Radiology: Cardiothoracic Imaging

COMMENTARY

The Puzzle of the Perifissural Nodule

Charles S. White, MD • Geoffrey D. Rubin, MD

Charles S. White, MD, FACR, FNASCI, is a professor of radiology and internal medicine at the University of Maryland School of Medicine and the director of thoracic imaging and vice chairman for clinical affairs at the University of Maryland Medical Center. He received his training at Columbia-Presbyterian Medical Center in New York. Dr White is certified by both the American Board of Radiology and the American Board of Internal Medicine. He has published widely in the areas of cardiothoracic radiology, including lung cancer screening and cardiac imaging. He is currently membership chairman of the Fleischner Society, past editor-in-chief of the *Journal of Thoracic Imaging*, past president of the Society of Thoracic Radiology, and past president of the North American Society of Cardiac Imaging.

Geoffrey D. Rubin, MD, MBA, FACR, FAHA, FSABI, FNASCI, is the George B. Geller Distinguished Professor for Cardiovascular Research, professor of radiology, and past chair of radiology at Duke University. He is a past president of the Fleischner Society and currently president and board chair of the International Society for Computed Tomography, founding board member of the Radiology Leadership Institute (RLI) of the American College of Radiology, board member of RAD-AID International, and host of the acclaimed RLI podcast, "Taking the Lead." He was previously professor of radiology at Stanford University, where he also served as associate dean for clinical affairs in the Stanford School of Medicine and chief of cardiovascular imaging. At Stanford, he pioneered the development of CT angiography and a variety of volumetric visualization and analysis techniques, cofounding one of the world's first clinical 3D Laboratories in 1996.

One of the most vexing problems to confront radiologists is the high frequency and proper management of lung nodules encountered at chest CT. This issue is compounded by the capability of newer CT scanners to create slices of thinner collimation and the associated increased generation of data. While it is well-known that smaller nodules less than 6 mm are unlikely to be malignant, subclassification using additional features such as morphology, density, and location to distinguish between benign and malignant nodules is proving to be enormously valuable to the radiologist to limit false-positive results (1). It is well-established, for example, that pure ground-glass nodules, in general, demonstrate more indolent growth than solid nodules (2). In this issue of *Radiology: Cardiothoracic Imaging*, Schreuder et al discuss an important group of nodules whose characteristics encompass morphology, density, and location, providing a comprehensive review of CT features of intrapulmonary lymph nodes, a topic on which they have considerable expertise (3).

The authors summarize the pathologic characteristics of intrapulmonary lymph nodes, which are described as solid; round, oval, or polygonal; within 15 mm of the pleura; 12 mm or less in diameter; and most often in the middle or lower lobes. The CT-equivalent term, *perifissural nodule*, has come to refer to a noncalcified solid nodule with sharp margins and a regular shape abutting or near the pleural or fissural margin. Unfortunately, as the authors note, the term *perifissural nodule* is imprecise and somewhat misleading, in part due to the lack of uniformity of its definition (3). As an alternative, *parapleural nodule* or a label such as a *LIPLN* (likely intrapulmonary lymph node) might be more accurate designations, although such change would be difficult because the term *perifissural nodule* has become highly engrained in the literature.

A further issue occurs because some of the characteristics that are defined at CT as characteristics of perifissural nodules differ from those based on pathologic studies. For example, at CT a perifissural nodule is often defined as being 5–15 mm or less from a pleural surface, which is somewhat different than the 15-mm delimitation described at pathology. In addition, the term *perifissural* implies that the nodule is located in relation to a fissure (major, minor, or accessory) and not the pleura, when in fact the pleura is a frequent location for perifissural nodules. Another point of confusion arises because the term *perifissural* suggests that the nodule is in direct contact with a pleural surface. However, atypical perifissural nodules need not abut the pleura provided they are within 5 mm of it and have appropriate characteristics. Finally, it is assumed that nodules that meet the CT criteria for perifissural nodules pathologically are intrapulmonary lymph nodes. But in the absence of proof for every such nodule, it is not possible to know this. Most of the radiologic-pathologic studies come from the era of relatively thick-section CT, and the smaller nodules that are often encountered today may in many cases represent other entities such as focal fat or small noncalcified granulomas. The important point is that whatever perifissural CT nodules are pathologically, they are overwhelmingly an indicator of a benign etiology, even at a size when a nonperifissural nodule would raise concern for malignancy.

From the Department of Radiology and Nuclear Medicine, University of Maryland School of Medicine, 22 S Greene St, Baltimore, MD 21201 (C.S.W.); and Department of Radiology, Duke University School of Medicine, Durham, NC (G.D.R.). Received June 25, 2020; revision requested June 30; revision received June 30; accepted June 30. **Address correspondence to** C.S.W. (e-mail: *cwhite@umm.edu*).

See also the article by Schreuder et al in this issue. Conflicts of interest are listed at the end of this article.

As the authors summarize, most studies have found no cancers among nodules classified as perifissural at CT (3). The handful of perifissural nodules that have proved to be malignant, and therefore not pathologically intrapulmonary lymph nodes, were most often located in the upper lobes and were usually designated as atypical. Even among new nodules found at follow-up CT imaging, those designated as perifissural did not prove to be malignant. Although perifissural nodules at CT are highly likely to be benign, even such benign nodules may show growth.

In a supplement, the authors estimate the frequency of perifissural nodules at CT as a minimum of 24% and maximum of 44% of all noncalcified nodules based on National Lung Screening Trial (NLST) data (3). This is worthwhile information but depends on a number of factors. The definition of what constitutes a perifissural nodule is certainly important and has varied from study to study. An additional influence is the type of CT protocol. The NLST data used for the authors' calculation employed relative thick-section reconstruction (up to 2 mm), which might lead to results that are not representative of current practice where thinner slice imaging is performed. However, the most important factor is likely to be observer variation.

The designation of a nodule as a perifissural nodule is based on interpretation of its size, shape and location, and sharpness. The authors suggest that error can be minimized by taking several actions (3). They advise that all perifissural nodule candidates be inspected in at least two orthogonal planes. This is excellent advice, although depending on whether the thinnest available slices are sent to the picture archiving and communication system (PACS) workstation, which is variable depending on the practice, the value of orthogonal views can be limited. However, this limitation may improve in the future as tools for seamless volumetric analysis of CT images are widely adopted on the PACS reading station and as better machine learning tools become available. The authors suggest excluding round nodules from consideration as perifissural nodules and including only those that are oval, triangular, and polygonal. However, doing so would eliminate as many as one-third of all potential perifissural nodules, which seems a high price to pay for a low rate of malignancy in these nodules that are often quite small. From a practical point of view, depending on image quality and nodule size, it can be difficult to distinguish round nodules from other nodule shapes that are more reliably associated with a perifissural nodule. Perhaps round nodules with both a direct attachment to the pleura or fissure and acute obtuse margins should retain consideration as perifissural nodules. It is clear that further investigation into this important question is required.

The concept of typical versus atypical perifissural nodules as described by de Hoop et al deserves further consideration (4). While there is general consensus that typical perifissural nodules are rarely if ever malignant, at least one study in which a nested cohort was used showed a higher likelihood of malignancy for atypical nodules. In the de Hoop et al classification, atypical perifissural nodules are defined as nodules that are not attached to a visible fissure that meet characteristics for a perifissural nodule or nodules that are attached to a fissure and are convex on one side and round on the other. Assuming atypical nodules do in fact have a higher risk of malignancy, it would be interesting to compare the atypical fissure-attached and nonfissure-attached nodule subgroups to determine whether one has a disproportionately greater risk of malignancy.

The authors describe the uncertain association between perifissural nodules and linear densities that may extend from them. Although frequently visualized in CT-pathologic correlative studies, linear stranding has been less well-documented in dedicated studies of perifissural nodules. The authors note that some of the strands related to intrapulmonary lymph nodes may represent veins but also point out that malignant nodules can have vascular attachments. They reasonably conclude that the value of such linear densities is limited. The authors have nicely organized their work-up preferences regarding perifissural nodules into a decision tree.

The adoption of recommendations for perifissural nodules by nodule guidelines has been variable, in one case because the guidelines have not been updated for several years. The three guidelines that do discuss perifissural nodules differ somewhat in their size criteria. The oldest of the three, the British Thoracic Society (BTS) guideline, recommends no further follow-up in nodules meeting morphologic criteria that are within 1 cm of a fissure or pleural surface and less than 10 mm, without specifically stating whether this reflects maximum or mean diameter (5). In the most recently revised American College of Radiology Lung-RADS version 1.1 guideline, nodules adjacent to fissures but not costal pleural nodules with a maximum diameter of 10 mm are downclassified to category 2, considered benign with a recommendation for routine 1-year follow-up in this screening population (6). Unlike the BTS guideline, there is no constraint regarding a distance limit from the fissure. Finally, the Fleischner guideline for incidental nodules does not specify an upper limit in size, noting only that if the perifissural nodule criteria are met, a follow-up CT is not recommended even if size exceeds 6 mm (7). The inclusion of the perifissural recommendations in these guidelines and the variations in their recommendations underscores the keen interest in this topic and the need for further investigation.

Disclosures of Conflicts of Interest: C.S.W. disclosed no relevant relationships. **G.D.R.** disclosed no relevant relationships.

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