

EN BLOC ESOPHAGECTOMY REDUCES LOCAL RECURRENCE AND IMPROVES SURVIVAL COMPARED WITH TRANSHIATAL RESECTION AFTER NEOADJUVANT THERAPY FOR ESOPHAGEAL ADENOCARCINOMA

To the Editor:

Dr Rizzetto and colleagues¹ concluded from their retrospective review of 58 patients that en bloc esophagectomy is the surgical treatment of choice for adenocarcinoma after neoadjuvant therapy. We, however, interpret this strong statement with a degree of reservations. A larger prospective study involving 151 patients (of which 116 had adenocarcinoma) has previously demonstrated no significant difference in recurrence and survival between en bloc transthoracic and transhiatal approaches.² The discrepancy of result could be due to several reasons.

The authors emphasized that despite a higher age and comorbidity profiles in the transhiatal arm, deaths in this group of patients were all cancer-related but one. However, surgical complication, particularly pulmonary infection, is an independent factor associated with poor survival.³ Older patients with more comorbidities are inevitably more predisposed to pulmonary complications. This factor, together with other functional and nutritional variables such as preoperative albumin level, weight loss, pulmo-

nary functions, and performance status, could have skewed the survival analysis. We feel that by including indices of tumor aggressiveness such as differentiation, lymphovascular and perineural invasion status, and the aforementioned functional and nutritional parameters, a multivariate Cox regression analysis is a more accurate means of determining the real impact of each surgical approach.

Lymph node yield from transhiatal resections is significantly lower than that from transthoracic en bloc resections. The relatively higher proportion of complete pathologic response in the transhiatal group (39% vs 25%) could have been incorrectly overestimated secondary to fewer lymph nodes retrieved. This is reflected in the higher proportion of patients with stage III disease in the en bloc group (37.5% vs 27.8%). The underestimation of patients with residual disease in the transhiatal group could have led to the marked difference of 5-year survival observed between the 2 groups.

We feel that more attention must be paid to interpreting this study and that younger and more medically fit patients might benefit from more aggressive en bloc resection; transhiatal approach does not necessarily account for worse oncologic outcomes among older patients with more comorbidities. If en bloc resection is preferred based on its more extensive oncologic dissection, we would be interested in the authors' views on 3-field lymphadenectomy, given the prevalence of positive cervical nodes shown to be as high as 24%.⁴

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Reply to the Editor:

We appreciate the questions and comments by Drs Chang and McAnena in regards to our study, which demonstrated significantly improved survival after neoadjuvant therapy with an en bloc esophagectomy compared with a transhiatal resection.¹ Regarding the nonrandomized study by Morgan et al that failed to show a difference between a transthoracic and transhiatal resection after neoadjuvant therapy, there are several points that bear mentioning.² First, in contrast to our study, their population was mixed adenocarcinoma and squamous cell cancer. Furthermore, although we reported a significantly greater number of nodes resected with the en bloc resection (median 29.5 versus 19 in the transhiatal group), Morgan et al inexplicably reported a median of 13 resected nodes with each procedure. Last, although our results with transhiatal resection mirror reports from other centers, their results were unusual. They reported a local recurrence rate of 6% and 5-year survival of 53% after neoadjuvant therapy and transhiatal resection compared with 17% and 22% in our study and 19% and 20%, respectively, in the randomized University of Michigan trial.³ These differences are difficult to explain but may represent significant selection bias in the study by Morgan et al and also indicate that although the incision may be

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similar, all transthoracic esophagectomies are not equal.

Drs Chang and McAnena also reference a report by Kinugasa et al and raise the concern that pulmonary complications may have adversely impacted long-term survival in the transhiatal group in our study.⁴ It is important to recognize that all patients in the study by Kinugasa et al had squamous cell cancer, and many had 3-field lymph node dissections. Pulmonary dysfunction is more likely in patients with squamous cancer and a significant smoking history, and recurrent laryngeal nerve palsy is more common after a 3-field dissection than after our 2-field lymphadenectomy. Nonetheless, pulmonary complications are known to be more common after transthoracic esophagectomy, so this is unlikely to be the cause of the worse survival in the transhiatal group. We recognize that patients who had a transhiatal resection were older and had more comorbidities, and consequently, we analyzed disease-specific survival for both groups and showed that the difference in favor of the en bloc resection was even more striking. Because all patients had advanced disease based on preoperative clinical staging and many had residual disease after therapy, we do not believe that a Cox analysis of relatively minor factors such as lymphovascular invasion and tumor differentiation would alter or add to the very clear findings in favor of an en bloc resection in our data.

We agree that stage migration likely explains some of the difference in survival that we found in the group of patients with complete pathologic response in favor of the en bloc resection group. However, the concern of stage migration is precisely why our finding of significantly improved survival in patients with residual disease after en bloc resection is so important, because stage migration is not possible in these patients: they all had residual disease, and survival in these patients is known to be poor. In our opinion,

there is no valid explanation for the difference in survival we report other than the type of resection and, in particular, the reduced incidence of local-regional recurrence after the en bloc technique. It is likely that even in patients thought to have complete pathologic response, the en bloc resection provides a survival advantage by the removal of micrometastatic disease that would otherwise be left behind with a transhiatal resection. The “underestimation of residual disease” only applies to the group with supposed complete pathologic response, and, importantly, this is the only group without a significant improvement in survival with the en bloc procedure. When residual disease was present, and therefore not underestimated, the patients who had en bloc resection had a significant survival advantage over those who had transhiatal resection. If Drs Chang and McAnena are implying that the disease is underestimated even in this group of patients who had a transhiatal resection, that may well be true, but that is also the point: residual disease needs to be removed to provide patients with a survival advantage, and the en bloc esophagectomy is the best procedure to accomplish this objective.

We recognize that some centers have reported a high prevalence of upper mediastinal and cervical nodal disease even with distal esophageal adenocarcinomas, but this has not been our experience. Our preference is to carefully watch these areas with serial computed tomography and positron emission tomography scans and to reoperate when necessary for nodal recurrence. It has not been our experience that the failure rate for localized nodal recurrence in these areas is high enough to justify the added morbidity of a 3-field dissection in everyone.

On a last note, we ask that readers keep an open mind about the possibility, or perhaps probability, that the type of resection does impact survival for patients with esophageal cancer and consider doing a thorough node

dissection in the chest and abdomen for all patients, including those who have had neoadjuvant therapy. After all, local control is what we as surgeons provide to patients with esophageal cancer, and the evidence is becoming irrefutable that this is best accomplished with a transthoracic en bloc esophagectomy.

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REMEDIASTINOSCOPY: A STATISTICAL REINTERPRETATION To the Editor:

We read with considerable interest the study by Marra and colleagues¹ in the April 2008 issue, “Remediastinoscopy in Restaging of Lung Cancer After Induction Therapy.” We do, however, have some issues with the statistical interpretation of their results.

First, there is the reporting of a *P* value of 0.0000 in their Table 2.¹ A *P* value is the probability of observing the value or more extreme values given that the null hypothesis is true (ie, no true difference). Marra and colleagues¹ give this as 0, which is not