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Introduction

Despite remarkable progress in diagnosis and treatment over the last two decades, lung cancer remains the leading cause of cancer-related death worldwide [1,2]. According to the most recent global cancer statistics, lung cancer accounts for approximately 2.5 million new cases and remains responsible for nearly one in five cancer-related deaths worldwide [1]. Patient survival is closely associated with the stage at diagnosis; therefore, identifying tumors at a surgically curable stage remains one of the principal objectives of thoracic oncology. Patients with completely resected stage I non-small cell lung cancer (NSCLC) may achieve 5-year survival rates exceeding 80%, whereas survival remains poor in patients with advanced-stage disease [3,4]. Consequently, early detection remains the most effective strategy for reducing lung cancer-related mortality.

The introduction of low-dose computed tomography (LDCT) has fundamentally changed the strategy for early lung cancer detection. The National Lung Screening Trial (NLST) first demonstrated a 20% reduction in lung cancer-specific mortality among high-risk

individuals undergoing annual LDCT screening compared with chest radiography [5]. Subsequently, the Dutch–Belgian NELSON trial confirmed an even greater reduction in lung cancer mortality through volume-based CT screening, providing robust evidence supporting implementation of organized screening programs [6]. These findings have formed the basis of current recommendations issued by the NCCN, USPSTF, CHEST and ERS [7-10]. Furthermore, the NCCN Guidelines for Non-Small Cell Lung Cancer recommend that incidentally detected pulmonary nodules should undergo systematic risk assessment based on clinical characteristics, smoking history, previous malignancy, family history, radiological features, and multidisciplinary evaluation before definitive management is considered, highlighting the importance of standardized follow-up algorithms in daily clinical practice.

Although implementation of low-dose CT screening has significantly improved early lung cancer detection, most pulmonary nodules encountered in routine clinical practice are still detected incidentally during CT examinations performed for unrelated indications. Consequently, clinicians frequently face the challenge of distinguishing transient inflammatory abnormalities from early-stage lung cancer while avoiding unnecessary invasive procedures.

Nevertheless, most pulmonary nodules encountered in routine clinical practice are detected incidentally rather than through organized screening programs. The increasing use of thoracic CT for a variety of clinical indications has resulted in a growing number of patients referred for evaluation of indeterminate pulmonary lesions. Appropriate management of these lesions has become increasingly important because unnecessary invasive procedures should be avoided without delaying diagnosis of potentially curable lung cancer [11,12]. Although the majority of these lesions are benign, distinguishing inflammatory abnormalities from early lung cancer remains one of the most challenging issues in thoracic practice.

To address this challenge, the Fleischner Society published updated recommendations in 2017 for the management of incidentally detected pulmonary nodules (Table 1) [13]. These recommendations have become an integral part of routine clinical practice by providing practical guidance regarding surveillance intervals and indications for further diagnostic evaluation according to nodule characteristics and patient-related risk factors.

During the COVID-19 pandemic, thoracic CT was frequently performed for evaluation of suspected SARS-CoV-2 pneumonia. An unintended consequence of this practice was the detection of a large number of incidental pulmonary nodules, ground-glass opacities, and pulmonary masses that otherwise might have remained undiagnosed [14,15]. This unprecedented increase in incidental pulmonary lesion detection provided a unique opportunity to determine whether adherence to the Fleischner Society recommendations could optimize patient selection for pulmonary resection, avoid unnecessary surgery for regressive inflammatory lesions, and facilitate earlier diagnosis of surgically curable lung cancer with favorable long-term outcomes.

Interpretation of these lesions was further complicated by persistent inflammatory abnormalities observed after COVID-19 infection. Organizing pneumonia, ischemic necrosis, post-inflammatory fibrosis and residual inflammatory nodules frequently mimicked early-stage lung cancer on CT imaging, making clinical decision-making considerably more challenging [16-18]. Therefore, differentiating inflammatory lesions from malignant pulmonary nodules became increasingly difficult, emphasizing the importance of structured radiological surveillance rather than immediate surgical intervention.

Although several studies have described incidental pulmonary findings during the COVID-19 era, very limited evidence exists regarding the long-term oncological outcomes of patients managed according to the Fleischner Society recommendations after incidental lesion detection [14,15,18]. Furthermore, few studies have evaluated whether guideline-based surveillance successfully reduces unnecessary pulmonary resections while simultaneously improving early diagnosis of surgically curable lung cancer.

We hypothesized that implementing the Fleischner Society's recommendations would optimize patient selection for surgery by preventing unnecessary lung resections, improving early diagnosis of malignant lesions, and enhancing long-term oncological outcomes.

Materials and Methods

Study Design and Ethical Approval

This is a retrospective, single-center observational study. The study protocol was reviewed and approved by the Clinical Research Ethics Committee of University of Health

Sciences Ankara Keçiören Training and Research Hospital (Approval No: 2012-KAEK-15/2250; March 9, 2021). Because of the retrospective study design, the Ethics Committee waived the requirement for written informed consent. The study complied with the ethical principles of the Declaration of Helsinki.

Patient Selection

Patients who underwent thoracic CT between April 1, 2019 and April 1, 2021 because of suspected COVID-19 infection were retrospectively reviewed. Thoracic CT examinations demonstrating incidental pulmonary GGOs, pulmonary nodules or pulmonary masses were included. Overall, 259 patients fulfilled the initial radiological inclusion criteria. Seven patients with a previous history of malignancy and twelve patients with incomplete clinical records were excluded. Patients presenting with pulmonary masses (n=61) underwent immediate multidisciplinary evaluation by the thoracic oncology board because of a high radiological suspicion of malignancy. Patients presenting with pulmonary nodules or GGOs (n=179) entered a structured surveillance program according to the 2017 Fleischner Society recommendations [13]. During surveillance, 43 lesions demonstrated complete regression or substantial radiological improvement and therefore did not require surgery. Persistent lesions, enlarging nodules or lesions with radiological features suspicious for malignancy underwent pulmonary resection (n=136). Overall, 197 patients with definitive postoperative histopathological diagnoses constituted the final study cohort. They were divided into two groups, malignant and benign, according to the pathology results (Figure 1) (Table 2).

Clinical Variables

Demographic characteristics, clinical risk factors, radiological findings, surgical data, histopathological diagnoses, and follow-up outcomes were retrieved from the hospital electronic medical records. The variables collected for analysis included age, sex, smoking status (never smoker, former smoker, and current or smoker with a cumulative smoking exposure of ≥20 pack-years), passive smoking exposure, family history of cancer, biomass exposure, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), type of pulmonary resection, final histopathological diagnosis, pathological tumor stage, overall survival (OS), and disease-free survival (DFS). These variables were selected to evaluate factors associated with malignant histopathology and to determine the effectiveness of

Fleischner Society-guided surveillance in achieving early diagnosis of surgically curable lung cancer and favorable long-term outcomes.

Surgical Management

Undiagnosed lung lesions were treated with wedge resection and frozen section analysis. Lesions reported as benign based on intraoperative frozen section evaluation were terminated with wedge resection. Lesions reported as malignant underwent surgical resection (segmentectomy, lobectomy, bilobectomy, pneumonectomy) and lymph node dissection according to lung reserve and oncological principles. Mass lesions were evaluated by a multidisciplinary thoracic oncology board, and surgical resection (segmentectomy, lobectomy, bilobectomy, pneumonectomy) and lymph node dissection were performed according to lung reserve and oncological principles.

Study Outcomes

The primary endpoint was identification of clinical predictors associated with malignant histopathology.

Secondary endpoints included: effectiveness of Fleischner Society-guided surveillance, avoidance of unnecessary surgery, distribution of surgical procedures, five-year overall survival, five-year disease-free survival.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range). Categorical variables were summarized as frequencies and percentages. Comparisons between benign and malignant groups were performed using Pearson's chi-square or Fisher's exact test where appropriate. Independent predictors of malignancy were evaluated using multivariable logistic regression analysis. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. Overall survival and disease-free survival were estimated using the Kaplan–Meier method. A two-sided p value <0.05 was considered statistically significant.

RESULTS

Regression During Fleischner Society-Guided Surveillance

Among the 179 patients with incidentally detected pulmonary ground-glass opacities (GGOs) or nodules who entered structured surveillance according to the 2017 Fleischner Society recommendations, 43 (24.0%) demonstrated spontaneous radiological regression and therefore did not require pulmonary resection. Follow-up data were available for 38 of these patients, who were monitored for a median of 8 months (range, 3–14 months). Complete radiological resolution was observed in all followed patients, and none subsequently required surgical intervention. These findings indicate that guideline-based surveillance safely prevented unnecessary pulmonary resection in patients with transient inflammatory pulmonary lesions.

Baseline clinical characteristics

The mean age of the total cohort was 59.7 ± 11.3 years. Patients with malignant lesions were older than those with benign pathology (62.3 ± 9.8 vs. 52.1 ± 12.4 years, $p<0.001$). Male sex was more frequent in the malignant group than in the benign group (75.0% vs. 51.0%, $p=0.003$). Smoking exposure was also more frequent among patients with malignant lesions. In particular, >=20 pack-year smoking exposure was observed in 96 malignant patients (64.9%) compared with 24 benign patients (49.0%) (Table 3).

Radiological findings and surgical management

Radiological presentation differed significantly between benign and malignant groups. Pulmonary masses were observed exclusively in patients with malignant pathology, whereas nodules and ground-glass opacities were more frequently represented among patients with benign or indeterminate lesions selected for surveillance. Surgical management also differed markedly between groups. Wedge resection was the predominant procedure for benign lesions, while lobectomy represented the most common procedure in malignant lesions (Table 3). Invasive adenocarcinoma was the most common malignant histology, followed by squamous cell carcinoma (Table 4).

Histopathological Findings

Among malignant lesions, invasive adenocarcinoma represented the most frequent histological subtype, followed by squamous cell carcinoma. Adenocarcinoma in situ and large-cell carcinoma accounted for only a small proportion of malignant tumors.

Among benign lesions, ischemic necrosis and organizing pneumonia predominated, together accounting for more than 80% of all benign pathological diagnoses. Hamartoma represented the remaining benign lesions. This pathological distribution reflects the unique inflammatory consequences of the COVID-19 pandemic and emphasizes the diagnostic challenges posed by persistent post-inflammatory pulmonary abnormalities (Table 4).

Independent Predictors of Malignancy

Multivariable logistic regression identified age ≥70 years (adjusted OR 5.50; 95% CI 1.51–20.10; p=0.010), male sex (adjusted OR 2.28; 95% CI 1.08–4.80; p=0.030), and heavy smoking (≥20 pack-years; adjusted OR 3.49; 95% CI 1.11–10.89; p=0.032) as independent predictors of malignant histopathology.

Former smoking demonstrated a positive but statistically non-significant association with malignancy. Similarly, COPD, interstitial lung disease, biomass exposure, and family history of cancer were not independently associated with malignant pathology after multivariable adjustment (Table 5, figure 2).

Overall survival and disease-free survival

After surgery, 52 patients received chemotherapy and 5 patients received chemoradiotherapy. During a median follow-up of approximately 60 months, recurrence occurred in two patients (1.4%), whereas distant metastases developed in nine patients (6.1%). These were: brain metastases in 4 patients, liver metastases in 2 patients, adrenal metastases in 1 patient, bone metastases in 1 patient, and contralateral lung metastases in 1 patient. One patient developed a bronchopleural fistula, one patient died due to respiratory failure, one patient died due to myocardial infarction, and one patient died due to heart failure in the early postoperative period. Nineteen patients (9.6%) with malignant disease died during follow-up. The overall 5-year survival rate was found to be 87.2%, and the 5-year disease-free survival rate was 92.6%.

The pathological stage distribution and survival rates in 148 patients with malignant lesions are summarized in Table 6. Early-stage disease was dominant: Stage I tumors were detected in 76 patients (51.4%), Stage II disease in 44 patients (29.7%), and Stage III disease in 28 patients (18.9%). No Stage IV disease was found in the surgically treated group. The outcomes for patients with Stage I-II tumors were more favorable than those with Stage III disease. The crude mortality rate was 8 (6.7%) in Stage I-II disease and 11 (39.3%) in Stage III disease (p=0.0000). The 5-year disease-free survival rate and 5-year survival rates were higher in Stage I-II disease compared to Stage III disease, respectively (90%, 40.4% and 92%, 57.9%, p=0.0000). (Figure 3). These findings support the observation, guided by the Fleischner Society, that follow-up and timely surgical resection are associated with diagnosis at a surgically treatable stage and positive long-term oncological outcomes. The predominance of Stage I–II disease indicates that structured radiological surveillance facilitated diagnosis before progression to advanced-stage disease. This finding is reflected by the excellent long-term overall and disease-free survival observed in the present cohort.

DISCUSSION

Principal Findings

The present study demonstrates that structured implementation of the 2017 Fleischner Society recommendations enabled early identification of surgically curable lung cancer while simultaneously preventing unnecessary pulmonary resection in patients with transient inflammatory pulmonary lesions detected during the COVID-19 pandemic [13]. Of the 179 patients with incidentally detected ground-glass opacities or pulmonary nodules who entered guideline-based surveillance, 43 demonstrated spontaneous radiological regression and therefore avoided surgery. None of the 38 patients with available follow-up data required subsequent pulmonary resection, confirming the safety and clinical effectiveness of structured surveillance for incidental pulmonary lesions.

Our study provides three clinically important observations. First, approximately one-quarter of patients undergoing Fleischner Society-guided surveillance avoided pulmonary resection because their lesions regressed spontaneously during follow-up. Second, unlike pre-pandemic surgical series, organizing pneumonia and ischemic necrosis constituted the predominant benign pathological diagnoses, reflecting the inflammatory and vascular

sequelae of SARS-CoV-2 infection [19-21]. Third, structured surveillance facilitated diagnosis of lung cancer predominantly at pathological Stage I–II, resulting in excellent five-year overall and disease-free survival. Together, these findings demonstrate that guideline-based surveillance not only improves patient selection for surgery but also enhances long-term oncological outcomes.

Comparison with Previous Studies

The predominance of early-stage lung cancer represents one of the most important findings of the present study. More than four-fifths of malignant tumors were diagnosed at pathological Stage I–II, and these patients demonstrated substantially better overall survival and disease-free survival than those with Stage III disease. Early-stage surgical treatment translated into excellent long-term oncological outcomes, with a five-year overall survival of 87.2% and a five-year disease-free survival of 92.6%.

These findings are consistent with the well-established survival benefit associated with CT-based lung cancer screening programs. Both the National Lung Screening Trial (NLST) and the NELSON trial demonstrated that low-dose CT screening substantially reduces lung cancer mortality by facilitating earlier diagnosis of surgically curable disease [5,6,19]. Likewise, the current NCCN Guidelines continue to recommend low-dose CT screening for individuals at increased risk because early-stage detection provides the greatest opportunity for curative surgical resection [4].

However, relatively limited evidence exists regarding patients with incidentally detected pulmonary lesions outside organized screening programs, particularly during the COVID-19 pandemic [14,15,18]. Our findings extend the current literature by demonstrating that structured surveillance based on the 2017 Fleischner Society recommendations safely reduced unnecessary pulmonary resections while maintaining excellent long-term oncological outcomes [13].

Furthermore, our results are consistent with the principles of the Slovak Lung Cancer Screening Initiative, which advocates standardized implementation of evidence-based screening and follow-up pathways to maximize early-stage lung cancer detection while minimizing unnecessary invasive procedures [22,23]. Although our cohort consisted of patients with incidentally detected pulmonary lesions rather than participants in a formal

screening program, both approaches share the common objective of identifying lung cancer at a surgically curable stage through structured radiological assessment.

COVID-19–Related Benign Pulmonary Mimickers

One of the most distinctive observations of the present study was the pathological spectrum of benign pulmonary lesions. Ischemic necrosis and organizing pneumonia accounted for the majority of benign surgical specimens. This distribution differs considerably from that reported in pre-pandemic surgical series, in which hamartoma and other benign tumors generally represent the predominant pathological diagnoses.

The increased frequency of organizing pneumonia and ischemic necrosis in our cohort is most likely related to the inflammatory and vascular sequelae of SARS-CoV-2 infection. COVID-19 is characterized by diffuse alveolar injury, endothelial dysfunction, microvascular thrombosis, and persistent inflammatory responses, all of which may produce residual pulmonary nodules or mass-like lesions that closely mimic lung cancer on CT imaging [19-21]. Previous pathological studies have similarly demonstrated that organizing pneumonia, fibro-inflammatory repair, and ischemic pulmonary necrosis are common late manifestations following COVID-19 pneumonia and frequently persist despite clinical recovery [20,21].

The observation that all patients with available follow-up demonstrated complete radiological resolution further supports this interpretation. Had surgery been performed immediately after the initial CT examination, many of these inflammatory lesions would have undergone unnecessary pulmonary resection. These findings emphasize the importance of short-term radiological surveillance before surgical intervention is considered in carefully selected patients [13].

Clinical Implications

Multivariable logistic regression identified advanced age, male sex, and heavy smoking (≥20 pack-years) as independent predictors of malignant pathology, findings that are consistent with previous epidemiological studies and current lung cancer screening recommendations (4-6,19). These results indicate that radiological surveillance should always be interpreted together with established clinical risk factors when estimating the probability of malignancy.

Our findings have direct implications for contemporary thoracic practice. Incidentally detected pulmonary nodules should not automatically prompt surgical intervention solely because of their radiological appearance. Instead, structured implementation of the Fleischner Society recommendations, combined with multidisciplinary evaluation and individualized clinical risk assessment, allows clinicians to distinguish transient inflammatory lesions from persistent malignant disease while minimizing unnecessary pulmonary resections.

This strategy appears particularly valuable in healthcare settings where inflammatory pulmonary abnormalities are common, such as during or after the COVID-19 pandemic [19,20]. Guideline-based surveillance enables clinicians to avoid unnecessary pulmonary resections without delaying diagnosis of surgically curable lung cancer [13]. Consequently, multidisciplinary evaluation integrating radiological findings, clinical risk factors, and interval imaging should remain the cornerstone of management of incidentally detected pulmonary lesions.

Strengths and Limitations

The principal strengths of this study include the relatively large surgically confirmed cohort, complete histopathological verification of all resected lesions, comprehensive long-term oncological follow-up, and evaluation of incidental pulmonary lesions during the unique period of widespread thoracic CT utilization associated with the COVID-19 pandemic. These strengths provide robust evidence regarding the real-world effectiveness of guideline-based surveillance in routine thoracic surgical practice.

Nevertheless, several limitations should be acknowledged. First, this was a retrospective single-center study, which may limit the generalizability of the findings. Second, only surgically treated patients with definitive pathological diagnoses were included, introducing unavoidable selection bias. Third, pulmonary nodules that remained stable without surgical intervention were not represented in the final pathological analysis. Finally, because the study reflects clinical practice during the COVID-19 pandemic, the spectrum of benign pathological diagnoses may differ from that observed in non-pandemic populations.

Clinical Perspective

The COVID-19 pandemic unexpectedly created one of the largest opportunities for incidental pulmonary lesion detection through widespread thoracic CT imaging [14,15]. Our findings demonstrate that standardized implementation of the Fleischner Society recommendations enabled clinicians to distinguish transient inflammatory lesions from persistent malignant disease while avoiding unnecessary pulmonary resections [13]. Importantly, structured surveillance facilitated diagnosis predominantly at surgically curable stages, resulting in excellent long-term oncological outcomes. These findings support routine implementation of the Fleischner Society recommendations together with multidisciplinary evaluation as the preferred management strategy for incidentally detected pulmonary lesions in contemporary thoracic practice.

Future Perspectives

Future multicenter prospective studies incorporating volumetric nodule assessment, artificial intelligence-assisted CT interpretation, and radiomics-based image analysis may further improve individualized risk stratification of incidentally detected pulmonary lesions. Integration of these emerging technologies with established Fleischner Society-guided surveillance protocols may optimize patient selection for surgery while preserving excellent long-term oncological outcomes [13].

Conclusions

The present study demonstrates that strict implementation of the Fleischner Society recommendations safely differentiates transient inflammatory pulmonary lesions from persistent malignant disease, thereby preventing unnecessary pulmonary resections while facilitating early diagnosis of surgically curable lung cancer. Structured guideline-based surveillance, combined with multidisciplinary evaluation and individualized risk assessment, resulted in excellent long-term oncological outcomes in this cohort. These findings support routine implementation of the Fleischner Society recommendations as an integral component of contemporary thoracic surgical practice for patients with incidentally detected pulmonary lesions [13].

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References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. doi: 10.3322/caac.21834.
2. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10-45. doi: 10.3322/caac.21871.
3. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol. 2016;11(1):39-51. doi: 10.1016/j.jtho.2015.09.009.
4. NCCN Clinical Practice Guidelines in Oncology: Lung Cancer Screening. Version 1.2026. Plymouth Meeting (PA): National Comprehensive Cancer Network; 2026.
5. National Lung Screening Trial Research Team; Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395-409. doi: 10.1056/NEJMoa1102873.
6. de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020;382(6):503-513. doi: 10.1056/NEJMoa1911793.
7. US Preventive Services Task Force; Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325(10):962-970. doi: 10.1001/jama.2021.1117.
8. Vachani A, Zheng C, Amy Liu IL, Huang BZ, Osuji TA, Gould MK. The Probability of Lung Cancer in Patients With Incidentally Detected Pulmonary Nodules: Clinical Characteristics and Accuracy of Prediction Models. Chest. 2022;161(2):562-571. doi: 10.1016/j.chest.2021.07.2168.

9. O'Dowd EL, Tietzova I, Bartlett E, Devaraj A, Biederer J, Brambilla M, et al. ERS/ESTS/ESTRO/ESR/ESTI/EFOMP statement on management of incidental findings from low dose CT screening for lung cancer. Eur Respir J. 2023;62(4):2300533. doi: 10.1183/13993003.00533-2023.
10. Wood DE, Kazerooni EA, Aberle DR, Argento C, Baines J, Boer B, et al. NCCN Guidelines® Insights: Lung Cancer Screening, Version 1.2025. J Natl Compr Canc Netw. 2025;23(1):e250002. doi: 10.6004/jnccn.2025.0002.
11. Callister ME, Baldwin DR, 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(12):1188. doi: 10.1136/thoraxjnl-2015-207168corr1.
12. Mazzone PJ, Lam L. Evaluating the Patient With a Pulmonary Nodule: A Review. JAMA. 2022;327(3):264-273. doi: 10.1001/jama.2021.24287.
13. 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.
14. Revel MP, Parkar AP, Prosch H, Silva M, Sverzellati N, Gleeson F, et al. COVID-19 patients and the radiology department - advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). Eur Radiol. 2020;30(9):4903-4909. doi: 10.1007/s00330-020-06865-y.
15. Dennie C, Hague C, Lim RS, Manos D, Memauri BF, Nguyen ET, et al. Canadian Society of Thoracic Radiology/Canadian Association of Radiologists Consensus Statement Regarding Chest Imaging in Suspected and Confirmed COVID-19. Can Assoc Radiol J. 2020;71(4):470-481. doi: 10.1177/0846537120924606.
16. Kory P, Kanne JP. SARS-CoV-2 organising pneumonia: 'Has there been a widespread failure to identify and treat this prevalent condition in COVID-19?'. BMJ Open Respir Res. 2020;7(1):e000724. doi: 10.1136/bmjresp-2020-000724.
17. Myall KJ, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, Preston R, et al. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. Ann Am Thorac Soc. 2021;18(5):799-806. doi: 10.1513/AnnalsATS.202008-1002OC.

18. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. Six-month Follow-up Chest CT Findings after Severe COVID-19 Pneumonia. Radiology. 2021;299(1):E177-E186. doi: 10.1148/radiol.2021203153.
19. Carsana L, Sonzogni A, Nasr A, Rossi RS, Pellegrinelli A, Zerbi P, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. Lancet Infect Dis. 2020;20(10):1135-1140. doi: 10.1016/S1473-3099(20)30434-5
20. de Oliveira Filho CM, Vieceli T, de Fraga Bassotto C, da Rosa Barbato JP, Garcia TS, Scheffel RS. Organizing pneumonia: A late phase complication of COVID-19 responding dramatically to corticosteroids. Braz J Infect Dis. 2021;25(1):101541. doi: 10.1016/j.bjid.2021.101541.
21. George PM, Barratt SL, Condliffe R, Desai SR, Devaraj A, Forrest I, et al. Respiratory follow-up of patients with COVID-19 pneumonia. Thorax. 2020;75(11):1009-1016. doi: 10.1136/thoraxjnl-2020-215314.
22. Juskanic D, Sandor F, Denkova L, Juhos P, Janik M, Hontzas J, et al. Lung Cancer Screening Initiative in Slovakia: Guidelines of screening implementation. Bratisl Lek Listy. 2023;124(2):109-115. doi: 10.4149/BLL_2023_016.
23. Chen H, Kim AW, Hsin M, Shrager JB, Prosper AE, Wahidi MM, et al. The 2023 American Association for Thoracic Surgery (AATS) Expert Consensus Document: Management of subsolid lung nodules. J Thorac Cardiovasc Surg. 2024;168(3):631-647.e11. doi: 10.1016/j.jtcvs.2024.02.026.

Table 1. Fleischner Society Recommendations for the Management of Incidentally Detected Pulmonary Nodules (2017)

CT finding	Low-risk patient	High-risk patient	Recommendation
Single solid nodule <6 mm	No routine follow-up	Optional CT at 12 months	No further imaging if stable
Single solid nodule 6–8 mm	CT at 6–12 months; consider CT at 18–24 months	CT at 6–12 months and again at 18–24 months	Continue surveillance if stable
Single solid nodule >8 mm	CT at 3 months, PET/CT and/or tissue sampling	CT at 3 months, PET/CT and/or tissue sampling	Multidisciplinary evaluation recommended
Multiple solid nodules <6 mm	No routine follow-up	Optional CT at 12 months	Individualize according to dominant nodule
Multiple solid nodules ≥6 mm	CT at 3–6 months; consider CT at 18–24 months	CT at 3–6 months and at 18–24 months	Management based on the most suspicious nodule
Pure ground-glass nodule <6 mm	No routine follow-up	No routine follow-up	Usually benign
Pure ground-glass nodule ≥6 mm	CT at 6–12 months, then every 2 years until 5 years	Same recommendation	Surgical evaluation if enlargement or increasing solid component
Part-solid nodule ≥6 mm	CT at 3–6 months; if persistent, annual CT for 5 years	Same recommendation	Consider resection if solid component ≥6 mm or progressive
Multiple subsolid nodules	CT at 3–6 months	CT at 3–6 months	Further management according to the dominant lesion

Abbreviations: CT, computed tomography; PET, positron emission tomography.

Table 2. Comparison of Fleischner Society Recommendations and Clinical Outcomes in the Present Study

Fleischner Society-guided clinical step	Findings in the present study
Initial CT surveillance for incidental GGOs/nodules	179 patients entered Fleischner-guided surveillance
Radiological regression during surveillance	43 patients avoided pulmonary resection
Follow-up after regression	38 patients had available follow-up
Follow-up duration after regression	Median 8 months (range, 3-14 months)
Complete radiological resolution	38/38 patients (100%)
Persistent, enlarging, or suspicious lesions	136 patients underwent pulmonary resection
Pulmonary masses	61 patients underwent direct MDT evaluation and surgery
Final cohort with histopathology	197 patients
Malignant pathology	148 patients (75.1%)
Benign pathology	49 patients (24.9%)
Five-year overall survival in malignant lesions	129/148 (87.2%)
Five-year disease-free survival in malignant lesions	137/148 (92.6%)

GGO, ground-glass opacity; MDT, multidisciplinary team.

Table 3. Baseline Clinical, Radiological, and Surgical Characteristics of the Study Cohort

Variable	Total (n=197)	Benign (n=49)	Malignant (n=148)	p value
Clinical characteristics				
Age, years (mean ± SD)	59.7 ± 11.3	52.1 ± 12.4	62.3 ± 9.8	<0.001
Age ≥70 years	44 (22.3%)	3 (6.1%)	41 (27.7%)	0.001
Male sex	136 (69.0%)	25 (51.0%)	111 (75.0%)	0.003
COPD	30 (15.2%)	9 (18.4%)	21 (14.2%)	0.634
Interstitial lung disease	13 (6.6%)	5 (10.2%)	8 (5.4%)	0.400
Biomass exposure	10 (5.1%)	4 (8.2%)	6 (4.1%)	0.269
Family history of cancer	10 (5.1%)	2 (4.1%)	8 (5.4%)	1.000
Never smoker	17 (8.6%)	8 (16.3%)	9 (6.1%)	0.039
Former smoker	59 (29.9%)	17 (34.7%)	42 (28.4%)	
≥20 pack-year smoker	120 (60.9%)	24 (49.0%)	96 (64.9%)	
Radiological characteristics				
Ground-glass opacity	59 (29.9%)	21 (42.9%)	38 (25.7%)	0.036
Pulmonary nodule	74 (37.6%)	28 (57.1%)	46 (31.1%)	0.002
Pulmonary mass	61 (31.0%)	0 (0.0%)	61 (41.2%)	<0.001
Surgical characteristics				
Right-sided resection	121 (61.4%)	37 (75.5%)	84 (56.8%)	0.030
Left-sided resection	76 (38.6%)	12 (24.5%)	64 (43.2%)	
Wedge resection	43 (21.8%)	43 (87.8%)	0 (0.0%)	<0.001
Segmentectomy	21 (10.7%)	0 (0.0%)	21 (14.2%)	
Lobectomy	102 (51.8%)	0 (0.0%)	102 (68.9%)	
Bilobectomy	6 (3.0%)	0 (0.0%)	6 (4.1%)	
Pneumonectomy	19 (9.6%)	0 (0.0%)	19 (12.8%)	
Other limited resection	6 (3.0%)	6 (12.2%)	0 (0.0%)	

Table 4. Histopathological Diagnosis According to Final Pathology

Histopathological diagnosis	Benign (n=49)	Malignant (n=148)	Total (n=197)
Malignant lesions			
Invasive adenocarcinoma	0	79 (53.4%)	79 (40.1%)
Squamous cell carcinoma	0	62 (41.9%)	62 (31.5%)
Adenocarcinoma in situ	0	3 (2.0%)	3 (1.5%)
Large-cell carcinoma	0	4 (2.7%)	4 (2.0%)
Benign lesions			
Ischemic necrosis	27 (55.1%)	0	27 (13.7%)
Organizing pneumonia	13 (26.5%)	0	13 (6.6%)
Hamartoma	9 (18.4%)	0	9 (4.6%)

Table 5. Multivariable Logistic Regression for Predictors of Malignancy

Variable	Adjusted OR	95% CI	p value
Age ≥70 years	5.50	1.51–20.10	0.010
Male sex	2.28	1.08–4.80	0.030
Former smoker	2.15	0.65–7.12	0.209
≥20 pack-year smoker	3.49	1.11–10.89	0.032
COPD	0.45	0.17–1.19	0.108
ILD	0.52	0.15–1.84	0.313
Biomass exposure	1.08	0.26–4.51	0.918
Family history of cancer	1.43	0.27–7.46	0.673

CI, confidence interval; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; OR, odds ratio. Reference categories: age <70 years, female sex, never smoker, and absence of the listed comorbidity/exposure.

Table 6. Association between pathological stage and survival outcomes among malignant patients.

Stage	n (%)	Deaths, n	Crude OS (%)	Mean OS, months	5-year OS (%)	Mean DFS, months	5-year DFS (%)
IA1	9 (6.1)	0	100.0	67.2 (n=6)	100.0	58.1 (n=7)	100.0
IA2	25 (16.9)	0	100.0	64.5 (n=22)	100.0	64.5 (n=22)	100.0
IA3	12 (8.1)	0	100.0	66.0 (n=9)	100.0	66.0 (n=9)	100.0
IB	30 (20.3)	3	90.0	59.2 (n=23)	87.0	58.6 (n=23)	87.0
IIA	15 (10.1)	1	93.3	61.4 (n=11)	90.9	61.4 (n=11)	90.9
IIB	29 (19.6)	4	86.2	54.4 (n=18)	82.4	51.5 (n=19)	73.7
IIIA	18 (12.2)	6	66.7	42.4 (n=11)	54.5	36.9 (n=12)	50.0
IIIB	10 (6.8)	5	50.0	43.6 (n=8)	62.5	31.8 (n=10)	26.7
Stage group	**n (%)**	**Deaths, n (%)**	**Crude OS (%)**	**Mean OS, months**	**5-year OS (%)**	**Mean DFS, months**	**5-year DFS (%)**
Stage I–II	120 (81.1)	8 (6.7)	93.3	61.0 (n=89)	92.0	59.6 (n=91)	90.0
Stage III	28 (18.9)	11 (39.3)	60.7	42.9 (n=19)	57.9	34.6 (n=22)	40.4
p value		0.0000					0.0000

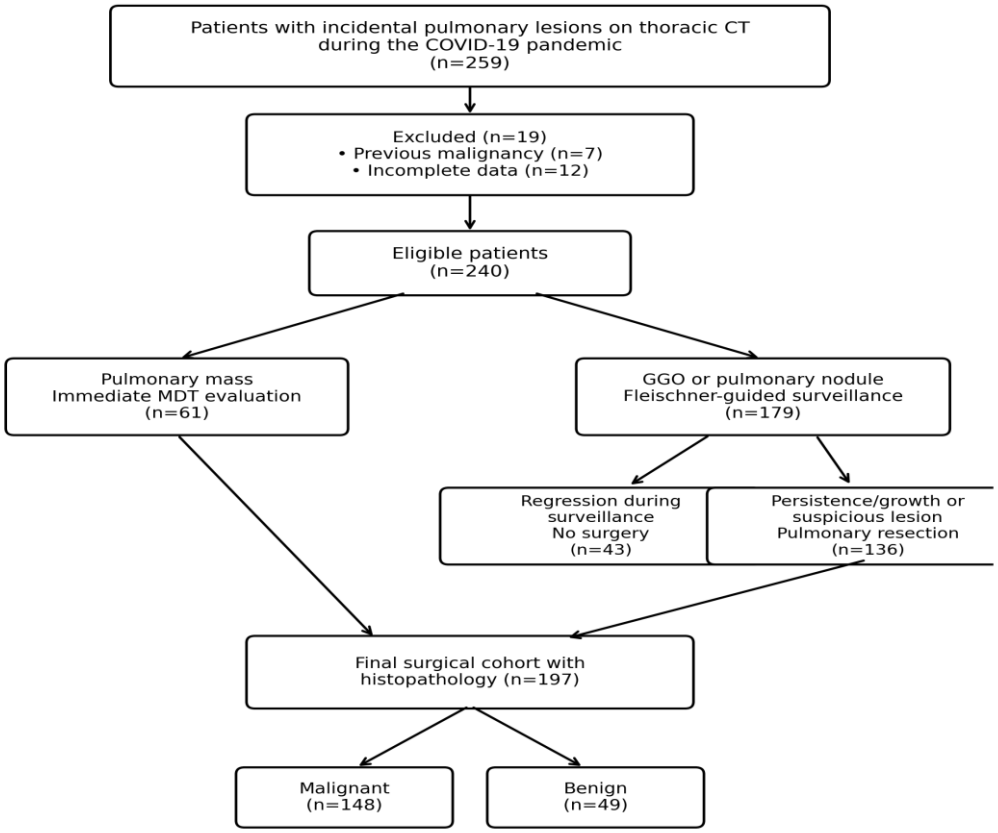


Figure 1. Patient selection flow diagram, Fleischner Society-guided surveillance, surgical management, and final histopathological classification. MDT, multidisciplinary thoracic oncology team; GGO, ground-glass opacity.

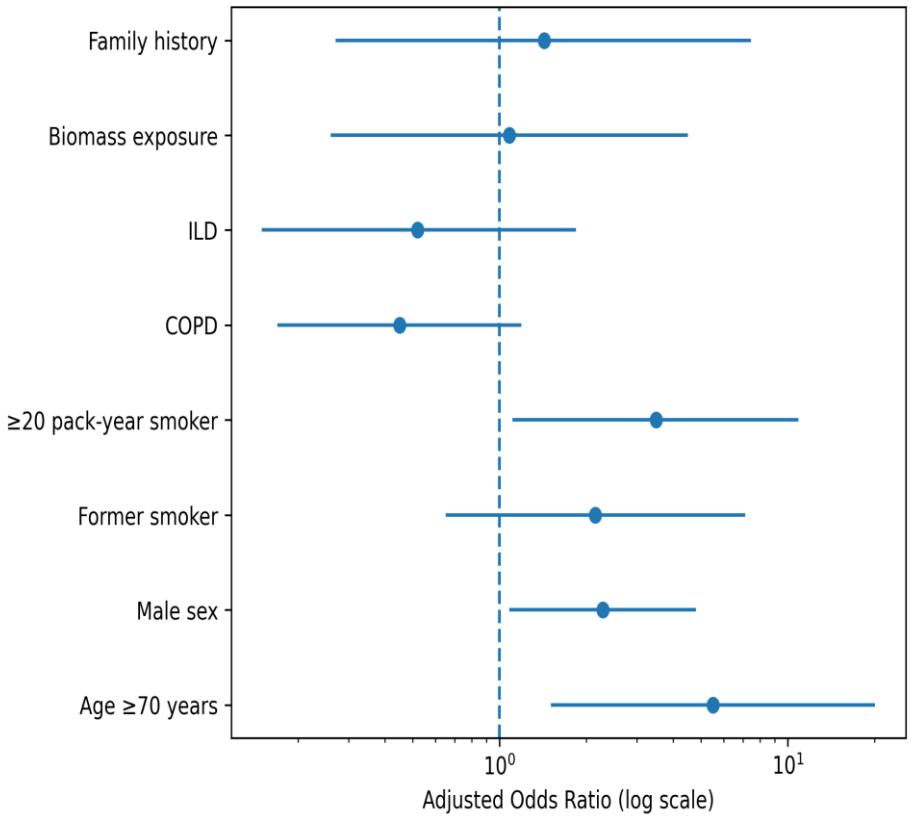


Figure 2. Forest plot of the multivariable logistic regression (Log Scale), Forest plot showing adjusted odds ratios (ORs) and 95% confidence intervals. The x-axis is logarithmic; the dashed vertical line indicates OR=1.0.

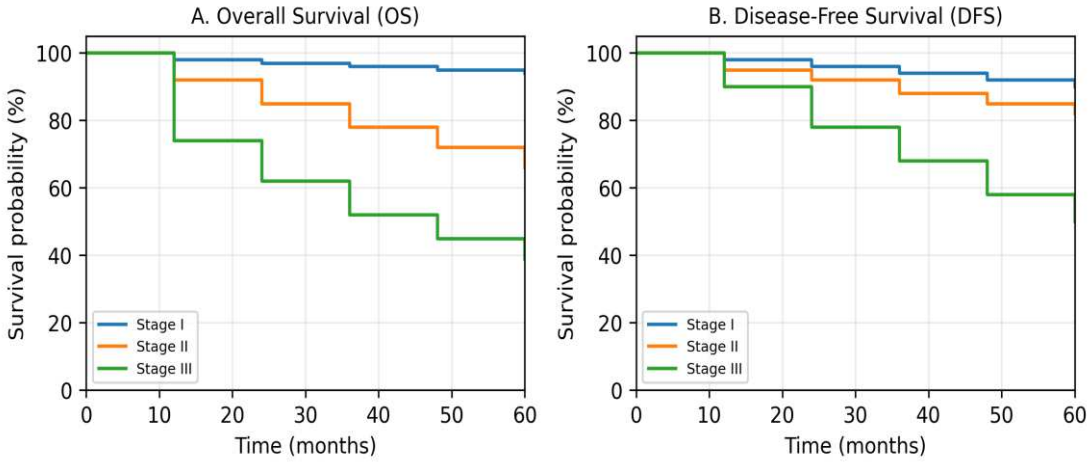


Figure 3. Kaplan-Meier curves for overall survival and disease-free survival according to pathological stage (Stage I vs. II vs. III).