A Simple Method Minimizes Chylothorax after Minimally Invasive Esophagectomy

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BACKGROUND: Postoperative chylothorax is a rare, but potentially fatal complication after esophagectomy. Preventive measures aimed at decreasing the incidence of chyle leakage after minimally invasive esophagectomy (MIE) could potentially reduce the high postoperative mortality associated with this complication. However, previous techniques are traumatic and time consuming. We present a simple method in the prophylaxis of chylothorax after MIE.

STUDY DESIGN: A total of 344 consecutive esophageal cancer patients who underwent 3-stage MIE between June 2006 and July 2012 were included. Of these, 178 patients were given preoperative milk orally 6 hours before surgery (Group M+) and 166 underwent MIE without preoperative milk and served as controls (Group M−). Patient demographics were retrospectively collected. The incidences of intraoperative thoracic duct identification and postoperative chylothorax were recorded and statistically compared between the 2 groups.

RESULTS: In this cohort, the 2 groups were comparable in clinical features including age, sex, tumor location, histologic type, and TNM stage. No patient was converted to open thoracotomy. During the thoracoscopic stage, a higher incidence of duct identification (95.5% vs 12.7%, p < 0.001) and a lower incidence of duct ligation (6.74% vs 13.25%, p = 0.039) were recorded in Group M+. Postoperatively, a total of 10 cases of chylothorax (2.91%) were observed. The incidence of chylothorax was significantly lower in Group M+ than in Group M− (0.56% vs 5.42%, p = 0.018).

CONCLUSIONS: Preoperative oral administration of milk facilitates visualization of the thoracic duct and minimizes the risk of iatrogenic injury to the thoracic duct during thoracoscopic esophagectomy. It is a simple and safe method for preventing chyle leakage after MIE. A randomized and controlled trial is required to confirm these findings. (J Am Coll Surg 2014;218:108–112. © 2014 by the American College of Surgeons)

CME questions for this article available at http://jacscme.facs.org

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METHODS
A total of 344 consecutive patients underwent 3-stage MIE at our institution between June 2006 and July 2012 and were enrolled in this study. Tumor lesions were clinically staged using endoscopy, tissue biopsy, abdominal-thoracic CT, and endoscopic ultrasound. Inclusion criteria for MIE were: clinically staged T1-3N0M0 tumors; no previous history of cancer; no previous history of neck or chest surgery; and an American Society of Anesthesiologists (ASA) score of I to III.

All operations were performed under the direction of the same senior consultant over the same time period. Patients who met inclusion criteria were assigned to 2 surgical groups. Preoperative milk was given to only 1 surgical group (Group M+), who received 500 mL of whole milk orally 6 hours before MIE. The other surgical group underwent MIE without preoperative milk and served as controls (Group M−). All patients fasted for at least 6 hours before surgery. Patient demographics are summarized in Table 1. The hospital ethics committee approved the study. All patients gave their written informed consent before the operation after receiving careful explanation of the goals of the study.

Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group M+ (n = 178)</th>
<th>Group M− (n = 166)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>62.2 ± 8.3</td>
<td>60.3 ± 9.1</td>
<td>0.740*</td>
</tr>
<tr>
<td>Sex, M:F</td>
<td>128:50</td>
<td>130:36</td>
<td>0.171</td>
</tr>
<tr>
<td>Location, U; M; L, n</td>
<td>31; 123; 24</td>
<td>26; 120; 20</td>
<td>0.810</td>
</tr>
<tr>
<td>Neoadjuvant therapy</td>
<td>7</td>
<td>9</td>
<td>0.512</td>
</tr>
<tr>
<td>Histology, SC; AD; others</td>
<td>167:8:3</td>
<td>155:7:4</td>
<td>0.941†</td>
</tr>
<tr>
<td>Stage, T1:T2:T3:T4**(1)</td>
<td>42:50:81:5</td>
<td>33:54:77:2</td>
<td>0.543</td>
</tr>
<tr>
<td>Thoracic duct visualisation</td>
<td>170</td>
<td>21</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Thoracic duct ligation</td>
<td>12</td>
<td>37</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td>158 ± 70</td>
<td>163 ± 67</td>
<td>0.328*</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>0</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Thoracic stage duration, min</td>
<td>87 ± 29</td>
<td>102 ± 35</td>
<td>0.054*</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>8.9 ± 3.3</td>
<td>10.1 ± 4.2</td>
<td>0.427*</td>
</tr>
</tbody>
</table>

Group M+ patients received preoperative milk; Group M− patients did not. ± values indicate standard deviation.
*Student’s t-test.
†Chi-square test.
‡Fisher’s exact test.
**Others: 3 cases of small cell carcinoma in both groups and 1 case of carcinoma sarcomatode in Group M+.
(1)Including 7 cases of T4b, and 1 case of T4 (in Group M+), which was invasive to the thoracic duct, and the patient had resection of thoracic duct during MIE.
* Mann-Whitney test.
AD, adenocarcinoma; L, lower; M, middle; SC, squamous cancer; U, upper.

Operative procedures
All patients received a combination of epidural and general anesthesia before the operation and were provided with patient-controlled analgesia postoperatively. Patients were intubated with a left-sided, double-lumen endotracheal tube to accomplish selective deflation of the right lung during the thoracic phase of the thoracic esophagectomy, and they were switched to double-lung ventilation during the abdominal and cervical stages. The MIE consisted of 3 stages: the thoracic, the abdominal, and the cervical stages.

Thoracic stage
The thoracic stage included esophageal mobilization and mediastinal lymphadenectomy. An observation port was placed at the seventh intercostal space along the mid-axillary line, and another 10-mm port was placed at the ninth intercostal space in the mid-scapular line. Two 5-mm ports were placed at the third intercostal space along the mid-axillary line and just inferior to the tip of the scapula, respectively. An artificial CO₂ pneumothorax was achieved at a pressure of 8 mmHg. After thorascopic exploration, the azygous vein was double-ligated by Hem-o-Lok (Teleflex) and then divided, after mobilization of the thoracic esophagus, which progressed from the tumor inspection site to the thoracic inlet cranially, and to the hiatus caudally.

Identification of the thoracic duct was confirmed if the vessel was visible without any additional dissection. One of 3 methods was used when handling the thoracic duct: ligation, dissection, or preservation; the method was selected according to the operative findings. During the surgical resection, the thoracic duct was ligated only if it were deemed inadvertently injured, or divided if it were involved in the tumor process. Otherwise, the duct was preserved.

Mediastinal lymphadenectomy was performed along the bilateral recurrent laryngeal nerves, together with the subcarinal and paraesophageal lymph node stations. The procedure was completed by placing an intercostal drain and closing the thoracic ports.

Abdominal and cervical stages
The abdominal and cervical stages were carried out as previously described. Jejunostomy was performed on all patients in order to provide enteral nutrition (usually begun on the second postoperative day). The operation concluded with closure of the cervical and abdominal incisions in layers.

Data collection and statistical analysis
Clinical data, including patient demographics and operative features of all patients, were collected from the clinical database at our institution. Postoperative chylothorax was
suspected when chylous drainage from the chest tube exceeded 400 mL. The diagnosis was then verified with laboratory confirmation of elevated triglycerides (>110 mL/dL) or positive Sudan III stain in the setting of sustained drainage. Clinical features of patients with postoperative chylothorax, their associated treatments, and their overall outcomes were also recorded.

All data were tabulated using Microsoft Excel for further analysis. Statistical analysis was undertaken using SPSS software (version 17.0). Variables were compared using the Mann-Whitney test, the Student’s *t*-test, and chi-square test. A 2-sided p value less than 0.05 was considered statistically significant.

RESULTS

Patient demographics

There was a male predominance in our cohort of 258 men and 86 women. The mean age at time of surgery was 61.0 ± 5.3 years (SD). There was no significant difference in age (p = 0.740) or sex (p = 0.171) between Group M+ and Group M−. According to the UICC (Union for International Cancer Control) esophageal cancer TNM staging system (7th Edition, 2010), there were 75 cases of pT1 (21.80%), 104 cases of pT2 (30.23%), 158 cases of pT3 (45.93%), and 7 cases of pT4 (2.03%) in our study. The depth of tumor invasion was similar between the 2 groups (p = 0.543). There was no significant difference in tumor location (p = 0.810) or histologic subtype (p = 0.941) between the 2 groups (Table 1).

Operative features

All patients underwent thoracoscopic esophagectomy without conversion to open thoracotomy. During surgery, the thoracic duct was visually identified (Fig. 1) in 191 of 344 patients (170 patients in Group M+ vs 21 patients in Group M−). A significantly higher rate of thoracic duct identification was recorded in Group M+ compared with Group M− (95.51% vs 12.65%, p < 0.001). Accidental injury requiring thoracic duct ligation was noted in 6.74% of patients in Group M+ vs 13.25% of patients in Group M− (p = 0.039). One patient in Group M+ was found to have tumor invasion to the thoracic duct, and the patient had resection of the thoracic duct during MIE.

No significant differences were found in the length of hospital stay, volume of blood loss, or number of blood transfusions between the 2 groups. Operative features are listed in Table 1.

Morbidity and mortality

No patients died during the operation in either group (Table 2). Complications were observed in 152 patients (39.89% in Group M+ vs 48.80% in Group M−, p = 0.096). In Group M−, 1 patient developed a gastric conduit leak on the eighth postoperative day and died 2 weeks later because of septic shock and multi-organ failure. No significant difference in 30-day mortality was noted between the 2 groups.

Management and outcome of chylothorax

There were 10 cases of chylothorax in this study, and the incidence of postoperative chylothorax was significantly lower in Group M+ compared with Group M− (0.56% vs 5.42%, respectively; p = 0.018). All 10 cases of chylothorax failed in thoracic duct identification during the operation, and 3 patients with postoperative

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group M+ (n = 178)</th>
<th>Group M− (n = 166)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0</td>
<td>1</td>
<td>0.972*</td>
</tr>
<tr>
<td>Morbidity</td>
<td>71</td>
<td>81</td>
<td>0.096†</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>1</td>
<td>9</td>
<td>0.018*</td>
</tr>
<tr>
<td>Cervical anastomotic leak</td>
<td>37</td>
<td>41</td>
<td>0.387†</td>
</tr>
<tr>
<td>Gastric conduit failure</td>
<td>2</td>
<td>1</td>
<td>0.952*</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>18</td>
<td>17</td>
<td>0.969†</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>9</td>
<td>11</td>
<td>0.534*</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>3</td>
<td>2</td>
<td>0.957†</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1</td>
<td>0</td>
<td>0.972*</td>
</tr>
</tbody>
</table>

Note: Group M+ patients received preoperative milk; Group M− patients did not.
* Fisher’s exact test.
† Chi-square test.
† A total of 3 patients required reoperation and religation of thoracic duct due to chylothorax (6% in Group M+ vs 12.2% in Group M−, p = 0.371). Including temporary and permanent recurrent laryngeal nerve palsy.
† Bleeding requiring reoperation.
chylothorax had undergone intraoperative thoracic duct ligation (0% in Group M+ vs 1.81% in Group M−, \( p = 0.222 \)).

Conservative chylothorax treatment consisted of intrapleural drainage via chest tube, total parenteral nutrition, and pleurodesis (50% hypertonic glucose injected into the thoracic cavity). Patients in whom conservative treatment was not successful underwent reoperation. In this study, 4 patients were treated conservatively and 6 patients (all from Group M−, Table 3) required reoperation due to persistent chyle leakage despite conservative treatment for at least 5 days. The incidence of reoperation for chylothorax was lower in Group M+ compared with Group M− (0% vs 3.61%, \( p = 0.032 \)). Thoracoscopic exploration was performed on all patients who underwent reoperation, and milk was given intraoperatively via nasal-gastric tube to facilitate identification of the thoracic duct. The injuries were identified and ligated under thoracoscopy, and chyle leakage resolved within 24 hours of reoperation in all patients. One patient developed a thoracic cavity infection 6 months after discharge (from Group M−, Table 3). The patient recovered without sequelae after reoperation for thoracic debridement.

**DISCUSSION**

As the most common subtype in the East, esophageal squamous cell cancer is more commonly located in the mid-upper thoracic esophagus, and the close relationship of the thoracic duct to the thoracic esophagus makes iatrogenic injury more frequent during operation. In a recent study from Shah and associates, squamous histology was identified as an independent predictor of chylothorax after esophagectomy, and it follows that patients from the East are at higher risk of chylothorax compared with their western counterparts. In the surgical resection of esophageal squamous cell cancer, we introduced preoperative milk 6 hours before surgery and observed a higher rate of intraoperative thoracic duct identification and a lower incidence of postoperative chylothorax, which suggested preoperative milk as an effective method in the prevention of chyle leakage.

Previously, researchers successfully used 50 mL of cream administered orally 3 hours before open esophagectomy to reduce the incidence of chylothorax. The success of this method for identifying the thoracic duct during minimally invasive surgery remains uncertain. Inspired by this idea, oral preoperative milk was given 6 hours before MIE and the thoracic duct was observed as a bright white vessel under thoracoscopy (Fig. 1). The presence of fat facilitated visualization of the thoracic duct, which had subsequently widened in diameter to 2 to 3 mm compared with the usual 1 to 2 mm. The change in size and appearance of the thoracic duct, as well as the magnified view afforded by thoracoscopy, improved identification of thoracic duct during MIE.

Given the improvements on duct visualization, preoperative milk was effective in preventing chylothorax in this study. First, preoperative milk administration minimized intraoperative thoracic duct ligation due to incidental injury (6.74% of Group M+ patients vs 13.25% of Group M−), which saved the time of ligation and assured continuity of the operation. Second, even when thoracic duct injury occurred during the surgery, chylous fluid would be suggestive in bright white due to preoperative milk, and ligation could be easily performed to stop the chyle leakage at the injury site, which saved patients from potential chylothorax. Because milk had been administered 6 hours before surgery, the improvements in identification would not interfere with the operation.

**Table 3. Clinical Features of Patients with Postoperative Chylothorax**

<table>
<thead>
<tr>
<th>Pt. no.</th>
<th>Group</th>
<th>Age, y</th>
<th>Sex</th>
<th>Location</th>
<th>Histology</th>
<th>Thoracic duct*</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M−</td>
<td>60</td>
<td>M</td>
<td>M</td>
<td>SC</td>
<td>−</td>
<td>Reoperation</td>
<td>Survival</td>
</tr>
<tr>
<td>2</td>
<td>M−</td>
<td>58</td>
<td>M</td>
<td>U</td>
<td>SC</td>
<td>−</td>
<td>Reoperation</td>
<td>Survival</td>
</tr>
<tr>
<td>3</td>
<td>M+</td>
<td>63</td>
<td>M</td>
<td>M</td>
<td>SC</td>
<td>−</td>
<td>−</td>
<td>Pleurodesis</td>
</tr>
<tr>
<td>4</td>
<td>M−</td>
<td>58</td>
<td>F</td>
<td>M</td>
<td>SC</td>
<td>−</td>
<td>+</td>
<td>Reoperation</td>
</tr>
<tr>
<td>5</td>
<td>M−</td>
<td>62</td>
<td>M</td>
<td>M</td>
<td>AD</td>
<td>−</td>
<td>−</td>
<td>Pleurodesis</td>
</tr>
<tr>
<td>6</td>
<td>M−</td>
<td>57</td>
<td>F</td>
<td>M</td>
<td>SC</td>
<td>+</td>
<td>−</td>
<td>Pleurodesis</td>
</tr>
<tr>
<td>7</td>
<td>M−</td>
<td>70</td>
<td>M</td>
<td>U</td>
<td>SC</td>
<td>−</td>
<td>−</td>
<td>Reoperation</td>
</tr>
<tr>
<td>8</td>
<td>M−</td>
<td>56</td>
<td>F</td>
<td>M</td>
<td>SC</td>
<td>−</td>
<td>+</td>
<td>Reoperation</td>
</tr>
<tr>
<td>9</td>
<td>M−</td>
<td>61</td>
<td>M</td>
<td>M</td>
<td>SC</td>
<td>−</td>
<td>−</td>
<td>Reoperation</td>
</tr>
<tr>
<td>10</td>
<td>M−</td>
<td>70</td>
<td>M</td>
<td>U</td>
<td>SC</td>
<td>−</td>
<td>−</td>
<td>Pleurodesis</td>
</tr>
</tbody>
</table>

Group M+ patients received preoperative milk; Group M− patients did not.

*Identification and injury to the thoracic duct recorded during MIE.

1This patient developed infection 6 months after discharge and recovered without sequelae after reoperation for thoracic debridement.

AD, adenocarcinoma; M, middle; MIE, minimally invasive esophagectomy; SC, squamous cancer; U, upper.
making administration of preoperative milk a simple method to prevent chylothorax after MIE.

To prevent the chyle leakage, prophylactic ligation of the thoracic duct is favored during esophagectomy. In a recent study, chyle leakage decreased from 2.1% to 1.2% when intraoperative thoracic duct ligation was performed on all patients operated on for esophageal cancer,7 which means that less than 1% of patients benefit from prophylactic ligation. In addition, the long-term effect of thoracic duct ligation on esophageal cancer patients remains uncertain. Because poor nutritional status is commonly noted in these patients,8 ligation of the thoracic duct may interfere with absorption of fats and other nutrients,9 which leads to the safety concerns regarding this procedure.

Reoperation due to chylothorax was observed in 6 patients in Group M−; 3 of these had a history of duct ligation during the original MIE. These results suggested that 3 of 21 ligations (14.29%) had failed during thoracoscopy esophagectomy. Although thoracic duct ligation has been proven effective,10 it does not completely eliminate the occurrence of chylothorax because there is considerable variation in duct anatomy, and some injury might be missed during the operation.11 On the other hand, preoperative milk minimized the incidence of reoperation in Group M+, which made MIE a safer procedure because reoperation for chylothorax carries high mortality when patients are nutritionally and immunologically depleted.12 We believe that identification and preservation of the thoracic duct using milk is a safe method for prevention of chylothorax after MIE.

In our study, thoracic ligation was performed in 6.74% of Group M+ patients compared with 13.25% in Group M−. The lower incidence of ligation in Group M+ could be explained by improvement in duct visualization during MIE because thoracic duct leakage appeared bright white. In Group M−, the chyle leakage was often observed as transparent liquid under thoracoscopy, and in some cases might be falsely positive without intraoperative laboratory testing. Therefore, more ligations were performed if indefinitely thoracic duct injury was suspected.

CONCLUSIONS

Although this study has limitations, including its retrospective design and lack of randomized controls, preoperative administration of milk has shown simplicity and safety in minimizing chylothorax after MIE. Further study based on larger samples is required to confirm this finding.

Author Contributions

Study conception and design: Shen
Acquisition of data: Feng, H Wang

Analysis and interpretation of data: Khan
Drafting of manuscript: Shen
Critical revision: Tan, Q Wang

REFERENCES