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Early View

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Digging mediastinal holes in vigor: a word of caution

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256 character summary: Transbronchial mediastinal cryobiopsy has a superior diagnostic yield vs. endobronchial ultrasonography. However, this is exclusively explained for diagnoses other than lung cancer. Uncertainties about safety hinder implementation in routine practice.

Dear editor,

With interest, we read the manuscript of Zhang et al (1), which investigated the diagnostic performance of transbronchial mediastinal cryobiopsy (TBMC) as compared to endobronchial ultrasonography (EBUS) with fine-needle aspiration. In patients presenting with mediastinal pathology in whom a pathological diagnosis was warranted, a diagnostic yield of 91,8% was found for TBMC. This is better than 79,9% reported for EBUS.

When scrutinizing the data, there is no obvious benefit in favor of TBMC in the group with lung cancer. Remarkably, there were 3 lung cancer patients in whom TBMC missed the diagnosis, where EBUS did not fail. This could be related to the convenience of taking biopsies in multiple locations within the same lesion with EBUS – and could be an indication that the negative predictive value of TBMC is not perfect. The possibility for additional molecular analysis on the cryo-specimens is very attractive. Recent meta-analyses reported over 90% of the EBUS-TBNA specimens were found suitable for molecular testing (2, 3). The inferior results of EBUS-TBNA in the current series (73,5% suitability) is however somewhat remarkable. One could speculate about a relationship with the additional TBMC the endoscopist also needed to do. Nevertheless, for the patient in whom EBUS falls short, the TBMC could be a very attractive alternative.

The results of TBMC obtained in the group without lung cancer appear spectacular. In the 12 patients with non-lung cancer malignancies, TCMB resulted in the diagnosis in 11 (91,7%), EBUS only in 3 (25,0%). In the 47 patients with non-malignant disorders such as sarcoidosis and tuberculosis, TCMB found the diagnosis in 38 (80,9%), EBUS in 25 (53,2%). Other well-designed studies reported that EBUS performed better for sarcoidosis (4) than reported here. For tuberculosis, largely better values were reported (5), although the latter were probably overestimated (6). If there is a relation with the study design remains unclear but a parallel with the lower than expected adequacy for molecular analysis in the lung cancer group is tempting.

Obviously, digging transbronchial holes in the mediastinum that results in diagnostic gain needs to be weighed against the risk of potentially serious complications. The mediastinum is a sterile interpulmonary region wherein besides high- and low-pressure blood vessels also the thoracic duct and recurrent nerves are crossing. With EBUS, infectious complications are rare but do exist (7). Descending necrotizing mediastinitis needing surgical exploration is a serious adverse event - especially when occurring in the diagnostic process of a benign pathology such as sarcoidosis or tuberculosis (8). With TBMC – the

samples measured on average 4,6 mm (2,2-8,1) which means that the holes where cryoprobe and obtained tissue are pulled through have a considerable diameter. Although no serious events needing medical intervention were encountered in the current series, common sense to stay highly vigilant for mediastinal infections and tissue ruptures beyond the nodes seems warranted. The authors already applied less than 50% freezing time as compared to the initial first-in-man report on TBMC (9). The nature of the investigation in the central airways precludes control of serious hemorrhage, especially in a patient who is under conscious sedation. This represents a potential disadvantage as compared to a video-assisted thoracoscopy or mediastinoscopy.

Obtaining a better diagnostic yield with as few as possible serious adverse events always comes down to the selection of the right patient for the right diagnostic procedure. Fortunately, the suspicion for a lung cancer diagnosis vs ‘uncommon and benign mediastinal pathology’ can be directed with great accuracy based on the imaging. The former most often has a suspect parenchymatous lesion, while the latter frequently but not exclusively presents as a unique mediastinal pathology. Until further data become available on the safety issue discussed above,

and based on the current data, a diagnostic EBUS remains the first option for those with a high a priori chance for lung cancer. TBMC potentially selects for those with a probability for an alternative diagnosis or as an adjunct procedure in the patients with presumed lung cancer after a negative EBUS.

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