Sub solid pulmonary nodules

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Introduction

Sub solid pulmonary nodules

- Multidetector CT, low-dose CT lung cancer screening programs
- Varieties of small peripheral lung nodules
- The importance and prevalence of subsolid pulmonary nodules
References

**Radiology:** Volume 253: Number 3—December 2009
Subsolid Pulmonary Nodules and the Spectrum of Peripheral Adenocarcinomas of the Lung:
Recommended Interim Guidelines for Assessment and Management
Myrna C. B. Godoy, MD; David P. Naidich, MD

**Radiology:** Volume 245: Number 1—October 2007
Persistent Pulmonary Nodular Ground-Glass Opacity at Thin-Section CT: Histopathologic Comparisons
Ha Young Kim, MD, Young Mog Shim, MD et al
• Bartjan de Hoop, et al, Pulmonary Ground-Glass Nodules: Increase in Mass as an Early Indicator of Growth; *Radiology* April 2010 255:199-206

• Sang Min Lee, et al, Transient Part-Solid Nodules Detected at Screening Thin-Section CT for Lung Cancer: Comparison with Persistent Part-Solid Nodules; *Radiology* April 2010 255:242-251
Subsolid nodules - definition

Subsolid nodules are defined as focal nodular areas of increased lung attenuation through which normal parenchymal structures such as airways, vessels, and interlobular septa can be defined

- part-solid
- nonsolid = completely GGO
- Solid nodules are defined as those that completely obscure the lung parenchyma
**Subsolid nodules - differential**

- Persistent: either no change or an increase in diameter for \( \geq 1 \) month

Atypical adenomatous hyperplasia (AAH)
Broncholoalveolar cell carcinoma (BAC)
Pulmonary lymphoproliferative disorder
Organizing pneumonia/fibrosis nodules
• new interim management guidelines.
BAC

- Presents a unique growth pattern along alveolar septa without stromal invasion and has an indolent course

- High incidence of multifocality (25% vs 5%)
Noguchi’s histologic classification for small, peripheral adenocarcinomas, 1995, 2004

six subtypes, on the basis of the patterns of tumor growth
• A localized BAC;
• B, localized BAC with foci of collapsed alveolar structures;
• C, localized BAC with foci of active fibroblastic proliferation;
• D, poorly differentiated adenocarcinoma;
• E, tubular adenocarcinoma; and
• F, papillary adenocarcinoma with evidence of compressive and destructive growth.

Types A, B, and C represent a distinct grouping, as they show in common a predominant growth pattern involving “replacement” of alveolar lining cells.
1999, 2004

• The addition of AAH as a premalignant lesion

• Documented at histologic evaluation of resected lung cancers, - accompanying adenocarcinomas in up to 60% of cases
AAH

BAC, mucinous type

mixed subtype adenocarcinoma

Godoy M C B, Naidich D P Radiology 2009;253:606-622
**AAH<-->BAC**

- Foci AAH of appear as GGO lesions typically measure less than 5 mm (may be larger)

- Noguchi type A and B lesions, which demonstrate purely lepidic growth pattern, typically manifest as pure GGO nodules greater than 5 mm

- Noguchi type C lesions showing fibroblastic proliferation with stromal invasion correlate with lesions with mixed solid component and GGO
CT < -- > Pathology

Progression of lesions from those with pure GGO to those with mixed solid component and GGO has been shown to occur in select cases, correlating to stepwise progression of Noguchi replacement-type adenocarcinomas.
BAC
Multifocal?
BAC
Illustration of the relationship between the Noguchi histologic classification of adenocarcinoma of the lung (Noguchi types A though F) and corresponding CT appearances of these lesions.

Premalignant AAH
A localized BAC
B localized BAC with foci of structural collapse
C localized BAC, active fibroblastic proliferation
D, E, F poorly differentiated tubular, papillary adenocarcinoma
C likely mixed BAC/invasive adenocarcinoma
C mixed BAC/invasive adenocarcinoma
Premalignant AAH
A localized BAC
D, E, F poorly differentiated, tubular, papillary adenocarcinoma
B localized BAC with foci of structural collapse

Godoy M C B, Naidich D P Radiology 2009;253:606-622

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CT scans (1-mm section) of BAC (Noguchi type B lesion), heterogeneous GGO, show a nodule with GGO with (a) superimposed reticulation and (b) air bronchiolograms.
CT scans (1-mm section) of BAC (Noguchi type B lesion), heterogeneous GGO, show a nodule with GGO with (a) superimposed reticulation and (b) air bronchiolograms.
CT scan of mixed subtype adenocarcinoma with BAC component.

Godoy M C B, Naidich D P Radiology 2009;253:606-622
• Benign conditions, including
  Organizing pneumonia
  Focal fibrosis
  Focal inflammation

• may also present as subsolid nodules
Focal inflammation mimicking adenocarcinoma.

Godoy M C B, Naidich D P Radiology 2009;253:606-622

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• High-risk patients screened with low-dose CT

• Malignancy rate was greater for part-solid (63%) than nonsolid (pure GGO) (18%) nodules

• 34% of subsolid nodules proved to be malignant compared with 7% for solid nodules
Kim et al

- Persistent nonsolid nodules in a non-screened population

- **81%** of proved to be either AAH, BAC, or adenocarcinoma with BAC features

- **19%** proved histologically to represent either organizing pneumonia or nonspecific fibrosis
The morphologic characteristics of nodules in terms of shape, marginal characteristics, internal characteristics, and presence of pleural tag were not significantly different between BAC or adenocarcinoma with predominant BAC component, AAH, and nonspecific fibrosis or organizing pneumonia groups.
The risk

- **75%** of pure persistent pulmonary GGO nodules turn out to be BAC or adenocarcinoma with predominant BAC component
Differences between benign and malignant

No differences between benign and malignant lesions when assessed by shape, marginal characteristics, or the presence of pleural tags
Metastases

They rarely represent metastases, even in patients with documented extrathoracic tumors
Current Concepts in the Diagnosis and Management of Subsolid Nodules

- Alternate approaches to diagnosis and management
- Follow-up surveillance CT??
- PET/CT??
- Biopsy??
Growth Rate

Volume doubling time:

- AAH: 988 days ± 470
- BAC: 567 days ± 168
- Adeno CA: 384 days ± 212
- Squamous cell CA: 122 days ± 68
Growth Rate

Previous concept that lack of growth over a 2-year follow-up indicates a benign etiology does not apply for subsolid nodules.
Two discrete GGOs
2nd lesion: adenocarcinoma
Change in the attenuation becoming part solid

A change in the attenuation of lesions in itself is indicative of substantial interval change
Mixed subtype adenocarcinoma, progression of GGO to a nodule with mixed solid component and GGO

Follow-up CT scan obtained 1 year later
Role of PET

• For lesions as small as 8–10 mm in size

• FDG PET is accurate in differentiating benign from malignant lesions, with an overall sensitivity, specificity, and accuracy of 96%, 88%, and 94%, respectively

• FDG PET, has a lower sensitivity for small (<10 mm) or slow-growing lesions, such as carcinoid tumors and BAC
Tsunezuka et al

Correlated the effectiveness of FDG PET to characterize adenocarcinomas (≤2 cm) with Noguchi classification:

**false-negative rate** for type A lesions was 100%,
for type B lesions was 80%,
for type C lesions was 47%,
true-positive rate for types D, E, and F lesions was 67%, 100%, and 86%, respectively.

Similar results have been reported by Yap and colleagues
Shimizu et al
Role of Transthoracic Needle Biopsy

- The diagnostic yield of CT-guided FNA biopsy for GGO nodules was 51.2%
- Lesions smaller than 10 mm with predominantly ground-glass appearance the diagnostic yield was as low as 35.2%
Kim et al

accuracy of CT-guided core biopsy

Overall concordance rate between core and surgical biopsies in malignant and premalignant lesions was 73%

transthoracic FNA should only be performed in patients with subsolid nodules at CT who are either nonsurgical candidates, surgical candidates for whom proof of malignancy is still considered necessary, or who present with multifocal disease
Patients with Multiple Subsolid Nodules

Variable-sized subsolid nodules. (a) Magnified 1-mm CT section through the right upper lobe shows multiple small lesions with GGO and one dominant larger nodule with GGO (arrow). (b) CT scan at 4-year follow-up shows no substantial interval change (arrow) and the lesions were presumed to represent AAH and BAC (dominant lesion).
Is there over diagnosis of Lung Cancer in Patients with Subsolid Nodules?

- The potential of low-dose CT lung cancer screening to decrease lung cancer mortality

- Preliminary reports do seem to indicate that in select cases identification of small subsolid lesions at CT may in fact lead to over diagnosis and unnecessary treatment
Multiple subsolid nodules with variable size and appearance. In such cases, selective limited resection of the dominant lesions may be acceptable, contrary to standard treatment of patients with multiple foci of BAC and/or adenocarcinoma.
Suggested Guidelines in the Management of Subsolid Nodules

• These do not differentiate between low- and high-risk group as per Fleischner criteria due to the increased incidence of adenocarcinomas in younger and nonsmoking patients

• In the light of individual clinical history.
Smaller than 5 mm

Incidentally identified, isolated pure GGOs smaller than 5 mm foci of AAH sufficiently often to obviate routine follow-up CT studies

- some of these lesions may prove to be BAC, the extreme rarity of invasive adenocarcinomas coupled with their extremely prolonged doubling times suggest that there is no reason to undergo either the added expense or radiation exposure necessary to follow these lesions presumably over prolonged time intervals measured in years
Subsolid nodule

>5 mm AAH

No additional imaging or follow up
Smaller than 10 mm, Pure GGO

- **Conservative management** requires an initial follow-up examination in 3–6 months to document that lesions have not resolved spontaneously (or following antibiotic therapy).

- For most of these lesions, continued long-term follow-up is likely preferable to surgical resection.

- Annual follow-up should extend for more than 2 years.

- 5 years?, the risk of subsequent development of cancer needs to be balanced against the risks of unnecessary radiation exposure and surgical intervention.

- Thin-section, Low dose CT, with as low as 80 mAs.
Subsolid nodule

- >5 mm AAH
  - No additional imaging or follow up

- ≥ 10mm
  - Conservative follow up, more than 2 years

5??
**Solitary Lesions 10 mm or Larger, pure GGO**

- Nodules with pure GGO that are larger than 1 cm in size should be assumed as BAC or invasive adenocarcinoma provided if there is an increase in attenuation or development of a solid component or persistence.

- Although 20%-25% will prove to be benign at resection.
Solitary Lesions 10 mm or Larger, pure GGO

- Solitary lesions 10 mm or larger with pure GGO should be **resected**, provided that **persistence or growth** of the lesion is again established over at least a 3–6-month period.

- Percutaneous needle biopsy are limited given substantial sampling error.

- PET or PET/CT remain doubtful as PET-negative studies do not exclude the possibility of invasive adenocarcinoma, while these lesions are also still unlikely to be associated with distant metastases.
Lesions with Mixed Solid Component and GGO

Should be presumed malignant and surgical resection should be considered, provided lack of interval change over at least 3 months
Lesions with Mixed Solid Component and GGO

- Any lesion with mixed solid component and GGO, **regardless of size**, represents malignancy with sufficient likelihood to warrant further **evaluation**.

The evaluation should include:

- **PET/CT**
  - greater likelihood for invasive tumors for which preoperative staging and assessment of prognosis is warranted.

- **Transthoracic biopsy**
  - limited value of accurate differentiation between BAC and invasive adenocarcinomas and the likelihood that these lesions will be resected, regardless.
Subsolid nodule

- >5 mm AAH
  - No additional imaging or follow up

- ≥ 10mm
  - Conservative follow up, more than 2 years,??

- <1 cm, mixed
  - ± further evaluation: PET CT Surgery
Multiple Subsolid Nodules smaller than 5 mm with pure GGO

- At least 1-year follow-up CT study
- May be at greater risk than the general population for developing cancer.
- However, continued long-term follow-up should not be considered necessary.

- In general, follow-up CT surveillance is to be preferred in cases in which multiple small (5–10-mm in size) lesions are identified, as these most likely represent either multifocal AAH or in smokers, respiratory bronchiolitis.
Multiple Subsolid Nodules - Dominant lesions
GGOs greater than 10 mm
mixed solid component and GGO

• Surgical resection should be considered

• PET/CT should be performed following a similar logic as outlined above for solitary lesions

• Limited lung-sparing resections may be considered as an option to routine lobectomy given the likelihood that at least some of the remaining lesions will continue to grow
Subsolid nodule

- >5 mm AAH
  - No additional imaging or follow up

- ≥ 10mm
  - Conservative follow up, more than 2 years, ??

- <1 cm, mixed
  - ± further evaluation: PET CT
    - Surgery

- Multiple
  - Without a dominant lesion
  - With a dominant lesion
  - 1 year follow up
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