3
Chest

Standard Imaging Methods for Chest

Chest radiography

1. Imaging method

The digital imaging systems currently used at nearly all facilities, such as flat-panel detectors and computed radiography systems, perform histogram analysis. Consequently, the radiation dose affects image quality without affecting the photographic density of the images. It has been reported that, although the increase in noise that results from a moderate reduction in dose reduces image quality, it has little effect on diagnostic performance. It is, therefore, appropriate to set the imaging conditions (radiation dose) to a level comparable to or lower than used for conventional film-screen imaging.

2. Image processing

With chest radiography that uses a digital imaging system, images of high diagnostic value need to be obtained through appropriate image processing, such as the use of gradients, frequencies, dynamic range reduction, and denoising.

3. Soft copy display requirements

According to the Guidelines for Handling Digital Images, 3rd Edition,[1] a compliant liquid-crystal monitor is one that has a resolution of 1 megapixel or greater and satisfies the requirements for control grade 1 of the Guidelines for Quality Control of Monitors for Displaying Medical Images (JESRAX-0093-*B^{-2017}) of the Japan Medical Imaging and Radiological Systems Industries Association.[2]

Computed tomography (CT)

1. Imaging method

For the performance required of a computed tomography (CT) system to diagnose diseases of the thoracic region, imaging with a high-resolution computed tomography (HRCT) system (Figs. 1A and 6A), early-phase imaging using bolus injection of a contrast medium (Fig. 6B), and a multidetector computer tomography (MDCT) system equipped with a multi-row detector that can withstand clinical use is desirable. The imaging method used depends largely on the performance of the CT system. Continuous scanning from the apex to the base of the lungs is generally recommended. Although a slice thickness of 5 mm is widely used, CT with intermediate slice thicknesses of 3 to 5 mm is used concurrently as needed. Adequate breath-holding is required during scanning.

2. High-resolution CT (HRCT)

HRCT imaging uses thin collimation. "Thin" is usually considered ≤ 2 mm. A high-spatial-frequency algorithm is used in reconstruction (Figs. 1A and 6A). The methods used are one that involves re-imaging of only the necessary sites and another that involves first performing continuous thin-collimation CT imaging of all lung fields by MDCT, then creating images of intermediate slice thickness by reconstruction.

① Imaging of diffuse lung disease

An imaging based on the method of Goddard is widely used in emphysema and chronic obstructive pulmonary disease (COPD). Specifically, the method involves HRCT imaging at the level of the aortic arch, tracheal bifurcation and 1 to 2 cm above either the left or right upper diaphragm and performing a visual assessment.[3] In pulmonary fibrosis, assessment at 1 to 2-cm intervals with a collimation thickness of 1 to 2 mm is commonly performed. Recently, a method involving the imaging of all lung fields by continuous thin-collimation CT using ≥ 16-row MDCT has been used for emphysema volumetry.[4] Expiratory imaging, as well as inspiratory imaging, is useful for purposes such as the qualitative diagnosis of obstructive pulmonary disease (see BQ 19).[5]

② Imaging method for pulmonary nodules

An imaging method based on HRCT is used. At the image reconstruction stage, coronal images (Fig. 1B), sagittal images, and target images of the nodules (FOV, approximately 20 cm) are generated as needed. Not only can nodules be qualitatively assessed, but quantitative changes in nodules over time can be assessed by volumetry.[6]

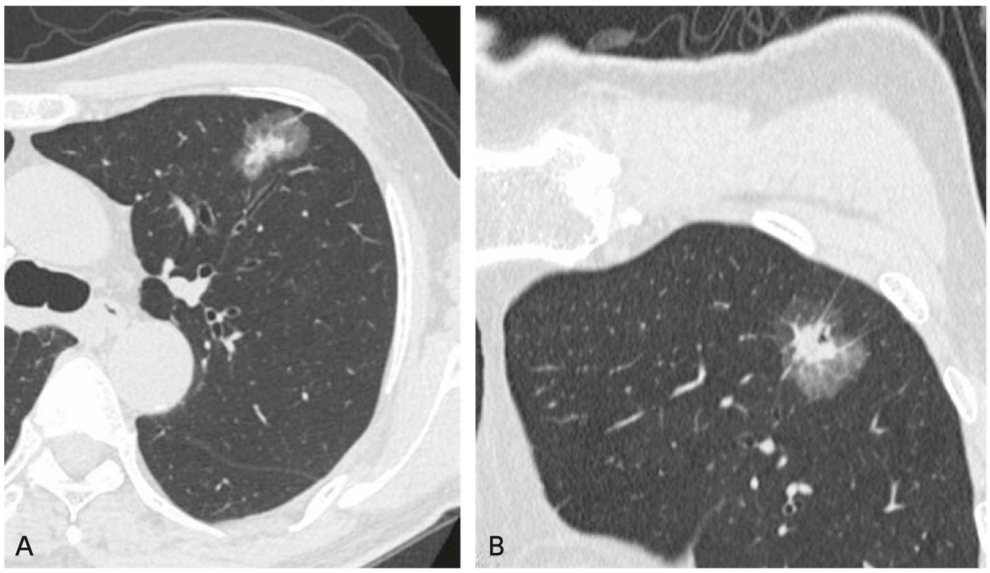

Figure 1. Invasive lung adenocarcinoma

A: HRCT, transverse image: A part-solid nodule with a whole-tumor diameter of 28 mm and solid-component diameter of 15 mm is seen in the left upper lobe.

B: HRCT, coronal reconstructed image: The whole-tumor diameter is 29 mm, and the solid-component diameter is 11 mm.

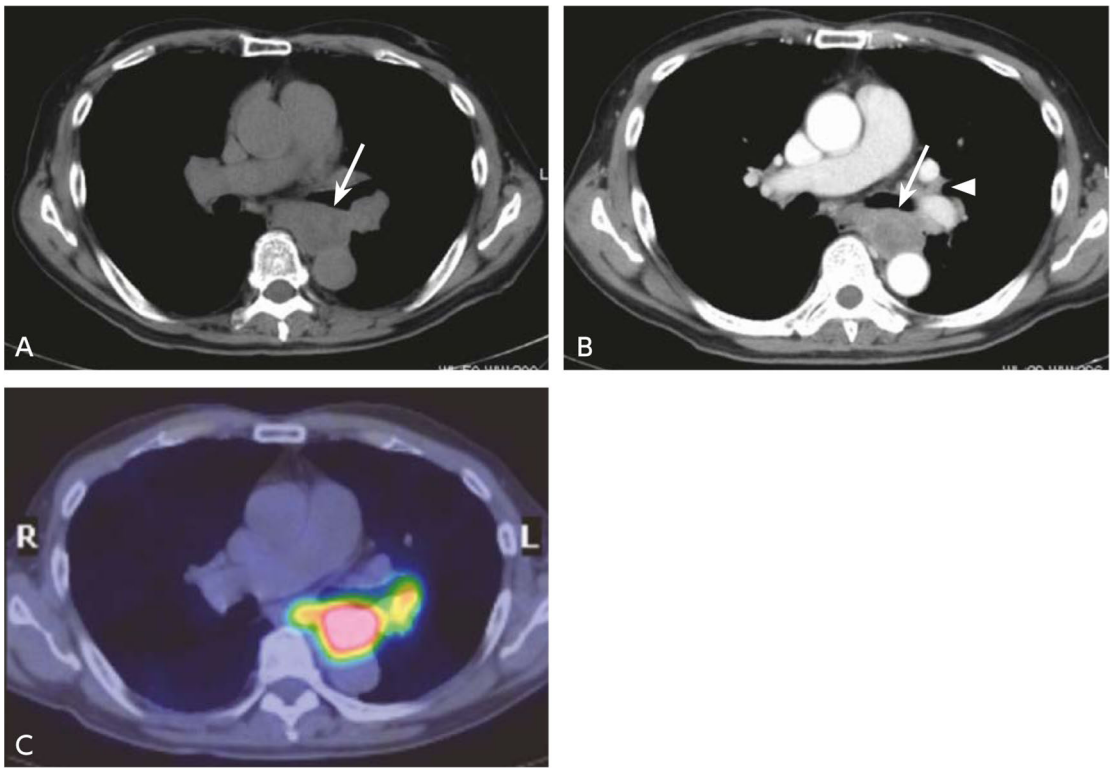

Figure 2. Hilar and mediastinal lymph node metastases of lung cancer

(c-T2N3M0, stage III B)

A: Non-contrast-enhanced CT, transverse image: Lymph node enlargement is seen dorsal to the left main bronchus and ventral to the descending aorta (⇨).

B: Contrast-enhanced CT, transverse image: The relationship between the enlarged lymph nodes and surrounding blood vessels is clearly seen (⇨). Left hilar lymph node enlargement is also suspected (▷).

C: FDG-PET/CT, transverse image: Accumulation consistent with enlarged lymph nodes is seen.

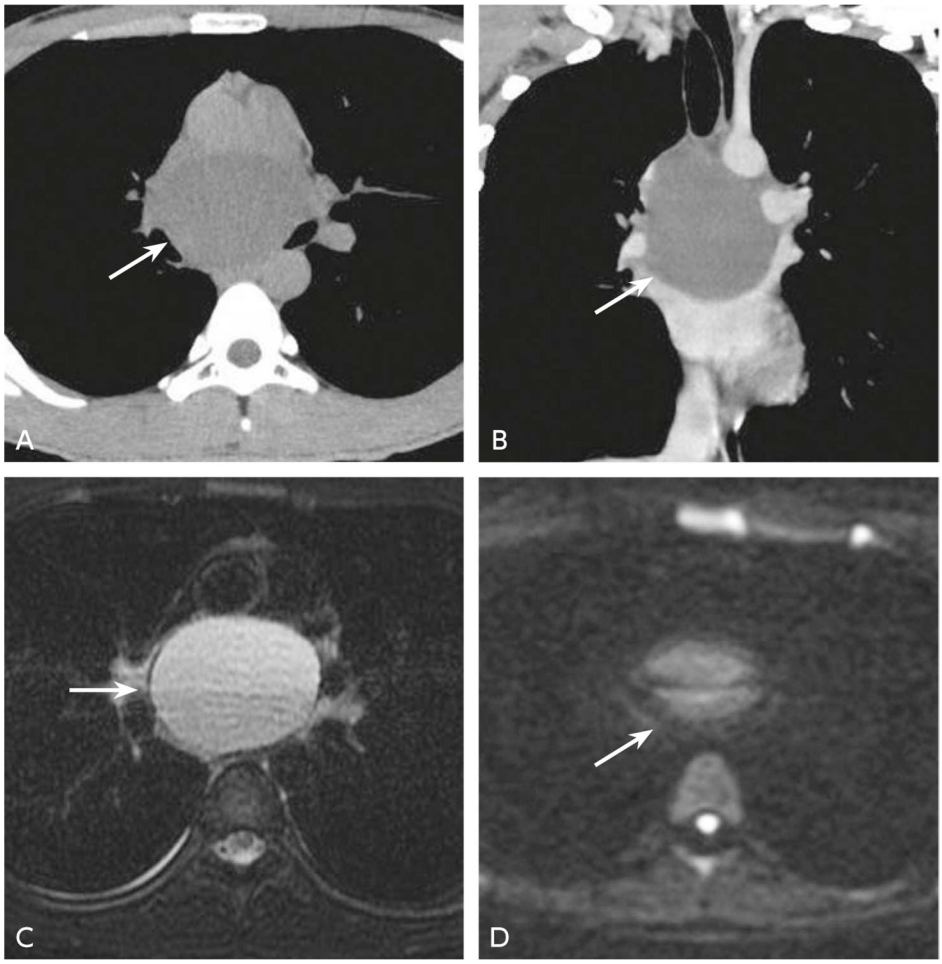

Figure 3. Bronchogenic cyst

A: Non-contrast-enhanced CT, transverse image: A mass with distinct borders is seen below the tracheal bifurcation. The mass is homogeneous and shows slightly higher attenuation than water (→).

B: Contrast-enhanced CT, coronal reconstructed image: Contrast enhancement is not seen in the mass (→).

C: MRI, fat-suppressed T2-weighted transverse image: The mass shows hyperintensity, and a fluid-fluid level (→) is seen in the mass.

D: MRI, diffusion-weighted transverse image, b-value = 1,000 s/mm^2: The mass shows slight hyperintensity (→).

3. Reducing the patient's radiation exposure

Although filtered back projection (FBP) has been used in CT for image reconstruction in the past, recent years have seen the emergence of systems that enable iterative reconstruction methods, which provide excellent noise reduction. Low-dose imaging and iterative reconstruction methods have made it possible to perform CT examinations with doses previously not considered feasible. For the thoracic region, image quality has been found to be comparable with 120-mA FBP imaging and 60-mA imaging using iterative reconstruction.[7)] The use of low-dose imaging using systems capable of iterative reconstruction methods should be emphasized in the future to reduce radiation exposure.

4. Display conditions

Window settings (WSs) of approximately 30 to 50 HU for window level (WL) and 250 to 400 HU for window width (WW) (mediastinum WS) are appropriate for observing soft tissue such as the mediastinum. Window settings of approximately -500 to -700 HU for WL and 1,200 to 2,000 HU for the WW (lung WS) are suitable when observing the lungs. Except in special cases, images are displayed using the pair of conditions for the mediastinum and lungs. The standard algorithm is used in reconstruction in the mediastinum WS, and reconstruction that accentuates the high-spatial-frequency algorithm is used in reconstruction in the lung WS.

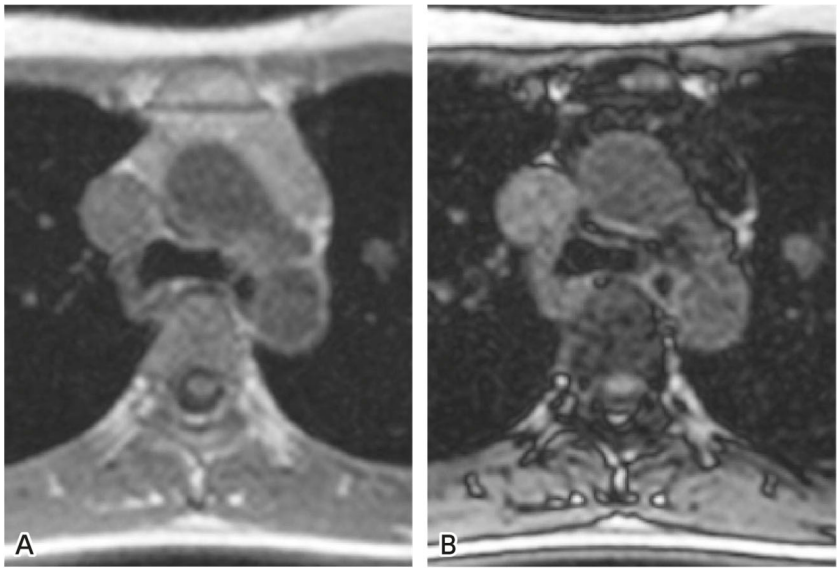

Figure 4. Thymic hyperplasia

A: MRI, GRE T1-weighted in-phase image, TR/163, TE/4.6, FA/75: The anterior mediastinal mass shows slightly higher signal intensity than muscle.

B: MRI, GRE T1-weighted opposed-phase image, TR/163, TE/2.3, FA/75: As compared with the in-phase image, a homogeneous signal decrease is seen in the mass.

5. Contrast imaging examinations

Automatic injectors are now widely used for bolus injections, with a total contrast medium dose of ≤ 100 mL and an injection rate of approximately 1 to 5 mL/s (Figs. 2B and 6B).[8)] To obtain good contrast enhancement over an extensive area, effort is needed to substantially improve temporal resolution by using an automatic injector in combination with MDCT. Perfusion imaging using dual-energy CT has recently been reported to be useful (Fig. 6C).[9)]

Magnetic resonance imaging (MRI)

1. Imaging method

Although imaging with a high-performance system with a strong magnetic field is preferable, artifacts caused by differences in magnetic susceptibility are always a problem for lung imaging. The thoracic region is prone to artifacts caused by heartbeats, blood flow in the great vessels, and breathing and is therefore an unfavorable location for MRI examination. However, these artifacts can be reduced by ECG and pulse-wave gating, respiratory gating and breath-holding, and the application of a presaturation pulse.

T1-weighted imaging and T2-weighted imaging are standard, and transverse images are usually acquired (Figs. 3C and 3D). However, coronal and sagittal images are also acquired for lung apex lesions (e.g., superior sulcus tumors), lung base lesions (e.g., diaphragmatic invasion of a malignancy), and mediastinal and chest wall lesions. A slice thickness of 5 to 8 mm is commonly used. A matrix size of $\geq 256 \times 192$ is preferred. The method called fast-spin echo (FSE), which has a short imaging duration, is generally used. Gradient echo (GRE) is used in MRA and cine imaging. The use of diffusion-weighted imaging has been examined for distinguishing between benign and malignant lesions and for diagnosing mediastinal lymph node metastasis in lung cancer and mediastinal tumors (Fig. 3D). However, there is poor reproducibility between MRI systems in determining an ADC cutoff, and this remains a challenge. Lesion blood flow status and the extent of progression can be evaluated by post-contrast T1-weighted imaging. However, depending on the location of the lesion, the evaluation may be more useful when combined with fat-suppressed imaging. In addition, chemical shift imaging has been reported to be effective for distinguishing thymic hyperplasia from thymoma. With this method, because protons in water and fat resonate at different frequencies, signals that strengthen each other (in phase) and signals that cancel each other (opposed phase) are generated, and changes in signal intensity are observed. In thymic hyperplasia, which is high in fat content, a decreased signal is seen in opposed-phase images. The imaging method mainly involves the use of GRE, with images acquired by increasing and decreasing the echo time (Figs. 4 and 5).[10)]

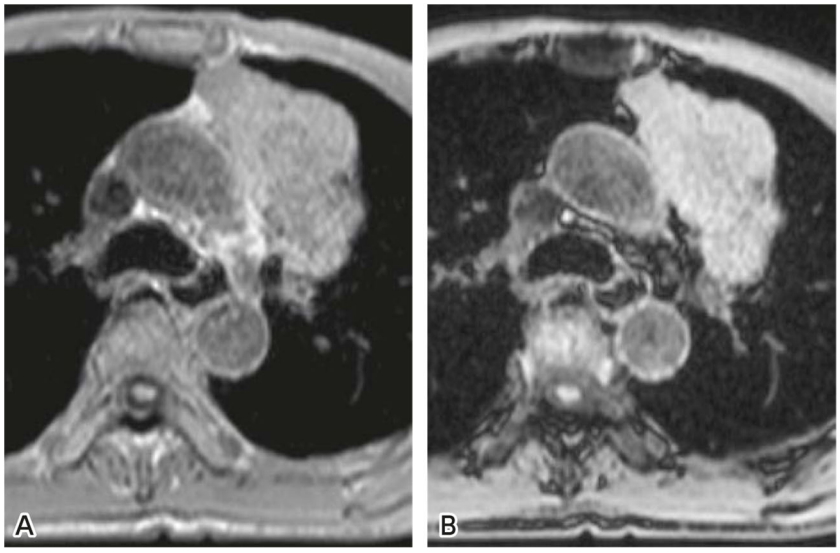

Figure 5. Thymoma

A: MRI, GRE T1-weighted in-phase image, TR/225, TE/4.6, FA/70: The anterior mediastinal mass shows slightly higher signal intensity than muscle.

B: MRI, GRE T1-weighted opposed-phase image, TR/225, TE/2.3, FA/70: No change in the signal of the mass is seen.

Nuclear medicine imaging

1. Pulmonary perfusion scintigraphy ^{99m}TC-macroaggregated albumin (^{99m}Tc-MAA)

In general, the patient lies supine at rest, the injection syringe is shaken immediately before intravenous infusion, and ^{99m}Tc-MAA is slowly injected intravenously at a dose of 111 to 185 MBq as the patient takes 2 to 3 deep breaths. Beginning 5 minutes after injection, images are acquired from 6 angles (or 8 with the addition of left and right anterior oblique), frontal (Fig. 6E), posterior, left and right lateral, and left and right posterior oblique, using a gamma camera equipped with a low-energy general-purpose (or high-resolution) collimator. It can also be imaged in combination with SPECT.

2. Ventilation scintigraphy (^{81m}Kr)

Imaging is generally performed with the patient sitting with his or her back to a gamma camera equipped with a medium- (or low-medium-) energy collimator. When ^{81m}Kr gas is used, humidified oxygen or air is passed through a generator at a flow rate of approximately 0.3 to 3.0 L/min. The patient then inhales the ^{81m}Kr gas that emerges through a mask or similar device, and imaging is performed. Because the physical half-life of ^{81m}Kr is a short 13 seconds, repeated imaging can be performed without the need for special equipment, and it can be performed from many angles (Figs. 6D and 6E). Ventilation scintigraphy is highly clinically useful in pulmonary thromboembolism, which is visualized as a defect only on perfusion scintigraphy when pulmonary blood flow scintigraphy and ventilation scintigraphy are performed concurrently.

3. ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) PET and PET/CT imaging

For 2D data acquisition, 185 to 444 MBq (3 to 7 MBq/kg) of FDG are administered intravenously; for 3D data acquisition, 111 to 259 MBq (2 to 5 MBq/kg) are administered. The dose is adjusted as appropriate depending on the equipment used and the patient's age and weight. Approximately 60 minutes after administration, a PET or PET/CT system is used to perform a whole-body emission scan. A transmission scan (in the case of PET) or CT imaging (in the case of PET/CT; Fig. 2C) is also performed. Delayed-phase imaging is added as necessary.

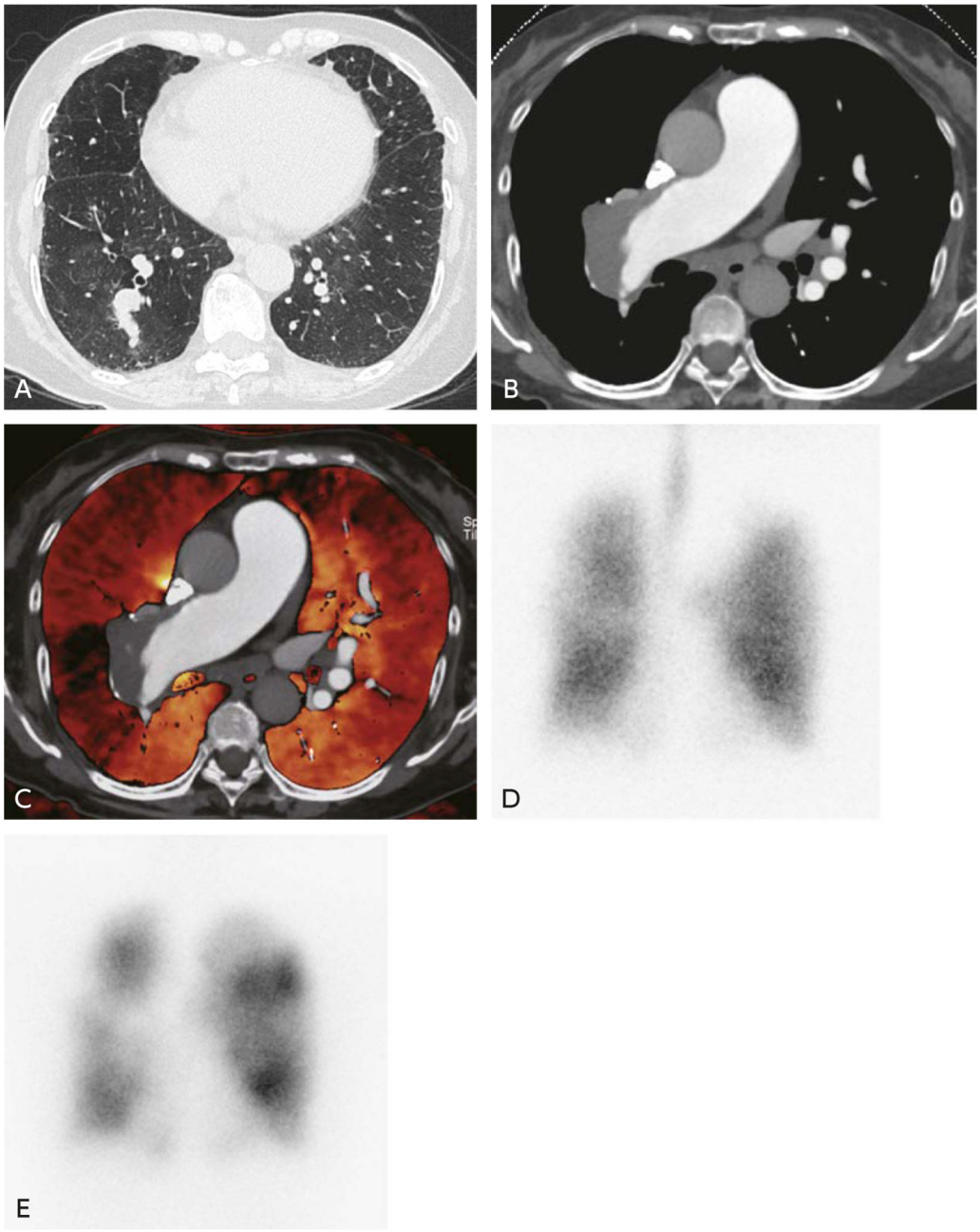

Figure 6. Chronic thromboembolic pulmonary hypertension

A: HRCT, transverse image: The lung attenuation shows an inhomogeneous mosaic pattern.
B: Contrast-enhanced CT, arterial phase, transverse image: The pulmonary arteries are markedly dilated, and a large thrombus is seen in the right pulmonary artery.
C: Contrast-enhanced CT, perfusion image: Blood flow in the lungs appears inhomogeneous, and areas of perfusion defects are seen.
D: Pulmonary ventilation scintigraphy (^{81m}Kr): Accumulation defects are not seen in either lung.
E: Pulmonary perfusion scintigraphy (^{99m}Tc-MAA): Multiple defects are seen in both lungs.

Secondary sources used as references

1) Japan Radiological Society, Ed.: Guidelines for Handling Digital Images, 3rd Edition. Japan Radiological Society, 2015.
2) Japan Medical Imaging and Radiological Systems Industries Association, Ed.: Guidelines for Quality Control of Monitors for Displaying Medical Images, revised on July 20, 2017. Japan Medical Imaging and Radiological Systems Industries Association, 2017.
3) Nishimura M et al: Annual change in pulmonary function and clinical phenotype in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 185: 44-52, 2012
4) Akira M et al: Quantitative CT in chronic obstructive pulmonary disease: inspiratory and expiratory assessment. AJR Am J Roentgenol 192: 267-272, 2009
5) Matsuoka S et al: Quantitative assessment of air trapping in chronic obstructive pulmonary disease using inspiratory and expiratory volumetric MDCT. AJR Am J Roentgenol 190: 762-769, 2008
6) van Klaveren RJ et al: Management of lung nodules detected by volume CT scanning. N Engl J Med 361: 2221-2229, 2009
7) Yamashiro T et al: Adaptive iterative dose reduction using three dimensional processing (AIDR3D) improves chest CT image quality and reduces radiation exposure. PLoS One 9: e105735, 2014
8) Yi CA et al: Efficacy of helical dynamic CT versus integrated PET/CT for detection of mediastinal nodal metastasis in non-small cell lung cancer. AJR Am J Roentgenol 188: 318-325, 2007
9) Le Faivre J et al: Impact of CT perfusion imaging on the assessment of peripheral chronic pulmonary thoromboembolism: clinical experience in 62 patients. Eur Radiology 26: 4011-4020, 2016
10) Inaoka T et al: Thymic hyperplasia and thymus gland tumors: differentiation with chemical shift MR imaging. Radiology 243: 869-876, 2007
11) Bajc M et al: EANM guidelines for ventilation/perfusion scintigraphy: part 1. pulmonary imaging with ventilation/perfusion single photon emission tomography. Eur J Nucl Med Mol Imaging 36: 1356-1370, 2009

CQ 1 Is CT recommended for the differential diagnosis of adult community-acquired pneumonia and non-infectious diseases?

Recommendation

CT is weakly recommended for the differential diagnosis of adult community-acquired pneumonia and non-infectious diseases.

Recommendation strength: 2, strength of evidence: D (very weak), agreement rate: 100% (15/15)

Background

There are a variety of lung diseases that must be differentiated from community-acquired pneumonia. Examples in immunocompetent individuals include pulmonary edema, eosinophilic pneumonia (EP), hypersensitivity pneumonitis, idiopathic interstitial pneumonia, and drug-induced lung disorders.[1)] In addition to these, several pathologies are possible in immunodeficient individuals, such as opportunistic infections and changes caused by malignancies.[2)] The role of CT was examined in the differential diagnosis of community-acquired pneumonia and these non-infectious diseases, particularly acute respiratory disorders, which appear as diffuse lung opacities.

Explanation

There is considerable overlap in the chest radiography findings of community-acquired pneumonia and diffuse lung disease, and no findings are considered disease-specific. However, it has been reported that the addition of CT, particularly HRCT, may provide new information (Figs. 1 and 2).[3-5)]

An investigation of the use of CT in patients with community-acquired pneumonia who required hospitalization found it useful for detecting lesion cavities and masses not detected by chest radiography and for excluding masses suspected of being present based on chest radiography.[3)] Although its usefulness does not extend as far as differentiating from infectious pneumonia, it has been found to be useful to some extent for diagnosis by exclusion or revealing important findings. A survey of pulmonologists was conducted to examine the status of HRCT use and its usefulness in diffuse lung disease.[4)] Of the valid responses received from the 230 physicians surveyed, 67% to 89% indicated that HRCT was useful in diagnosing diseases such as idiopathic interstitial pneumonia, EP, Langerhans cell histiocytosis, lymphangioleiomyomatosis, and bronchiectasis.

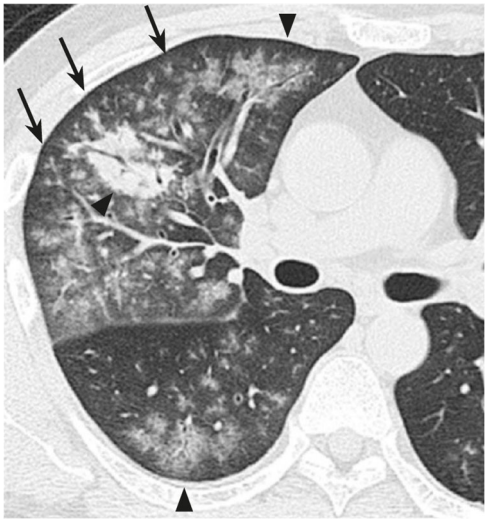

Figure 1. *Mycoplasma pneumoniae* pneumonia (man in his 40s)

HRCT: Centrilobular branching opacities and nodules (→), acinar to lobular ground-glass opacities and consolidations (►) are seen in the right upper and lower lobes. Bronchovascular bundle thickening is also prominent.

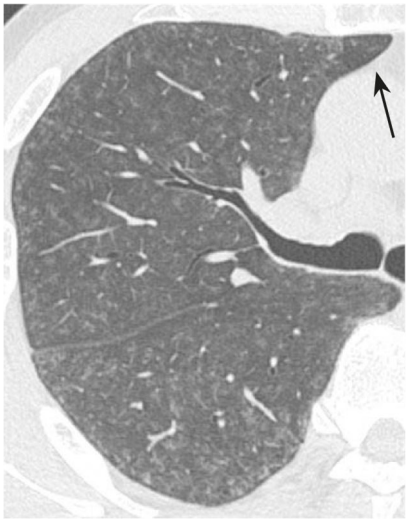

Figure 2. Non-fibrotic (subacute) hypersensitivity pneumonitis (man in his 60s)

HRCT: Centrilobular ground-glass opacities are seen diffusely. A low-attenuation area (→) caused by air-trapping is seen in the periphery of S3. No centrilobular branching opacities are seen.

Five of the articles describing investigations of the use of HRCT to differentiate between infectious and non-infectious diseases indicated that there are several common distinguishing features in images.[2, 6-9)] An investigation of acute lung parenchymal lesions in immunocompetent individuals found that the most important finding for distinguishing infectious from non-infectious disease was centrilobular nodules,[6)] which are typically not seen in non-infectious diseases other than hypersensitivity pneumonitis. Other findings specific to infection were the presence of segmental distribution and wedge-shaped consolidation associated with the segmental bronchi. The sensitivity of these findings was 83% for infectious disease and 94% for non-infectious disease.[6)] An examination of a group with multiple consolidations seen on chest radiography found that important HRCT findings for distinguishing infectious from non-infectious disease were a centrilobular branching structure caused by centrilobular nodules and endobronchial mucus plugs.[7)] Neither the centrilobular branching structure nor a tree-in-bud appearance is seen in non-infectious lung diseases such as hypersensitivity pneumonitis, emphysema, obstructive bronchiolitis, and cryptogenic organizing pneumonia.[8, 9)] An examination of the diagnostic rate for various diseases in a group of immunodeficient patients who did not have acquired immune deficiency syndrome and who developed acute lung injuries,[2)] including infection, showed variability in the diagnostic rate depending on the disease, with sensitivity ranging from 27% to 100% and positive predictive value ranging from 25% to 100%. HRCT findings frequently seen in bacterial pneumonia include centrilobular lesions and lesions of secondary lobules, and the CT halo sign and cavities tend to be common in mycosis and tuberculosis. Malignancies included leukemia, malignant lymphoma, and lymphangitis carcinomatosa, with

bronchovascular bundle thickening, nodules, and lymph node enlargement frequently seen in these diseases. An examination of differentiation between infectious pneumonia and invasive mucinous adenocarcinoma mimicking pneumonia found that bronchial wall thickening proximal to a lesion and pleural thickening adjacent to a lesion were findings suggestive of infectious pneumonia.[10)]

Although not differentiation based on imaging, examples of the purposes for which CT is useful include determining locations for alveolar lavage fluid collection, transbronchial lung biopsy, and surgical biopsy, which may contribute to the differentiation of pneumonia and non-infectious disease.

Although the above findings are insufficient scientific evidence to establish that CT is effective in this role, there are HRCT findings that are relatively characteristic of community-acquired pneumonia and non-infectious disease, making their differentiation possible to some extent, which may aid in determining a treatment plan. It was therefore concluded that CT can be weakly recommended for the differential diagnosis of adult community-acquired pneumonia and non-infectious diseases.

Search keywords and secondary sources

PubMed was searched using the following keywords: pneumonia and computed tomography.

References

1) Shorr AF et al: Pulmonary infiltrates in the non-HIV-infected immunocompromised patient: etiologies, diagnostic strategies, and outcomes. Chest 125: 260-271, 2004
2) Emoto T et al: HRCT findings of pulmonary complications in non-AIDS immunocompromised patients: are they useful in differential diagnosis? Radiat Med 21: 7-15, 2003
3) Beall DP et al: Utilization of computed tomography in patients hospitalized with community-acquired pneumonia. Maryland Med J 47: 182-187, 1998
4) Scatarige JC et al: Utility of high-resolution CT for management of diffuse lung disease: results of a survey of U.S. pulmonary physicians. Acad Radiol 10: 167-175, 2003
5) Tanaka N et al: Community-acquired pneumonia: a correlative study between chest radiographic and HRCT findings. Jpn J Radiol 33: 317-328, 2015
6) Tomiyama N et al: Acute parenchymal lung disease in immunocompetent patients: diagnostic accuracy of high-resolution CT. AJR Am J Roentgenol 174: 1745-1750, 2000
7) Johkoh T et al: Usefulness of high-resolution CT for differential diagnosis of multi-focal pulmonary consolidation. Radiat Med 14: 139-146, 1996
8) Aquino SL et al: Tree-in-bud pattern: frequency and significance on thin-section CT. J Comput Assist Tomogr 20: 594-599, 1996
9) Okada F et al: Clinical/pathological correlations in 553 patients with primary centrilobular findings on high-resolution CT scan of the thorax. Chest 132: 1939-1948, 2007
10) Kim TH et al: Differential CT features of infectious pneumonia versus bronchioloalveolar carcinoma (BAC)mimicking pneumonia. Eur Radiol 16: 1763-1768, 2006

BQ 17 Is CT recommended for differentiating between bacterial pneumonia and atypical pneumonia?

Statement

CT is recommended for differentiating between *Streptococcus pneumoniae* pneumonia and *Mycoplasma pneumoniae* pneumonia. Although evidence for its usefulness in the case of other prophlogistic microorganisms is limited, their CT characteristics have been established to some degree.

Background

The guidelines of the Japanese Respiratory Society recommend that atypical pneumonias be screened from among the community-acquired pneumonias and treated early. The usefulness of CT for distinguishing between bacterial pneumonia and atypical pneumonias in adults was examined.

Explanation

The main CT findings examined were those of *Streptococcus pneumoniae* pneumonia (Fig. 1), the most common type of bacterial pneumonia, and frequently occurring atypical pneumonias (*Mycoplasma pneumoniae* pneumonia, *Chlamydophila pneumoniae* pneumonia, and influenza virus pneumonia; Fig. 2). The characteristics of the findings have been established to some extent for *Streptococcus pneumoniae* pneumonia, *Mycoplasma pneumoniae* pneumonia, and influenza virus pneumonia.

Tanaka et al. compared the CT findings of 18 patients with bacterial pneumonia and 14 patients with atypical pneumonia.[1)] Centrilobular shadows, acinar shadows, air space consolidations, and ground-glass opacities with lobular distribution were seen more frequently in atypical pneumonia than in bacterial pneumonia. An investigation by Nambu et al. (24 patients with *Chlamydophila pneumoniae* pneumonia, 30 patients with *Mycoplasma pneumoniae* pneumonia, 41 patients with *Streptococcus pneumoniae* pneumonia) showed that findings of bronchovascular bundle thickening and centrilobular nodules were more frequent in *Mycoplasma pneumoniae* pneumonia and *Chlamydophila pneumoniae* pneumonia than in *Streptococcus pneumoniae* pneumonia.[2)]

An investigation by Reittner et al. of CT findings in a total of 114 patients, comprising 35 patients with bacterial pneumonia, 28 with *Mycoplasma pneumoniae* pneumonia, and 9 with viral pneumonia, found a higher frequency of centrilobular nodules in *Mycoplasma pneumoniae* pneumonia and viral pneumonia than in bacterial pneumonia, with no consolidation seen in viral pneumonia.[3)] Ito et al. examined bacterial pneumonia in 94 patients (including 65 patients with *Streptococcus pneumoniae* pneumonia) and atypical pneumonia in 31 patients (including 20 patients with *Mycoplasma pneumoniae* pneumonia and 7 with *Chlamydophila pneumoniae* pneumonia).[4)] Centrilobular nodules, bronchovascular bundle thickening, and lobular ground-glass opacities were seen significantly more frequently in atypical pneumonia, making these

findings useful for differentiating atypical pneumonia from bacterial pneumonia. However, distinguishing *Chlamydophila pneumoniae* pneumonia from bacterial pneumonia was difficult.

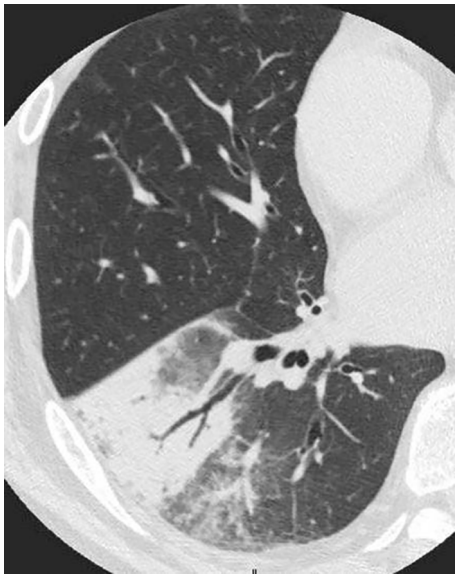

Figure 1. *Streptococcus pneumoniae* pneumonia

HRCT, transverse image: Consolidation and ground-glass opacities associated with air bronchograms are seen in the right lower lobe. Bronchial wall thickening is unremarkable.

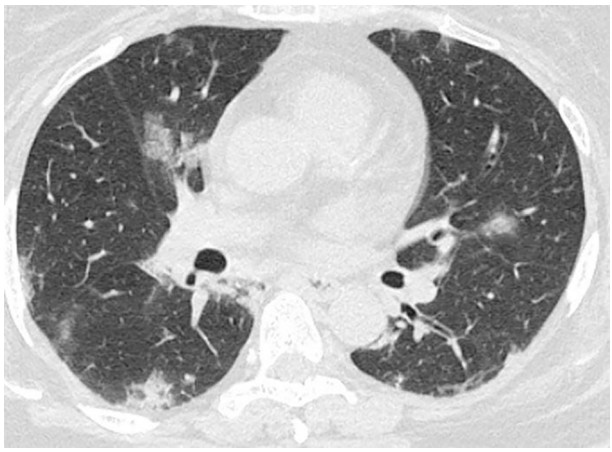

Figure 2. Influenza virus pneumonia

HRCT, transverse image: Multiple ground-glass opacities and consolidations are seen in both lungs, with intralobular reticular opacities seen in the ground-glass opacities.

Investigations by Miyashita et al. (64 patients with *Mycoplasma pneumoniae* pneumonia and 68 with *Streptococcus pneumoniae* pneumonia)[5] and Nei et al. (36 patients with *Mycoplasma pneumoniae* pneumonia and 52 with community-acquired pneumonia, including 20 with *Streptococcus pneumoniae* pneumonia)[6] found bronchial wall thickening and centrilobular nodules at significantly higher frequencies in *Mycoplasma pneumoniae* pneumonia. There are other, similar reports of CT findings in *Streptococcus pneumoniae* pneumonia and *Mycoplasma pneumoniae* pneumonia, indicating that findings of bronchial wall thickening and centrilobular nodules are useful for distinguishing between these two conditions.

There have been few summary reports of the imaging findings for *Chlamydophila pneumoniae* pneumonia. As compared with *Mycoplasma pneumoniae* pneumonia, bronchial wall thickening and centrilobular nodules are seen less frequently in *Chlamydophila pneumoniae* pneumonia, whereas lobular ground-glass opacities and lobular consolidation are seen more frequently.[7] However, differentiation from *Streptococcus pneumoniae* pneumonia is considered difficult.[4]

With regard to influenza virus pneumonia, summary reports of seasonal and novel influenza viruses have indicated that intralobular reticular opacities are frequently seen in these conditions.[8-10] Ono et al. compared CT findings in seasonal influenza virus pneumonia (30 patients) and *Streptococcus pneumoniae* pneumonia (71 patients).[11] Ground-glass opacities and reticular opacities were frequently seen in influenza

virus pneumonia, and consolidation, intrabronchial mucus plugs, and centrilobular nodules were common in *Streptococcus pneumoniae* pneumonia. Significant differences were seen for each finding.

Fujita et al. examined the CT findings of 12 patients with virus-associated pneumonia and found segmental consolidation in patients with mixed infections with bacterial pneumonia, which distinguished them from pure viral pneumonia.[8)] In an examination of the CT findings of 93 patients with viral pneumonia and 22 patients with bacterial pneumonia, Miller et al. frequently observed diffuse ground-glass opacities or consolidation in bacterial pneumonia.[12)]

Numerous reports have described findings similar to those seen in influenza virus pneumonias in other viral pneumonias such as adenoviral pneumonia. CT may therefore be useful for distinguishing viral pneumonia from bacterial pneumonia.[3, 8)]

Search keywords and secondary sources

PubMed was searched using the following keywords: pneumonia and computed tomography.

In addition, the following were referenced as secondary sources.

1) Japanese Respiratory Society, Ed.: 2017 Guidelines for the Management of Community-acquired Pneumonia. Japanese Respiratory Society, 2017.
2) Japan Radiological Society, Japanese College of Radiology, Ed.: 2007 Diagnostic Imaging Guidelines for Adult Community-acquired Pneumonia, Japan Radiological Society, 2007.
3) Murayama S: CT diagnosis of lung infections. Tuberculosis 77: 79-86, 2002.
4) Murata K, et al.: CT appearance of respiratory tract infections. Nippon Acta Radiologica 59: 371-379, 1999.
5) Ashizawa K: Bacterial pneumonia. Japanese Journal of Clinical Medicine 28: 231-234, 2007.
6) Tanaka H, et al.: CT appearance of mycoplasma pneumonia lesions. Japanese Journal of Clinical Radiology 30: 979-986, 1985.

References

1) Tanaka N et al: High resolution CT findings in community-acuired pneumomonia. J Comput Assist Tomogr 20: 600- 608, 1996
2) Nambu A et al: Chlamydia pneumoniae: comparison with findings of mycoplasma pneumoniae and streptococcus pneumoniae at thin-section CT. Radiology 238: 330-338, 2006
3) Reittner P et al: Pneumonia: high-resolution CT findings in 114 patients. Eur Radiol 13: 515-521, 2003
4) Ito I et al: Differentiation of bacterial and non-bacterial community-acuired pneumomonia by thin-section computed tomography. Eur J Radiol 72: 388-395, 2009
5) Miyashita N et al: Radiographic features of mycoplasma pneumoniae pneumonia: differential diagnosis and performance timing. BMC Med Imaging 9: 7, 2009
6) Nei T et al: Mycoplasma pneumoniae pneumonia: differential diagnosis by computerized tomography. Intern Med 46: 1083-1087, 2007
7) Okada F et al: Chlamydia pneumoniae pneumonia mycoplasma pneumoniae pneumonia: comparison of clinical finfings and CT findings. J Comput Assist Tomogr 29: 626-632, 2005
8) Fujita J et al: Chest CT findings of influenza virus- associated pneuonia in 12 adult patients. Influenza Other Respi Viruses 1: 183-187, 2007
9) Agarwal PP et al: Chest radiographic and CT findings in novel swine-origin influenza A (H1N1) virus (S-OIV) infection. AJR Am J Roentgenol 193: 1488-1493, 2009
10) Marchiori E et al: High resolution computed tomography findings from adult patients with influenza A (H1N1) virus-associated pneumonia. Eur J Radiol 74: 93-98, 2010
11) Ono A et al: A comparative study of thin-section CT findings between seasonal influenza virus pneumonia and Streptococcus pneumoniae pneumonia. Br J Radiol 87: 20140051, 2014
12) Miller WT Jr et al: CT of viral lower respiratory tract infestions in adults: comparison among viral organisms and between viral and bacterial infections. AJR Am J Roentgenol 197: 1088-1095, 2011

BQ 18 Is CT recommended for diagnosing pneumoconiosis?

Statement

CT is useful and recommended for determining the distribution and extent of pneumoconiosis lesions and diagnosing complications.

Background

Under the Pneumoconiosis Law in Japan, chest radiography plays the central role in the diagnosis of pneumoconiosis, and its severity is determined according to the PR classification for chest radiography. Clinically, however, CT findings are used complementarily in diagnosis.

Explanation

In silicosis, CT has been reported to provide excellent detection of coalescence and large opacities.[1)] CT has also been found to improve the rate of inter-reader agreement on findings.[2)] In patients who exhibit small granular opacities classified as type-p opacities on chest radiography, the addition of HRCT improves the rate of detection of granular opacities themselves[3)] and makes it possible to determine whether granular opacities are actually present, or if the findings indicate peribronchiolar fibrosis alone,[4)] enabling more accurate PR classification.

In the case of asbestosis, diagnosis is difficult with chest radiography of general lung lesions alone when severe pleural plaques are present, and the combined use of CT is therefore considered advisable.[5)] A subpleural curvilinear shadow (SCLS) is a characteristic CT finding in asbestosis (Fig.) and is observed frequently in patients with this disease.[6)] Such findings of mild fibrosis are not visualizable without CT and therefore require it.

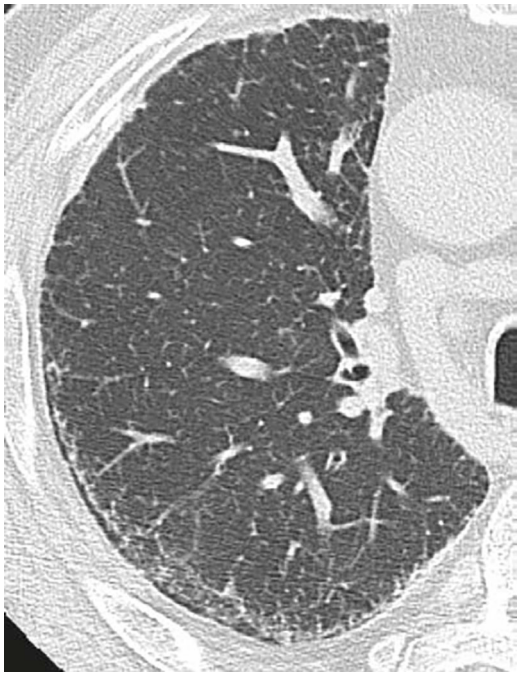

Figure. Asbestosis

HRCT, transverse image: A linear shadow that follows the pleura is seen immediately below the upper dorsal pleura, and findings suggestive of aggregated partially granular opacities are seen. This is the typical appearance of SCLSs seen in asbestosis.

Search keywords and secondary sources

PubMed was searched using the following keywords: CT, pneumoconiosis, silicosis, asbestosis, and PR classification.

References

1) Remy-Jardin M et al: Coal worker's pneumoconiosis: CT assessment in exposed workers and correlation with radiographic findings. Radiology 177 (2): 363-371, 1990
2) Antao VC et al: High-resolution CT in silicosis: correlation with radiographic findings and functional impairment. J Compt Assist Tomo; 29 (3): 350-356, 2005
3) Begin R et al: Computed tomography scan in the early detection of silicosis. Am Rev Resp Dis 144 (3 Pt 1): 697-705, 1991
4) Akira M et al: Radiographic type p pneumoconiosis: high-resolution CT. Radiology 171 (1): 117-123, 1989
5) Friedman AC et al: Asbestos-related pleural disease and asbestosis: a comparison of CT and chest radiography. AJR Am J Roentgenol 150 (2): 269-275, 1988
6) Yoshimura H et al: Pulmonary asbestosis: CT study of subpleural curvilinear shadow. Radiology 158 (3): 653-658, 1986

FQ 1 Is CT recommended for diagnosing the severity of chronic obstructive pulmonary disease (COPD)?

Statement

Although CT is not required to diagnose the severity of COPD, there is scientific evidence supporting its usefulness in this role.

Background

The severity of COPD is determined comprehensively based on respiratory symptoms, spirometric classification, and/or risk of exacerbation. CT is not required (secondary sources 1 and 2). However, the structural abnormalities on CT, such as the extent of emphysema, peripheral airway narrowing, and a decrease in the pulmonary vascular bed, are correlated with airflow limitation on spirometry, acute COPD exacerbation, and patients' prognosis.

Explanation

Emphysema is defined as a region of low attenuation not bounded by a visible wall on CT. Visual assessment of low-attenuation areas is a simple method for evaluating emphysema extent on CT.[1, 2] Recently, computer-based quantification has been increasingly used. The ratio of low-attenuation area on CT (LAA%) is widely used as a measure of emphysema extent.[3] The mean CT attenuation values of the whole lung,[4] the Hounsfield Unit (HU) points below 15% of the voxels (Perc15),[5] are also useful measures. A previous study reported that a lower Perc15 value was significantly related to a greater decline in FEV1.[6] Moreover, quantitative evaluations of emphysematous lung based on artificial intelligence were found to be correlated with patient prognosis.[7]

A histological analysis of surgical specimens showed that COPD severity is associated with bronchial wall thickening and lumen narrowing.[8] Various methods of computer measurement on CT have been proposed for evaluating the airways [airway wall area,[9] percent airway wall area corrected for total airway area (WA%),[10] peak attenuation of the bronchial wall,[11] and intrathoracic airway volume measurement[12]].

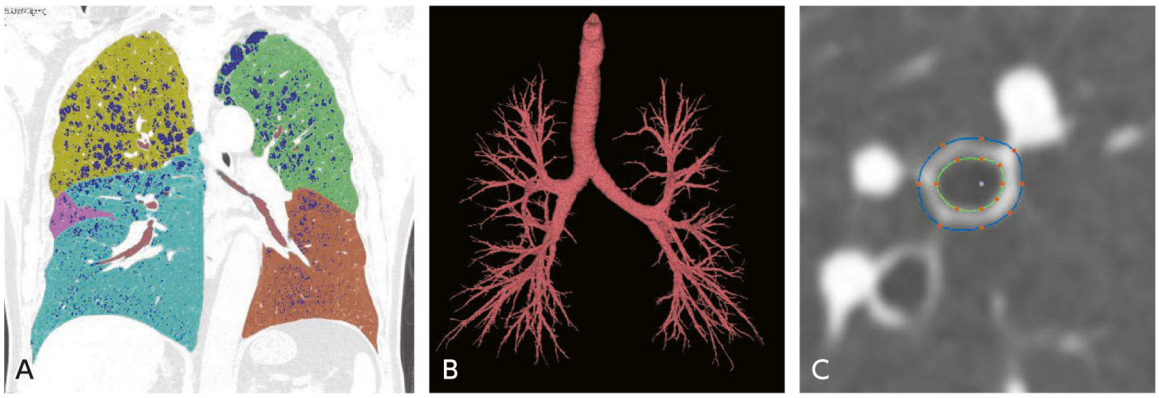

Figure. Examples of CT quantitative evaluation of COPD

The patient was a man in his 70s.

A: Quantitative measurement of emphysema (areas with ≤ -950 HU shown in blue), B: Extraction of bronchial tree, C: Measurement of bronchial wall area (WA%)

Expiratory CT is useful for evaluating emphysematous lung and airway lesions (see BQ 19).

A method using the percent cross-sectional area of small pulmonary vessels (% CSA < 5) has been proposed to evaluate vascular lesions. A % CSA < 5 has been found to be highly correlated with LAA% (r = -0.83)[13] and to be strongly correlated with mean pulmonary arterial pressure measured by right heart catheterization in patients with COPD.[14] The diameter of the main pulmonary artery on CT is a predictive factor for acute exacerbation of COPD.[15]

COPD severity should be evaluated comprehensively based on not only spirometry, but also exercise tolerance, nutritional status, and systemic comorbidities. Morphological evaluation of the erector spinae muscles by CT also correlates with prognosis.[16]

Search keywords and secondary sources

PubMed was searched using the keywords "COPD" and "CT," and 3,230 articles were retrieved, of which 16 were cited.

In addition, the following were referenced as secondary sources.

1) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2020 REPORT, 2020
2) Japanese Respiratory Society, Ed.: 2018 Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (COPD), 5th Edition. Medical Review, 2018.

References

1) Lynch DA et al: CT-based visual classification of emphysema: association with mortality in the COPDGene study. Radiology 288 (3): 859-866, 2018
2) Goddard PR et al: Computed tomography in pulmonary emphysema. Clin Radiol 33 (4): 379-387, 1982
3) Gevenois PA et al: Comparison of computed density and macroscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 152 (2): 653-657, 1995
4) Camiciottoli G et al: Spirometrically gated high-resolution CT findings in COPD: lung attenuation vs lung function and dyspnea severity. Chest 129 (3): 558-564, 2006

5) Mohamed Hoesein FA et al: CT-quantified emphysema in male heavy smokers: association with lung function decline. Thorax 66 (9): 782-787, 2011
6) Lowe KE et al: COPDGene ((R)) 2019: Redefining the diagnosis of chronic obstructive pulmonary disease: Chronic Obstr Pulm Dis 6 (5): 384-399, 2019
7) Humphries SM et al: Deep learning enables automatic classification of emphysema pattern at CT. Radiology 294 (2): 434-444, 2020
8) Hogg JC et al: The nature of small-airway obstruction in chronic obstructive pulmonary disease. N Engl J Med 350 (26): 2645-2653, 2004
9) Nakano Y et al: Computed tomographic measurements of airway dimensions and emphysema in smokers: correlation with lung function. Am J Respir Crit Care Med 162 (3 Pt 1): 1102-1108, 2000
10) Berger P et al: Airway wall thickness in cigarette smokers: quantitative thin-section CT assessment. Radiology 235 (3): 1055-1064, 2005
11) Yamashiro T et al: Quantitative assessment of bronchial wall attenuation with thin-section CT: an indicator of airflow limitation in chronic obstructive pulmonary disease. AJR Am J Roentgenol 195 (2): 363-9, 2010
12) Tanabe N et al: Associations of airway tree to lung volume ratio on computed tomography with lung function and symptoms in chronic obstructive pulmonary disease. Respir Res 20 (1): 77, 2019
13) Matsuoka S et al: The relationship between small pulmonary vascular alteration and aortic atherosclerosis in chronic obstructive pulmonary disease: quantitative CT analysis. Acad Radiol 18 (1): 40-46, 2011
14) Matsuoka S et al: Pulmonary hypertension and computed tomography measurement of small pulmonary vessels in severe emphysema. Am J Respir Crit Care Med 181 (3): 218-225, 2010
15) Wells JM et al: Pulmonary arterial enlargement and acute exacerbations of COPD. N Engl J Med 367 (10): 913-921, 2012
16) Tanimura K et al: Quantitative assessment of erector spinae muscles in patients with chronic obstructive pulmonary disease: novel chest computed tomography-derived index for prognosis. Ann Am Thorac Soc 13 (3): 334-341, 2016

BQ 19 Is expiratory CT recommended for the diagnosis of obstructive pulmonary disease?

Statement

Although scientific evidence is lacking, the use of expiratory CT can be considered after reduction of radiation exposure.

Background

Expiratory CT is basically used as a technique for functional respiratory imaging for research purposes, such as evaluating air trapping and the collapse of the trachea and bronchi that occur during expiration as a result of obstruction caused by peripheral airway stenosis in bronchial asthma and COPD. Whether expiratory CT is useful for the diagnosis of obstructive pulmonary disease was evaluated.

Explanation

As indicated in references such as the GOLD documents and the Japanese Respiratory Society's guidelines for the diagnosis and treatment of COPD (secondary sources 1 and 2), CT is not considered essential for diagnosing obstructive pulmonary disease. Fundamental to the diagnosis of obstructive pulmonary disease is respiratory function testing. That is, CT is unnecessary for the actual diagnosis of various obstructive pulmonary diseases. However, even the above-mentioned guidelines indicate that CT is useful in cases such as when morphological differentiation from other diseases is required or to detect mild emphysematous lesions. There also have been no reports indicating that expiratory CT is necessary for the actual diagnosis of various obstructive pulmonary diseases. However, as a technique for functional respiratory imaging of conditions such as air trapping (Fig.) and the collapse of the trachea and bronchi in obstructive pulmonary disease, expiratory CT may be used in the clinical setting to plan treatment and evaluate treatment efficacy. Therefore, the use of expiratory CT imaging may be desirable depending on the purpose.

Typical uses of expiratory CT in obstructive pulmonary disease include ① evaluating air trapping, ② evaluating airway collapse, ③ quantitatively evaluating emphysematous lesions, and ④ diagnosing obstructive pulmonary disease that appears normal on inspiratory CT, but abnormal on expiratory CT.

1. Evaluating air trapping and respiratory function with expiratory CT

The methods used to evaluate air trapping with expiratory CT include using the lung density threshold and mean lung density. The severity of air trapping seen with either method in various obstructive pulmonary diseases has been found to be correlated with the severity of airflow limitation indicated by respiratory function tests.[1-3] However, air trapping is also seen in healthy individuals and must therefore be interpreted carefully.[4]

2. Evaluating collapse of the trachea and bronchi and pulmonary function with expiratory CT

Collapse of the bronchi is evaluated based on the changes in the luminal areas of the segmental, subsegmental, and sub-subsegmental bronchi as compared with inspiratory CT. The ratio of the luminal area during inspiration versus the luminal area during expiration was found to be correlated with the severity of the airflow limitation in patients with COPD, with this trend being the strongest for peripheral sub-subsegmental bronchi.[5)]

3. Evaluating emphysematous lesions with expiratory CT

A tendency for expiratory CT to underestimate emphysema severity has been identified,[6)] and inspiratory CT has been found to be superior to expiratory CT for quantitatively evaluating emphysematous lesions.[7)]

4. Obstructive diseases with normal inspiratory CT and abnormal expiratory CT findings

Typical obstructive diseases with normal inspiratory CT and abnormal expiratory CT findings include bronchiolitis obliterans and bronchial asthma. There is evidence suggesting that expiratory CT may enable milder abnormalities to be detected at an early stage in these diseases.[6)] In particular, expiratory CT has been found to be useful for diagnosing bronchiolitis obliterans syndrome, which occurs in lung transplants, with sensitivity of 83% and specificity of 89%.[8)]

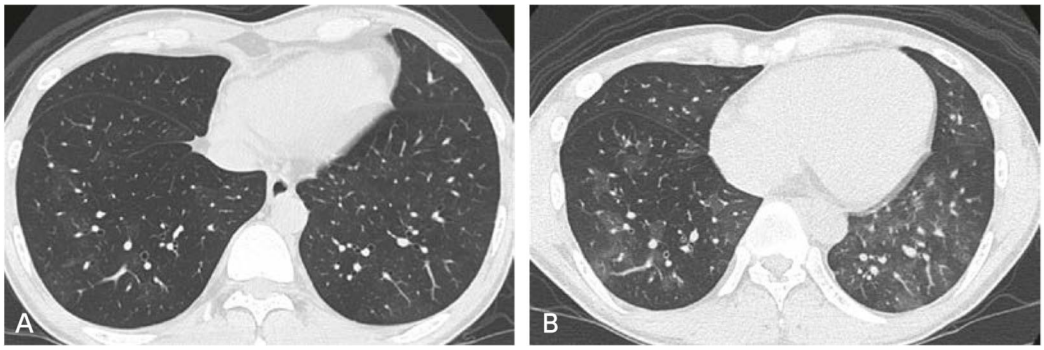

Figure. Bronchiolitis obliterans syndrome

A: Inspiratory CT, B: Expiratory CT

A region of air trapping that shows no increase in density with expiratory CT is accentuated.

The imaging protocol used for expiratory CT must reduce radiation exposure. Although the inter-reader agreement rate and confidence in image evaluations decrease in proportion to decreases in the tube current, reducing the current to 20 mAs has been found to not be problematic.[9)]

Search keywords and secondary sources

PubMed was searched for the period from January 1985 through March 2020 using the following keywords: CT, expiratory, and expiration.

In addition, the following were referenced as secondary sources.

1) Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for diagnosis, management, and prevention of COPD (2019 Report)
2) Japanese Respiratory Society, Ed.: 2018 Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (COPD), 5th Edition. Medical Review, 2018.

References

1) Lamers RJ et al: Chronic obstructive pulmonary disease: evaluation with spirometrically controlled CT lung densitometry. Radiology 193: 109-113, 1994
2) Arakawa H et al: Air trapping on expiratory high-resolution CT scans in the absence of inspiratory scan abnormalities: correlation with pulmonary function tests and differential diagnosis. AJR Am J Roentgenol 170: 1349-1353, 1998
3) Matsuoka S et al: Quantitative assessment of air trapping in chronic obstructive pulmonary disease using inspiratory and expiratory volumetric MDCT. AJR Am J Roentgenol 190: 762-769, 2008
4) Tanaka N et al: Air trapping at CT: high prevalence in asymptomatic subjects with normal pulmonary function. Radiology 227: 776-785, 2003
5) Matsuoka S et al: Airway dimensions at inspiratory and expiratory multisection CT in chronic obstructive pulmonary disease: correlation with airflow limitation. Radiology 248: 1042-1049, 2008
6) Nishimura K et al: Comparison of different computed tomography scanning methods for quantifying emphysema. J Thorac Imaging 13: 193-198, 1998
7) Gevenois PA et al: Pulmonary emphysema: quantitative CT during expiration. Radiology 199: 825-829, 1996
8) Bankier AA et al: Bronchiolitis obliterans syndrome in heart-lung transplant recipients: diagnosis with expiratory CT. Radiology 218: 533-539, 2001
9) Bankier AA et al: Air trapping: comparison of standard-dose and simulated low-dose thin-section CT techniques. Radiology 242: 898-906, 2007

BQ 20 Is HRCT recommended for diagnosing idiopathic pulmonary fibrosis (IPF)?

Statement

HRCT is an essential test for diagnosing IPF and is therefore recommended.

Background

IPF is an idiopathic interstitial pneumonia that typically presents the usual interstitial pneumonia (UIP) pattern on CT. CT is now essential for diagnosing IPF, and a multidisciplinary discussion (MDD) that combines CT findings with clinical and pathological findings is fundamental to diagnosis.

Explanation

IPF is an idiopathic interstitial pneumonia that presents the UIP imaging pattern. Because its CT findings are distinctive, the usefulness of CT in the diagnosis of IPF has long been recognized. Moreover, CT has been found to be superior even to chest radiography in diagnostic performance and correlation with clinical severity.[1, 2)]

A characteristic CT finding in IPF is bibasilar-predominant honeycombing (Fig.), and the IPF diagnostic accuracy rate is extremely high when typical findings are seen. The 2019 IPF diagnostic guidelines, the most recent guidelines, divided CT findings into 4 classifications, UIP pattern, probable UIP, indeterminate for UIP, and alternative diagnosis, and they recommended that IPF be diagnosed based on an MDD that combines clinical and pathological findings. Patients who show the UIP pattern on CT and have no clinical findings inconsistent with IPF can be diagnosed with IPF without making a pathological diagnosis.[1)] CT is also important for diagnosing interstitial pneumonias in general. A retrospective study found that CT findings changed ≥ 50% of the initial diagnoses made by internists.[3)] A separate investigation found that the diagnostic concordance rate for multiple clinicians was a κ value of 0.41 for diagnosis by HRCT alone. The rate increased to 0.51 when the CT findings were augmented with clinical information and to 0.67 when a radiologist was included. It increased further, to 0.75, with the addition of pathological diagnosis and to 0.85 with the consensus diagnosis of a clinician, radiologist, and pathologist.[4)] However, many patients do not show the typical UIP pattern on CT. An examination of HRCT findings in patients clinically diagnosed with IPF found that 34% had the typical definite UIP pattern with honeycomb lung; 36% did not have honeycomb lung, but had findings consistent with UIP, which is suggestive of IPF; and 30% had findings suggestive of an alternative diagnosis to UIP.[5)] The rate of inter-reader agreement on honeycomb lung, which is important for diagnosing the UIP pattern, is not very high, with κ values ranging from 0.40 to 0.58.[6)] This is related to the low rate of agreement on the classification of CT findings. The rates of inter-reader agreement on UIP classification in reports that used the previous (2013) classification were moderate, with κ values ranging from 0.48 to 0.52.[8)]

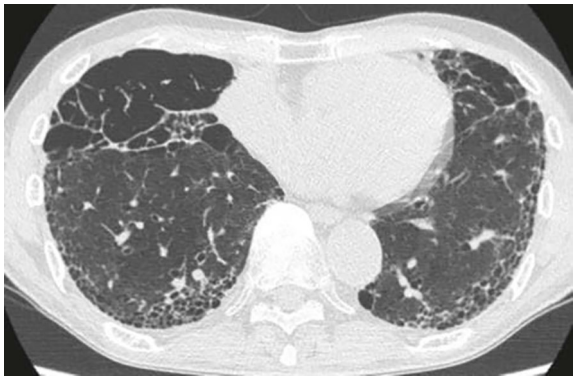

Figure. IPF

HRCT, transverse image: Reticular opacities and honeycomb lung are seen predominantly in the bilateral basilar subpleural regions.

CT is used for prognostic assessment, as well as diagnosis. The observed extent of traction bronchiectasis has been reported to be linked to prognosis in IPF.[5] CT also plays an important role in IPF follow-up. Reticular and ground-glass opacities and honeycomb lung increase during the clinical course of IPF.[9] Acute exacerbation and lung cancer occur occasionally and are important prognostic factors in IPF.[10] Depending on the CT pattern, acute exacerbation is divided into peripheral, diffuse, and multifocal patterns. The multifocal pattern has been reported to have a significantly better prognosis than the other patterns.[11]

In addition to being essential for IPF diagnosis, CT is important for evaluating its status and stage of its clinical course.

Search keywords and secondary sources

PubMed was searched using the following keywords: CT, usual interstitial pneumonias, imaging, and idiopathic pulmonary fibrosis.

In addition, the following were referenced as secondary sources.

1) Raghu G et al: Diagnosis of Idiopathic pulmonary fibrosis: an official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med 198 (5): e44-e68, 2018
2) Travis WD et al: An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med 188 (6): 733-748, 2013

References

1) Mathieson JR et al: Chronic diffuse infiltrative lung disease: comparison of diagnostic accuracy of CT and chest radiography. Radiology 171 (1): 111-116, 1989
2) Staples CA et al: Usual interstitial pneumonia: correlation of CT with clinical, functional, and radiologic findings. Radiology 162 (2): 377-381, 1987
4) Aziz ZA et al: Interstitial lung disease: effects of thin-section CT on clinical decision making. Radiology 238 (2): 725-733, 2006
5) Flaherty KR et al: Idiopathic interstitial pneumonia: what is the effect of a multidisciplinary approach to diagnosis? Am J Respir Crit Care Med 170 (8): 904-910, 2004
6) Sumikawa H et al: Computed tomography findings in pathological usual interstitial pneumonia: relationship to survival. Am J Respir Crit Care Med 177 (4): 433-439, 2008
7) Watadani T et al: Interobserver variability in the CT assessment of honeycombing in the lungs. Radiology 266 (3): 936-944, 2013

8) Walsh SL et al: Interobserver agreement for the ATS/ERS/JRS/ALAT criteria for a UIP pattern on CT. Thorax 71 (1): 45-51, 2016
9) Hartman TE et al: Disease progression in usual interstitial pneumonia compared with desquamative interstitial pneumonia. Assessment with serial CT. Chest 110 (2): 378-382, 1996
10) Natsuizaka M et al: Epidemiologic survey of Japanese patients with idiopathic pulmonary fibrosis and investigation of ethnic differences. Am J Respir Crit Care Med 190 (7): 773-779, 2014
11) Akira M et al: CT findings during phase of accelerated deterioration in patients with idiopathic pulmonary fibrosis. AJR Am J Roentgenol 168 (1): 79-83, 1997

BQ 21 Is HRCT recommended for differentiating among collagen vascular diseases?

Statement

There is a good deal of overlap between the HRCT findings for lung lesions in various collagen vascular diseases, which makes it difficult to find clear differences in the findings. However, differentiation is possible to some extent if characteristic findings are observed.

Background

The treatment strategy and prognosis for collagen vascular disease lesions of the lungs vary with the type of collagen vascular disease. Moreover, collagen vascular disease preceded by lung lesions is somewhat frequent. Identifying the collagen vascular disease may therefore be difficult initially. The question of whether the type of collagen vascular disease present can be inferred based on the HRCT findings for lung lesions was examined, and the findings are outlined below.

Explanation

Few articles have examined the differences in HRCT findings depending on the type of collagen vascular disease [rheumatoid arthritis (RA), systemic sclerosis (SSc), polymyositis/dermatomyositis (PM/DM), mixed connective tissue disease (MCTD), primary Sjögren's syndrome (pSjS), and systemic lupus erythematosus (SLE)]. One article compared the findings for RA, SSc, PM/DM, pSjS, and MCTD.[1)] Another compared the findings for all of the diseases: RA, SSc, PM/DM, pSjS, MCTD, and SLE.[2)] The report by Daimon et al. focused on collagen vascular disease lesions in the lungs in 49 patients who were found to have nonspecific interstitial pneumonia (NSIP) pattern based on surgical biopsy. The type of collagen vascular disease was inferred in 22 of the 49 patients (45%). Diagnostic accuracy for the various collagen vascular diseases varied widely depending on the type of disease: RA, 47%; SSc, 38%; PM/DM, 61%; pSjS, 25%; and MCTD, 0%.[1)] The authors concluded that diagnosis was possible to some extent if typical findings were observed, such as intralobular reticular opacities in SSc and subpleural linear opacities in PM/DM. Tanaka et al. compared collagen vascular disease lesions of the lungs in 187 patients (RA, 55 patients; SSc, 50 patients; PM/DM, 46 patients; MCTD, 15 patients; pSjS, 11 patients; and SLE, 10 patients) using multivariate analysis and the chi-squared test. They found that, compared with other collagen vascular diseases, findings of honeycombing and traction bronchiectasis were more frequent for RA lung lesions; lymph node enlargement, esophageal dilatation, and extensive ground-glass attenuation (GGA) were more frequent for SSc lung lesions; and consolidation and the absence of honeycombing were more frequent for PM/DM lung lesions.[2)] For the other 3 collagen vascular diseases, the only differences detected were chi-squared test results showing that GGA along the bronchovascular bundle and consolidation were more frequent findings for pSjS and SLE lung lesions than for the other collagen

vascular diseases.[2)] RA, SSc, and PM/DM have characteristic findings that differ from those of the other collagen vascular diseases and these characteristic findings may contribute to differentiation.

As mentioned above, few articles have compared the characteristics of the various collagen vascular diseases systematically. Differentiation is therefore currently attempted by means of an analysis that takes into account reports of the CT findings for these diseases.[3-15)]

Airway lesions are seen frequently in RA, and bronchial dilatation, bronchiolitis obliterans, and follicular bronchiolitis (FB) are observed with moderate frequency.[3)] Reflecting these conditions, mosaic perfusion and centrilobular opacities (air trapping) are observed on CT.[3, 4)] In interstitial pneumonia, the usual interstitial pneumonia (UIP) and NSIP patterns are seen with roughly equal frequency,[6)] and the organizing pneumonia (OP) pattern is seen occasionally.[3, 6, 7)] The most recent articles have reported that the greatest number of patients with RA show the UIP pattern.[7-9)] Reflecting these findings, ground-glass and reticular opacities and consolidation are seen on HRCT, and honeycombing is more prominent than in other collagen vascular diseases.[3, 6)]

In SSc, the NSIP pattern is the most common pathologically. Reflecting this, overlapping of fine reticular opacities in dorsal and subpleural GGAs is characteristic and associated with traction bronchiectasis. The findings more closely resemble those seen in idiopathic NSIP than they do those seen in IPF or UIP.[3, 10)]

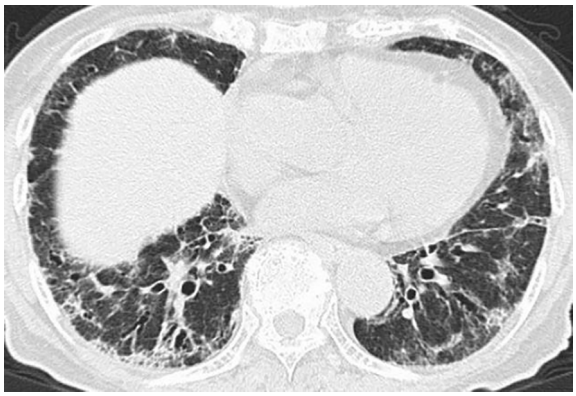

Figure. Dermatomyositis (DM)-related lung disease

(NSIP pattern + OP pattern)

HRCT, transverse image: GGAs are seen immediately below the pleura and along the bronchi in the bilateral lower lung fields, and the internal bronchi are dilated (traction bronchiectasis). Mixed consolidation is also present, and bandlike opacities are seen parallel to the pleura.

In PM/DM, findings of overlapping GGAs and consolidation are seen predominantly in the lower lung field, in addition to subpleural linear or bandlike opacities, reflecting the NSIP and OP patterns, which are frequent pathological findings in these conditions.[11, 12)] Characteristics of PM/DM are more frequent consolidation and less frequent honeycombing compared with other collagen vascular diseases (Fig.).[3, 11, 12)] In patients with DM who do not exhibit muscle symptoms (amyopathic DM, or ADM), rapidly progressing

interstitial pneumonia may be seen.[13] If the findings described above are seen in such patients, caution should be exercised clinically regarding the presence of ADM.

In MCTD, the UIP or NSIP pattern has been seen pathologically,[3, 14] and findings such as GGAs, consolidation, honeycombing, and centrilobular nodular opacities have been reported.[14]

In pSjS, as in RA, airway lesions such as FB are frequent, and centrilobular opacities and the tree-in-bud pattern are seen.[15] The interstitial pneumonias, including lymphocytic interstitial pneumonia (LIP), NSIP, and UIP have been reported, with centrilobular opacities and cyst formation being characteristics of LIP.[3, 15]

In SLE, acute lupus pneumonitis and diffuse alveolar hemorrhage are important complications,[3] with diffuse or patchy GGAs or consolidation seen in both conditions.

Collagen vascular disease lung lesions are diverse, and the NSIP pattern is the most frequent pattern for such lesions. Consequently, GGAs are a frequent finding on HRCT, and identifying differences between collagen vascular diseases is difficult. However, RA and pSjS are suggested by airway lesions, RA by prominent honeycombing, SSc by GGAs with internal reticular opacities, and PM/DM by peripheral consolidation or consolidation along the bronchi. Thus, the type of collagen vascular disease can be inferred.

Search keywords and secondary sources

In addition to the previous literature, articles were identified by searching PubMed using the following keywords: CT (tomography, X-ray computed), lung, collagen vascular disease, and connective tissue disease. In addition, the following keywords related to the various collagen vascular diseases were used: rheumatoid arthritis, scleroderma, polymyositis, dermatomyositis, mixed connective tissue disease, primary Sjogren syndrome, and systemic lupus erythematosus. The period searched was from September 1, 2015 to June 30, 2019.

References

1) Daimon T et al: Nonspecific interstitial pneumonia associated with collagen vascular disease: analysis of CT features to distinguish the various types. Intern Med 48: 753-761, 2009
2) Tanaka N et al: HRCT findings of collagen vascular disease-related interstitial pneumonia (CVD-IP): a comparative study among individual underlying diseases. Clin Radiol 73: 833.e831-833.e810, 2018
3) Lynch DA: Lung disease related to collagen vascular disease. J Thorac Imaging 24: 299-309, 2009
4) Jokerst C et al: An overview of collagen vascular disease-associated interstitial lung disease. Semin Roentgenol 50: 31-39, 2015
5) Chung MH et al: Airway obstruction in rheumatoid arthritis: CT manifestations, correlated with pulmonary function testing. Yonsei Med J 45: 443-452, 2004
6) Tanaka N et al: Rheumatoid arthritis-related lung diseases: CT findings. Radiology 232: 81-91, 2004
7) Kelly CA et al: Rheumatoid arthritis-related interstitial lung disease: associations, prognostic factors and physiological and radiological characteristics: a large multicentre UK study. Rheumatology 53: 1676-1682, 2014
8) Assayag D et al: Rheumatoid arthritis-associated interstitial lung disease: radiologic identification of usual interstitial pneumonia pattern. Radiology 270: 583-588, 2014
9) Chansakul T et al: Intra-thoracic rheumatoid arthritis: Imaging spectrum of typical findings and treatment related complications. Eur J Radiol 84: 1981-1991, 2015

10) Desai SR et al: CT features of lung disease in patients with systemic sclerosis: comparison with idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia. Radiology 232: 560-567, 2004
11) Ikezoe J et al: High-resolution CT findings of lung disease in patients with polymyositis and dermatomyositis. J Thorac Imaging 11: 250-259, 1996
12) Mino M et al: Pulmonary involvement in polymyositis and dermatomyositis: sequential evaluation with CT. AJR Am J Roentgenol 169: 83-87, 1997
13) Tanizawa K et al: HRCT features of interstitial lung disease in dermatomyositis with anti-CADM-140 antibody. Respir Med 105: 1380-1387, 2011
14) Kozuka T et al: Pulmonary involvement in mixed connective tissue disease: high-resolution CT findings in 41 patients. J Thorac Imaging 16: 94-98, 2001
15) Taouli B et al: Thin-section chest CT findings of primary Sjogren's syndrome: correlation with pulmonary function. Eur Radiol 12: 1504-1511, 2002

BQ 22 Is HRCT recommended for diagnosing drug-induced lung injury?

Statement

CT is the standard method for diagnosing drug-induced lung injury, although there is little definitive scientific evidence to support such use.

Background

There is no reliable non-invasive method for clinically diagnosing drug-induced lung injury. The diagnosis is determined by a comprehensive assessment that includes clinical evaluation, imaging, and pathology. The roles of CT include confirming that there are findings consistent with a drug-induced lung injury, differentiating from other diseases, and evaluating the status of the condition when drug administration is discontinued and resumed.

Explanation

Although there is little definitive evidence that CT is useful for diagnosing drug-induced lung injury, it has become indispensable for diagnosing such disorders in the actual clinical setting. There is no reliable non-invasive method for clinically diagnosing drug-induced lung injury. The diagnosis needs to be determined by a comprehensive assessment that includes clinical information, such as the patient's medical history and clinical course, and testing and pathology findings. The diagnostic criteria for a drug-induced lung injury include ① ingestion of a drug that could cause the disorder, ② reports that the clinical disease type is attributable to a drug, ③ the exclusion of other causative diseases, ④ improvement of the condition with discontinuation of the drug, and ⑤ worsening when administration is resumed.[1)] The roles of CT in examining these criteria include: determining whether the imaging findings are consistent with those for previously reported drug-induced lung injury (criterion ②); differentiating from other types of lesions, such as those resulting from infection, pulmonary edema, and worsening of underlying disease (criterion ③); evaluating any improvement in opacities resulting from discontinuation of the drug (criterion ④); and evaluating any worsening of opacities resulting from the resumption of drug administration (criterion ⑤). CT is also used to evaluate the presence or absence of lung lesions before a drug is administered. A survey study concerning the drug gefitinib found that the presence of chronic interstitial pneumonia and ≤ 50% normal lung on CT were risk factors for a drug-induced lung injury.[4)]

The imaging findings for drug-induced lung injury are extremely varied. Typical findings include extensive bilateral ground-glass opacities or infiltrative shadows, which may be associated with interlobular wall thickening and intralobular reticular opacities. The findings are classified according to imaging pattern, using expressions that indicate the imaging pattern of the idiopathic lung disease, such as hypersensitivity pneumonitis (HP)-like, eosinophilic pneumonia (EP)-like, organizing pneumonia (OP)-like, nonspecific interstitial pneumonia (NSIP)-like, and diffuse alveolar damage (DAD)-like patterns. It should be noted

that, unlike the original diseases, the radiology-pathology correlations for these imaging pattern classifications have not been adequately examined. An examination of CT and pathology in 20 patients with drug-induced lung injury found that the 2 diagnoses agreed for only 9 patients (45%).[3] However, correlations are seen between imaging patterns and prognosis. The DAD-type imaging pattern indicates a serious lung disorder and suggests a poor prognosis.[4] With drugs such as m-TOR inhibitors, patients may have no subjective symptoms and only abnormal CT findings.[2] Other types of drug-induced lung injury that have been reported include the appearance of peritumoral infiltrative shadows and ground-glass opacities (peritumoral infiltration) caused by immune checkpoint inhibitors,[5] and the radiation recall phenomenon, in which acute inflammation occurs in the previously treated radiation field when chemotherapy is administered after radiotherapy.[6]

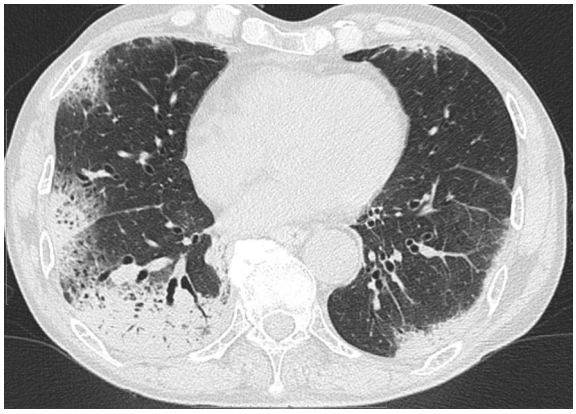

Figure. Pembrolizumab-induced lung injury

HRCT, transverse image: Consolidation and ground-glass opacities are seen predominantly in the bilateral periphery. They show an OP-like imaging pattern.

To summarize, the roles of CT in drug-induced lung injury include ① assessing disease present before drug administration, such as chronic interstitial pneumonia, ② confirming the onset of a lung disorder, ③ differentiating from other conditions, ④ predicting prognosis, and ⑤ evaluating treatment efficacy. CT is therefore considered clinically useful in drug-induced lung injury.

Search keywords and secondary sources

PubMed was searched using the keyword “pneumonitis drug,” and 46,491 articles were retrieved, of which 6 were cited.

In addition, the following was referenced as a secondary source.

1) Japanese Respiratory Society, Ed.: 2018 Guide for the Diagnosis and Treatment of Drug-induced Lung Injury, 2nd Edition. Medical Review, 2018.

References

1) Camus P et al: Interstitial lung disease induced by drugs and radiation. Respiration 71: 301-326, 2004
2) White DA et al: Noninfectious pneumonitis after everolimus therapy for advanced renal cell carcinoma. Am J Respir Crit Care Med 182: 396-403, 2010
3) Cleverley JR et al: Drug-induced lung disease: high-resolution CT and histological findings. Clin Radiol 57: 292-299, 2002
4) Inoue A et al: Severe acute interstitial pneumonia and gefitinib. Lancet 361: 137-139, 2003
5) Baba T et al: Radiologic features of pneumonitis associated with nivolumab in non-small-cell lung cancer and malignant melanoma. Future Oncol 15: 1911-1920, 2019
6) Ding X et al: Radiation recall pneumonitis induced by chemotherapy after thoracic radiotherapy for lung cancer. Rad Oncol 6: 24, 2011

FQ 2 Is CT recommended for diagnosing acute respiratory distress syndrome (ARDS)?

Statement

Although CT is not essential for diagnosing ARDS, it is useful for this purpose, and there is scientific evidence supporting its use.

Background

The presence of bilateral lung opacities on chest radiography is the criterion for the diagnosis of ARDS. Although CT is not essential for diagnosis, its diagnostic performance is higher than that of chest radiography, and it is useful for pathological evaluation.

Explanation

ARDS was first identified in a report by Ashbaugh et al. in 1967. Since then, the presence of bilateral diffuse infiltrative shadows on chest radiography has been regarded as being a characteristic of ARDS.[1] The diagnostic criteria referred to as the Berlin Definition, developed in 2012, are currently widely used. They are: PaO_2/FiO_2 (arterial blood oxygen pressure/fraction of inspired oxygen) ≤ 300 mmHg; onset within 1 week; the presence of bilateral opacities on chest radiography not fully explained by pleural effusion, atelectasis, or nodules; and the exclusion of pulmonary edema due to heart failure or fluid infusion (secondary source 1). The use of CT in the diagnostic criteria was considered, but deferred, and CT was ultimately designated for use as an adjunct diagnostic test. The reasons given for this were the risk of moving critically ill patients to perform imaging and the fact that CT imaging is not available globally, as it is in Japan. Consequently, although CT is not essential for diagnosing ARDS, it is recommended that it be considered when possible causes such as pleural effusion, atelectasis, and nodules cannot be excluded by chest radiography; when an opacity cannot be definitively attributed to ARDS; or when differentiation from other diseases is necessary. The diagnostic performance of chest radiography in ARDS is inferior to that of CT. In a study that examined chest radiography in patients with ARDS diagnosed using CT, sensitivity was 0.73, specificity was 0.70, and the positive and negative predictive values were 0.88 and 0.47, respectively.[2]

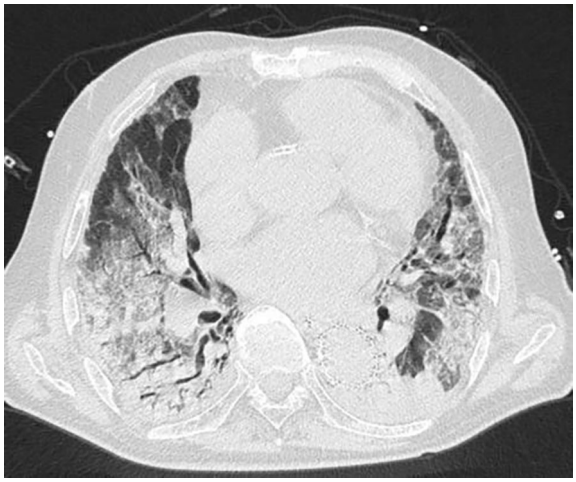

Figure. ARDS

HRCT, transverse image: Extensive ground-glass opacities, consolidation, and bronchodilatation are seen in both lungs. A homogeneous distribution associated with normal regions is seen predominantly dorsally.

CT can be used not only for ARDS diagnosis, but also for purposes such as predicting the causal and pathological condition s and prognosis and detecting complications. The causes of ARDS can be broadly divided into direct lung injury (e.g., pneumonia, aspiration, lung injury) and indirect lung injury (e.g., sepsis, nonthoracic trauma), and CT is useful for differentiating between them. With direct lung injury, ground-glass opacities and consolidation seen on CT tend to be distributed asymmetrically between the left and right lungs. With indirect lung injury, ground-glass opacities tend to be distributed symmetrically between the lungs.[3)] CT findings predictive of pathological conditions have been found to accurately reflect the advanced stages of DAD, pathological findings in ARDS. Ground-glass opacities and infiltrative shadows without traction bronchiectasis have been found to indicate the exudative or early proliferative phase. Ground-glass opacities and infiltrative shadows with traction bronchiectasis have been found to indicate the proliferative and fibrotic phases.[4)] With regard to predicting prognosis, a study of patients with ARDS that scored fibroproliferative CT findings found that they were independent predictors of prognosis and responsiveness to treatment and were related to the need for long-term mechanical ventilation.[5)] A separate study found that abnormal shadows in ≥ 80% of the lung field, a right atrium to left atrium ratio of ≥ 1, and the appearance of varicoid traction bronchiectasis on CT were adverse prognostic factors in ARDS.[6)] Complications such as pneumomediastinum, pneumothorax, and subcutaneous emphysema occur frequently with the use of positive-pressure ventilation in ARDS. Complications such as atelectasis, pneumonia, and abscess also occur and may be detected by CT.[7)]

As indicated above, CT is not essential, but it is useful for diagnosing ARDS. It is also clinically important for purposes other than diagnosis.

Search keywords and secondary sources

PubMed was searched using the following keywords: acute respiratory distress syndrome and CT. A total of 831 articles were retrieved, of which 7 were cited.

In addition, the following were referenced as secondary sources.

1) Ranieri VM et al: Acute respiratory distress syndrome: the Berlin definition. Jama 307 (23): 2526-2533, 2012
2) Japanese Respiratory Society et al., Ed.: 2016 Guidelines for the Diagnosis and Treatment of ARDS. Sogo Igaku Sha, 2016.

References

1) Ashbaugh DG et al: Acute respiratory distress in adults. Lancet 2 (7511): 319-323, 1967
2) Figueroa-Casas JB et al: Accuracy of the chest radiograph to identify bilateral pulmonary infiltrates consistent with the diagnosis of acute respiratory distress syndrome using computed tomography as reference standard. J Crit Care 28 (4): 352-357, 2013
3) Goodman LR et al: Adult respiratory distress syndrome due to pulmonary and extrapulmonary causes: CT, clinical, and functional correlations. Radiology 213 (2): 545-552, 1999
4) Ichikado K: High-resolution computed tomography findings of acute respiratory distress syndrome, acute interstitial pneumonia, and acute exacerbation of idiopathic pulmonary fibrosis. Seminars in ultrasound, CT, and MRI 35 (1): 39-46, 2014
5) Ichikado K et al: Fibroproliferative changes on high-resolution CT in the acute respiratory distress syndrome predict mortality and ventilator dependency: a prospective observational cohort study. BMJ open 2 (2): e000545, 2012
6) Chung JH et al: CT predictors of mortality in pathology confirmed ARDS. Eur Radiol 21 (4): 730-737, 2011
7) Gattinoni L et al: The role of CT-scan studies for the diagnosis and therapy of acute respiratory distress syndrome. Clin Chest Med 27 (4): 559-570, 2006

BQ 23 Is chest radiography recommended for lung cancer screening?

Statement

Although scientific evidence is lacking, chest radiography is now widely used in Japan for lung cancer screening, and its use in conjunction with adequate quality control can be considered.

Background

The lung cancer mortality rate in Japan is increasing, and lung cancer has been the leading cause of death among males since the late 1990s. The statistics for 2018 show that there were 74,328 deaths from lung cancer among males and females combined, and the number is said to be further increasing. Chest radiography is used for tuberculosis screening in Japan, as well as for lung cancer screening (Fig.). However, this practice is viewed unfavorably in some other countries. The following provides background, such as the results and interpretations of randomized, controlled studies conducted in other countries and case-control studies in Japan, and it summarizes the basis for the statement given in answer to this BQ.

Explanation

During the 1970s, two large, randomized, controlled studies were conducted in Europe and the United States to examine the effectiveness of the combined use of chest radiography and sputum cytology in reducing lung cancer mortality among smokers. However, no significant reduction in mortality was seen in either study.[1, 2] A subsequent examination of long-term prognosis found that, although some patients in the group that underwent screening had a good prognosis, the group showed no reduction in mortality.[3]

No randomized, controlled studies have been conducted in Japan. However, case-control studies in Japan reported reductions of 20% to 60% in lung cancer mortality when the chest radiography screening used for tuberculosis was applied to lung cancer screening.[4-7] Chest radiography is widely used in Japan for lung cancer screening based on these results.

The Mayo Lung Project, which was conducted before these other studies, was the subject of controversy regarding the control group and study methods used. One point of controversy was the fact that the group designated as the screening intervention group underwent chest radiography and sputum cytology once every 4 months, whereas the non-intervention group underwent these procedures annually. A 2004 meta-analysis, which excluded reports from Japan because they were case-control studies, focused on the analysis of randomized, controlled studies and found no reduction in mortality with screening.[8]

Against this backdrop, a study examined the effectiveness of screening for 4 types of cancer (prostate, lung, colorectal, and ovarian; PLCO study), including lung cancer, in reducing mortality. The study found no difference in mortality between the intervention group, which underwent chest radiography once a year for a total of 4 examinations, and the non-intervention group, which did not undergo screening, after follow-up for 13 years.[9] Questions have been raised about the results of this study. For example,

re-analysis of the screening methods and conclusions showed the screening to be effective. Other questions have concerned aspects such as the initial observation period specified and a change in the follow-up period. Moreover, it has been noted that randomized, controlled studies of screening are not always conducted with strong quality control. The problems noted include low compliance (the proportion of subjects for whom screening is recommended who actually undergo screening) and high contamination (subjects for whom screening is recommended who undergo it at a different location).[10] Articles from Europe and the United States have noted a variety of problems with the randomized, controlled studies that have been conducted, including the Mayo Lung Project and PLCO studies.[11]

Although scientific evidence is lacking, lung cancer screening by chest radiography is now widely performed in Japan. Based on the above considerations, such screening can be considered if adequate quality control is implemented.

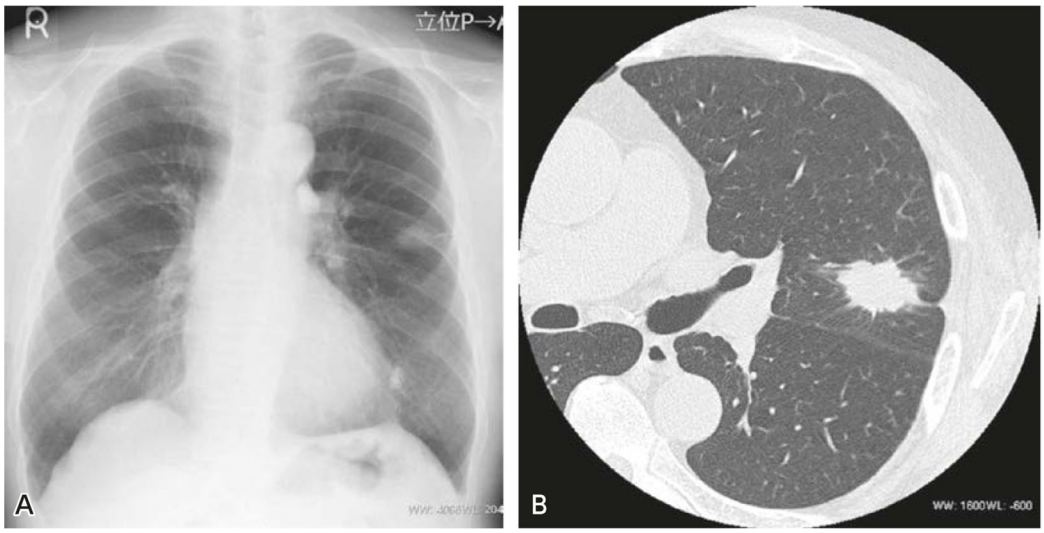

Figure. Primary lung squamous cell carcinoma found on screening (pT2aN0M0, stage IB)

The patient was an asymptomatic man in his 70s.

A: Chest radiography: An irregular marginal nodule, 3 cm in diameter, is seen in the lateral left middle lung. A linear opacity continuous with the pleura is also seen.

B: HRCT, transverse image: An irregular marginal nodule associated with indrawn pleura is seen in the dorsal left upper lobe.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung cancer, screening, and chest radiograph.

In addition, the following was referenced as a secondary source.

1) Tomotaka S: New evidence regarding lung cancer screening and interpretation of that evidence: PLCO. Journal of the Japanese Association For Cancer Detection And Diagnosis 20: 156-159, 2012.

References

1) Fontana RS et al: Lung cancer screening: the Mayo Program. J Occup Med 28: 746-750, 1986
2) Kubik A et al: Lung cancer detection: results of a randomized prospective study in Czechoslovakia. Cancer 57: 2427-2437, 1986
3) Marcus PM et al: Lung cancer mortality in the Mayo Lung Project: impact of extended follow-up. J Nati Cancer lnst 92: 1308-1316, 2000

4) Nishii K et al: A case-control study of lung cancer screening in Okayama prefecture, Japan. Lung Cancer 34: 325-332, 2001
5) Nakayama T et al: An evaluation of chest X-ray screening for lung cancer in Gunma prefecture, Japan: a population-based case-control study. Eur J Cancer 38: 1380-1387, 2002
6) Tsukada H et al: An evaluation of screening for lung cancer in Niigata prefecture, Japan: a population-based case-control study. Br J Cancer85: 1326-1331, 2001
7) Sagawa M et al: A case–control study for evaluating the efficacy of mass screening program for lung cancer in Miyagi prefecture, Japan. Cancer 92: 588-594, 2001
8) Manser RL et al: Screening for lung cancer: The Cochrane Collaboration. 1-18, 2004
9) Oken MM et al: Screening by chest radiograph and lung cancer mortality: the prostate, lung colorectal, and ovarian (PLCO) randomized trial. JAMA 306: 1865-1873, 2011
10) Sagawa M et al: Revised recommendation (2010 edition) on lung cancer screening in “lung cancer clinical practice guidelines” of the Japanese lung cancer society. JJLC 52: 938-942, 2012
11) Strauss GM et al: Chest X-ray screening for lung cancer: overdiagnosis, endpoints, and randomized population trials. J Surg Oncol 108: 294-300, 2013

CQ 2 Is low-dose CT recommended for lung cancer screening?

Recommendation

Low-dose CT is strongly recommended for population-based screening of the high-risk group (men and women aged ≥ 50 years, smoking index ≥ 600)

Recommendation strength: 1, strength of evidence: strong (A), agreement rate: 100% (15/15)

Low-dose CT is weakly recommended for opportunistic screening of the non-high-risk group.

Recommendation strength: 2, strength of evidence: weak (C), agreement rate: 93% (14/15)

Background

Until recently, lung cancer screening using low-dose CT (LDCT) was performed on a limited basis as opportunistic screening rather than population-based screening, because there was insufficient evidence of its effectiveness in reducing mortality. Recently, however, LDCT screening was found to reduce lung cancer mortality in two large, randomized, controlled studies.

Explanation

1. Indirect evidence (detection rate, 5- and 10-year survival rates)

In studies by Sobue et al.,[1] Sone et al.,[2] Nawa et al.,[3] and Yoshimura et al.[4] in Japan and by the International Early Lung cancer Action Program (I-ELCAP),[5] the detection rate for stage I lung cancer with LDCT screening was found to be high, ranging from 75% to 100% on initial screening and from 79% to 100% with repeated screening.

Sobue et al. reported that the 5-year survival rate for detected lung cancer was 76.2% for that detected on initial screening and 64.9% for that detected with repeated screening.[1] Nawa et al. reported rates of 91% and 84% for initial and repeated screening, respectively. Moreover, their analysis showed female sex, nonsmoking, small tumor diameter, and non-solid morphology to be factors contributing to a high survival rate.[6] The I-ELCAP investigators reported that the 10-year survival rate was 80% for all patients with lung cancer detected on screening and 88% for those with stage I lung cancer.[7]

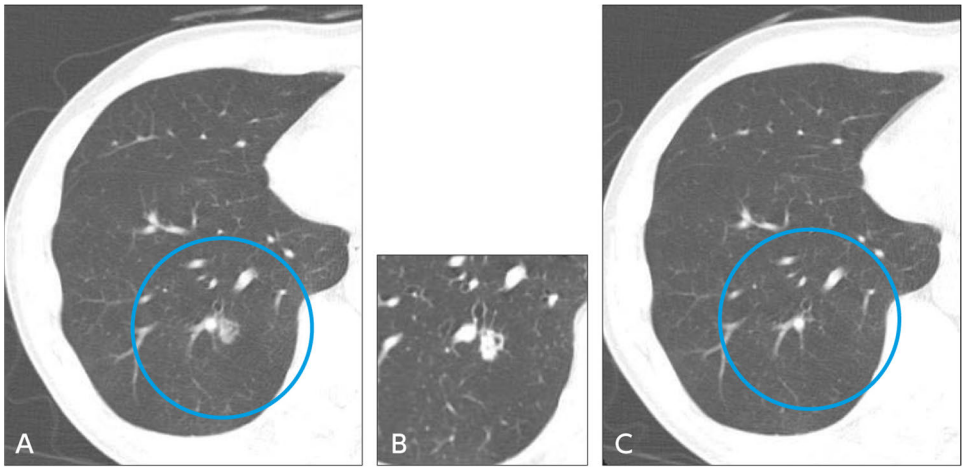

Figure 1. Lung cancer detected by LDCT screening: high-risk group

60-year-old man. Current smoker, 20 cigarettes/day × 40 years (smoking index, 800 = 40 pack-years). Squamous cell carcinoma, pT1N0M0.

A: MDCT at detection (tube current, 25 mAs), B: Thin-section CT on same day (tube current, 150 mAs)

C: MDCT 1 year prior (tube current, 25 mAs)

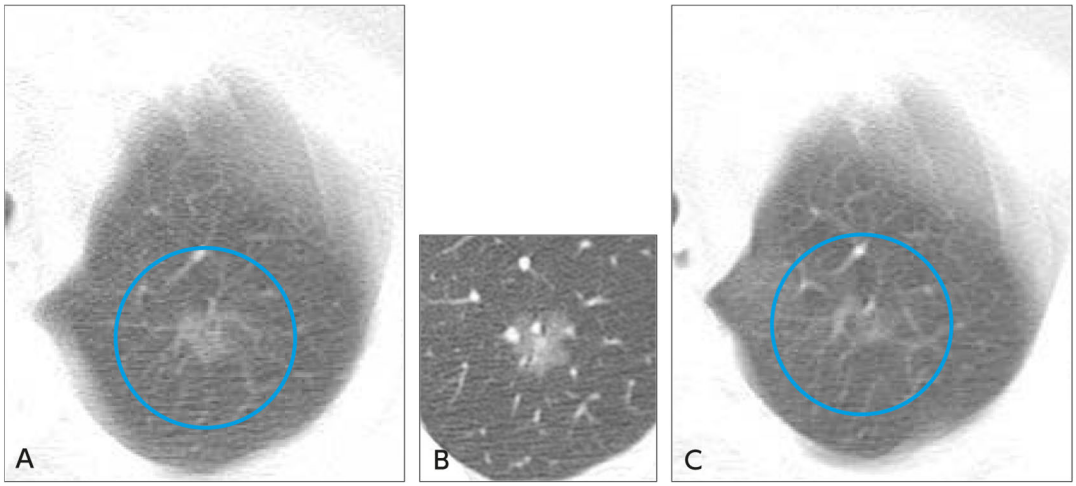

Figure 2. Lung cancer detected by LDCT screening: non-high-risk group

The patient was a woman in her 50s. Nonsmoker. Well-differentiated adenocarcinoma, pT1N0M0.

A: Single-slice CT at detection (tube current, 25 mAs), B: Thin-section CT on same day (tube current, 150 mAs)

C: 36 months prior (tube current, 50 mAs)

2. Direct evidence

① High-risk group

In 2011, the National Lung Screening Trial, a large, randomized, controlled study conducted in the United States, reported that, with LDCT screening in a high-risk group (smoking index ≥ 600 = 30 pack-years) aged 55 to 74 years, there were 2.47 deaths per 1,000 person-years, compared with 3.09 deaths per 1,000 person-years in a group that underwent chest radiography, a relative reduction in mortality of 20% (95% CI, 6.8 to 26.7, p = 0.004).[8] In the Dutch-Belgian lung cancer screening trial (NELSON), a

large, randomized, controlled study that was conducted in Europe, 15,789 individuals aged 50 to 74 years with a history of smoking (smoking index ≥ 300 = 15 pack-years) were randomly assigned to a group that underwent LDCT screening or to an unscreened group. The results of the study, which were reported in 2020, showed that the relative risk of death from lung cancer was 0.76 in the LDCT screening group, significantly lower than in the unscreened group.[9)]

② Non-high-risk group

There have been no reports of a large study with a randomized, controlled design on LDCT screening that has included non-high-risk group patients. However, a cohort study in Japan using sequential observations suggested that LDCT screening that included the non-high-risk group reduced lung cancer mortality. Nawa et al. analyzed an LDCT screening group (25,385 individuals) between 50 and 59 years old through 2009 in Hitachi, Ibaraki Prefecture (population 199,218 in 2009, according to the national census).[10)] Nonsmokers accounted for 54% of those screened. Although 210 individuals were eventually diagnosed with lung cancer, the standardized mortality ratio (SMR) for the city of Hitachi as a whole was comparable to that of the nation as a whole during the period before the introduction of LDCT screening (1995 to 1999), and, early after its introduction (2000 to 2004), the ratio was 24% lower (SMR = 0.76; 95% CI, 0.67 to 0.86) after introduction (2005 to 2009), indicating that LDCT screening that included the non-high-risk group was effective.

Currently underway is the Japanese Randomized Trial for Evaluating the Efficacy of Low-dose Thoracic CT Screening for Lung cancer (JECS study),which is being conducted by the Working Group on Randomized, Controlled Studies for the Application of Lung cancer Screening Using Low-Dose CT of the Innovative Cancer Medical Application Research Project of the Japan Agency for Medical Research and Development. The study is a randomized, controlled investigation of LDCT screening in nonsmokers and smokers with a smoking index of < 600 (30 pack-years), aged ≥ 50 years and ≤ 70 years, and the results are awaited.[11, 12)]

As the above discussion indicates, large, randomized, controlled studies have found reductions in lung cancer mortality in the high-risk group with the use of LDCT in lung cancer screening. It was therefore concluded that its use can be recommended for population-based screening involving comprehensive assessment. However, the actual implementation of screening requires a nationwide system and facilities that can accommodate it, and a variety of problems remain to be solved. Moreover, there is a lack of scientific evidence that LDCT screening reduces mortality in the non-high-risk group, and it therefore cannot be recommended for population-based screening of this group. However, its use in opportunistic screening is permissible if the fact that its effectiveness is unclear and disadvantages such as overdiagnosis and radiation exposure are first explained appropriately. It was therefore concluded that its use in opportunistic screening involving comprehensive assessment can be weakly recommended.

Remarks

CT under non-low-dose imaging conditions must not be used in the screening of healthy individuals in either the high-risk or non-high-risk group. In addition, to ensure the appropriate implementation of LDCT lung cancer screening, it is important to give careful consideration to the individuals to be screened, radiation exposure management, screening criteria, quality control, informed consent regarding the benefits and disadvantages of screening, and conditions of screening providers. This is the stated view of the Japanese Society of CT Screening. Appropriate imaging and reconstruction conditions are needed to manage radiation exposure. In recent years, however, the clinical use of methods such as iterative approximation for image reconstruction has advanced with increases in computational speed. Consequently, further decreases in dose and improvements in image quality are anticipated for lung cancer CT screening.

Search keywords and secondary sources

PubMed and MEDLINE were searched using the following keywords: lung cancer, screening, low-dose, reduced dose, CT, sensitivity, specificity, mortality, and risk factor.

In addition, the following were referenced as secondary sources.

1) Ministry of Health, Labour and Welfare grant-in-aid, Working Group on Research to Establish Suitable Methods of Cancer Screening and its Evaluation: Guidelines for lung cancer screening based on efficacy evaluation, 2006.
2) Joint committee on lung cancer screening using low-dose CT: Guide for lung cancer screening using low-dose CT—database to support interpretation training/lung cancer CT screening, KANEHARA & Co., 2005.

References

1) Sobue T et al: Screening for lung cancer with low-dose helical computer tomography: anti-lung cancer association project. J Clin Oncol 20 (4): 911-920,2002
2) Sone S et al: Results of three-year mass screening programme for lung cancer using mobile low-dose spiral computed tomography scanner. Br J Cancer 84 (1): 25-32,2001
3) Nawa T et al: Lung cancer screening using low-dose spiral CT: results of baseline and 1-year follow-up studies. Chest 122 (1): 15–20 2002
4) Yoshimura A, et al.: Pilot study of primary screening for lung cancer using low-dose helical CT. Japanese Journal of Lung Cancer 40(2): 99-105, 2000.
5) Henschke CI et al: Early lung cancer action project: initial findings on repeat screening. Cancer 92 (1): 153-159, 2001
6) Nawa T et al: Long-term prognosis of patients with lung cancer detection on low-dose chest computed tomography screening. Lung Cancer 75: 197-202, 2012
7) The International Early Lung Cancer Action Program Investigators: Survival of patients with stage Ⅰ lung cancer detected on CT screening. N Engl J Med 355: 1763–1771, 2006
8) The National Lung Screening Trial Research Team: Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 365: 395-409, 2011
9) de Koning HJ et al: Reduced lung-cancer mortality with volume CT screening in a randomized trial. New Eng J Med 382: 503-513, 2020
10) Nawa T et al: A decrease in lung cancer mortality following the introduction of low-dose chest CT screening in Hitachi, Japan. Lung Cancer 78: 225–228, 2012
11) Sagawa M et al: A randomized controlled trial on the efficacy of thoracic CT screening for lung cancer in non-smokers and smokers of ＜30 pack-years aged 50-64 years (JECS Study): ressearch design. Jpn J Clin Oncol 42 (12): 1219-1221, 2012
12) Working Group on Randomized, Controlled Studies for the Application of Lung Cancer Screening Using Low-Dose CT, Innovative Cancer Medical Application Research Project, Japan Agency for Medical Research and Development: Controlled study of lung cancer CT screening—JECS study (http://www.jecs-study.jp/index.html).

BQ 24 Which imaging examinations are recommended for the differential diagnosis of benign and malignant lung nodules?

Statement

Because it enables micromorphology to be evaluated, HRCT is considered a standard test for the differential diagnosis of benign and malignant lung nodules.

With the use of contrast-enhanced CT for the differential diagnosis of benign and malignant lung nodules, the information obtained is increased not only by visually assessing enhancement, but also by measuring the change in density within the nodules.

Background

Lung nodules detected by chest radiography or CT during lung cancer screening and follow-up observations for other diseases are currently addressed by first performing HRCT and comprehensively assessing features such as the size of the nodule, the nature of its margins, its degree of enhancement, its internal structure, and the status of the surrounding lung tissue. Whether to perform invasive tests such as bronchoscopy and percutaneous biopsy is then determined. However, there is no objective standard for interpreting morphology, and interpretations may therefore differ depending on the diagnosing physician. Moreover, even if invasive testing is not performed, change over time is determined by follow-up observation. In recent years, the assessment of malignancy by measuring the volume-doubling time of lung nodules has been applied clinically. For differential diagnosis using contrast-enhanced CT, the degree of enhancement before and after contrast-enhanced imaging and the enhancement pattern in dynamic studies are also analyzed.

Explanation

1. HRCT

Many studies have compared HRCT and pathology findings,[1, 2] and HRCT is elucidating the histological background of attributes of the margins and interior of nodules (Fig.). However, the interpretation of HRCT findings is performed using subjective criteria that depend on the reader; no objective criteria for benign and malignant lesions have been established. Consequently, the fact that the criteria used vary from study to study has been noted to be problematic. As a result, large variability has been seen in sensitivity and specificity depending on the tissue type and attributes of the nodules included in studies and on the status of the surrounding lung tissue.[3-6] The current approach to the non-invasive differential diagnosis of solitary lung nodules is to first determine their size by HRCT, with follow-up 1 year later for nodules < 5 mm in diameter and 3 months later for those ≥ 5 mm and < 10 mm in diameter. If a growth trend is seen, the

approach shifts to invasive testing. For nodules ≥ 10 mm in diameter, FDG-PET is performed concomitantly, and highly invasive testing is recommended based on the results.[7)]

If a lung nodule is detected by chance in an asymptomatic patient, a helical HRCT scan can be performed to measure its volume. In this way, the volume-doubling time of nodules can also be calculated based on the interval between 2 CT scans performed sequentially. The volume-doubling time is also calculated with this type of quantitative method when there appears to be no change visually in short-term follow-up observations, and this method has begun to be used when the volume-doubling time is brief, based on a cutoff of 400 days, and malignancy is considered a possibility.[8)]

2. Contrast-enhanced CT

Contrast enhancement is stronger in malignant nodules than in benign nodules. Consequently, a method of differentiating benign from malignant nodules was examined by establishing a cutoff for the difference in the CT numbers of noncalcified lung nodules before and after administration of an iodine contrast medium. The results of this multicenter study showed that when malignant nodules were defined as those with contrast enhancement of ≥ 15 HU and benign nodules as those with contrast enhancement of < 15 HU, sensitivity and specificity were 98% and 58%, respectively.[9)] Based on these results, contrast enhancement of < 15 HU on contrast-enhanced CT strongly suggests that the nodule is benign. However, if contrast enhancement is ≥ 15 HU, it may be attributable to a disease such as organizing pneumonia (OP), and a benign condition therefore cannot be ruled out. A meta-analysis of studies of benign-malignant differentiation using dynamic contrast-enhanced CT found that sensitivity and specificity in differentiating benign and malignant lung nodules ranged from 88% to 97% and from 68% to 97%, respectively. These results were comparable to those for contrast-enhanced CT, indicating that further improvement in diagnostic performance cannot be expected with dynamic contrast-enhanced CT.[10)]

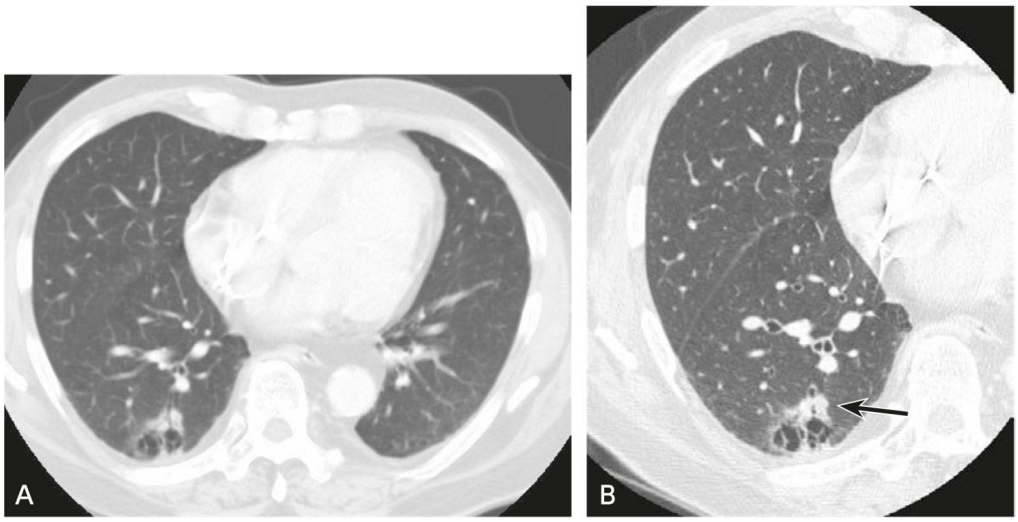

Figure. Assessment of lung nodule attributes using HRCT

A: CT, FOV includes both lungs, slice thickness of 5 mm: The presence of a small number of solid lesions on the margin of a cystic lesion in the dorsal right lower lobe is suspected, but determining their attributes is difficult.

B: HRCT, FOV limited to 1 lung, slice thickness of 1.3 mm: A distinct border (→) is seen between the normal lung and the lesions on the margin of the cystic lesion in the dorsal right lower lobe, a finding suggestive of lung cancer. Adenocarcinoma was diagnosed on resection.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung nodule, differential diagnosis, and CT.

In addition, the following were referenced as secondary sources.

1) David S et al: NCCN Guidelines®: non-small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021
2) Silvestri GA et al: Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143 (5): e211S-250S, 2013
3) Japan Lung Cancer Society, Ed.: 2020 Guidelines for the Diagnosis and Treatment of Lung Cancer: Includes Malignant Pleural Mesothelioma and Thymic Tumors. KANEHARA & Co., 2021.
4) MacMahon H et al: Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology 237: 395-400, 2005

References

1) Aoki T et al: Evolution of peripheral lung adenocarcinomas: CT findings correlated with histology and tumor doubling time. AJR Am J Roentgenol 174: 763-768, 2000
2) Furuya K et al: New classification of small pulmonary nodules by margin characteristics on high-resolution CT. Acta Radiol 40: 496-504, 1999
3) Zwirewich CV et al: Solitary pulmonary nodule: high-resolution CT and radiologic-pathologic correlation. Radiology 179: 469-476, 1991
4) Seemann MD et al: Usefulness of morphological characteristics for the differentiation of benign from malignant solitary pulmonary lesions using HRCT. Eur Radiol 9: 409-417, 1999
5) Takanashi N et al: The diagnostic accuracy of a solitary pulmonary nodule, using thin-section high resolution CT. Lung Cancer 13: 105-112, 1995
6) Sakai S et al: Lung cancer associated with diffuse pulmonary fibrosis: CT-pathologic correlation. J Thorac Imaging 18: 67-71, 2003
7) Winer-Muram HT et al: The solitary pulmonary nodule. Radiology 239: 34-49, 2006
8) van Klaveren RJ et al: Management of lung nodules detected by volume CT scanning. N Engl J Med 361: 2221-2229, 2009
9) Swensen SJ et al: Lung nodule enhancement at CT: multicenter study. Radiology 214: 73-80, 2000
10) Cronin P et al: Solitary pulmonary nodules: meta-analytic comparison of cross-sectional imaging modalities for diagnosis of malignancy. Radiology 246: 772-782, 2008

CQ 3 Is FDG-PET/CT recommended for the differential diagnosis of benign and malignant lung nodules?

Recommendation

FDG-PET/CT is weakly recommended for the differential diagnosis of benign and malignant lung nodules.

Recommendation strength: 2, strength of evidence: weak (C), agreement rate: 100% (15/15)

Background

FDG-PET/CT, which can now be performed at many facilities, provides information on the glucose metabolism of lung nodules, in addition to enabling the interpretation of morphology by CT. This additional information can improve the accuracy of benign-malignant differentiation.

Explanation

FDG-PET/CT is used to diagnose the benign or malignant nature of lung nodules based on their level of glucose metabolism. Its diagnostic performance has been shown to be superior to that of CT and MRI in many studies (Fig.).[1-6] The standardized uptake value (SUV), which is used as a semi-quantitative index, is affected by factors such as the type of PET system and imaging method used, the patient's blood glucose level, and lesion localization (lung apex or base). Consequently, a cutoff is established and used for benign-malignant differentiation, which is a limitation. Benign-malignant differentiation using the SUV alone is therefore not recommended in routine clinical practice. Moreover, the volume effect is known to be strong in relatively small tumors with FDG-PET/CT. Consequently, the diagnostic performance of FDG-PET/CT is markedly lower for nodules < 10 mm in diameter. It is therefore recommended that it be used for benign-malignant differentiation of lesions ≥ 10 mm in diameter. Histologically, false negatives are known to occur for tumors such as those in the moderately malignant group, tumors with alveolar epithelial replacement growth, mucin-producing tumors, and tumors with strong central scar formation that are ≥ 10 mm in diameter. On the other hand, false positives are known to occur for some granulomatous inflammatory nodules, such as tuberculomas and cryptococcosis nodules.[7, 8] Current PET/CT involves performing thin-layer CT imaging and fusing it with PET images. Consequently, the CT images are of high diagnostic value. The radiation dose that the examinee is exposed to can be kept to a low level, which means the test has little adverse effect on the examinee. Thus, a comprehensive diagnosis can be performed by adding the information on glucose metabolism obtained by FDG-PET to the morphological diagnosis obtained by thin-layer CT.

FDG-PET/CT is more expensive than other tests. Based on the above considerations, however, the net benefits are commensurate with the cost if its use is limited to nodules ≥ 10 mm in diameter, for which benign-malignant differentiation is difficult with HRCT. It was therefore concluded that FDG-PET/CT can be weakly recommended for the differential diagnosis of benign and malignant lung nodules.

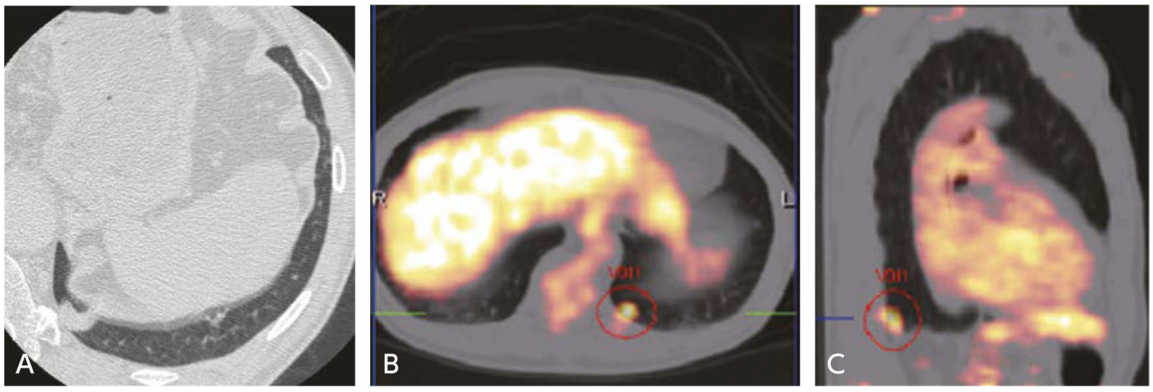

Figure. Lung squamous cell carcinoma

A: HRCT, slice thickness of 0.6 mm: A nodule with distinct margins is seen in the left lung base. There is no accompanying tendency for lobulation or spicula, and benign-malignant diagnosis is difficult.

B, C: FDG-PET/CT performed 10 days after A (B: transverse image, C: sagittal image): SUV max of 2.43 for the nodule in the left lung base. Comprehensive diagnosis that included HRCT was performed, and malignancy was more strongly suspected. Squamous cell carcinoma was diagnosed on resection.

Search keywords and secondary sources

PubMed was searched using the following keywords: pulmonary nodule, differential diagnosis, FDG-PET, and PET/CT.

In addition, the following was referenced as a secondary source.

1) Japan Lung Cancer Society, Ed.: Guidelines for Diagnosis and Treatment of the Lung Cancer/Malignant Pleural Mesothelioma/Thymic Tumors 2020. KANEHARA & Co., 2021.

References

1) Cronin P et al: Solitary pulmonary nodules: meta-analytic comparison of cross-sectional imaging modalities for diagnosis of malignancy. Radiology 246: 772-782, 2008
2) Lowe VJ et al: Prospective investigation of PET in lung nodules. J Clin Oncol 16: 1075-1084, 1998
3) Gould MK et al: Accuracy of positron emissioon tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis. JAMA 285: 914-924, 2001
4) Fletcher JW et al: A comparison of the diagnostic accuracy of 18F-FDG PET and CT in the characterization of solitary pulmonary nodules. J Nucl Med 49: 179-185, 2008
5) Basso Dias A et al: Fluorine 18-FDG PET/CT and diffusion-weighted MRI for malignant versus benign pulmonary lesions: a meta-analysis. Radiology 290: 525-534, 2019
6) Hou S et al: Combination of positron emission tomography/computed tomography and chest thin-layer high-resolution computed tomography for evaluation of pulmonary nodules: correlation with imaging features, maximum standardized uptake value, and pathology. Medicine 97: 31, 2018
7) Kim SK et al: Accuracy of PET/CT in characterization of solitary pulmonary lesions. J Nucl Med 48: 214-220, 2007
8) Nomori H et al: Evaluation of 18F fluorodeoxyglucose (FDG) PET scanning for pulmonary nodules less than 3 cm in diameter, with special reference to the CT images. Lung Cancer 45: 19-27, 2004

BQ 25 Is CT recommended for determining the T stage of lung cancer?

Statement

There is strong scientific evidence for the use of CT to determine the T stage of lung cancer, and it is the standard test for this purpose.

Background

The usefulness of CT for determining the T stage of lung cancer before treatment was examined, and the findings are summarized below.

Explanation

CT is essential for accurately measuring the tumor diameter component of the T stage. Reconstructed coronal images and sagittal images are particularly useful for tumors that are long in the cranial-caudal direction (Fig.). They are also useful for determining the presence or absence of atelectasis and postobstructive pneumonia, whether there has been invasion of neighboring structures, and the extent of invasion of the central bronchi.[1-3)] Although there are no significant differences between CT and MRI with respect to sensitivity and specificity in differentiating stages T0 to T2 and T3 to T4 (CT: 63% and 84%, respectively; MRI: 56% and 80%, respectively), MRI is superior to CT for assessing mediastinal invasion.[1)] MRI has been reported to be superior to CT for determining the presence or absence and extent of invasion of the chest wall, vertebral bodies, brachial plexus, subclavian arteries and veins, and mediastinum.[1, 4-6)] There have been an especially large number of reports indicating that it is useful for pulmonary apical tumors (Pancoast tumors).[4, 5)] MRI is recommended when CT shows no obvious masses in the chest wall or costal bone destruction present, and the diagnosis is indeterminate with CT.

However, there have been no prospective studies comparing sagittal and coronal reconstruction CT and MRI using isotropic data obtained by MDCT. In diagnosing invasion of the interlobar pleura, chest wall, and mediastinum, the diagnostic accuracy of MDCT reconstructed sagittal images with a slice thickness of 1.25 mm has been reported to be significantly higher than that of CT with a slice thickness of 5 mm.[7)] However, it has not been compared with MRI, and MRI therefore cannot be definitively concluded to be superior.

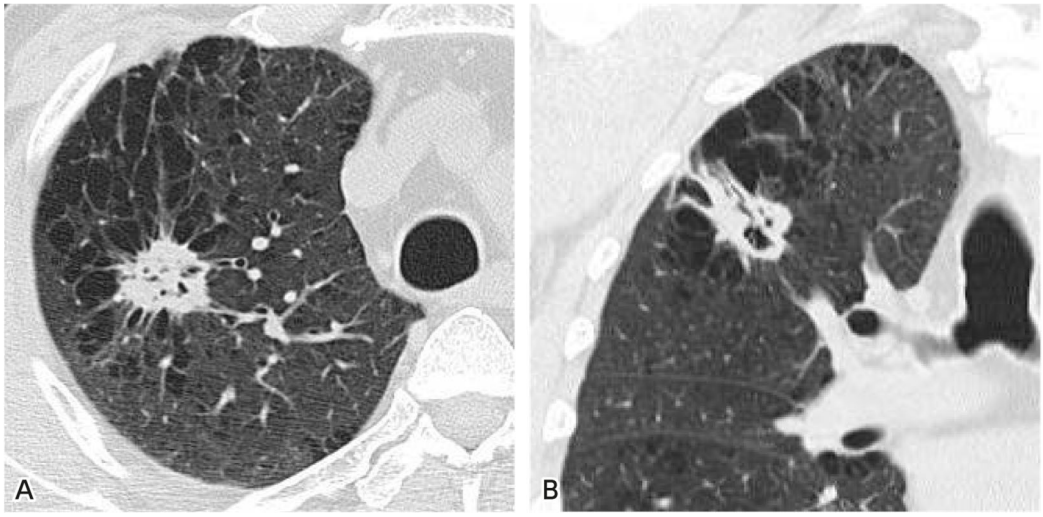

Figure. Primary lung cancer (pT2bN0M0, stage IIA)

A: HRCT, transverse image: Maximum diameter is 28 mm (> 2 cm, ≤ 3 cm, cT1c).

B: HRCT, coronal reconstructed image: The morphology of the tumor features a long length from top to bottom and a maximum diameter of 48 mm (> 4 cm, ≤ 5 cm), and the tumor was judged to be stage cT2b.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung cancer, T-factor, invasion, and CT.

In addition, the following were referenced as secondary sources.

1) David S: NCCN Guidelines®: non-small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021
2) Silvestri GA et al: Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143 (5): e211S-250S, 2013
3) Gaga M et al: An official American Thoracic Society/European Respiratory Society Statement: The role of the pulmonologist in the diagnosis and management of lung cancer. Am J Respir Crit Care Med 188 (4): 503-507, 2013

References

1) Webb WR et al: CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiologic Diagnostic Oncology Group. Radiology 178: 705-713, 1991
2) White PG et al: Preoperative staging of carcinoma of the bronchus: can computed tomographic scanning reliably identify stage III tumours? Thorax 49 (10): 951-957, 1994
3) Herman SJ et al: Mediastinal invasion by bronchogenic carcinoma: CT signs. Radiology 190 (3): 841-846, 1994
4) Rapoport S et al: Brachial plexus: correlation of MR imaging with CT and pathologic findings. Radiology 167: 161-165, 1988
5) Laissy JP et al: Assessment of vascular involvement with magnetic resonance angiography (MRA) in Pancoast syndrome. Magn Reson Imaging 13 (4): 523, 1995
6) Tang W et al: The presurgical T staging of non-small cell lung cancer: efficacy comparison of 64-MDCT and 3.0 T MRI. Cancer Imaging 15 (1): 14, 2015
7) Higashino T et al: Thin-section multiplanar reformats from multidetector-row CT data: utility for assessment of regional tumor extent in non-small cell lung cancer. Eur J Radiol 56 (1): 48-55, 2005

CQ 4 Is MRI recommended for determining the T stage of lung cancer?

Recommendation

MRI is weakly recommended for determining the T stage of lung cancer when diagnosis of invasion of the chest wall, pericardium, brachial plexus, diaphragm/mediastinum/heart/great vessels, and vertebral bodies (T3 to T4) by CT is indeterminate.

Recommendation strength: 2, strength of evidence: weak (C), agreement rate: 93% (14/15)

Background

Accurate measurement of ground-glass opacities and the solid-component diameter and accurate diagnosis of invasion from the main bronchus to the tracheal bifurcation are required for determining the Tis, T1, and T2 components of the T stage of lung cancer. Consequently, diagnosis is performed using CT.

MRI has been reported to be superior to CT for determining the T3 and T4 components for the presence or absence and extent of invasion of the chest wall, pericardium, brachial plexus, diaphragm, heart, great vessels, and vertebral bodies. There have been an especially large number of reports indicating that it is useful for pulmonary apical tumors (Pancoast tumors).[1-3] Moreover, cine-MRI using respiratory motion has been reported to be useful for diagnosing involvement of the chest wall, mediastinum, heart, and great vessels.[4] If the chest wall, mediastinum, heart, and great vessels can be observed to move separately from the tumor, invasion of these structures can be ruled out (Fig. 1). MRI is indicated when there is extensive contact between a tumor and mediastinal structures such as the chest wall and great vessels and invasion is suspected on CT. To answer the question, Is MRI recommended for determining the T stage of lung cancer?, a systematic review was performed, and the diagnostic performance of MRI and CT was compared.

Explanation

In conducting this systematic review, diagnostic accuracy, sensitivity, specificity, cost, and contrast media adverse reactions were selected as outcome variables. Using the keywords indicated below, a literature search was performed for studies that compared the diagnostic performance of MRI and CT in determining the T stage in adults suspected of having lung cancer. There were no articles relevant to cost and contrast media adverse reactions. The 3 articles discussed below were relevant to the comparison of the diagnostic accuracy, sensitivity, and specificity of MRI and CT in determining the T stage.[5-7]

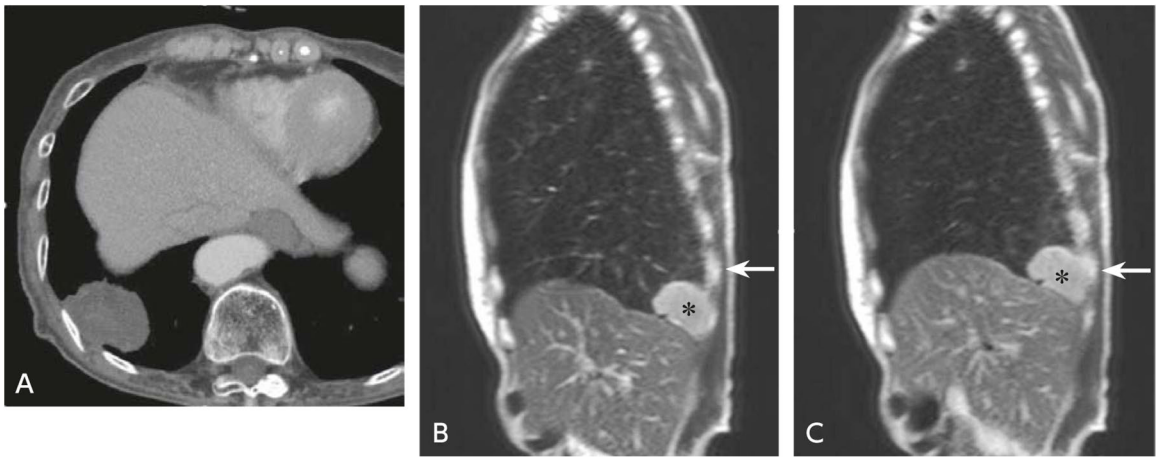

Figure 1. Primary lung cancer (Sq, cT1cN0M0, Stage IA3)

The patient was a woman in her 70s.

A: Chest CT: An irregular marginal solid nodule with a long-axis diameter of 2.6 cm is seen in the dorsal right lower lobe. Although it has extensive contact with the right 10th rib, there is no apparent rib destruction or involvement of the chest wall.

B, C: Respiratory dynamic MRI (B: inspiratory phase, C: expiratory phase): The tumor (*) slides in relation to the right 10th rib (←) on inspiration.

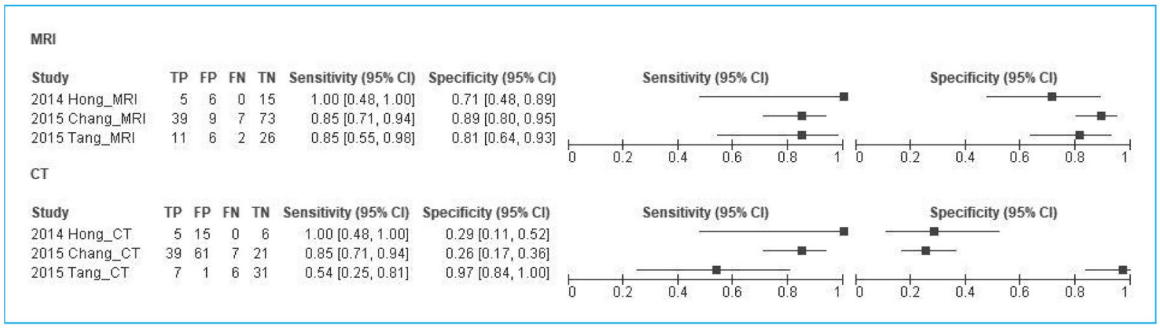

Figure 2. Meta-analysis results

In all 3 reports, the patients were selected consecutively, and no patient attrition bias was seen. With regard to index test (MRI) interpretation in the 3 articles, there may have been flow bias between facilities. Although blinding was used, none of the reports indicated whether the reference standard (pathological diagnosis) was interpreted without index test (MRI) information, and 2 of the 3 reports did not indicate the interval between the index test (MRI) and the control test (CT). The MRI methods and diagnostic criteria were not uniform (mixture of contrast-enhanced dynamic MRI and respiratory dynamic MRI), and the studies examined were a mix of prospective and retrospective studies.

Tang et al. compared T stage diagnostic performance in 45 consecutive patients diagnosed with non-small cell lung cancer who prospectively underwent contrast-enhanced dynamic MRI and contrast-enhanced CT within 1 week.[5] The criteria in the assessment of chest wall invasion were contact between the mass and chest wall > 3 cm, the presence of an obtuse angle contact between the mass and chest wall, extension of the mass into the chest wall, loss of the extra-pleural fat plane, or rib destruction.

The following criteria were used in the identification of mediastinal invasion: extensive contact between the mass and mediastinum; pleural and pericardial thickening; contact of ≥ 180 degrees between the mass and mediastinal great vessels; and loss of the fat plane between the mass and the mediastinal structures. Sensitivity and specificity for stages T3 and T4 were 85% and 91%, respectively, with MRI and 69% and 97%, respectively, with CT. Although the differences were not statistically significant, MRI showed superior sensitivity. Because this was a prospective study in consecutive patients, it included patients with chest wall and great vessel involvement that was not obvious on CT (32/45 patients with stages T1 and T2). Specificity was therefore high for both: 91% (29/32) for MRI and 97% (31/32) for CT.

Hong et al. compared the presence or absence of great vessel involvement (whether stage T4) observed by respiratory dynamic MRI and contrast-enhanced CT. Sensitivity and specificity were 100% and 71%, respectively, with MRI and 100% and 29%, respectively, with CT; the MRI specificity was statistically significantly superior.[6] Similarly, Chang et al. compared the presence or absence of chest wall and great vessel involvement (whether stage T3 or T4) observed by respiratory/contrast-enhanced dynamic MRI and contrast-enhanced CT. Sensitivity and specificity were 85% and 89%, respectively, with MRI and 85% and 26%, respectively, with CT; the MRI specificity was statistically significantly superior.[7]

In a meta-analysis of these 3 articles (Fig. 2), the pooled sensitivity, pooled specificity, AUC of the symmetric summary receiver-operating characteristic curve (SROC), and pooled diagnostic odds ratio were 86%, 84%, 0.92, and 36.9, respectively, for MRI and 80%, 43%, 0.80, and 5.7, respectively, for CT. No tests for significant differences were performed due to the small number of articles. However, MRI was superior to CT in all of these measures.

However, 2 of the 3 studies were retrospective studies, and MRI was not performed in patients with apparent invasion or no apparent chest wall or great vessel involvement.[6, 7] Thus, patient selection bias was present in these studies. Based on the above considerations, it was concluded that MRI can be weakly recommended for determining the T stage of lung cancer, on condition that it be used in patients with an indeterminate T3/T4 diagnosis.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung, pulmonary, neoplasms, magnetic resonance imaging, MRI, cancer, invasiveness, invasion, neoplasm invasion, staging, and neoplasm staging. The period searched was through June 2020; hits were obtained for 278 articles.

References

1) Webb WR et al: CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiologic Diagnostic Oncology Group. Radiology 178: 705-713, 1991
2) Rapoport S et al: Brachial plexus: correlation of MR imaging with CT and pathologic findings. Radiology 167: 161-165, 1988
3) Laissy JP et al: Assessment of vascular involvement with magnetic resonance angiography (MRA) in Pancoast syndrome. Magn Reson Imaging 13 (4): 523, 1995
4) Sakai S et al: Bronchogenic carcinoma invasion of the chest wall: evaluation with dynamic cine MRI during breathing. J Comput Assist Tomogr 21 (4): 595-600, 1997

5) Tang W et al: The presurgical T staging of non-small cell lung cancer: efficacy comparison of 64-MDCT and 3.0 T MRI. Cancer Imaging 15 (1): 14, 2015
6) Hong YJ et al: Respiratory dynamic magnetic resonance imaging for determining aortic invasion of thoracic neoplasms. J Thorac Cardiovasc Surg 148 (2): 644-650, 2014
7) Chang S et al: Usefulness of thin-section single-shot turbo spin echo with half-Fourier acquisition in evaluation of local invasion of lung cancer. J Magn Reson Imaging 41 (3): 747-754, 2015

CQ 5 Is MRI recommended for diagnosing lymph node metastasis of lung cancer?

Recommendation

MRI is weakly recommended for diagnosing lymph node metastasis of lung cancer.

Recommendation strength: 2, strength of evidence: weak (C), agreement rate: 73.3% (11/15)

Background

CT is an essential test not only for determining the T stage, but also for determining the anatomical location of lymph nodes (lymph node mapping) for N stage determination. However, the diagnostic performance of FDG-PET is higher than that of CT in determining the presence or absence of metastasis (N0 or N1/2/3), and FDG-PET is therefore more widely used for this purpose. Moreover, as advances have been made in MRI technology, it has also been reported to be useful for N-staging. A systematic review was conducted to examine and compare the diagnostic performance of MRI and FDG-PET/CT in detecting lymph node metastasis.

Explanation

With CT, a short-axis diameter of ≥ 1 cm is often used as the criterion for enlargement, and its sensitivity and specificity range from 52% to 75% and 66% to 88%, respectively. These are inferior to the sensitivity and specificity of PET, which range from 83% to 91% and 86% to 92%, respectively.[1-3] A meta-analysis of 36 articles on FDG-PET/CT reported pooled sensitivity and specificity of 72% and 91%, respectively, in an examination of lymph node diagnostic performance for each patient.[4] FDG-PET/CT was therefore recommended for N stage determination.

In recent years, there have been many reports indicating that MRI is useful for N-staging. Short-inversion-time inversion-recovery turbo-spin-echo (STIR turbo SE) imaging and diffusion-weighted imaging have been used for this purpose, with the diagnostic performance of short-inversion-time inversion-recovery (STIR) imaging found to be superior to that of FDG-PET/CT, and FDG-PET/CT and diffusion-weighted imaging found to be comparable in diagnostic performance (Fig. 1).[5] Since 2016, three meta-analyses of the diagnostic performance of MRI in N-staging have been reported in major radiology journals.[6-8] The sensitivity and specificity of MRI for each patient in the 3 meta-analyses were high: 68% and 92%, 87% and 88%, and 72% and 97%, respectively. The article by Shen et al., which compared the diagnostic performance of MRI and FDG-PET/CT, reported sensitivity and specificity of 72% and 97%, respectively, for MRI and 65% and 93%, respectively, for FDG-PET/CT. Thus, although the differences were not statistically significant, a trend toward higher sensitivity and specificity was seen with MRI.[8]

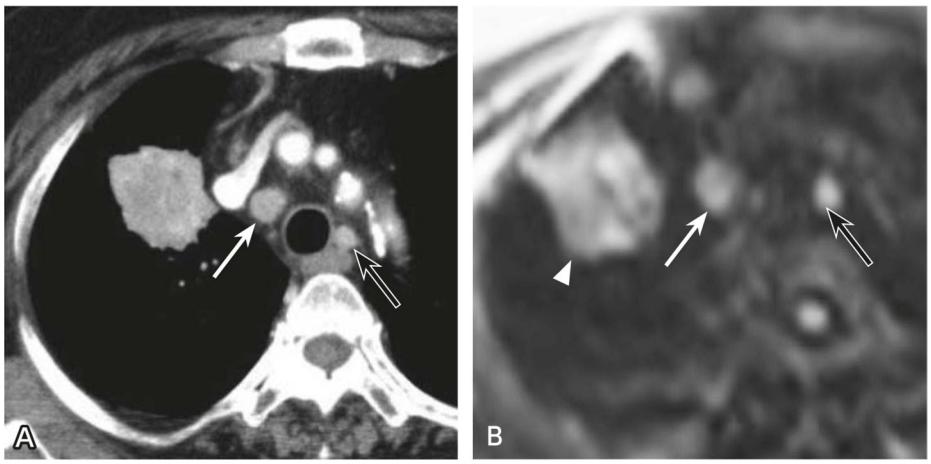

Figure 1. Lung cancer (cT2aN3M1b, stage IV)

A: Contrast-enhanced CT: An enlarged right lower paratracheal lymph node (#4R), with a short-axis diameter of > 1 cm, is seen (⇨). Also seen is a left lower paratracheal lymph node (#4L) with a short-axis diameter of < 1 cm.
B: MRI, diffusion-weighted imaging, b-value = 1,000 s/mm^2: The primary lesion in the right upper lobe (▷) and the #4R (⇨) and #4L (→) lymph nodes all show hyperintensity.

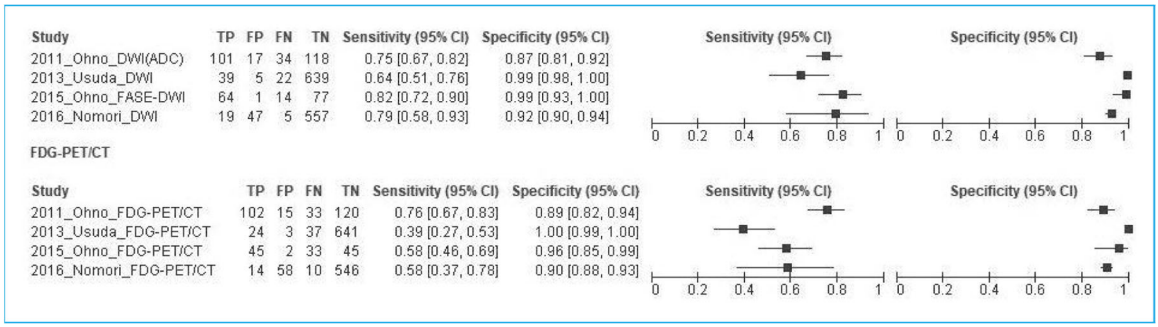

Figure 2. Meta-analysis results

Only one of these meta-analyses compared the diagnostic performance of MRI and FDG-PET/CT by collecting and analyzing reports published between 2003 and 2014.[8)] The MRI imaging method used is generally diffusion-weighted imaging; the use of STIR is reported by only certain institutions. Consequently, included in the search performed for the present systematic review were new reports published since 2015 that compared the diagnostic performance of diffusion-weighted imaging and FDG-PET/CT with respect to N stage determination. In addition, diagnostic accuracy, sensitivity, specificity, and cost were specified as outcome variables. Using the keywords indicated below, a literature search was performed for studies that compared the diagnostic performance of MRI (diffusion-weighted imaging) and the sensitivity and specificity of FDG-PET/CT in determining the N stage in adults suspected of having lung cancer. There were no articles relevant to cost. The four articles indicated below were relevant.[5, 9-11)]

The patients were selected consecutively, and no patient attrition bias was seen. With regard to index test (MRI) interpretation, there was a risk of bias. Although blinding was used, none of the reports indicated whether the reference standard (pathological diagnosis) was interpreted without index test (MRI) information. Moreover, the reports did not indicate the interval between the index test (MRI) and the control test (FDG-PET/CT). Consequently, there may have been flow bias between facilities. The results for diagnostic performance showed that the pooled sensitivity, pooled specificity, AUC of SROC, and pooled diagnostic odds ratio were 75%, 95%, 0.84, and 55.9, respectively, for MRI and 62%, 95%, 0.84, and 34.9, respectively, for FDG-PET/CT. No tests for significant differences were performed due to the small number of articles. However, a trend toward higher values for pooled sensitivity and the pooled diagnostic odds ratio was seen for MRI (Fig. 2).

As in the 3 meta-analyses mentioned above, the results of this meta-analysis showed that MRI provided high diagnostic performance. Additional advantages include the absence of radiation exposure and its lower cost compared with FDG-PET/CT. However, the N and M stages of lung cancer can be simultaneously determined during FDG-PET/CT, and it is an essential test for staging. Moreover, problems with MRI remain, such as standardizing the imaging and evaluation methods to use MRI as the standard imaging method and the fact that performing MRI in the brief period before surgery is difficult at some facilities. Based on the above considerations, it was concluded that MRI can be weakly recommended for diagnosing lymph node metastasis of lung cancer.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: lung, pulmonary, neoplasms, magnetic resonance imaging, MRI, lymph nodes, metastasis, lymphatic metastasis, and neoplasm metastasis. The period searched was through June 2020; hits were obtained for 78 articles.

References

1) McLuod TC et al: Bronchogenic carcinoma: analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. Radiology 182 (2): 319-323, 1992
2) Birim O et al: Meta-analysis of positron emission tomographic and computed tomographic imaging in detecting mediastinal lymph node metastases in nonsmall cell lung cancer. Ann Thorac Surg 79 (1): 375-382, 2005
3) van Tinteren H et al: Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial. Lancet 359 (9315): 1388-1393, 2002
4) Wu Y et al: Diagnostic value of fluorine 18 fluorodeoxyglucose positron emission tomography/computed tomography for the detection of metastases in nonsmall-cell lung cancer patients. Int J Cancer 132 (2): E37–E47, 2013
5) Ohno Y et al: N stage disease in patients with non-small cell lung cancer: efficacy of quantitative and qualitative assessment with STIR turbo spin-echo imaging, diffusion-weighted MR imaging, and fluorodeoxyglucose PET/CT. Radiology 261 (2): 605-615, 2011
6) Shen G et al: Performance of DWI in the nodal characterization and assessment of lung cancer: a meta-analysis. AJR Am J Roentgenol 206 (2): 283-290, 2016
7) Peerlings J et al: The diagnostic value of MR imaging in determining the lymph node status of patients with non-small cell lung xancer: a meta-analysis. Radiology 281 (1): 86-98, 2016
8) Shen G et al: Comparison of 18F-FDG PET/CT and DWI for detection of mediastinal nodal metastasis in non-small cell lung cancer: a meta-analysis. PLoS One 12 (3): e0173104, 2017

9) Usuda K et al: Advantages of diffusion-weighted imaging over positron emission tomography-computed tomography in assessment of hilar and mediastinal lymph node in lung cancer. Ann Surg Oncol 20 (5): 1676-1683, 2013
10) Ohno Y et al: Diffusion-weighted MR imaging using FASE sequence for 3T MR system: preliminary comparison of capability for N-stage assessment by means of diffusion-weighted MR imaging using EPI sequence, STIR FASE imaging and FDG PET/CT for non-small cell lung cancer patients. Eur J Radiol 84 (11): 2321-2331, 2015
11) Nomori H et al: Diffusion-weighted imaging can correctly identify false-positive lymph nodes on positron emission tomography in non-small cell lung cancer. Surg Today 46 (10): 1146-1151, 2016

BQ 26 Is PET recommended for N and M staging of lung cancer?

Statement

PET is recommended for N and M staging of lung cancer.

Background

PET is a modality that involves administering a positron-emitting isotope, imaging its biodistribution, and performing a diagnosis based on the distribution and kinetics of the tracer. Features of FDG-PET include its ① high detection sensitivity, ② good resolution, and ③ ability to correct for absorption in the body. It is used together with CT for lung cancer staging. FDG-PET and FDG-PET/CT are also recommended for lung cancer staging in the guidelines of the National Cancer Comprehensive Network (NCCN) and the American College of Chest Physicians (ACCP) and as the official statement of the American Thoracic Society/European Respiratory Society (ATS/ERS).

Explanation

1. N stage determination

The most important factor in the staging of lung cancer, particularly preoperative staging, is determining the mediastinal lymph node (N2) stage. The advantages of FDG-PET include its ① high detection sensitivity, ② good resolution, and ③ ability to correct for absorption in the body. However, for determining the mediastinal lymph node (N2) stage, it has 4 drawbacks: ① the lack of a diagnostic cutoff based on a semi-quantitative index; ② limited resolution of 7 to 10 mm; ③ weak uptake in well-differentiated, low-grade tumors; and ④ false positives due to inflammation. There have been numerous reports of N2 staging with FDG-PET.[1-3] Silvestri et al. reviewed 44 studies of mediastinal lymph node (N2) staging published between 1994 and 2006.[4] An SROC analysis of data for 2,865 patients with lung cancer showed sensitivity of 74% (95% CI, 69% to 79%) and specificity of 85% (95% CI, 82% to 88%). The results indicated that although FDG-PET/CT is more accurate than CT for mediastinal lymph node (N2) staging, it is not perfect. Mediastinal lymph node (N2) staging with FDG-PET is particularly important in patients predicted to have clinical stage IB to IIIB disease. If an abnormal finding is obtained by FDG-PET, a preoperative investigation of the lymph node diagnosis is recommended by means such as endobronchial ultrasonography (EBUS), thoracoscopy, or mediastinoscopy.

Taking into account the fact that the resolution limit of FDG-PET is 7 to 10 mm, Gould et al. performed a meta-analysis of only lymph node lesions that enlarged to ≥ 10 mm.[5] FDG-PET sensitivity and specificity were 100% and 78%, respectively. In a similar analysis of lymph nodes < 10 mm in size, sensitivity and specificity were 82% and 93%, respectively, indicating that false-negative results are obtained with FDG-PET in approximately 20% of patients. The results of a randomized, controlled,

multicenter study using FDG-PET/CT conducted by Fischer et al. showed sensitivity and specificity of 95% and 85%, respectively, an improvement on the data for FDG-PET.[6)]

2. M stage determination

With M staging of lung cancer by FDG-PET, unexpected metastasis is seen in 10% to 20% of patients.[4)] Although the clinical impact of this is strong, most of the data were obtained in small, single-center, prospective studies. The problems with using FDG-PET for M staging include ① non-standardized evaluation methods, ② the handling of brain metastasis, ③ the method of confirmation used when FDG-PET is negative, and ④ the contribution to patient prognosis. Li et al. examined the sensitivity of FDG-PET in the M staging of lung cancer in a meta-analysis of 9 studies and found that its sensitivity and specificity were 93% and 96%, respectively.[7)] In a meta-analysis of 10 studies, Yu et al. examined the sensitivity of FDG-PET/CT in the M staging of non-small cell lung cancer and found that its sensitivity and specificity were 81% and 96%, respectively.[8)] An examination by organ of metastasis found that the diagnostic sensitivity of FDG-PET for brain metastasis was only 60%, and that MRI was the most accurate modality for determining the extent of small lesions and tumors.[4)] Although diagnostic accuracy for liver metastasis ranges from 92% to 100%, the amount of relevant data is considered inadequate.[9,10)] FDG-PET sensitivity and specificity for bone metastasis have both been reported to be ≥ 90%. Moreover, the accuracy of FDG-PET in detecting bone metastasis has been found to be higher than that of both MRI and bone scintigraphy.[11, 12)] On the other hand, it is known to produce false negatives for the osteoblastic bone metastasis characteristic of breast or prostate cancer. Although its diagnostic accuracy for adrenal metastasis is 100%, the amount of relevant data is inadequate. Because accumulation by small nodules several mm in size is underestimated, lung and pleural metastases need to be determined by diagnostic chest CT.

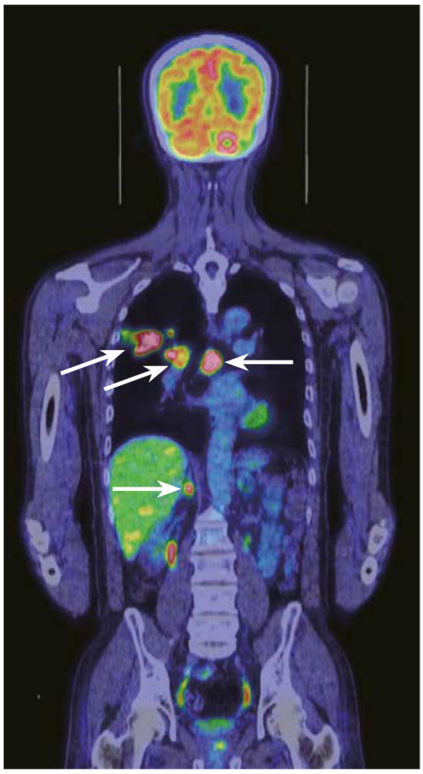

Figure. Lung cancer and multiple metastases

FDG-PET/CT fusion imaging: In addition to the primary tumor in the right lung, abnormal accumulation (→) is seen in the right lung, mediastinal lymph nodes, and right adrenal gland.

Search keywords and secondary sources

PubMed, the Cochrane Library database, and the National Guideline Clearing House database were searched using the following keywords: lung cancer, bronchogenic carcinoma, staging, PET, PET/CT, and FDG. Important articles with high-level medical evidence were used in the review.

In addition, the following were referenced as secondary sources.

1) David S: NCCN Guidelines®: non-small cell lung cancer Ver 5. 2021. National Comprehensive Cancer Network, 2020
2) Silvestri GA et al: Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143 (5): e211S-250S, 2013
3) Gaga M et al: An official American Thoracic Society/European Respiratory Society Statement: the role of the pulmonologist in the diagnosis and management of lung cancer. Am J Respir Crit Care Med 188 (4): 503-507, 2013

References

1) De Wever W et al: Integrated PET/CT in the staging of nonsmall cell lung cancer: technical aspects and clinical integration. Eur Respir J 33: 201-212, 2009
2) Antoch G et al: Non-small cell lung cancer: dual –modality PET/CT in preoperative staging. Radiology 229: 526-533, 2003
3) Lardinois D et al: Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. N Engl J Med 348: 2500-2507, 2003
4) Silvestri GA et al: Noninvasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines, 2nd ed. Chest 132: 178S-201S, 2007
5) Gould MK et al: Test performance of positron emission tomography and computed tomography for mediastinal staging in patients with non-small-cell lung cancer: a meta-analysis. Ann Intern Med 139: 879-892, 2003
6) Fischer BM et al: Preoperative staging of lung cancer with combined PET-CT. N Engl J Med 361: 32-39, 2009
7) Li J et al: Meta-analysis: accuracy of 18FDG PET-CT for distant metastasis staging in lung cancer patients. Surg Oncol 22: 151-155, 2013
8) Yu B et al: Clinical usefulness of ^{18}F-FDG-PET/CT for the detection of distant metastases in patients with non-small cell lung cancer at initial staging: a meta-analysis. Cancer Management and Research 10: 1859-1864, 2018

9) Cerfolio RJ et al: The accuracy of integrated PET-CT compared with dedicated PET alone for the staging of patients with non-small cell lung cancer. Ann Thorac Surg 78: 1017-1023, 2004
10) Fischer BM et al: A prospective study of PET/CT in initial staging of small-cell lung cancer: comparison with CT, bone scintigraphy and bone marrow analysis. Ann Oncol 18: 338-345, 2007
11) Qu X et al: A meta-analysis of ^{18}FDG-PET-CT, ^{18}FDG-PET, MRI and bone scintigraphy for diagnosis of bone metastases in patients with lung cancer. Eur J Radiol 81: 1007-1015, 2012
12) Chang MC et al: Meta-analysis: comparison of F-18 fluorodeoxyglucose-positron emission tomography and bone scintigraphy in the detection of bone metastasis in patients with lung cancer. Acad Radiol 19: 349-357, 2012

BQ 27 Is contrast-enhanced cranial MRI recommended for diagnosing brain metastasis of lung cancer?

Statement

There is strong scientific evidence for the use of contrast-enhanced cranial MRI for diagnosing brain metastasis of lung cancer, and it is the standard test for this purpose. However, it can be omitted for non-small cell lung cancer that shows pure ground-glass nodules (GGNs) or part-solid nodules with a solid-component diameter of ≤ 1 cm on CT, because there is little possibility of brain metastasis in such cases.

Background

The brain is the organ where distant metastasis from lung cancer most frequently occurs. Consequently, the diagnosis of brain metastasis is important. The diagnostic performance of contrast-enhanced MRI in detecting brain metastasis was examined by comparison with contrast-enhanced CT, and the findings are summarized below.

Explanation

Contrast-enhanced MRI has been found to detect brain lesions with higher sensitivity and to detect more and smaller metastases than non-contrast MRI, contrast-enhanced CT, and non-contrast CT.[1, 2] This is attributed to factors such as the fact that contrast-enhanced MRI provides higher density resolution and greater contrast medium enhancement than CT and has no bone artifacts (Fig.). However, although the detection rate of contrast-enhanced MRI is higher than that of contrast-enhanced CT, and contrast-enhanced MRI can detect smaller metastases, it has also been found that there was no significant difference between these modalities with respect to mean survival time or the 2-year survival rate.[3]

A meta-analysis of 18 reports compared clinical evaluation and CT with respect to brain metastasis in 1,830 patients with non-small cell lung cancer. In the 9 reports that were limited to patients without clinical symptoms, the median prevalence of brain metastasis was 3%, and the median negative predictive value was 97%. In the 9 reports that included both patients with and without clinical symptoms, the median rate of brain metastasis was 14%, sensitivity was 76%, and specificity was 82%. On the other hand, in a study of brain metastasis detection in small cell lung carcinoma, the detection rate with MRI (24%) was higher than with CT (10%), and all of the patients found to have brain metastasis by CT were symptomatic. However, 11% of the patients found to have brain metastasis by MRI were asymptomatic.[4]

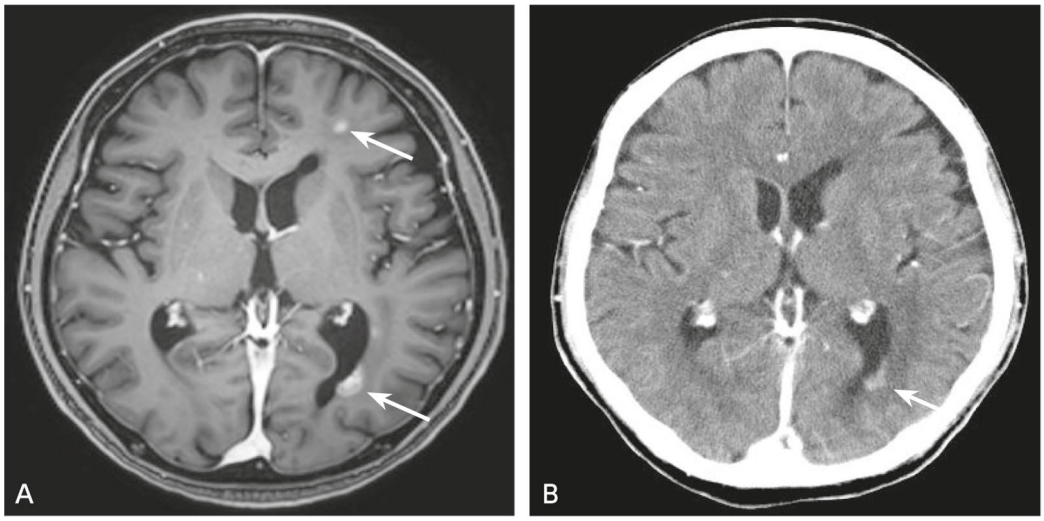

Figure. Multiple brain metastases of lung cancer (cT2aN2M1c, stage IVB)

A: Contrast-enhanced MRI: Hyperintense nodules are seen at 2 sites (→) in the left frontal and left parietal lobes.
B: Contrast-enhanced CT: Although the hyperintense region in the left parietal lobe (→) is identifiable, the lesion in the left frontal lobe is difficult to identify with CT alone.

The 3rd edition of the ACCP guidelines recommend that brain MRI be performed in patients with clinical stage I or II non-small cell lung cancer if CNS signs and symptoms are observed clinically. This is because the percentage of patients found to be positive for brain metastasis is low, at 3%, and the negative predictive value of brain MRI is extremely high in patients who are negative for brain metastasis on clinical evaluation. Another factor in this recommendation is cost-effectiveness. However, patients with asymptomatic brain metastasis have been found to have a better prognosis than patients with symptomatic brain metastasis.[5)] Consequently, the NCCN guidelines (NSCLC, version 3, 2020) recommend cranial MRI in patients with non-small cell lung cancer ≥ stage II (optional for stage IB) regardless of symptoms in order to enable asymptomatic brain metastasis to be detected and treated early. In view of the high prevalence of brain metastasis in asymptomatic small cell lung carcinoma, cranial MRI is recommended for all such patients, whether the disease is localized or advanced (SCLC, version 2, 2018). However, a histological diagnosis is often not obtained at the stage of preoperative staging, and contrast-enhanced cranial MRI is therefore recommended for all lung cancer staging.

However, there have been numerous reports that brain metastasis almost never occurs in adenocarcinoma that shows predominant ground-glass opacities and lepidic growth on CT.[4-6)] Sakurai et al. reported that all of the 25 patients with bronchioloalveolar carcinomas ≤ 3 cm that they examined had stage T1N0M0 disease.[6)] Cho et al. found that, of 109 patients with adenocarcinomas that showed pure GGNs on CT who underwent preoperative MRI, only 1 had brain metastasis 30 months after surgery (1/109, 0.9%).[7)] Suzuki et al. showed that, in patients whose primary lesions were GGNs ≤ 2 cm in size with a consolidation ratio of ≤ 25%, the cancer was also noninvasive pathologically, and there was very little distant metastasis.[8)] Brain imaging can therefore be omitted in non-small cell lung cancer that shows pure GGNs and part-solid nodules with a solid-component diameter of ≤ 1 cm on CT, because there is little possibility of brain

metastasis in such cases. If contrast-enhanced MRI cannot be performed for a reason such as the presence of an electronic device or metal in the patient's body, contrast-enhanced CT is considered appropriate.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung cancer, brain metastasis, MRI, and CT.

In addition, the following were referenced as secondary sources.

1) David S: NCCN Guidelines®: non-small cell lung cancer Ver 3. 2020. National Comprehensive Cancer Network, 2020
2) David S: NCCN Guidelines®: small cell lung cancer Ver 2. 2018. National Comprehensive Cancer Network, 2018
3) Silvestri GA et al: Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143 (5): e211S-250S, 2013
4) Gaga M et al: An official American Thoracic Society/European Respiratory Society Statement: the role of the pulmonologist in the diagnosis and management of lung cancer. Am J Respir Crit Care Med 188 (4): 503-507, 2013
5) Japan Lung Cancer Society, Ed.: Guidelines for Diagnosis and Treatment of the Lung Cancer/Malignant Pleural Mesothelioma/Thymic Tumors 2020. KANEHARA & Co., 2021.

References

1) Davis PC et al: Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. AJNR Am J Neuroradiol 12 (2): 293-300, 1991
2) Akeson P et al: Brain metastases-comparison of gadodiamide injection-enhanced MR imaging at standard and high dose, contrast-enhanced CT and non-contrast-enhanced MR imaging. Acta Radiol 36 (3): 300-306, 1995
3) Yokoi K et al: Detection of brain metastasis in potentially operable non-small cell lung cancer. Chest 115 (3): 714-719, 1999
4) Seute T et al: Detection of brain metastases from small cell lung cancer: consequences of changing imaging techniques (CT versus MRI). Cancer 112 (8): 1827-1834, 2008
5) Sánchez de Cos J et al: Non-small cell lung cancer and silent brain metastasis: survival and prognostic factors. Lung Cancer 63 (1): 140-145, 2009
6) Sakurai H et al: Bronchioloalveolar carcinoma of the lung 3 centimeters or less in diameter: a prognostic assessment. Ann Thorac Surg 78 (5): 1728-1733, 2004
7) Cho H et al: Pure ground glass nodular adenocarcinomas: are preoperative positron emission tomography/computed tomography and brain magnetic resonance imaging useful or necessary? J Thorac Cardiovasc Surg 150 (3): 514-520, 2015
8) Suzuki K et al: A prospective radiological study of thin-section computed tomography to predict pathological noninvasiveness in peripheral clinical IA lung cancer (Japan Clinical Oncology Group 0201). J Thorac Oncol 6 (4): 751-756, 2011

BQ 28 Is bone scintigraphy recommended for diagnosing bone metastasis of lung cancer?

Statement

Although scientific evidence supporting the use of bone scintigraphy to diagnose bone metastasis is lacking, its use can be considered, particularly when bone metastasis is suspected clinically and FDG-PET cannot be performed.

Background

Diagnosing bone metastasis during the initial examination for primary lung cancer is important for prognosis prediction and treatment selection. Screening for bone metastasis previously involved bone scintigraphy. Recently, however, bone scintigraphy is being replaced by FDG-PET. FDG-PET and FDG-PET/CT are also recommended for lung cancer staging in the NCCN and ACCP guidelines and as the official statenebt of the ATS/ERS. That is because the sensitivity of FDG-PET is comparable to the sensitivity of bone scintigraphy,[1-3] whereas accumulation in bone scintigraphy is increased by factors such as trauma, infection, and joint disease, resulting in low specificity. Conversely, the advantages of bone scintigraphy are its short test duration, and the fact that it results in fewer false-negatives for osteoblastic bone metastasis than FDG-PET. Bone scintigraphy and FDG-PET were compared with respect to their performance in diagnosing bone metastasis of primary lung cancer, and the findings are summarized below.

Explanation

In a meta-analysis of 8 articles (723 patients), the sensitivity and specificity of bone scintigraphy for bone metastasis were 82% and 62%, respectively, in primary lung cancer patients with a mean prevalence of 20%. Thus, the specificity of bone scintigraphy was found to be somewhat low. However, a separate meta-analysis of 17 articles (2,940 patients), comprising 9 on FDG-PET/CT, 6 on FDG-PET, 6 on MRI, and 16 on bone scintigraphy, found sensitivity and specificity of 92% and 98%, 87% and 94%, 77% and 92%, and 86% and 88%, respectively. Moreover, the odd ratios for FDG-PET/CT (449.17) and FDG-PET (118.25) were significantly higher than those for MRI (38.27) and bone scintigraphy (63.37).[1] A meta-analysis of 7 articles found that the sensitivity and specificity of either FDG-PET/CT or FDG-PET and bone scintigraphy for bone metastasis were 93%, 95%, 87%, and 82%, respectively, on a per-patient basis (1,746 patients). On a per-lesion basis (1,263 lesions), sensitivity and specificity were 93%, 92%, 91%, and 57%, respectively.[3]

FDG-PET is recommended for staging in the NCCN and ACCP guidelines and as the official statement of the ATS/ERS. The ACCP guidelines state that bone scintigraphy can be used as an alternative to FDG-PET if it cannot be performed.

Search keywords and secondary sources

PubMed was searched using the following keywords: lung cancer, bone metastases, bone scintigraphy, and PET. Important articles with high-level medical evidence were used in the review.

In addition, the following were referenced as secondary sources.

1) David S: NCCN Guidelines®: non-small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021
2) David S: NCCN Guidelines®: small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021
3) Silvestri GA et al: Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143 (5): e211S-250S, 2013
4) Gaga M et al: An official American Thoracic Society/European Respiratory Society Statement: the role of the pulmonologist in the diagnosis and management of lung cancer. Am J Respir Crit Care Med 188 (4): 503-507, 2013

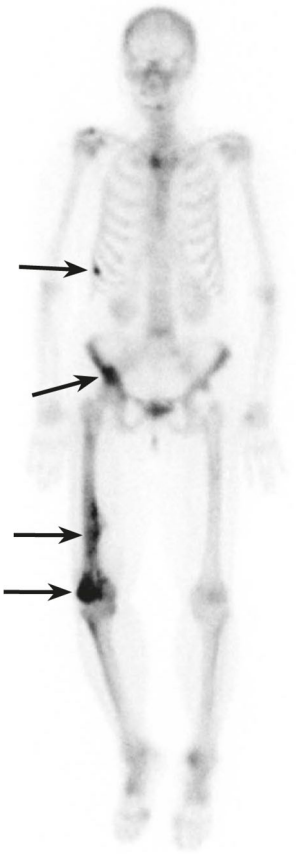

Figure. Lung cancer and multiple bone metastases

Bone scintigraphy, frontal view: Abnormal accumulation is seen in a right rib and the right ilium, right femur, and right patella (→).

References

1) Qu X et al: A meta-analysis of ^{18}FDG-PET-CT, ^{18}FDG-PET, MRI and bone scintigraphy for diagnosis of bone metastases in patients with lung cancer. Eur J Radiol 81: 1007-1015, 2012
2) Chang MC et al: Meta-analysis: comparison of F-18 fluorodeoxyglucose-positron emission tomography and bone scintigraphy in the detection of bone metastasis in patients with lung cancer. Acad Radiol 19: 349-357, 2012
3) Schirrmeister H et al: Omission of bone scanning according to staging guidelines leads to futile therapy in non-small cel lung cancer. Eur J Nucl Med Mol Imaging 31: 964-968, 2004

BQ 29 Is PET recommended for detecting lung cancer recurrence?

Statement

PET is useful and recommended for detecting lung cancer recurrence. In some cases, tumor markers may be elevated, but a lesion at a site where recurrence is difficult to identify only by morphological diagnostic imaging using a modality such as CT and MRI may be detectable using PET.

Background

Lung cancer recurrence is usually detected using a morphological imaging modality such as CT or MRI. PET using FDG is a functional imaging method for imaging glucose metabolism that may be even more useful than diagnostic imaging based on conventional morphological diagnosis. This section summarizes the literature on the usefulness of PET for detecting lung cancer recurrence.

Explanation

Periodic morphological diagnostic imaging and examination of changes in tumor marker levels are the main methods used to detect lung cancer recurrence. However, in some cases, it is difficult to distinguish between postoperative changes and local recurrence with chest CT (Fig.). It can also be difficult to identify the site of recurrence based on tumor marker elevation alone, and detection may complicated by false positives.

Investigations of the diagnostic accuracy of PET/CT and PET with respect to the posttreatment recurrence of non-small cell lung cancer have reported sensitivity ranging from 81% to 100%, specificity of 77% to 98%, and diagnostic accuracy rates of 88% to 97%, indicating its usefulness in detecting recurrence.[1-11] In examinations of patients suspected of having a recurrence based on elevated tumor marker carcinoembryonic antigen (CEA) levels and other clinical findings, the diagnostic accuracy rates of PET and PET/CT ranged from 90% to 95%,[2-6] higher than the diagnostic accuracy rate of CT (50%), and confidence in the diagnosis was also better.[3] On the other hand, examinations of postoperative patients with asymptomatic non-small cell lung cancer found that PET/CT identified recurrence in 18% to 38% of patients.[7, 8]

In some cases, determining and differentiating local recurrence can be difficult with morphological diagnostic imaging by CT because pulmonary fibrosis occurs after stereotactic radiation therapy. With PET/CT, however, recurrence can be distinguished from fibrotic inflammation based on accumulation strength and shape.[12-14]

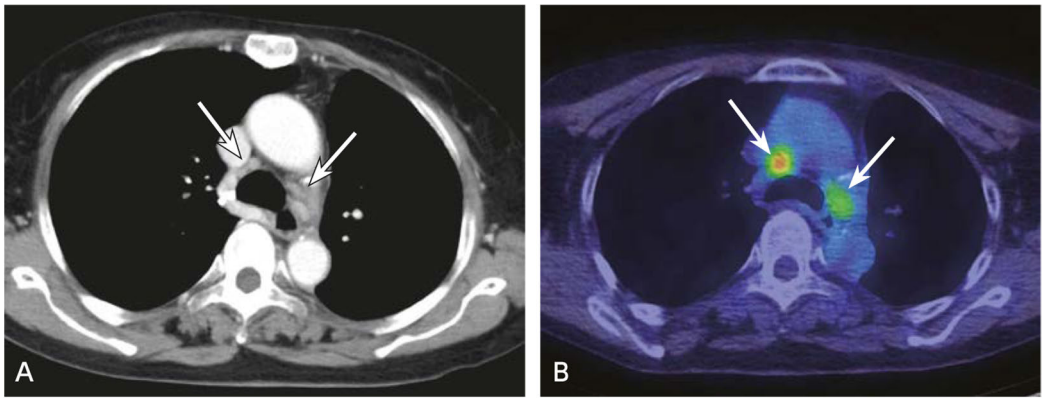

Figure. Screening for recurrence performed due to CEA elevation after surgery for right lower lobe, ALK fusion gene-positive lung cancer.

A: Contrast-enhanced CT, transverse image; B: PET/CT fusion imaging, transverse image
Although only small mediastinal lymph nodes are seen on contrast-enhanced CT, FDG accumulation (SUVmax = 3.8 to 5.7, →) is subsequently seen on PET/CT, suggesting recurrence. Alectinib administration was started, CEA decreased over time, and a reduction in the size of the mediastinal lymph nodes was seen (not shown).

An investigation of the use of PET/CT to examine recurrence and residual neoplasms following treatment for non-small cell lung cancer found that the examination resulted in treatment resumption in 20% of patients, a change of treatment in 6%, and treatment discontinuation in 2%. Thus, PET/CT resulted in a change in the treatment plan for 28% of the patients as a whole.[15)]

Although there have been very few reports of studies of the usefulness of PET in detecting small cell lung carcinoma recurrence, the results of one such study were similar to those obtained for non-small cell lung cancer: sensitivity of 100%, specificity of 80%, and a diagnostic accuracy rate of 92%.[16)] In an investigation of the use of PET to evaluate posttreatment recurrence and residual neoplasms, changes such as a change in the type of treatment and treatment resumption were made in the treatment plans of approximately half of the patients as a result of the evaluation.[17)]

Recurrent lung cancer lesions are not limited to a single location, but they can be present in multiple organs. PET, which can be used to evaluate the whole body, is therefore highly useful for detecting such lesions. Moreover, because the specificity of PET is also high, the likelihood of recurrence can be concluded to be low if the results of PET are negative, permitting follow-up to be carried out without performing other tests.

Search keywords and secondary sources

PubMed was searched using the following keywords: FDG, PET, lung cancer, and recurrence. The period searched was from 2015 to June 2019, and there were no new studies that ought to have been selected for review.

In addition, the following was referenced as a secondary source.

1) Japanese Society of Nuclear Medicine Subcommittee, Respiratory Nuclear Medicine Research Group, Ed.: Respiratory Nuclear Medicine Diagnostic (Clinical Practice) Guidelines, 2nd Edition. Japanese Society of Nuclear Medicine, 2015.

References

1) He YQ et al: Diagnostic efficacy of PET and PET/CT for recurrent lung cancer: a meta-analysis. Acta Radiol 55: 309-317, 2014
2) Opoka L et al: Assessment of recurrence of non-small cell lung cancer after therapy using CT and Integrated PET/CT. Pneumonol Alergol Pol 81: 214-220, 2013
3) Jiménez-Bonilla JF et al: Diagnosis of recurrence and assessment of post-recurrence survival in patients with extracranial non-small cell lung cancer evaluated by 18F-FDG PET/CT. Lung Cancer 81: 71-76, 2013
4) Isobe K et al: Usefulness of fluoro-2-deoxyglucose positron emission tomography for investigating unexplained rising carcinoembryonic antigen levels that occur during the postoperative surveillance of lung cancer patients. Int J Clin Oncol 14: 497-501, 2009
5) Keidar Z et al: PET/CT using 18F-FDG in suspected lung cancer recurrence: diagnostic value and impact on patient management. J Nucl Med 45: 1640-1646, 2004
6) Hellwig D et al: Diagnostic performance and prognostic impact of FDG-PET in suspected recurrence of surgically treated non-small cell lung cancer. Eur J Nucl Med Mol Imaging 33: 13-21, 2006
7) Toba H et al: 18F-fluorodeoxyglucose positron emission tomography/computed tomography is useful in postoperative follow-up of asymptomatic non-small-cell lung cancer patients. Interact Cardiovasc Thorac Surg 15: 859-864, 2012
8) Cho S, Lee EB: A follow-up of integrated positron emission tomography/computed tomography after curative resection of non-small cell lung cancer in asymptomatic patients. J Thorac Cardiovasc Surg 139: 1447-1451, 2010
9) Takenaka D et al: Integrated FDG-PET/CT vs. standard radiological examinations: comparison of capability for assessment of postoperative recurrence in non-small cell lung cancer patients. Eur J Radiol 74: 458-464, 2010
10) Kanzaki R et al: Clinical value of F18-fluorodeoxyglucose positron emission tomography-computed tomography in patients with non-small cell lung cancer after potentially curative surgery: experience with 241 patients. Interact Cardiovasc Thorac Surg 10: 1009-1014, 2010
11) Onishi Y et al: Non-small cell carcinoma: comparison of postoperative intra- and extrathoracic recurrence assessment capability of qualitatively and/or quantitatively assessed FDG-PET/CT and standard radiological examinations. Eur J Radiol 79: 473-479, 2011
12) Takeda A et al: Evaluation for local failure by 18F-FDG PET/CT in comparison with CT findings after stereotactic body radiotherapy (SBRT) for localized non-small-cell lung cancer. Lung Cancer. 79: 248-253, 2013
13) Zhang X et al: Positron emission tomography for assessing local failure after stereotactic body radiotherapy for non-small-cell lung cancer. Int J Radiat Oncol Biol Phys 83: 1558-1565, 2012
14) Nakajima N et al: Differentiation of tumor recurrence from radiation-induced pulmonary fibrosis after stereotactic ablative radiotherapy for lung cancer: characterization of 18F-FDG PET/CT findings. Ann Nucl Med 27: 261-270, 2013
15) Marcus C et al: 18F-FDG PET/CT and lung cancer: value of fourth and subsequent posttherapy follow-up scans for patient management. J Nucl Med 56: 204-208, 2015
16) Zhao DS et al: 18F-fluorodeoxyglucose positron emission tomography in small-cell lung cancer. Semin Nucl Med 32: 272-275, 2002
17) Blum R et al: Impact of positron emission tomography on the management of patients with small-cell lung cancer: preliminary experience. Am J Clin Oncol 27: 164-171, 2004

BQ 30 Is MRI recommended for diagnosing mediastinal tumors?

Statement

MRI is useful for diagnosing cystic tumors of the mediastinum and may also provide additional information about the internal attributes of solid tumors of the mediastinum. It is also highly useful and recommended for diagnosing tumors of the posterior mediastinum.

Background

CT is often used for diagnostic imaging of mediastinal tumors, and MRI is subsequently added in some cases. However, the necessity and usefulness of MRI in this role have not been adequately examined. Although few reports have directly compared the diagnostic performance of CT and MRI in diagnosing mediastinal tumors, several reports have indicated that MRI is useful for this purpose. Consequently, the usefulness of MRI in diagnosing mediastinal tumors was examined, and the findings are summarized below.

Explanation

The sites of mediastinal tumor development are chiefly classified as the anterior, middle, and posterior mediastinum. In addition, the tumors are broadly classified as cystic or solid tumors according to their internal attributes. When discussing the usefulness of MRI, it is necessary to consider the sites of development and internal attributes. There have been very few reports that have directly compared the usefulness of CT and MRI in evaluating mediastinal tumors. In an investigation of the diagnostic performance of CT and MRI in anterior mediastinal tumors, the diagnostic accuracy of CT and MRI was 83% and 84%, respectively, for thymomas; 38% and 13% for thymic carcinomas; 58% and 38% for teratomas; 35% and 27% for malignant germ cell tumors; and 55% and 43% for malignant lymphomas.[1)] Thus, the diagnostic performance of CT was comparable or superior to that of MRI in these solid anterior mediastinal tumors. Moreover, CT was significantly better than MRI in diagnosing teratomas.

Cystic mediastinal lesions, such as thymic cysts, bronchial cysts, and esophageal cysts, are known to show a variety of densities and signals on non-contrast CT and T1-weighted MRI images due to hemorrhage and protein content,[2)] making differentiation from solid tumors difficult. However, in the report mentioned above, the diagnostic performance of MRI (diagnostic accuracy, 71%) was significantly higher than that of CT (46%) for the diagnosis of thymic cysts.[1)] In an examination of the use of diffusion-weighted imaging to differentiate solid from cystic tumors of the mediastinum, the ADC values were significantly higher for cystic tumors than for solid tumors.[3)] Particularly when a contrast medium cannot be used, MRI can readily distinguish between cystic and solid tumors. Cystic teratomas, abscesses, and lesions that contain viscous fluids such as blood may show hyperintensity on diffusion-weighted imaging, and the ADC value may be relatively low. The signal intensities and ADC values of T1- and

T2-weighted images and diffusion-weighted images vary depending on the attributes of the intracystic fluid. Consequently, it may be possible to obtain additional information about the nature of the intracystic fluid by comprehensively evaluating each sequence.

In a report that compared the visualizability of various CT and MRI findings for thymic epithelial tumors, the visualization rate with CT and MRI was 18% and 75%, respectively, for the peritumoral capsule, 13% and 43% for intratumoral septa, and 5% and 17% for intratumoral hemorrhage. Thus, visualizability was significantly better with MRI. Moreover, visualization by MRI of a fibrous septum that divided the tumor or a capsule surrounding the tumor was found to be suggestive of a low-risk thymoma (Fig.).[4] An examination of MRI findings and the WHO histological classifications of thymic epithelial tumors found that type A thymomas were often smaller than those of other tissue types, encapsulated, had a distinct border, and were round masses with smooth margins. It also found that thymic carcinomas were often internally inhomogeneous on T2-weighted images, frequently showed hypointense areas that reflected fibrous components in the lesion, and were often associated with mediastinal lymph node enlargement.[5] Because CT and MRI are comparable for evaluating great vessel invasion of thymic epithelial tumors,[4] MRI can be used for this purpose when contrast-enhanced CT cannot be performed for a reason such as iodine allergy. An investigation of the use of dynamic contrast-enhanced MRI for thymic epithelial tumors found that enhancement peaked early in noninvasive thymomas, while a late peak with a pattern of gradually increasing enhancement was seen in invasive thymomas and thymic carcinomas with an abundant intratumoral fibrous component.[6] An investigation of the differentiation of thymic epithelial tumors, malignant lymphomas, and malignant germ cell tumors reported that a pattern of early enhancement and late washout on dynamic contrast-enhanced MRI was a characteristic of thymic epithelial tumors, while a pattern of gradually increasing enhancement was seen in malignant lymphomas and malignant germ cell tumors.[7] An investigation of the differentiation of benign and malignant solid tumors of the mediastinum using diffusion-weighted imaging found that the ADC values of malignant tumors were lower than those of benign tumors.[8] Particularly low ADC values have been reported for malignant lymphoma, reflecting high cell density.[8, 9] Investigations of diffusion-weighted imaging for thymic epithelial tumors showed that ADC values were lower for high-risk thymomas and thymic carcinomas than for low-risk thymomas and also lower for advanced tumors of Masaoka stages III and IV than for early-stage tumors of stages I and II.[10, 11] The use of diffusion-weighted imaging may provide additional information for the qualitative diagnosis of mediastinal tumors and the evaluation of their malignancy.

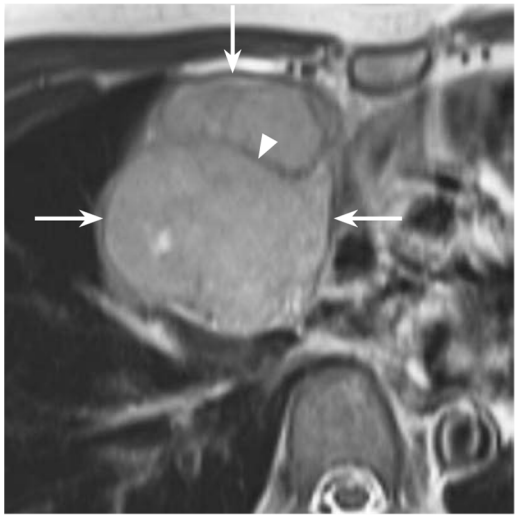

Figure. Low-risk thymoma (type AB thymoma)

MRI, T2-weighted transverse image: A lobulated mass with a distinct border and smooth margin is seen in the right anterior mediastinum. The entire circumference of the mass is covered with a hypointense capsule (→), and a hypointense septum (▷) that appears to divide the tumor interior is also seen.

In thymic hyperplasia, fat is often interposed between the thymic tissues, and the signal intensity is lower with opposed-phase chemical shift imaging (CSI) by MRI than with in-phase imaging. This has been found to be useful for differentiating from tumorous lesions such as thymomas.[12] A study examining the differentiation of thymoma from normal thymus and thymic hyperplasia in patients with myasthenia gravis found MRI to be superior to CT. The diagnostic accuracy rate of CT and MRI in a qualitative evaluation based on factors such as morphology and other attributes was 86.7% and 96.6%, respectively. Moreover, the diagnostic accuracy rate in a quantitative evaluation using non-contrast CT density and CSI signal changes was 75% and 98.9%, respectively.[13]

Nearly all tumors that develop in the posterior mediastinum are neurogenic tumors such as schwannomas, neurofibromas, ganglioneuromas, neuroblastomas, and paragangliomas, and MRI is useful for evaluating the relationships between tumors and structures such as nerves and intervertebral foramina.[14] In recent years, multiplanar reconstruction (MPR) has made it possible to easily perform evaluations using coronal and sagittal CT images, and the predominance of MRI is fading. However, an advantage of MRI is the high tissue contrast it provides, even with non-contrast-enhanced imaging. There have no reports that have compared the usefulness of CT and MRI in evaluating posterior mediastinal tumors.

Search keywords and secondary sources used as references

PubMed was searched using the following keywords: MRI, thymoma, thymic epithelial tumor, thymic hyperplasia, lymphoma, germ cell tumor, neurogenic tumor, mediastinum, and mediastinal tumor.

In addition, the following were referenced as secondary sources.

1) Japan Lung Cancer Society, Ed.: Guidelines for Diagnosis and Treatment of the Lung Cancer/Malignant Pleural Mesothelioma/Thymic Tumors 2020. KANEHARA & Co., 2021.

References

1) Tomiyama N et al: Anterior mediastinal tumors: diagnostic accuracy of CT and MRI. Eur J Radiol 69: 280-288, 2009
2) Murayama S et al: Signal intensity characteristics of mediastinal cystic masses on T1-weighted MRI. J Comput Assist Tomogr 19: 188-191, 1995
3) Shin KE et al: Diffusion-weighted MRI for distinguishing non-neoplastic cysts from solid masses in the mediastinum: problem-solving in mediastinal masses of indeterminate internal characteristics on CT. Eur Radiol 24: 677-684, 2014
4) Sadohara J et al: Thymic epithelial tumors: comparison of CT and MR imaging findings of low-risk thymomas, high-risk thymomas, and thymic carcinomas. Eur J Radiol 60: 70-79, 2006
5) Inoue A et al: MR imaging of thymic epithelial tumors: correlation with World Health Organization classification. Radiat Med 24: 171-181, 2006
6) Sakai S et al: Differential diagnosis between thymoma and non-thymoma by dynamic MR imaging. Acta Radiol 43: 262-268, 2002
7) Yabuuchi H et al: Anterior mediastinal solid tumours in adults: characterisation using dynamic contrast-enhanced MRI, diffusion-weighted MRI, and FDG-PET/CT. Clin Radiol 70: 1289-1298, 2015
8) Razek AA et al: Assessment of mediastinal tumors with diffusion-weighted single-shot echo-planar MRI. J Magn Reson Imaging 30: 535-540, 2009
9) Zhang W et al: A whole-tumor histogram analysis of apparent diffusion coefficient maps for differentiating thymic carcinoma from lymphoma. Korean J Radiol 19: 358-365, 2018
10) Abdel Razek AA et al: Diffusion-weighted MR imaging in thymic epithelial tumors: correlation with World Health Organization classification and clinical staging. Radiology 273: 268-275, 2014
11) Priola AM et al: Diffusion-weighted magnetic resonance imaging of thymoma: ability of the apparent diffusion coefficient in predicting the World Health Organization (WHO)classification and the Masaoka-Koga staging system and its prognostic significance on disease-free survival. Eur Radiol 26: 2126-2138, 2016
12) Inaoka T et al: Thymic hyperplasia and thymus gland tumors: differentiation with chemical shift MR imaging. Radiology 243: 869-876, 2007
13) Priola AM et al: Comparison of CT and chemical-shift MRI for differentiating thymoma from non-thymomatous conditions in myasthenia gravis: value of qualitative and quantitative assessment. Clin Radiol 71: e157-169, 2016
14) Sakai F et al: Intrathoracic neurogenic tumors: MR-pathologic correlation. AJR Am J Roentgenol 159: 279-283, 1992

BQ 31 Is CT recommended for distinguishing benign from malignant pleural lesions?

Statement

CT is useful for distinguishing benign from malignant pleural lesions and provides information that can be used to decide whether to perform thoracocentesis or thoracoscopy. Although it has limitations in detecting malignant disease, the use of contrast-enhanced CT is recommended.

Background

Pleural lesions are often asymptomatic, and detection by diagnostic imaging is important, However, the use of chest radiography to detect such lesions has limitations. The usefulness of differential diagnosis between benign and malignant tumors by CT was examined.

Explanation

Distinguishing pleural lesions from intrapulmonary lesions is not necessarily easy by chest radiography, and CT is therefore performed to diagnose pleural lesions. CT can provide information such as the extent and morphology of pleural lesions, their level of intrathoracic growth, and the presence or absence of bone destruction and chest wall invasion.

CT is considered capable of distinguishing between benign and malignant pleural lesions in the vast majority of cases. A 1990 retrospective study of CT in 74 patients with diffuse pleural disease (39 with malignant disease, 35 with benign disease; contrast media used except in those with asbestos exposure) used the following 4 parameters for diagnosis: ① circumferential/rind pleural involvement; ② nodular pleural thickening; ③ parietal pleural thickening greater than 1 cm; and ④ mediastinal pleural lesions. The results showed specificity of 100%, 94%, 94% and 88%, respectively, and sensitivity of 41%, 51%, 36%, and 56%, respectively. Moreover, the presence of 1 or more of these parameters enabled diagnosis in 28 of the 39 patients with malignancies.[1)] In a 2001 prospective study of contrast-enhanced chest CT in 40 patients with pleural effusion that used diagnostic criteria similar to those used in the study described above, evaluation of the pleural surface (nodular or irregular) enabled diagnosis in 28 of the 32 patients with malignant disease and all 8 patients with benign disease (sensitivity, 84%; specificity, 100%). The study found that circumferential pleural involvement/pleural rind was seen with nearly equal frequency in benign and malignant lesions and was, therefore, an unreliable finding.[2)] A 2002 retrospective study of the use of contrast-enhanced CT in 215 patients with pleural disease included 99 with malignant pleural mesothelioma (MPM), 39 with metastatic pleural disease (MPD), 32 with tuberculous pleurisy, 26 with empyema, and 19 with asbestos-related advanced benign pleural disease (ARBPD). Circumferential/rind pleural involvement was seen in 70% with MPM, 15% with MPD, 9% with tuberculous pleurisy, 5% with ARBPD, and none of the patients with empyema. Nodular pleural thickening was seen in 48% with MPM

and 13% with MPD; it was not seen with tuberculous pleurisy or empyema, but was seen in 16% with ARBPD. Pleural thickening greater than 1 cm was observed in 59% with MPM, 17% with MPD, 75% with tuberculous pleurisy, 61% with empyema, and 53% with ARBPD. Pleural thickening greater than 1 cm is therefore considered unreliable as a diagnostic finding. Mediastinal pleural lesions were found in 85% with MPM, 33% with MPD, 22% with tuberculous pleurisy, 12% with empyema, and 16% with ARBPD.[3)] A 2005 investigation of 146 patients (59 patients with malignant disease and 87 with benign disease) used similar diagnostic criteria: ① pleural nodularity; ② pleural rind; ③ pleural thickening greater than 1 cm; and ④ mediastinal pleural involvement. The results showed specificity of 97%, 97%, 85%, and 87%, respectively, and sensitivity of 37%, 22%, 31%, and 35%, respectively. Thus, low sensitivity was seen.[4)] Findings from evaluations of the pleural surface (nodular or irregular) and the presence of mediastinal pleural lesions are particularly reliable findings, and circumferential pleural involvement/pleural rind and parietal pleural thickening greater than 1 cm are findings with high specificity that can be used for reference depending on the circumstances (Figs. 1 and 2). However, all of the studies indicate that sensitivity is limited to a certain extent. A contrast medium should be used.

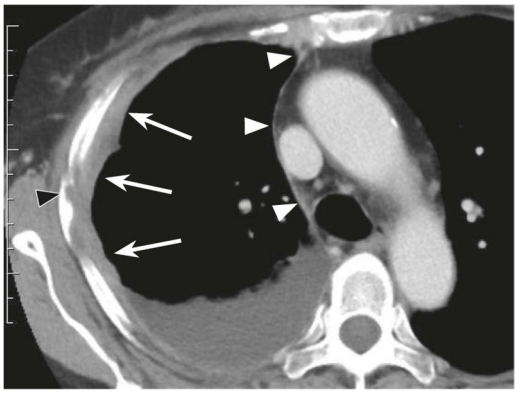

Figure 1. Malignant pleural mesothelioma

Contrast-enhanced CT, transverse image: Irregular parietal pleural thickening (11 mm, →) and pleural effusion are seen, accompanied by mediastinal pleural lesions (▷) and rib invasion (►).

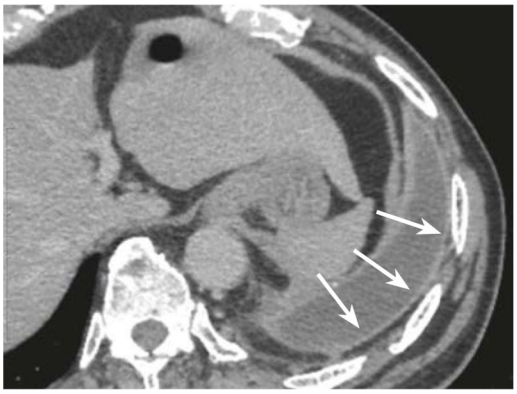

Figure 2. Tuberculous pleurisy

Contrast-enhanced CT, transverse image: Smooth parietal pleural thickening (4 mm, →) and pleural effusion are seen.

In a retrospective study of 370 patients who underwent thoracoscopy (211 patients with malignant disease and 159 with benign disease), sensitivity was 68% for CT reports of imaging performed before thoracoscopy that indicated malignant disease, and specificity was 78% for reports that indicated benign disease. Moreover, the positive predictive value was 80%, and the negative predictive value was only 65% for reports that indicated malignant disease.[5)]

Malignant pleural disease is often present even in the absence of CT findings indicating malignancy. It is therefore difficult to exclude malignancy based on CT alone.[4, 5)] Even in the absence of CT findings indicating malignancy, the possibility of clinical malignancy should be considered, and the appropriate means of thorough examination by thoracocentesis or thoracoscopy selected.

Search keywords and secondary sources

PubMed was searched using the following keywords: pleural tumor, pleural mesothelioma, differential diagnosis, and CT.

In addition, the following were referenced as secondary sources.

1) Japan Lung Cancer Society, Ed.: Guidelines for Diagnosis and Treatment of the Lung Cancer/Malignant Pleural Mesothelioma/Thymic Tumors 2018. KANEHARA & Co., 2018.

References

1) Leung AN et al: CT in differential diagnosis of diffuse pleural disease. AJR Am J Roentgenol 154 (3): 487-492, 1990
2) Traill ZC et al: Thoracic computed tomography in patients with suspected malignant pleural effusions. Clin Radiol 56 (3): 193-196, 2001
3) Metintas M et al: Computed tomography features in malignant pleural mesothelioma and other commonly seen pleural diseases. Eur J Radiol 41 (1): 1-9, 2002
4) Yilmaz U et al: CT in differential diagnosis of benign and malignant pleural disease. Monaldi Arch Chest Dis 63 (1): 17-22, 2005
5) Hallifax RJ et al: Role of CT in assessing pleural malignancy prior to thoracoscopy. Thorax 70 (2): 192-193, 2015

BQ 32 Is PET/CT recommended for diagnosing malignant pleural mesothelioma?

Statement

Although PET/CT has limitations for determining the degree of progression of primary tumors, it is useful for diagnosing lymph node and distant metastases, for patients considering surgical resection, and those with suspected posttreatment metastasis or recurrence.

Background

Malignant pleural mesothelioma has been shown to be closely associated with asbestos exposure, and it is a malignancy with an extremely poor prognosis. There is concern that the number of patients with this disease in Japan will increase between 2020 and 2030. The reasons for its poor prognosis include the fact that no method of early detection or standard treatment has been established.

PET/CT has been established to be useful for clinical staging malignancies and diagnosing metastasis and recurrence. However, malignant pleural mesothelioma is a relatively rare disease, and most of the reported studies on the usefulness of PET/CT in diagnosing it have been single-center studies. Moreover, there have been few systematic reviews or meta-analyses of the relevant literature.[1, 2] This section summarizes the literature on the usefulness of PET/CT in clinically staging malignant pleural mesothelioma and diagnosing its metastasis and recurrence.

Explanation

Diagnostic imaging plays a major role in diagnosing malignant pleural mesothelioma and evaluating the response to treatment. One aspect of this role, clinical staging, is important for its strong influence on treatment strategy. The most commonly used staging classification for this disease is currently TNM staging established by the International Mesothelioma Interest Group.

Diagnostic imaging modalities such as CT, MRI, and PET/CT are used as appropriate to determine the clinical stage. CT may in some cases underestimate changes such as chest wall invasion and mediastinal lymph node metastasis. However, it is widely available and offers excellent cost-effectiveness. It is therefore often the first choice for the diagnostic imaging of malignant pleural mesothelioma. PET/CT is considered effective for purposes such as detecting unforeseen distant metastasis that cannot be identified with the normal diagnostic imaging methods, and it can aid in selecting an appropriate treatment.

1. Usefulness of PET/CT in clinical staging

① T stage

Accurate T staging is vital for the surgical resection of a tumor. Particularly important is differentiating between T3 tumors, which are resectable even when locally advanced, and T4 tumors, which are unresectable when locally advanced. However, microinvasion of the abdominal cavity by tumors can occur transdiaphragmatically, making it difficult to accurately determine the degree of progression with either CT or PET/CT.[3)]

The reported sensitivity of PET/CT in T4 diagnosis ranges from 67% to 78%, and identifying transdiaphragmatic invasion of the abdominal cavity and invasion of the pericardium was found to be difficult with PET/CT.[4, 5)] Thoracoscopy or laparoscopy should be considered if diagnostic imaging suggests that lesions may have spread to the contralateral side of the thoracic cavity or abdominal cavity.

② N stage

Mediastinal lymph node metastasis of malignant pleural mesothelioma is an adverse prognostic factor. In evaluating hilar or mediastinal lymph node metastasis using CT, a lymph node with a short-axis diameter of ≥ 1 cm is often considered positive. Examination of the diagnostic performance of CT in evaluating mediastinal lymph node metastasis showed that sensitivity and specificity were 60% and 71%, respectively, and mediastinal lymph node diagnostic performance with MRI was comparable to the diagnostic performance with CT.

The reported sensitivity, specificity, and diagnostic accuracy rate of PET/CT in mediastinal lymph node diagnosis (N2) ranged from 11% to 50%, 78% to 93%, and 59% to 66%, respectively, which resulted in part from false negatives for micrometastasis and false positives caused by inflammation. Thus PET/CT has certain limitations in diagnosing hilar or mediastinal lymph node metastasis.[4-6)] However, in a comparative investigation of CT, PET, PET/CT, and MRI in operable (stage II and III) malignant pleural mesothelioma conducted by Plathow et al., the diagnostic accuracy rate of PET/CT was the highest obtained.[7)]

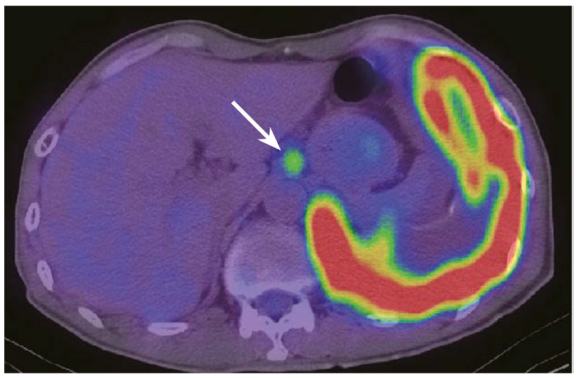

Figure. Malignant pleural mesothelioma

PET/CT fusion image, transverse image: FDG accumulation consistent with left pleural lesions is seen. FDG accumulation is also seen in an abdominal lymph node (→), suggesting lymph node metastasis.

③ M stage

Distant metastasis of malignant pleural mesothelioma occurs as unifocal or multifocal metastases in areas such as the brain, lungs, liver, adrenal glands, abdominal lymph nodes, and bones (Fig.). Erasmus et al. reported that extrathoracic metastasis that could not be identified with normal diagnostic imaging was detectable by PET/CT in 24% of patients.[4] Thus, PET/CT is useful for improving the accuracy of distant metastasis diagnosis and, therefore, may contribute to identifying patients who are candidates for surgery and inhibiting early postoperative recurrence.

2. Usefulness of PET/CT in diagnosing posttreatment metastasis and recurrence

Examination of the diagnostic performance of PET/CT with respect to local recurrence and distant metastasis occurring after treatment has shown sensitivity and specificity of 94% to 98% and 75% to 100%, respectively. PET/CT is highly useful when there are signs of malignant pleural mesothelioma recurrence, and recurrence and metastasis cannot be determined with other methods of diagnostic imaging.[8, 9]

Search keywords and secondary sources

PubMed was searched using the following keywords: mesothelioma, PET, and CT. The period searched was from 2015 to June 2019, and there were no new studies that should have been selected for review.

In addition, the following were referenced as secondary sources.

1) David S: NCCN Guidelines®: non-small cell lung cancer Ver 5. 2021. National Comprehensive Cancer Network, 2021
2) David S: NCCN Guidelines®: small cell lung cancer Ver 2. 2021. National Comprehensive Cancer Network, 2021

References

1) Basu S et al: Current evidence base of FDG-PET/CT imaging in the clinical management of malignant pleural mesothelioma: emerging significance of image segmentation and global disease assessment. Mol Imaging Biol 13: 801-811, 2011
2) Zahid I et al: What is the best way to diagnose and stage malignant pleural mesothelioma? Interact Cardiovasc Thorac Surg 12: 254-259, 2011
3) Wilcox BE et al: Utility of integrated computed tomography-positron emission tomography for selection of operable malignant pleural mesothelioma. Clin Lung Cancer 10: 244-248, 2009
4) Erasmus JJ et al: Integrated computed tomography-positron emission tomography in patients with potentially resectable malignant pleural mesothelioma: staging implications. Thorac Cardiovasc Surg 129: 1364-1370, 2005
5) Sørensen JB et al: Preoperative staging of mesothelioma by 18F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography fused imaging and mediastinoscopy compared to pathological findings after extrapleural pneumonectomy. Eur J Cardiothorac Surg 34: 1090-1096, 2008
6) Pilling J et al: Integrated positron emission tomography-computed tomography does not accurately stage intrathoracic disease of patients undergoing trimodality therapy for malignant pleural mesothelioma. Thorac Cardiovasc Surg 58: 215-219, 2010
7) Plathow C et al: Computed tomography, positron emission tomography, positron emission tomography/computed tomography, and magnetic resonance imaging for staging of limited pleural mesothelioma: initial results. Invest Radiol 43: 737-744, 2008
8) Tan C et al: Role of integrated 18-fluorodeoxyglucose position emission tomography-computed tomography in patients surveillance after multimodality therapy of malignant pleural mesothelioma. J Thorac Oncol 5: 385-388, 2010
9) Gerbaudo VH et al: FDG PET/CT patterns of treatment failure of malignant pleural mesothelioma: relationship to histologic type, treatment algorithm, and survival. Eur J Nucl Med Mol Imaging 38: 810-821, 2011