Clinical outcomes after implementation of a lung nodule surveillance programme in Hong Kong

Lynn YW Shong, WC Chong, PI Cheang, WC Choy, Florence KP Chan, WC Kwok, Mary SM Ip, David CL Lam *

ABSTRACT

Introduction: To facilitate early and accurate identification and risk stratification of lung nodules, a surveillance programme was implemented at a tertiary hospital in Hong Kong. This study examined the clinical outcomes of patients recruited during the first year of programme implementation.

Methods: This prospective cohort study included patients enrolled in the lung nodule surveillance programme between 1 January 2022 and 31 December 2022. Recruitment criteria included patients attending the respiratory outpatient clinic for lung nodules or lung masses. Patient demographics and clinical outcomes were analysed. Primary outcomes were the number of lung cancer cases detected and their stage at diagnosis. Secondary outcomes included the invasive investigations performed, adverse events related to these procedures, and details of lung cancer treatment and survival.

Results: Of the 1471 patients recruited to the programme, 291 (19.8%) underwent invasive investigations, and 133 (9.0%) were diagnosed with lung cancer. Among those diagnosed, 62 (46.6%) had stage I disease and 10 (7.5%) had stage II disease. Overdue scans and missed follow-ups were identified and rescheduled. Significantly better survival was observed in female patients compared with male patients (P=0.037 for progression-free survival and P=0.030 for overall survival), and in patients with early-stage cancer compared with those with late-stage lung cancer (P<0.001). Age was also independently associated with survival outcomes (P<0.001).

Conclusion: The implementation of a lung nodule surveillance programme resulted in the detection of early-stage lung cancer in more than half of diagnosed cases, with the potential to improve patient survival.

Hong Kong Med J 2025;31:Epub
https://doi.org/10.12809/hkmj2412168

[1] **LYW Shong,** PhD, FHKAM (Medicine)
[2] **WC Chong,** MScEPB, MN
[1] **PI Cheang,** BNurs
[2] **WC Choy,** MSc
[2] **FKP Chan,** MD, FHKAM (Medicine)
[2] **WC Kwok,** MD, FHKAM (Medicine)
[2] **MSM Ip,** MD, FRCP (UK)
[2] **DCL Lam *,** MD, PhD

[1] *Division of Respiratory Medicine, Department of Medicine, Queen Mary Hospital, Hong Kong SAR, China*
[2] *Division of Respiratory Medicine, Department of Medicine, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China*

* Corresponding author: dcllam@hku.hk

This article was published on 6 Aug 2025 at www.hkmj.org.

This version may differ from the print version.

New knowledge added by this study

- The implementation of a lung nodule surveillance programme improved compliance with follow-up. The proportion of early-stage lung cancer diagnoses in this programme was higher than that reported by the Hong Kong Cancer Registry in 2021.
- Patients with early-stage lung cancer and female patients demonstrated better survival outcomes.

Implications for clinical practice or policy

- This lung nodule surveillance programme has the potential to improve lung cancer survival rates and reduce healthcare costs.
- Further research on the cost-effectiveness of such programme is essential to inform healthcare policy and optimise care for patients with lung nodules.

Introduction

Lung cancer is the leading cause of cancer-related deaths in Hong Kong, with a high incidence and low 5-year survival rate.[1] Early diagnosis and treatment are crucial to improving survival outcomes, as demonstrated in lung cancer screening trials and real-world experiences.[2-5] To date, low-dose computed tomography (CT) screening has not been implemented in Hong Kong.[6] However, the widespread clinical use of CT has led to increased detection of lung nodules on thoracic CT scans.[7] Despite general awareness of lung nodule management guidelines, adherence is often suboptimal.[8,9] Over the past few decades, an increasing number of centres have developed programmes to manage incidental lung nodules.[10]

香港推行肺結節監測計劃後的臨床結果

桑艷華、莊詠芝、鄭寶盈、蔡詠晴、陳璟珮、郭宏駿、葉秀文、林志良

引言：為了及早和準確發現肺部結節，並評估其惡化風險，香港一所大型公立醫院推行了一項肺結節監測計劃。本研究旨在評估該計劃實施首年內參與患者的臨床結果。

方法：這項前瞻性隊列研究納入於2022年1月1日至12月31日期間參加肺結節監測計劃的患者，招募對象為到呼吸科專科門診接受肺結節或肺部腫塊評估的患者。研究分析了患者的人口學特徵及臨床結果，主要研究結果包括確診的肺癌病例數及其確診時的分期；次要研究結果則包括侵入性檢查、與這些檢查相關的不良事件，以及肺癌的治療方式與存活情況。

結果：在參加肺結節監測計劃的1471名患者中，291人（19.8%）接受了侵入性檢查，當中133人（9.0%）確診為肺癌。在這133名肺癌患者中，62人（46.6%）在第I期被確診，10人（7.5%）在第II期被確診。研究期間發現部分患者的影像檢查逾期或未如期覆診，已安排重新追蹤。女性患者的無惡化存活期與總體存活率明顯優於男性患者（無惡化存活期 P=0.037；總體存活率 P=0.030）。此外，早期肺癌患者的存活情況亦顯著較晚期肺癌患者為佳（P<0.001）。年齡與患者的存活結果有獨立相關性（P<0.001）。

結論：肺結節監測計劃使超過一半確診個案能在肺癌早期被發現，顯示該計劃具潛力改善患者的存活率。

This study aimed to review the clinical outcomes of a lung nodule surveillance programme at a tertiary hospital in Hong Kong. It outlines the structure of this comprehensive programme, characteristics of lung nodules, invasive interventions, stage distribution, treatment modalities, and initial survival data.

Methods

Participants

This single-centre prospective cohort study included all patients enrolled in a lung nodule surveillance programme at Queen Mary Hospital, Hong Kong, during its first year of implementation, from 1 January to 31 December 2022. The programme was launched with the following objectives: (1) to streamline the referral process and promote cohesive care among practitioners; (2) to identify high-risk lung nodules requiring timely invasive intervention; (3) to provide a multidisciplinary platform with a nurse navigator coordinating care across specialties; and (4) to establish rapport between patients and healthcare staff, thereby improving compliance. Recruitment criteria included patients under surveillance for lung nodules (lesions <3 cm) or lung masses. Patients with lung cancer receiving active treatment were excluded. Referral sources included lung cancer screening, incidental findings on CT or chest radiographs, and symptomatic presentations. All recruited cases were followed until the lung nodule was confirmed as benign or malignant, or until participants declined follow-up or died. The programme algorithm is shown in Figure 1. Upon entry into the pathway, a nurse coordinator conducts initial screening and monitors patients' waiting time. The clinical team, comprising doctors and nurses, reviews each case to perform risk stratification, formulate investigation and follow-up plans, arrange appropriate interventions, provide patient education, and ensure timely follow-up. Patients are managed according to the 2017 Fleischner Society Guidelines[11] and the Clinical Practice Consensus Guidelines for Asia.[12] Lung nodules requiring intensive evaluation or tissue sampling are discussed by a multidisciplinary team that includes respiratory physicians, chest radiologists, cardiothoracic surgeons, and clinical oncologists. Nurse coordinators regularly review consultation notes and track investigation results. Overdue scans or missed follow-ups are identified and rescheduled. Surveillance continues until the lung nodule is confirmed as benign or malignant.

The demographic and clinical characteristics of all recruited individuals including sex, age, smoking history, and co-morbidities were retrieved from the Clinical Management System of the Hospital Authority. In pathology reports, cases where non–small-cell lung cancer (NSCLC) could not be further classified were recorded as NSCLC. In the results, adenocarcinoma, squamous cell carcinoma, small-cell lung cancer, and NSCLC were listed as mutually exclusive categories. Cancer staging was assigned based on pathological staging when available, or clinical staging otherwise, in accordance with the eighth edition of the International Association for the Study of Lung Cancer staging classification.[13] Patients with stage I or II lung cancer were categorised as early-stage, and those with stage III or IV disease as late-stage. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guideline was followed in the preparation of this manuscript. Primary outcomes were the proportion of lung cancer cases detected and their stage at diagnosis. Secondary outcomes included invasive investigations performed, adverse events related to invasive procedures, subgroup analysis by referral source, avoidance of overdue scans and loss to follow-up, and lung cancer treatment and survival.

Statistical analyses

Continuous variables were reported as mean with standard deviation or median with interquartile range, as appropriate. Categorical variables were reported as number and percentage. Clinical characteristics between subgroups were analysed using Student's *t* test or Chi squared test. Progression-free survival (PFS) and overall survival (OS) were analysed using the Kaplan–Meier method, and

factors affecting survival were evaluated using Cox regression analysis. All analyses were performed using SPSS (Windows version 23.0; IBM Corp, Armonk [NY], US).

Results

Study population

A total of 1471 adult patients with lung nodules or lung masses were enrolled in the lung nodule surveillance programme. Demographic characteristics are summarised in online supplementary Table 1. The mean age was 68 years; 726 (49.4%) were men, 954 (64.9%) were never-smokers, 150 (10.2%) were current smokers, and 367 (24.9%) were ex-smokers. Regarding co-morbidities, 140 patients (9.5%) had chronic obstructive pulmonary disease, 35 (2.4%) had interstitial lung disease, 59 (4.0%) had asthma, and 105 (7.1%) had a history of tuberculosis. Of the 1471 participants, 291 (19.8%) underwent invasive diagnostic procedures, resulting in the diagnosis of lung cancer in 133 patients (9.0%), including 131 primary lung cancers and two cases of lung metastasis from pancreatic carcinoma (online supplementary Fig 1). Pathological findings of the 158 patients without lung cancer are presented in online supplementary Table 2. Referral sources and radiographic characteristics of 266 patients, including 133 with lung cancer and 133 matched controls (matched by age, sex, and smoking history) without lung cancer, are presented in online supplementary Table 3. Among these 266 patients, 193 (72.6%) had more than one pulmonary lesion, 67.3% of dominant nodules were solid, and 50.0% were located in the upper lobes. The median size of the dominant lung lesion was 12 mm (interquartile range, 6-26). Patients with lung cancer had significantly larger pulmonary lesions (median size: 24 mm vs 6 mm, P<0.001) and a higher proportion of part-solid nodules (21.1% vs 3.0%, P<0.001) than those without lung cancer. Referral sources among the 266 patients included lung cancer screening (29/266, 10.9%), incidental findings on CT or chest radiographs (153/266, 57.5%), and symptomatic presentation (84/266, 31.6%). There were no significant differences between groups in referral source, nodule number, or location. Among the 133 patients without lung cancer, 31 (23.3%) missed scheduled follow-up and 12 (9.0%) had overdue scans. All were identified by programme coordinators and rescheduled for follow-up.

Characteristics of patients with confirmed lung cancer

The characteristics of patients with confirmed lung cancer (n=133), both overall and stratified by sex (men: n=69; women: n=64) and smoking history (non-smokers: n=81; current/ex-smokers: n=52), are presented in Table 1. The mean age of patients with lung cancer was 69.4 years; 51.9% were men and 60.9% were non-smokers. There were no significant differences between groups in terms of age or body mass index. Compared with male patients, female patients had significantly lower cigarette exposure (mean pack-years: 1.7 vs 25.7, P<0.001) and a higher prevalence of epidermal growth factor receptor (*EGFR*) mutations (66.7% vs 38.2%, P=0.008). Compared with current or ex-smokers, non-smokers were more likely to have adenocarcinoma (90.1% vs 73.1%, P=0.003), *EGFR* mutations (69.6% vs 22.5%, P<0.001), and stage I lung cancer (55.6% vs 32.7%, P=0.041).

Of the 133 patients with lung cancer, 92 (69.2%) had more than one pulmonary lesion. Among the dominant lesions, 60.9% were solid and 56.4% were located in the upper lobes. The median size of the dominant lesion was 24.0 mm (interquartile range, 16.0-39.3), and 48 (36.1%) cases presented with lung masses. Male patients and individuals with a history of smoking had significantly larger pulmonary lesions (mean size: 37.2 mm vs 26.1 mm for men and women, P=0.013; 38.8 mm vs 27.5 mm for current or ex-smokers and non-smokers, P=0.014). Female patients exhibited a higher prevalence of ground-glass opacities (GGOs) compared with male patients (28.1% vs 4.3%, P=0.002) and a lower proportion of solid lesions (50.0% vs 71.0%, P=0.004). Non-smokers were more likely to have pure GGOs (23.5% vs 3.8%, P=0.004) and part-solid GGOs (28.4% vs 9.6%, P=0.016) but fewer solid lesions (48.1% vs 80.8%, P<0.001), compared with current or ex-smokers.

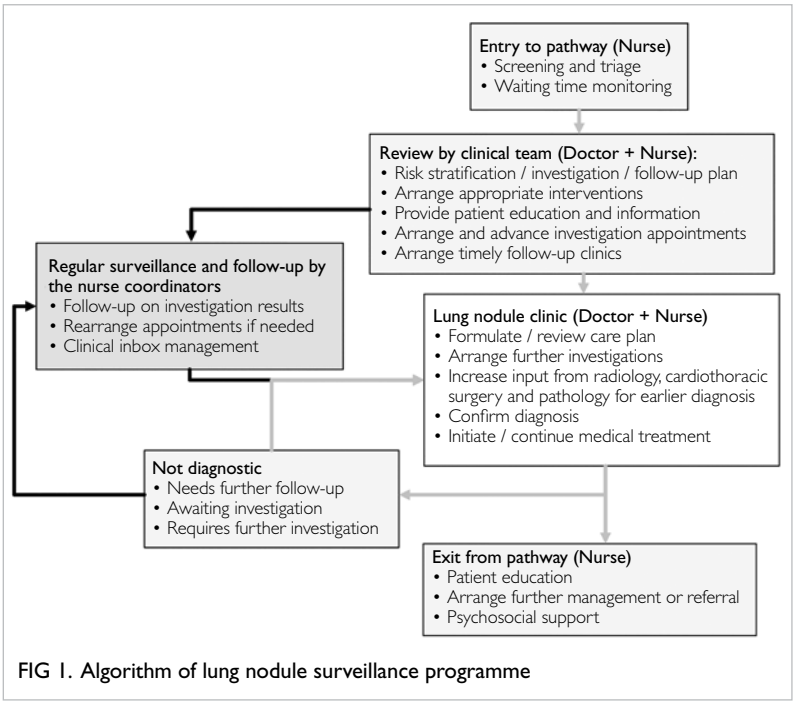

FIG 1. Algorithm of lung nodule surveillance programme

TABLE 1. Characteristics of patients with confirmed lung cancer*

	2021 Hong Kong Cancer Registry	All patients	Male patients	Female patients	P value	Non-smokers	Current/ex-smokers	P value
No. (%)	5231†	133	69 (51.9%)	64 (48.1%)		81 (60.9%)	52 (39.1%)	
Age, y	69	69.4 ± 8.4	69.4 ± 8.5	70.1 ± 10.4	0.682	68.6 ± 10.3	71.5 ± 7.7	0.082
BMI, kg/m^2		23.3 ± 4.0	23.3 ± 3.4	23.3 ± 4.6	0.969	23.6 ± 4.0	23.3 ± 4.0	0.401
Non-smoker		81 (60.9%)	23 (33.3%)	58 (90.6%)	<0.001	81 (100%)	0	<0.001
Smoking history, pack-years		13.5 ± 21.9	25.7 ± 25.2	1.7 ± 7.3	<0.001	0	39.9 ± 19.9	<0.001
Nodule size, mm‡		24.0	27.0	21.0	0.013	22.0	30.0	0.014
No. of nodules								
1		40 (30.1%)	23 (33.3%)	17 (26.6%)	0.641	18 (22.2%)	22 (42.3%)	0.139
2		28 (21.1%)	14 (20.3%)	14 (21.9%)		19 (23.5%)	9 (17.3%)	
3		13 (9.8%)	5 (7.2%)	8 (12.5%)		10 (12.3%)	3 (5.8%)	
4		15 (11.3%)	6 (8.7%)	9 (14.1%)		10 (12.3%)	5 (9.6%)	
≥5		36 (27.1%)	20 (29.0%)	16 (25.0%)		24 (29.6%)	12 (23.1%)	
Unknown		1 (0.8%)	1 (1.4%)	0		0	1 (1.9%)	
Nodule density§								
Solid		81 (60.9%)	49 (71.0%)	32 (50.0%)	0.001	39 (48.1%)	42 (80.8%)	<0.001
Part-solid		28 (21.1%)	14 (20.3%)	14 (21.9%)		23 (28.4%)	5 (9.6%)	
Pure GGO		21 (15.8%)	3 (4.3%)	18 (28.1%)		19 (23.5%)	2 (3.8%)	
Cystic		2 (1.5%)	2 (2.9%)	0		0	2 (3.8%)	
Unknown		1 (0.8%)	1 (1.4%)	0		0	1 (1.9%)	
Lobar location of nodule								
LUL		36 (27.1%)	18 (26.1%)	18 (28.1%)	0.986	24 (29.6%)	12 (23.1%)	0.577
LLL		23 (17.3%)	12 (17.4%)	11 (17.2%)		14 (17.3%)	9 (17.3%)	
RUL		39 (29.3%)	21 (30.4%)	18 (28.1%)		20 (24.7%)	19 (36.5%)	
RML		6 (4.5%)	1 (1.4%)	5 (7.8%)		5 (6.2%)	1 (1.9%)	
RLL		26 (19.5%)	14 (20.3%)	12 (18.8%)		18 (22.2%)	8 (15.4%)	
Mediastinum		3 (2.3%)	3 (4.3%)	0		0	3 (5.8%)	
Histology								
AdenoCa	3644 (69.7%)	111 (83.5%)	56 (81.2%)	55 (85.9%)	0.113	73 (90.1%)	38 (73.1%)	0.003
NSCLC‖	729 (13.9%)	10 (7.5%)	4 (5.8%)	6 (9.4%)		6 (7.4%)	4 (7.7%)	
SCC	522 (10.0%)	6 (4.5%)	5 (7.2%)	1 (1.6%)		0	6 (11.5%)	
SCLC	300 (5.7%)	3 (2.3%)	3 (4.3%)	0		0	3 (5.8%)	
Others¶	36 (0.7%)	3 (2.3%)	1 (1.4%)	2 (3.1%)		2 (2.5%)	1 (1.9%)	
Mutations								
WT		37 (33.9%)	28 (50.9%)	9 (16.7%)	0.008	10 (14.5%)	27 (67.5%)	<0.001
EGFR	47.5%	57 (52.3%)	21 (38.2%)	36 (66.7%)		48 (69.6%)	9 (22.5%)	
ALK	3.8%	6 (5.5%)	1 (1.8%)	5 (9.3%)		6 (8.7%)	0	
ROS1	2.6%	3 (2.8%)	1 (1.8%)	2 (3.7%)		2 (2.9%)	1 (2.5%)	
Others††		6 (5.4%)	4 (7.3%)	2 (3.7%)		3 (4.3%)	3 (7.5%)	
Stages								
I	17.4%	62 (46.6%)	26 (37.7%)	36 (56.3%)	0.160	45 (55.6%)	17 (32.7%)	0.041
II	5.0%	10 (7.5%)	6 (8.7%)	4 (6.3%)		5 (6.2%)	5 (9.6%)	
III	12.9%	16 (12.0%)	11 (15.9%)	5 (7.8%)		6 (7.4%)	10 (19.2%)	
IV	56.9%	45 (33.8%)	26 (37.7%)	19 (29.7%)		25 (30.9%)	20 (38.5%)	

Abbreviations: ALK = anaplastic lymphoma kinase; AdenoCa = adenocarcinoma; BMI = body mass index; *EGFR* = epidermal growth factor receptor; GGO = ground-glass opacity; LLL = left lower lobe; LUL = left upper lobe; NSCLC = non–small-cell lung cancer; RLL = right lower lobe; RML = right middle lobe; ROS1 = ROS proto-oncogene 1; RUL = right upper lobe; SCC = squamous cell carcinoma; SCLC = small-cell lung cancer; WT = wild type

* Data are shown as No. (%), mean ± standard deviation or median, unless otherwise specified

† 747 unknown cases (clinically/radiologically diagnosed) are not listed in the table

‡ Pulmonary lesion size, median largest diameter

§ Dominant pulmonary lesion

‖ Adenocarcinoma, SCC, other malignancies, and NSCLC were mutually exclusive

¶ Include two cases of secondary lung cancer and one case of spindle cell tumour

†† Include *MET* abnormalities, *RET* rearrangements, *HER2* mutations and amplifications, and *RAS* mutations

Diagnostic investigations

Among the 291 patients who underwent invasive investigations, two experienced a small pneumothorax following transbronchial biopsy during bronchoscopy, and five developed a minor pneumothorax after CT-guided biopsy of a lung lesion; all resolved with conservative management. Another two patients had a large pneumothorax following CT-guided biopsy of a lung nodule, requiring chest drain insertion, which was removed after 3 days. One patient developed trace perilesional haemorrhage after CT-guided biopsy of a lung lesion, which was managed conservatively. No patients who underwent invasive procedures experienced complications such as haemothorax, respiratory failure requiring mechanical ventilation, or death. The diagnoses for the 133 patients with lung cancer were established using various diagnostic procedures: 39 (29.3%) cases via bronchoscopy with or without endobronchial ultrasound; 32 (24.1%) via CT-guided biopsy of a lung lesion; 44 (33.1%) through surgical biopsy; nine (6.8%) through cytological analysis of sputum, pleural fluid, ascites, or pericardial effusion; seven (5.3%) by ultrasound-guided fine needle biopsy of cervical lymph nodes or subcutaneous nodules; one (0.8%) via endoscopic ultrasound-guided biopsy of an adrenal lesion; and one (0.8%) through liquid biopsy detecting *EGFR* mutations as the patient declined tissue biopsy (online supplementary Fig 2). Of the 133 patients, 17 (12.8%) underwent invasive investigations at metastatic sites.

Lung cancer stages

Among the 133 lung cancer cases, 62 (46.6%) were stage I, 10 (7.5%) were stage II, 16 (12.0%) were stage III, and 45 (33.8%) were stage IV. No cases of adenocarcinoma in situ arising from GGOs were identified among the 291 patients who underwent invasive investigations; however, five cases of minimally invasive adenocarcinoma (pT1mi, pathological stage IA1) were detected. The proportion of stage I lung cancer in the lung nodule surveillance programme (46.6%) was significantly higher than that reported by the Hong Kong Cancer Registry (HKCR) in 2021 (17.4%, P<0.001).[1] Conversely, the proportion of stage IV cases was significantly lower in the surveillance programme (33.8%, 45 of 133) compared with the HKCR data (56.9%, P<0.001) [Fig 2a]. Overall, 54.1% (72 of 133) of cases in the surveillance programme were diagnosed at an early stage (stage I-II), compared with 22.4% in the HKCR data (P<0.001) [Fig 2b].

Lung cancer treatments

Of the 133 lung cancer patients, 60 (45.1%) underwent surgical resection; seven (5.3%) received stereotactic body radiation therapy; 27 (20.3%) were treated with systemic chemotherapy with or without radiotherapy, combined chemoimmunotherapy (chemoIO), or IO alone; and 21 (15.8%) received targeted therapy. Three patients (2.3%) received palliative radiotherapy as their first-line treatment. The remaining 12 (9.0%) patients opted for best supportive care, one (0.8%) patient pursued traditional Chinese medicine, and two moved out of Hong Kong. Two cases who left Hong Kong were lost to follow-up after diagnosis.

Compared with non-smokers, a lower proportion of patients with a history of smoking underwent surgical resection (45 of 79 [57.0%] non-smokers vs 15 of 52 [28.8%] current/ex-smokers, P=0.0014) and targeted therapy (19 of 79 [24.1%] vs 2 of 52 [3.8%], P=0.0019). In contrast, a higher proportion of current/ex-smokers received chemotherapy, chemoradiotherapy, chemoIO, or IO alone (8 of 79 [10.1%] vs 19 of 52 [36.5%], P<0.001) and best supportive care (2 of 79 [2.5%] vs 10 of

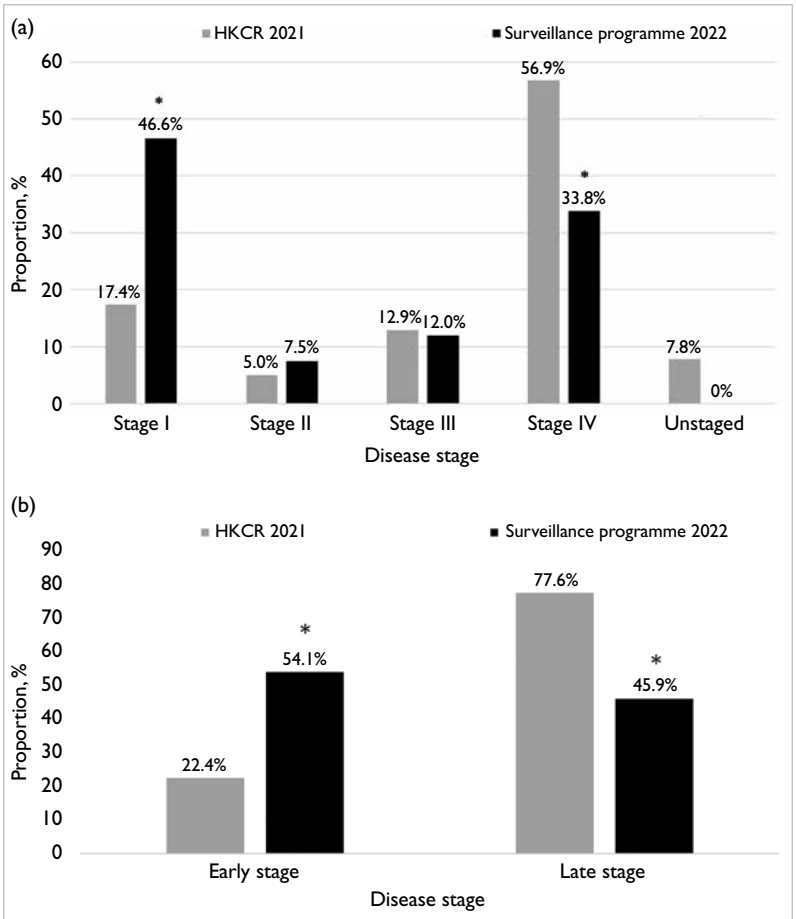

FIG 2. Stages of lung cancer patients. (a) Comparison of lung cancer stage distribution between patients from the lung nodule surveillance programme in 2022 and the Hong Kong Cancer Registry (HKCR) in 2021. (b) Lung cancer cases stratified into early-stage and late-stage groups

* P<0.001

52 [19.2%], P=0.0014) [Fig 3a]. Patients diagnosed with stage I lung cancer primarily received surgical resection or curative RT, whereas those diagnosed at stage III or IV were more likely to receive systemic therapy or best supportive care (Fig 3b).

Lung cancer patient survival

As of the survival analysis conducted in April 2024, the median survival for all patients had not been reached. Among patients with late-stage lung cancer, the median PFS was 282 days (95% confidence interval [95% CI]=52-512), and the median OS was 438 days (95% CI=137-739). Both the median disease-free survival and OS for patients with early-stage lung cancer had not been reached at the time of analysis (Fig 4).

Univariate Cox regression analysis revealed that female sex (P<0.02), age (P<0.001), smoking history (P<0.02), lung lesion size (P≤0.001), disease stage (P<0.001), and surgical resection (P<0.001) were significant predictors of both PFS and OS. Multivariate Cox regression analysis showed that male sex, age, and late-stage disease were independently associated with survival. For male sex, the hazard ratios were 2.831 (95% CI=1.066-7.517) for PFS and 2.931 (1.107-7.756) for OS (P=0.037 and 0.030, respectively). For age, the hazard ratios were 1.082 (1.040-1.136) for PFS and 1.117 (1.067-1.170) for OS, and for late-stage disease, the hazard ratios were 12.664 (4.405-36.408) and 11.791 (4.132-33.651) for PFS and OS, respectively (all P<0.001) [Table 2]. There were no statistically significant differences in survival rates based on nodule characteristics or locations.

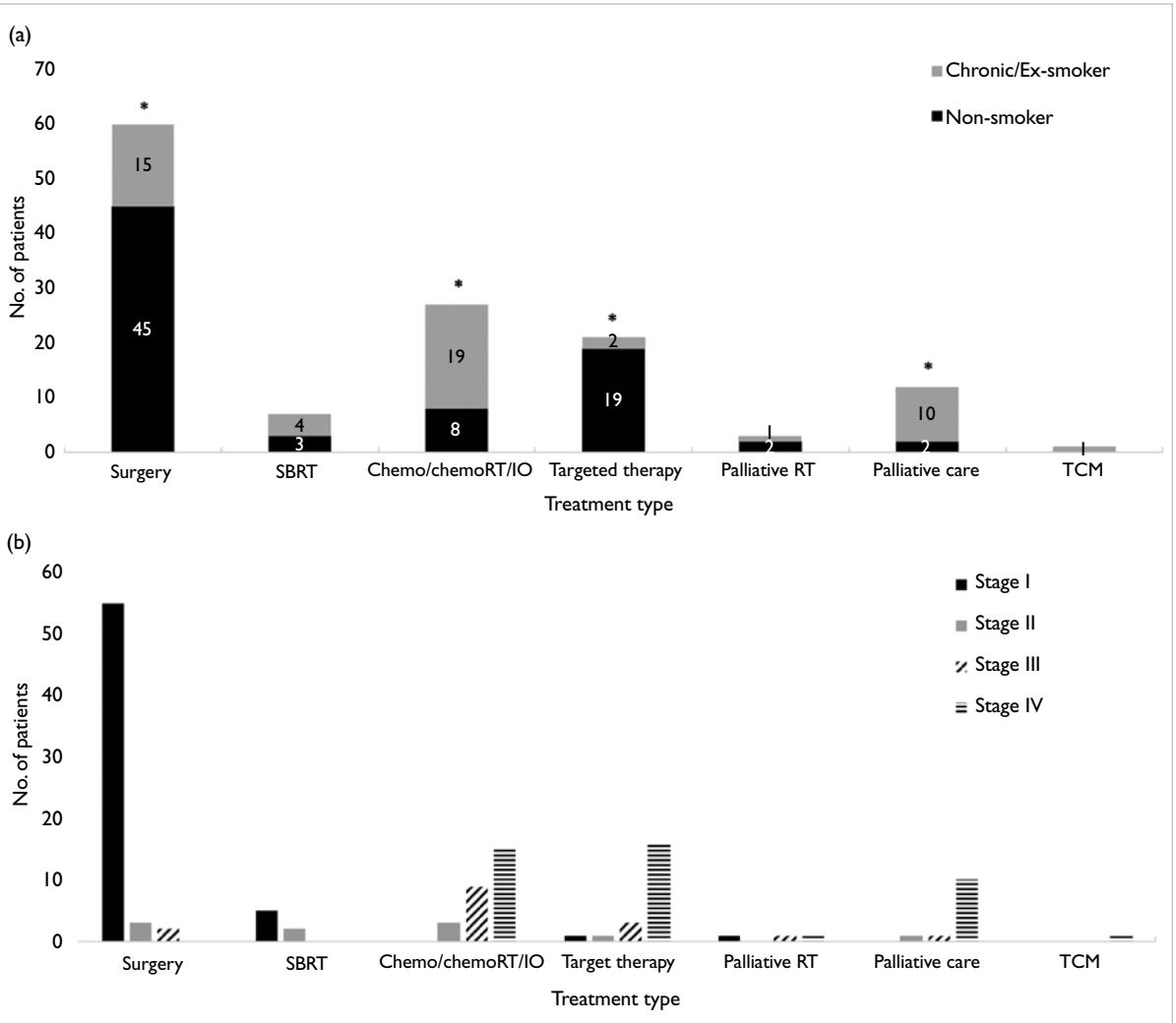

FIG 3. Lung cancer treatments stratified by (a) smoking history and (b) disease stage
Abbreviations: Chemo = chemotherapy; ChemoRT = chemoradiotherapy; IO = immunotherapy; RT = radiotherapy; SBRT = stereotactic body radiation therapy; TCM = traditional Chinese medicine
* P<0.05

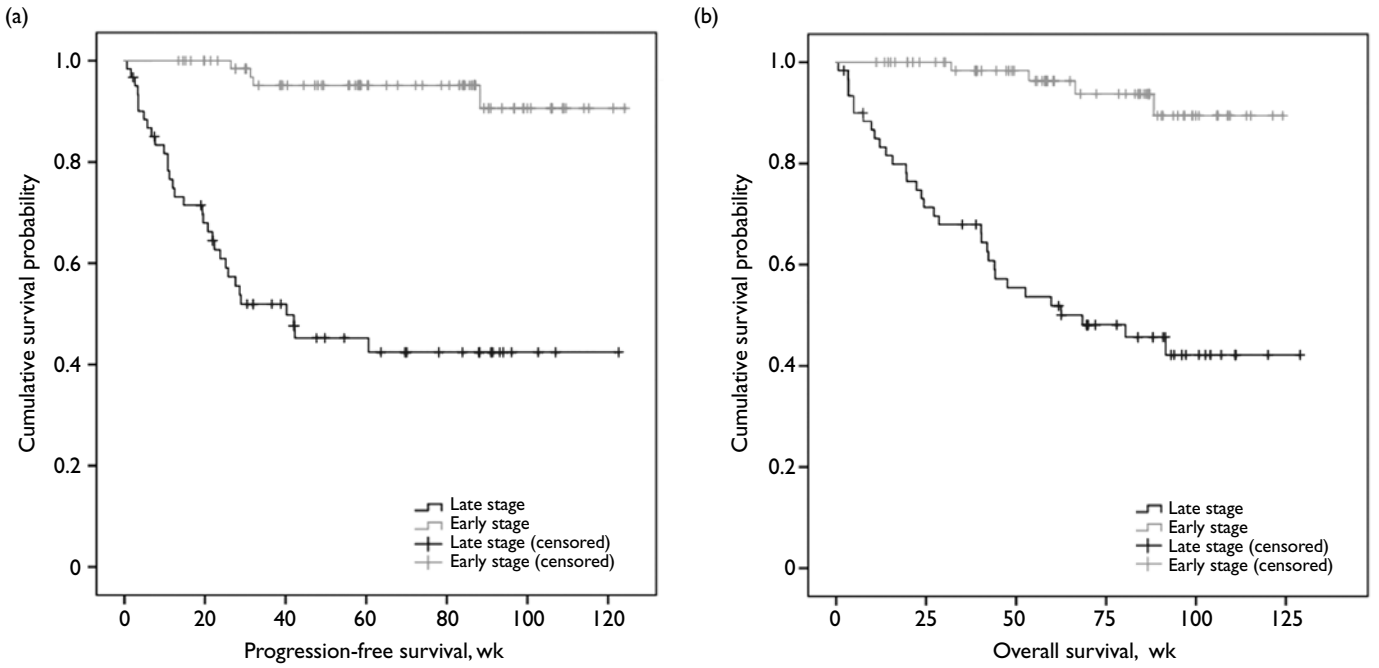

FIG 4. Survival curves for lung cancer cases stratified by stage. (a) Progression-free survival. (b) Overall survival

Discussion

In this single-centre study, the implementation of a lung nodule surveillance programme resulted in 54.1% of lung cancer patients being diagnosed at an early, potentially curable stage, which may contribute to improved survival outcomes. Compared with HKCR 2021 data, this reflects a 31.7% increase in the proportion of early-stage diagnoses (from 22.4% to 54.1%) and a potential 23.1% reduction in the proportion of patients diagnosed with stage IV disease (from 56.9% to 33.8%).

The prevalence of lung nodules detected in lung cancer screening trials varies considerably, with reported rates ranging from 6.8% to 50.9%.[7,14-19] The National Lung Screening Trial showed that 96% of nodules detected in high-risk smokers were non-malignant.[2] The Taiwan Lung Cancer Screening in Never-Smoker Trial, a multicentre cohort of 12 011 never-smokers, revealed a lung nodule prevalence of 17.4% and a cancer prevalence of 2.6% at baseline screening.[20] An ongoing clinical trial in Hong Kong is investigating lung cancer screening in individuals with a smoking history or a family history of lung cancer.[21] Although low-dose CT screening is a proven modality that significantly reduces lung cancer mortality in some countries, current guidelines recommend screening only for a limited high-risk population. Moreover, the detection of incidental lung nodules has increased with the widespread use of CT scans.[22] In our study, such nodules accounted for 57.5% of all cases. Increased referrals for incidental nodules likely contributed to longer waiting times for follow-up appointments. Previous studies have reported delayed or failed tracking of incidental pulmonary nodules in 40% to 70% of patients,[8,23] and one study reported a 27% loss to follow-up.[19] A dedicated lung nodule surveillance programme can complement lung cancer screening by facilitating early detection in individuals who do not meet current screening criteria but present with incidental pulmonary nodules. In our study, overdue scans (9.0%) and missed follow-up appointments (23.3%) were promptly identified and rescheduled by programme coordinators, ensuring close monitoring and timely intervention to optimise patient outcomes.

TABLE 2. Multivariate logistic regression analysis for survival of lung cancer patients

	Progression-free survival*		Overall survival	
	HR (95% CI)	P value	HR (95% CI)	P value
Sex†	2.831 (1.066-7.517)	0.037	2.931 (1.107-7.756)	0.030
Age	1.082 (1.040-1.136)	<0.001	1.117 (1.067-1.170)	<0.001
Smoking‡	1.154 (0.493-2.699)	0.741	1.075 (0.466-2.484)	0.865
Stage§	12.664 (4.405-36.408)	<0.001	11.791 (4.132-33.651)	<0.001

Abbreviations: 95% CI = 95% confidence interval; HR = hazard ratio

* Disease-free survival for patients with early-stage cancer

† Male vs female

‡ Non-smoker vs current/ex-smoker

§ Late-stage vs early-stage

Lung nodule surveillance programmes have shown success across various settings. For example, the lung nodule registry at National Jewish Health established a database of patients with identified nodules, resulting in improved follow-up imaging and a stage shift towards earlier lung cancer diagnosis.[24,25] Similarly, a comprehensive programme in Tennessee in the US reported an increase in the proportion of stage I or II cancer diagnoses from 23% to 38% following the implementation of electronic and manual chart reviews.[10] The lung nodule surveillance programme in this study not only actively tracked reports but also provided clinical assessments, estimated patient cancer risk, and optimised guideline adherence. Our findings echo those of previous studies: stage I and II lung cancer was detected in 54.1% of cases, compared with 22.4% reported in the 2021 HKCR report.

Smoking remains a significant risk factor for lung cancer in both men and women.[26] Our study showed that smokers presented with larger nodules, more advanced disease stages, and a lower likelihood of undergoing surgical resection compared with non-smokers. Unlike Western populations where 10% to 20% of lung cancer patients are non-smokers,[27] approximately 38% of lung cancer cases in Asia occur in non-smokers.[2,18,28-35] Our findings reflect this regional trend, with 60.9% of confirmed lung cancer patients being non-smokers; among them, 38.3% were diagnosed at a late stage. Non-smokers in our cohort were more likely to have GGOs, adenocarcinoma, *EGFR* mutations, and early-stage lung cancer at diagnosis—findings consistent with previous studies.[23,35-37] These results suggest that lung cancer control efforts in Hong Kong should target both smokers and non-smokers with relevant risk factors.[5] Beyond smoking status, emerging research highlighted sex-based differences in lung cancer biology, including hormonal factors, molecular changes, genetic predispositions, the presence of human papillomavirus, nontuberculous mycobacteria, and prior radiation therapy for breast cancer.[35]

Previous studies have shown that improved survival is associated with stage shifts.[38,39] For example, Yang et al[5] reported an increase in stage I disease from 15.9% to 58.8% and a decrease in stage IV disease from 60.3% to 25.7% between 2006 and 2019, during which the 5-year survival rate for lung cancer in Taiwan rose from 22.1% to 54.9%. In the present study, although the median PFS and OS had not yet been reached at the time of analysis; patients with early-stage lung cancer had significantly better survival outcomes. Multivariate analysis identified sex, stage, and age as independent predictors of survival, while no significant survival differences were observed based on nodule density or location. These findings suggest that although the physical attributes of lung nodules are important for diagnosis, survival outcomes are more strongly influenced by factors such as stage at diagnosis, patient demographics, and treatment strategies.

Limitation

This study has several limitations. First, the follow-up period was relatively short at just over 15 months, and the median PFS and OS were not reached for early-stage patients. Second, the observational design of this single-centre study limits the ability to establish a causal relationship between the lung nodule surveillance programme and the observed stage shift. Although patients with clinically metastatic lung cancer were not excluded, the study cohort may not fully represent the broader lung cancer population in Hong Kong. Nevertheless, the findings provide indirect evidence that a lung nodule surveillance programme may facilitate early-stage detection. To confirm the programme's impact on stage shift and survival outcomes, randomised controlled trials or case-control studies comparing enrolled patients with non-enrolled but eligible patients are warranted. Furthermore, local studies evaluating the cost-effectiveness of such programmes would provide further evidence to optimise care for patients with lung nodules.

Conclusion

This lung nodule surveillance programme improved follow-up compliance and facilitated timely, appropriate investigations for high-risk patients. Consequently, more than half of lung cancer cases were diagnosed at an early stage, enabling provision of curative treatments and potentially contributing to improved survival outcomes.

Author contributions

Concept or design: DCL Lam, LYW Shong.
Acquisition of data: WC Chong, LYW Shong, PI Cheang, WC Choy.
Analysis or interpretation of data: LYW Shong, FKP Chan, WC Kwok, WC Chong, MSM Ip, DCL Lam.
Drafting of the manuscript: DCL Lam and LYW Shong.
Critical revision of the manuscript for important intellectual content: DCL Lam, LYW Shong, WC Kwok.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, WC Kwok was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

Acknowledgement

The authors thank all patients for their participation.

Declaration

Part of the research data was presented at the Hospital Authority Convention 2024, 16-17 May 2024, Hong Kong.

Funding/support

The research described in this report was supported in part by the Lee and the Ho Families Respiratory Research Fund.

Ethics approval

This study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster, Hong Kong (Ref No.: UW23-101) and was conducted in full compliance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki. The requirement for patient consent was waived by the ethics board as the study involved minimal risk and used data collected during routine clinical care without altering patient management.

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj2412168).

References

1. Hospital Authority. Hong Kong Cancer Registry 2021. Available from: https://www3.ha.org.hk/cancereg/. Accessed 19 Apr 2024.
2. Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011;365:395-409.
3. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. N Engl J Med 2020;382:503-13.
4. Becker N, Motsch E, Trotter A, et al. Lung cancer mortality reduction by LDCT screening—results from the randomized German LUSI trial. Int J Cancer 2020;146:1503-13.
5. Yang CY, Lin YT, Lin LJ, et al. Stage shift improves lung cancer survival: real-world evidence. J Thorac Oncol 2023;18:47-56.
6. Centre for Health Protection, Department of Health, Hong Kong SAR Government. Cancer Expert Working Group on Cancer Prevention and Screening. Recommendations on Prevention and Screening for Lung Cancer For Health Professionals. Jun 2023. Available from: https://www.chp.gov.hk/files/pdf/lung_cancer_professional_hp.pdf. Accessed 31 Aug 2024.
7. Gould MK, Tang T, Liu IL, et al. Recent trends in the identification of incidental pulmonary nodules. Am J Respir Crit Care Med 2015;192:1208-14.
8. Shelver J, Wendt CH, McClure M, et al. Effect of an automated tracking registry on the rate of tracking failure in incidental pulmonary nodules. J Am Coll Radiol 2017;14:773-7.
9. Wiener RS, Gould MK, Slatore CG, Fincke BG, Schwartz LM, Woloshin S. Resource use and guideline concordance in evaluation of pulmonary nodules for cancer: too much and too little care. JAMA Intern Med 2014;174:871-80.
10. LeMense GP, Waller EA, Campbell C, Bowen T. Development and outcomes of a comprehensive multidisciplinary incidental lung nodule and lung cancer screening program. BMC Pulm Med 2020;20:115.
11. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. Radiology 2017;284:228-43.
12. Bai C, Choi CM, Chu CM, et al. Evaluation of pulmonary nodules: clinical practice consensus guidelines for Asia. Chest 2016;150:877-93.
13. Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT. The eighth edition lung cancer stage classification. Chest 2017;151:193-203.
14. Bach PB, Mirkin JN, Oliver TK, et al. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA 2012;307:2418-29.
15. Field JK, Duffy SW, Baldwin DR, et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. Thorax 2016;71:161-70.
16. Pedersen JH, Ashraf H, Dirksen A, et al. The Danish randomized lung cancer CT screening trial—overall design and results of the prevalence round. J Thorac Oncol 2009;4:608-14.
17. Horeweg N, Scholten ET, de Jong PA, et al. Detection of lung cancer through low-dose CT screening (NELSON): a prespecified analysis of screening test performance and interval cancers. Lancet Oncol 2014;15:1342-50.
18. Krist AH, Davidson KW, Mangione CM, et al. Screening for lung cancer: US Preventive Services Task Force recommendation statement. JAMA 2021;325:962-70.
19. Weinstock TG, Tewari A, Patel H, et al. No stone unturned: Nodule Net, an intervention to reduce loss to follow-up of lung nodules. Respir Med 2019;157:49-51.
20. Chang GC, Chiu CH, Yu CJ, et al. Low-dose CT screening among never-smokers with or without a family history of lung cancer in Taiwan: a prospective cohort study. Lancet Respir Med 2024;12:141-52.
21. ClinicalTrials.gov. Screening for lung cancer in subjects with family history of lung cancer (Identifier NCT05762731). 2023. Available from: https://www.clinicaltrials.gov/study/NCT05762731. Accessed 19 Apr 2024.
22. Schmid-Bindert G, Vogel-Claussen J, Gütz S, et al. Incidental pulmonary nodules—what do we know in 2022. Respiration 2022;101:1024-34.
23. Digby GC, Habert J, Sahota J, Zhu L, Manos D. Incidental pulmonary nodule management in Canada: exploring current state through a narrative literature review and expert interviews. J Thorac Dis 2024;16:1537-51.
24. Carr LL, Dyer DS, Zelarney PT, Kern EO. Improvement in stage of lung cancer diagnosis with incidental pulmonary nodules followed with a patient tracking system and computerized registry. JTO Clin Res Rep 2022;3:100297.
25. Dyer DS, Zelarney PT, Carr LL, Kern EO. Improvement in follow-up imaging with a patient tracking system and computerized registry for lung nodule management. J Am Coll Radiol 2021;18:937-46.

26. O'Keeffe LM, Taylor G, Huxley RR, Mitchell P, Woodward M, Peters SA. Smoking as a risk factor for lung cancer in women and men: a systematic review and meta-analysis. BMJ Open 2018;8:e021611.
27. McCarthy WJ, Meza R, Jeon J, Moolgavkar SH. Chapter 6: Lung cancer in never smokers: epidemiology and risk prediction models. Risk Anal 2012;32 Suppl 1(Suppl 1):S69-84.
28. Church TR, Black WC, Aberle DR, et al. Results of initial low-dose computed tomographic screening for lung cancer. N Engl J Med 2013;368:1980-91.
29. Kovalchik SA, Tammemagi M, Berg CD, et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. N Engl J Med 2013;369:245-54.
30. Aberle DR, DeMello S, Berg CD, et al. Results of the two incidence screenings in the National Lung Screening Trial. N Engl J Med 2013;369:920-31.
31. Patz EF Jr, Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography screening for lung cancer. JAMA Intern Med 2014;174:269-74.
32. Hong Kong Cancer Registry, Hospital Authority. Cancer Facts. 2020. Available from: https://www3.ha.org.hk/cancereg/facts.html. Accessed 19 Apr 2024.
33. Cho J, Choi SM, Lee J, et al. Proportion and clinical features of never-smokers with non–small cell lung cancer. Chin J Cancer 2017;36:20.
34. Chinese Expert Group on Early Diagnosis and Treatment of Lung Cancer, China Lung Oncology Group. China National Lung Cancer Screening Guideline with Low-dose Computed Tomography (2023 Version) [in Chinese]. Zhongguo Fei Ai Za Zhi 2023;26:1-9.
35. MacRosty CR, Rivera MP. Lung cancer in women: a modern epidemic. Clin Chest Med 2020;41:53-65.
36. Horeweg N, van Rosmalen J, Heuvelmans MA, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. Lancet Oncol 2014;15:1332-41.
37. Tolwin Y, Gillis R, Peled N. Gender and lung cancer–SEER-based analysis. Ann Epidemiol 2020;46:14-9.
38. Flores R, Patel P, Alpert N, Pyenson B, Taioli E. Association of stage shift and population mortality among patients with non–small cell lung cancer. JAMA Netw Open 2021;4:e2137508.
39. Potter AL, Rosenstein AL, Kiang MV, et al. Association of computed tomography screening with lung cancer stage shift and survival in the United States: quasi-experimental study. BMJ 2022;376:e069008.

