Editorial Commentary

Hybrid esophagectomy: the best of both worlds

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In the study entitled "*Hybrid minimally invasive esophagectomy for esophageal cancer*", Mariette *et al.* report the results of a multi-institution randomized controlled trial comparing open Ivor-Lewis esophagectomy to a hybrid approach (laparoscopic abdominal mobilization and right thoracotomy) from the standpoint of postoperative complications. Overall, 207 patients were randomized on an intention to treat basis, with 104 and 103 patients assigned to the open and hybrid groups respectively. The primary endpoint was the rate of major intra-operative complications or postoperative complications within 30 days. Major complications were defined, rather liberally as Clavien-Dindo (CD) grade 2 or more. Secondary outcomes assessed included 30-day mortality, 30-day overall complication rate (minor and major), major pulmonary complication rate at 30 days and overall and disease free survival (1).

Patients who underwent an open approach experienced a roughly 2-fold increase in major complications at 30 days (64% *vs.* 36%). This difference was predominantly driven by grade 2 complications of which the bulk was related to excess sputum and atelectasis necessitating bronchoscopy, and to a lesser extent pneumonia. Along these lines, no difference in CD 3 or 4 complications was observed between the two groups. Similarly, there was no difference in intensive care unit (ICU) admission rates or hospital length of stay (LOS). Conversely, there was an increase in minor (grade 1) complications in the hybrid group compared to the open surgery group (1).

Esophagectomy is a complex operation with significant morbidity and mortality. Approximately 50% of patients who die in the postoperative period do so as a result of pulmonary complications (2,3). Accordingly, minimally invasive techniques have been increasingly adopted in an attempt to minimize postoperative complications; minimally invasive esophagectomy (MIE) has demonstrated fewer postoperative complications (2-4). This being said, its implementation is associated with a significant learning curve potentially limiting its widespread adoption. It has been estimated that 119 cases are necessary to reach proficiency and during early experience, morbidity may be increased (3). Hybrid esophagectomy, wherein gastric mobilization and lymphadenectomy are performed laparoscopically followed by standard open right thoracotomy is a procedure that appears to demonstrate similar outcomes. Furthermore, the learning curve is significantly shorter, with 25 laparoscopic gastric mobilizations required to reach proficiency, thus significantly increasing the potential for adoption (3). Accordingly, a comparative study of a completely open approach to a hybrid approach is warranted.

From the standpoint of the primary endpoint, the results of the present study clearly demonstrate superiority of a less invasive approach over a more invasive one. The robust methodology, wherein only experienced surgeons at high volume centres were able to enroll patients ensured that complications were predominantly related to surgical approach as opposed to effects of a learning curve. This feature is further supported by the lack of any institutional differences related to the outcomes measured. Combining this with the randomized nature in a large cohort of patients

further cements the superiority of a hybrid approach over an open one from the standpoint of surgical morbidity. Furthermore, these results are in keeping with the findings of the TIME trial, wherein patients were randomized to open esophagectomy compared to a completely minimally invasive approach (laparoscopic and thoracoscopic) (2). Therein, a near three fold reduction in pulmonary complications was observed. In the present study, the increased rate of atelectasis necessitating bronchoscopy in the open group supports the hypothesis that avoidance of an upper midline incision reduces splinting thus improving clearance of secretions. This being said, it is important to note that bronchoscopy is a somewhat subjective indicator of morbidity given that its implementation varies widely among surgeons, at whose discretion the procedure is performed. This is particularly true since the adoption of enhanced recovery pathways following esophagectomy, wherein patient care pathways vary widely among institutions (5,6). Nonetheless, this study further corroborates the seemingly intuitive benefit of minimizing surgical trauma (1).

Three major findings in the present study warrant further analysis. First, no difference in LOS was observed between the two groups in contrast to the bulk of studies to date, diminishing the impact of reduced morbidity with a hybrid approach (7-9). This, coupled with the generous inclusion of CD 2 complications as major, suggests that grouping of complications was skewed towards producing a result excessively against an open approach. Second, while 90-day mortality was included in the present study, no data regarding readmission rates were reported. Third, the survival data presented, although not significant from a statistical standpoint appears to suggest a benefit, both with respect to overall and disease free survival.

With respect to the first finding, that complications were grouped with a skew towards a dramatic result, it is true. Grade 2 complications in addition to bronchoscopy drove the difference between major and minor complications in favour of hybrid esophagectomy. However, minor (grade 1) complications were increased in the hybrid group. This was concurrent with a reduction in grade 2 complications suggesting that migration of some grade 2 to grade 1 complications occurred. This suggests that while complications in this complex operation are common, their severity can be mitigated by employing a hybrid approach. This being said, one would not expect diminished rates of grade 3 or 4 complications following adoption of a less invasive approach. These are largely related to anastomotic complications which appear to be unaffected by surgical approach and likely explain the lack of a difference in ICU admission rates. In the meta-analysis by Yibulayin *et al*, a minimally invasive approach was strongly associated with reduced overall and pulmonary complication rates [odds ratio (OR) 0.7, P<0.05; OR 0.527, P<0.05; respectively] (10). Conversely, no difference in anastomotic leak rate was observed when employing a MIE over an open Ivor-Lewis esophagectomy (OR 1.02, P=0.785) (10). Thus, a reduction in surgical trauma reduces its associated complications without affecting more severe anastomotic or deep organ space infections.

While the grouping of grade 2 complications as severe is somewhat disingenuous, these complications, encompassing urinary tract infections, pneumonia and surgical site infections have been shown to drive readmission rates in US hospitals (7,8). In addition, they have been shown to drive increases in LOS. However, LOS was not different among groups in the present study. Although LOS may be used a surrogate for complication rates in population based studies, this may not be applicable in this study population. Centres who enrolled patients in the study demonstrated proficiency in caring for patients post-esophagectomy. High volume centres are associated with improved outcomes in part due to early recognition and prompt treatment of post-operative complications (9). Coupled with a relatively long median LOS of 14 days compared to the US average of 9, patients who developed complications may have been recognized relatively early and promptly treated mitigating their impact on the LOS variable in the study (5,7). A more robust measure for the morbidity related to the procedure could have been gleaned from an examination of readmission rates. According to NSQIP data, readmission occurs in approximately 10% of patients within 30 days (7). The majority of patients develop complications 7 days post discharge, outside the LOS window defied in the study (7). Furthermore, these complications are predominantly infectious in nature comprising pneumonia and wound infections in nearly 1/3 of patients (7). Given the data shown, one would expect a lower readmission rate in patients with fewer pulmonary complications, which would further support the adoption of a hybrid approach.

Finally, the study was not powered to detect a survival difference. Accordingly, decisive conclusions regarding the oncologic efficacy of a hybrid compared to an open approach cannot be drawn. Lymph node retrieval (median 22 in both groups) and R0 resection rates were comparable between the two groups, a finding that has

been corroborated in the TIME trial and meta-analyses (2,10). This being said, the study did not demonstrate an overt increase in cancer specific mortality nor a decrease in disease specific survival. Median survival was on the order of 50 months in both groups. Furthermore, 3- and 5-year overall survival were a very respectable 67% and 60% in the hybrid group and 55% and 40% in the open group respectively. This difference did not reach statistical significance. However, the excellent survival likely attests to the surgical quality provided due to the criteria for enrolment of patients; namely high surgical volume and thus experience in caring for patients with esophageal cancer. This single feature certainly plays a significant role in the excellent outcomes reported herein and is a testament to the importance of regionalization for this complex disease (9).

Acknowledgments

None

Footnote

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

Ethical Statement: The authors are accountable for all 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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