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Editorial

Minimally Invasive Surgery for Esophageal Cancer in Japan

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Minimally invasive esophagectomy (MIE) has been increasingly performed to treat esophageal cancer since the procedure was first reported by Cuschieri et al. in 1992.[1] In 1996, Akaishi et al. became the first to report performing thoracoscopic esophagectomy and regional lymph node dissection to treat esophageal cancer in Japan.[2] The Japan Study Group for Esophageal Endoscopic Surgery was established in 1998 to discuss and learn endoscopic surgical procedures for esophageal diseases. This editorial describes the history of minimally invasive surgery to treat esophageal cancer in Japan and the achievements of the Japan Study Group for Esophageal Endoscopic Surgery.

History of Minimally Invasive Surgery for Esophageal Cancer

Minimally invasive esophagectomy in the left lateral decubitus position

In Japan, in 1994, Akaishi et al. reported the first case of treatment of esophageal cancer by thoracoscopic esophagectomy and regional lymph node dissection with the patient in the left lateral decubitus position, and, in 1996, Akaishi et al. reported the results of treatment of 39 cases by the same procedure.[2] In their series, six trocars were inserted into the right chest, and the rates of postoperative complication by pneumonia and recurrent laryngeal nerve palsy (RLNP) were 7.7% and 17.9%, respectively. There were no in-hospital deaths within 30 days postoperatively. Akaishi et al. concluded that thoracoscopic mediastinal lymphadenectomy was technically feasible, that its completeness was comparable to that of the open procedure, and that the decrease in pulmonary function was significantly less than the decrease in their previous experience with the open procedure. Their positive clinical results led to the widespread adoption of thoracoscopic esophagectomy throughout Japan. Thoracoscopic esophagectomy has been covered by Japanese National Health Insurance since April 2002, and the numbers of cases treated by thoracoscopic esophagectomy increased from 49 in 1995, to 227 in 2000, 480 in 2005, 1065 in 2010, 1766 in 2015, and 2315 in 2017.[3] In 1999, Kawahara et al. reported applying thoracoscopic esophagectomy to the treatment of 23 patients with intrathoracic esophageal cancer.[4] In their series, six trocars were inserted into the right chest. The rates of postoperative systemic inflammatory response syndrome and RLNP were 0% and 21.7%, respectively, and there were no deaths within 30 days postoperatively. In 2002, Osugi et al. reported applying thoracoscopic esophagectomy to the treatment of 75 patients with intrathoracic esophageal cancer.[5] In their series, four trocars were inserted into the right chest, and a 5-cm mini-thoracotomy was created. The rates of postoperative pneumonia and RLNP in the last 39 of their 75 patients were 5.1% and 15.4%, respectively, and there were no in-hospital deaths. They concluded that the mini-thoracotomy was essential to performing the procedure safely and effectively. All

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three surgeons' groups chose to perform thoracoscopic esophagectomy with the patient in the left lateral decubitus position, the same position as used to perform esophagectomy through a right thoracotomy, because the thoracic anatomy was easily to grasp, and emergency thoracotomy could be performed easily. For some time thereafter, the left lateral decubitus position was adopted to perform thoracoscopic esophagectomy in almost all hospitals in Japan.

Minimally invasive esophagectomy in the prone position

Although in 1994 Cuschieri et al. had reported that 6 of the 26 thoracoscopic esophagectomies in their series had been performed in the prone position,[6] the prone position did not receive much attention until Palanivelu et al.[7] reported their surgical experience with 130 patients in the prone position in 2006. In their series, three trocars were inserted into the right chest, and a flexible upper gastrointestinal endoscope was inserted into the esophagus to lift it as a means of facilitating the dissection. The rates of postoperative pneumonia and RLNP were 1.5% and 1.5%, respectively, and 30-day postoperative mortality was 1.5%. The main advantages of thoracoscopic esophagectomy in the prone position were thought to be a shorter anesthesia time; the use of a single-lumen endotracheal tube to allow intermittent inflation of the right lung; decreased lung injury (lung retraction was avoided) because the lung collapses mostly as a result of the positive pressure pneumothorax and gravity in the prone position; decreased bronchial and tracheal injury; excellent exposure of the operative field; and better ergonomics in terms of the surgeon's stance.

Thoracoscopic esophagectomy in the prone position rapidly became widely adopted in Japan. In 2010, Noshiro et al. reported 43 esophageal cancer cases that had been treated by esophagectomy in the prone position.[8] In their series, four trocars were inserted into the right chest. The rates of postoperative pneumonia and RLNP were 11.6% and 14.0%, respectively, and 30-day postoperative mortality was 2.3%. They concluded that thoracoscopic esophagectomy in the prone position was technically feasible and safe, ergonomically superior for the surgeon, and provided better operative exposure around the left recurrent laryngeal nerve during aggressive esophagectomy. In theory, the surgical outcome of treatment of esophageal cancer by thoracoscopic esophagectomy should be superior when performed with the patient in the prone position than in the lateral decubitus position.[9] The number of thoracoscopic esophagectomy procedures performed in the prone position has increased in Japan, and the percentage of esophagectomies performed in the prone position rose from 11% in 2007 to 75% in 2017.

Minimally invasive esophagectomy by a transmediastinal approach

Transhiatal esophagectomy consists of esophageal mobilization through both the neck and the esophageal hiatus and is considered less invasive than transthoracic esophagectomy (TTE). Mediastinoscopic esophagectomy was developed in an effort to improve the safety of esophageal mobilization, the accuracy of mediastinal lymph node dissection, and the security of the workspace. In 1994, Bumm et al. reported 57 cases of adenocarcinoma of the esophagus treated by mediastinoscopic esophagectomy. The rate of major intraoperative complications in their series was low (5.3%), and the rates of pulmonary complications and recurrent nerve palsy were also low.[10] The 30-day postoperative mortality in their cases was 5.3%.

In Japan, in 2001, Ikeda et al. described a mediastinoscopic esophagectomy procedure in which they created a pneumomediastinum by carbon dioxide insufflation to provide a larger workspace, and they used it to treat six patients with superficial esophageal cancer.[11] There were no postoperative complications, but the mediastinal lymph node dissection was difficult to perform. In 2004, Tangoku et al. reported treating 42 esophageal cancer cases by a mediastinoscopic esophagectomy procedure in which they used a 5-mm-diameter mirror scope attached to a retractor with a transparent flat tip (Subcu-dissector, Endopath Saphenous Vein Harvest Tray; Ethicon Endosurgery), and they succeeded in performing mediastinal lymph node dissections by this method.[12] The rates of postoperative pneumonia and RLNP were 24.4% and 36.6%, respectively, and 30-day postoperative mortality was 2.4%. Fujiwara et al. established a mediastinoscopic esophagectomy with mediastinal lymph node dissection procedure that involved creating a pneumomediastinum, and, in 2017, they reported postoperative results that included a low rate of complication by pneumonia (6.7%) and a high rate of RLNP (33.3%).[13] There were no in-hospital deaths. To reduce the rate of RLNP, they introduced an intraoperative nerve monitoring system to use when performing lymph node dissection around the left recurrent laryngeal nerve. In 1997, Bumm et al. described this method of mediastinoscopic esophagectomy with cervical anastomosis as a

transmediastinal esophagectomy (TME).[14] Although the cost of TME has been covered by Japanese National Health Insurance since April 2018, its adoption in Japanese hospitals has been limited because the technique itself is relatively difficult to perform.

Robot-assisted minimally invasive esophagectomy

In 2002, Melvin et al. reported having performed robot-assisted esophagectomy in a patient with distal esophageal cancer, and no perioperative or long-term complications related to the use of the robotic instruments were identified in their patient.[15] In 2006, Van Hillegersberg et al. reported performing robot-assisted thoracoscopic esophagectomy and mediastinal lymph node dissection in 21 cases of esophageal cancer.[16] In their series, three ports for the robotic instruments and two assistant ports were inserted into the right chest, and 18 (86%) of the 21 procedures were completed thoracoscopically. The rates of postoperative pneumonia and RLNP were 47.6% and 14.3%, respectively. The in-hospital mortality rate was 4.8%, and the deaths were attributable to tracheoesophageal fistulas. They concluded that robot-assisted thoracoscopic esophagectomy was feasible and enabled effective lymphadenectomy with little blood loss, and suggested that standardizing the technique and increased experience would reduce the complication rate.

In Japan, in 2012, Suda et al. reported performing robot-assisted thoracoscopic esophagectomy and mediastinal lymph node dissection to treat 16 esophageal cancer patients.[17] In their series, four ports for robotic instruments and one assistant port were inserted into the right chest. The rates of postoperative pneumonia and RLNP were 6.3% and 56.3%, respectively, and in-hospital mortality was 0%. Robot assistance significantly reduced the incidence of RLNP from 85.0% to 56.3% in addition to reducing ventilator time. They concluded that robot-assisted thoracoscopic esophagectomy with total mediastinal lymphadenectomy was feasible and safe, and was promising as a means of preventing RLNP. Robot-assisted thoracoscopic esophagectomy has been covered by Japanese National Health Insurance since April 2018, and the number of robot-assisted thoracoscopic esophagectomy procedures has gradually been increasing.

In 2003, Horgan et al. reported the first case in which robot-assisted transhiatal esophagectomy with cervical anastomosis was performed to treat a patient with distal esophageal cancer.[18] The robot was used for transhiatal dissection of the middle and lower esophagus. In 2008, Galvani et al. reported the surgical outcomes of 18 patients who were treated by the same procedure, and they concluded that robot-assisted transhiatal esophagectomy is a safe, effective operation that is accompanied by minimal blood loss, minimal respiratory complications, and no hospital mortality.[19]

In 2013, Mori et al. were the first to report the performance of robot-assisted transhiatal esophagectomy in a patient with esophageal cancer in Japan.[20] In their series, three ports for robotic instruments and one assistant port were inserted into the abdomen, and the surgical robot was used for transhiatal dissection of the middle and lower esophagus and lymphadenectomy in the middle mediastinum. In 2016, Mori et al. reported the surgical outcome of 22 patients treated by the same procedure.[21] None of the patients in that series developed pneumonia postoperatively, and the incidences of other major postoperative complications were similar to their incidences in patients who had undergone TTE. Moreover, there was no significant difference between the numbers of mediastinal lymph nodes harvested in the group who underwent robot-assisted transhiatal esophagectomy and in the group who underwent TTE (median, 30 vs. 29). They concluded that robot-assisted transhiatal esophagectomy enables better prevention of pulmonary complications in the management of esophageal cancer. Nakauchi et al. reported performing robot-assisted mediastinoscopic esophagectomy by a newly developed procedure in which they used a robot during both transcervical and transhiatal procedures to treat six patients with esophageal cancer.[22] They concluded that robot-assisted mediastinoscopic esophagectomy was technically feasible and safe, and that using a surgical robot is helpful in overcoming the technical difficulties involved in transcervical middle mediastinal lymph node dissection. Since April 2020, robot-assisted mediastinoscopic esophagectomy has also been covered by Japanese National Health Insurance.

Both the operator requirements and the hospital requirements established by the Japan Society for Endoscopic Surgery should be adhered to in order to ensure the safe introduction and popularization of robot-assisted thoracoscopic esophagectomy in hospitals. Because robot-assisted esophagectomy shows great promise, vigorous research and development of surgical robots is under way.

Achievements of the Japan Study Group for Esophageal Endoscopic Surgery

Because esophageal diseases are less common than other gastrointestinal diseases, most surgeons have little

opportunity to perform esophageal surgery. Surgery for esophageal cancer is one of the most difficult surgeries for gastrointestinal diseases. Since endoscopic surgery is usually more difficult than open surgery, endoscopic surgery for esophageal diseases, especially for esophageal cancer, should be performed by surgeons who are proficient in both esophageal surgery and endoscopic surgery. The existence of a growing need for a study meeting where surgeons could learn endoscopic surgery for esophageal diseases eventually led to the formation of the "Japan Study Group for Esophageal Endoscopic Surgery," whose establishment was initially proposed by Dr. Takashi Akaishi, Dr. Haruhiro Inoue, and myself. The Study Group met for the first time in June 1998. As of December 2019, a total of 43 meetings had been held, and a total of 2996 surgeons had participated. A timely topic related to esophageal endoscopic surgery has been enthusiastically discussed at each meeting.

In anticipation of the Japan Society for Endoscopic Surgery instituting an Endoscopic Surgical Skill Qualification System later in 2004, in July of that year Dr. Masayuki Higashino and I hosted the "Advanced Esophageal Endoscopic Surgery Training Seminar," and an animal model was used for the trainees to learn esophageal endoscopic surgery during the seminar. The training seminar has been held 31 times as of August 2019, and a total of 848 surgeons have had hands-on experience in performing various esophageal surgery procedures on animals. On the first day of the seminar, expert esophageal endoscopic surgeons have delivered lectures on performing thoracoscopic esophagectomy with the patient in the left lateral decubitus position, on thoracoscopic esophagectomy with the patient in the prone position, and on how to practice performing the procedures on animals during the training session. On the second day, the trainees have practiced esophageal endoscopic surgery on pigs that had been placed under general anesthesia. About 95% of the trainees rated the whole seminar as "Good" or "Very Good" in the post-seminar survey.

Surgical training programs use various models, including live animals and human cadavers, to simulate human tissue and anatomy in vivo. Although human cadavers currently represent the model closest to the situation in clinical practice, the cost, limited availability, infection risk, and poor compliance of cadaveric tissue restrict their use.[23] Since the Guidelines for Cadaver Dissection in Education and Research of Clinical Medicine by the Japan Surgical Society and the Japanese Association of Anatomists were published in 2012,[24] the use of cadavers for surgical training has been formally legalized, and the Study Group's surgical training program has begun using human cadavers. This training seminars have been using Thiel-embalmed cadavers, which are soft, flexible, and retain almost natural colors.[23] The training seminars have been held three times as of January 2020, and a total of 42 trainees have practiced esophageal endoscopic surgery on cadavers. An expert esophageal endoscopic surgeon delivered a lecture about TME to the trainees on the first day of the seminar, and the trainees practiced TME on cadavers on the second day. All of the trainees in the third seminar rated the whole seminar as "Good" or "Very Good" in the post-seminar survey. There seems to be a very great need for these seminars, because, for anatomical reasons, trainees can practice TME only on cadavers.

Surveys designed to clarify the status of endoscopic surgery for esophageal diseases in Japan were conducted in 2007, 2012, and 2017, and the results will be published shortly.

Minimally invasive esophagectomy (MIE), including thoracoscopic esophagectomy and TME, is becoming a standard procedure for the treatment of esophageal cancer in Japan. According to a recent review article, the incidences of postoperative complications in the form of pneumonia, arrhythmia, anastomotic leakage, and RLNP are about 10% each.[25] In the near future, we hope to further develop and/or improve the procedures and the instruments used for MIE to enable better long-term survival and lower incidences of postoperative complications.

Disclosure Statement

The author has no conflict of interest to declare.

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