Editorial

Impact of pulmonary fibrosis on tumor measurements

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Lung cancer is a frequent sequela in interstitial pulmonary disease, like idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD) with an incidence rate of 10–20%. Furthermore, the morbidity of lung cancer in IPF patients ranges from 3% to 22% (1). Patients with combined pulmonary fibrosis and emphysema (CPFE) have an odds ratio (OR) of 9.06 to develop lung cancer, compared with cancer population with a normal lung—and the median survival of 20 months compared to 53 months (2). The mechanisms of development of lung cancer in the areas of interstitial lung changes are not yet fully understood (3). First, most affected patients have a history of smoking, but also other effects like increased shear stress and inflammatory processes in IPF lung areas may play a role in lung cancer origin (1,3,4).

In general, three major therapeutic options are available: surgical resection, medical treatment, or radiation. For all of these options, precise tumor measurements are essential. However, especially the latter two are less well investigated, as patients with underlying lung diseases are usually excluded from trials. Therefore, surgical resection is the main stay of treatment.

Patients with pulmonary fibrosis have a higher risk of surgical mortality compared to non-fibrotic patients (17% *vs.* 3.1%). IPF patients have a higher mortality rate for pneumonectomy (33% *vs.* 5.1%) and lobectomy (12% *vs.* 2.6%). They also have a higher incidence of postoperative lung injury (21% *vs.* 3.7%), and a longer mean hospital stay (17 *vs.* 9 days) (5). Furthermore, patients can develop postoperative acute respiratory distress or acute exacerbation of the fibrotic disease. The incidence is increasing with more affected fibrotic lung parenchyma. Given this, and the increased rates of complications, the larger the resected volume of lung parenchyma is, surgeons aim to resect only as much lung parenchyma, that is required.

To plan sub-segmental (or wedge) resection, it is essential to determine the size of the malignant lesion within the fibrotic tissue in the preoperative planning examination as exact as possible. The mainstay imaging technique is computed tomography (CT).

The only other study by Sakai *et al.* who investigated the morphology of lung cancer in fibrotic lung tissue did not report on the impact on tumor size measurement (6).

The current study by Ishizawa *et al.* is therefore the first study exploring the impact of different lung abnormalities on tumor measurements (7). They included 896 patients with lung cancer, operated in one center. Two radiologists with more than 20 years of experience in chest radiology reviewed all images and classified the lung parenchyma adjacent to the lung carcinoma. Tumors were in 15 honeycomb, 30 reticulated, 207 emphysematous and 628 normal lungs. The inclusion time for this retrospective study was 5 years with a bandwidth of CT acquisition parameters. The majority of CT datasets (n=786) were acquired with a slice thickness of ≤2 mm and only 55 CT datasets with ≥5 mm. Underestimation of tumor size was defined as

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≥10 mm in pathological maximum compared with radiological one. All tumor specimen were pathologically evaluated. While squamous cell lung carcinoma was detected in 10% of normal lungs, it contributed to 40% of cases in the non-normal lungs. Tumor size underestimation occurred in 33% of cases with back-ground honeycombing, while only in 7% to 8% of cases with reticulation, emphysema or normal lung. The multivariate analysis revealed an OR of 8.58 for tumor size underestimation if honeycombing is present adjacent to the tumor.

The pathological examination of the underestimated tumor cases revealed, that the tumor infiltrated the dilated airways within the honeycomb lung. This led to the most extreme underestimation of 120 and 65 mm pathological size compared to 21 and 11 mm radiological, respectively. Also, infiltration to the fibrotic lung tissue and a subpleural cyst obscured the true tumor dimensions. This finding pronounces the importance of the use of multiplanar reformations in the evaluation of tumor extent. The tumor within the fibrotic lungs were more localized peripherally, so surgical resection should take this into account, as a 10 cm safety margin may be required.

On the other hand, it has to be kept in mind, that the underlying lung disease itself is extremely life limiting. Patients with interstitial lung disease with a diffusion capacity of the lung for carbon monoxide (DLCO%) <38% showed only a median survival of 10 month (4).

Given the impact of reliable tumor measurement for minimized perioperative complications it might be worth to facilitate more advanced imaging techniques. The low incidence rate of significant fibrosis and lung cancer would only lead to a minimal increase in health care cost. For this purpose, magnetic resonance imaging (MRI) might be an interesting technique, especially using ultra high-resolution sequences in combination with contrast media uptake.

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