Editorial

Editorial on "Complications after esophagectomy are associated with extremes of body mass index"

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Comment on: Mitzman B, Schipper PH, Edwards MA, *et al.* Complications After Esophagectomy Are Associated With Extremes of Body Mass Index. Ann Thorac Surg 2018;106:973-80.

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There is overwhelming evidence that obesity has become a public health epidemic, with more than one third of American adults classified as obese (1). While many have demonstrated that obesity is a risk factor for a variety of disease processes, including hypertension, diabetes mellitus, obstructive sleep apnea, and cardiovascular disease, there is increasing awareness that obesity may play a role in complications following surgery (2-4). When compared to normal weight patients, those who are classified as overweight or obese have been shown to be at increased risk of several adverse events in the postoperative setting, including infections, deep venous thrombosis, cardiovascular events, pneumonia, increased length of intensive care unit and hospital stays, and postoperative mortality (5).

Despite advances in the treatment of esophageal carcinoma, this disease continues to be a leading cause of cancer-related death in the United States. In those with limited disease, esophageal resection is a mainstay to cure. While innovations in surgical approaches have been integrated into the armamentarium of the practicing thoracic surgeon, esophagectomy remains a procedure associated with significant operative morbidity and mortality. Though the relationship between body mass index (BMI) and postoperative outcomes has been demonstrated in the setting of other oncologic resections, the effect of obesity following esophagectomy has been less clear. Similar to many abdominal operations, some authors have suggested that esophagectomy is associated with increased risk in obese populations, while other authors have failed to demonstrate worse outcomes or, rather, have reported an "obesity paradox" in which mildly overweight patients experience some benefit compared to their underweight or morbidly obese counterparts (6-11). In their retrospective review of over 9,000 patients from the Society of Thoracic Surgeons (STS) General Thoracic Surgery Database, Mitzman *et al.* conclude that complications following esophagectomy are associated with extremes of BMI, namely underweight and class III obesity (12).

The authors performed a retrospective analysis using the STS General Thoracic Surgery Database, and obtained the records for patients who underwent elective esophagectomy for cancer between 2009 and 2016. They identified 9,389 patients who met inclusion criteria and postoperative complications and death, defined as during hospitalization or within 30 days of operation, were examined. The cohort was categorized according to BMI as follows: underweight (2.8%, n=261), normal (31.8%, n=2,984), overweight (36.2%, n=3,399), class I obesity (18.9%, n=1,775), class II obesity (7.0%, n=659), and class III obesity (3.3%, n=311). Surgical approaches were defined as either open or minimally invasive transhiatal, three hole, or Ivor Lewis esophagectomy, and did not differ across BMI categories. Histopathology, however, differed across BMI categories (P<0.0001), with squamous cell carcinoma (SCC) more prevalent among Underweight patients, while adenocarcinoma was more common in other BMI

categories, pointing to the unique disease etiologies of SCC versus adenocarcinoma, with the former associated with smoking and alcohol, and the latter with obesity and gastroesophageal reflux disease. In their analyses, BMI was evaluated as both a categorical and continuous variable.

Operative duration differed among BMI categories (P<0.0001), with class III obesity patients spending an average of 45 minutes longer in the operating room. Hospital length of stay (P<0.0001) was longest among underweight and class III obesity patients. The highest rate of 30-day readmissions was also seen in those categorized with class III obesity at 18% (P=0.0294). The incidence of any major postoperative event was 32.5%. Multivariate analysis revealed that among underweight patients, infectious (P=0.016) and other (P=0.005) complications were found to be more prevalent in multivariate analysis, while pulmonary (P=0.0021), cardiovascular (P=0.0236), thromboembolic (P=0.045), and infectious (P=0.015) complications were common among class III obesity patients. Cardiovascular (P<0.0001) and thromboembolic (P=0.013) events were associated with any BMI increase above overweight. When evaluating BMI as a continuous variable, those with BMI's less than normal were found to be at an increased risk of all complications analyzed.

The authors concluded that BMI is associated with postoperative complications following esophagectomy for esophageal carcinoma. Mitzman and colleagues demonstrated increased risk of adverse events in populations with BMI classification of both underweight as well as class III obesity. They additionally observed an "obesity paradox" in mildly overweight patients who experienced better perioperative outcomes as compared to other patients in the study cohort; this finding appears to be consistent in the literature. Similar results suggestive of this relationship were observed in sizeable cohort of non-small cell lung cancer patients undergoing surgical resection (11). Perhaps, it should not be referred to as "paradox" anymore.

While the authors addressed the differences in histological classification between BMI categories, with SCC more prevalent among underweight individuals while those with higher BMI were more likely to have adenocarcinoma, the authors did not specifically address differences in clinical stage among BMI categories (P<0.0001). Clinical stage I disease was more common in those categorized as having class II or III obesity (22.0% and 22.5%, respectively), while stage III disease was most common among underweight and normal BMI populations (37.9% and 38.7%, respectively). Consistent with the current investigation, prior authors have also described differences in sarcopenia based upon histologic type (7,8,13). It is possible, therefore, that interactions exist between BMI, clinical stage, and histology in the present investigation, which may, at least in part, account for differences in postoperative complications.

Although there are limitations of this study attributable to its retrospective nature, use of BMI as an imperfect surrogate for overall body composition, possible BMI migration prior to resection, and incomplete knowledge in the timing of BMI measurements with respect to neoadjuvant therapies and surgical date, the value of this investigation should not be understated. By using the STS General Thoracic Surgery Database, the authors were able to assemble the largest cohort to date, evaluated across multiple regions and practices, to definitively determine the effects of BMI on postoperative outcomes following esophagectomy. Because of this respectable study population, Mitzman and colleagues were able to evaluate outcomes across BMI categories, which has been a limitation of prior investigations. Furthermore, perhaps most unique to this study is the authors' ability to provide evidence for poorer outcomes in underweight populations following esophageal resection. Prior investigations were underpowered to allow for adequate evaluation of this population of patients.

However, the authors' conclusion and suggestion for "pre-habilitation regimen prior to esophagectomy" will require further study. Effecting change in body weight and composition is generally difficult for most healthy people, let alone for patients dealing with a cancer diagnosis. Whether BMI could be meaningfully adjusted respective to timing of esophagectomy remains to be seen. Likewise, we will need to identify other nutritional or other biomarkers associated with BMI, which could serve as surrogates of BMI in pre-habilitation success prior to esophagectomy.

In conclusion, by capitalizing on the large scale population data available in the STS database, Mitzman and colleagues present a thorough investigation detailing increased risk for a variety of postoperative adverse events in those with a BMI classification of underweight or class III obesity. Consistent with some prior investigations, the current study highlights both higher complications in the extremes of BMI as well as protective effect in mildly overweight patients. Future investigations should be aimed at methods to best optimize patients to reduce the morbidity associated with esophageal resection. The study of endocrine, inflammatory, and other molecular pathways

among various BMI groups is also warrantied to improve our understanding of varied perioperative risks based on BMI.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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