Editorial

How to diagnose pulmonary nodules: from screening to therapy

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Lung cancer is still the leading cause of cancer-related death worldwide and early detection allows for a better survival for lung cancer, which is supported by the results of the National Lung Screening Trial (NLST) in 2011 (1). Early screening by low-dose computed tomography (LDCT) in high-risk patients can induce a 20% reduction in lung cancer-specific mortality, therefore LDCT is now recommended for lung cancer screening. It is demonstrated that the implementation of early screening could increase the number of detected pulmonary nodules by an estimated 875,000 per year (2). However, it is suggested that the majority of screen detected nodules were benign, making it necessary to establish a comprehensive criterion of screening, diagnosis and therapy of pulmonary nodules so that lung cancer can be early detected and not over-diagnosed.

Screening

As we know that a pulmonary nodule is identified as a focal rounded or irregular opacity in the lung, can be well or poorly defined, measures less than 30 mm, and surrounded by aerated lung and is not associated with atelectasis or lymph node enlargement (1,3).

The current evaluation criteria of nodules are mainly divided according to the opacity and diameter of the nodules, and the patients are identified as low-risk and high-risk according to the age, smoking history, former tumor history, etc. (4). The recommendation of screening is differed on the solid and sub-solid nodules, and as a special part of sub-solid nodules, ground-glass nodules (GGN) are listed as a separate category, since it is demonstrated that the ground-glass opacity (GGO) has a more possibility of histology of adenocarcinoma, and Claudia I. Henschke *et al.* found in their recent research that a part-solid or nonsolid nodule is more likely to be malignant than a solid one, even when nodule size is taken into account (5,6).

In 2016, the Fleischner Society pulmonary nodule recommendations are still using the cutoff value of diameter in solid nodules as 4, 4–6, >6–8 and >8 mm, since nodule <4 mm is proved to have a low probability of malignant disease (7). The cutoff value of diameter sub-solid nodule is set as 5 mm in the statement from the Fleischner Society and if solitary pure GGNs ≤5 mm, no CT follow-up require and multiple pure GGNs ≤5 mm should obtain follow-up CT at 2 and 4 years. Initial follow-up CT at 3 months is needed and recommended to confirm persistence. If persistent, dominant nodules with part-solid or solid component are suggested to be biopsied or surgical resected, especially for lesions with >5 mm solid component (8).

Diagnosis

During the follow-up, there are several nodule features presented in the CT image may give the evidence that the nodule could be malignant and the iconic features are margin, size, growth and the presence and the distribution of calcification (5,9).

Recent studies suggest some new aspects of the nodule features helping to diagnose a malignant nodule. Another famous lung cancer screening trial—Dutch-Belgian randomised lung cancer multi-slice screening (NELSON) trial first reported to using the volumetric measurements as a remarkable nodule since it yielded high specificity and sensitivity, a nodule with a volume <100 mm^3 is not predictive for lung cancer and the volume doubling time assessment is recommended for the nodules with a volume

ranging between 100–300 mm^3 (10). The British Thoracic Society guidelines for the investigation and management of pulmonary nodules published in 2015 also take the volume as the characteristic of nodule (8,11). As a result, dynamic contrast-enhanced CT (DCE-CT) is demonstrated to be a useful screening method besides LDCT (12).

When the features suggesting the malignance of the nodule are detected, the diagnostic approaches will then be approved. In clinic, the diagnostic approaches are divided as non-invasive and invasive methods. As the most common non-invasive method using in clinic, fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT was considered to have limited value in nodule <8 mm, especially in pure GGN (11). However, recent studies have rebuilt the diagnostic value of ^{18}F-FDG PET/CT for evaluation of solitary pulmonary nodules. A latest meta-analysis suggested that although current evidence showed moderate accuracy, PET/CT is still a useful method for detecting malignant pulmonary nodules qualitatively (13).

Besides the surgery, the invasive diagnostic method is percutaneous lung biopsy and bronchoscopy. Endobronchial ultrasonography with guide sheath (EBUS-GS), electromagnetic navigation bronchoscopy (ENB) and virtual bronchoscopic navigation (VBN) are the up-to-date technologies in the interventional pulmonology (14). The combination of these methods has been proven to have precisely diagnostic value for pulmonary nodules, especially for GGNs.

Therapy

When the malignance of the nodule is confirmed or highly suspected, surgery is recommended depending on number of the nodules and the fitness of the individual. Lobectomy or anatomical segmentectomy is the treatment of choice (2).

Non-surgical recommended treatments are stereotactic ablative radiotherapy (SABR) and radiofrequency ablation (RFA). As an effective therapy, RFA has been increasingly reported for the treatment of primary lung cancer and becomes an accepted treatment for primary non-small cell lung cancer (NSCLC) in patients who are not candidates for surgery. SABR is proved to revolutionize radiation therapy for early stage lung cancer in the literature, having the advances in imaging and highly conformal and accurate radiation delivery and can achieve tumor control rates compared with surgery.

Conclusions

"*The best way to predict the future is to invent it*." The combination of early detection strategies and innovative therapies can give patients more confidence, aim to find earlier cancer, give optimal treatment, and make life better.

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Footnote

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