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Commentary: Ground-glass opacity—an unexpected silver lining

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CENTRAL MESSAGE

The presence of ground-glass opacity around a solid tumor predicts a favorable prognosis. In future TNM staging systems, tumors with ground glass opacity should be placed in a distinct category.

In the accompanying article by Hattori and colleagues,[1] the authors further investigate the outcomes of patients registered in JCOG0201. This was a multi-institutional prospective study on the definition of radiologic early lung cancer—cancer without nodal metastasis or vascular or lymphatic invasion.[2] Patients enrolled in this landmark trial had the preoperative radiology findings correlated with the pathologic specimen. Lung carcinoma $\leq$2.0 cm in size and with a consolidation $\leq$25% of the maximum tumor diameter was considered to be radiologic early lung cancer.

Since the publication JCOG0201 in 2011, the 8th edition of the TNM staging system has incorporated the extent of solid component in a partially solid lesion to the TNM schema but not necessarily the features of the ground-glass pathologic correlate. Other investigators have noted the prognostic significance of ground glass on long-term outcomes. Hattori and colleagues[3,4] have previously demonstrated that the mere presence of ground-glass opacity (GGO) as part of an otherwise solid lesion had a favorable prognosis. In fact, the presence of GGO negated the predictive value of maximum tumor size or solid component on long-term survival.[3] This effect was also seen in patients with multiple synchronous tumors.[5] The presence of GGO indicates less risk of invasive tumor[6] and rendered the prognostic impact of visceral pleural invasion moot.[4,7] Patients with pure GGO have almost zero risk of nodal involvement.[8] Radiologic lesions without any GGO component exhibit a more malignant behavior.

The ability to predict the biologic behavior of a tumor based on computed tomography findings has profound implications for choosing treatment. The patients with GGO may be the most likely to benefit from sublobar resection, or looking at it another way, not have to endure overtreatment with more extensive lung resection. This biologically distinct behavior of 2 nodules with solid components but distinguished by the mere presence or absence of GGO has broad implications for the extent of surgical therapy.

While AJCC 8th edition characterizes the T stage according to the extent of solid component in a partially solid lesion, the result of JCOG0201 and other large series suggest that in future schemas, the mere presence or absence of GGO should determine stage, as pure ground-glass lesions and those with partial solid components behave in a distinct manner separate from purely solid lesions, with far less malignant potential. In the accompanying manuscript,[1] the 5-year overall survival was significantly different between the "with GGO" and the "pure Solid" groups (95.1% vs 81.1%). Most interesting was the survival of more than 90% in patients with GGO, regardless of the solid component size. However, for patients without GGO component, survival diminished drastically with increasing size of tumor (c-T1a: 87.5%, c-T1b: 85.9%, c-T1c: 73.7%). The presence of GGO component to a lung cancer may be the silver lining for patient survival.

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THOR

Commentary: A picture really is worth a thousand words

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CENTRAL MESSAGE

Imaging data may contribute to much greater prognostic information than previously appreciated.

Hattori and colleagues[1] present compelling data that demonstrate the beneficial impact of ground-glass characteristics when accompanying solid lung cancers. Strengths of this study include the inclusion of a sizable number of patients, the inclusion of data from several institutions, carefully performed measurements verified by multiple investigators, and the long follow-up necessary to reach reliable and valid conclusions. The results add another dimension to the issue of ground-glass lesions that, while not as common in the West, are increasingly being seen due to the adoption of computed tomography–based lung cancer screening. The main limitation of the data gathered in the authors' work is the lack of positron emission tomography scan information. Notwithstanding this limitation, the utility of these findings over and above pathologic examination of the lesions is the ability to use the data for surgical decision-making instead of simply determining prognosis after the fact.

The utility of the results published here provoke important questions. First, in this era of the creation of large databases, should we not be collecting images along with clinical data to facilitate the conduct of such investigations in the future? Surely, with the logarithmic expansion of data-storage capacity, this should be feasible. Second, it is clear that we have not maximized the use of relatively straightforward measures such as imaging characteristics and pathology information (spread through air spaces [STAS][2] as a prime example), whereas the emphasis on more complex genomic data has

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