Review

Perioperative Management for the Prevention of Postoperative Pneumonia with Esophageal Surgery

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An esophagectomy, especially for esophageal cancer, is extremely invasive surgery.[1,2] Patients have potential risks of respiratory, cardiovascular, and liver complications and are often quite elderly. Although several new devices for surgery, perioperative management, and some minimally invasive surgeries[3–6] have been developed, an esophagectomy is still frequently accompanied with high risks of morbidity and mortality. The recent development of additional preoperative or postoperative therapy may improve the postoperative survival of esophageal cancer patients, but the risk of postoperative complications increase.[7–13] Once complication occurs, it causes seriously shortened survival after surgery.

Therefore postoperative complications cannot be overlooked. These complications, especially pneumonia, the major respiratory complication, are frequently seen in the postoperative course of an esophagectomy.[14,15]

Early detection and appropriate management for these conditions are important. Prevention is the first line of treatment, but this has not been sufficiently achieved. Preventive protocols are suggested in the Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus, April 2007 edition[16,17]; however, little evidence exists of their efficacy. This article discusses the traditional and recent ideas for the prevention of postoperative complications with a review of the latest literature.

Smoking Cessation

Smoking is a high-risk factor for cardiopulmonary postoperative complications.[18,19] The relative risk of complications after surgery for smokers increases from 1.4-fold to 4.3-fold in comparison to nonsmokers[20–22]; therefore smoking cessation is an effective strategy to prevent postoperative pulmonary complications. A decrease in these complications by smoking cessation is closely associated with physiological improvements in ciliary action, macrophage activity, small airway function, decreases in sputum production, among others. So smoking cessation is encouraged for a certain period prior to surgery. The incidence of postoperative pulmonary complications is 22.0% in current smokers, 12.8% in past smokers, and 4.9% in never smokers, respectively.[23] Barrera et al.[24] evaluated 300 patients who had undergone thoracic surgery and divided them into 4 groups: nonsmokers, past quitters (who stopped smoking > 2 months), recent quitters (who stopped > 1 week and ≤ 2 months) and ongoing smokers. The incidence of postoperative pneumonia was significantly different ($p = 0.04$) between nonsmokers and all smokers in the 4 groups, (3%, 10%, 15%, and 23%, respectively). Thus preoperative smoking cessation is recommended at least 1 month or more before surgery. However, there is no such data concerning esophagectomies.

Preoperative Respiratory Rehabilitation

Preoperative rehabilitation to improve the activity of the respiratory muscles and thoracic compliance is a traditional means for the prevention of postoperative pulmonary complications. It is useful in both cardiothoracic and major abdominal surgery,[25] as well as in radical surgery for thoracic esophageal cancer patients.[26] Randomized controlled trials investigated the efficacy of this physiotherapy.[27–29] Chumillas et al.[28] reported the result of a single blind randomized clinical trial of 81 patients following upper abdominal surgery. The incidence of postoperative pulmonary complication was 7.5% in the rehabilitation group and 19.5% in the control group. There is no direct evidence of efficacy following an esophagectomy, though very few such investigations have been reported.[30]

Preoperative pulmonary rehabilitation is easily performed, so this measure could be recommended.

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Table 1. Incidence of postoperative pneumonia after an esophagectomy with/without steroid

Author	Year	n	Control (%)	Steroid (%)	p value
Shimada et al.[47]	2000	107	40	28	0.14
Sato et al.[48]	2002	66	30	9	0.03
Yano et al.[49]	2005	40	30	15	N.S.
Tsukada et al.[50]	2006	36	27	14	0.62

N.S., not significant.

Oral Care

Ventilator-associated pneumonia is reduced by appropriate oral care.[31–34]

A close relationship exists between the oral environment and pneumonia.[35–37] Dental plaque is a specific reservoir of colonization and can be a cause of subsequent aspiration pneumonia; therefore the colonization of dental plaque is reported as a risk.[38] If patients have pathogenic bacteria in their dental plaque, the risk of postoperative pneumonia rises after an esophagectomy.[39]

Farran et al. reported that the empiric use of antibiotics is not effective. Postoperative pneumonia is reduced only from 19.6% to 12.5% by antibiotics.[40] This is because antibiotics cannot infiltrate into the deep part of the biofilm of dental plaque. Therefore mechanical removal is preferred to reduce the oral bacteria.

The leading cause of postoperative pneumonia other than systemic inflammatory response syndrome (SIRS) in esophageal surgery is thought to be due to mis-swallowing. Recurrent nerve paralysis and subsequent dysfunction of swallowing are frequently observed in the postoperative course of an esophagectomy, and this causes the progression of postoperative pneumonia.[41]

Adopting preoperative oral care is reasonable and effective,[42] but there have been few reports that address this issue.[39]

Steroids

Inflammatory cytokines produced in the midst of surgery play an important role in eliciting a systemic inflammatory response.[43,44] Steroids directly attenuate surgical stress-induced inflammatory responses by suppressing the release of proinflammatory cytokines, such as IL-6. The use of steroids during the perioperative periods of several types of surgery,[45] including an esophagectomy, is effective for blocking this inflammatory cascade and prevention of postoperative complications.[46–50] The influence of steroids on the reduction of inflammatory responses is examined in several reports.[43,46,51–53] These studies evaluate the effectiveness of administration of steroids prior to the surgery, and the results are reviewed in Table 1. Sato et al.[48] reported that steroid use significantly reduces the incidence of postoperative pneumonia ($p = 0.03$). Although other reports have no statistical significance,[47,49,50] their p values are all low.

Furthermore, steroid use is also reported to reduce the duration of SIRS and the risk of organ failure. The Guidelines for Diagnosis and Treatment of Carcinoma of the Esophagus, April 2007 edition,[16,17] recommends steroids for the management of an esophagectomy.

Neutrophil Elastase Inhibitor

A newly developed neutrophil elastase inhibitor (NEI) may be helpful for the prevention of postoperative respiratory complications after an esophagectomy. NEI is a selective inhibitor of neutrophil elastase, and this reagent is often used in severe respiratory conditions, especially in SIRS.

A phase III study was conducted in Japan; it demonstrated that NEI improved pulmonary function and reduced the duration of the patients' ICU stay.[54]

Recently, the efficacy of NEI has been evaluated for the prevention of postoperative pneumonia in a wide variety of surgeries,[55] including esophagectomies.[56,57] Akamoto et al.[58] investigated the postoperative serum levels of several inflammatory cytokines, such as IL-6 and the TH1/Th2 balance. Suda et al.[56] concluded that the duration of postoperative SIRS after esophagectomy, the duration of mechanical ventilation, and the ICU stay were significantly shortened in NEI-treated patients. Ono et al.[57] similarly reported that the preventive administration of NEI could reduce the rate of postoperative SIRS in patients in severe conditions with mechanical ventilation who undergo surgery. There has been no large-scale test to evaluate the effect of NEI for a reduction of the postoperative respiratory complications, but it is a very promising

candidate. Since steroid use is thought to be effective, a comparison between steroids and NEI for the treatment of esophagectomy patients would be of immense interest.

Minimally Invasive Surgical Procedures

Surgical procedures themselves have been reevaluated to reduce postoperative complications. Several less-invasive surgeries, such as a vertical muscle-sparing thoracotomy without a costectomy, have been discussed.[59] These procedures decreased the number of postoperative respiratory complications from 10.5% in a conventional esophagectomy to 1.5%[59] in less-invasive surgery.

On the other hand, the development of scope-guided surgery was first reported by Cuschieri in 1992[60] to have the potential to minimize the invasiveness of esophageal surgery.[61] However, he used this technique in only 5 patients, so it is unclear whether it is truly less invasive.[62]

Others have investigated whether minimally invasive surgery is superior to a conventional open esophagectomy,[63–66] but the latest report indicates[63] that the overall surgical morbidity is not reduced by minimally invasive surgery ($p = 0.156$). Pulmonary morbidity was slightly reduced to 30.9% in minimally invasive surgery, from 38.8% in open surgery, though there was no significant difference ($p = 0.340$). Minimally invasive surgery may have the potential to reduce postoperative complications, and there may be other benefits, such as less blood loss, shortened hospital stay, and preservation of respiratory muscles, though these techniques require further application.[67,68] On the other hand, some problems are associated with these methods. This minimally invasive surgery may limit the quality of lymph node dissection in comparison to a traditional esophagectomy, and the prognosis has been unknown.

Immunonutrition

Nutrition by enteral feeding with additional ingredients, such as arginine, ω-3 fatty acid, and ribonucleic acids, is called immunonutrition. It may be effective to enhance the immune system and reduce the risk of postoperative infection,[69,70] medical costs, postoperative hospital stay,[71–73] and the duration of SIRS.[74] These data imply that an initiation of postoperative pneumonia could be blocked by this modality because the initial aspiration of bacteria in the upper respiratory tract may cause consequent infectious pneumonia.[41]

Adopting immunonutrition for esophageal surgery is promising,[74] but there is no direct evidence that overall infection rates are significantly lower with immunonutrition, and the rates of pneumonia did not differ.[75] It is not known which is best: preoperative or postoperative use of immunonutrition. As a result, the effectiveness of using it for esophageal cancer surgery remains to be elucidated.

Summary

Complications after an esophagectomy are a serious problem. It is important to minimize the risk, but there are few major randomized controlled trials that address the prevention. The efforts must be concentrated not only on improvement of the survival, but also on the prevention of complications.

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