AABIP JOURNAL CLUB

Small Shadows, Big Decisions: Surgery or Surveillance?

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The clinical question

Does upfront surgical intervention lead to higher survival than watchful waiting in patients with pulmonary subsolid nodules (SSNs) with a diameter of ≤2 cm and consolidation to tumor ratio (CTR) of ≤ 0.25?

Take Home Message

(AABIP conclusion for the manuscript)
In small, low-CTR subsolid nodules, watchful waiting is as safe as surgery and helps avoid overtreatment without compromising outcomes.

Background

CT-based screening has led to increased detection of SSNs, which vary widely in prognosis. While larger part-solid nodules behave aggressively and generally warrant surgery, small pure ground-glass nodules and low-CTR SSNs often follow a more indolent course. As such, many guidelines recommend surveillance in these cases; however, many patients undergo surgery due to diagnostic uncertainty and anxiety, raising concern for overtreatment and possibly loss of function without clear benefit.

Therefore, determining whether surgery improves outcomes for small, radiographically noninvasive SSNs is extremely relevant to prevent overtreatment or excessive follow-up.

Current guidelines recommend varying management strategies for pure ground-glass nodules (pGGNs) and for part-solid nodules with solid components <5–6 mm, reflecting their generally indolent course and favorable prognosis (2–7). Evidence from large prospective studies support this approach: Kakinuma et al. demonstrated that many SSNs, particularly small pGGNs, remain stable for years without progression (8), while Sawada et al. reported excellent long-term outcomes for patients with ground-glass opacities managed with careful surveillance (9). Despite this, existing guidelines remain inconsistent. The American College of Chest Physicians (CHEST) and the British Thoracic Society recommend follow-up for SSNs >5 mm, with the latter endorsing resection if growth or morphologic change occurs (3,4). In Asia, CHEST consensus guidelines recommend surveillance for SSNs of any size (2). The National Comprehensive Cancer Network (NCCN) advises biopsy or surgery for pGGNs ≥20 mm with growth and recommends PET/CT or tissue sampling for part-solid nodules with solid components >6 mm or new/growing components >4–6 mm (4,6). The Japanese Society for CT Screening is more aggressive, suggesting biopsy or surgery even for smaller part-solid nodules (solid components ≤5 mm), reflecting the higher malignancy risk observed in East Asian populations (6).

The Japan Clinical Oncology Group (JCOG) and the Western Japan Oncology (WJO) group have conducted multiple prospective studies (JCOG 0804, 0802, 1211; WJOG 4506L/4507L) confirming that SSNs ≤2 cm and with CTR ≤ 0.25 are rarely invasive, with excellent long-term survival after limited, parenchyma preserving resection. These findings begged the question of whether surgery is even necessary in all cases, and the ongoing JCOG 1906 will prospectively explore observation as a strategy, however the results have not yet been published. This study aims to build on this body of evidence by retrospectively comparing observation and surgery in patients with an SSN of ≤2 cm in diameter and a CTR ≤ 0.25.

Study design

Type of trial: Retrospective, observational cohort study

Randomization, blinding, controls: No randomization or blinding (retrospective study). Controls were patients who underwent observation (watchful waiting), compared against those who had upfront surgery.

N: 1,676 patients (1,122 in the surgery group, 554 in the observation group)
Study groups:
Surgery group: Patients who underwent resection.
Observation group: Patients who were managed with watchful waiting.

Settings:
Single-country, multi-center study in China (large retrospective database, tertiary hospital settings)

Enrollment:
Patients with SSNs (thin-section CT confirmed)
Treatment period:
Between Feb 2005 – Dec 2018.

Follow up:
Patients were followed up through December 2023, with a median follow-up of about 5 years, with some patients followed up to 10 years.

Primary outcome:
Event-Free Survival (EFS), defined as absence of all-cause death, lung cancer recurrence, or metastasis.

Population

Inclusion criteria: Patients with SSNs ≤2 cm in diameter and consolidation-to-tumor ratio (CTR) ≤0.25 were included
Exclusion criteria:
Patient with a follow-up period of < 5 years
Nodules that were solid-type lung cancers (not SSNs).
Patients with other malignant tumors.
Patients who had received chemotherapy.
Cases with incomplete imaging or clinical data.
Insufficient follow-up (< 1 year or inadequate CT follow-up).

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Baseline Characteristics:

Age
- Surgery: 57 (51–63)
- Observation: 54 (46–60)

Sex
- Surgery: 26% male, 74% female
- Observation: 32% male, 68% female

Smoking history
- Surgery: 84% never, 8% previous, 8% current
- Observation: 74% never, 3% previous, 7% current, 17% NA

Tumor markers (abnormal values)
- **CEA (carcinoembryonic antigen)**
  - Surgery: 130 / 1,065 (12.2%)
  - Observation: 19 / 270 (7.0%)
- **NSE (neuron-specific enolase)**
  - Surgery: 379 / 1,067 (35.5%)
  - Observation: 39 / 243 (16.0%)
- **CYFRA 21-1**
  - Surgery: 383 / 1,067 (35.9%)
  - Observation: 54 / 241 (22.4%)
- **ProGRP (pro-gastrin-releasing peptide)**
  - Surgery: 92 / 1,048 (8.8%)
  - Observation: 29 / 242 (12.0%)
- **SCCA (squamous cell carcinoma antigen)**
  - Surgery: 171 / 1,065 (16.1%)
  - Observation: 26 / 245 (10.6%)

Lung lobe location
- Right upper lobe
  - Surgery: 429 (38.2%)
  - Observation: 236 (42.6%)
- **Right middle lobe**
  - Surgery: 70 (6.2%)
  - Observation: 26 (4.7%)
- **Right lower lobe**
  - Surgery: 171 (15.2%)
  - Observation: 69 (12.5%)
- **Left upper lobe**
  - Surgery: 298 (26.6%)
  - Observation: 162 (29.2%)
- **Left lower lobe**
  - Surgery: 154 (13.7%)
  - Observation: 61 (11.0%)
- **Peripheral location**
  - Surgery: 856 (76.3%)
  - Observation: 419 (75.6%)

SSN type
- Surgery: 35% pure GGN, 65% part-solid
- Observation: 85% pure GGN, 15% part-solid

Morphologic features
- **Irregular shape**
  - Surgery: 461 (41.1%)
  - Observation: 37 (6.7%)
- **Ill-defined margin**
  - Surgery: 951 (84.8%)
  - Observation: 314 (56.7%)
- **Lobulation**
  - Surgery: 952 (84.9%)
  - Observation: 222 (40.1%)
- **Spiculation**
  - Surgery: 301 (26.8%)
  - Observation: 3 (0.5%)
- **Cystic change**
  - Surgery: 517 (46.1%)
  - Observation: 54 (9.8%)
- **Pleural tag**
  - Surgery: 526 (46.9%)
  - Observation: 55 (10.0%)
- **Vascular change**
  - Surgery: 362 (32.3%)
  - Observation: 37 (6.7%)

CT attenuation (HU)
- Surgery: −431 (−598 to −229)
- Observation: −622 (−700 to −522)

Mean nodule diameter (mm)
- Surgery: 14.3 (9.9–19.9)
- Observation: 7.3 (6.1–9.1)

Solid component size (mm)
- Surgery: 1.3 (0–6.8)
- Observation: 0 (0–0)

Consolidation-to-tumor ratio (CTR)
- Surgery: 0.08 (0–0.34)
- Observation: 0 (0–0)

Outcomes

Primary outcomes:

- Event-Free Survival (EFS), defined as absence of all-cause death, lung cancer recurrence, or metastasis.

Secondary outcomes:

- EFS in various subgroups.
  - Age ≤62 vs > 62
  - Sex male vs female
  - CEA normal vs higher than normal
  - RLL vs non-RLL
  - Deep lobulated vs non-deep lobulated
  - CTR ≤0.22 vs CTR > 0.22
  - CT HFU value ≤-346.5 vs >. -346.5
  - Mean diameter ≤13.6 vs > 13.6 mm

Adverse events:

- Adverse events related to surgery were specifically not reported.

Commentary

(AABIP criticism)

This study's chief strengths are its scale, duration, and outcome choice: a large cohort of >1,600 patients, long follow-up (mean ~70 months), and a clinically meaningful primary endpoint (event-free survival) together provide robust evidence on the natural history and management of subsolid nodules. That said, important limitations temper interpretation. Selection bias is likely as patients triaged to surgery tended to have larger, denser nodules with more aggressive morphology, which could worsen their prognosis relative to those observed. Generalizability is also constrained: this is a single-country, multicenter cohort from China, where epidemiology, screening practices, and surgical thresholds may differ from other settings. Excluding patients with prior malignancies or chemotherapy further narrows applicability to real-world, diverse populations. Finally, the research question is framed as a binary "surgery vs observation," omitting relevant non-surgical options such as SBRT or ablation that many clinicians would consider for select patients.

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Suggested Reading

(References in Vancouver style)

1. Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, et al. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5 Suppl):e93S-e120S.
2. Baldwin DR, Callister MEJ, Akram AR, Barnard S, Cane P, Draffan J, et al. British Thoracic Society guidelines for the investigation and management of pulmonary nodules. *Thorax*. 2015;70(Suppl 2):ii1-ii54.
3. MacMahon H, Naidich DP, Goo JM, Lee KS, Leung ANC, Mayo JR, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: From the Fleischner Society 2017. *Radiology*. 2017;284(1):228-243. doi:10.1148/radiol.2017161659.
4. The 2023 American Association for Thoracic Surgery (AATS) Expert Consensus Document: Management of subsolid lung nodules
Chen, Haiquan et al. The Journal of Thoracic and Cardiovascular Surgery, Volume 168, Issue 3, 631 - 647.e11

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(Vancouver style)

1. Li F, Qi L, Xia C, Liu J, Chen J, Cui S, et al. Pulmonary subsolid nodules: upfront surgery or watchful waiting? *Chest*. 2025 Jun;167(6):1764-1777. doi:10.1016/j.chest.2024.12.028. Epub 2025.

2. Bai C, Choi C-M, Chu C-M, Anantham D, Chung-Man Ho J, Khan AZ, et al. Evaluation of pulmonary nodules: clinical practice consensus guidelines for Asia. Chest. 2016;150(4):877-93.
3. Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP, et al. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 Suppl):e93S-e120S.
4. Baldwin DR, Callister MEJ, Akram AR, Barnard S, Cane P, Draffan J, et al. British Thoracic Society guidelines for the investigation and management of pulmonary nodules. Thorax. 2015;70(Suppl 2):ii1-ii54.
5. Wood DE, Kazerooni EA, Aberle D, Berman A, Brown LM, Eapen GA, et al. NCCN guidelines insights: lung cancer screening, version 1.2022. J Natl Compr Canc Netw. 2022;20(7):754-64.
6. Ashizawa K, Maruyama Y, Kobayashi T, Kondo T, Nakagawa T, Hatakeyama M, et al; Lung Cancer Diagnostic Criteria Subcommittee of the Japanese Society of CT Screening. Guidelines for the management of pulmonary nodules detected by low-dose CT lung cancer screening, 6th edition. Jpn J Radiol. 2025;43(3):333-46. doi:10.1007/s11604-024-01695-0.
7. American College of Radiology. Lung CT screening reporting & data system (Lung-RADS®) version 2022. Reston (VA): American College of Radiology; 2022.
8. Kakinuma R, Noguchi M, Ashizawa K, Aoki T, Yamamoto T, Kuriyama K, et al. Natural history of pulmonary subsolid nodules: a prospective multicenter study. J Thorac Oncol. 2016;11(7):1012-28.
9. Sawada S, Yamashita N, Sugimoto R, Ueno T, Yamashita M, Yamanaka T, et al. Long-term outcomes of patients with ground-glass opacities detected using CT scanning. Chest. 2017;151(2):308-15.

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