Enucleation of Esophageal Submucosal Tumors: A Single Institution’s Experience

Sumin Shin, MD, Yong Soo Choi, MD, PhD, Young Mog Shim, MD, PhD, Hong Kwan Kim, MD, PhD, Kwhanmien Kim, MD, PhD, and Jhingook Kim, MD

Department of Thoracic and Cardiovascular Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

Department of Thoracic and Cardiovascular Surgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam-si, Gyeonggi-do, Republic of Korea

Background. Esophageal submucosal tumors (SMTs) are usually benign, and surgical enucleation is widely accepted as the treatment of choice. The goals of this study were to investigate the surgical outcomes after enucleation of esophageal SMTs and to establish the feasibility of video-assisted thoracoscopic enucleation.

Methods. We performed a retrospective review of 87 patients who underwent enucleation of esophageal SMTs between 1995 and 2011 at Samsung Medical Center.

Results. There were 59 men and 28 women in the study group, with a mean age of 43.3 years (range, 20–73 years). Fifty-eight (67%) patients were asymptomatic. Among the remaining patients, the most common symptom was dysphagia (n = 12). Transthoracic approaches were used in 79 patients, including 63 patients who underwent video-assisted thoracoscopic enucleation. Transabdominal approaches were performed in 8 patients. Pathologic diagnosis included leiomyoma (n = 78 [89.7%]), gastrointestinal stromal tumors (GISTs) (n = 5 [5.7%]), schwannoma (n = 3 [3.4%]), and hemangioma (n = 1 [1.1%]). The thoracoscopic enucleation group had a significantly shorter median hospital stay compared with the thoracotomy groups (5 versus 6 days; p = 0.013). Overall, there were 2 postoperative leaks, including in 1 patient who underwent reoperation after enucleation. With the exception of 2 patients, there was no other major complications. One patient underwent esophagectomy for tumor recurrence after enucleation of GISTs.

Conclusions. Overall, surgical outcomes were excellent after enucleation. The thoracoscopic approach was feasible for most patients and was correlated with a shorter hospital stay. However, careful management is warranted after enucleation of GISTs considering the recurrence risk.

(Eur J Cardiothorac Surg 2014;45:964–9)

© 2014 by The Society of Thoracic Surgeons

Esophageal submucosal tumors (SMTs) represent a heterogeneous group that accounts for less than 1% of all esophageal neoplasms; autopsies show an incidence of 8 to 43 cases per 10,000 populations [1, 2]. Leiomyoma is the most common benign tumor of the esophagus and accounts for 70% to 80% of esophageal SMTs [2]. Other types, such as gastrointestinal stromal tumors (GISTs) are very rare. Because of the similar clinical, endoscopic, and radiologic features of these tumors, definitive diagnosis may not be possible until postoperative histologic and immunohistochemical examination is performed [3].

Surgical treatment has been the therapy of choice for esophageal SMTs, and enucleation is widely accepted as sufficient treatment [4, 5]. However, some cases of GISTs with malignant potential may require esophageal resection, which has higher rates of morbidity and mortality [3, 5–7]. Traditionally, thoracotomy and laparotomy have been popular methods for enucleation [4, 5]. Recent reports on the feasibility of enucleation using minimally invasive techniques have suggested that such techniques may be difficult to use on large lesions and may increase surgical complications [8–13].

We present surgical outcomes after the enucleation of esophageal SMTs and evaluate the feasibility of enucleation using video-assisted thoracic surgery (VATS).

Patients and Methods

Study Population

Eighty-seven patients who underwent enucleation of esophageal SMTs between February 1995 and November 2011 at Samsung Medical Center were included in this study. Their medical records were reviewed retrospectively. The Institutional Review Board of the Samsung Medical Center approved this study and waived the requirement for informed consent.

Preoperative Evaluation

Patients underwent comprehensive preoperative evaluations, which included esophagogastroduodenoscopy (EGD), endoscopic ultrasonography (EUS), esophagography, and chest computed tomography (CT) scans.

Accepted for publication Oct 11, 2013.

Address correspondence to Dr Choi, Department of Thoracic Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul, 135-710, Korea; e-mail: choi.smcts@gmail.com.

© 2014 by The Society of Thoracic Surgeons

Published by Elsevier Inc

http://dx.doi.org/10.1016/j.athoracsur.2013.10.030

0003-4975/$36.00
Operative Approach and Technique
Preoperative surgical evaluations were discussed with the members of our thoracic surgery department. Indications for operation included the presence of symptoms, evidence of an increase in tumor size, and the need to confirm the pathologic diagnosis. The surgical approaches were largely dependent on the location and size of the tumors. We preferred to approach tumors located in the upper and middle esophagus through the right side of the chest. However, if the tumors leaned to 1 side, the tumor was also approached through the affected side, depending on the surgeon’s preference. Tumors located in the distal esophagus that had not reached the esophagogastric junction (EGJ) were mostly approached through the right side. Tumors located near the EGJ or lying over the EGJ were approached transthoracically through the left side or transabdominally. In terms of transthoracic enucleation, if the overall dissection of the esophagus was anticipated because of the shape of tumor, we preferred to approach through the right side regardless of the location of the tumor. All transthoracic approaches were performed at the lateral decubitus position.

After the first successful video-assisted thoracoscopic enucleation in 2001, we preferred to use VATS for cases that required a transthoracic approach. For this operation, patients were intubated with a double-lumen tube to allow for single-lung ventilation. Subsequently, a 3- or 4-port placement was chosen based on the preference of the operator.

After localization of the tumor, the mediastinal pleura was incised longitudinally, and a myotomy was performed over the tumor. The tumor was removed gently to prevent mucosal damage. Air inflation of the esophagus through endoscopy was used to check the dissected area, or a Levin tube was used to confirm the integrity of the mucosa. In all patients, the muscular layer was approximated with interrupted sutures after enucleation to prevent the formation of a pseudodiverticulum.

Follow-Up
For patients who underwent repair of mucosa during enucleation, the patient received nothing by mouth until we confirmed the mucosal integrity by esophagography. The choice of procedure depended on surgeon choice and extent of injury. If the surgeon thought the extent of mucosal injury considerable, the patient usually received nothing by mouth until the seventh day after the operation. In contrast, if the injury was not significant, an oral diet was resumed 2 to 3 days after the operation. We also kept the chest tube in place until we confirmed the mucosal integrity with esophagography. For patients with mucosal injury, follow-up esophagography was performed on approximately the seventh postoperative day before discharge. In contrast, patients without mucosal injury in whom leakage was not anticipated, follow-up esophagography was undertaken earlier in the hospital or later in the outpatient department. If a patient had symptoms that were suspected to be related to the operation or an abnormal finding was observed in the esophagogram, we performed follow-up in the outpatient department. The interval of follow-up was based on each case. For patients with GISTs, chest CT scans with contrast was performed every 6 months postoperatively for 2 years and then annually. EGD was also performed in patients with GISTs every 1 or 2 years.

Statistical Analysis
Categorical data are presented as frequencies and were compared by χ² tests or Fisher’s exact tests. Continuous data are described by the mean ± standard deviation or range for normally distributed data or by the median and the interquartile range (IQR) for data that were not normally distributed. Continuous data were compared using the independent t test or the Mann-Whitney U test according to the distribution of the data. To assess the feasibility of VATS enucleation, we limited the analysis to patients who underwent enucleation through a transsthoracic approach (thoracotomy versus VATS). Patients whose operation was converted to thoracotomy were included in the thoracotomy group. Statistical significance was assumed at a probability (p) value less than 0.05. All statistical analyses were performed using IBM SPSS Statistics, version 19.0 (SPSS Inc, Chicago, IL).

Results
Patient Characteristics
Patient characteristics are described in Table 1. There were 59 men and 28 women, with a mean age of 43.4 years (range, 20–73 years). The majority of the tumors arose in the middle (n = 36 [41.4%]) and lower thirds of the esophagus or at the EGJ (n = 35 [40%]). Fifty-eight (67%) patients were asymptomatic and their tumors were discovered incidentally by screening EGD during health examinations. The most common symptom that patients reported was dysphagia (n = 12). The mean tumor size in all patients was 5.5 ± 3.26 cm (range, 0.8–20 cm). A comparison of the mean tumor size according to the presence of symptoms revealed that patients with symptoms had a significantly larger mean tumor size than did patients without symptoms (6.0 ± 2.41 cm versus 5.2 ± 3.60 cm; p = 0.046).

Operative Approach and Postoperative Outcomes
The transthoracic approach was performed in 79 patients and the transabdominal approach was performed...
in 8 patients. Mucosal injury occurred in 20 patients (23%). If mucosal injury was detected intraoperatively, the mucosa was repaired with an interrupted suture. An intraoperative EGD was performed in 33 patients to confirm mucosal integrity. For the remaining 54 patients, mucosal integrity was confirmed by air inflation using a Levin tube. Eleven cases of mucosal injury occurred in the VATS group and 9 cases of injury occurred in the open group, which included thoracotomy and laparotomy.

There were 2 postoperative leaks after enucleation. Enucleation using VATS through the left side was performed on 1 patient who had a 7-cm leiomyoma arising between the subclavian vessel and aortic arch. During enucleation, mucosal injury was detected and repaired. However, follow-up esophagography revealed leakage and the patient underwent exploratory thoracotomy and primary repair 5 days after operation. That patient continued to receive nothing by mouth until 53 days after operation. The other patient, who had an 11-cm horseshoe-shaped leiomyoma encircling the distal esophagus to the EGJ, underwent enucleation through laparotomy. During enucleation, mucosal injury was also detected and repaired. He was able to start oral intake 23 days postoperatively without additional surgical intervention. There were no other major complications. The median length of the hospital stay was 5 days (IQR, 4–7 days).

Pathologic Results
Leiomyoma was the most common pathologic diagnosis. Seventy-eight patients (89.7%) were diagnosed with leiomyoma. GIST was diagnosed in 5 patients (5.7%). Schwannoma and hemangioma were diagnosed in 3 patients (3.4%) and 1 patient (1.1%), respectively.

VATS Versus Thoracotomy
Among the patients who underwent enucleation transorally (n = 79), a total of 63 patients (79.7%) underwent enucleation using VATS, and 16 patients (18.4%) underwent enucleation through a thoracotomy. Seven patients had their operations converted to thoracotomies from VATS, for a conversion rate of 11% (7 of 63). Causes of VATS failure included mucosal adhesion and fibrosis (n = 3), failure of single-lung ventilation (n = 2), pleural adhesion (n = 1), and localization failure (n = 1).

The clinical characteristics and surgical outcomes according to surgical approach in patients who underwent transantral enucleation are presented in Table 2. The VATS group showed a statistically significant smaller mean tumor size (4 versus 6.5 cm; p = 0.002), shorter median hospital stay (5 versus 6 days, p = 0.013), and shorter duration of chest tube placement (3 versus 4 days; p = 0.034) than the thoracotomy group. There was no significant difference in the median operative time between the 2 groups.

Follow-Up
The mean follow-up period was 21.4 months (range, 1–194 months). During this period, 1 patient had a GIST recurrence. He underwent esophageal mass excision at 31 months after enucleation. After the operation, he was treated with imatinib for 2 months. However, we detected a second recurrence at 32 months after the second operation. Thus, we performed an esophagectomy; he was then maintained on treatment with imatinib mesylate.

There were 9 patients who had symptoms of reflux. One patient underwent Nissen fundoplication for persistent gastroesophageal reflux 26 months after tumor resection. He had a 10-cm horseshoe-shaped leiomyoma that encircled his distal esophagus. He had gastroesophageal reflux symptoms before undergoing VATS enucleation, and there was no structural abnormality seen in follow-up esophagography. Another 8 patients had new-onset gastroesophageal reflux. Their symptoms improved after treatment with proton pump inhibitors.

Four patients had pseudodiverticula in the follow-up esophagogram. The mean tumor size in patients with pseudodiverticula was significantly larger than that in the patients without pseudodiverticula (9.8 ± 2.72 cm versus 5.6 ± 3.94 cm; p = 0.007). All patients with pseudodiverticula had tumors located in the lower esophagus that did not involve the EGJ.

Comment
The primary goal of this study was to investigate surgical outcomes after enucleation of esophageal SMTs. Our study indicated that enucleation was sufficient surgical management for most SMTs, with low morbidity. The thoracoscopic approach is also feasible for most patients, with shorter hospital stays compared with the thoracotomy group (5 versus 6 days; p = 0.013). Even though the
The mean tumor size was larger in the thoracotomy group than in the VATS group (6.5 versus 4.0 cm; \( p = 0.002 \)), we have also been successful in removing large tumors up to 10 cm.

There are several options for the treatment of esophageal SMTs, including observation, endoscopic treatment, and surgical treatment [5]. Surgical treatment has been the therapy of choice for esophageal SMTs, and enucleation is widely accepted as an adequate treatment [4, 5]. Transthoracic enucleation by thoracotomy has been the most common procedure performed for the treatment of esophageal SMTs [4, 5]. Since Everitt and coworkers [8] reported the first successful thoracoscopic enucleation in 1992, thoracoscopic approaches have been used increasingly, and several studies have examined their feasibility and safety [9–13]. von Rahden and associates [9] reported that compared with open surgery, enucleation of esophageal SMTs using a minimally invasive approach reduced pulmonary complications, hospital stay, and postoperative wound-related pain. Kent and colleagues [11] reported that the minimally invasive resection of esophageal SMTs was associated with a shorter length of hospital stay compared with open approaches. In the current study, we also found that the thoracoscopic approach was associated with a shorter hospital stay and shorter duration of chest tube placement compared with the thoracotomy group.

The indications for thoracoscopic enucleation have not been established. Jiang and associates [12] suggested that esophageal leiomyomas 1 to 5 cm in diameter would be the best candidates for thoracoscopic enucleation. Tumors larger than 5 cm can also be candidates for enucleation by thoracoscopy, even though there is an increased possibility of thoracotomy conversion [11]. In our study, although the tumor size in the VATS group was smaller than that in the thoracotomy group, we successfully performed enucleation for large-sized tumors as well. Early in the study period, we performed enucleation mostly using the open technique. After the first successful VATS enucleation in 2001, we preferred to use VATS when a transthoracic approach was necessary. After 2006, VATS was attempted in all cases in which patients needed a transthoracic approach, even if the tumor was large, because of the high level of experience of the surgeon. The overall thoracotomy conversion rate was 11% (7 of 63). Over the past 5 years, this conversion rate decreased to 4.2% (2 of 48), which is similar to the conversion rate in VATS lobectomy for non–small-cell lung cancer at our institution (4.9%) [14]. Kent and coworkers [11] also demonstrated that the mean tumor size in the open group was larger than in the minimally invasive group and reported successful enucleation of tumors up to 8 cm. In our study, most mucosal injuries during enucleation were successfully repaired, and the majority of patients were discharged without complication. However, based on our experience, patients should receive nothing by mouth for an extended time in the presence of postoperative leakage. We also had 1 patient with postoperative leakage after VATS. In this patient, the tumor was located in the left side of the upper third of the esophagus, and the subclavian artery

### Table 2. Clinical Characteristics and Surgical Outcomes According to Surgical Approach in Patients Who Underwent Enucleation Using the Transthoracic Method

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Thoracotomy</th>
<th>VATS</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>79 (100)</td>
<td>16 (20.3)</td>
<td>63 (79.7)</td>
<td>0.389</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper or upper to middle</td>
<td>12 (15.2)</td>
<td>3 (18.8)</td>
<td>9 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Middle or middle to lower</td>
<td>40 (50.6)</td>
<td>8 (50.0)</td>
<td>32 (50.8)</td>
<td></td>
</tr>
<tr>
<td>Lower or lower to EGJ</td>
<td>27 (34.2)</td>
<td>5 (31.3)</td>
<td>22 (34.9)</td>
<td></td>
</tr>
<tr>
<td>Laterality</td>
<td></td>
<td></td>
<td></td>
<td>0.249</td>
</tr>
<tr>
<td>Right</td>
<td>67 (84.8)</td>
<td>12 (75.0)</td>
<td>55 (87.3)</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>12 (15.2)</td>
<td>4 (25.0)</td>
<td>8 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Histologic type</td>
<td></td>
<td></td>
<td></td>
<td>0.315</td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>70 (88.6)</td>
<td>13 (81.3)</td>
<td>57 (90.4)</td>
<td></td>
</tr>
<tr>
<td>GIST</td>
<td>5 (6.3)</td>
<td>2 (12.5)</td>
<td>3 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (5.1)</td>
<td>1 (6.3)</td>
<td>3 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Median tumor size, cm (IQR)</td>
<td>4.5 (3.0–6.5)</td>
<td>6.5 (4.9–7.5)</td>
<td>4.0 (3.0–5.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median operative time, min (IQR)</td>
<td>105 (81–128)</td>
<td>105 (76–134)</td>
<td>105 (85–128)</td>
<td>0.643</td>
</tr>
<tr>
<td>Mucosal injury</td>
<td>15 (19.0)</td>
<td>2 (12.5)</td>
<td>13 (20.6)</td>
<td>0.723</td>
</tr>
<tr>
<td>Postoperative leakage</td>
<td>1 (1.3)</td>
<td>–</td>
<td>1 (1.6)</td>
<td>0.797</td>
</tr>
<tr>
<td>Duration of chest tube placement, median, d (IQR)</td>
<td>3 (2–5)</td>
<td>4 (3–5)</td>
<td>3 (2–5)</td>
<td>0.034</td>
</tr>
<tr>
<td>Median hospital stay, d (IQR)</td>
<td>5 (3–7)</td>
<td>6 (5.3–7)</td>
<td>5 (3–7)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

\( ^a \) Seven patients whose operations were converted to thoracotomies from VATS were included in the VATS group.

EGJ = esophagogastric junction; GIST = gastrointestinal stromal tumor; IQR = interquartile range; VATS = video-assisted thoracic surgery.
and aorta obstructed the surgeon’s field of vision, which made it difficult to repair the mucosa. For most patients, VATS enucleation was feasible; a large tumor itself is not a contraindication for VATS. Ultimately, after considering the size and location of the tumor, an appropriate approach should be selected. Because of the similarities in clinical appearance between esophageal leiomyoma and GIST, tumor resection may be needed to confirm the diagnosis. Likewise, a frozen section was usually unreliable in differentiating GISTs from other types of benign esophageal tumors. Blum and coworkers [3] reported 4 cases of GISTs, which were successfully differentiated from leiomyoma by immunohistochemical evaluation of a fine-needle aspirate obtained during EUS. Guidelines published by the European Society of Gastrointestinal Endoscopy documented that the diagnostic yield of EUS-guided sampling for submucosal tumor was 34% to 90%. However, the impact of EUS-guided fine-needle aspiration on patient management has not been evaluated, and the EUS-guided sampling is not likely to impact management. Therefore, they recommend EUS-guided sampling for patients with unresectable GIST or patients with previous history of malignancy [15], because a preoperative diagnosis would allow presurgical treatment with imatinib if a GIST was confirmed. Thus, routine biopsy is not required but may be helpful in discrete clinical situations such as large tumors of channeling anatomical locations.

One patient with a GIST who had a recurrence was not examined by immunohistochemistry with c-kit at the first operation. Therefore, we concluded that the tumor was some sort of spindle-cell tumor with malignant potential, so we performed a second mass excision when recurrence was detected. After the second operation, the patient was diagnosed with a GIST. Considering the high morbidity associated with esophagectomy, we decided to administer adjuvant imatinib instead of performing an additional operation. However, after adjuvant therapy failed to prevent a second recurrence, we performed an esophagectomy. The remaining 4 patients with GISTs showed no signs of recurrence even after enucleation. Lee and associates [6] showed that tumor recurrence after surgical treatment for GISTs is associated with tumor size and tumor characteristics such as mitotic activity, rather than the surgical therapy selected. Taking into account the incidence of leiomyoma, esophagectomy might be excessive as the initial surgical intervention for esophageal SMTs.

The principle of follow-up after enucleation of esophageal benign tumors has not been established. In cases of GIST, regular follow-up was recommended based on the probability of recurrence. In contrast, recurrence of other types of esophageal SMTs is rarely reported, so it may not be necessary to apply oncologic follow-up for these tumors. Instead, functional outcomes such as reflux should be considered. Kent and associates [11] reported that after enucleation of 20 patients with esophageal SMTs, 5 underwent fundoplication for new-onset or worsening gastro-esophageal reflux during follow-up. In the present study, only 1 patient underwent fundoplication for reflux, because the reflux in the other patients was adequately controlled with proton pump inhibitors. Follow-up esophagography revealed several cases of pseudodiverticulum. We found that the presence of pseudodiverticulum was associated with tumor size and location. The significance of a pseudodiverticulum was not investigated in the current study. However, for patients with large tumors, especially those located in the lower esophagus, the possibility of pseudodiverticulum should be considered.

This study has several limitations. Because our data were retrospectively collected and reviewed, this study has many intrinsic drawbacks. In addition, all trans-abdominal approaches were performed with open techniques because laparoscopic surgical procedures were seldom carried out by the thoracic surgeon at our institution.

In summary, we have shown that enucleation is a sufficient method of surgical management for most esophageal SMTs, and it results in low morbidity. The thoracoscopic approach is also feasible for selected patients and is associated with a shorter hospital stay compared with that for the thoracotomy group. In patients with GISTs, regular follow-up is recommended based on the probability of recurrence. In contrast, oncologic management may not be necessary for leiomyoma because of the very small chance of recurrence, but functional outcomes would be considered during follow-up.

References

INVITED COMMENTARY

The series by Shin and colleagues [1] represents one of the largest reported experiences with video-assisted thoracic surgery (VATS) for esophageal submucosal tumors. In their series, 63 patients underwent VATS, and the results were compared with those in 16 patients treated by thoracotomy. Chest tube duration and length of stay were less in the VATS patients, suggesting that VATS is superior; however, this was not a matched comparison. Not unexpectedly, the tumors treated with thoracotomy were larger. Other studies, such as that by Kent and colleagues (reference 11 in the article), also reported decreased length of stay with VATS, but again their thoracotomy patients had larger tumors.

Conversion rates in the Shin paper decreased with time. Additionally, the authors’ comfort with VATS increased with experience, so that all patients are now offered a VATS approach. Other series have also reported successful resection of larger tumors up to 10 cm in size (reference 12 in the article), confirming the reproducibility of this approach across different centers.

Our own preference has been to use a robotic approach, as described by Cerfolio and colleagues [2]. We believe that it offers additional advantages, which include improved visualization and easier ability to dissect the esophageal tumor from the underlying mucosa and normal esophageal muscle using robotic wristed instrumentation.

It is unlikely that a randomized comparison of VATS with thoracotomy for esophageal smooth muscle tumors will ever be possible, given the relatively small incidence of these lesions and the disparate nature of these approaches. A comparison of robotic resection with VATS, inasmuch as both use minimally invasive techniques, may be more acceptable to patients and is a reasonable question to investigate in the future. The results of studies such as this series by Shin and colleagues support the role of VATS as a standard of care for patients with esophageal submucosal tumors.

Hiran C. Fernando, MD
Cardiothoracic Surgery
Boston Medical Center
88 E. Newton St
Robinson B402
Boston, MA 02118
e-mail: hiran.fernando@bmc.org

References