important hints to our case and future device applications. Regarding our case, we explicitly asked the patient for any known allergies at the time of the operation and repeated this query after the comment from Kounis and colleagues. The patient denied any allergies; however, a skin test for sensitivity to nickel or other metals was not performed. In addition, after initial interventional Amplatzer PFO occluder implantation, the patient was without any signs of discomfort, palpitations, dyspnea, headache, pericardial effusion, or conspicuously altered laboratory values, the main symptoms of Kounis hypersensitivity-associated syndrome, for almost 33 months. The symptom that precipitated readmission to the hospital was a stroke, which was most likely due to the thrombus formation on the atrial disk of the Amplatzer device. We cannot rule out, the possibility that the Kounis hypersensitivity-associated syndrome played some role in development of this thrombus formation; however, the histologic examination of the explanted device and thrombus did not reveal any inflammatory cells. In a multicenter-study of PFO closure device explants, the rate of explants was 0.28%.³ Most of these explants were due to persistent or unknown chest pain, and half of these patients had a known nickel allergy. In addition it is shown, that in patients with known nickel allergy the rate of chest discomfort and palpitations is significantly increased after PFO device closure.⁴ None of these signs were found in our patient.

We fully agree with Kounis and colleagues that a possible nickel allergy should be ruled out before elective implantation of intracardiac metal devices. Otherwise, the patient should be made aware of the possibility of device explantation when informed consent is obtained.

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ENDOBRONCHIAL ULTRASOUND-GUIDED MEDIASTINAL LYMPH NODE NEEDLE ASPIRATION IN NON-SMALL CELL LUNG CANCER: FROM THEORY TO PRACTICE

To the Editor:

We read with pleasure the article by Lee and colleagues.¹ Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a new diagnostic technique that provides a minimally invasive option for mediastinal staging in patients with lung cancer. This technique was described by Krasnik and colleagues² in 2003 and rapidly gained the interest of the scientific community. Nonrandomized studies demonstrate that EBUS-TBNA affords excellent diagnostic performance with a sensitivity ranging from 70% to 99% and a negative predictive value up to 98%.³ Those excellent preliminary results convinced the American College of Chest Physicians to advocate EBUS-TBNA to stage the mediastinum only 4 years after the first description of the technique.

In 2006, we had the opportunity to use the first dedicated bronchoscope imported to Italy, and the potential of EBUS-TBNA was immediately obvious. The short learning curve,

high diagnostic accuracy, minimal invasiveness, and possible surgical sparing encouraged us to use EBUS-TBNA even outside of lung cancer staging.⁴

In a paradoxical way, the excellence of the preliminary results delayed the production of randomized studies, and to date only Annema and colleagues,⁵ pioneers in endobronchial ultrasound, published the randomized clinical trial, ASTER (Assessment of Surgical Staging Versus Endosonographic Ultrasound in Lung Cancer). In the aseptic world of scientific trials, the report by Lee and colleagues¹ attracts our attention for its ability to focus interest on clinical practice. The brilliant results reported by the authors demonstrate the high diagnostic value of EBUS-TBNA and the undoubtable skill of the operators. We do recommend rapid on-site evaluation of the specimen because it can decrease the rate of inadequate tests.

Reports with strong clinical characteristics, as well as randomized trials, are needed to validate EBUS-TBNA, especially for its potential capability of avoiding unnecessary surgery.

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Reply to the Editor:

We thank Drs Nosotti, Simone, and Cioffi for their kind remarks and excellent commentary regarding our recent publication.¹ Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is truly an emerging technology that allows safe and accurate assessment of the mediastinum in patients with non-small cell lung cancer. We also anticipate the results of the ASTER trial² with hopes that it will further validate our findings.

We also understand the valid point made regarding the utility of rapid on-site evaluation during EBUS-TBNA. To this end, recent studies have sought to investigate the utility of rapid on-site evaluation.^{3,4} However, in a practical sense, it may not always be possible to have access to the service of an experienced cytopathologist at all times during the performance of EBUS-TBNA. Practice patterns ultimately are developed with the resources that are available within a given institution.

Altogether, EBUS-TBNA provides a safe and reliable method of assessing the mediastinum in patients with non-small cell lung cancer. Whether the results are available instantaneously or in a couple of days, what matters the most is achieving an accurate result.

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BENEFITS AND RISKS OF USING CLOPIDOGREL BEFORE CORONARY ARTERY BYPASS SURGERY: A ROLE OF PLATELET FUNCTION ASSESSMENT

To the Editor:

We read with great interest the recently published systematic review and meta-analysis of randomized trials and observational studies by Biancari and colleagues.¹ When assessing the influence of preoperative antiplatelet therapy (APT) administration management on bleeding and adverse ischemic events, the objective quantification of platelet activity should inextricably be included in the considerations. Expected inhibition of platelet function is not always achieved after APT administration. The frequency of low responsiveness to aspirin and clopidogrel has been reported to range from 1% to 45% for the 2 drugs.² The efficacy of platelet inhibition with aspirin and clopidogrel varies widely among patients, from intensive platelet inhibition to poor platelet response. The effect of clopidogrel on bleeding mainly depends on 2 factors: (1) observed platelet inhibition, which depends on inherent platelet activity before clopidogrel administration and platelet inhibitory response to clopidogrel, and (2) the ability of newborn platelets to restore normal aggregation after clopidogrel

discontinuation. This results in individual widespread variability in the activity of adenosine diphosphate platelet receptors, which consequently reflects similar variability in proclivity to excessive bleeding or adverse ischemic events. Awidi and colleagues³ found that the combination of aspirin and clopidogrel had greater inhibitory effects on platelet aggregation than either agent alone. There is evidence that certain patients have an accentuated response to the usual doses of preoperative aspirin that may result in increased perioperative blood loss.⁴ Therefore, the benefits and risks of using clopidogrel before coronary artery bypass grafting (CABG) should be individually assessed according to platelet function tests, and the role of aspirin should inevitably be included in the considerations. For patients receiving dual APT (aspirin + clopidogrel) before CABG, the influence of aspirin on bleeding and ischemic adverse events should be examined separately using an aspirin-sensitive platelet function test. The role of aspirin and clopidogrel should be assessed separately by drug-specific platelet function tests to provide the most precise and reliable information on the benefits and risks of preoperative administration for each antiplatelet agent, thus facilitating an individual approach to patients with the aim of reducing bleeding and adverse ischemic events. Evaluation of the effect of APT (aspirin or clopidogrel) on both bleeding and ischemic events should be based on platelet function assessment with subsequent distinction of patients with high residual platelet activity, thus a proclivity to ischemic events, or enhanced platelet inhibition, thus a proclivity to excessive bleeding. The group of patients with pronounced platelet inhibition observed during APT could benefit from early preoperative APT withdrawal in terms of excessive bleeding prevention. For patients undergoing CABG, individually tailored APT administration management based on platelet function tests, both pre- and