Authors have nothing to disclose with regard to commercial support.

on vein graft integrity has been demonstrated previously by our group, and we reported a technique that preserves endothelial and media viability.³ The SV is harvested with a no-touch technique but without surrounding soft tissue, and overdilation is avoided by connecting the SV to the arterial cannula and allows the vein to distend at the patient's own arterial pressure.

In a recent randomized study of on- versus off-pump coronary surgery where a no-touch technique was used without the surrounding pedicle tissue, we reported a SV patency rate of 89% at 8 years' follow-up.⁵ We also found that by using this approach, long-term survival was similar in patients receiving SV or radial artery in the context of bilateral internal thoracic artery grafting.¹ In conclusion, although every effort should be made to avoid SV damage and overdilation during harvesting, the role of no-touch technique and surrounding soft tissue still needs to be clarified. Despite preliminary promising data, this technique currently remains largely underused because of the potentially increased risk of surgical-site infection in the leg. A randomized clinical trial investigating the effect of pressure distention and no-touch soft tissue pedicle harvesting on SV on medial-intimal proliferation at 1-year follow up using intravascular ultrasound has just been completed in our institution, and it is expected to report in the next few months.

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MANAGEMENT OF N2 NON-SMALL CELL LUNG CANCER

To the Editor:

We commend Yang and colleagues¹ on their recent article in the *Journal* evaluating long-term outcomes after surgery for unsuspected ipsilateral mediastinal nodal metastases (N2) in non-small lung cancer (NSCLC). The treatment of N2 disease is controversial, with various options recommended by different guidelines. This study lends considerable data to support the recommendation that when occult N2 disease is recognized at thoracotomy, the most appropriate option is probably to go ahead with surgery and administer postoperative chemotherapy. Taking this a step further, is there really strong evidence to suggest that neoadjuvant chemotherapy (NACT) followed by lung resection is actually superior to upfront surgery followed by postoperative chemotherapy, even in the setting of preoperatively diagnosed N2 disease? All the studies supporting NACT for N2 disease used surgery alone as the control arm.² In the current era, in which the standard of care for operable NSCLC is surgery followed by adjuvant chemotherapy, we wonder whether we need a reexamination of the need for NACT (as opposed to adjuvant chemotherapy) in N2 disease.

Two meta-analyses^{2,3} evaluating the outcomes of NACT in all (stages I-IIIa) as well as N2 NSCLC arrived at almost identical 5-year survival benefits of about 5%; incidentally, this is also identical to the 5% survival benefit seen with adjuvant chemotherapy in operable NSCLC.⁴ Although we are acutely aware of the perils of comparing results across trials (or meta-analyses!), there seem to be some data to suggest that outcomes with these two strategies could be similar even for N2 NSCLC. Let us assume for a moment that the hypothesis that postoperative chemotherapy would have equivalent survival to that seen with NACT in the setting of proven N2 NSCLC is true; if so, this would obviate the need for accurate mediastinal staging before lung resection in a large number of patients. The longstanding controversy as to whether endobronchial ultrasound or mediastinoscopy is superior would be buried as a clinically irrelevant question, and implications for resource saving (cost, operating room time) would be enormous. The argument that N3 nodal metastases would need to be ruled out is only theoretic, because the incidence of occult N3 nodes in otherwise operable NSCLC is remarkably low when the positron emission tomographic-computed tomographic scan does not indicate metastatic disease. The role of endobronchial ultrasound and mediastinoscopy would then be reserved for the small proportion of patients with increased uptake in contralateral mediastinal lymph nodes.

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In summary, we hypothesize that postoperative chemotherapy is noninferior to neoadjuvant chemotherapy for N2 NSCLC and call for a large multicenter randomized trial to answer this question. We recognize the inherent challenges in conducting such a trial; however, the implications on reducing patient morbidity, costs, and resource use would be immense.

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HECATE: THE MANY FACES OF N2 DISEASE

Reply to the Editor:

In their letter to the editor, Pramesh and colleagues¹ propose 2 substantial changes to the management of N2 disease based on a recent paper by Yang and colleagues,² which evaluated outcomes after lobectomy in patients with unsuspected pN2 disease in the National Cancer Database, providing further support for proceeding with resection followed by adjuvant chemotherapy. Pramesh and colleagues¹ hypothesize that adjuvant chemotherapy for preoperatively diagnosed N2 disease will have equivalent outcomes to neoadjuvant chemotherapy. They should be cautious, however, about extrapolating these findings that compare unsuspected pN2 disease in postsurgical patients undergoing mediastinal lymph node dissection with cN2 disease diagnosed by clinical staging alone. The authors propose a multicenter trial testing this hypothesis for clinical N2 disease. Boffa and colleagues³ evaluated

patients with cN2 disease in the National Cancer Database and found no difference in survival between those undergoing neoadjuvant or adjuvant chemotherapy with complete resection, supporting the authors' proposal for a clinical trial.

On the basis of their hypothesis, Pramesh and colleagues¹ propose that preoperative invasive mediastinal staging would no longer be necessary and could be reserved for fludeoxyglucose-avid contralateral mediastinal nodes. In the most recent National Comprehensive Cancer Network and European Society of Thoracic Surgeons guidelines, patients with peripheral cN0 tumors ≤ 3 cm do not require invasive mediastinal staging because of a low risk of occult mediastinal disease. Patients with cN1 disease, central tumors, increased tumor fludeoxyglucose uptake, and adenocarcinomas, however, have a greater risk of N2 and N3 disease.⁴ Although most well-staged cN0-1/pN2 patients will have single-station, microscopic disease, the clinical N2 patients the authors propose to study without mediastinal staging would be more likely to have occult multistation N2 or N3 disease, which have a poorer prognosis, and N3 disease should be treated with definitive chemoradiation.

N2 disease is heterogeneous, ranging from occult to clinically suspected N2 to bulky disease and from single to multistation disease, making study comparisons and the uniform application of treatment recommendations difficult. Gomez-Caro and colleagues⁵ found unsuspected N2 disease in 14.4% of patients staged cN0 and in 4.8% with multistation N2 disease. Cho and colleagues⁶ found a decreased 5-year survival with occult multistation N2 disease of 36% versus 67% for single-station disease. Size >3 cm, cN1, adenocarcinomas, and middle lobe tumors were predictors of multistation disease, and they suggest that these patients should be staged aggressively.

Like Hecate, the 3-headed Greek goddess of the crossroads, it is important to recognize the many faces of N2 disease in choosing which pathway to follow. Accurate mediastinal staging remains important in defining the extent of disease, guiding treatment, and determining prognosis, especially in trials, so results can be better compared between studies. The extent of mediastinal disease should be considered in deciding a treatment option for N2 disease. Although studies support a role for surgery in the multimodal treatment of N2 disease, the exact role continues to be defined. Recent papers suggest a benefit after surgery and adjuvant chemotherapy for occult N2 disease and provide an opportunity for trials evaluating the primary role of surgery in N2 disease, focusing on