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EBUS-TBNA in the differential diagnosis of pulmonary artery sarcoma and thromboembolism

To the Editors:

We read with interest the correspondence published by PARK *et al.* [1] suggesting a potential role for endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) to differentiate pulmonary artery sarcoma and thromboembolism.

Pulmonary artery sarcoma usually has its origin in the pulmonary arterial trunk and extends towards pulmonary branches, and is indeed sometimes difficult to differentiate from chronic thromboembolic disease. However, we believe that the authors' conclusions suggesting that EBUS-TBNA is safe in this setting are premature. Indeed, such an approach could be associated with significant complications.

Even if pulmonary artery sarcoma may mimic acute or chronic pulmonary thromboembolism, it has been reported [2, 3] that a careful analysis including medical history, chest computed tomography (CT), magnetic resonance imaging (MRI), pulmonary angiogram and positron emission tomography CT with ^{18}F-2-fluoro-2-deoxy-D-glucose [4, 5] may be sufficient to detect patients with pulmonary artery sarcoma. Chest CT classically shows hyperdense lesions, beaded peripheral pulmonary arteries, and contiguously soft tissue-filled pulmonary arteries and extravascular spread [2]. Moreover, MRI may be more specific for pulmonary artery sarcoma, showing enhancement with gadolinium contrast [2].

PARK *et al.* [1] performed EBUS-TBNA in a patient with acute pulmonary embolism, which was later confirmed by the complete reversibility of endovascular clots after 6 weeks of anticoagulation. Performing EBUS-TBNA in a patient with acute thromboembolism is certainly debatable and hazardous, and it is important to state that a diagnosis of acute thromboembolic disease is based on established imaging techniques, such as ventilation/perfusion lung scan, chest CT and pulmonary angiography [6].

Diagnosis of an endovascular tumour could be made by endovascular catheter biopsy [7]. In addition, as stated by PARK *et al.* [1], surgery is the treatment of choice in the management of pulmonary artery sarcoma (pneumonectomy, pulmonary artery resection/reconstruction or pulmonary endarterectomy) and chronic thromboembolic pulmonary disease (pulmonary endarterectomy) [6]. It is therefore important to highlight that surgery should be proposed to eligible patients with pulmonary artery sarcoma or chronic thromboembolic pulmonary hypertension, allowing diagnosis confirmation and management.

Finally, a large proportion of patients with proximal pulmonary artery chronic obstruction by sarcoma or thromboembolic material may present with pulmonary hypertension, a condition associated with a high risk of complication following transbronchial needle aspiration. Indeed, it has been clearly demonstrated that proximal obstruction of pulmonary arteries may be associated with hypertrophy of systemic bronchial arteries (fig. 1), increasing the risk of haemorrhage from transbronchial needle aspiration.

To conclude, we believe that physicians should be aware of the potential complications of EBUS-TBNA in patients with pulmonary artery sarcoma or pulmonary thromboembolic disease, and we consider that EBUS-TBNA should not be

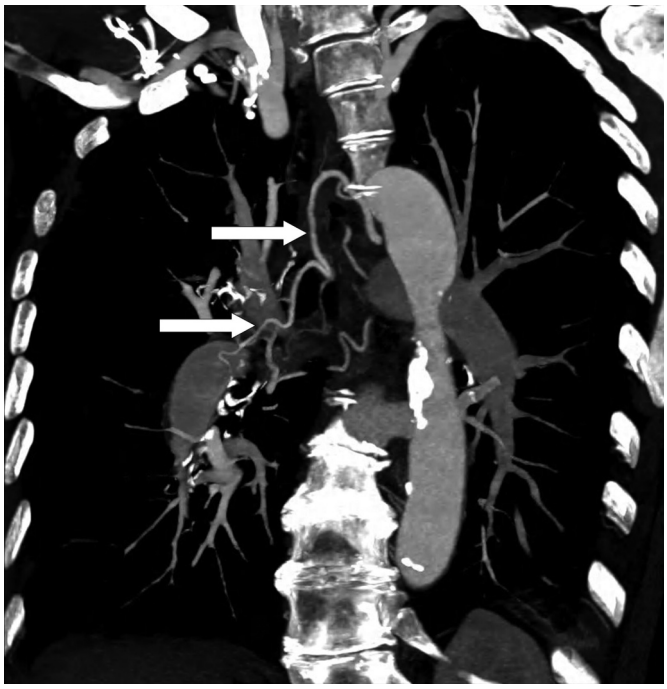

FIGURE 1. Computed tomography angiography with maximum-intensity reconstruction in the coronal plane showing hypertrophy of systemic bronchial arteries (arrows) in a case of proximal chronic thromboembolic pulmonary disease.

proposed in the management of pulmonary artery sarcoma or thromboembolic disease.

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Nomogram to predict the presence of *EGFR* activating mutation in lung adenocarcinoma

To the Editors:

GIRARD *et al.* [1] developed a nomogram to predict the presence of epidermal growth factor receptor (*EGFR*) activating mutations. Before using it in practice, however, the precision and limitations must be considered. Patient selection for tyrosine kinase inhibitors (TKIs) based exclusively on *EGFR* mutations is still controversial, because clinical response rates to TKI are nearly 70% in tumours harbouring *EGFR* activating mutations. Other factors, such as amplification of the *EGFR* gene and the activity of molecules downstream of EGFR, such as phosphorylated protein kinase B, and mutations of KRAS can play a role in the sensitivity to EGFR inhibitors. Again, 10–20% of patients with a partial response to gefitinib did not have identifiable EGFR mutations, signifying that *EGFR* mutations are not the only determinants of TKI response [2]. The incidence of *EGFR* mutations in East Asia is nearly 40%, compared with 10% in Europe and the USA. The prediction accuracy of the nomogram for *EGFR* mutation is unsatisfactory as the concordance index is low (0.64) in the East-Asian population, where the need for reliable predictive nomograms is higher [1].

Differences in all the above factors and population characteristics can challenge the accuracy and concordance of nomograms when they are applied to an Asian/non-Asian population. Before a nomograms is put to widespread use, it needs external independent validation. Despite external validitation, we do not know whether the existing evidence supports the impact of nomograms on medical decision making. There are no randomised studies that clearly reveal that the use of prediction nomograms improves decision making or patient care, reduces patient anxiety and is harmless.

In Chinese nonsmall cell lung cancer patients, the *EGFR* mutation status determined in serum DNA using mutant-enriched sequencing corresponds to that demonstrated in paired tumour tissues (concordance rate of 93.1%) suggesting that serum DNA is a practical and reliable source of tumour DNA for detecting *EGFR* mutations [3]. This concordance rate (93.1) is higher than the nomogram's concordance index of 0.84 and 0.64 in non-Asian and East-Asian populations, respectively. Another study confirmed high sensitivity (92%) and specificity (100%) of plasma *EGFR* mutation analysis by microfluidics digital PCR [4]. If we are unable to obtain tumour tissue or block, where diagnosis is based only on needle aspiration or cytology, it is practicable now to use serum DNA to detect *EGFR* mutation status and to evaluate its potential as a predictor of response to EGFR–TKIs without waiting for biopsy tissue.

In this scenario, nomograms can be built to predict the treatment outcome of TKIs. Predictive models can help