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Clinical and radiological findings in relation to histopathological results of pulmonary nodule resections

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ABSTRACT

Objective: Despite technological advances and well-defined clinical scoring, pulmonary nodule management still remains a controversial issue. Due to conflicting situations, many patients are referred to reference centers for evaluation.
The aim of this study is to reveal the relationship between clinical, radiological, and histopathological findings of patients with surgically resected pulmonary nodules who were followed-up by a multicisciplinary team at a 3rd level reference center.

Patients and Methods: Patients, who were followed-up by the multidisciplinary team and underwent surgical resection per the multidisciplinary team's recommendations between October, 2018 and December, 2021, were included in the study.

Results: A total 209 eligible patients were identified. 133 (63.6%) patients had solitary pulmonary nodules, 61 (29.3%) patients had 2-4 nodules and 15 (7.2%) patients had 5 nodules, 29 (13.9%) of patients had the largest nodule less than 1 cm diameter. According to nodule nature, solid nodules were detected in 154 (73.7%), subsolid in 43 (25.6%) and ground glass in 12 (5.7%) patients and malignant histopathology was detected in 107 (69.5%), 37 (86%) and in 8 (66.6%) respectively. Among twenty-nine (13.9%) patients with subcentimetric nodules, 16 (61.5%) patients were diagnosed with malignancy. Thirty-three (15.8%) patients showed no avidity in PET-CT scan of whom 4 (12.1%) were diagnosed with adenocarcinoma metastasis. Totally, 185 (88.5%) surgical procedures were performed by video assisted thoracic surgery (VATS), 24 (11.5%) patients needed thoracotomy without mortality. Multivariate analysis showed that previous malignancy history ($p<0.019$), diameter of a nodule (>1 cm) ($p<0.027$), emphysema in lung parenchyma ($p<0.003$), high Brock risk score ($p<0.011$), high Herder risk score ($p<0.001$), increased avidity of PET scan ($p<0.001$) were risk factors for malignancy.

Conclusion: Clinical scoring, radiological findings and patient history are important factors in the prediction of malignancy, but multidisciplinary follow-up, especially, in conflicting cases plays a critical role in terms of detecting malignancy. VATS is a safe surgical method that can be used for definitive diagnosis in these patients.

Keywords: Pulmonary nodule, Malignancy prediction, PET-CT, VATS

1. INTRODUCTION

Pulmonary nodules are common incidental findings on thoracic computed tomography (CT) and are still a problem in daily pulmonology practice [1]. The increasing and widespread use of CT scan has led to an increase in the number of patients followed-up for pulmonary nodules. Nodules may be secondary to benign diseases, but the primary concern is malignancies, for which early diagnosis and treatment options are crucial [2,3]. In contrast, it is not cost-effective to treat benign lesions with an additional cumulative radiation dose, especially over an extended period of time.

Several prediction models have been proposed to assess the malignant potential of clinical and radiological findings. Mayo Clinic [4], Veterans Association [5], Brock University [6] and Herder risk model [7] are the most common risk stratification models. Herder risk model also evaluates fluorodeoxyglucose

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(FDG) uptake in positron emission tomography-computed tomography (PET-CT). These models were found to be non-superior in a comparative study; the added value of PET-CT is undeniable for larger nodules but unclear for smaller nodules (<8mm) [8]. Especially, for indeterminate nodules, multidisciplinary follow-up, careful observation, and diagnostic testing are still strongly recommended [9].

The purpose of this study is to evaluate the clinical, radiological, and histopathological findings of patients with resected pulmonary nodules that were followed-up at a tertiary care center, compare the risk models, and determine procedure-related risk and complications.

2. PATIENTS and METHODS

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Marmara University School of Medicine Clinical Research Ethics Committee (date: 08.10.2021, approval number: 09.2021.1100).

All patients followed for pulmonary nodules and discussed in the multidisciplinary team (pulmonary medicine, thoracic surgery, radiology, oncology, nuclear medicine) meeting between October 2018 and December 2021 were evaluated retrospectively. Patients who underwent surgical resection per the multidisciplinary team's recommendations were included in the study.

Pulmonary nodules were described as spherical, well-circumscribed, and less than or equal to 3 cm in diameter radiologic opacities surrounded by lung parenchyma. Patients with nodules larger than 3 cm or with pleural effusion, atelectasis, enlarged lymph nodes (≥15mm), consolidation, or appearance of ground glass on lung parenchyma were excluded from the study. Patients with active malignancies of solid organs, with or without metastasis, were excluded from the study. Patients with prior malignancies who had been cured for more than 5 years and had no active findings were included in the study.

Age, gender, occupation, body mass index (BMI), smoking status (packet/year, former-current smoker), exposure to asbestosis and biomass, comorbidities, other medical diagnoses, duration of nodule follow-up, malignancy history (belong to the patient or patient's first-degree relatives), and radiological reports of thorax CT and FDG PET-CT scanning were extracted from medical records. FDG PET-CT avidity was measured on a four-point scale, based on no uptake, low (SUV_{max} ≤2.5), moderate (SUV_{max}:2.5-10), and intense (SUV_{max} ≥ 10) uptake. The probability of malignancy of the nodules was calculated using the Brock model and the Herder risk model. The Brock model incorporates clinical and radiologic variables including age, sex, family history of lung cancer, emphysema, nodule size, location (upper lobe), nodule type (part-solid, ground-glass), and the presence of spiculation [6]. The Herder model is built upon the Brock model by additionally integrating FDG PET-CT avidity (classified as none, low, moderate, or intense) [7].These models were used to calculate the probability of malignancy for each case, based on data extracted from the electronic medical records and imaging reports.

The history, clinical and radiological findings, and functional status of the patients were re-consulted by physicians of the multidisciplinary team with at least 10 years of experience, each as an expert in their fields. The patients were evaluated primarily by taking into account the current guidelines [10].

Histopathological diagnoses were obtained by surgical resection of nodules. The primary surgical procedure was video-assisted thoracoscopic surgery (VATS) performed by thoracic surgeons with at least 10 years of experience. Some patients required thoracotomy due to the localization of nodules, the results of intraoperative frozen biopsies, or the complications.

Statistical Analyses

Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 25.0 program. The distribution of variables was examined using histogram graphs and the Kolmogorov-Smirnov test. Descriptive analyses were presented using mean ± standard deviation or median, IQR (interquartile range) values. Categorical variables were compared using the Pearson Chi-square test. The Mann Whitney-U Test was used to compare non-parametric variables between two groups that did not show normal distribution. ROC (receiver operating characteristic) analysis was utilized to examine significant cut-off values for predicting malignancy for Brock risk and Herder risk scores. Results with a p-value below 0.05 were deemed statistically significant.

3. RESULTS

Demographics

A total of 209 eligible patients were identified. One hundred and thirty-five (64.6%) patients were male. The mean age was 61.7±11.4 years (range 26-88 years), the mean BMI was 23.7±3.1, and the mean Charlson comorbidity index was 5.2±3.2 [11]. There were no gender differences in these parameters. Fifty-six (26.8%) patients had no smoking history, the mean smoking history for men was 37.3±19.7 packet/year and for women was 27.8±11.9 pack/year (p<0.001). Six (2.9%) patients had direct asbestos exposure while eleven (5.3%) had biomass exposure. In total, 15 (7.2%) patients had a history of tuberculosis, 58 (28%) patients had a history of malignancy, and 9 (4.3%) of them had lung cancer in the past (Table I).

CT characteristics

According to nodule characteristics, 133 (63.6%) patients had solitary pulmonary nodules, 61 (29.2%) patients had 2-4 nodules and 15 (7.2%) patients had 5 nodules, 29 (13.9%) patients had the largest nodule with a diameter of less than 1 cm. Most patients had morphologically solid nodules [154 (73.7%)], subsolid appearance was detected in 43 (20.6%) patients, and 12 (5.7%) patients had nodules in pure ground-glass nature. The right upper lobe was the most common location for the largest nodule with 81 (38.8%) patients, followed by the left upper lobe with 55 (26.3%) patients, and the right lower lobe with 37 (17.7%) patients. Lung parenchyma revealed emphysema in 73 (35%) and fibrosis in 4 (2%) patients (Table I).

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Table I. *Baseline demographics and clinical data*

		n (%)
Gender, male		135 (64.5)
Malignancy history		92 (44)
Malignancy in first-degree relatives		145 (69.3)
Rheumatological disorder		4 (1.9)
Smoking history		153 (73.2)
Asbestos exposure		6 (2.9)
Biomass exposure		11 (5.3)
Nodule characteristics	Solid	154 (73.7)
	Subsolid	43 (20.6)
	Ground glass	12 (5.7)
Number of nodules	1	133 (63.6)
	2-4	61 (29.2)
	5	15 (7.2)
Location of nodules	Right lower lobe	37 (17.7)
	Right middle lobe	11 (5.2)
	Right upper lobe	81 (38.8)
	Left lower lobe	25 (12.0)
	Left upper lobe	55 (26.3)
Nodule Size	<1 cm	29 (13.9)
	≥1 cm	180 (86.1)
Presence of emphysema		73 (35)
Presence of fibrosis		4 (2)
PET-CT characteristics	Z0	33 (15.8)
	Z1	68 (32.5)
	Z2	47 (22.5)
	Z3	34 (16.3)
Brock risk score	Low	18 (8.6)
	Moderate	179 (85.7)
	High	12 (5.7)
Herder risk score	Low	51 (24.4)
	Moderate	84 (40.2)
	High	74 (35.4)
Surgery	Thoracotomy	24 (11.4)
	VATS	185 (88.5)
Postoperative complication		11 (5.2)
Malignant histopathology		151 (72.2)

PET-CT: positron emission tomography-computed tomography, Z0: no avidity, Z1: low uptake, Z2: moderate uptake, Z3: intense uptake, VATS: video-assisted thoracoscopic surgery

PET-CT characteristics

Positron emission tomography-computed tomography results were classified using the four-point intensity reading. Twenty-seven (12.9%) patients had no PET-CT evaluation, 33 (15.8%) patients showed no avidity (Z_0), 68 (32.5%) patients had low uptake (Z_1), 47 (22.5%) patients had moderate uptake (Z_2) and 34 (16.3%) patients had intense uptake (Z_3) (Table I).

Risk scores

Predicting the malignancy based on the Brock risk score, 18 (8.6%) patients were in the low-risk group, 179 (85.7%) in the moderate-risk group, and 12 (5.7%) in the high-risk group [12]. Herder risk scores were classified as low-risk in 51 (24.4%) patients, moderate-risk in 84 (40.2%) patients and high-risk in 74 (35.4%) patients [13] (Table I).

The coherence of the two tests was 46.4%. With a cut-off value of 12.7% for predicting malignancy, the Brock risk model demonstrated a sensitivity of 79.4% and a specificity of 62.1%. In contrast, the Herder risk test had a sensitivity of 69.5% and a specificity of 77.5% with a 26.5% cut-off value (Table II) (Figure I).

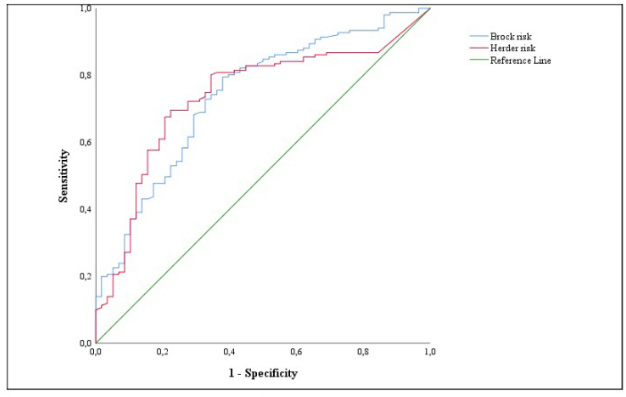

Figure 1. *Sensitivity and specificity of Brock and Herder risk scores*

Correlation of clinical and radiological findings for predicting malignancy

Comparison of clinical, radiological findings and risk scores between non-malignant and malignant pulmonary nodules are shown in Table III.

Table II. *Sensitivity and specificity of Brock and Herder risk tests according to malignancy prediction*

	AUC	SD	p-value	95% CI		Cut-off	Sensitivity	Specificity	PPV	NPV
				Upper limit	Lower Limit					
Brock risk score	0.739	0.038	**<0.001**	0.664	0.813	>12.75%	79.47%	62.07%	84.51%	53.73%
Herder risk score	0.736	0.038	**<0.001**	0.661	0.810	>26.50%	69.54%	77.59%	88.98%	49.45%

CI: Confidence Interval, AUC: Area under the curve, SD: Standard deviation, PPV: Positive predictive value, NPV: Negative predictive value

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Table III. *Comparison of clinical, radiological characteristics and risk scores between non-malignant and malignant pulmonary nodules*

	Malignancy		P
	No	Yes	
Age (mean±SD)	56.9±11.5	63.6±10.9	**<0.001**
BMI (mean±SD)	24.1±3.1	23.5±3.1	0.104
Charlson CI, median (IQR)	3 (1-5)	6 (3-9)	**<0.001**
Smoking history (pack year) (mean±SD)	29.5±13.5	37.5±22.0	**0.043**
Patients' age at nodule diagnosis, median (IQR)	53.5 (45-63)	62 (53-69)	**<0.001**
Size (mm), median (IQR)	12 (10-17)	15 (12-20)	**0.003**
Brock risk score, median (IQR)	8.6 (5.7-25.3)	27.2 (15.2-45.0)	**<0.001**
Herder risk score, median (IQR)	9.50 (1.10-25.30)	59.7 (17.1-88.0)	**<0.001**
Length of ICU stay (days), median (IQR)	1.5 (1-2.5)	1 (1-1.5)	0.291
Length of hospital stay (days), median (IQR)	3 (3-5)	6 (4-7)	**<0.001**

SD: Standard deviation, IQR: Interquartile Range, BMI: Body mass index, CI: Comorbidity index, ICU: Intensive care unit

Table IV. *Multivariate analysis of risk factors for malignancy*

		Malignancy		p value
		Yes	No	
		n (%)	n (%)	
Gender, male		37 (27.41)	98 (72.59)	0.881
Malignancy history		18 (19.57)	74 (80.43)	**0.019**
Malignancy in first-degree relatives		13 (20.31)	51 (79.69)	0.111
Rheumatological disorder		2 (50.00)	2 (50.00)	0.316
Smoking history		40 (26.14)	113 (73. 86)	0.391
Asbestos exposure		3 (50.0)	3 (50.0)	0.217
Biomass exposure		4 (36.36)	7 (63.64)	0.512
Nodule characteristic	Solid	48 (31.17)	106 (68.83)	0.076
	Subsolid	6 (13.95)	37 (86.05)	
	Ground Glass	4 (33.33)	8 (66.67)	
Number of nodules	1	37 (27.82)	96 (72.18)	0.859
	2-4	16 (26.23)	45 (73.77)	
	5	5 (33.33)	10 (66.67)	
Location of nodule	Right lower lobe	13 (35.14)	24 (64.86)	0.777
	Right middle lobe	3 (27.27)	8 (72.73)	
	Right lower lobe	22 (27.16)	59 (72.84)	
	Left lower lobe	5 (20.00)	20 (80.00)	
	Left upper lobe	15 (27.27)	40 (72.73)	
Size	<1 cm	13 (44.83)	16 (55.17)	**0.027**
	≥1 cm	45 (25.00)	135 (75.00)	
Presence of emphysema		11 (15.07)	62 (84.9)	**0.003**
Presence of fibrosis		2 (50.00)	2 (50.00)	0.316
PET-CT characteristics	No	7 (25.93)	20 (74.07)	**<0.001**
	Z0	24 (72.73)	9 (27.27)	
	Z1	16 (23.53)	52 (76.47)	
	Z2	8 (17.02)	39 (82.98)	
	Z3	3 (8.82)	31 (91.18)	
Brock risk score	Low	9 (50.00)	9 (50.00)	**0.011**
	Moderate	49 (27.37)	130 (72.63)	
	High	0 (0.0)	12 (100.00)	
Herder risk score	Low	26 (50.98)	25 (49.02)	**<0.001**
	Moderate	25 (29.76)	59 (70.24)	
	High	7 (9.46)	67 (90.54)	

PET-CT: Positron emission tomography-computed tomography, Z0: no avidity, Z1: low uptake, Z2: moderate uptake, Z3: intense uptake, VATS: video-assisted thoracoscopic surgery

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Age (p<0.001), Charlson Comorbidity Index (p<0.001), smoking history (p=0.043), patient's age at nodule diagnosis (p<0.001), size of nodule (p=0.003), Brock and Herder risk scores (p<0.001 and p<0.001, respectively) and the length of hospital stay (p <0.001) showed statistically significantly differences between patients with or without a malignant histopathological diagnosis.

Multivariate analysis showed that previous malignancy history (p<0.019), diameter of nodule (>1 cm) (p<0.027), presence of emphysema in the lung parenchyma (p<0.003), higher Brock risk score (p<0.011), higher Herder risk score (p<0.001), and increased avidity of PET-CT (p<0.001) were risk factors for malignancy (Table IV).

Surgical procedures

In total, 185 (88.5%) surgical procedures were performed by VATS, while 24 (11.5%) patients required thoracotomy. Twenty-eight patients (13.3%) were followed-up in the intensive care unit (ICU) due to pre-operatively planned comorbidities; 11 (5.3%) patients required ICU stay due to post-operative complications during hospitalization (4 pulmonary embolism, 3 atelectasis, 1 pneumonia, 1 pneumothorax, 1 pulmonary artery injury, 1 urinary sepsis); however, no mortality was observed. For the entire study population, the median length of hospital stay was 5 (2-12) days and the median length of ICU stay was 1 (1-4) day.

According to histopathological diagnoses, the median (IQR) hospital stay for patients with benign nodules was 3 (3-5) days and for patients with malignant nodules was 6 (4-7) days (p<0.001); for the length of ICU stay, it was 1 (1-2.5) day and 1 (1-1.5) day respectively (p=0.291).

Histopathological results

One-hundred fifty-one patients were diagnosed with malignancy with the most common type of primary adenocarcinoma of the lung (61 (40.4%) patients), while 51 (33.8%) patients had metastasis of primary carcinomas other than the lung, 20 (13.2%) patients had squamous cell carcinoma. Metastases mostly originated from the breast in 16 (31.3%), colon in 2 (23.5%), sarcoma in 8 (15.6%), and bladder in 5 (9.8%) patients.

Anthracosis was the most common benign histopathology with 25 (43.1%) patients, followed by chondroid hamartoma with 15 (25.9%), and granulomatous reactions with 4 (6.8%) patients.

Twenty-nine (13.9%) patients had subcentimetric nodules, of which 16 (55.17%) were diagnosed with malignancy. The most common malignancy was adenocarcinoma while anthracosis was the most common benign diagnosis.

Thirty-three (15.8%) patients showed no avidity in PET-CT scan, and 4 (12.1%) were diagnosed with metastatic adenocarcinoma.

According to morphological characteristics, 154 (73.7%) nodules had solid appearance, 43 (20.6%) had subsolid and 12 (5.7%) had ground glass morphology. One hundred and six (68.83%) patients with solid nodules were diagnosed with malignancy. Metastasis of other carcinomas (46 (30%)), adenocarcinoma (33 (21%)), and squamous cell carcinoma (12 (8%)) were detected as the common types. Anthracosis and chondroid hamartoma were seen in 17 (11%) and 15 (9%) patients respectively as the most common benign pathologies in solid nodules.

Thirty-seven (86.05%) patients with subsolid nodules were diagnosed with malignancy. Adenocarcinoma (24 (56%)), squamous cell carcinoma (8 (19%)), and metastasis of other than lung carcinomas (3 (7%)) were common malignant diagnoses in this group and anthracosis (4 (9%)) was in the benign group.

Only 4 (33.33%) patients with ground-glass nodules had benign diagnoses, the malignancy rate in this group was 66.67%. Adenocarcinomas (4 (49%)) and metastasis of other than lung carcinomas (2 (17%)) were mostly detected as malignant diagnoses. Morphological characteristics and histopathological diagnoses are shown in Figure 2.

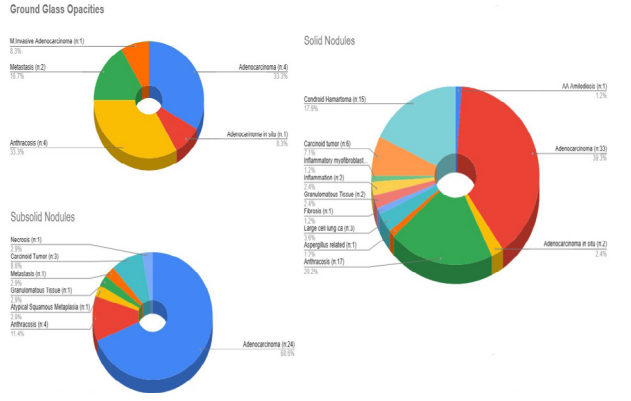

Figure 2. *Histopathological diagnosis of nodules according to CT characteristics*

4. DISCUSSION

In this study, 209 patients with pulmonary nodules were clinically, radiologically, and histopathologically evaluated. Most nodules were solid (73.7%) and predominantly located in the right upper lobe (38.8%). Increased PET-CT avidity was associated with malignancy. Brock and Herder risk scores were significant in malignancy prediction, with Herder showing higher specificity (77.5%) and Brock demonstrating higher sensitivity (79.4%). Independent risk factors for malignancy included a history of malignancy, nodule size >1 cm, presence of emphysema, higher risk scores, and increased PET-CT avidity. Adenocarcinoma was the most common histopathological diagnosis (40.4%), followed by metastatic lesions (33.8%).

Even though, the frequency of incidental pulmonary nodules is on the rise, there are still challenging and controversial aspects in their management [14]. While, the majority of centers select the most appropriate, cost-effective and patient-centered method of follow-up, the follow-up criteria also adapt to the changing technological capabilities.

In this article, we evaluated the patients who applied or were referred to a tertiary care hospital for follow-up on incidental

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nodules and who underwent surgical resection on the recommendation of a multidisciplinary team due to a high likelihood of malignancy.

We demonstrated that a history of malignancy, the diameter of the nodule (>1 cm), emphysema in the lung parenchyma, a high Brock risk score, a high Herder risk score, and an increased avidity of PET-CT scan were all risk factors for malignancy. Literature identifies age, smoking history, diameter of the nodule, and upper lobe location as risk factors for malignancy [5,15]. The anticipated reason for the upper lobe location not being a risk factor in our study may be associated with common infection, tuberculosis, and smoke or biomass exposure in our country, which is supported by the frequency with which anthracosis and granulomatous reactions were detected in histopathologically benign diagnoses.

The presence of pulmonary parenchymal emphysema was found to be associated with a high risk, indicating that emphysema is a severe complication of smoking, and that these patients tended to be at a higher risk for cancer [16].

In the current study, we used the Brock and Herder risk models to identify the risk groups as described in Shultz et al., Mayo Clinic and Veterans Affairs (VA) models appear inadequate, particularly at the point of making a clinical decision [17]. The coherence between the Brock and Herder risk scores was 46.4% when compared. In the Brock risk score, the majority of patients were classified in the moderate-risk group whereas in the Herder risk score, the proportion of moderate and high-risk patients was nearly equal. These results also align with those of Ameri et al [8]. The Herder risk model has a tendency toward greater dependability, which is consistent with the literature [1,8,18]. This study also revealed that 33 (15.8%) patients had no uptake avidity on PET-CT scan, while 4 (12.1%) were diagnosed with malignancy and their nodule diameters were also less than 1 centimeter. PET-CT scans are recommended by the American College of Chest Physicians for patients with a diameter of 8-10 mm who have a low to moderate pre-test probability of malignancy [19]. Predictive models may be insufficient, particularly for low-risk patients [7]. If the pretest probability is low and PET-CT is negative, malignancy risk is usually low (2%) and follow-up is suggested but if the pretest is in the high-risk group and PET-CT is negative, risk for malignancy is approximately more than 10% and biopsy or resection should be considered [20]. In our study 33 (15.8%) patients with negative PET-CT results had surgical nodule resection due to high-risk group classification based on the Herder model, and 4 (12.1%) patients were diagnosed with malignancy, which is consistent with the literature.

The VATS technique is widely utilized worldwide for both diagnosis and treatment. The main indications include mediastinal and pleural biopsies, wedge resection, treatment of pneumothorax, and pleurectomy. Recently, segmentectomy, lobectomy, and pneumonectomy were added to the list of surgical procedures that can be performed using this technique [21]. VATS can be used to resect peripherally located solitary pulmonary nodules with fewer complications, a shorter hospital stay, and a shorter convalescence [22]. Thoracotomy carries a 3 to 4 percent mortality rate for resection of a malignant solitary pulmonary nodules and a 0.3 percent mortality rate for resection of a benign nodule [23].

The literature indicates that the complication rate of VATS technique ranges – between 3.2% and 4.3% [23-25]. The most common complications are prolonged air leakage, bleeding, atelectasis, cardiac arrhythmias, pneumonia, and wound infections [24]. Similarly, Imperatori et al., demonstrated identical complication rates with a 0.6% mortality rate [21]. Conversion to thoracotomy range may vary between 1.04% and 33.1% based on the indication for surgery or complication [26,27]. In our study, the overall complication rate was 5.3% without mortality and conversion to thoracotomy was 11.5%. Thoracotomy is required in 24 patients, all for definitive surgery excluding a patient with complications. The fact that our center was a reference center and the patients were relatively complicated cases with high Charlson comorbidity indices may have affected the results, given the higher complication rates. Another possible explanation is that we accepted every unexpected medical condition after surgery as a complication, such as urinary tract infection or atelectasis caused by secretions. Bleeding, arrhythmia, prolonged air leakage, and wound infection, which are anticipated to occur more frequently in the postoperative period, were not observed in our study.

Subsolid structured nodules are made of ground glass and have a partially solid appearance. Malignant subsolid nodules are typically diagnosed as adenocarcinomas and are expected to grow more slowly than malignant solid nodules [28]. Kakinuma et al., monitored 439 patients with pure ground glass nodules smaller than 6 mm and found that 45 (10.3%) grew and 4 (0.9%) developed adenocarcinomas [29]. In another series of 226 patients with subsolid nodules, 4.1% of pure ground-glass nodules and 70% of subsolid nodules with more than 25% solid components were malignant [30]. Solid, subsolid, and ground glass appearance were, in order, the most prevalent radiologic nodule appearances in our study. The majority of solid and subsolid nodules, along with 66.6% of ground-glass nodules, were diagnosed with malignant histopathology. The high rate of malignancy in ground-glass nodules in our study is due to the fact that these patients were sampled by a multidisciplinary team that considered not only radiologic but also clinical characteristics and risk factors. In addition, there were 29 (13.9%) patients with subcentimetric nodules, among these patients, 16 (61.5%) patients were diagnosed with malignancy. Furthermore, 33 (15.8%) patients showed no avidity on PET-CT scans, but among these 33 patients, 4 (12.1%) patients were diagnosed with adenocarcinoma metastasis. The biopsy decisions of the patients in this group were made after multidisciplinary evaluation, despite the fact that they belong to low-risk clinical scoring or radiological evaluation groups.

According to histopathology, 33.8% of the nodules were metastases of cancers other than the lung carcinomas, with the majority originating from breast, colon, sarcomas, and bladder. Similarly, Ginsberg et al., also reported the VATS results of 426 patients with nodules. The number of patients with primary known tumors was 315 and most of the resections originated

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in breast, colon, lymphoma, bladder, and sarcoma respectively [31].

Considering the limitations of our study, some data were lost due to the fact that it was primarily a retrospective study. Due to the change in our hospital's registration system, the files of a subset of the patients who were screened could be accessed. For this reason, the number of patients remained lower compared to other studies in the literature that made similar evaluations. The radiological criteria evaluated in our study were not assessed by a single radiologist, and the evaluations made on official reports were recorded. Therefore, other potential radiological parameters could not be utilized in this study. The absence of a single physician's evaluation can be cited as a separate source of bias. Nodules extracted surgically were evaluated in this study. Transthoracic fine needle aspiration biopsies, tru-cut biopsies, or central endoscopic interventions were excluded from this study due to the fact that they were performed by multiple different physicians. Surgical interventions were performed by a thoracic surgery team with diverse educational backgrounds and academic designations. Despite the absence of mortality, postoperative complications and morbidity may have affected the results.

Conclusion

In this retrospective study, the risk factors for malignancy were found as a history of malignancy, the diameter of nodules, emphysema in the lung parenchyma, a high Brock risk score, a high Herder risk score, and increased avidity of PET-CT scan. VATS is a secure and definitive sampling technique for nodules. Multidisciplinary evaluation and decision making is vital in reference centers.

Compliance with Ethical Standards

Ethical approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Marmara University School of Medicine Clinical Research Ethics Committee (date: 08.10.2021, approval number: 09.2021.1100).

Conflict of interest: The authors declare that there is no conflict of interest.

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