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Commentary: Surgery for ground-glass nodules: Free lunch or slippery slope?

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The widespread use of computed tomography of the chest in routine clinical practice and the implementation of computed tomography scanning for lung cancer screening has dramatically increased the detection of ground-glass or subsolid (SSN) pulmonary nodules. In most instances, persistent SSN less than 5 mm in size represent focal proliferative lesions known as atypical alveolar hyperplasia that are considered the earliest progenitor lesions of invasive adenocarcinoma of the lung. Larger SSNs typically harbor adenocarcinoma in situ, minimally invasive adenocarcinoma, and less commonly frankly invasive adenocarcinoma. The precise biological behavior of these lesions is unclear, as many remain unchanged in size and appearance for many years. However, approximately 20% to 40% of these nodules either grow or develop a solid component suggestive of a more invasive malignancy.¹ This uncertainty in clinical behavior commits patients to either frequent, repeat imaging or even occasionally to surgical resection. When surgical resection is contemplated, the extent of parenchymal resection is an important consideration, given the indolent nature of these nodules.

In this issue of the *Journal*, Zhang and colleagues² from Fudan University present what to our knowledge is the largest series comparing lobar with sublobar resection in patients presenting with adenocarcinoma in situ and minimally invasive adenocarcinoma. Impressively, 97% of patients had their resection performed using minimally

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CENTRAL MESSAGE

Wedge resection for small GGOs harboring AIS or MIA is associated with equivalent survival and fewer complications when compared with those after segmentectomy and lobectomy.

invasive techniques despite the fact that the median nodule size was only 9 mm. Complications occurred in 2% of patients, and there were no 30-day deaths among 1644 patients. Five-year recurrence-free and overall survival were 100% and 98.8%, respectively, regardless of the extent of parenchymal resection.

The message is loud and clear; do not do a lobectomy when a sublobar resection (preferably wedge) should suffice. We congratulate the authors on their impressive perioperative results and agree with their principal message. However, it is far from certain that surgical resection is or should be the principal recommendation for patients with SSN, particularly those <1 cm in size. The risk of radiation-induced cancers as a result of frequent repeat imaging cited by the authors as one rationale for resection is based on hypothetical mathematical modelings based on radiation doses extrapolated from atomic bombings. In fact, the American Association of Physicists in Medicine (AAPM) states that “predictions of hypothetical cancer incidence and mortality from the use of diagnostic imaging are highly speculative. The AAPM, and other radiation protection organizations, specifically discourages these predictions of hypothetical harm.”³ Given the large number of patients with SSN seen by the Fudan group, we believe that the authors are uniquely positioned to answer the seminal question about SSN: active surveillance or resection?

A randomized trial allocating patient to immediate versus delayed resection based on predefined criteria will not only provide guidance about the optimal

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strategy but more precisely define the triggers for surgical intervention. Without data from controlled clinical trials, surgical resection with the intention of intercepting cancer progression rather than being a “free lunch” may be a slippery slope toward unnecessary and potentially harmful interventions that betray our “do no harm” axiom.

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Commentary: Computed tomography screening for lung cancer at large in China: Early cure or definitive overtreatment?

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CENTRAL MESSAGE

Lung cancer screening without consideration for pretest probability leads to surgeries of unclear benefit.

In this issue of the *Journal*, Zhang and colleagues¹ report the results of surgical resection of incidentally found pure ground-glass opacities (GGO; 76.3%) or part solid-GGO (22.6%). In this single-center study of predominantly female, middle-aged, never-smokers, patients underwent computed tomography (CT) scans for arbitrary reasons. Almost none of these patients would qualify for lung cancer screening based on current guidelines.² CT imaging was completed as part of a regular health examination due in part to the low cost and wide availability of CT scans. Now faced with a lesion found on a CT scan, these patients uniformly underwent surgery. Patients in this study did remarkably well with wedge resection. None had nodal spread of disease, and 5-year recurrence-free survival was 100%. Even in those patients found to have invasive cancer on final pathological evaluation, lack of a lobectomy did not

worsen the recurrence rate. Are the authors documenting a strategy of curing lung cancer early, or is this an exercise in overtreatment?

Previously reported results from JCOG0201 show significantly different 5-year overall survival between patients with any GGO and those with “pure solid” lesions.³ With the presence of GGO, survival was >90%, regardless of solid (invasive cancer) component size.³ In the study cohort of Zhang and colleagues (98.9% with GGO), efforts to classify tumor invasion on frozen sections might have been unnecessary, given the positive prognostic advantages associated with GGO. As shown in JCOG0201, and substantiated in the current article, nodal spread is rare in these cases, and aggressive surgery is not required.³

The authors note that one motivation to pursue surgery is to avoid unnecessary CT scans. This poses a conundrum, as these patients still required CT scans for long-term follow-up even when surgical resection was completed. Although

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