Third, in the era of molecular biology, we are finding evidence of disease aggressiveness regarding microvascular invasion [4] and gene mutations [5] despite the stage. The trend is to find evidence of benefit from adjuvant therapy to epidermal growth factor-mutated patients, even for early stage of lung cancer (e.g., the Randomized, Double-Blind Trial in Adjuvant NSCLC with Tarceva (RADIANT) trial, double-blind randomized of erlotinib in the adjuvant setting of I–IIa NSCLC). Moreover, the authors have accurately stated that extended lymphadenectomy is not more morbid than sampling.

As a conclusion, regarding the benefit/risk expected of extended lymphadenectomy and the absence of accuracy of PET/CT for small-size structures, I was expecting the authors to conclude that PET/CT is not relevant for small-size tumor or node metabolic evaluation. A trial evaluating the omission of extended lymphadenectomy in small-size tumors with no lymph node uptake on PET–CT appears unethical and obviously exposes the arm of the patient without lymphadenectomy to a loss of chance (risk of under staging and under treatment). In addition, a wait-for–grow–attitude for non-uptaking nodes with suspect morphologic characteristics is a misbenefit of technology.

REFERENCES


LETTER TO THE EDITOR RESPONSE

Reply to Durand

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Received 20 April 2011; accepted 26 April 2011

Keywords: Non-small-cell lung cancer • Lymph node involvement • Tumor size • SUV • Positron emission tomography

We read with great interest the comment of Durand [1] whom we thank for giving us the opportunity to focus further on some topics of our article [2].

First of all, we would like to stress that we routinely perform lobectomy with radical lymphadenectomy as a standard treatment for early-stage lung cancer for both staging and treatment purposes. For this very reason, we were able to retrospectively analyze our patients, all of whom underwent the same radical surgery, identifying a homogeneous group of cases with ‘very small’ non-small-cell lung cancer (NSCLC), <1 cm in size and pathological N0 status. In addition, all our patients were preoperatively staged by computed tomography (CT) and (not or) positron emission tomography/CT (PET/CT) with fluorodeoxyglucose.

Considering that in the 7th edition TNM the definitions of the TNM descriptors and the stage groups were based on the outcome measure of the overall survival [3], we focused our attention on NSCLC <1 cm in size, that in our opinion was not studied enough in detail and in which survival was probably underestimated, in order to highlight how the size of the tumor could be an important predictor of lymph node involvement and survival.

All our patients with ‘very small’ NSCLC had different lymph node involvement and a 5-year survival rate when compared with staging group of origin (T1a) which had a 5-year survival rate of 77% after radical excision [3]. Specifically, none of these patients had any pathological lymph node involvement and their 5-year overall survival was 100%. Besides, all of them had nodule size >8 mm in diameter, which was above the spatial resolution of the PET device.

In 2011, Fischer et al. demonstrated in their prospective randomized study that sensitivity and specificity of PET/CT were the same both for lymph nodes <1 cm and for enlarged nodes (>1 cm) [4]. In particular, they showed that the negative predictive value was significantly higher in the group with small nodules (96% vs 70%) and the positive predictive value was lower (43% vs 71%). This means that a negative PET/CT was highly valid in patients with normal-sized lymph nodes, considering ‘normal size lymph nodes’, as defined by Silvestri et al.,
the lymph nodes with short-axis diameter of ≤1 cm on a CT scan image [5].

In detail, we used CT as an anatomical tool for thorax imaging, and PET/CT as a functional tool offering information about metabolic activity of structures identified with fusion images of a low-resolution CT in order to have a complete preoperative staging.

In conclusion, our study confirms the literature reports suggesting that tumor size, measured by CT and intra-operatively confirmed by the pathologist, and standardized uptake value (SUV), measured by PET/CT, could be reliable independent predictors of tumor aggressiveness and lymph node involvement. Radical lymphadenectomy could be omitted in patients with stage I NSCLC tumors <1 cm in diameter or SUV <2.0, considering the complete absence of lymph node involvement and the demonstrated 100% 5-year survival rate.

REFERENCES


LETTER TO THE EDITOR

Prevalence and clinical significance of elevated preoperative glycosylated hemoglobin in diabetic patients scheduled for coronary artery surgery

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Received 3 May 2011; accepted 7 June 2011

Keywords: Glycosylated hemoglobin • Coronary surgery • Diabetes mellitus • Platelet function

We read with great interest the recently published retrospective study by Knapik et al. [1]. The authors postponed coronary artery surgery (CAS) in majority of patients with glycosylated hemoglobin (HbA1C) exceeding 8%. However, 15% of patients underwent CAS despite high HbA1C. It would be interesting if authors separately presented outcome evaluation in that subgroup of patients. A major drawback of this study is the lack of early postoperative platelet-function (PF) assessment. A greater proportion of patients with elevated HbA1C were scheduled to on-pump surgery. Cardiopulmonary bypass results with postoperative platelet-count turnover with platelet count exceeding preoperative values [2], which inevitably results with higher thromboxane level, thereby may contribute to aspirin resistance onset [2]. In addition, Zimmermann et al. [2] summarized in a review article the facts indicating that aspirin is more effective after off-pump revascularization comparing to on-pump and described diabetes-associated permanent aspirin resistance. Diabetes-related aspirin resistance, together with procedurally acquired resistance, can lead to a hyperaggregability state, thus influencing perioperative myocardial-infarction (MI) onset. Knapik et al. [1] did not describe the postoperative anti-platelet therapy (APT) regimen and differences in regimens with respect to off- or on-pump revascularization. They mentioned that literature sources are reporting conflicting data about the impact of diabetes on mortality after CAS, which is suggestive of the presence of other factors influencing the outcome in the diabetics group. Increased PF has already been described in diabetics, in particular in the insulin-dependent group [3], and that may influence the outcomes in the ‘elevated HbA1c group’, which is mainly consisted of insulin-dependent diabetics in the present study. Early thrombosis with a crucial role of platelets is a major cause of vein-graft attrition during the first month after CAS [2], and aspirin has a beneficial effect on a vein-graft patency in the first month after CAS [4]. Taking into consideration the above mentioned, postoperative PF assessment with aspirin-resistant patients’ detection could bring a clear distinction between role of elevated HbA1C and platelet hyperactivity on perioperative MI in diabetics. More aggressive early postoperative APT in diabetics with elevated HbA1C may be an alternative approach to procedure postponement, which carries risks.