (n = 53)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67 (34–79)</td>
<td>66 (27–91)</td>
<td>0.994</td>
</tr>
<tr>
<td>ASA-PS(1:2:3)</td>
<td>11 (20.8%):42 (79.3%):0</td>
<td>11 (20.8%):42 (79.3%):0</td>
<td>1.000</td>
</tr>
</tbody>
</table>
| BMI: body mass index, cT: clinical T stage, cN: clinical N stage, ESD: endoscopic
Table 2 Operative and postoperative outcomes in patients who underwent laparoscopic distal gastrectomy for gastric cancer

<table>
<thead>
<tr>
<th></th>
<th>FLICS group (n = 53)</th>
<th>NR group (n = 53)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reoperation</td>
<td>0</td>
<td>1 (1.9%)</td>
<td>0.237</td>
</tr>
<tr>
<td>Postoperative hospital stay (day)</td>
<td>9.1 ± 1.8</td>
<td>15.1 ± 7.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Overall surgical complications</td>
<td>3 (5.7%)</td>
<td>20 (37.7%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Clavien–Dindo grade &gt;III</td>
<td>0</td>
<td>1* (1.9%)</td>
<td>0.237</td>
</tr>
<tr>
<td>Liver dysfunction</td>
<td>0</td>
<td>0</td>
<td>0.237</td>
</tr>
<tr>
<td>Organ damage (including liver injury)</td>
<td>0</td>
<td>0</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Figure 1. Described Schematic of the flexible liver retraction with clipping and suturing method of handling 2.0 PLOLINE in extracorporeal operation. (a).

Figure 2. Our procedure of Flexible liver retraction with Internal Organ retractor. Puncture the clipping and suturing in situ during laparoscopic distal gastrectomy. (a–c). The right hypochondrium and lift is punctured by the suture needle and the hepatic crown lifted to the right temporal side (b–c). After dissection of lesser omentum.

Comment [SE52]: All first-time use abbreviations in main text or peripheral text must be defined.
Comment [SE53]: Please note that you discount this item in discussing the study limitations. Please consider deleting it from the table. If not, please at least mention it in the text of the Results, e.g. “Although the FLICS group had a shorter mean hospital stay, changes in hospital policy during the study period may have influenced this result.”
Comment [SE54]: Please note that this item was indented. When left aligned, it appeared that it referred to all the items indented below it. However, it might be best to delete this item from the table entirely.
Comment [SE55]: As noted above in the text, this required definition.
Comment [SE56]: Please note that this is unclear. Do you mean “gross liver injury”? The fact that enzyme levels were elevated indicates at least microscopic injury.
Comment [SE57]: Please note that the journal requests that figure legends be brief, with no more than 4 or 5 lines. We have revised them to shorten them as much as possible.
Comment [QA58]: Please consider reversing panels a and b in the figure, as well as the descriptions written here in the legend. The intraabdominal schematic should come first. The external tension only makes sense when one understands how the sutures are situated internally.
Comment [SE59]: Please consider rearranging the panels so that a–c are the top row, d–f the middle row, and g–i the bottom row. Because readers of English normally read from left to right, the natural tendency is also to look at a figure with multiple panels the same way. It’s initially a bit confusing for the sequence of steps to be oriented vertically rather than horizontally.
Comment [SE60]: Please note that figure 2 is not been cited in the text. Please check.
Comment [SE61]: Please check that this correctly conveys the intended meaning. There was no description for panel a.