An Update on Randomized Clinical Trials in Gastric Cancer

Jennifer Tseng, MD[a,*], Mitchell C. Posner, MD[b,c]

KEYWORDS

• Esophageal cancer • Randomized clinical trial • Surgery • Chemotherapy
• Neoadjuvant therapy • Adjuvant therapy • Lymphadenectomy

KEY POINTS

- There is no difference in oncologic outcomes comparing transhiatal with transthoracic esophagectomy.
- Nasogastric tubes assist in decreasing perioperative complications.
- Preoperative chemotherapy trials are difficult to evaluate because studies have examined squamous cell carcinoma versus adenocarcinoma and inconsistently included gastro-esophageal junction and gastric cardia tumors.
- Standard of care in Europe includes preoperative cisplatin and 5-fluoracil; however, ongoing studies are needed to study the subgroups of patients who benefit most from neoadjuvant chemotherapy.
- Randomized trials of preoperative radiation therapy have not increased resectability rates; a few recent trials show variable results in survival and pathologic complete responses with preoperative chemoradiotherapy.

SURGICAL MANAGEMENT

The surgical approach to esophageal cancer involves either transhiatal or transthoracic esophagectomy. Hulscher and colleagues[1] randomized 220 patients with middle or distal esophageal cancer to either transhiatal or transthoracic esophagectomy. Original results revealed no difference in R0 resection rates, although the lymph node retrieval was significantly higher in the transthoracic group (31 vs 16; $P<.001$).

Disclosures: None.
[a] Department of Surgery, University of Chicago Medicine, 5841 South Maryland Avenue, Room G209, MC 5094, Chicago, IL 60637, USA; [b] Surgical Oncology, Section of General Surgery, Department of Surgery, UCM Comprehensive Cancer Center, University of Chicago Medicine, 5841 South Maryland Avenue, Room G209, MC 5094, Chicago, IL 60637, USA; [c] Department of Radiation and Cellular Oncology, UCM Comprehensive Cancer Center, University of Chicago Medicine, 5841 South Maryland Avenue, Room G209, MC 5094, Chicago, IL 60637, USA
* Corresponding author.
E-mail address: jennifer.tseng@uchospitals.edu

Surg Oncol Clin N Am 26 (2017) 621–645
http://dx.doi.org/10.1016/j.soc.2017.05.003
surgonc.theclinics.com

Postoperative pulmonary complications and hospital duration of stay were higher in patients who underwent transthoracic esophagectomy. However, there were no differences in the perioperative mortality rates. Additionally, there were no differences in local or distant recurrence rates. Five-year survival analysis was comparable (34% and 36%; $P = .71$). Three other phase III trials prospectively examined the outcomes of patients assigned to transhiatal and transthoracic esophagectomy, but no definitive conclusions could be reached owing to small sample sizes.[2–4]

Various reconstructive techniques have been addressed by 3 prospective, randomized, controlled trials. Gupta and colleagues[5] found a lower leak rate of 4.3% versus 20.8% ($P = .03$) and stricture rate of 8.5% versus 29.2% ($P = .02$) after a "novel" hand-sewn esophagogastric anastomosis compared with a standard hand-sewn anastomosis. Bhat and colleagues[6] found the anastomotic leak rate to be dramatically reduced after omental wrap of the esophagogastric anastomosis versus standard anastomosis (3.09% vs 14.43%; $P = .005$). Tabira and colleagues[7] found no difference in anastomotic leak or postoperative nutritional status at 6 and 12 months after use of a slender gastric tube for reconstruction after esophagectomy when compared with a more generous gastric tube. Nederlof and colleagues[8] studied using an end-to-end (ETE) versus an end-to-side (ETS) esophagogastrostomy after esophageal cancer resection. This Dutch trial found the anastomotic stricture rate to be higher with the ETE anastomosis, but that the anastomotic leak rate, pulmonary complications, and duration of hospital stay were greater with an ETS anastomosis.

A number of trials addressed other surgical technique issues. A comparison of the Ivor-Lewis and Sweet esophagectomy techniques was performed for esophageal squamous cell carcinoma in 2015 by Li and colleagues[9] Operative morbidity was higher with the Sweet technique, and Ivor-Lewis esophagectomy led to higher lymph node yield. A small institutional randomized trial also found that in prone versus decubitus positioning for minimally invasive esophagectomy, the prone positioning may decrease surgeon workload and lead to better ergonomic results.[10] A multicenter, open-label, randomized, controlled trial by Biere and colleagues[11] evaluated open esophagectomy versus minimally invasive esophagectomy. Short-term pulmonary complications were better with the minimally invasive technique, suggesting the usefulness of the minimally invasive approach over open esophagectomy in clinical practice and as an area for further research into long-term outcomes.

PERIOPERATIVE OUTCOMES

Shackcloth and colleagues[12] completed a well-planned and executed study addressing the most appropriate use of nasogastric tubes (NGT) in the first 48 hours after esophagectomy. Thirty-four patients were randomized to NGT with continuous sump suction, single-lumen NGT with 4-hourly aspirations, or no NGT. The patients receiving continuous suction via the sump system spent significantly less time with a pH of less than 5.5 than either of the other 2 groups (4.3% vs 39.7% vs 40.3% [$P = .007$]). Patients randomized to no NGT had significantly more pulmonary complications, 7 of 12 versus 4 of 22 ($P = .02$), and required an NGT to be inserted in 7 of 12 cases. This study argues for the use of sump NGT in patients in the immediate perioperative period. A follow-up study by Mistry and colleagues[13] hypothesized that early removal of NGT would not adversely affect major pulmonary complications and anastomotic leak rates. This was confirmed in their single-center, parallel-group, open-label randomized trial of 150 patients.

Other recent trials have focused on perioperative interventions. The safety analysis of the Japan Clinical Oncology Group 9907 trial compared preoperative and