Editorial

Individualized and Minimally Invasive Surgical Treatment for Esophageal Cancer

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Introduction

Intralumenal endoscopic treatment is an optimal and minimally invasive treatment for superficial esophageal cancer without risk of regional lymph node metastasis. Definitive chemoradiation therapy for potentially resectable esophageal cancer is another hot topic. A randomized control trial (RCT) with definitive chemoradiation and curative esophagectomy for cT1bN0 thoracic esophageal cancer is now ongoing as a study by the Japan Clinical Oncology Group. We must await the final results of this RCT to optimize an initial treatment for cT1bN0 thoracic esophageal cancer.

Radical esophagectomy with extensive lymph node dissection is a basic requirement of curative surgical treatment for esophageal cancer with a potential risk of lymph node metastasis. This procedure is one of the most invasive surgeries in the field of management of gastrointestinal malignancies. Since the mid-1980s, radical esophagectomy with 3-field lymphadenectomy has been established and intensively performed in leading institutes in Japan.[1,2] Although relatively acceptable long-term outcomes have been reported, substantial evidence of survival benefit is not proved by randomized controlled trials. In most Western countries, surgical resection is generally considered to be a part of multimodal approaches for esophageal cancer because of limited local control and high morbidity. Even in Japan, the mortality rate after esophageal surgery is reported in a nationwide survey to reach 3%–4%. On the other hand, the number of poor-risk patients with comorbidity is increasing. To reduce mortality and morbidity rates after radical esophagectomy, the establishment of minimally invasive and individualized surgical approaches is required. In this article, I would like to focus on the surgical approaches to relatively early stage esophageal cancer without indication of endoscopic treatment.

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Introduction of Thoracoscopic Esophagectomy

Since the 1990s, the minimization of surgical invasiveness to reduce postoperative complications has become a major topic in the management of relatively early gastrointestinal cancers. In the field of esophageal surgery, initial challenges were reported in 1993 by Cuschieri[3] and Gossot et al.[4] Since the extent of lymph node dissection performed with thoracoscopy and laparoscopy-assisted esophagectomy also varies among institutes, indication of this procedure is still based on the experience in each institute.[5–7] As with the indications of the procedure, the technical details of the procedures of endosopic esophageal cancer surgery differ among institutes. Several technical options are available, including complete endoscopic approaches, a thoracoscopy-assisted method with minithoracotomy, and hand-assisted thoracoscopic esophagectomy.[8,9] Recently, thoracoscopic esophagectomy by means of a prone position is one of the hot topics in this field.[10] No standard procedure has been established in terms of instruments or positions of the port sites and monitors.

Benefits and Limitations of Thoracoscopic Surgery for Esophageal Cancer

Compared with conventional open surgery, endoscopic surgery for gastrointestinal cancer is reported to have several benefits for patients, including less pain, less inflammatory response, faster recovery of gastrointestinal functions, preserved postoperative immune functions, shorter hospital stay, reduced medical costs, and better quality of life (QOL). Several controversial reports are found on the biological assessment of surgical invasiveness measured by chemical mediators in

thoracoscopic esophagectomy. Preserved postoperative pulmonary functions and a lower incidence of pulmonary complications might be a possible benefit of thoracoscopic esophageal surgery. Preserved functions of respiratory muscles and less pain resulting from the smaller incision may contribute to a faster recovery of vital capacity after surgery.[11,12] Although the initial reports of thoracoscopic esophagectomy failed to show a lower incidence of postoperative complications compared with conventional open surgery, recent reports that have cleared the initial learning phase indicate a lower morbidity in endoscopic surgery.[12,13] A magnified view by endoscope enables us to perform a precise dissection of lymph nodes and to reduce total blood loss. However, no large-scale randomized controlled trial is available to prove these benefits in thoracoscopic esophageal surgery.

On the other hand, the most critical concern for thoracoscopic esophagectomy is surgical curability. Although several reports exist to support its oncological relevance in regard to the long-term outcome of thoracoscopic surgery for esophageal cancer compared with conventional open surgery,[6,13] no randomized controlled trial is available to prove this issue. Several reports demonstrate no difference in the number of harvested lymph nodes between open surgery and endoscopic surgery.[12,13]

A lack of tactile sensation is one of the critical limitations in endoscopic surgery. Bulky tumors and metastatic lymph nodes adjacent to vital organs, such as the trachea, bronchus, and aorta, are not suitable indications of this procedure. Scar formation after neoadjuvant radiotherapy or chemoradiotherapy is also an obstacle to the safe application of endoscopic surgery.

A large surgical invasion of radical esophagectomy is mainly due to the extensive mediastinal lymph node dissection. A reduction of superficial incision by thoracoscopic esophagectomy is insufficient to minimize the surgical invasiveness of the procedure. Modification and individualization of lymph node dissection is a highly important issue in the control of surgical morbidity.

Clinical Significance of Lymphatic Mapping in an Individualized Surgical Approach to Esophageal Cancer

To realize an individualized surgical approach to esophageal cancer, we introduced lymphatic mapping in 1999.[14] The first possible sites of metastasis along the route of lymphatic drainage from the primary lesion are known as sentinel nodes (SNs), and these are detectable by the use of injected dyes or radioactive tracers, or both.[15] We have established the procedure of radio-guided lymphatic mapping for esophageal cancer using 99m-technutium tin colloid and reported the validity of the SN concept in cT1-T2N0 esophageal cancer.[16] Preoperative lymphoscintigraphy after the endoscopic injection of a radioactive tracer into the submucosal layer of the lesion has been found to be very useful in detecting SNs. A handheld gamma probe is used to locate the radioactive nodes. Intraoperative gamma probing is also feasible in thoracoscopic or laparoscopic surgery using a special gamma detector introducible from a trocar port.

In esophageal cancer, SNs are multiple and widely spread from cervical to abdominal areas. In more than 80% of the cases, at least one SN is located in the 2nd or 3rd compartment of regional lymph nodes. This characteristic distribution of SNs is attributed to the multidirectional lymphatic drainage routes from the esophagus.[16]

A complete dissection of multiple and widespread SNs as nodes in a "functional" first compartment of regional lymph nodes is essential and oncologically important. We are currently performing thoracoscopic esophagectomy combined with lymphatic mapping for cT1 or T2N0 esophageal cancer to secure the curability of surgery. If intraoperative pathological and molecular diagnoses focused on harvested SNs show an absence of metastasis, uniform extended lymph node dissection, such as 3-field lymphadenectomy, may be unnecessary.

The incidence of carcinoma of the esophagogastric junction, including Barrett's carcinoma, is increasing in Western countries and more recently Japan, but several surgical approaches to this clinical entity are available.[17] Recently, the long-term outcome of RCT comparing extended transthoracic esophagectomy and transhiatal esophagectomy to adenocarcinoma of the esophagogastric junction has been reported.[18] A lower operative morbidity and shorter hospital stay in the transhiatal group were reported. Although there is no significant difference between overall survival after transthoracic-extended esophagectomy and transhiatal-limited esophagectomy, transthoracic lymph node dissection showed significant survival benefits in a certain subgroup with lymph node metastases from 1 to 8. Therefore an individualized extent of resection and lymph node dissection for Barrett's carcinoma based on lymphatic mapping will become an important topic. If abdominal SNs are all

negative and no hot spot is detected in the mediastinal area by preoperative scintigram, transthoracic extensive lymph node dissection is not required.

An individualized lymph node dissection and esophageal resection based on the distribution and status of SNs will soon become feasible even in an endoscopic setting.[19)]

Conclusions

Although an optimal multimodal approach to esophageal cancer is still under investigation, we must pay attention to the reduction of surgical mortality and morbidity after curative surgery. To develop a minimally invasive and individualized surgical approach to esophageal cancer, we may expect thoracoscopic surgery and lymphatic mapping to be powerful tools. Well-designed clinical trials to develop new evidence that supports these novel technologies are required without delay.

References

1. Akiyama H, Tsurumaru M, Udagawa H, Kajiyama Y. Radical lymph node dissection for cancer of the thoracic esophagus. *Ann Surg* 1994; **220**: 364–73.
2. Ando N, Ozawa S, Kitagawa Y, Shinozawa Y, Kitajima M. Improvement in the results of surgical treatment of advanced squamous esophageal carcinoma during 15 consecutive years. *Ann Surg* 2000; **232:** 225–32.
3. Cuschieri A. Endoscopic subtotal oesophagectomy for cancer using the right thoracoscopic approach. *Surg Oncol* 1993; **2** (Suppl 1): 3–11.
4. Gossot D, Fourquier P, Celerier M. Thoracoscopic esophagectomy: technique and initial results. *Ann Thorac Surg* 1993; **56**: 667–70.
5. Peracchia A, Rosai R, Fumagalli U, Bona S, Chella B. Thoracoscopic dissection of the esophagus for cancer. *Int Surg* 1997; **82**: 1–4.
6. Osugi H, Takemura M, Higashino M, Takada N, Lee S, et al. Video-assisted thoracoscopic esophagectomy and radical lymph node dissection for esophageal cancer. A series of 75 cases. *Surg Endosc* 2002; **16**: 1588–93.
7. Lin TS, Kuo SJ, Lai CY, Chou MC. Combination of video-assisted thoracoscopic surgery and hand-assisted laparoscopic surgery for early cancer of the thoracic esophagus. *Int Surg* 2004; **89**: 131–5.
8. Kawano T, Iwai T. Hand-assisted thoracoscopic esophagectomy using a new supportive approach. *Surg Endosc* 2001; **15**: 330.
9. Suzuki Y, Urashima M, Ishibashi Y, Abo M, Omura N, et al. Hand-assisted laparoscopic and thoracoscopic surgery (HALTS) in radical esophagectomy with three-field lymphadenectomy for thoracic esophageal cancer. *Eur J Surg Oncol* 2005; **31**: 1166–74.
10. Palanivelu C, Prakash A, Senthilkumar R, Senthilnathan P, Parthasarathi R, et al. Minimally invasive esophagectomy: thoracoscopic mobilization of the esophagus and mediastinal lymphadenectomy in prone position—experience of 130 patients. *J Am Coll Surg* 2006; **203**: 7–16.
11. Akaishi T, Kaneda I, Higuchi N, Kuriya Y, Kuramoto J, et al. Thoracoscopic en bloc total esophagectomy with radical mediastinal lymphadenectomy. *J Thorac Cardiovasc Surg* 1996; **112**: 1533–41.
12. Osugi H, Takemura M, Higashimoto M, Takada N, Lee S, et al. A comparison of video-assisted thoracoscopic oesophagectomy and radical lymph node dissection for squamous cell cancer of the esophagus with open operation. *Br J Surg* 2003; **90**: 108–13.
13. Nguyen NT, Roberts P, Follette DM, Rivers R, Wolfe BM. Thoracoscopic and laparoscopic esophagectomy for benign and malignant diseases: lessons learned from 46 consecutive procedures. *J Am Coll Surg* 2003; **197:** 902–13.
14. Kitagawa Y, Fujii H, Mukai M, Kubota T, Ando N, et al. The role of the sentinel lymph node in gastrointestinal cancer. *Surg Clin North Am* 2000; **80**: 1799–809.
15. Morton DL, Wen DR, Wong JH, Economou JS, Cagle LA, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg* 1992; **127**: 392–9.
16. Takeuchi H, Fujii H, Ando N, Ozawa S, Saikawa Y, et al. Validation of radio-guided sentinel lymph node navigation in esophageal cancer. *Ann Surg* 2009. (in press)
17. Vizcaino AP, Moreno V, Lambert R, Parkin DM. Time trends incidence of both major histologic types of esophageal carcinomas in selected countries, 1973-1995. *Int J Cancer* 2002; **99**: 860–8.
18. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg* 2007; **246**: 992–1001.
19. Kitajima M, Kitagawa Y. Surgical treatment of esophageal cancer—the advent of the era of individualization. *N Engl J Med* 2002; **347**: 1705–9.