



Expanding indications of minimally invasive esophagectomy in elderly patients

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Esophagectomy has always been associated with a high risk of morbidities. Using the recent definitions reported by the Esophageal Complication Consensus Group (ECCG), the same group published results of >2,700 esophagectomy performed in 24 centers from a newly developed web-based database system (1,2). The overall complication rate was 59.0% and the 30-day mortality was 2.4%. The incidence of complications was much higher than those previously reported in some other national audits, and could be due to a standardized approach to report complications in the most recent report. In addition, 22.2% of the study population was elderly patients (age 70–80: 19.7%; age >80: 2.5%). Given the high complication rate of the procedure, performing esophagectomy on this age group has been a major concern of causing more harm than benefit. A cohort study published in 2013 by Stahl *et al.* demonstrated that increasing age was associated with an increase in mortality, length of stay, discharged to rehabilitative care and cost (3). Using propensity score analysis, mortality was almost double between age above 80 and between 70–79 (8.0% *vs.* 4.2%). Another systematic review and pooled analysis also found that elderly patients undergoing esophagectomy had significantly increased in-hospital mortality, cardiac and pulmonary complications (4). Conventional open esophagectomy was the standard approach of surgery in both studies.

In this issue of the *Annals of Esophagus*, Hol *et al.* presented a retrospective cohort study of minimally invasive esophagectomy in a single high volume center

from the Netherlands focusing on elderly patients more than 70 years old (5). Sixty patients were identified from a 3-year period, and were divided into age ≥ 76 (Group 1: n=19) and age 71–75 (Group 2: n=41). The outcomes were reported according to the ECCG definitions. There was no significant difference identified in the overall incidence of complications (Group 1: 57.9%, Group 2: 65.9%, $P=0.552$), anastomotic leakage (Group 1: 21.1%, Group 2: 14.6%, $P=0.535$) and 90 days mortality (Group 1: 10.5%, Group 2: 4.9%, $P=0.415$). The 1-year survival was 46.2% and 76.2% respectively in Group 1 and Group 2, almost reaching statistical significance ($P=0.075$).

The 90-day mortality of 10.2% in the ≥ 76 years old cohort was high compared to the 71–75 years old group and was also higher than the overall ECCG cohort of 2.1%. The complications were not significantly different between the two groups and were similar to other reported cohorts. Of note, the cardiovascular complication rate was 31.6% in the older age group. These results suggest that while the surgery did not increase the overall complication rate, the elderly patients had poor tolerance to these complications and hence a higher mortality is observed. In addition, deconditioning and nutritional issues after surgery might also explain the higher intermediate term mortality rate. In another recent Dutch multicenter cohort study, the morbidities and mortality were not found to be different for age above or lower than 75 (6). The discrepancy might be due to difference in the selection criteria of surgery between different centers. In both studies, the criteria for operation

among elderly patients were not clearly stated.

Performing esophagectomy with minimally invasive approach could reduce postoperative complications. Multicenter prospective randomized study conducted in Europe demonstrated a reduction in the incidence of pneumonia, as well as a better short-term quality of life scores with thoracoscopic esophagectomy (7). Results from another single center randomized study comparing robotic assisted minimally invasive esophagectomy (RAMIE) and open esophagectomy was recently reported as well (8). There was a significantly lower overall surgery related complications with RAMIE, in particular pulmonary (RR 0.54; 95% CI, 0.34–0.85) and cardiac events (RR 0.47; 95% CI, 0.27–0.83). Similar to the aforementioned study, the quality of life scores at short-term follow-up were significantly better with RAMIE compared with open esophagectomy.

Prospective randomized studies were conducted mostly in high volume expert centers by experienced surgeons with strict inclusion and exclusion criteria, results of which may not be replicable in real clinical settings. Utilizing Japanese National Clinical Database, Yoshida *et al.* reported results comparing 12,711 MIE and 11,512 open esophagectomy, with the aim of recruiting cases in daily clinical practice (9). In the study, MIE was associated with a significant reduction in pulmonary morbidities, sepsis and the need for blood transfusion. In addition, the in-hospital mortality rate was also significantly lower in the MIE group. These findings provide further proof that short-term outcomes with minimally invasive esophagectomy is significantly better than that of open esophagectomy. The authors from this large national cohort study also conducted multivariate analysis for risk factors of surgery related mortality. Increasing age was identified as an independent risk factor, among other factors including low activity of daily living, diabetes mellitus on insulin, chronic obstructive pulmonary disease, congestive heart failure and chronic renal impairment (Creatinine >1.2 mg/dL). Comparing with baseline age of <59, patients of age 75–79 and >80 had odds ratio of 4.78 and 5.27 respectively for surgery related mortality. However, the proportion of patients at these extreme age groups were not described in the study. While minimally invasive esophagectomy may reduce the incidence of postoperative complications, careful selection and risk stratification are still required to achieve good clinical outcomes for patients of advanced age.

In recent decade, frailty, defined as an age-related cumulative decline in multiple physiological systems, was

identified a better predictor of mortality and morbidity than chronological age. In addition to the original model proposed by Fried *et al.*, multiple scales were proposed to quantify the degree of frailty among elderly patients (10). Numerous studies have been published in the last 5 years using frailty as a surgical risk predictor of general surgical, colorectal, vascular and cardiac surgeries (11). In a retrospective study, assessment of the modified frailty index in predicting the surgical outcomes of esophagectomy was performed using data of 2,095 patients from an U.S. national database (12). The odds ratio of mortality for frail patients was 31.84, and the odds ratio for elderly was 1.05. In the elderly patients, the frailty index could be a useful way of predicting surgical mortality and selecting patients for surgery. Optimizing nutritional status in the elderly may also be beneficial in reducing surgical morbidity. A study is being conducted at the Memorial Sloan-Kettering Cancer Center examining the use of a nutritional algorithm with objective guidelines for nutritional counseling and feeding tube placement for patients ≥ 65 years old receiving chemoradiotherapy for locally advanced esophageal cancer (NCT02027948). A structured nutritional therapy as such could also be applied in the surgical patients in order to achieve satisfactory surgical outcomes.

In summary, surgical mortality has been much decreased after esophagectomy in recent decades, with the use of minimally invasive techniques and improvement in perioperative care. Esophagectomy in the elderly patients particularly those >75 years is not absolutely contraindicated, but careful case selection is mandatory to achieve satisfactory clinical outcomes after surgery.

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aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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