EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Correspondence

Reply to: “Digging mediastinal holes in vigor: a word of caution”

Jing Zhang, Zan-Sheng Huang, Felix J. F. Herth, Ye Fan

Please cite this article as: Zhang J, Huang Z-S, Herth FJF, *et al*. Reply to: “Digging mediastinal holes in vigor: a word of caution”. *Eur Respir J* 2021; in press (https://doi.org/10.1183/13993003.01528-2021).

Reply to: “Digging mediastinal holes in vigor: a word of caution”

Jing Zhang, Zan-Sheng Huang, Felix JF Herth, Ye Fan

Department of Respiratory Disease, Xinqiao Hospital, Third Military Medical University (JZ, ZSH, YF), Chongqing, China; Department of Pneumology and Critical Care Medicine, Thoraxklinik, and Translational Lung Research Center Heidelberg, University of Heidelberg (FJH), Heidelberg, Germany

Corresponding author:

Ye Fan, MD; Department of Respiratory Disease, Xinqiao Hospital, Third Military Medical University, Chongqing, China; E-mail: fanye2008728@googlemail.com

From the authors:

We thank T.K. Tournoy and the co-worker for their thoughtful letter in response to our manuscript on transbronchial mediastinal cryobiopsy[1]. We agree that our study shows no differences in the diagnostic yield of lung cancer between endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and mediastinal cryobiopsy, thus it would be premature to consider mediastinal cryobiopsy as the standard nodal staging strategy in lung cancer. In our cohort, a diagnosis of non-small cell lung cancer is established by EBUS-TBNA but not cryobiopsy in 3 patients, which might be attributed to the relatively fixed biopsy location of mediastinal cryobiopsy. Nevertheless, it should be noted that there were 6 lung cancer cases only diagnosed by mediastinal cryobiopsy.

T.K. Tournoy and co-worker raise an important question on the adequacy of mediastinal tissues for molecular analysis. The data regarding the suitability of specimens obtained by EBUS-TBNA for tumor genotyping vary considerably in the literature. As such, our data on EBUS-TBNA sample adequacy for genotyping are in line with the findings from several large EBUS-TBNA clinical studies published over the past 5 years[2-5]. In our study, we considered a minimum of 200 viable tumor cells necessary for molecular testing. Using the same criterion, Rooper and colleagues reported similar results in that 71% of EBUS-TBNA specimens were eligible for molecular testing[4]. In the meta-analysis mentioned in T.K. Tournoy's correspondence and the largest report included in this meta-analysis, no specific information is provided as to the quality criteria for TBNA sample adequacy for molecular testings[6, 7]. Hence, the differential findings between these may result from the use of different quality criteria. To avoid bias, we applied the same criteria to evaluate quality for both EBUS-TBNA and cryobiopsy samples.

The diagnostic yield of EBUS-TBNA for sarcoidosis in our cohort (67%) is only slightly lower compared to von Bartheld's study (74%) mentioned in T.K. Tournoy's correspondence, which might be due to the relatively small number of sarcoidosis patients in our trial[8]. We agree with T.K. Tournoy and the co-worker that the sensitivity of EBUS-TBNA for tuberculosis in the current series is inferior than that of Navani's study; however, it might be potentially overestimated because of their study design[9].

As this is the first trial of transbronchial mediastinal cryobiopsy, patient safety is our primary concern. The procedure has now been performed in more than 300 patients in our center, and we have observed no procedure-related serious complications (such as severe bleeding, mediastinitis, and death), which is in accordance with the safety data from EBUS-guided electrocautery-assisted forceps biopsy report[10]. Based on our experience, transbronchial mediastinal cryobiopsy might be a safe approach for the acquirement of

mediastinal tissue. We agree with T.K. Tournoy and the co-worker that further research in transbronchial mediastinal cryobiopsy is indicated.

Conflict of interest statement

Felix JF Herth received personal money for adboard activities and lecture fees from Pulmonx, Erbe, Olympus, and Uptake. The other authors declare no competing interests.

Support statement

This study was supported by a grant from the National Natural Science Foundation of China (81873414).

References

1. Zhang J, Guo JR, Huang ZS, Fu WL, Wu XL, Wu N, Kuebler WM, Herth FJF, Fan Y. Transbronchial mediastinal cryobiopsy in the diagnosis of mediastinal lesions: a randomised trial. Eur Respir J. 2021. Epub ahead of print.

2. Centeno C, Serra Mitja P, Avila M, Carcereny E, Muñoz-Mármol AM, Moran T, Castellà E, Sanz-Santos J, García-Olivè I, Ramirez Serrano JL, Rosell Gratacos A, Andreo García F. Molecular analysis in cytological samples obtained by endobronchial or oesophageal ultrasound guided needle aspiration in non-small cell lung cancer. Pulmonology. 2020:S2531-0437(20)30099-4.

3. Zhang Y, Xie F, Mao X, Zheng X, Li Y, Zhu L, Sun J. Determining factors of endobronchial ultrasound-guided transbronchial needle aspiration specimens for lung cancer subtyping and molecular testing. Endosc Ultrasound. 2019;8(6):404-411.

4. Rooper LM, Nikolskaia O, Carter J, Ning Y, Lin MT, Maleki Z. A single EBUS-TBNA procedure can support a large panel of immunohistochemical stains, specific diagnostic subtyping, and multiple gene analyses in the majority of non-small cell lung cancer cases. Hum Pathol. 2016;51:139-145.

5. Hopkins E, Moffat D, Parkinson I, Robinson P, Jersmann H, Dougherty B, Birader MI, Francis K, Nguyen P. Cell block samples from endobronchial ultrasound transbronchial needle aspiration provide sufficient material for ancillary testing in lung cancer-a quaternary referral centre experience. J Thorac Dis. 2016;8(9):2544-2550.

6. Labarca G, Folch E, Jantz M, Mehta HJ, Majid A, Fernandez-Bussy S. Adequacy of Samples Obtained by Endobronchial Ultrasound with Transbronchial Needle Aspiration for Molecular Analysis in Patients with Non-Small Cell Lung Cancer. Systematic Review and Meta-Analysis. Ann Am Thorac Soc. 2018;15(10):1205-1216.

7. Navani N, Brown JM, Nankivell M, Woolhouse I, Harrison RN, Jeebun V, Munavvar M, Ng BJ, Rassl DM, Falzon M, Kocjan G, Rintoul RC, Nicholson AG, Janes SM. Suitability of endobronchial ultrasound-guided transbronchial needle aspiration specimens for subtyping and genotyping of non-small cell lung cancer: a multicenter study of 774 patients. Am J Respir Crit Care Med. 2012;185(12):1316-1322.

8. von Bartheld MB, Dekkers OM, Szlubowski A, Eberhardt R, Herth FJ, in 't Veen JC, de Jong YP, van der Heijden EH, Tournoy KG, Claussen M, van den Blink B, Shah PL, Zoumot Z, Clementsen P,

Porsbjerg C, Mauad T, Bernardi FD, van Zwet EW, Rabe KF, Annema JT. Endosonography vs conventional bronchoscopy for the diagnosis of sarcoidosis: the GRANULOMA randomized clinical trial. JAMA. 2013;309(23):2457-2464.

9. Navani N, Molyneaux PL, Breen RA, Connell DW, Jepson A, Nankivell M, Brown JM, Morris-Jones S, Ng B, Wickremasinghe M, Lalvani A, Rintoul RC, Santis G, Kon OM, Janes SM. Utility of endobronchial ultrasound-guided transbronchial needle aspiration in patients with tuberculous intrathoracic lymphadenopathy: a multicentre study. Thorax. 2011;66(10):889-893.

10. Ray AS, Li C, Murphy TE, Cai G, Araujo KLB, Bramley K, DeBiasi EM, Pisani MA, Cortopassi IO, Puchalski JT. Improved Diagnostic Yield and Specimen Quality With Endobronchial Ultrasound-Guided Forceps Biopsies: A Retrospective Analysis. Ann Thorac Surg. 2020;109(3):894-901.