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ORIGINAL ARTICLE

Outcomes of multidisciplinary management of pulmonary nodules in a tertiary center

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ABSTRACT

Objective: A multidisciplinary approach is recommended for managing pulmonary nodules. This study aimed to examine the malignancy rates, malignancy determinants, and follow-up results of patients with pulmonary nodules whom the multidisciplinary team evaluates.

Methods: Clinical characteristics of the patients, radiological and histological characteristics of the nodules, and the follow-up outcomes were documented retrospectively. A total of 94 patients with solitary pulmonary nodules (SPNs) (n=58) and multiple pulmonary nodules (MPNs) (n=36) were included in the study.

Results: Our study showed that malignancy risk increased with irregular nodule margins ($p < 0.008$). Patients who had tissue sampling from suspected nodules exhibited markedly higher rates of previous malignancy than those who did not (58.5% vs. 19.5% $p<0.001$). For the patients with solitary pulmonary nodule (SPN), the group for whom biopsy was planned had more underlying malignancy ($p=0.011$) and had a bigger nodule size of 10 mm (range, 8.0-13.25 mm) vs 15.00 mm (range, 10.0-19.75 mm) ($p=0.003$). Among the patients who have multiple pulmonary nodules (MPN), eighty-four percent of patients in the biopsy group had underlying malignancy diagnoses, whereas this rate was 26% in the CT follow-up group ($p=0.002$). Adenocarcinoma was the most common SPN histology and squamous cell carcinoma for MPNs. The Multidisciplinary Thoracic Oncology Board identified malignancy in 60% of patients with SPNs and 92.3% of those with MPNs/

Conclusions: Patients evaluated in the multidisciplinary tumor board consist of a very diverse patient group. Discerning between malignant and benign conditions relies heavily on examining nodule features and assessing malignancy history.

Keywords: pulmonary nodule, multidisciplinary board, multiple pulmonary nodules.

INTRODUCTION

Pulmonary nodules are frequently discovered incidentally during CT scans performed for other reasons, and the frequency of nodule detection on a given scan increased from 24 to 31% [1,2]. In patients with a solitary pulmonary nodule (SPN), the overall frequency of malignancy ranges from 2% to 23% [3]. Various guidelines have been published to evaluate pulmonary nodules [4-6]. Tumor boards provide the highest level of patient evaluation for complex cases. Multiple studies have indicated that multidisciplinary care benefits patients with malignancy[7-9]. Although most Multidiciplinary Throacic Oncology Boards (MTB) adhere to guidelines, some judgments deviate owing to patient characteristics [10]. All characteristics should be taken into account when evaluating the risk of malignancy in this complex patient population. At our center, patients reviewed

by the board undergo a comprehensive evaluation using a multidisciplinary approach based on current guidelines. This study aimed to examine the malignancy rates, malignancy determinants, and follow-up results of patients with pulmonary nodules whom the Hacettepe University Medical Faculty Thoracic Oncology Board evaluated.

METHODS

This study was designed retrospectively, and the Hacettepe University Medical Faculty Ethics Committee, Turkey, approved the study protocol (13.02.2013, LUT 12/163-11). Patients with pulmonary nodules that evauated by The Multidisciplinary Board that held weekly with representatives from Chest Diseases, Cardiovascular and Thoracic Surgery, Radiology, Radiation Oncology, Nuclear Medicine, and Pathology at Hacettepe University between June 2003 and February 2013 included to the study. The patients with solitary pulmonary nodules (SPNs) and multiple pulmonary nodules (MPNs) were recorded. Age, gender, smoking habits, history of other malignancies, and the results of thorax CT scans of the patients, nodule characteristics, pathology results examined. Dominant nodule was sampled for patients with multiple nodules. The follow-up results and post-procedure complications recorded. The study examined the incidence of malignancy in patients who had diagnostic testing and calculated the efficacy of the MTB in detecting malignancies.

The Statistical Package for the Social Sciences (SPSS) Ver. 18 program was used for the statistical analyses; categorical variables were calculated using frequency, and continuous variables were calculated using median and standard deviation. Nominal variables were analyzed using the Chi-square test, and the interval variables of the two groups were analyzed using the t-test. A p-value of <0.05 was considered significant.

RESULTS

A total of 94 patients, 58 with SPN and 36 with MPN were included in the study. Of the 58 patients with SPNs, 30 were advised to undergo surgical biopsy, 10 were suggested to undergo transthoracic biopsy, and the remaining 18 underwent thorax CT scans for follow-up per the Board's directive.

Out of the total cohort of 36 patients identified with multiple pulmonary nodules (MPNs), surgical intervention was advised for nine patients, while transthoracic biopsy was deemed appropriate for four patients. The remaining 23 subjects were suggested to undergo follow-up examinations with computed tomography (CT) scans. Sankey diagram of study is shown in Figure 1.

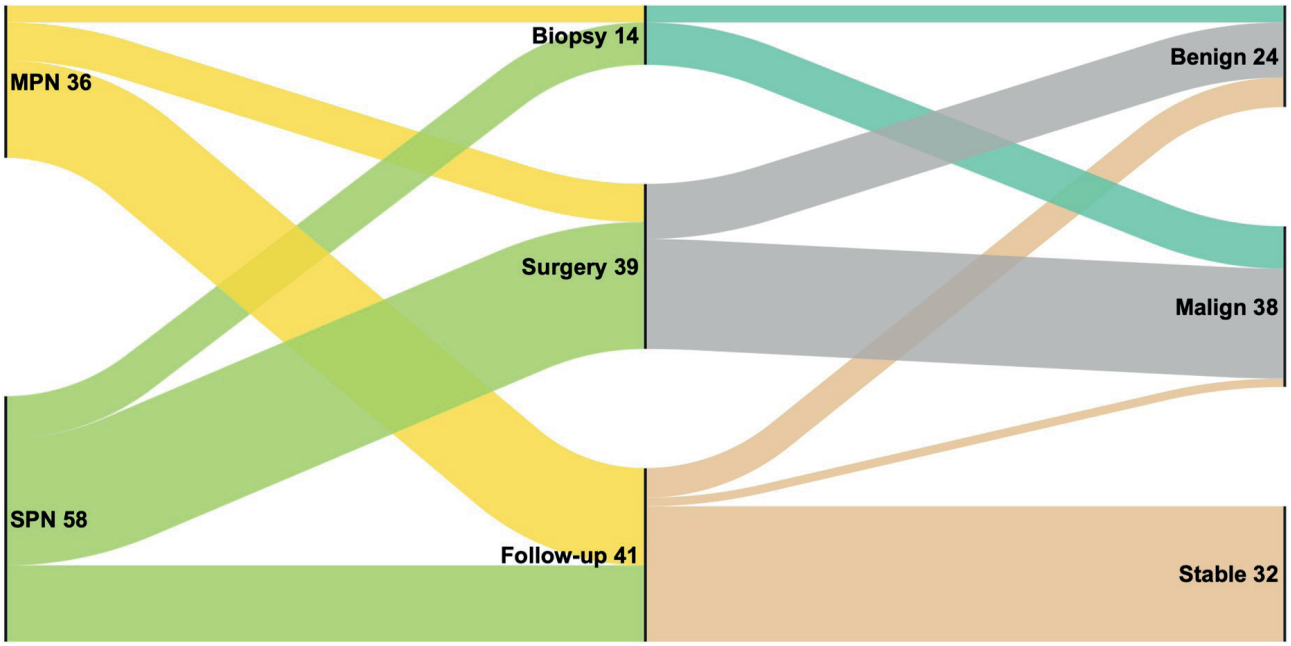

Figure 1. Sankey diagram of outcome of all the pulmonary nodules evaluated by Multidisciplinary Thoracic Oncology Board. SPN: Solitary pulmonary nodule, MPN: Multiple pulmonary nodule. (Numbers represent the number of patients in the relevant group).

The mean age of the patients was 62 years. Thirty-two (34%) of the patients were women, and 62 (66%) were men. The demographic characteristics of all patients were categorized based on whether they had tissue sampling. Patients who had tissue sampling exhibited markedly higher rates of previous malignancy than those who did not (58.5% vs. 19.5% p<0.001). Among patients with SPN, for whom biopsy was planned, 50% of patients had underlying malignancy diagnoses, whereas this rate was 11% in the follow-up group (p=0.011). The mean nodule size of patients in the follow-up group was 10 mm (range, 8.0-13.25 mm) [6-19], whereas it was 15.00 mm (range, 10.0-19.75 mm) [6-26] in the biopsy group (p=0.003) (Table 1).

Thirteen (81.3%) of the sharp-borders SPNs were benign, and 8 (33.3%) were malignant. Three irregular-borders SPNs were benign (18.8%), and 16 were malignant (66.7%). SPNs with irregular borders revealed a higher prevalence of malignant histology (p=0.008) (Table 2).

Twenty-one nodules were identified in the upper lobes; however, no significant relation with the location was confirmed in terms of being malignant or benign (p=0.50).

The pathologic results of all three spiculated nodules were determined as malignant. According to the pathology results, 16 nodules had benign histology, and 24 were malignant. Although patients with malign histology had more smoking history, these associations weren't statistically significant. When evaluating the pathology results of patients with SPNs, benign causes were diagnosed in 16 patients, and malignant etiology was diagnosed in 24 patients. Adenocarcinoma (54.6%) was identified most commonly among the malignancies, followed by squamous cell (12.5%) ca and typical carcinoid (12.5%). Chronic inflammation/fibrotic causes (37.5%) were identified most frequently among benign causes, followed by chondroid hamartoma (25%), necrotizing granulomatous inflammation (25%), and lung parenchymal tissue (12.5%).

Table 1. Comparison of baseline characteristics of patients with SPN and MPN who underwent tissue sampling and were followed up

	Patients with Solitary Pulmonary nodule (n= 58)			Patients with Multiple Pulmonary nodule (n=)		
	Follow- up (n: 18)	Tissue sampling (n: 40)	p value	Follow- up (n: 23)	Tissue sampling (n: 13)	p value
Age, (mean±SD) years	66±13.7	59.7±12.4	0.058	64.26±11.17	62.69±14.20	0.71
Sex, n (%)						
Male	14 (77.8)	26 (65.0)	0.50	17 (73.9)	5(38.5)	0.082
Female	4 (22.2)	14 (35)		6 (26.1)	8(61.5)	
Smoking history +, n, (%)	9 (50.0)	24 (60.0)	0.67	12 (52.2)	4 (30.8)	0.37
Pack/years, (mean±SD*)	35.22±25.17	28.13±30.49	0.45	21.36±10.53	9.50±2.51	0.04
COPD, n, (%)	3 (16.7)	12 (30.0)	0.45	4 (17.4)	5 (38.5)	0.317
Emphysema, n, (%)	5 (27.8)	14 (35.0)	0.81	7 (30.4)	5 (38.5)	0.90
Underlying malignancy, n, (%)	2 (11.0)	20 (50.0)	**0.011**	6(26.1)	11 (84.6)	**0.002**
Nodule size, mm, range, median (IQR**)	10 (8.0-13.25) [6-19]	15.0 (10.0-19.75) [6-26]	**0.003**	N/A		
Nodule type, n, (%)				N/A		
Non-solid, ground glass	2 (11)	14 (35)	0.117	N/A		
Solid	16 (88.9)	26 (65)		N/A		
Egde type, n, (%)				N/A		
Irregular	6 (33.3)	19 (47.5)	0.47	N/A		
Sharp	12 (66.7)	21 (52.5)		N/A		
Nodule localization, n, (%)				N/A		
Upper lobes	12 (66.0)	18 (45)	0.21	N/A		

*SD standart deviation ,N/A not applicable

** Interquartile range

Table 2. Demographic and radiological characteristics of patient wtih SPN according to pathology

	Benign (n: 16)	Malign (n: 24)	p value
Age, (mean±SD*) years	58.1±7.6	60.7±14.9	0.52
Sex, n (%)			
Male	10 (62.5)	16 (66.7)	1.00
Female	6 (37.5)	8 (33.3)	
Smoking history, n, (%)	6 (37.5)	10 (41.7)	1.00
Pack/ years,(mean±SD*)	24.1±17.7	30.5±22.5	0.56
COPD, n, (%)	5 (31.3)	7 (29.2)	1.00
Emphysema, n, (%)	6 (37.5)	8 (33.3)	1.00
Underlying malignancy, n, (%)	5 (31.3)	15 (62.5)	0.10
Nodule size mm, range, median (IQR**)	15 (10.5-18.0) [9-22]	16.5 (10.0-24.25) [6-26]	0.45
Nodule type, n, (%)			
Non-solid, ground glass	6 (37.5)	8 (33.3)	1.00
Solid	10 (62.5)	16 (66.7)	
Egde type, n, (%)			
Irregular	3 (18.8)	16 (66.7)	**0.008**
Sharp	13 (81.3)	8 (33.3)	
Nodule localization, n, (%)			
Upper lobes	7 (43.8)	15 (62.5)	0.50
Right middle lobe	3 (18.8)	3 (12.5)	
Lower lobes	6 (37.5)	6 (25.0)	

*Standart deviation

** Interquartile range

The mean follow-up duration of nodules was 6-12 months (range, 3-36 months). It was confirmed that two nodules disappeared after 3 months, and two regressed. Among the patients with MPNs, 84% of patients in the biopsy group had underlying malignancy diagnoses, whereas this rate was 26% in the CT follow-up group (p=0.002). Also, it was similar for the patients with MPN; the most common malign pathology among multiple nodules was adenocarcinoma (33.3%), and one patient that was diagnosed as benign was chronic inflammation. Nodules disappeared in 3 of the 23 follow-up patients, and one of the nodules grew in one patient. The growing nodule was identified as malignant using transthoracic biopsy. Nineteen patients' nodules were stable. Considering that the patients who underwent tissue biopsy were predicted to be malignant, the malignancy detection success of the MTB was 60% for SPN and 92.3% for MPN. One of the 18 follow-up patients with an SPN was determined to have a malignant disease. Post-procedure pneumothorax in 2 patients, air leak in 3 patients, pneumonia in 1 patient, and renal dysfunction in 1 patient was observed.

DISCUSSION

Over the past ten years, there has been a consistent rise in the detection of incidental pulmonary nodules on chest CT scans, which has been linked to an increase in the number of stage I lung cancer diagnoses[11]. Guidelines recommend discussing patients with malignancy suspicion by multidisciplinary tumor boards. According to previous studies, a multidisciplinary approach is the most effective way to provide patients with suspected malignancy [7,12] Multidisciplinary tumor boards are supposed to enhance overall treatment and results for patients at high risk; MTB recommendations deviate from the management clinicians' original plan [13].

According to a study; age, female sex, cancer background in the family, emphysema, large nodule size, nodule being in the upper lobe, being half-solid, being few, and spiculation were predictors for cancer risk [14,4]. In a large series of studies, results show that nodules in the upper lobe increase the risk of malignancy [15,16,7]. This may be related to more carcinogens being inhaled in the upper lobes, depending on smoking. In our study,

the majority of malignant solitary nodules (62.5%) were located in the upper lobes. In a recent study among individuals with SPNs, smoking increased the probability of developing lung cancer in men. However, there was no substantial correlation found between smoking and the diagnosis or mortality of lung cancer in women with an SPN [17]. This may be related to more carcinogens being inhaled in the upper lobes, depending on smoking. In our study, most malignant solitary nodules (62.5%) were in the upper lobes. In a recent study among individuals with SPNs, smoking increased the probability of developing lung cancer in men. However, there was no substantial correlation found between smoking and the diagnosis or mortality of lung cancer in women with an SPN [18]. A recent meta-analysis, only centrilobular emphysema was significantly associated with lung cancer [19]. These results support the existence of different malignancy variables for different patient groups. Similarly, in our study, there was no significant relation between smoking, COPD, and radiologic emphysema diagnosis in patients with malignant and benign results, but all nodules with spiculated borders were found to be malignant, and irregular-edged SPNs showed significantly more malignant features when compared with those with smooth edges. A study investigating the clinical practice consensus guidelines for Asia has found that the populations used to validate the models for assessing pretest may not be accurate when applied to Asian populations due to several factors including high rates of granulomatous and other infectious diseases, air pollution, and the occurrence of lung cancer among nonsmokers [20]. This result supports the finding that unique characteristics can be seen in different patients subgroups including multidisciplinary board patients.

The present study determined malignancy histopathologically in 38 (40.4%) patients. The pathology results of 13 (32%) of 40 patients with SPNs and 5 (38%) of 13 patients with multiple nodules who underwent biopsy were diagnosed as adenocarcinoma. Similar to our study, in a study by Gould et al., most SPNs were diagnosed with adenocarcinoma (50%). The increased solid content in ground-glass nodules shows more invasive pathologic conditions [14]. A study shows sub-solid lesions have a 34% malignancy risk, whereas solid lesions have 7% [21]. In our study, the pathology of malignant SPN patients who had a malignancy history showed 40% cancer metastasis, 35% primary lung cancer, and 25% benign pathology. According to a study examining the surgical results of 131 patients with solitary pulmonary nodules with a previous cancer history, metastases were detected in 65 patients, primary lung cancer in 57 patients, and benign lesions in 9 patients [22].

Our study observed benign pathology in 40% of patients with SPNs who underwent sampling. The MTB had a 60% success rate in identifying cancer in patients who underwent tissue sampling and were expected to have malignant diseases. This rate was 92.3% for patients with MPN. Although the general frequency of malignancy in patients with solitary pulmonary nodule (SPN) varies between 2% and 23% in the literature [3], the high rate of malignancy observed in MTB in our study supports that tissue biopsy should be prioritized for the diagnosis of malignancy in MTB patients, even if the patients do not have other malignancy criteria.

The primary limitation of this study is the limited sample size. The lack of significance of malignancy-risk variables in our study can be attributed to the fact that our study did not screen and instead focused on a specific population. The patient cohort deliberated by the MTB exhibits a higher prevalence of comorbidities and necessitates the implementation of interdisciplinary techniques for both diagnosis and therapy. Furthermore, our research was limited to the available data because we used existing data from hospital records. Therefore, the study could not include additional important information, such as the effects of PET CT.

CONCLUSIONS

Multidisciplinary board patients present unique subgroup characteristics. When deciding on the light of the guidelines, it should be kept in mind that the patient group may not show classical features due to its complexity, and a patient-specific plan should be made.

Author contribution

Study conception and design: OOA, AUD, and ZTS; data collection: OOA ; analysis and interpretation of results: OOA and AUD; draft manuscript preparation:

OOA, AUD and ZTS. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Clinical Research Ethics Committee of Hacettepe University. (Protocol no: LUT 12/163-11, 13.02.2013)

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Conflict of interest

The authors declare that there is no conflict of interest.

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