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Diagnostic yield of CT-guided needle biopsy for subsolid pulmonary nodules: Correlation with postoperative pathology

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Abstract:

BACKGROUND AND AIM: Subsolid pulmonary nodules (SSNs), encompassing pure ground-glass nodules (pGGNs) and part-solid nodules (PSNs), may represent a spectrum of pulmonary adenocarcinoma. Accurate preoperative diagnosis is essential to guide treatment decisions and avoid unnecessary surgeries. This study aimed to evaluate the diagnostic performance of computed tomography-guided transthoracic core needle biopsy (CT-TNB) in SSNs, with correlation to final surgical pathology.

METHODS: This retrospective cohort study included 41 SSNs from 40 patients who underwent CT-TNB followed by surgical resection between 2012 and 2022. Radiological and histopathological characteristics were evaluated. Descriptive statistics and diagnostic performance metrics were calculated using Python.

RESULTS: Of the 41 SSNs, 13 (31.7%) were pGGNs and 28 (68.3%) were PSNs. CT-TNB diagnosed 36 nodules (87.8%) as adenocarcinoma, four (9.8%) as atypical epithelial cells, and one (2.4%) as benign pathology. Final pathology revealed 28 (68.3%) invasive adenocarcinomas (IA), 10 (24.4%) minimally invasive adenocarcinomas (MIA), one adenocarcinoma in situ, one atypical adenomatous hyperplasia, and one breast cancer metastasis. CT-TNB demonstrated 97.6% sensitivity and 100% positive predictive value (PPV) for malignancy. For invasive carcinoma (MIA or IA), sensitivity was 94.7%, with 100% specificity and PPV.

CONCLUSIONS: CT-TNB demonstrates high diagnostic accuracy for SSNs and correlates reliably with postoperative pathology. It remains a valuable tool for preoperative assessment when performed by experienced teams using core needle techniques.

Keywords:

Adenocarcinoma, lung, needle biopsy, subsolid nodules

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Introduction

Subsolid pulmonary nodules (SSNs) are a distinct category of lung lesions characterized by a ground-glass opacity component on computed tomography (CT), allowing visualization of bronchial and vascular structures. Based on radiological appearance, they are classified as pure ground-glass nodules (pGGNs) or part-solid nodules (PSNs). Although less prevalent than solid nodules, SSNs carry a higher probability of malignancy and often represent a spectrum of pulmonary adenocarcinoma, including atypical adenomatous hyperplasia (AAH), adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), and invasive adenocarcinoma (IA).[1,2]

Management of SSNs is challenging due to their variable growth patterns and overlapping benign and malignant features. While some resolve spontaneously, others progress slowly and may develop invasive components, particularly in PSNs.[3,4] Risk factors for malignancy include larger nodule size, a solid component, spiculated margins, and pleural retraction.[1]

Given their heterogeneity, the management of SSNs poses significant diagnostic and therapeutic challenges. Accurate preoperative diagnosis is critical to guide treatment decisions and avoid unnecessary surgical resections.[5] Computed tomography-guided transthoracic needle biopsy (CT-TNB) is a minimally invasive procedure widely used for tissue diagnosis. Although it has demonstrated high diagnostic accuracy and safety in the evaluation of pulmonary nodules, concerns persist regarding its diagnostic yield in SSNs, particularly in smaller or predominantly ground-glass lesions.[6,7]

The present study aimed to evaluate the diagnostic performance of CT-TNB in patients with subsolid pulmonary nodules who subsequently underwent surgical resection.

Materials and Methods

Study design and population

This retrospective cohort study was derived from a medical specialty thesis conducted at our institution and included adult patients who underwent surgical resection for SSNs between 2012 and 2022. Eligible patients were identified through a systematic review of surgical and histopathology records (n=4497). Cases involving non-parenchymal surgeries, resection of masses larger than 3 cm, purely solid nodules, non-oncological procedures, or incomplete data were excluded. Among the 86 patients with a total of 92 resected SSNs identified in the thesis cohort, a subset of 41 nodules that had undergone preoperative CT-TNB was selected for inclusion in the present study [Fig. 1]. In cases where multiple nodules were excised from the same patient, each nodule was evaluated independently.

Data collection

Demographic and clinical data, including age, sex, smoking history, comorbidities, and family history of malignancy, were obtained from the hospital information management system. Radiological assessments were based on the most recent preoperative thoracic CT scans, with additional imaging studies reviewed when available. Nodule characteristics, including location, size, shape, borders, internal structure, and relationship to adjacent bronchial, vascular, and pleural structures, were evaluated. All CT-TNBs were performed using a core needle. Data on diagnostic outcomes and post-procedural complications were recorded. Patient epicrises and post-procedural chest radiographs were reviewed to assess for complications. Histopathological diagnoses were determined by an experienced pulmonary pathologist blinded to radiological findings. Classification of lesions was performed according to the 2021 World Health Organization Classification of Lung Tumors.[8]

TNB technique

All patients underwent a clinical evaluation, including medical history and hematological testing. Eligibility required an International Normalized Ratio (INR) <1.5 and a platelet count >50×10□/L, confirmed within five days. Antiplatelet and anticoagulant agents were discontinued per guidelines: nonsteroidal anti-inflammatory drugs (NSAIDs) and clopidogrel five days, heparin six hours, rivaroxaban one day, and dabigatran/edoxaban three days before the procedure. Biopsies were performed by four board-certified interventional radiologists (8–20 years of experience) under CT guidance (Siemens Somatom) with an 18- or 20-gauge coaxial needle. Planning used non-contrast chest CT reconstructed at 3-mm intervals, following standardized protocols to optimize trajectory and minimize risk. Pulmonary vessels, fissures, and effusion-associated targets were avoided. Patient positioning was individualized based on operator judgment and anatomical considerations.

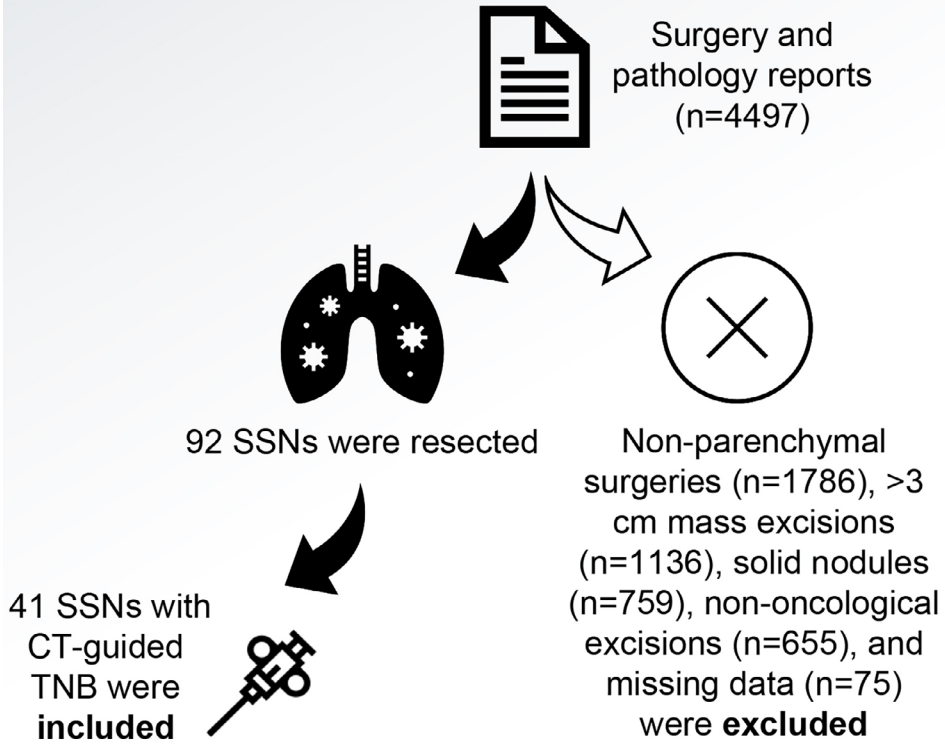

Figure 1: Flow chart of the study
SSNs: Subsolid pulmonary nodules, TNB: Transthoracic needle biopsy

Statistical analysis

All statistical analyses were conducted using Python version 3.13 (Python Software Foundation, Wilmington, DE, USA). Descriptive statistics were applied to summarize demographic and radiological features. Continuous variables were reported as mean±standard deviation (SD) or median with range, and categorical variables as counts and percentages. Diagnostic accuracy metrics, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were calculated using the scikit-learn library. To provide a measure of precision for these estimates, particularly given the study's sample size, 95% confidence intervals (CIs) were calculated for each metric using the Clopper-Pearson exact method. Data management and summary statistics were performed with pandas and numpy, while confusion matrices were created using matplotlib and seaborn.

Ethical considerations

This study is derived from the medical specialty thesis of the first author. It was approved by Hacettepe University Non-interventional Clinical Research Ethics Committee (Approval Number: 2023/03-01, Date: 21.02.2023) and conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study.

Artificial intelligence–based tools (ChatGPT, OpenAI, San Francisco, CA, USA) were used exclusively to improve the clarity, fluency, and grammar of the manuscript text. All content generated with artificial intelligence (AI) assistance was critically reviewed, revised, and approved by the authors, who take full responsibility for the final version.

Results

The study included 40 patients (23 males, 17 females) with a mean age of 61.5±9.6 years (range: 27–75). One patient underwent CT-TNB for two different nodules at separate time points. All SSNs included in the study were incidentally detected. Baseline characteristics of the patients are detailed in Table 1.

Of the 41 nodules evaluated with CT-TNB, 13 (31.7%) were classified as pGGNs and 28 (68.3%) as PSNs. The most frequent location was the right upper lobe (39.0%), followed by the left upper lobe (31.7%), left lower lobe (17.1%), right lower lobe (9.8%), and right middle lobe (2.4%).

Table 1: Baseline characteristics of the patients

Characteristics	n	%
Total number of patients	40	
Male	23	57.5
Female	17	41.5
Age at diagnosis (mean±SD) (years)	61.5±9.6	
Smoking status		
Active smoker	10	25.0
Former smoker	20	50.0
Never smoker	10	25.0
Comorbidities		
Hypertension	21	52.5
Malignancy	18	45.0
Lung cancer	2	5.0
Other cancers	16	40.0
Diabetes mellitus	15	37.5
Coronary artery disease	6	15.0
COPD	4	10.0
Others	25	62.5
Family history of cancer	12	30.0

SD: Standard deviation, COPD: Chronic obstructive pulmonary disease

Table 2: Radiological characteristics of subsolid nodules

Characteristics	n	%
Total number of nodules	41	
SSN subtype		
pGGN	13	31.7
PSN	28	68.3
Longest diameter, median (range), mm	17 (10–30)	
Lesion-pleura distance, median (range), mm	12 (0–55)	
Location		
Right upper lobe	16	39.0
Right middle lobe	1	2.4
Right lower lobe	4	9.8
Left upper lobe	13	31.7
Left lower lobe	7	17.1
Border		
Indistinct	36	87.8
Spiculated	5	12.2
Shape		
Irregular	28	68.3
Oval	7	17.1
Round	5	12.2
Lobulated	1	2.4
Internal structure		
Air bronchogram	17	41.5
Air bubble or cyst	7	17.1
Vascular sign	28	68.3
Bronchial sign	15	36.6
Pleural contact	16	39.0
Pleural retraction	23	56.1

SSN: Subsolid nodule, pGGN: Pure ground-glass nodule, PSN: Part-solid nodule

The median longest diameter of the nodules was 17 mm (range: 10–30 mm). Detailed radiological characteristics are presented in Table 2. A total of 22 nodules (53.7%) were biopsied immediately after detection, whereas 19 nodules (46.3%) were biopsied after a follow-up period of at least three months. Among those followed radiologically with serial CT, the median follow-up duration was 27 months (range: 4–105). The 19 nodules under surveillance exhibited diverse progression patterns: 16 showed a size increase of >2 mm/year, nine demonstrated increased density, five showed growth in the solid component, and three developed a new solid component [Fig. 2]. Among those with diameter progression, the median volume doubling time was 460 days (range: 168–5918). The surgical procedure was lobectomy in 36 nodules (87.8%), wedge resection in four (9.8%), and segmentectomy in one (2.4%).

On CT-TNB, 36 nodules (87.8%) were diagnosed as adenocarcinoma, four (9.8%) as atypical epithelial cells, and one (2.4%) as benign pathology. Postoperative pathological diagnoses included 28 (68.3%) IA, 10 (24.4%) MIA, one (2.4%) metastasis, one (2.4%) AIS, and one (2.4%) AAH. A confusion matrix illustrating the correlation between preoperative biopsy and postoperative pathological diagnoses is shown in Figure 3. The nodule that yielded a benign result on preoperative biopsy was a PSN located in the right lower lobe, with a maximum diameter of 10 mm and a solid component of 4 mm, exhibiting spiculated and irregular margins. It was ultimately diagnosed as IA after surgical resection. The four nodules interpreted as atypical epithelial cells on CT-TNB were later diagnosed as AAH, AIS, IA, and breast cancer metastasis, respectively. Among the 36 nodules diagnosed as adenocarcinoma on CT-TNB, 10 were confirmed as MIA and 26 as IA.

The sensitivity and PPV of CT-TNB for diagnosing malignancy were 97.6% (95% CI: 87.1–99.9) and 100% (95% CI: 91.2–NA), respectively. Specificity and NPV for malignancy could not be calculated, as the surgically resected cohort contained no confirmed benign lesions. The sensitivity, specificity, PPV, and NPV of CT-TNB for identifying invasive carcinoma (MIA or IA) were 94.7% (95% CI: 82.3–99.4), 100% (95% CI: 29.2–NA), 100% (95% CI: 90.3–NA), and 60% (95% CI: 14.7–94.7), respectively.

No complications were observed in 40 (97.6%) of the biopsy procedures. However, one 52-year-old male patient with comorbidities that increased the risk of hemorrhagic complications, including multiple myeloma, chronic kidney disease, hypertension, and coronary artery disease, died due to biopsy-related hemorrhage.

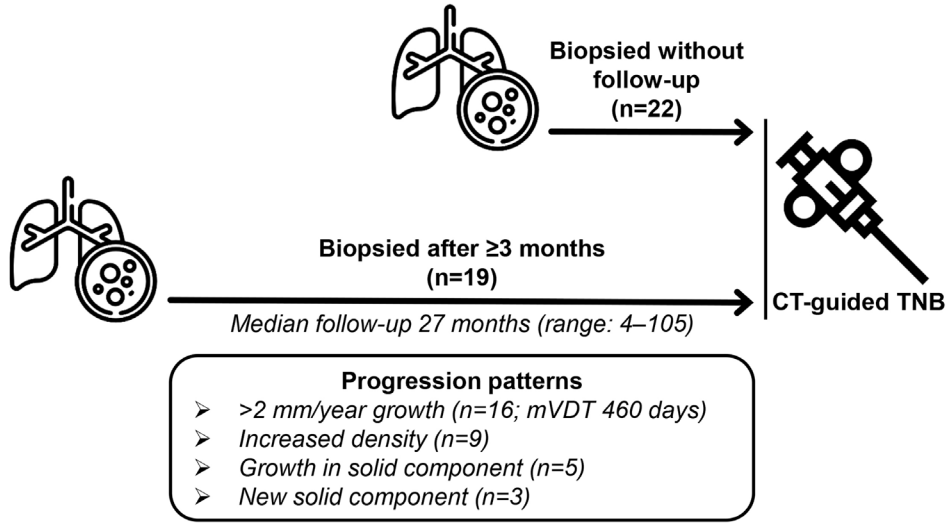

Figure 2: Timeline and progression patterns of subsolid nodules undergoing computed tomography-guided biopsy
TNB: Transthoracic needle biopsy, mVDT: Median volume doubling time

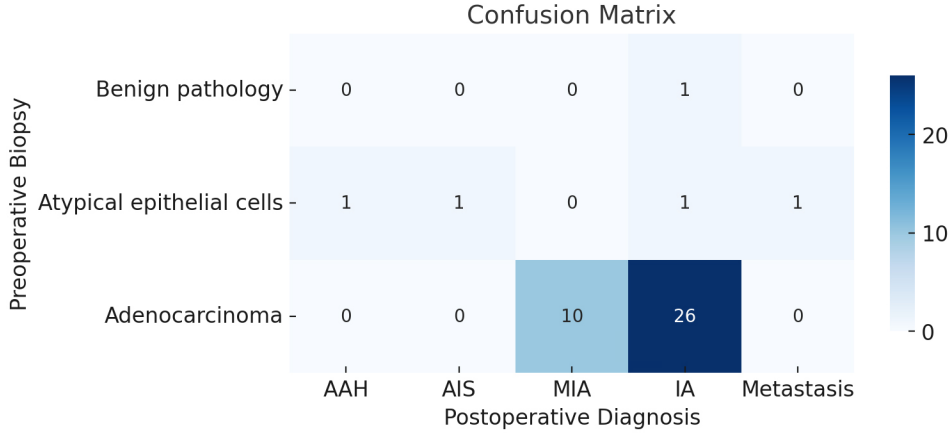

Figure 3: Confusion matrix showing the correlation between preoperative biopsy results and postoperative pathological diagnoses of subsolid nodules
AAH: Atypical adenomatous hyperplasia, AIS: Adenocarcinoma in situ, MIA: Minimally invasive adenocarcinoma, IA: Invasive adenocarcinoma

Discussion

This study evaluated the diagnostic performance of CT-TNB in SSNs, with correlation to final surgical pathology. Our findings demonstrate that CT-TNB provides high diagnostic accuracy in this population, with a sensitivity of 97.6% and a PPV of 100% for malignancy. For predicting invasive adenocarcinoma (IA or MIA), the sensitivity was 94.7%, and the specificity and PPV remained at 100%.

Our results are consistent with the existing literature. The robust performance of CT-TNB for SSNs, including both PSNs and GGNs, has been increasingly recognized. Kim et al.[6] performed a systematic review and meta-analysis involving 744 SSNs and demonstrated pooled sensitivity and specificity of 90% and 99%, respectively, for percutaneous TNB. Comparable accuracy across solid and subsolid nodules has also been highlighted by Yun et al.,[9] who reported similar sensitivity, specificity, and predictive values for both lesion types, suggesting that the presence of ground-glass components does not inherently compromise diagnostic accuracy. Another study using propensity score matching showed that ground-glass and solid nodules yield similar diagnostic and safety outcomes in CT-TNB, further reinforcing our findings.[10]

The slightly higher sensitivity in our study may be attributable to the exclusive use of core needle biopsies and a relatively experienced interventional team, consistent with Kim et al.'s[6] observation that core needle biopsies

trend toward higher diagnostic yield than fine-needle aspiration. This preference for core biopsy is further supported by a study on nodules smaller than 1 cm, which found that using aspiration alone was a significant independent risk factor for diagnostic failure.[11]

Kiranantawat et al.[7] reported sensitivities ranging from 88.6% to 95.6%, with 100% specificity in SSNs, regardless of nodule size or ground-glass opacity proportion. Their findings support our observation that CT-TNB is reliable even for small or predominantly ground-glass lesions. High diagnostic accuracy for small lesions (≤20 mm) has also been reported by Li et al.,[12] who achieved an overall accuracy of 93.5% and a sensitivity of 90.4%, and by Choi et al.[11] for nodules <1 cm, with a sensitivity of 93.1% and accuracy of 95.0%. However, it is worth noting that Huang et al.[13] found that diagnostic accuracy was significantly lower for small nodules (≤15 mm) at 83.7% compared to 96.8% for larger nodules (>15 mm), suggesting that lesion size can still pose a challenge.

Tsai et al.[14] explored the ability of CT-guided core biopsy to predict predominant histologic subtypes in adenocarcinoma and reported a 64% concordance rate with surgical pathology. Our findings complement this by demonstrating a strong correlation between CT-TNB and postoperative histology in both MIA and IA cases. However, in four cases initially diagnosed as atypical epithelial cells, the final pathology ranged from AAH to metastasis, indicating limitations in sampling accuracy and the need for careful interpretation of atypical findings. Such indeterminate results are not uncommon; Borelli et al.[15] reported a nondiagnostic biopsy rate of 18% in their cohort, with subsequent analysis revealing that 66.7% of these nondiagnostic cases were ultimately malignant. They also identified lesions ≤20 mm and a final benign diagnosis as risk factors for nondiagnostic results, which underscores the complexities of biopsying smaller SSNs or those with subtle malignant foci. The challenge of accurately targeting the solid component of PSNs during biopsy has been highlighted by Halpenny et al.,[16] who found that inadequate targeting may lead to underestimation of invasiveness. In our study, the single false-negative case involved a PSN with spiculated and irregular margins that yielded a benign biopsy result but was later confirmed as IA. This reinforces the importance of precise radiologic-pathologic correlation and targeting strategies during CT-TNB.

Complication rates in our cohort were lower than those reported in several studies. A large meta-analysis reported a pooled overall complication rate for CT-guided core biopsy of 38.8% and a major complication rate of 5.7%.[17] Overall complication rates were also significantly higher for core biopsy compared to fine-needle aspiration, highlighting a trade-off between increased diagnostic yield and procedural risk associated with core biopsies. Lee et al.[18] found that SSNs were associated with a significantly higher incidence of pulmonary hemorrhage compared to solid nodules (29.7% vs. 8.9%, $p<0.001$). This observation is supported by a study that reported comparable diagnostic accuracy between lesion types; however, the incidence of hemorrhage on post-biopsy follow-up CT was significantly higher in part-solid lesions compared to solid lesions, despite no significant difference in rates of symptomatic major hemorrhage or pneumothorax.[9] Although only one patient in our series experienced a major complication, the outcome was fatal, underscoring the need for careful preprocedural evaluation, particularly in patients with comorbidities. Azour et al.[19] emphasized that lesion- and patient-related variables significantly impact both diagnostic yield and safety outcomes and advocated for tailored procedural planning. Several studies have identified specific risk factors for complications: Huang et al.[13] identified longer needle path length from pleura to lesion, lower lobe location, and obstructive lung function as risk factors for pneumothorax, while longer needle path, smaller lesions, and non-pleural contact were associated with pulmonary hemorrhage. Li et al.[12] found that for small (≤20 mm) lesions, a lesion-pleural distance ≥21 mm and a needle-pleural angle ≥51° were significant risk factors for pneumothorax, with the former also being a risk for bleeding. Furthermore, An et al.[10] noted an increased incidence of significant pneumothorax with small lesion size, deep lesion location, and traversing an interlobar fissure, and interestingly reported that post-biopsy hemorrhage may be a protective factor for pneumothorax. In contrast to these single-center findings, the meta-regression did not identify significant risk factors for complications specifically for core biopsy procedures, which may reflect heterogeneity across pooled studies or limitations in the granularity of data available for meta-regression.[17]

A primary limitation of our study is the selection bias inherent in its design. By exclusively including patients who underwent both CT-TNB and subsequent surgical resection, our cohort is enriched with nodules that were highly

suspicious for malignancy, leading to a high prevalence of cancer in the final pathology. This design was chosen to ensure a definitive histopathological gold standard for every case but prevents the inclusion of true-negative cases (i.e., patients with a benign biopsy who were correctly managed with surveillance). Consequently, our calculated specificity and PPV of 100% are likely inflated and do not reflect the performance of CT-TNB in a broader, unselected population of patients with SSNs. Furthermore, this makes a meaningful calculation of the negative predictive value impossible. A study incorporating a control group of biopsied SSNs with benign final diagnoses confirmed by long-term follow-up would be necessary to establish the true specificity and NPV of the procedure. Other limitations of our study include its retrospective design and single-center setting, which may limit generalizability. Additionally, the small sample size limited our statistical power and, importantly, precluded any meaningful subgroup analyses, such as comparing the diagnostic performance of CT-TNB between pGGNs and PSNs or evaluating the impact of lesion size on accuracy. Future studies should focus on assessing how variables such as lesion-pleural distance, needle trajectory, and consolidation ratio within SSNs affect diagnostic accuracy and complication profiles. Moreover, integration of radiomics or AI-based biopsy guidance systems could enhance lesion targeting and reduce false-negative rates, especially in complex PSNs.

Conclusion

Computed tomography–guided transthoracic needle biopsy provides high diagnostic accuracy in the evaluation of SSNs, with strong correlation to final surgical pathology. While the procedure is generally safe, clinicians should remain vigilant for hemorrhagic complications, especially in patients with multiple comorbidities. Our findings reinforce the value of CT-TNB in preoperative planning, particularly when performed by experienced teams using core needle techniques, and contribute to the growing body of evidence supporting its role in the management of SSNs.

Ethics Committee Approval

The study was approved by the Hacettepe University Non-interventional Clinical Research Ethics Committee (No: 2023/03-01, Date: 21/02/2023).

Informed Consent

Informed consent was waived due to the retrospective nature of the study.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Funding

The authors declared that this study received no financial support.

Use of AI for Writing Assistance

Artificial intelligence–based tools (ChatGPT, OpenAI) were used solely to enhance the clarity, fluency, and grammar of the manuscript. The authors critically reviewed and edited all AI-assisted text, accepting full responsibility for the final content.

Author Contributions

Concept – D.K.; Design – U.I., R.I., D.K.; Supervision – D.K.; Resource – U.I., R.I., D.K.; Materials – U.I., O.K., G.D.; Data Collection and/or Processing - U.I., R.I., G.D.; Analysis and/or Interpretation - U.I., R.I., T.T.Ç.; Literature Review – R.I., U.K., E.Ü.; Writing – R.I., O.K., T.T.Ç.; Critical Review – T.T.Ç., D.K.

Peer-review

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