

Follow-up of Solitary Pulmonary Nodules at Mater Dei Hospital

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Abstract

Background: Solitary Pulmonary Nodules (SPNs) are a very common diagnostic challenge. Under-evaluation may delay the diagnosis of early lung cancer whilst over-evaluation increases expenditure and radiation, as well as increases patient concerns and anxiety. The aim of this audit was to evaluate whether the Fleischner Society Recommendations¹ are adhered to in the follow-up of SPNs locally.

Methodology: This retrospective study included SPNs diagnosed incidentally on Computed Tomography (CT) between January 2013 and December 2014, excluding patients with a history of malignancy. The follow-up of the nodules was compared with Fleischner Society Recommendations (FSR) as the gold standard, which stratifies nodules based on size and smoking history.

Results: From a cohort of 100 patients, guideline-concordant care was identified in 48%. SPNs were under-evaluated in 32% of cases, while over-evaluation occurred in 20% of the total. From the patient cohort, lung malignancy was diagnosed in 31%. The risk of malignancy increased with increasing nodule size (0% in ≤ 4 mm, 1% in $>4-8$ mm, and 30% in >8 mm). The risk of malignancy was 39.5% in current smokers, 47.8% in ex-smokers and 29.4% in non-smokers.

Conclusion: Our data confirm that the risk of malignancy increases with the size of the nodule, and this reflects international figures. It is the responsibility of the ordering physician to include the correct smoking history when requesting imaging. Appropriate specific booking request information and standardised medical imaging reporting systems should be implemented to ensure adequate follow-up of SPNs according to international recommendations.

Introduction

A Solitary Pulmonary Nodule (SPN) is defined as a discrete, well-marginated, rounded pulmonary opacity less than or equal to 3 cm in diameter that is completely surrounded by lung parenchyma, does not touch the hilum or mediastinum, and is not associated with adenopathy, atelectasis or pleural effusion.²

SPNs are an increasingly common radiological finding on Computed Tomography (CT) since the improvement in spatial resolution of CT scanners has led to the detection of smaller and smaller nodules. The reported incidence of SPNs on CT is up to 51% in smokers aged 50 years or older.¹ Such incidental lung nodules represent a diagnostic challenge to physicians. Most pulmonary nodules are not malignant, however follow-up is essential since suspicious lesions may be biopsied early, leading to timely intervention. Radiological features of the SPN, including size, morphology, and rate of growth, help to determine the likelihood of malignancy.¹

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Both under-evaluation and over-evaluation of SPNs are potentially harmful. Under-evaluation may delay the diagnosis of early lung cancer. On the other hand, over-evaluation may increase expenditure and radiation. This may also increase patient anxiety, leading to unnecessary physical and emotional damage.³⁻⁵ The Fleischner Society is an international, multidisciplinary medical society for thoracic radiology, dedicated to the diagnosis and treatment of diseases of the chest, which was founded in 1969.⁶ The society first issued recommendations for the management and follow-up of solid SPNs in 2005, focusing on nodules which were solid, <8mm in size, in individuals above 35 years of age, and which were found on CT scans requested for non-screening purposes.¹ In 2013, the society published guidelines for the management of sub-solid nodules, which refers to both non-solid nodules (ground glass) and partly solid nodules (part solid, part ground glass).⁷ In

2017, the society updated their guidelines for both solid and sub-solid nodules.⁸ At the time of our data collection, the 2005 Fleischner Society Recommendations (FSR) were the mostly widely used guidelines in the follow-up of incidental lung nodules. The FSR 2005 stratify SPNs based on size of nodule and patient risk, and suggest the appropriate follow-up time-frame for each category of patients (Table 1). A high risk patient signifies the presence of smoking history, history of lung cancer amongst first-degree relatives, and/or exposure to asbestos, uranium or radon. A low risk patient is defined by minimal or absent smoking history and pollutant exposure, and absence of family history of lung cancer. The 2005 recommendations refer to completely solid nodules, while noting that sub-solid nodules may require longer follow-up to exclude indolent adenocarcinoma.¹

Table 1: Fleischner Society Recommendations

Size of Nodule (mm)	Low Risk Patient	High Risk Patient
≤4mm	No follow-up required	CT in 12 months. No further investigations if CT remains unchanged.
>4-6mm	CT in 12 months. No further investigations if CT remains unchanged.	First follow up in 6-12 months then in 18-24 months if CT scan remains unchanged
>6-8mm	First follow up in 6-12 months then in 18-24 months if CT scan remains unchanged	First follow up in 3-6 months then in 9-12 months and 24 months if CT scan remains unchanged
>8	CT scan in 3, 9 and 24 months, dynamic contrast-enhanced CT, PET +/- biopsy	CT scan in 3, 9 and 24 months, dynamic contrast-enhanced CT, PET +/- biopsy

Excluding:

- individuals younger than 35 years
- History of intrathoracic or extra-thoracic malignancy
- Those with hilar lymph nodes
- Masses larger than 3cm
- Immunocompromised individuals

Adapted from: Guidelines for Management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society, MacMahon H, Austin JH, Gamsu G, Herold CJ, Jett JR, Naidich DP, Patz EF Jr, Swensen SJ, Radiology, 2005 Nov; 237(2):395-400.

Method

Study Design

Approval was obtained from the Data Protection Office at Mater Dei Hospital, and the University Research Ethics Committee (UREC) at the University of Malta. A search was performed on PACS® for the keyword 'nodule' in the reports of all CTs performed during the years 2013 and 2014. SPNs diagnosed incidentally on CT (both thoracic and non-thoracic) between January 2013 and December 2014 were included in the study. The following nodules were excluded: age less than 35 years, sub-solid nodules, known history of malignancy or immunosuppression, presence of hilar lymph nodes, pulmonary lesions above 3cm (this is defined as a mass). FSR criteria 2005 do not apply to patients younger than 35 years, and to sub-solid nodules. Patients with a history of malignancy or with hilar lymph nodes were excluded because the risk of the nodule being malignant is much higher in these cases, while immunocompromised patients were excluded because SPNs are most likely to be viral in origin if less than 10mm in diameter.⁹ A sample of 100 nodules which fit the inclusion criteria and did not meet any of the exclusion criteria, was analysed.

Data was collected from PACS®, iSoft Clinical Manager® and Electronic Case Summary® relating to patient age, nodule size, smoking history, initial and follow-up CTs, and final diagnosis (benign vs malignant) based on the final radiology report and/or histology.

Gold Standard

The Fleischner Society Recommendations from 2005 were used as the gold standard, based on size of nodule and patient risk (mostly referring to positive smoking history). The follow-up of each pulmonary nodule was analysed according FSR criteria and hence classified as either guideline-concordant, under-evaluated or over-evaluated. Nodules classified as guideline-concordant were timely followed-up according to FSR, and received the correct number of follow-up CTs. Under-evaluated SPNs received a lower number of follow-

up CTs when compared to FSR, when considering their size and smoking history, and/or follow-up was stopped prematurely. Over-evaluated nodules on the other hand received a higher number of follow-up CTs when compared to FSR, and/or follow-up was continued beyond the time frame suggested by FSR.

Results

From a sample of 100 patients, 61% had a positive smoking history: 38% current smokers and 23% ex-smokers (Figure 1). A total of 35% of SPNs were found in patients aged between 56-65 years (Figure 2). Figure 3 shows the distribution of the SPNs according to size, with more than half measuring more than 8mm. 31% of SPNs were found incidentally on CTs performed for non-thoracic purposes such as post pacemaker insertion, in patients with abdominal pain and in trauma scans.

The management of solitary pulmonary nodules (SPNs) was guideline-concordant in 48%. Thirty two percent of SPNs were under-evaluated and 20% were over-evaluated as seen in Figure 4. Radiographic surveillance lasted a median of 24 months in patients with nodules with a size of >8mm, 12 months in nodules measuring >4-8 mm and 18 months in nodules ≤ 4mm. In 26% of radiology reports, the recommended follow-up was optimal, where the radiologist's report included both the recommended investigation as well as the correct time interval (Figure 5). 46% of radiology reports were sub-optimal – this included 33% with absent time frame recommendations, 10% with absent investigation recommendations, and 3% where the radiologist included the term 'follow-up' without giving a specific time frame. In 28% of radiology reports, there were no follow-up recommendations.

From the total cohort, lung malignancy was diagnosed in 31%, and the risk of malignancy increased with the size of the nodule (Figure 6). Tobacco smoking also increased the risk of malignancy as seen in Figure 7.

Figure 1: Smoking Status of Patients with Pulmonary Nodules

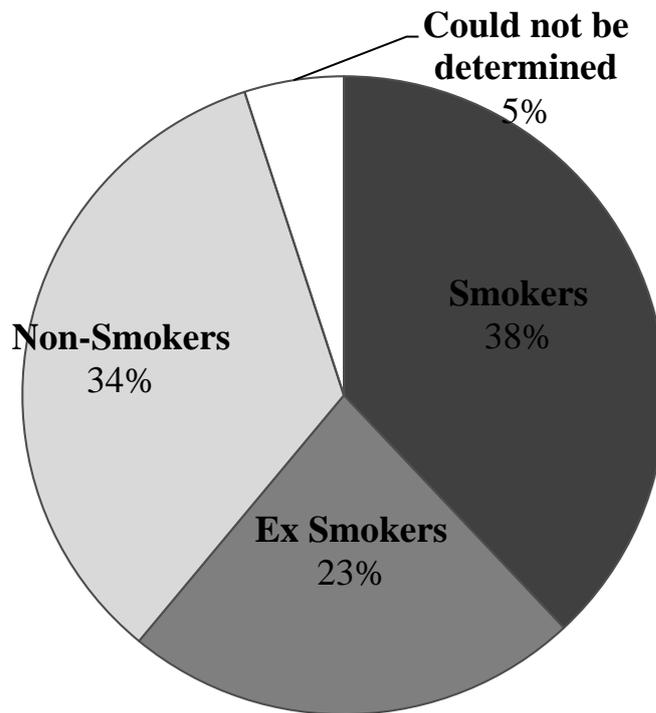


Figure 2: Age of Patients with Pulmonary Nodules

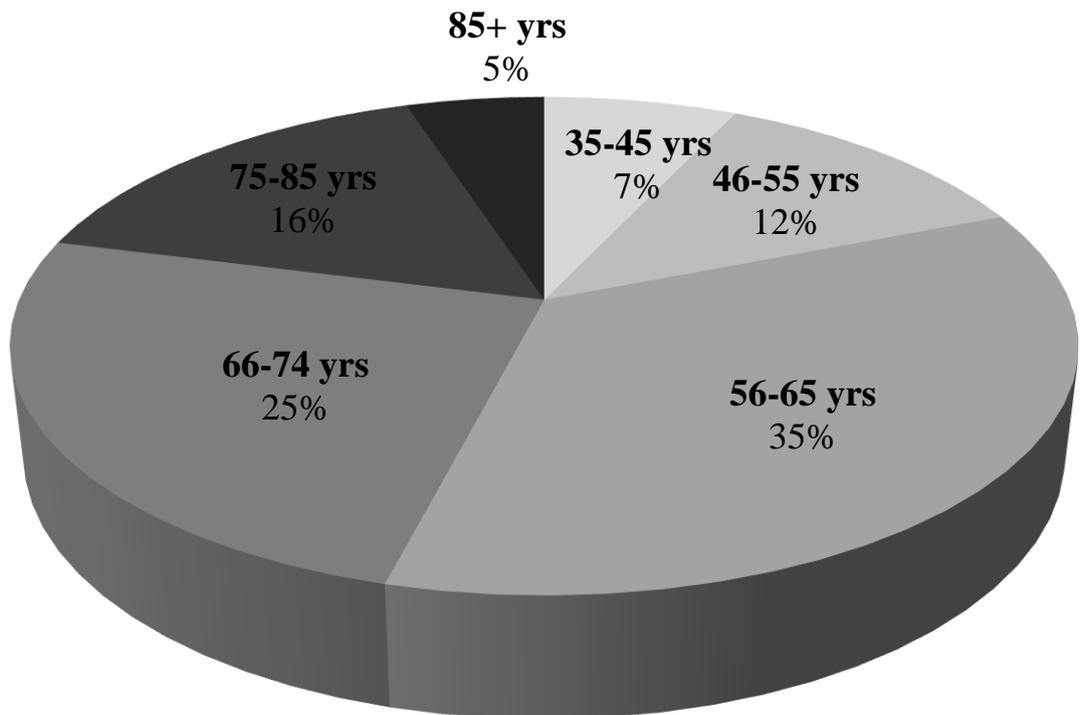


Figure 3: Size of Pulmonary Nodules

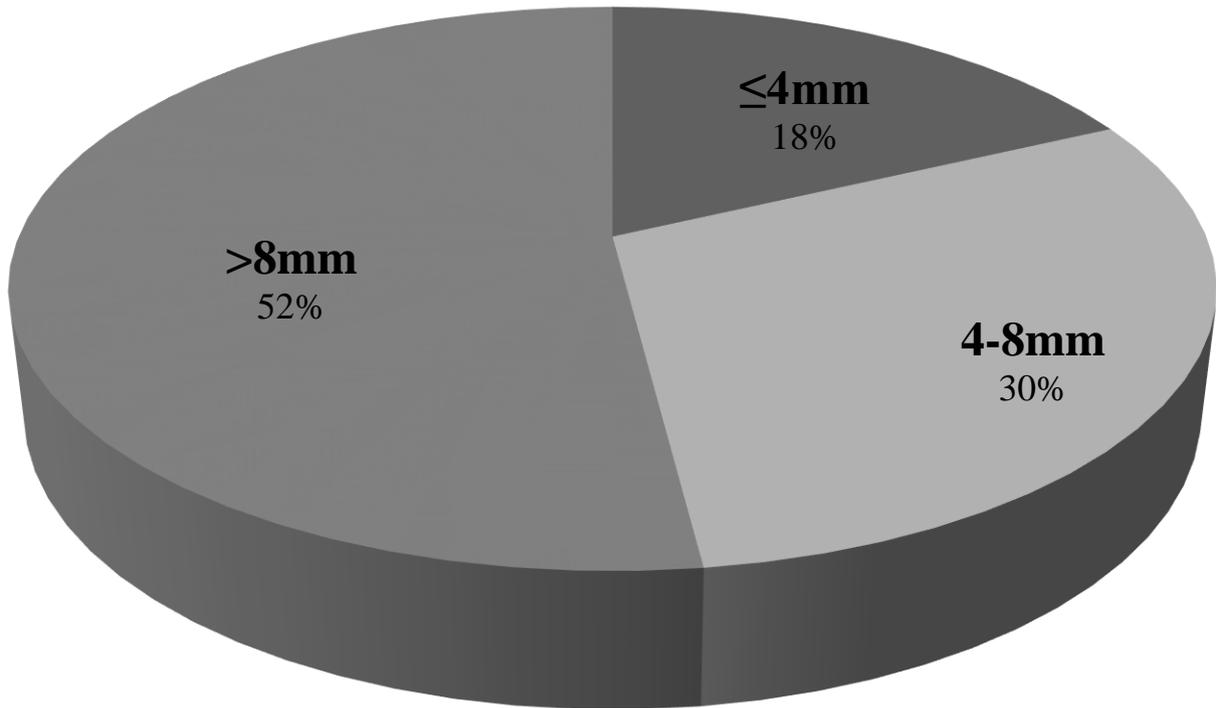


Figure 4: Are We Following the Fleischner Criteria?

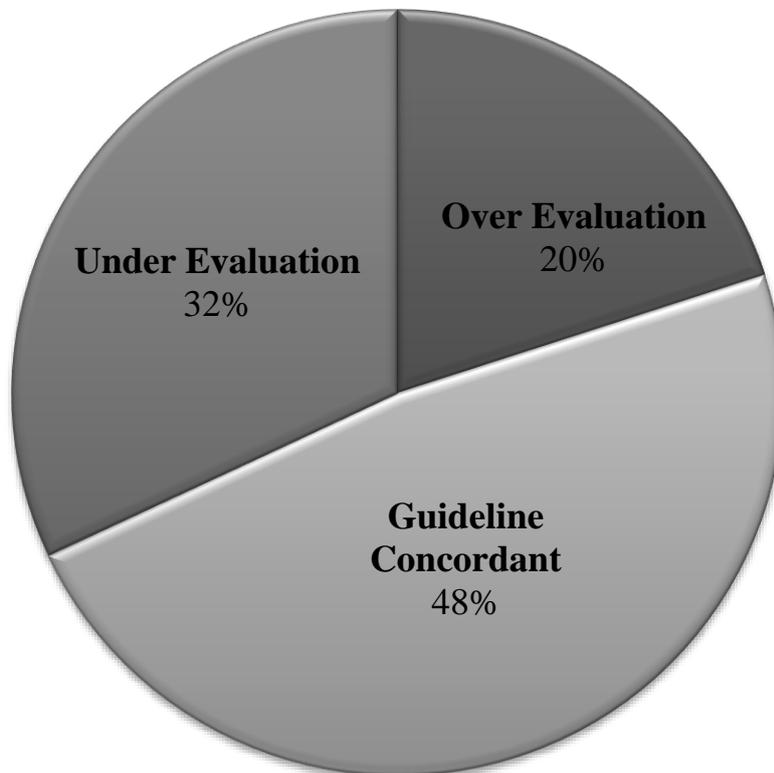


Figure 5: Documented Recommended Follow up Investigation by Radiology

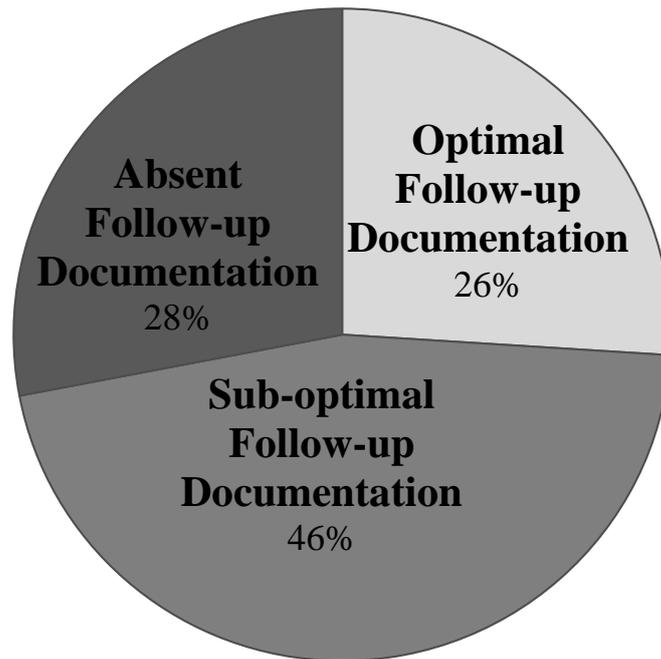


Figure 6: Risk of Malignancy of Lung Nodule In Relation to Size

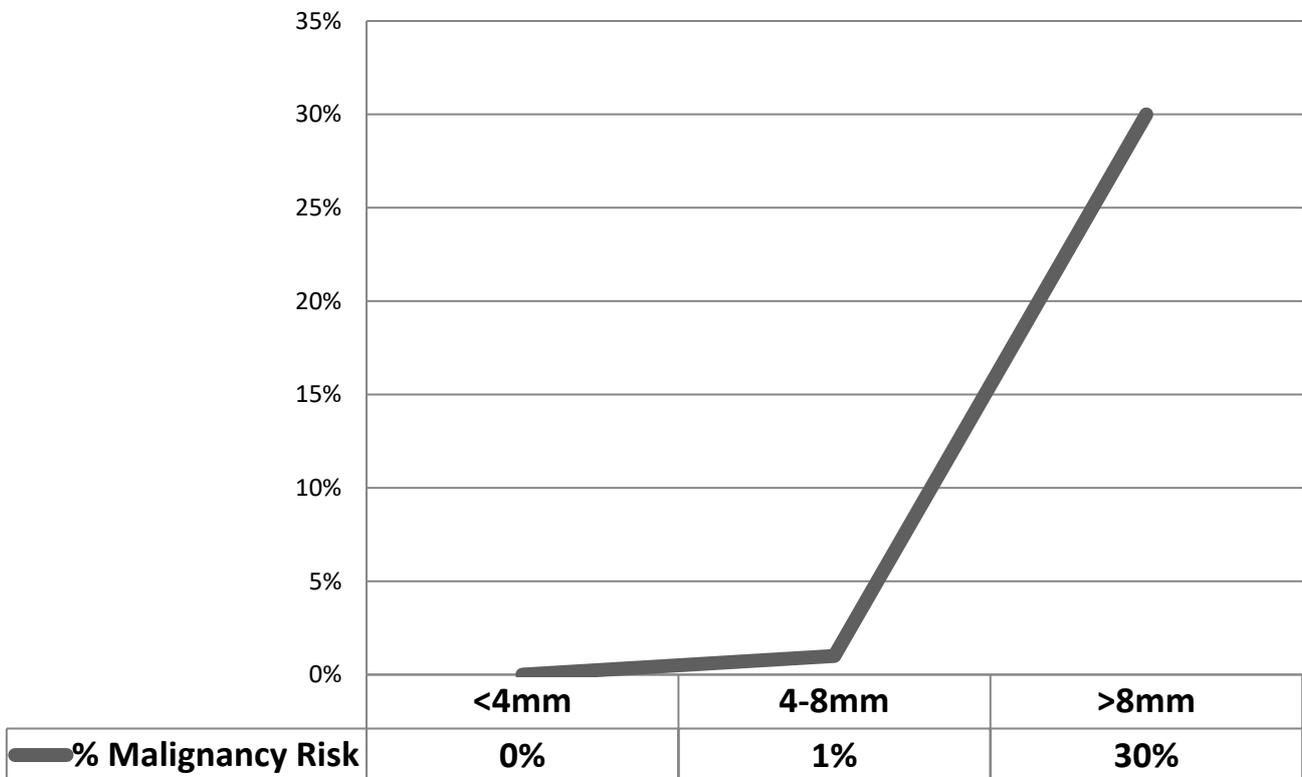
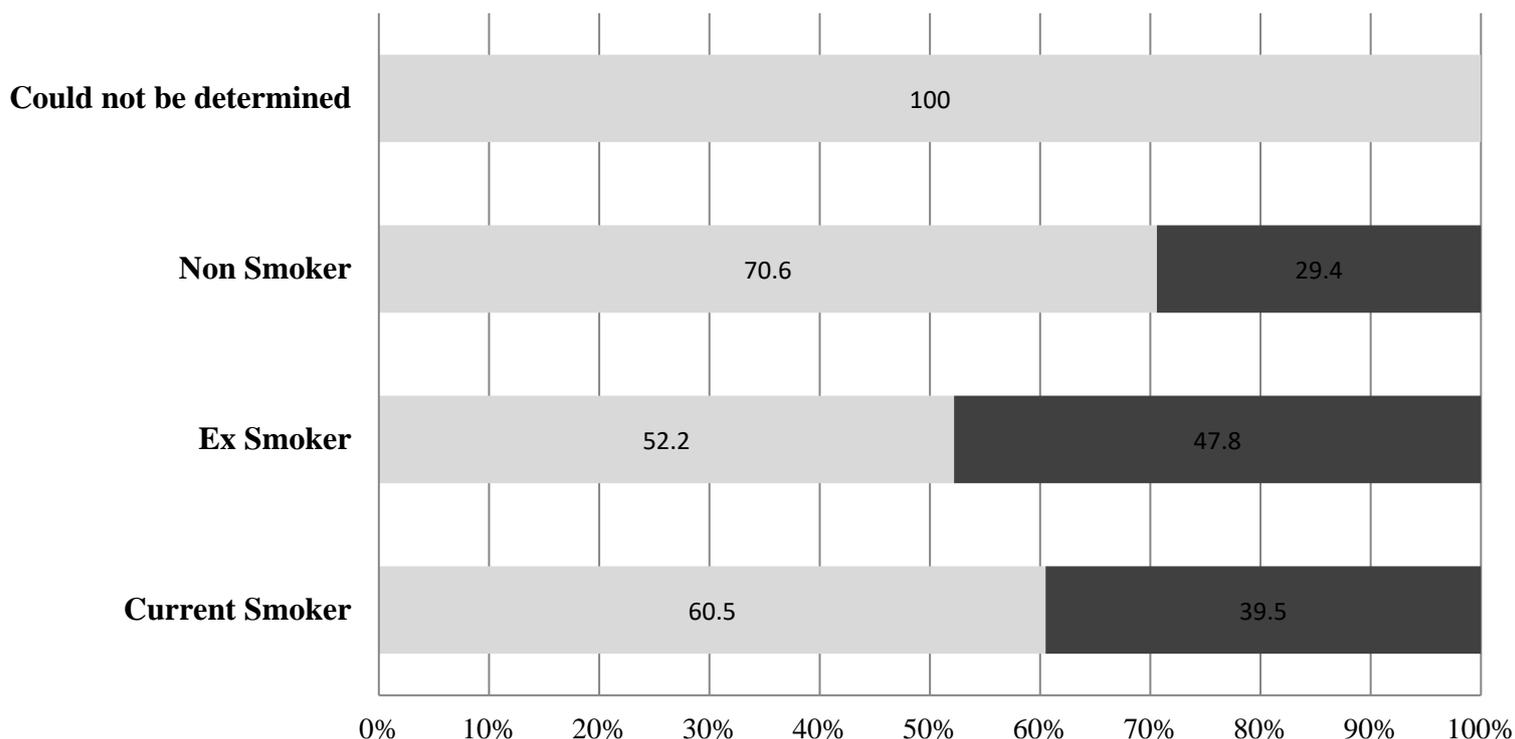


Figure 7: Risk of Malignancy of Lung Nodule In Relation to Smoking Status



	Current Smoker	Ex Smoker	Non Smoker	Could not be determined
■ Benign %	60.5	52.2	70.6	100
■ Malignant %	39.5	47.8	29.4	0

Discussion

Detection and follow up of SPNs is essential in the early diagnosis of lung cancer, which remains the most effective way of managing and potentially curing such an aggressive cancer. Lung cancer is often diagnosed late in view of late symptomatology and delay in seeking medical attention by the patient. From the total cohort in this study, lung malignancy was diagnosed in 31%, concordant with international data for malignancy risk in SPNs quoted at 30 to 40%.³ The size of the nodule is strongly related to malignancy risk with US data from 2005 showing a 0% risk of malignancy in nodules measuring <4mm, 1% risk in nodules 4-8mm, 15% risk in nodules 8-20mm, and 75% risk in nodules 20-30mm.¹⁰ Our study has comparable results, with a 0% risk of malignancy in nodules <4mm, 1% risk in nodules 4-8mm, and 30% risk in nodules 8-30mm.

Our data show that nodules in patients with a positive smoking history are more likely to be malignant (47.8% in ex-smokers, and 39.5% in

current smokers). Positive smoking history has been reported in other studies as a risk factor for malignancy in SPNs, along with increasing age, size and number of nodules, and reduced FEV₁ and FVC on spirometry.¹¹

Strict adherence to FSR was observed in just under half of the diagnosed SPNs (Figure 4). Possible reasons for under-evaluation of the SPN included lack of awareness on the Fleischner recommendations, patient co-morbidities, patient refusing follow-up, patient being lost to follow-up, or patients undergoing further investigations privately. SPNs were over-evaluated in 20% of cases, possibly due to lack of awareness or due to patient and/or physician anxiety. A similar study conducted in the USA in 2014 revealed similar data, with 55% of SPNs receiving guideline-concordant care, 27% being under-evaluated and 18% being over-evaluated.⁵ In order to improve adherence to guidelines, the radiologist should make recommendations in the CT report, giving clear documented advice on follow-up. Optimal

recommendations were made in 26% of our cohort. Impaired communication between different specialties undermines the delivery of good quality of care and ultimately delays the diagnosis of lung cancer at a stage where it can be potentially curable.⁵ Clear communication between the reporting radiologist and the ordering doctor is essential. A common problem is that the requesting physician is not a respiratory physician, and may not be familiar with the FSR. Negotiating a management plan over the phone is not always possible, and is associated with lack of documentation; therefore, standardised medical imaging reporting systems should be implemented to prompt the radiologist to make recommendations for follow-up. A further proposal is the initiation of a logbook for the entry of all patients found to have SPNs, which would be then forwarded to the respiratory multidisciplinary team. As these patients are often referred across specialties, documented hand-over should always be made in the case notes and on the referral ticket. Discussion at multidisciplinary team meetings is to be encouraged and this will lead to better decisions regarding follow-up and timely intervention.

It is the responsibility of the requesting physician to include all the clinical details in the CT request, particularly the smoking history. Appropriate radiology recommendations are not possible without the smoking history, as this forms the basis for the FSR. The authors propose the addition of more specific clinical data fields on the standard CT thorax booking request, prompting the ordering doctor to include the smoking history, as well as the presence of a history of lung cancer amongst first-degree relatives, and exposure to other lung carcinogens such as asbestos, uranium or radon. A similar system of specific clinical data fields is already in place in the online request form for High Resolution CT Thorax.

The most recent Fleischner Society Guidelines from 2017⁸ and the British Thoracic Society Guidelines from 2015¹² include nodule volume as well as nodule diameter for more precise assessment of malignant potential. The 2017 criteria have since been adopted as standard of care at Medical Imaging Department, Mater Dei Hospital, Malta. More importance is being given to subsolid (ground glass) nodules, since they have a higher risk of malignancy than solid nodules.¹³ More emphasis is also being placed on the prognostic

implications of nodule location, contour, morphology and doubling time. Upper lobe nodules, nodules with an irregular border and nodules with a doubling time <400 days have a higher incidence of malignancy. Peri-fissural and subpleural nodules that have a triangular or polygonal shape and a fine linear extension to the pleura are consistent with benign intrapulmonary lymph nodes.⁸

Limitations of the Study

One of the limitations of our study is that the smoking status could not be determined in 5% of the patients from the available online sources of data. Furthermore, there was limited data available on family history and exposure to asbestos, uranium or radon.

A second limitation is that the study focused on recommendations made in the official radiology report; there may have been verbal discussion of the nodule between the radiologist and the referring physician.

Investigations done in the private sector that were not uploaded on PACS® might have also led to the erroneous conclusion that patient was either not followed up or under-evaluated.

Conclusion

We recommend more accurate and streamlined implementation of Fleischner Society Recommendations for follow-up of lung nodules through standardisation of online CT booking request forms; standardisation of medical imaging reports; and documentation of multidisciplinary discussion in patient case notes. We also recommend re-auditing of local practice within two years of implementation of the new 2017 Fleischner Society Recommendations.

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