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Surgical Outcomes of Incidentally Detected Solid Solitary Pulmonary Nodules in a Cohort at Risk for Lung Cancer Screening

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Abstract

Background

A solitary pulmonary nodule (SPN) is a single pulmonary opacity smaller than 3 cm in diameter and completely surrounded by lung parenchyma. Detection of SPNs is one of the principal aims of lung cancer screening programs. According to current guidelines, surgical treatment is recommended for nodules with a high probability of malignancy. This study evaluated surgical outcomes, malignancy rates, and predictors of malignancy in incidentally detected solid SPNs resected after multidisciplinary team assessment in patients at risk for lung cancer screening.

Methods

This retrospective single-center study included adults who underwent surgery between January 2016 and January 2026 for asymptomatic, incidentally detected, solid SPNs measuring 8–30 mm. Patients had no preoperative tissue diagnosis or prior lung cancer history. Eligible individuals either fulfilled lung cancer screening criteria (age ≥ 50 years and smoking history ≥ 20 pack-years) or had additional risk factors, including family history of cancer or previous extrathoracic malignancy. Demographic, radiological, operative, and histopathological findings were analyzed. Mayo Clinic, Brock, and Herder risk scores were calculated. Independent predictors of malignant pathology were assessed using multivariable logistic regression.

Results

A total of 112 patients were included (mean age 58.2 ± 12.5 years; 59.8% male). Final histopathology demonstrated malignancy in 78 patients (69.6%). Among all patients, 74 (66.1%) fulfilled lung cancer screening eligibility criteria. Malignancy was more frequent in screening-eligible than non-eligible patients (76.9% vs. 41.2%, $p < 0.001$). Patients with malignant nodules were older (60.4 vs. 53.2 years, $p = 0.007$), more frequently male (67.9% vs. 41.2%, $p = 0.012$), and had greater tobacco exposure (52.7 vs. 37.9 pack-years, $p = 0.021$). Previous extrathoracic malignancy was more common in malignant cases (41.0% vs. 11.8%, $p = 0.002$). Mayo Clinic, Brock, and Herder scores were significantly higher in malignant nodules. On multivariable analysis, male sex ($p = 0.029$) and previous malignancy history ($p = 0.001$) were independently associated with malignant pathology.

Conclusions

In patients at risk for lung cancer screening who underwent surgery for incidentally detected SPNs, careful selection resulted in a high malignancy yield. Careful and individualized multidisciplinary

assessment guides treatment or surveillance decisions, and may help reduce overdiagnosis and overtreatment.

Introduction

A solitary pulmonary nodule (SPN) is defined as a single, marginated, rounded radiological lung opacity smaller than or equal to 3 cm in diameter [1, 2]. It is completely surrounded by aerated lung tissue, and not associated with additional lung pathology such as atelectasis and pleural effusion [3]. SPNs may occur due to either benign or malignant pathologies. In recent years, the increasing and more sensitive use of computed tomography (CT) has led to higher detection rates of SPNs and, consequently, early-stage lung cancer [4].

SPNs may be detected incidentally or identified in a targeted manner as part of a lung cancer screening program [5]. Incidental pulmonary nodules are frequently discovered during trauma evaluation, cardiac or abdominal imaging, or general health examinations (e.g., pre-employment assessments) [6]. In recent years, implementation of lung cancer screening programs has further increased SPN detection rates. According to current guidelines, lung cancer screening is recommended for individuals aged ≥ 50 years with a smoking history of ≥ 20 pack-years or a smoking duration of ≥ 20 years [7–11]. Occupational exposure, radon exposure, family history of cancer, personal history of malignancy, and certain pulmonary diseases are also recognized as independent risk factors for lung cancer. However, they are not yet considered absolute indications for screening in current guidelines [12].

Radiologically, SPNs may be classified as ground-glass, subsolid, or solid nodules. Previous studies have indicated that solid pulmonary nodules have a higher probability of malignancy [13, 14]. Thus, due to their increased malignant potential, current guidelines emphasize surgical resection as a treatment option for solid SPNs larger than 8 mm in diameter [15, 16].

In this study, patients with incidentally detected solid pulmonary nodules larger than 8 mm who underwent surgery following a multidisciplinary team (MDT) evaluation were retrospectively analyzed. The study aimed to select patients at risk for lung cancer screening, examine surgical outcomes, assess the likelihood of malignancy detectable by screening, and evaluate the characteristics of malignant nodules.

Materials and Methods

This study was designed as a retrospective cohort study, and patients who underwent thoracic surgery at the same institution between January 2016 and January 2026 were evaluated. Asymptomatic patients operated on following the evaluation of a MDT for a solid SPN detected incidentally, identified after a trauma, general health examination for a job application, or follow-up for another cancer, were considered for inclusion. According to current guidelines, patients at risk for lung cancer screening—defined as those aged over 50 years with a smoking history of at least 20 pack-years or prolonged smoking exposure (> 20 years)—were enrolled. In addition, patients who did not meet these criteria but

had recognized risk factors for lung cancer screening per the same guidelines, including a history of cancer in a first-degree relative or a history of extrathoracic malignancy, were also included.

Ultimately, the study population consisted of asymptomatic patients older than 18 years with solid SPNs measuring 8–30 mm in diameter detected incidentally, without a preoperative diagnosis, who had not undergone a nodule biopsy, and for whom complete data were available. Patients younger than 18 years, those with multiple nodules, those with a preoperative diagnosis, those with a prior history of lung cancer, and those with incomplete data were excluded. As a result, a total of 112 patients who met the inclusion criteria were enrolled in the study.

Demographic, radiological, operative, and histopathological characteristics of all patients were retrieved from the hospital database. As previously defined in the literature, the probability of malignancy for each SPN was assessed using the Mayo Clinic, Brock, and Herder risk prediction models. In the Mayo Clinic model, patient age, nodule diameter, smoking history, history of extrathoracic malignancy diagnosed previous ≥ 5 years, upper lobe location, and nodule spiculation were included as variables [17]. The Brock model consists of sex, age, nodule size, family history of cancer, presence of emphysema, number of nodules, nodule type (solid, semisolid, or ground-glass), upper lobe location, and spiculation [18]. The Herder model includes age, smoking history, history of malignancy, nodule size, spiculation, upper lobe location, and fluorodeoxyglucose (FDG) uptake on positron emission tomography (PET) [15]. In the Herder model, FDG uptake is categorized as “No FDG,” “Faint FDG,” “Moderate FDG,” or “Intense FDG.” However, the original model does not define these categories according to specific maximum standardized uptake value (SUVmax) thresholds. Therefore, FDG uptake in the present study was classified according to the criteria proposed by El-Amari et al., where SUVmax ≤ 2.5 was considered “Faint FDG,” SUVmax 2.6–10.0 as “Moderate FDG,” and SUVmax > 10.0 as “Intense FDG” [19].

Based on final histopathological examination, nodules were categorized as benign or malignant. The two groups were compared regarding demographic, radiological, and operative characteristics. In addition, malignancy rates were compared between patients who fulfilled lung cancer screening criteria based on age and smoking history and those included because of family history of cancer or personal history of malignancy.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 24. Normality of data distribution was assessed using the Kolmogorov–Smirnov test. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as number (n) and percentage (%). Continuous variables were compared using the independent samples Student’s t-test or Mann–Whitney U test, as appropriate. Categorical variables were compared using the Chi-square test or Fisher’s exact test. Variables showing stronger associations with malignant nodules in univariable analysis and meeting a threshold of $p < 0.10$ were entered into multivariable analysis. Logistic regression analysis was performed to determine independent predictors of malignancy. Independent factors were presented as Odds Ratio (OR) and 95% Confidence Interval (CI) (Minimum to Maximum) values. A two-sided p-value < 0.05 was considered statistically significant.

Results

A total of 112 patients who met the inclusion criteria were evaluated in the study. The mean age was 58.22 ± 12.48 years, and 67 patients were male (59.8%). A history of smoking was observed in 94 patients (83.9%), with a mean tobacco exposure of 48.61 ± 27.92 pack-years. Thirty-four patients (30.4%) had a first-degree family history of cancer, while 36 patients (32.1%) had a history of extrathoracic malignancy. Among patients with a previous malignancy, the most common primary cancers were head and neck cancer (n = 8) and breast cancer (n = 8), followed by colorectal cancer (n = 4), gynecological malignancies (n = 4), and hematological malignancies (n = 4). Prostate cancer (n = 2) and mesenchymal tumors (n = 2) were less frequent, while adrenal malignancy, renal cell carcinoma, malignant melanoma, and pancreatic cancer were each present in one patient.

Overall, 78 nodules (69.6%) were malignant and 34 (30.4%) were benign. Compared with patients with benign nodules, those with malignant nodules were significantly older (60.40 ± 11.73 vs. 53.24 ± 12.88 years, p = 0.007) and more frequently male (67.9% vs. 41.2%, p = 0.012). Although the smoking status did not differ significantly between the groups (p = 0.171), tobacco exposure was higher in the malignant group (52.69 ± 28.93 vs. 37.92 ± 22.19 pack-years, p = 0.021). A family history of cancer was significantly more common in the benign group (44.1% vs. 24.4%, p = 0.032), while a personal history of malignancy was more frequent in patients with malignant nodules (41.0% vs. 11.8%, p = 0.002). When grouped according to current lung cancer screening eligibility criteria, 74 patients (66.1%) were eligible. Patients with malignant nodules were significantly more likely to meet screening criteria than those with benign nodules (76.9% vs. 41.2%, p < 0.001). Demographic and clinical characteristics are summarized in Table 1.

Table 1
Demographic and clinical characteristics of the patients

Characteristic	**Total (n:112)**	**Malignant (n:78)**	**Benign (n:34)**	**p-value**
Age (years)	58.22 ± 12.48	60.40 ± 11.73	53.24 ± 12.88	**0.007**
Sex (male, %)	67 (59.8)	53 (67.9)	14 (41.2)	**0.012**
Smoking History (%)	94 (83.9)	68 (87.2)	26 (76.5)	0.171
Tobacco Consumption (package years)	48.61 ± 27.92	52.69 ± 28.93	37.92 ± 22.19	**0.021**
Cancer History in Family (%)	34 (30.4)	19 (24.4)	15 (44.1)	**0.032**
History of extrathoracic malignancy (%)	36 (32.1)	32 (41.0)	4 (11.8)	**0.002**
Lung Cancer Screening-Eligible Patients (%)	74 (66.1)	60 (76.9)	14 (41.2)	**< 0.001**

Radiological characteristics of the nodules were also evaluated and compared. Nodules were located in the right lung in 65 patients (58.0%), which was statistically significantly more frequent in the malignant group (66.7% vs. 38.2%, p = 0.007). The nodules were localized in the upper lobe in 61 patients (54.5%), with no significant difference between malignant and benign groups. Emphysematous changes were observed in 44 patients (39.3%), while spiculation was identified in 72 patients (64.3%). Spiculated nodules were significantly more common in the malignant group (71.8% vs. 47.1%, p = 0.018). Mean SUVmax was 4.76 ± 5.66, and mean nodule diameter was 16.46 ± 6.59 mm. Neither SUVmax nor nodule size differed statistically significantly between groups. Mean Mayo Clinic, Brock, and Herder risk scores were 45.09 ± 25.55, 26.11 ± 17.82, and 54.41 ± 35.81, respectively, and all three scores were significantly higher in malignant nodules than in benign nodules. Radiological findings are presented in Table 2.

Table 2
Radiological characteristics of the patients

Characteristic	Total (n:112)	Malignant (n:78)	Benign (n:34)	p-value
Side (Right, %)	65 (58.0)	52 (66.7)	13 (38.2)	**0.007**
Localization (Upper Lobe, %)	61 (54.5)	45 (57.7)	16 (47.1)	0.299
Emphysema (%)	44 (39.3)	33 (42.3)	11 (32.3)	0.402
Spiculation (%)	72 (64.3)	56 (71.8)	16 (47.1)	**0.018**
SUVmax	4.76 ± 5.66	5.45 ± 5.38	3.18 ± 6.03	0.064
Nodule Diameter (mm)	16.46 ± 6.59	16.50 ± 6.64	16.35 ± 6.56	0.914
Mayo Clinic Risk Score	45.09 ± 25.55	51.52 ± 25.51	30.33 ± 18.83	**< 0.001**
Brock Risk Score	26.11 ± 17.82	28.34 ± 19.46	21.01 ± 12.09	**0.045**
Herder Risk Score	54.41 ± 35.81	63.70 ± 33.39	33.11 ± 32.26	**< 0.001**

Operative and histopathological outcomes were subsequently analyzed. Diagnostic resection was performed by wedge resection in 105 patients (93.8%), while segmentectomy was performed in 1 patient (0.9%) and lobectomy in 6 patients (5.4%) because of centrally located lesions. Patients diagnosed with malignancy on frozen section after wedge resection who were medically fit underwent completion lobectomy during the same operation. The most common histopathological diagnoses were adenocarcinoma (26.8%), squamous cell carcinoma (20.5%), metastasis (17.9%), and granulomatous inflammation (12.5%). Operative and histopathological findings, and their distribution according to the lung cancer screening eligibility, history of cancer, and family history of cancer are summarized in Table 3.

Table 3
Operative and histopathological features of the patients

Diagnostic Method	**n, %**			
Wedge resection	105 (93.8)			
Segmentectomy	1 (0.9)			
Lobectomy	6 (5.4)			
Histopathological Diagnosis	**All Patients (n, %)**	**Patients Eligible for Lung Cancer Screening (n,%)**	**Patients with a Cancer History (n, %)**	**Patients with a Family History of Cancer (n, %)**
Adenocarcinoma	30 (26.8)	26 (35.1)	3 (8.3)	7 (20.6)
Squamous Cell Carcinoma	23 (20.5)	22 (29.7)	7 (19.3)	5 (14.7)
Metastasis	20 (17.9)	7 (9.4)	20 (55.6)	7 (20.6)
Granulomatous Inflammation	14 (12.4)	5 (6.7)	2 (5.6)	5 (14.7)
Organizing Pneumonia	8 (7.1)	4 (5.4)	1 (2.8)	5 (14.7)
Pulmonary Hamartoma	6 (5.4)	2 (2.7)	-	3 (8.8)
Carcinoid Tumor	4 (3.6)	4 (5.4)	1 (2.8)	-
Intrapulmonary Lymph Node	2 (1.8)	1 (1.4)	-	1 (2.9)
Pulmonary Myelolipoma	2 (1.8)	1 (1.4)	1 (2.8)	-
Large Cell Carcinoma	1 (0.9)	1 (1.4)	1 (2.8)	-
Solitary Fibrous Tumor	1 (0.9)	-	-	1 (2.9)
Pulmonary Amyloidosis	1 (0.9)	1 (1.4)	-	-
Total	**112 (100.0)**	**74 (100.0)**	**36 (100.0)**	**34 (100.0)**

For multivariable analysis, variables differing between groups in univariable analysis (age, sex, tobacco exposure, family history of cancer, history of malignancy, side, spiculation, and SUVmax) were entered into a logistic regression model. Multivariate logistic regression analysis identified male sex (OR: 4.31, 95% CI: 1.17–15.93, p = 0.029) and a history of additional malignancy (OR: 23.58, 95% CI: 3.48–159.80, p

= 0.001) as independent predictors of malignancy. Age (per year) showed a borderline association (OR: 1.06, p = 0.061). (Table 4).

Table 4
Multivariate analysis to determine independent variables affecting nodules being malignant

Variable	Odds Ratio (95% CI)	p-value
Age (per year)	1.06 (0.998–1.12)	0.061
Sex (male vs. female)	**4.31 (1.17–15.93)**	**0.029**
Pack-years of tobacco	1.02 (0.99–1.05)	0.170
Family history of cancer	1.92 (0.36–10.22)	0.442
History of malignancy	**23.58 (3.48–159.80)**	**0.001**
Side (right vs. left)	2.63 (0.80–8.68)	0.113
Spiculation	2.34 (0.63–8.72)	0.207
SUVmax	1.07 (0.93–1.24)	0.352

Discussion

Early detection of lung cancer through screening programs before the onset of symptoms is of vital importance since according to the most recent global data published in 2022, lung cancer remains the most frequently diagnosed cancer worldwide and the leading cause of cancer-related mortality [20]. Two landmark randomized controlled trials, the National Lung Screening Trial (NLST) and the Dutch-Belgian NELSON (Nederlands-Leuvens Longkanker Screenings Onderzoek) trial, demonstrated that low-dose computed tomography (LDCT)-based lung cancer screening can reduce lung cancer–specific mortality by 20% and 24%, respectively [21, 22].

Current guidelines primarily define age and smoking history as the principal eligibility criteria for lung cancer screening, and these criteria are also most commonly applied in countries with established screening programs [23]. However, screening criteria vary among countries according to geographic characteristics and the target populations selected for screening [24]. Although a personal history of malignancy is recognized as a risk factor in lung cancer guidelines, it is not generally considered a formal screening indication. Nevertheless, previous malignancy is highly relevant both for the detection of pulmonary metastases and for the development of second primary lung cancer [25, 26]. Previous studies have shown that cancer survivors have a higher risk of developing second primary lung cancer compared with the general population, in addition to their risk of pulmonary metastatic disease [27]. This increased risk has been reported particularly among survivors of head and neck, bladder, breast, and hematological malignancies. However, many such patients do not meet conventional age or smoking-history thresholds and therefore remain outside current screening criteria [28–30]. Consistent with the

literature, the most common previous malignancies in our cohort were head and neck cancer and breast cancer. Among 36 patients with a prior cancer history, 20 were diagnosed with pulmonary metastases and 12 with second primary lung cancer. Moreover, multivariable analysis demonstrated that previous malignancy history was the strongest independent predictor of malignant pathology in resected nodules.

Although family history of cancer has been associated with increased malignancy risk in SPNs and is recognized as a lung cancer risk factor, it is still not included as a formal criterion in current screening guidelines [7, 10, 18]. However, prior studies have suggested that family history may be an important marker for early lung cancer detection, particularly in non-smokers. Lee et al. reported that family history of cancer significantly increased lung cancer risk in never-smokers, especially in individuals older than 45 years [31]. Furthermore, a meta-analysis confirmed a significant association between family history of cancer and lung cancer risk [32]. The major concern regarding incorporation of family history into screening criteria is the potential increase in overdiagnosis [33, 34]. For this reason, we included such patients only after careful multidisciplinary evaluation. In our cohort, family history of cancer was significantly more frequent in the benign nodule group, suggesting that perceived cancer risk may have prompted more intensive diagnostic workup and referral for surgery. Nevertheless, 19 of 34 patients with a family history were ultimately diagnosed with malignancy, indicating that this remains a clinically relevant subgroup. To minimize overdiagnosis and overtreatment, these patients should undergo meticulous preoperative evaluation by a MDT.

Lung cancer screening also carries several recognized disadvantages, including false-positive findings, psychological burden, radiation exposure, overdiagnosis, and overtreatment [35–38]. Economic burden, unnecessary surgery, and treatment-related morbidity further emphasize the need for cautious patient selection [39]. Previous screening studies have reported malignancy rates of only 1–5% among detected nodules [18, 40, 41]. In contrast, malignancy was identified in 69.6% of all patients in our cohort and in 76.9% of those meeting standard screening criteria. This substantially higher yield likely reflects the fact that our population consisted of surgically selected patients with solid nodules > 8 mm who had already undergone prior evaluation and were considered high-risk lesions. These findings also indicate that patients were carefully assessed preoperatively, MDT recommendations were appropriately followed, and unnecessary treatment was likely minimized.

Management algorithms for SPNs detected through screening represent a critical clinical decision-making process. According to the Fleischner Society 2017, British Thoracic Society 2015, and NCCN guidelines, pulmonary nodules are first categorized as solid, part-solid, or ground-glass lesions. Solid SPNs larger than 8 mm may be referred for surgical treatment according to validated risk models and MDT evaluation [7, 15, 42]. The Mayo Clinic, Brock, and Herder models are among the most widely used malignancy prediction systems. The British Thoracic Society recommends the Brock model as the initial tool and the Herder model for nodules with a malignancy probability > 10% [42]. Susam et al. compared these three models and found the Herder score to be the most accurate predictor of malignancy [43]. Similarly, although all three scores differed significantly between benign and malignant nodules in our study, the Herder model showed the greatest discriminatory difference.

Many factors are considered when evaluating malignancy risk in SPNs, including age, sex, cancer history, family history, upper lobe location, spiculation, and emphysema, all of which are incorporated into risk prediction models [44]. Erdogdu et al. identified SUVmax as the most important predictor of malignancy [45]. In our cohort, multivariable analysis incorporating variables significant in univariable testing demonstrated that male sex (OR: 4.31, 95% CI: 1.17–15.93, p = 0.029) and previous malignancy history (OR: 23.58, 95% CI: 3.48–159.80, p = 0.001) were independently associated with malignant nodules. These two factors remained statistically significant in the multivariable model after demonstrating significant associations in the univariable analysis. These findings suggest that male sex and a history of malignancy are two important parameters that should be taken into consideration when planning screening, surveillance, or treatment strategies.

This study has several limitations. First, its retrospective design introduces inherent bias. Second, although family history and previous malignancy were included as additional risk factors, other recognized factors such as radon exposure and occupational exposure could not be analyzed due to incomplete medical records. Third, the cohort consisted exclusively of patients who had already undergone surgical treatment, meaning that the study did not directly evaluate initial screening eligibility or surveillance decisions. Inclusion of patients at the end of the diagnostic pathway may also have introduced selection bias and may explain differences from broader screening cohorts. Lastly, in the multivariate analysis performed, we observed that some variables had a wide range of CI interval. Wide confidence intervals for some estimates likely reflect limited subgroup sample size.

In conclusion, although a national lung cancer screening program has not yet been implemented in our country, analysis of surgically treated patients meeting screening criteria demonstrated that careful selection can yield a high rate of malignant diagnoses. Every screened patient determined to have an SPN should ideally undergo individualized MDT assessment to guide surveillance or treatment decisions. In addition to age and smoking history, a personal history of malignancy may increase the probability that a detected pulmonary nodule is more likely to be malignant. In contrast, the higher frequency of family history in benign cases suggests that perceived risk may lead to more aggressive investigation and surgical preference. To avoid overtreatment, careful risk stratification remains essential before proceeding to invasive management.

Abbreviations

SPN, solitary pulmonary nodüle; CT, computed tomography; MDT, multidisciplinary team; FDG, fluorodeoxyglucose; PET, positron emission tomography; SUVmax, maximum standardized uptake value; OR, odds ratio; CI, confidence interval; LDCT, low-dose computed tomography.

Declarations

Ethics approval and consent to participate: The study protocol was reviewed and approved by Manisa Celal Bayar University Instutional Ethics Committee (approval date and number: February 25, 2026, and 20.478.486/3911). The study was conducted per the ethical principles of the Declaration of Helsinki. All patient data were anonymized before the analysis. Given the retrospective design and the use of anonymized data, the requirement for informed consent was waived by the ethics committee.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: AA: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. DY: Methodology, Supervision, Writing – review & editing. RGP: Investigation, Data curation, Writing – review & editing. All authors read and approved the final manuscript.

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