Nodule Characterization
Subsolid Nodules

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KEYWORDS

• Subsolid lung nodule • Ground-glass lung nodule • Computed tomography • Nodule characterization • Lung cancer • Adenocarcinoma classification • Management • Guidelines

KEY POINTS

- Subsolid lung nodules, including both pure and part-solid ground-glass nodules, are increasingly detected and characterized on chest computed tomography scans, in conjunction with thin-section imaging.
- Different etiologies exist for subsolid nodules, including both benign and malignant causes.
- Subsolid lung nodules when persistent have a high likelihood of representing part of the pathologic spectrum of lung adenocarcinoma.
- Recently published management guidelines from the Fleischner Society and American College of Chest Physicians serve as aids to both clinicians and radiologists.

Recent advances in technology, including the widespread availability of multidetector computed tomography (CT) scanners and emerging data in support of lung cancer screening, have broadened our understanding and awareness about small pulmonary nodules. In particular, knowledge of the subsolid nodule has grown as detection with CT has increased in conjunction with thin-section imaging capabilities.[1,2] Subsolid nodules include both "pure" ground-glass (pGGN) and part-solid (PSNs) lesions. Although these nodules may be inflammatory or infectious in etiology, a high association with the recently redefined pathologic spectrum of lung adenocarcinoma has been established, rendering subsolid nodules of heightened clinical importance.

In this review, we focus on the radiologic, clinical, and pathologic aspects primarily of solitary subsolid pulmonary nodules. Particular emphasis will be placed on the pathologic classification and correlative CT features of adenocarcinoma of the lung.[3] The capabilities of fluorodeoxyglucose positron emission tomography-CT (FDG PET-CT) and histologic sampling techniques, including CT-guided biopsy, endoscopic-guided biopsy, and surgical resection, are discussed. Finally, recently proposed management guidelines by the Fleischner Society and the American College of Chest Physicians (ACCP) are reviewed.[1,2]

DEFINITIONS AND TERMINOLOGY

A lung nodule is technically defined as a rounded opacity that is smaller than 3 cm in diameter. Subsolid nodules are those containing at least some component of ground-glass attenuation. Subsolid nodules are further classified as either "pure ground glass" (pGGN) or "part solid" (PSN) in appearance. According to the Fleischner Society glossary of terms for thoracic imaging,[4] a ground-glass opacity (GGO) is defined as "a hazy increased opacity of lung, with preservation of bronchial and vascular

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margins. It is caused by partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these, the common factor being the partial displacement of air." The term "pure GGN" refers to nodules of only ground-glass attenuation on CT, whereas the term "part-solid GGN" describes those that exhibit a combination of ground-glass and solid attenuation, which obscures the underlying lung architecture on CT. The term opacity can be used when the subsolid focal opacity is less round or very poorly defined from the adjacent parenchyma, although the delineation between nodule and opacity is challenging. In distinction, the term ground-glass "attenuation" should be applied to larger, less distinct areas of poorly defined areas of increased lung density through which normal lung structures may still be identified. It should be noted that although the term "CT halo sign" and its opposite, the "reverse halo sign" incorporate both solid and ground-glass elements, these lesions should be considered as separate and distinct entities and therefore are considered separately.

EPIDEMIOLOGY

Knowledge of the frequency of subsolid nodules has been gained primarily through screening CT studies. The frequency of subsolid nodules among all nodules has varied among reports. Henschke and colleagues[5] reported that the frequency of subsolid nodules among all (233) nodules in the Early Lung Cancer Action Project (ELCAP) was 19%. Lung cancer screening studies in Korea[6] and Ireland[7,8] reported the frequency of subsolid nodules to be 6.3% of 4037 nodules and 7.7% of 168 nodules, respectively. Another study from Japan by Li and colleagues[9] reported a 38% frequency of subsolid nodules. The NELSON study (Dutch-Belgian Randomized Lung Cancer Screening Trial) reported an incidence of 2.5% for "partially solid" and 3.5% for "nonsolid" nodules among the 2236 nodules that were detected.[10]

ETIOLOGY

Subsolid nodules may be transient or persistent. Although a close association between subsolid nodules and the recently redefined spectrum of adenocarcinomas of the lung has been reported, a considerable percentage of subsolid nodules (both transient and persistent) will prove to be benign. Benign etiologies include infectious and inflammatory conditions, including organizing pneumonia, focal interstitial fibrosis, and hemorrhage. Malignant etiologies include the spectrum of adenocarcinoma and, rarely, pulmonary metastasis especially due to malignant melanoma.

Transient Subsolid Nodules

A substantial proportion of subsolid nodules are transient, ranging between 38% and 70%,[11–13] resolving either spontaneously or after a course of antibiotics. Felix and colleagues[11] reported that 43.8% of 75 pure GGOs in a lung cancer screening program disappeared on follow-up chest CT. Oh and colleagues[12] reported 37.6% of 69 pGGNs and 48.7% of 117 mixed GGNs resolved. Lee and colleagues[13] reported that and 69.8% of 126 subsolid nodules were transient. Oh and colleagues identified young patient age, blood eosinophilia, lesion multiplicity, polygonal shape, ill-defined borders, and a large degree of solid component as among the suggested clinical and CT features that predicted transient rather than persistent lesions.[11–13] Felix and colleagues[11] found that nodules that resolved were more often lobular GGOs, with mixed attenuation, and larger size than those that persisted. For this reason, follow-up thin-section CT imaging has been recommended to confirm the persistence or disappearance of subsolid nodules such as at 3 months (**Fig. 1**).[1] Although antibiotics have been used before obtaining follow-up examinations,[14,15] their use is not included in current management guidelines.[1,2,16]

Although transient subsolid nodules are due to a variety of nonspecific infectious and inflammatory conditions, most often the precise etiology remains unknown. Interestingly, *Aspergillus* is one reported potential etiology for a transient subsolid nodule.[17] Eosinophilia has been noted to occur with some frequency in patients with transient subsolid nodules, although, as reported by Oh and colleagues,[12] short-term follow-up chest CT should be obtained for GGNs in the presence of high blood eosinophilic count, regardless of lesion size, to confirm clearance.

Other inflammatory etiologies resulting in transient subsolid nodules include antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, Kaposi sarcoma, and other fungal infections, more commonly multiple than solitary.[18] Thoracic endometriosis related to ectopic endometrial tissue can also lead to focal hemorrhage,[19] resulting in subsolid lesions.[19]

Persistent Subsolid Nodules

The most common causes of persistent subsolid nodules are lesions that fall within the pathologic spectrum of lung adenocarcinoma.[5,20–23] Less