

## INCIDENTAL LUNG NODULE REPORTED. WHAT DO I DO NEXT?

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### ABSTRACT

**A lung nodule (white spot < 3 cm in diameter) can either be first detected on a chest radiograph or a Computed Tomography (CT) scan. When detected on the radiograph, the next step is almost always a CT scan. When first detected on a CT scan, the next step is the comparison with any imaging studies available from the past. If no past imaging is available for comparison, then the next step is a biopsy, which is also the gold standard for diagnosis. Although observation with interval imaging has been advocated, this approach is only safe when the likelihood of the nodule being benign is very high. Otherwise, a biopsy should be undertaken to exclude or confirm cancer in the early stage as it carries implications for survival.**

**It should be kept in mind that missing lung cancer when it is just a nodule is a bigger error than missing a lung cancer when someone presents with a mass on the imaging studies. This is because the former error can render a curable patient incurable whereas the latter may not make big difference in terms of survival.**

**CT scan does not carry a significant risk of harm from radiation as the prevalent notion in the society. Modality for biopsy largely depends on the location of the nodule and its accessibility via various modalities. The peripheral nodules are easier to access by transthoracic needle aspiration whereas the central nodules are easier to access via bronchoscopy or Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA). Occasionally, video assisted surgical biopsy may be needed and should be offered promptly when indicated. Reliance on Chest radiograph alone and lung cancer probability calculators should be minimised.**

**Key words: Lung cancer, nodule, non-smokers, CT scan, women**

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### INTRODUCTION

A lung nodule refers to a “white spot,” or a “lump” in your lung that is three centimetres or smaller in diameter. Similar to how women (or even men) can develop lumps in their breasts, a lump or several lumps can also appear in their lungs. The nodule can be either benign or malignant.<sup>1,2</sup> The most benign cause of nodule in Singapore is Tuberculosis or Nontuberculous mycobacteria (NTM) or fungal infection.

### IS CHEST X-RAY SUFFICIENT TO DETECT A NODULE?

CT scans are generally more accurate in picking up a lung nodule compared to a chest X-ray – with 5 out of 500 CT scans detecting a nodule, compared to only 1 in 500 X-rays. This is because a nodule needs to be at least one centimetre in size before it can be seen on a chest X-ray, whereas nodules as small as one millimetre can be seen on a CT scan.<sup>3</sup>

### WHY CHEST X-RAY SHOULD NOT BE RELIED UPON COMPLETELY?

The most common disease with which lung cancer gets confused with is Tuberculosis (TB). This is because TB is almost as common as lung cancer in Singapore and Asia, with 1300 new cases of TB and 1500 cases of lung cancer every year in Singapore. They look alike on the chest X-ray. TB affects the upper parts of the lung, similar to lung cancer. The shape & features of the white spot in the lungs caused by TB (cavity) are similar to the appearance of the spot caused by lung cancer. Therefore, if one is not careful, the diagnosis of TB may be confused with lung cancer. This issue is compounded by the fact that the confirmatory result of TB takes two months. So, if one decides to start a trial of TB treatment when the patient is having cancer, a two-month delay may be detrimental.

It is possible for someone to be told that a chest X-ray is normal only to find out about the cancer months or years later. More than 20 percent of chest X-rays in people with symptoms of lung cancer have been found to be falsely negative for lung cancer.

Paradoxically, lung cancer is missed in the people in whom it could have been cured if detected early. This group of people are those with small size cancer that is not picked up by the chest X-ray, people who have hazy nodules (ground glass) which have higher potential for being cancerous, nodule in young people because of the false belief that lung cancer only affects older people, nodules in never smokers because of the notion that lung cancer is only caused by smoking, and women because of the notion that women only get breast or ovarian cancer.<sup>4,5</sup>

## IS CT SCAN REALLY HARMFUL AS IT IS THOUGHT TO BE?

The risk of radiation-induced harm from a chest X-ray or a CT scan is overestimated in the community. A CT scan of the chest carries a radiation dose of 0.66 milli-gray whereas the harmful dose is >100 milli-gray. Moreover, we are always exposed to natural cosmic radiations all the time. A low-dose CT scan may be performed for concerned individuals.<sup>6</sup>

Test	Milli-gray
Chest X-Ray	0.002
CT scan	0.03-0.66
V/Q scan	0.32-0.74
Abdomen X-Ray	3.5-13.9
X-Ray Pelvis	1.6-13.1

## WHY SHOULD A LUNG NODULE IN YOUNG PEOPLE (AS YOUNG AS 30) NOT BE IGNORED?

Most people think that only older people get lung cancer although it has been reported in people as young as 20 years old. The average age at diagnosis is indeed 70 years but that is only an average. Ten percent of lung cancers occur in people under 55, and 1.5 percent occurs in people under 35. In Singapore where around 1500 patients are diagnosed with lung cancer every year, this means 150 patients under 55 and 23 patients under 35 are diagnosed every year. Young women are affected more by the disease than young men. When lung cancer affects younger people, it tends to present in an advanced stage with most presenting with stage four disease.<sup>7</sup>

Genetic abnormalities are thought to be the reason in younger lung cancer patients. For example, ROS1 mutations and ALK rearrangements are more common in young people with lung cancer and are almost always associated with aggressive disease. About 60 percent of young people with lung cancer will have these and other genetic mutations. Having a first-degree relative with lung cancer increases the risk of having lung cancer by 50 percent compared to an absent family history.

## WHY SHOULD A LUNG NODULE IN A NON-SMOKER NOT BE IGNORED?

Although smoking is a risk factor for developing lung cancer, it does not mean non-smokers are protected from the disease. Globally, about 25 percent of lung cancer patients have never smoked, while almost 40 percent of lung cancer patients in Singapore are never smokers. Lately, it has been found that the proportion of never-smokers with lung cancer has more than doubled from 13 percent to 28 percent. Lung cancer in non-smokers is often misdiagnosed initially as respiratory infection or even allergies, only to realise the correct diagnosis after a significant delay.<sup>8</sup>

## WHY SHOULD A LUNG NODULE IN A YOUNG WOMAN WHO NEVER SMOKED NOT BE IGNORED?

Lung cancer has been thought to be a man's disease for a long time. However, research shows an 80 percent rise in lung cancer in women. Almost 50 percent of lung cancer is diagnosed in women. It is also the leading cause of cancer deaths in women globally, killing more women each year than breast, uterine, and ovarian cancer combined. In Singapore, it is the second leading cause of cancer death after breast cancer.

Women are more sensitive to cancer-causing chemicals in cigarettes and can develop lung cancer from smoking for fewer number of years than men likely because they are unable to repair their DNA damaged by smoking. Oestrogen has also been shown to be responsible as it makes women more sensitive to cancer-causing chemicals making the cancer cells grow as studies have found that menopause (with a drop in oestrogen levels) reduces the risk of lung cancer. Among women, certain cancer-driving mutations like EGFR are more common.

Men are commonly diagnosed with squamous cell carcinoma type of lung cancer which affects the windpipes. The irritation of these windpipes causes cough and coughing out blood forcing the person to seek medical help early. However, women are commonly diagnosed with adenocarcinoma type of lung cancer which starts at the periphery of the lung. Since this type of lung cancer is located far away from the windpipes, it does not cause symptoms of cough and result in a late diagnosis.<sup>9, 11</sup>

## WHY IS IT HARD TO IMPLEMENT LUNG CANCER SCREENING IN SINGAPORE & ASIA EVEN WHEN IT IS THE NUMBER 1 KILLER AMONG ALL CANCERS?

Population-based screening is only recommended for colon cancer, breast cancer, cervical cancer, and liver cancer in Singapore. However, in the USA, population-based screening is also done for lung cancer as it has been shown to reduce risk of dying from it. Why is lung cancer screening not implemented in Singapore? To answer this question, we need to know who fulfils the criteria for screening for lung cancer in the USA. The people who should go for lung cancer screening based on USA-based studies & guidelines are those who are 55 to 74 years old and currently smoke or have quit smoking in the past 15 years and have at least a 30 pack-years smoking history. (A pack-year is one pack of cigarettes per day per year. One pack per day for 30 years or two packs per day for 15 years would both be 30 pack-years).<sup>10</sup>

About 40 percent of lung cancer patients in Singapore are never smokers. If we were to use USA-based lung cancer screening guidelines on our population, we will miss out 40 percent of the patients who have never touched a cigarette.<sup>12</sup>

In addition, lung cancer has affected people as young as 31-year-old in Singapore and hence the age criteria of the USA-based guidelines cannot be applied to the population of Singapore. Due to differences in *who* and *how* lung cancer affects Asians versus the western population, there is a need to come up with lung cancer screening guidelines that are applicable to the local and regional population. This has not taken place yet.

In summary, the first consideration after picking up a lung nodule in anyone is to rule out a diagnosis of lung cancer. The subsequent work-up which may include doing a CT scan, comparing the current imaging studies with the previous ones, doing a biopsy, or conservative approach with the plan of doing an interval CT scan, should anchor around the thinking of “what if this nodule turns out to be cancerous later on”. The goal should be to minimise this possibility as lung cancer is the most common cause of death among all cancers globally.

## REFERENCES

- Gould MK, Donington J, Lynch WR, et al. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e93S-e120S. doi: 10.1378/chest.12-2351. PMID: 23649456; PMCID: PMC3749714.
- Khan AN, Al-Jahdali HH, Irion KL, Arabi M, Koteyar SS. Solitary pulmonary nodule: A diagnostic algorithm in the light of current imaging technique. *Avicenna J Med*. 2011 Oct;1(2):39-51. doi: 10.4103/2231-0770.90915. PMID: 23210008; PMCID: PMC3507065.
- Bradley SH, Abraham S, Callister ME, et al. Sensitivity of chest X-ray for detecting lung cancer in people presenting with symptoms: a systematic review. *Br J Gen Pract*. 2019 Nov 28;69(689):e827-e835. doi: 10.3399/bjgp19X706853. PMID: 31636130; PMCID: PMC6805164.
- Del Ciello A, Franchi P, Contegiacomo A, Cicchetti G, Bonomo L, Larici AR. Missed lung cancer: when, where, and why? *Diagn Interv Radiol*. 2017 Mar-Apr;23(2):118-126. doi: 10.5152/dir.2016.16187. PMID: 28206951; PMCID: PMC5338577.
- Stapley S, Sharp D, Hamilton W. Negative chest X-rays in primary care patients with lung cancer. *Br J Gen Pract*. 2006 Aug;56(529):570-3. PMID: 16882373; PMCID: PMC1874519.
- U.S. Food and Drug Administration. What are the radiation risks from CT? [Internet]. USA: FDA [updated 2017 Dec 5; cited 2021 June]. Available from: <https://www.fda.gov/radiation-emitting-products/medical-x-ray-imaging/what-are-radiation-risks-ct>
- Liu B, Quan X, Xu C, et al. Lung cancer in young adults aged 35 years or younger: A full-scale analysis and review. *J Cancer*. 2019 Jun 9;10(15):3553-3559. doi: 10.7150/jca.27490. PMID: 31293660; PMCID: PMC6603399.
- Pelosof L, Ahn C, Gao A, et al. Proportion of Never-Smoker Non-Small Cell Lung Cancer Patients at Three Diverse Institutions. *J Natl Cancer Inst*. 2017 Jan 28;109(7):djw295. doi: 10.1093/jnci/djw295. PMID: 28132018; PMCID: PMC6279285.
- American Cancer Society. Key Statistics for Lung Cancer [Internet]. USA: American Cancer Society [updated 2021 Jan 12; cited 2021 June]. Available from: <https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html>
- Harvard Health Publishing. Lung cancer in women [Internet]. USA: Harvard Medical School [updated 2014 Mar; cited 2021 June]. Available from: [https://www.health.harvard.edu/newsletter\\_article/Lung\\_cancer\\_screening\\_in\\_women](https://www.health.harvard.edu/newsletter_article/Lung_cancer_screening_in_women)
- Jemal A, Miller KD, Ma J, et al. Higher Lung Cancer Incidence in Young Women Than Young Men in the United States. *N Engl J Med*. 2018 May 24;378(21):1999-2009. doi: 10.1056/NEJMoa1715907. PMID: 29791813; PMCID: PMC7717174.
- US Preventive Services Task Force, Krist AH, Davidson KW, Mangione CM, et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021 Mar 9;325(10):962-970. doi: 10.1001/jama.2021.1117. PMID: 33687470.

## LEARNING POINTS

- Chest x-ray alone should not be relied upon to diagnose or follow-up a patient with a lung nodule.**
- Every nodule should invoke thinking about its etiology and lung cancer should be considered first in the thought process of the workup.**
- Upper lobe nodules, cavitating nodules, nodules in young women, and non-smokers should not be assumed to be TB-related or non-malignant.**