Outcomes, quality of life, and survival after esophagectomy for squamous cell carcinoma: A propensity score–matched comparison of operative approaches

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Background: Minimally invasive esophagectomy (MIE) theoretically offers advantages compared with open esophagectomy (OE). However, the long-term outcomes have not been well studied, especially for esophageal squamous cell carcinoma. We retrospectively compared postoperative outcomes, quality of life (QOL), and survival in a matched population of patients undergoing MIE, with a control (OE) group.

Methods: From May 2004 to August 2013, MIE was performed for a group of 735 patients, which was compared with a group of 652 cases of OE. Eventually, 444 paired cases, matched using propensity-score matching, were selected for further statistical analysis.

Results: Compared with the OE group, the MIE group had shorter operation duration (191 $\pm$ 47 minutes vs 211 $\pm$ 44 minutes, $P < .001$); less blood loss (135 $\pm$ 74 ml vs 163 $\pm$ 84 ml, $P < .001$); similar lymph node harvest (24.1 $\pm$ 6.2 vs 24.3 $\pm$ 6.0, $P = .607$); shorter postoperative hospital stay (11 days [range: 7-90 days] vs 12 days [range: 8-112 days], $P < .001$); fewer major complications (30.4% vs 36.9%, $P = .039$); a lower readmission rate to the intensive-care unit (5.6% vs 9.7%, $P = .023$); and similar perioperative mortality (1.1% vs 2.0%, $P = .281$). At a median follow-up of 27 months, the 2-year overall survival rates in the MIE and OE group were: (1) stage 0 and I: 92% versus 90% ($P = .864$); (2) stage II: 83% versus 82% ($P = .725$); (3) stage III: 59% versus 55% ($P = .592$); (4) stage IV: 43% versus 43% ($P = .802$). The generalized estimating equation analysis showed that MIE had an independently positive impact on patients' postoperative QOL.

Conclusions: In our experience, MIE is a safe and effective procedure for the treatment of esophageal squamous cell carcinoma. It may offer better perioperative outcomes, better postoperative QOL, and equal oncologic survival, compared with OE. (J Thorac Cardiovasc Surg 2015;149:1006-15)

See related commentary on pages 1016-7.

Supplemental material is available online.

Although traditional open esophagectomy (OE) offers a potential cure for esophageal cancer, it is associated with high perioperative morbidity and mortality. Recently, minimally invasive esophagectomy (MIE) has become the recommended approach, popularized in centers with experienced surgeons.[1] Theoretically, MIE offers advantages, compared with conventional OE, and has been preliminarily shown to provide benefits in perioperative outcomes. Nevertheless, the long-term efficacy of MIE compared with OE has not been well studied, especially for esophageal squamous cell carcinoma (ESCC), which is quite different from esophageal adenocarcinoma in terms of area of prevalence, tumor location, biological behavior, and prognosis.

We started our practice of MIE in 2004 and have performed more than 700 such procedures, most of which were for ESCC. Thus, we retrospectively studied postoperative outcomes, quality of life (QOL), and cancer survival in a matched population of patients undergoing MIE, with a control (OE) group.

MATERIALS AND METHODS

Patients

From May 2004 to August 2013, patients with ESCC were enrolled in this study. All patients underwent esophagogastroduodenoscopy and were given a diagnosis of pathologic disease. Imaging examinations, including thoracoabdominal, enhanced computed tomography, cervical ultrasonography, and endoscopic ultrasonography (as well as positron

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Disclosures: Authors have nothing to disclose with regard to commercial support.

Y. Shen contributed equally to this work.

Read at the 94th Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 26-30, 2014.

Received for publication April 24, 2014; revisions received Nov 26, 2014; accepted for publication Dec 25, 2014; available ahead of print March 7, 2015.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.12.063

Abbreviations and Acronyms

cTis = Clinical Trials Information System
cTNM = clinical tumor-node-metastasis
ESCC = esophageal squamous cell carcinoma
MIE = minimally invasive esophagectomy
OE = open esophagectomy
pTNM = pathologic tumor-node-metastasis
QOL = quality of life

emission tomography, if possible), were used to determine the clinical stage.

For patients with cTis 3 N1 M0 or more-advanced disease, neoadjuvant therapy was performed. The treatment was determined by a multidisciplinary team. For patients with a cTis 3 N0 M0 classification (including cases that were down-staged after neoadjuvant therapy), surgery was performed after risk assessment. Patients chose which procedure (MIE or OE) to undergo, during the preoperative interview. The CONSORT (Consolidated Standards of Reporting Trials) flow diagram is shown in Figure 1. The institutional review board of Zhongshan Hospital, Fudan University approved the use of a prospectively maintained database of patients with esophageal carcinoma for this retrospective study (No. 2013154).

Surgical Procedures

Anesthesia and ventilation. All patients received a combination of epidural (0.1875% bupivacaine and morphine) and general anesthesia (inhaled sevoflurane) during the operation. For the OE group, patients were intubated with a left-side double-lumen endotracheal tube and single-lung ventilation. The intraoperative, mechanical ventilation parameters were set to a tidal volume of 8 ml/kg. For the MIE group, intubation and ventilation were the same as in the OE group, early on[2]; later, however, we adopted a single-lumen endotracheal tube and double-lung ventilation with a tidal volume of 6 to 8 ml/kg, which was assisted by an artificial CO_2 pneumothorax at 8 mm Hg.

Surgical position. For the MIE group, initially, patients were placed in the left lateral decubitus position. The surgeon and 2 assistants stood on either side of the patient, and 4 thoracoscopic ports of approximately 0.5 to 1.2 cm were placed on the thoracic cavity. Details are described in our previous publication.[3] Afterward, we adopted the prone position for patients, and then the semiprone position, for better surgical exposure and operative ergonomics. The surgeon and 1 assistant stood on the ventral side of the patient, and 4 ports were used.[2] For the OE group, patients were placed in the left lateral decubitus position.

Operation procedures. In the MIE group, for the majority of cases (in which the tumor was located in the thoracic esophagus), the procedures consisted of the following 3 stages: (1) mobilization of the intrathoracic esophagus and dissection of the intrathoracic lymph node by thoracoscopy; (2) mobilization of the stomach, with dissection of the celiac lymph node via laparotomy (mainly in the early period) or laparoscopy; and (3) resection of the tumor, pulling up of the gastric conduit, and gastroesophageal reconstruction with cervical anastomosis. For the tumors located in the upper esophagus, cervical lymphadenectomy was performed. For the other cases (in which the tumor was located in the abdominal esophagus), the procedures comprised the following 2 stages: (1) mobilization of the stomach, with dissection of the celiac lymph node via laparoscopy; and (2) mobilization of the intrathoracic esophagus and dissection of the intrathoracic lymph node via thoracoscopy, pulling up of the gastric conduit, resection of the tumor, and gastroesophageal reconstruction with intrathoracic anastomosis. Details of the techniques are described elsewhere.[2,4] In the OE group, the procedure involved open Ivor-Lewis esophagectomy and open Ivor-Lewis McKeown esophagectomy.

Mediastinal lymphadenectomy. In the early period (before June 2009), conventional lymphadenectomy was performed for the dissection of the subcarinal and paraesophageal lymph nodes. Later, we added the extensive lymphadenectomy along the bilateral recurrent laryngeal nerves, which had been our regular procedure. Details of the techniques are described elsewhere.[5]

Perioperative management. Milk was administered to patients orally, 6 hours before surgery, which facilitated visualization of the thoracic duct, thereby minimizing the risk of it sustaining iatrogenic injury during MIE.[6] Postoperatively, epidural analgesia was used until the thoracic drainage was removed (within approximately 3-5 days). A feeding jejunostomy was established in all cases, and enteral nutrition was started on postoperative day 1. An examination of the patient's water-soluble swallow was performed on postoperative day 7, before oral feeding was started.

Follow-up

Patients were evaluated at regular intervals: every 3 months in the first year, and every 6 months beginning in the second year. Follow-up investigations included clinical examinations, evaluation of the biochemistry of tumor-marker (carcino-embryonic antigen, squamous cell carcinoma–related antigen, etc) levels, CT scanning of the thorax and abdomen, and gastroendoscopy whenever indicated.

Health-Related Quality-of-Life Assessment

The assessment of health-related QOL was based on a previously validated questionnaire, QLQ-C30 (version 3.0; quality-of-life questionnaire), combined with an esophageal cancer-specific module, QLQ-OES18, which were developed by the European Organization for Research and Treatment of Cancer.[7] That organization's questionnaire includes: 1 global QOL scale; 5 functional scales (physical, role, emotional, cognitive, and social); and 19 symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties, dysphagia, eating, reflux, esophageal pain, swallowing saliva, choking when swallowing, dry mouth, taste problem, coughing and speech problem). After obtaining informed consent from the patients, we asked them to complete the questionnaires, before the operation and at multiple follow-up intervals (1, 3, 6, 12, 18, and 24 months postoperatively), via mail, in-person visit, or outpatient consultation.

Data Collection and Statistical Analysis

Clinical data for all cases were collected from the prospectively maintained database at our institution. The pathologic classification was made according to the Union for International Cancer Control esophageal cancer TNM (tumor-node- metastasis) staging system (6th edition). All collected data were tabulated using Microsoft Excel (Microsoft, Redmond, Wash) for further analysis.

Statistical analyses were performed according to the intent-to-treat principle. To control for potential differences in the characteristics of patients between the 2 groups, the method of propensity-score matching was used. By using a logistic regression model, which included variables such as age, gender, body mass index, Charlson Comorbidity Index, ASA (American Society of Anesthesiologists) grade, tumor location, cTNM (clinical) stage, neoadjuvant therapy, pTNM (pathologic) stage, and historical period of surgery, propensity scores were computed as the conditional probability of receiving cases, via either MIE or OE. Using the nearest neighbor–matching algorithm, we created propensity score–matched pairs without replacement (a 1:1 match). The caliper