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

possible, when what they mean is that the probability (P value) is less than .0001. They do not state in the table to what test or null hypothesis the P value refers, so it is not possible for the reader to interpret the statistical significance.

Second, Marra and colleagues¹ report that remediastinoscopy is associated with 100% specificity. That in itself is to be expected, simply because for the vast majority of tests (endobronchial ultrasonography included) performed with diagnostic biopsy, when tumor is seen in a biopsy specimen, it is invariably confirmed on the reference test (there would be serious problems if tumor diagnosed on the index test proved to be normal on the reference test). Therefore specificity (ability to rule in disease) is not the major focus for surgeons when evaluating remediastinoscopy for restaging the mediastinum. The same specificity will be obtained with any other tests combined with tissue biopsy, such as endobronchial ultrasonography (as referenced by Marra and colleagues¹).

Third, what is critical is sensitivity (the ability to rule out disease), so that patients with residual N2 disease are not brought to operation mistakenly, and the reported sensitivity for remediastinoscopy was 61%. It is important for readers to bear in mind that sensitivity truly starts at 50% (a test with no sensitivity, or equipoise), not 0%. Marra and colleagues¹ do not report a confidence interval for this estimate; when one is calculated, it ranges from 42% to 77%. That is, it crosses 50%. This low value of sensitivity is entirely in keeping with the previous literature on remediastinoscopy. De Leyn and associates² attributed this to the technical difficulty in obtaining adequate biopsy specimens from the areas of previous lymph node involvement.

Fourth, Marra and colleagues¹ have used their own arbitrary definition of "diagnostic accuracy," which includes (see footnote in their Table 3) in the denominator "no biopsy." This does not

comply with current Standards for Reporting of Diagnostic Accuracy (STARD).³ The importance of STARD was previously highlighted by Eugene Blackstone⁴ in this Journal in 2004. We believe that compliance with STARD is crucial for readers (which is why it is part of this Journal's policy), and we are surprised that a non-STARD compliant article was highlighted for continuing medical education credit.

On the basis of these findings, we believe that the conclusion that "remediastinoscopy provides a histologic proof of mediastinal downstaging with high diagnostic accuracy" cannot be sustained by the results presented by Marra and colleagues.¹ The results do indicate that residual disease can be ruled in with repeated mediastinoscopy, but the procedure is unable to rule out residual mediastinal disease with any degree of certainty (sensitivity of 61%, 95% confidence interval 42%–77%). Futile thoracotomy thus would not be avoided for a large proportion of patients were this technique used to restage the mediastinum after induction chemotherapy.

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Reply to the Editor:

We thank Drs Lim and Dusmet for their comments. We would like to answer some issues they addressed in the statistical analysis of our article.

As concerns the need to report specificity, competing methods for mediastinal restaging are of noninvasive (positron emission tomography, integrated positron emission tomography and computed tomography), or invasive (endoesophageal ultrasonography with fine-needle aspiration biopsy, endobronchial ultrasonography with transbronchial needle aspiration, remediastinoscopy) nature. Noninvasive methods do not provide histologic proof of their positive findings, so specificity varies to a high of 90% (and thus is lower than 100%). Invasive methods are able to provide a histologic or cytologic biopsy specimen of lymph nodes. In the first case, specificity is as high as 100%; in the second, however, cytologic examination may yield false-positive findings. In a review of the literature on cytologic study in pulmonary medicine, Policarpo-Nicolas and Wick¹ reported overall sensitivity and specificity values ranging from 60% to 96%, even in the most conscientious laboratories and considering the increased confidence of pathologists in cytomorphologic diagnosis.

The reported value of sensitivity of 61% in our series is consistent with the previous literature on remediastinoscopy (70%–83%), if slightly lower, with the exception of the study of De Leyn and colleagues,² who reported a disappointing 29% sensitivity in a small series of patients. That report was heavily biased by the inadequate reexploration of the subcarinal station in two thirds of cases (in which persistent nodal disease was found in 50% of cases at thoracotomy) and thus cannot be cited as a standard reference for the diagnostic value of remediastinoscopy. In most cases, sensitivity values of remediastinoscopy are comparable to or higher than those of the other methods for mediastinal restaging.