Original Article

Impact of lung cancer screening with low-dose chest computed tomography on an older population: a retrospective cohort study

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Background: The older population is at high risk of lung cancer (LC). However, the importance of lung cancer screening (LCS) in this population is rarely investigated. Herein, we evaluated the effect of LCS with low-dose computed tomography (LDCT) in the older population.

Methods: This retrospective cohort study was conducted in a single center and included patients aged 70–80 years who had undergone LCS with LDCT. They were categorized into the early 70s (70–74 years) and late 70s (75–80 years) groups based on their age. Using propensity score matching, the control group included patients with non-screening-detected LC from an LC cohort. LC detection, characteristics, and treatment were compared between the early and late 70s groups and between screening-detected LC and non-screening-detected LC.

Results: The study included 1,281 participants who underwent LDCT for LCS, of whom 1,020 were in their early 70s and 261 in their late 70s. Among the screening groups, 87.7% of the patients were ever-smokers. The overall LC detection rate was 2.8%. Interestingly, the LC detection rate in the late 70s group was similar to that in the early 70s group (3.4% *vs.* 2.7%, P=0.485). Furthermore, the incidence of LC was 6.1 cases and 8.3 cases per 1,000 person-years in the early 70s and late 70s groups, respectively (P=0.428). When comparing LC characteristics, patients with screening-detected LC showed a higher proportion of stage I LC (52.8% *vs.* 30.6%, P=0.010) and a lower proportion of stage IV LC (19.4% *vs.* 42.2%, P=0.010) than those with non-screening-detected LC. Moreover, 80.6% of patients with screening-detected LC received appropriate tumor reduction treatment based on the cancer stage.

Conclusions: In the older population, LCS using LDCT showed remarkable detection of LC, with a higher proportion of cases detected at an early stage.

Keywords: Lung cancer (LC); cancer screening; early detection of cancer; low-dose computed tomography (LDCT); elderly

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Introduction

Background

Lung cancer (LC), the second most common cancer, is the leading cause of cancer-related mortality worldwide (1,2). The National Lung Screening Trial (NLST) and Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) study provided compelling evidence on the reduction of LC-related mortality among individuals aged 50–75 years with a significant smoking history who underwent lung cancer screening (LCS) using low-dose computed tomography (LDCT) compared to those undergoing chest radiography and those not undergoing screening, respectively (3,4).

The incidence of LC tends to increase with advancing age, particularly in the population aged 75–80 years (5). However, most LCS studies have primarily focused on patients aged ≤74 years (2-4,6,7). As a result, only a few studies have investigated the effectiveness of LCS with LDCT scans in patients aged >74 years (8). The current guidelines for LCS commonly recommend age restrictions. The US Preventive Services Task Force specifically advises LCS with LDCT scans for individuals aged 55–80 years. In addition to age, eligible patients should have a history of smoking of at least 20 pack-years, be current smokers, or have quit smoking within the last 15 years (9). In addition to the guidelines of the US Preventive Services Task Force, other recommendations are available regarding LCS with LDCT. The American Association for Thoracic Surgery suggests considering LCS with LDCT for patients aged 50–79 years. Similarly, the *Chest* journal recommends screening individuals aged 55–77 years (10,11). Meanwhile, based on the Korean Lung Cancer Screening Project (K-LUCAS), only patients aged 55–74 years with a current smoking history of more than 30 pack-years are eligible to undergo LCS with LDCT in the current National Cancer Screening Program of Korea (12).

Highlight box

Key findings

- Lung cancer screening using low-dose computed tomography (LDCT) showed significant lung cancer detection rate in older people.

What is known and what is new?

- The effectiveness of lung cancer screening (LCS) using LDCT has been proven in heavy smokers aged 50–75 years.
- This study demonstrates the significant early-stage lung cancer detection from LCS in the older population, including individuals aged 75–80 years.

What is the implication, and what should change now?

- Given that LCS with LDCT could improve the early detection of lung cancer in the older population, more studies on lung cancer screening are needed in older smokers, considering the potential benefits of improved survival.

Rationale and knowledge gap

In the older population, poor general condition, decreased cognitive function, and aging-related frailty are issues in active cancer diagnosis and treatment (13,14). Even with early LC diagnosis via LCS with LDCT, further pathologic diagnosis or treatment is not easily accessible by the older population. Considering the life expectancy, the survival gain from the LCS is unclear. Thus, LCS with LDCT has been considered complicated and rarely performed in the older population. However, there are concerns about the excess mortality caused by LC in an older population, and if left untreated, LC can be aggressive and lead to substantial morbidity and mortality, irrespective of age or comorbidity burden (15,16).

Objective

This study aimed to examine the results of LCS with LDCT on LC detection in the older population. This study also aimed to evaluate the trend of early-stage detection through screening. We present this article in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-266/rc).

Methods

Study design and participants

This single-center retrospective cohort study was conducted at a teaching hospital, Veterans Health Service Medical Center (VHSMC), in Seoul. Two retrospective cohorts were used for the study. The first cohort consisted of patients who underwent LCS with LDCT, and the second cohort comprised patients with LC treated at the hospital, regardless of their screening status (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the Veterans Health

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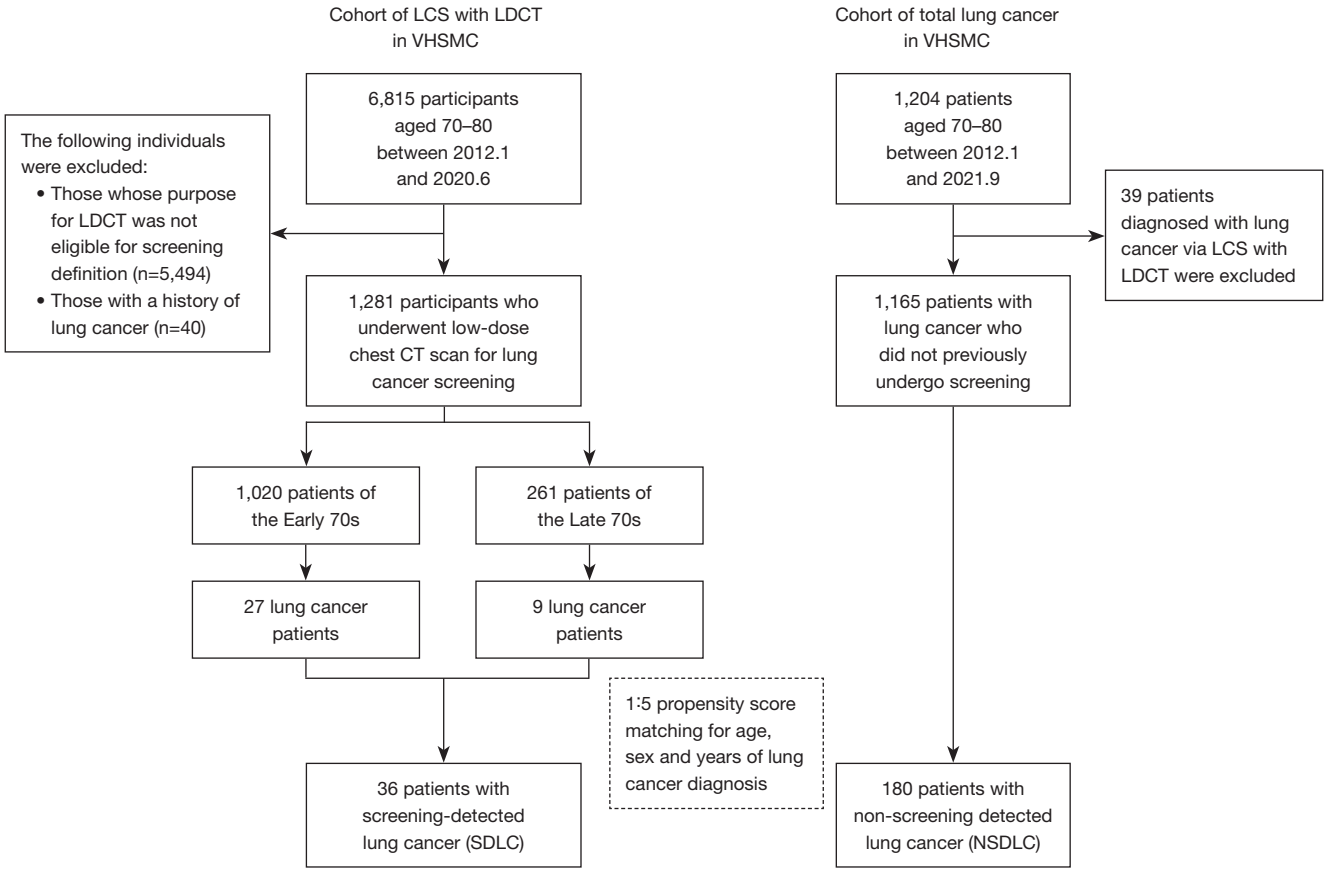

Figure 1 Flow chart of patient enrollment. LCS, lung cancer screening; LDCT, low-dose computed tomography; VHSMC, Veterans Health Service Medical Center; CT, computed tomography.

Service Medical Center (No. BOHUN 2023-02-004-001), the requirement for written informed consent was waived due to the retrospective nature of the study.

The VHSMC pulmonology clinic provides LCS using LDCT to veterans, regardless of their smoking history or age limits. Among participants who visited the pulmonologists' clinic, only patients who had their first LCS with LDCT between January 2012 and June 2020 and whose age at the initial screening was between 70 and 80 years were included. To avoid including patients who underwent LDCT for purposes other than LCS, the following patient groups were excluded: those with a previous history of LC, those who underwent LDCT due to abnormalities found at an earlier chest radiography or other medical images (such as lung nodules, focal inflammation, haziness in the lung field, or other abnormalities suggestive of LC), and those who underwent LDCT for symptoms such as severe cough, dyspnea, hemoptysis, and weight loss.

Then, the patients were categorized into two age groups: the early 70s group, comprising individuals aged 70–74 years, and the late 70s group, comprising consisting of individuals aged 75–80 years. LC diagnosed in the screening cohort was defined as screening-detected lung cancer (SDLC). Among patients with LC in the LC cohort, which included all patients diagnosed with LC in VHSMC between January 1, 2012, and September 30, 2021, patients with non-screening-detected lung cancer (NSDLC) were selected. After excluding patients with SDLC from that cohort, using propensity score matching (PSM), the number of patients with NSDLC was selected five times, ensuring compatibility with the SDLC group. The PSM variables were age, sex, and year of LC diagnosis (*Figure 1*).

Data collection

The medical records of patients were retrospectively reviewed until death or September 30, 2021. The initial LDCT was performed based on the patient's request for

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a health check or on the discretion of pulmonologists to perform LCS. Subsequent LDCT intervals were basically 1–2 years. The following data were collected: age, sex, smoking history, comorbidity with chronic obstructive pulmonary disease (COPD), body mass index, date of LDCT, LDCT interval, LDCT report and image, and number of LDCT scans taken. Nodules with a diameter of ≥4 mm were defined as non-calcified lumps (2,3). Moreover, lung nodules were evaluated using the Lung Imaging Reporting and Data System (Lung-RADS). In patients with nodules, subsequent LDCTs were performed based on the recommendations of the Lung-RADS (17). Patients with lung nodules with a RADS score of 3–4 points were considered positive on LCS with LDCT (18). In addition, survival data of all individuals in the screening cohort were collected from the medical records. All patients are veterans, and their medical records are linked to their survival data from the Ministry of Patriots and Veterans Affairs.

Patients were diagnosed with LC through pathological confirmation. However, for patients who cannot undergo a biopsy because of poor general condition, LC can be diagnosed based on imaging findings and multidisciplinary discussion. Data on LC pathology, diagnostic methods, and treatment modalities of patients with LC were gathered. Treatment was determined by each pulmonologist, oncologist, or surgeon according to National Comprehensive Cancer Network guidelines and decision from multidisciplinary discussions.

The screening rounds were defined based on the CT interval of patients who regularly underwent LCS. The initial LDCT was round 1 of screening. Round 2 was defined as subsequent screening with LDCT between 1 and 2 years after round 1. Round 3 was defined as subsequent screening with LDCT between 1 and 2 years after round 2, and rounds 4–7 were defined in the same way.

LCs detected during the screening were classified into three based on the screening round when the LC was diagnosed: prevalent cancer, subsequent screening-detected cancer, and interval cancer. Prevalent cancer referred to LC diagnosed based on lung abnormalities such as nodules detected in round 1. Subsequent screening-detected cancer was defined as LC diagnosed based on lung abnormalities or nodules detected in subsequent screening rounds except for round 1. Conversely, an interval cancer was defined as LC that arise between scheduled LCS, with the previous screening showing a negative or "normal" result. These cancers are detected in the interval period between screenings and may be cases that were either missed or not detectable in previous screenings (19).

Outcomes

The main outcome of this study is LC detection in the screening groups, and this outcome was compared between the early and late 70s groups. The cumulative LC detection rate was evaluated based on the follow-up duration and LC detection rate for each LDCT round. The characteristics of LC, biopsy methods, and treatments between the early and late 70s groups were compared in patients diagnosed with LC. In addition, differences in LC characteristics, such as stage, histology, and initial treatment, were evaluated between patients with SDLC and NSDLC.

Statistical analyses

Categorical variables were presented as numbers and percentages, and between-group comparisons were conducted using Pearson's chi-square or Fisher's exact test, as appropriate. Continuous variables were expressed as means and standard deviations and compared between the two groups using Student's *t*-test.

LC detection rates were defined in two ways. First, it was defined as the ratio of total LC cases to the entire population screened. The LC detection ratio was calculated for each LDCT screening round and its subgroups. Second, the rate of LC events per person-years at risk for the event was analyzed. Person-years were measured from the time of the first screening to the date of LC diagnosis.

Kaplan-Meier estimation and log-rank tests were used to evaluate the cumulative estimated LC detection rate between the early and late 70s groups. Kaplan-Meier estimation was used to compare survival differences between the LC-diagnosed group and the non-diagnosed group within the screening cohort. It was performed for the total population and separately for the early and late 70s groups, respectively. Survival duration was defined as the time from the initial date of LDCT to the date of death.

To mitigate potential imbalances in factors between patients with SDLC and NSDLC, PSM was applied to reduce selection bias between the SDLC and NSDLC groups. PSM was performed using logistic regression models, with age, sex, and year of LC diagnosis as covariates. PSM was performed at a 1:5 ratio without replacement, with a caliper value of 0.005. Following PSM, the differences between the matched groups were <0.1, indicating a successful balancing of covariates.

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Table 1 Patient characteristics and initial lung nodule characteristics in individuals undergoing lung cancer screening with LDCT

Characteristics	Total number of participants (N=1,281)	Early 70s (N=1,020)	Late 70s (N=261)	P value
Male sex	1,212 (94.6)	973 (95.4)	239 (91.6)	0.015
Age (years)	72.5±2.4	71.5±1.4	76.4±1.4	<0.001
BMI (kg/m^2)	24.6±3.2	24.7±3.2	24.5±5.5	0.625
Smoking status				0.008
Current smoker	419 (32.7)	354 (34.7)	65 (24.9)	
Former smoker	704 (55.0)	551 (54.0)	153 (58.6)	
Never smoker	135 (10.5)	97 (9.5)	38 (14.6)	
Unknown	23 (1.8)	18 (1.8)	5 (1.9)	
Median pack-years of smoking among smokers	40 [25–50]	40 [25–50]	36 [20–50]	0.083
Chronic obstructive pulmonary disease	510 (39.8)	398 (39.0)	112 (42.9)	0.252
Median number of LDCT scans	2 [1–4]	2 [1–4]	2 [1–3]	0.032
Compliance				
Had ≥2 CT scans	889 (69.4)	723 (70.9)	166 (63.6)	0.023
Had ≥3 CT scans	603 (47.1)	495 (48.5)	108 (41.4)	0.039
Median follow-up duration (years)	3.6 [2.6–5.7]	3.7 [2.7–5.7]	3.2 [2.2–5.9]	0.006
Initial lung nodule	708 (55.3)	569 (55.8)	139 (52.3)	0.464
Lung-RADS score				0.552
2	558/708 (78.8)	454/569 (79.8)	104/139 (74.8)	
3	87/708 (12.3)	64/569 (11.2)	23/139 (16.6)	
4A	44/708 (6.2)	36/569 (6.3)	8/139 (5.8)	
4B	15/708 (2.1)	12/569 (2.1)	3/139 (2.2)	
4X	4/708 (0.6)	3/569 (0.5)	1/139 (0.7)	

Data are presented as n (%), mean ± standard deviation, or median [interquartile range]. LDCT, low-dose computed tomography; BMI, body mass index; Lung-RADS, Lung Imaging Reporting and Data System; CT, computed tomography.

All P values were two-sided, and a P value of <0.05 was considered statistically significant. All analyses were performed using Stata 17.0 (Stata Corp., College Station, TX, USA).

Results

Characteristics of the screened populations

Between January 2012 and June 2020, a total of 6,815 participants underwent LDCT at a pulmonary clinic. Among them, 5,494 participants whose purpose for screening was not LCS were excluded. In addition, 40 patients with a previous history of LC were excluded, resulting in the inclusion of 1,281 participants. Among these, 1,020 and 261 participants were included in the early and late 70s groups, respectively (*Figure 1*).

Table 1 shows the baseline characteristics of the participants undergoing LCS. Among the participants, 94.6% were men, and 39.8% had COPD. Moreover, 32.7% were current smokers, 55.0% were former smokers, and 10.5% were never-smokers, indicating that 87.7% of the participants had a history of smoking. Compared with the late 70s group, the early 70s group had a higher proportion of current smokers and a lower proportion of never-smokers (P=0.008). The median pack-years of smoking among smokers were 40, with the early and late 70s groups having

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Table 2 Lung cancer detection during lung cancer screening

Outcomes	Total number of participants (N=1,281)	Early 70s (N=1,020)	Late 70s (N=261)	P value
Lung cancer incidence per 1,000 person-years	6.5	6.1	8.3	0.428
Total lung cancer	36 (2.8)	27 (2.7)	9 (3.4)	0.485
Lung cancer diagnosed at the first screening (prevalent cancer)	14 (1.1)	10 (1.0)	4 (1.5)	0.716
Screening-detected lung cancer*	33 (2.6)	27 (2.6)	6 (2.3)	0.751
Interval cancer§	4 (0.3)	1 (0.1)	3 (1.2)	0.024

Data are presented as incidence per 1,000 person-years, or n (%). *, this included prevalent cancer and subsequent screening-detected lung cancer; §, interval cancer: lung cancer detected between scheduled screenings.

median pack-years of 40 and 36, respectively (P=0.083).

Each participant had a median number of LDCT scans of 2. Among the participants, 889 (69.4%) underwent ≥2 LDCT scans, and 603 (47.1%) underwent ≥3 LDCT scans. Compliance with LCS was higher in the early 70s group than in the late 70s group. Specifically, 723 participants (70.9%) in the early 70s group and 166 participants in the late 70s group underwent ≥2 LDCT (63.6%) (P=0.023). Similarly, a higher proportion of participants in the early 70s group (48.5%) had undergone ≥3 LDCT scans compared with the late 70s group (41.4%) (P=0.039). The median follow-up durations from the initial LDCT were 3.7 years (25th/75th percentile: 2.7–5.7) in the early 70s group and 3.2 years (25th/75th percentile: 2.2–5.9) in the late 70s group (P=0.006).

In this study, the initial LDCT detected nodules in 708 (55.3%) patients. Among them, 569 (55.8%) in the early and 139 (52.3%) in the late 70s group had nodules, respectively, with no significant difference between the two groups (P=0.464) (*Table 1*). The initial Lung-RADS score, based on the characteristics of the lung nodules, is described in *Table 1*. According to the Lung-RADS score, no significant differences were found in the initial lung nodule characteristics between the early and late 70s groups (P=0.552).

LC detection during screening

In a median of 3.6 years of follow-up, 36 (2.8%) of 1,281 patients were diagnosed with LC. No statistically significant differences were found in the proportion of participants diagnosed with LC between the early and late 70s groups. Of the 1,020 participants in the early 70s group, 27 (2.7%) were diagnosed with LC, and of the 261 participants in the late 70s group, 9 (3.4%) were diagnosed with LC (P=0.485). The incidence of LC per 1,000 person-years in the overall group was 6.5. However, the incidence of LC per 1,000 person-years was slightly higher in the late 70s group (8.3) than in the early 70s group (6.1), and this difference was not statistically significant (P=0.428). In round 1, 14 (1.1%) patients were diagnosed with LC, which included 10 (1.0%) patients in the early 70s group and 4 (1.5%) in the late 70s group. However, no significant difference was found between the two groups (P=0.716) (*Table 2*).

The LC detection rate was analyzed for each round among patients who participated in subsequent regular screening programs. In round 2, a total of 812 patients (63.4% of the baseline participants) underwent LCS with LDCT. Among the baseline participants, 604 (47.2%) underwent round 3 of screening, and 372 (29.0%) and 189 (14.8%) patients completed rounds 4 and 5 of screening (*Table 3*). *Table 3* shows the nodule-positive rates and LC detection rates in each round, and *Figure 2* illustrates the initial nodule-positive rates and subsequent LC rates in each screening round. The lung nodule positivity rate in each round was 4.8–11.7% without any tendency to increase or decrease. In round 2, the late70s group showed higher nodule positivity rates (6.1% *vs.* 12.3%, P=0.008); however, the cancer detection rate was comparable between the age groups (1.1% and 0.6% in the early and late 70s groups, respectively, P=0.634). *Table 3* and *Figure 2* show the LC detection rates and the number of lung cancers detected, respectively, according to screening rounds and age groups, specifically the SDLC in rounds 2 and 3 in the early 70s group. However, no LC was detected in the subsequent screening in rounds 2 and 3 in the late 70s group, whereas two SDLCs were found in round 3. Regarding interval cancer, one interval cancer was found between rounds 1 and 2 in the early 70s group, and three interval cancers (1 between rounds 1 and 2, 1 between rounds 3 and 4, and

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Table 3 Results in each screening round in the screening group

Screening	Total number of participants who were screened	Positive lung nodule*				Detection of lung cancer			
		Total number of patients	Number of patients in the early 70s	Number of patients in the late 70s	P value	Total number of patients	Number of patients in the early 70s	Number of patients in the late 70s	P value
First round	1,281 (100.0)	150/1,281 (11.7)	115/1,020 (11.3)	35/261 (13.4)	0.338	14/1,281 (1.1)	10/1,020 (1.0)	4/261 (1.5)	0.444
Second round	812 (63.4)†	59/812 (7.3)	40/657 (6.1)	19/155 (12.3)	0.008	8/812 (1.0)	7/657 (1.1)	1‡/155 (0.6)	0.634
Third round	604 (47.2)†	44/604 (7.3)	40/498 (8.0)	7/106 (6.6)	0.618	7/604 (1.2)	7/497 (1.4)	0/106 (0.0)	0.221
Fourth round	372 (29.0)†	18/372 (4.8)	13/307 (4.2)	5/65 (7.7)	0.238	3/372 (0.8)	0/307 (0.0)	3/65§ (4.6)	<0.001
Fifth round	189 (14.8)†	16/189 (8.5)	13/151 (8.6)	3/38 (7.9)	0.888	3/189 (1.6)	2/151 (1.3)	1/38‖ (2.6)	0.564

Data are presented as n (%). One patient in the early 70s was diagnosed with lung cancer at the seventh screening round. *, patients who had lung nodules (Lung-RADS score of 3–4); †, proportion of patients who underwent this screening round to the baseline number of patients; ‡, one patient was diagnosed with lung cancer between the first and second rounds as an interval cancer; §, one patient was diagnosed with lung cancer between the third and fourth rounds as an interval cancer; ‖, one patient was diagnosed with lung cancer between the fourth and fifth rounds as an interval cancer. Lung-RADS, Lung Imaging Reporting and Data System.

1 between rounds 4 and 5) were diagnosed in the late 70s group. In round 4, the LC detection rate in the late 70s group was higher than that in the early 70s group (4.6% *vs.* 0.0%, P<0.001), and one was an incident cancer. During the screening periods, the detection rate of interval cancer was higher in the late 70s group than in the early 70s group (P=0.014) (*Table 4*). In total, 21 of 27 (77.8%) participants were finally diagnosed with LC from the initial positive nodules in the early 70s group, whereas 4 of 9 (44.4%) were finally diagnosed with LC from initial positive nodulesin the late 70s group (*Figure 2*).

Figure 3A shows the cumulative probability of LC detection in the total population. During the screening, the cumulative probabilities of being diagnosed with LC within 1, 2, 4, and 6 years of follow-up were 1.33%, 1.65%, 2.44%, and 3.08%, respectively. *Figure 3B* shows the probabilities of LC detection according to the two age groups. At 4 years of follow-up, the cumulative LC detection rates were 2.35% and 2.94% in the early and late 70s group, respectively. However, the cumulative LC detection rates did not show a significant difference between the two groups (P=0.523, *Figure 3B*).

Table S1 and Table S2 present the LC detection rates and incidences, respectively, according to subgroups, including sex, smoking history, COPD, and emphysema. The analysis did not reveal any significant differences in the LC detection rates between the early 70s and late 70s groups across these subgroups.

Characteristics and treatment approaches for older individuals with SDLC

In total, 36 patients with LCs were identified in the screening cohorts, with 27 patients from the early 70s group and 9 from the late 70s group. *Table 4* shows the cancer classification according to the screening round, LC diagnostic methods, LC stage, and types of treatment according to age groups. The cancer classification (prevalent, subsequent screening-detected, and interval cancer) is shown in *Table 4*. Four interval cancers were detected, 3 of 9 (33.3%) in the late 70s group and 1 of 27 (3.7%) in the early 70s group, with a higher proportion in the late 70s group than in the early 70s group (P=0.014). In the pathologic diagnoses, the four interval cancers included two small cell LC and one squamous cell carcinoma in the late 70s group and one adenocarcinoma in the early 70s group.

Among patients diagnosed with LC in the early 70s group, only one did not undergo biopsy because of poor general medical condition. All patients with LC in the late 70s group underwent biopsy. The proportion of patients who underwent biopsy was not statistically different between LCs detected in the early and late 70s groups (P=0.379). Among the patients in the early 70s group, 15 (55.6%) presented with adenocarcinomas, whereas 4 (44.4%) in the late 70s group presented with squamous cell carcinomas (P=0.442). Moreover, 15 (55.6%) and 4 (44.4%)

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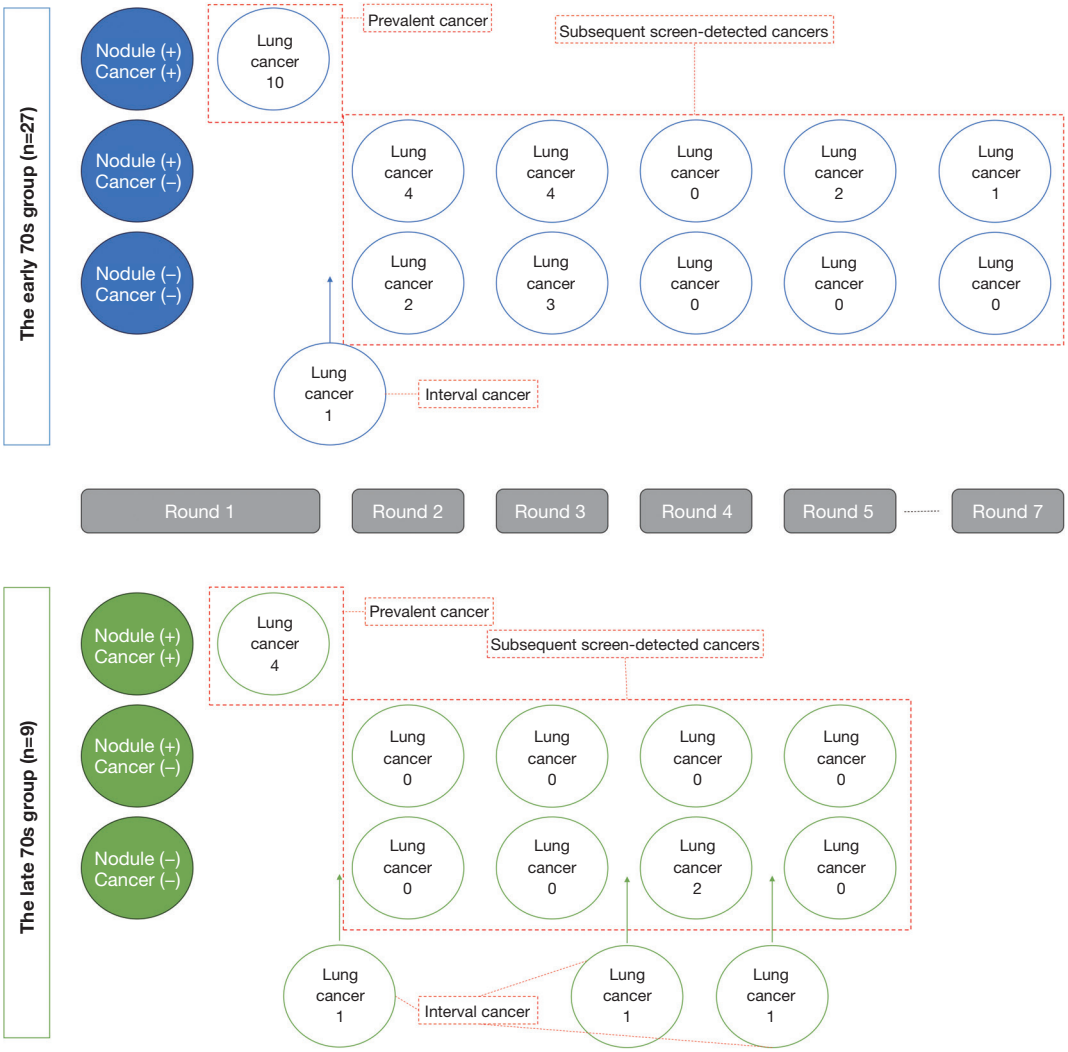

Figure 2 Classification based on the diagnosis time during screening and initial positive nodule in a group of 36 patients with lung cancer.

patients in the early and late 70s groups were diagnosed with stage I LC, and 4 (14.8%) and 3 (33.3%) patients with LC in the early and late 70s groups were diagnosed with stage IV cancer, respectively. The stage distribution between the early and late 70s was not statistically different (P=0.666). Regarding the initial treatment, 16 (59.3%) and 2 (22.2%) patients in the early and late 70s groups received surgical treatment, respectively (P=0.054). Moreover, the proportion of patients who received appropriate LC treatment based on stage was higher in the early 70s group (n=23, 85.2%) than in the late 70s group (n=6, 66.7%), without a statistical difference (P=0.216) (*Table 4*).

Survival comparison between patients with LC and individuals without LC

When evaluating all-cause mortality, significantly lower survival was observed in screened patients with LC than in screened participants without LC. The Kaplan-Meier survival curves presented in *Figure 4* demonstrate a substantial disparity in overall survival between patients diagnosed with LC and those without LC. This trend in survival was consistent across all subgroups, including the entire screened population, as well as the early and late 70s groups. Notably, the survival probability among patients with LC was consistently lower than in those without LC

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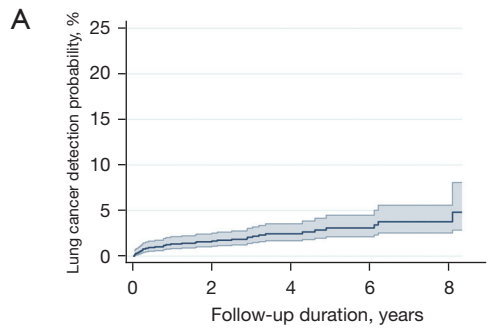
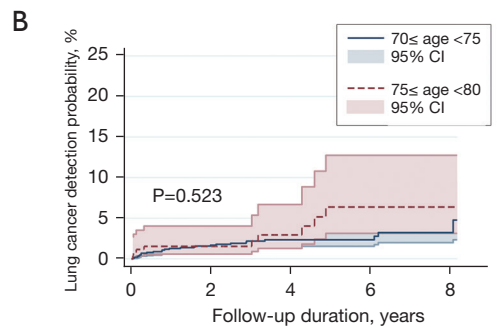


Lung cancer detection, %	1-year	2-year	4-year	6-year	8-year
70≤ age <80	1.33	1.65	2.44	3.08	3.77



Lung cancer detection, % / Age, years	1-year	2-year	4-year	6-year	8-year
70≤ age <75	1.28	1.68	2.35	2.35	3.23
75≤ age <80	1.53	1.53	2.94	6.38	6.38

Figure 3 Cumulative lung cancer detection probability. (A) Estimated lung cancer detection probability in the overall population; (B) estimated lung cancer detection probability according to age. CI, confidence interval.

in each subgroup, with P values of <0.001. The estimated 5-year survival of the group with screening-detected LC was 69.1% in the total population, including 75.4% and 35.6% in the early and late 70s groups, respectively.

Differences in LC characteristics and treatment between the screened and non-screened groups

Regarding the baseline characteristics, the SDLC and NSDLC groups had comparable sex proportion and age after PSM; however, BMI was significantly higher in the SDLC group than in the NSDLC group (24.2 *vs.* 22.8, P=0.041). *Table 5* presents the baseline characteristics of patients with LC and the cancer characteristics of these two groups, indicating that the SDLC group had higher rates of stage I LC (52.8% *vs.* 30.6%, P=0.010) and lower rates of stage IV (19.4% *vs.* 42.2%, P=0.010) than the NSDLC group. No significant differences were observed in the distributions of the pathological types of LC (P=0.204). Moreover, 18 (50.0%) and 64 (35.6%) patients with SDLC and NSDLC underwent surgery, respectively (P=0.103). In addition, 2 (5.6%) patients in the SDLC group and 23 (12.8%) in the NSDLC group received the best supportive care without any cancer treatment (P=0.216). In the SDLC group, 29 (80.6%) patients received appropriate treatment based on their cancer stage, and in the NSDLC group, 141 (78.3%) received appropriate treatment (P=0.766).

Discussion

Key findings

To our knowledge, this study is one of the few studies that have reported LCS results in older individuals. Specifically, this study focused on the group aged 75–80 years, which has not been adequately represented in previous randomized controlled trials (RCTs) such as the NLST or NELSON studies. This study recruited 1,281 older individuals in their 70s and retrospectively reviewed the results of LCS using LDCT, which was performed for a median of 2 and at a median follow-up duration of 3.6 years. Moreover, the LC detection rate was comparable between the early and late 70s groups; however, the incidence of interval cancer, which is diagnosed between screenings, was significantly higher in the late 70s group. The rates of stage I LC between the early and late 70s groups were comparable. This study provides a new insight into the characteristics of LC in the early and late 70s groups. The proportion of patients who received surgical treatment and best supportive care based on stage was lower in the late 70s group than in the early 70s group, without showing statistical significance. Moreover, the SDLC group had earlier LC stages than the NSDLC group. Thus, this study indicates that LC can be diagnosed in the early stage even in individuals in their late 70s through LCS, although LC survival data were not shown appropriately. This finding highlights the need for further research regarding LCS in this age group.

Strengths and limitations

Despite our efforts to include a diverse older population undergoing LCS, 90% of the participants were smokers, and 40% had COPD. The screening was primarily conducted at a pulmonologist's clinic, and this study was conducted at the

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Table 4 Characteristics and treatment patterns of lung cancer in patients detected through screening

Characteristics	Patients with lung cancer in the early 70s (N=27)	Patients with lung cancer in the late 70s (N=9)	P value
Cancer diagnosis			
Prevalent cancer*	10 (37.0)	4 (44.4)	0.693
Subsequent screening-detected cancer†	16 (59.3)	2 (22.2)	0.054
Interval cancer§	1 (3.7)	3 (33.3)	0.014
Median interval between baseline screening and lung cancer diagnosis (years)	1.0 [0.2–2.9]	3.0 [0.1–4.3]	0.897
Diagnostic methods			0.116
Percutaneous needle biopsy	2 (7.4)	2 (22.2)	
Bronchoscopy	8 (29.6)	6 (66.7)	
Surgery	14 (51.9)	1 (11.1)	
Biopsies performed at other sites	2 (7.4)	0 (0.0)	
Patients who did not undergo biopsy because of poor medical condition	1 (3.7)	0 (0.0)	0.376
Histologic type			0.442
Adenocarcinoma	15 (55.6)	3 (33.3)	
Squamous cell carcinoma	7 (25.9)	4 (44.4)	
Small-cell lung cancer	3 (11.1)	2 (22.2)	
Unknown	2 (7.4)	0 (0.0)	
Stage			0.666
I	15 (55.6)	4 (44.4)	
II	3 (11.1)	1 (11.1)	
III	5 (18.5)	1 (11.1)	
IV	4 (14.8)	3 (33.3)	
Initial treatment			0.144
Surgery	16 (59.3)	2 (22.2)	0.054
SABR	1 (3.7)	0 (0.0)	
CCRT	3 (11.1)	1 (11.1)	
Radiation therapy	1 (3.7)	0 (0.0)	
Chemotherapy	3 (11.1)	4 (44.4)‖	
Best supportive care	2 (7.4)	0 (0.0)	
Unknown	1 (3.7)	2 (22.2)	
Appropriate treatment based on stage	23 (85.2)	6 (66.7)	0.216

Data are presented as n (%) or median [interquartile range]. *, prevalent cancer: lung cancer diagnosed after initial LCS with LDCT; †, subsequent screening-detected cancer; §, interval cancer: lung cancer detected between scheduled screenings; ‖, one patient was treated with tyrosine kinase inhibitors. SABR, stereotactic ablative radiotherapy; CCRT, concurrent chemoradiation therapy.

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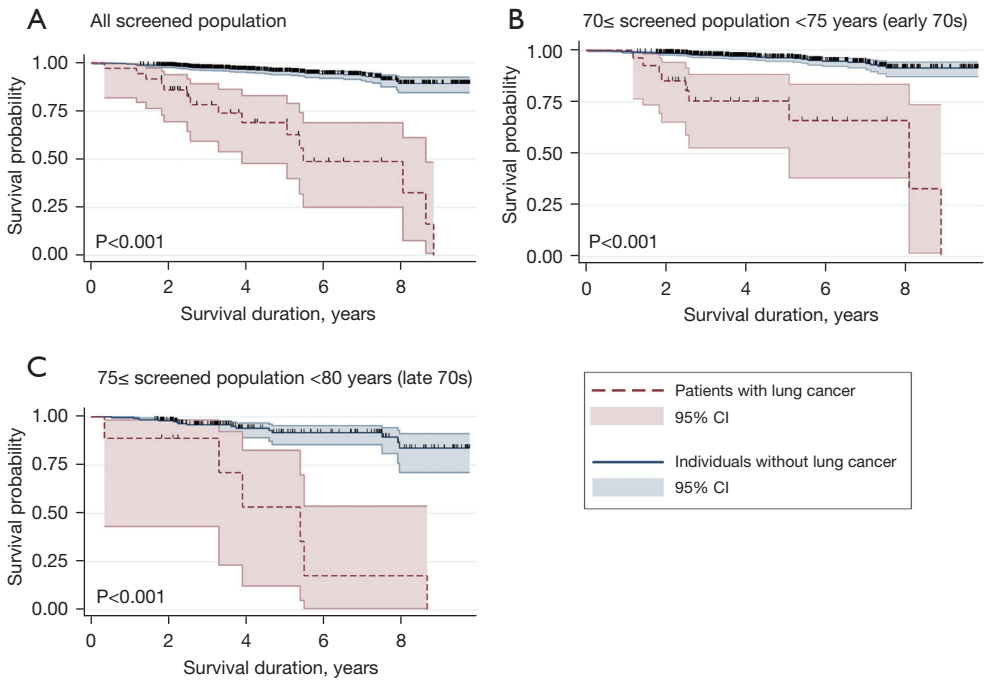

Figure 4 Survival comparisons between patients with and without lung cancer by age. (A) All participants; (B) 70≤ screened population <75 years (early 70s); (C) 75≤ screened population <80 years (late 70s). CI, confidence interval.

largest veteran health service center in Korea, resulting in a predominantly male group. As a result, the cohort primarily consisted of male participants who were smokers and had a higher prevalence of comorbidities compared with the general population, which introduces potential selection bias and limits generalizability. While this may not fully represent the characteristics of the general population, it aligns with previous LCS studies such as NLST, NELSON, and UKLS (3,4,20). Therefore, we are convinced that this study provides valuable insights into the outcomes of LCS, specifically in the older high-risk population.

This study has several limitations. Owing to the retrospective setting, no comparative control group such as non-screening population or chest radiography group was employed. To minimize selection bias, patients with respiratory symptoms were excluded. This led to the exclusion of a large number of participants, resulting in a small sample and statistical power. In addition, no data on the fitness/Eastern Cooperative Oncology Group (ECOG) performance status of the participants at the time of screening were analyzed, which hinders the comprehensive evaluation of the older population. Moreover, the median follow-up period of 3.7 years was relatively short, which is shorter than follow-up periods (7–11 years) in current LCS studies (3,4,21).

Comparison with similar researches

The overall LC incidence rate in the screening group was 6.5 per 1,000 person-years, with rates of 6.1 per 1,000 person-years in the early 70s group and 8.3 per 1,000 person-years in the late 70s group. These incidence rates are comparable to the findings of previous large RCTs, such as NLST with an incidence rate of 645 cases per 100,000 person-years (3), slightly higher than the incidence rate reported in the NELSON trial of 5.58 cases per 1,000 person-years, and in the ITALUNG trial of 49.9 per 10,000 person-year (4,7).

The LC detection rates observed in round 1 (prevalent cancer) of the present study were 1.1% in the total participant population and 1.5% in the early 75s group. These rates are comparable or slightly higher to the findings reported in previous well-powered RCTs such as the NELSON trial (0.9%), NLST trial (1.0%), and Asian studies such as K-LUCAS (0.7%), and study by Li *et al.* (0.7%) (3,4,12,22). The similarities in prevalent cancer rates in round 1 suggest that our study population, consisting of older individuals aged 70–80 years could be considered suitable for LCS. However, after round 1, the late 70s

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Table 5 Comparative analysis of baseline characteristics, lung cancer characteristics, and treatment approaches between patients with SDLC and NSDLC

Characteristics	Patients with SDLC (N=36)	Patients with NSDLC (N=180)	P value
Male sex	35 (97.2)	177 (98.3)	0.652
Age (years)	72.8±2.4	72.7±2.3	0.854
Body mass index (kg/m^2)	24.2±4.1	22.8±3.6	0.041
Smoking status			0.102
Current smoker	20 (55.6)	58 (32.2)	
Former smoker	14 (38.9)	110 (61.1)	
Never smoker	2 (5.6)	9 (5.0)	
Unknown	0 (0.0)	3 (1.7)	
Median pack-years of smoking among smokers	46 [35–50]	50 [40–50]	0.916
Stage			0.070
I	19 (52.8)	55 (30.6)	0.010
II	4 (11.1)	17 (9.4)	0.758
III	6 (16.7)	31 (17.2)	0.936
IV	7 (19.4)	76 (42.2)	0.010
Unknown	0 (0.0)	1 (0.6)	
Histologic type			0.204
Adenocarcinoma	18 (50.0)	58 (32.2)	
Squamous cell carcinoma	11 (30.6)	69 (38.3)	
Small-cell lung cancer	5 (13.9)	33 (18.3)	
Large cell lung cancer	0 (0.0)	6 (3.3)	
Other lung cancer*	0 (0.0)	9 (5.0)	
Unknown	2 (5.6)	5 (2.8)	
Initial treatment			0.063
Surgery	18 (50.0)	64 (35.6)	0.103
SABR	1 (2.8)	2 (1.1)	
CCRT	4 (11.1)	15 (8.3)	
Radiation therapy	1 (2.8)	6 (3.3)	
Chemotherapy	7 (19.4)	65 (36.1)	
Best supportive care	2 (5.6)	23 (12.8)	0.216
Unknown	3 (8.3)	5 (2.8)	
Appropriate treatment based on cancer stage	29 (80.6)	141 (78.3)	0.766

Data are presented as n (%), mean ± standard deviation, or median [interquartile range]. *, other lung cancer: 4 poorly differentiated carcinomas, 2 pseudosarcomatous carcinomas, 1 neuroendocrine carcinoma, 1 carcinosarcoma, and 1 spindle-cell carcinoma. SDLC, screening-detected lung cancer; NSDLC, non-screening-detected lung cancer; SABR, stereotactic ablative radiotherapy; CCRT, concurrent chemoradiation therapy.

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group showed a lower proportion of SDLC but higher rates of interval cancer than the early 70s group. This suggests that the subsequent LCS in this study might not have been as effective in diagnosing LC in the late 70s group. Further studies are warranted to assess the effectiveness of subsequent LCS using LDCT in this age group.

The late 70s group showed higher rates of interval cancer than the early 70s group. Two of 3 interval cancer cases in the later 70s group were small cell LC, and this is not surprising because of the high proportion of interval cancer in the late 70s group. Patients with small LC do not get any survival benefit from LCS (23); It is worth noting that in this study, the compliance was lower in the late 70s group than in the early 70s group, resulting in a higher proportion of interval cancers in the late 70s group. collectively ,we think our data are not sufficient to conclude that the late 70s group showed higher rates of interval cancer in general. Further research is needed to support the difference in the proportion of interval cancer between age groups.

In the total screening group, 50.0% of the patients were diagnosed with stage I LC, including 55.6% in the early 70s group and 44.4% in the late 70s group. These findings align with the results of a previous study, which reported stage I LC rates ranging from 36% to 67% (21,24). In the present study, 19.4% in the total screening group and 33.3% in the late 70s group had stage IV LC. These proportions are consistent with the range of 10–30% reported in previous studies for the diagnosis of stage IV LC (24). Importantly, in the present study, the proportion of patients diagnosed with stage I LC was higher in the SDLC group than in the NSDLC group. In addition, the proportion of patients diagnosed with stage IV LC in the SDLC group (19.4%) was considerably lower than that observed in the NSDLC group (42.7%). These findings suggest a potential change in the staging in this patient population undergoing LCS. More studies are needed to explore whether this change in stage distribution has any effect on survival outcomes.

The issue of overdiagnosis is widely discussed in the field of screening. Previous RCTs have reported varying proportions of overdiagnosis, ranging from 0% to 67% (25). However, our data are sufficient to assess the potential issue of overdiagnosis. Unfortunately, our study did not include a control group, which makes it challenging to calculate the exact proportion of overdiagnosis.

Our data show promising results of LC treatment in the older population. In this study, 81% of the patients in the SDLC group received treatment appropriate to their cancer stage. Pham *et al.* showed that 73.7% of patients aged 70s with LC were presented for treatment discussion at a multidisciplinary meeting (16). Walter *et al.* (26) showed that 79.8% of the patients with LC aged 75–84 years received any tumor-directed treatment. Ganti *et al.* showed that 75% of patients with LC aged >65 years received any tumor-directed treatment (27). Despite concerns regarding treatment toxicity, shorter expected life expectancy, treatment intolerability, and nihilism in an older population, the proportion of SDLC that received cancer treatment in our study was comparable to those in previous studies (15,26,27). Even though this could not guarantee survival gain from screening, at least, results show that a significant number of patients actively pursued aggressive treatment after screening.

In this study, 59% of the early 70s group underwent surgery, whereas only 20% of the late 70s group received surgical treatment. The lower rate of surgical interventions in the late 70s group suggests that the possibility of achieving complete recovery from LC may be lower in this group. However, in older patients, stereotactic ablative radiation therapy has been reported to have comparable treatment efficacy to surgery for early-stage LC (28-30). Therefore, it would be inappropriate to conclude solely based on the lower surgical rate that older patients who underwent screening have lower treatment rates.

Explanations of finding

Unfortunately, our data were not sufficient to estimate the LC mortality reduction between the screening group and the non-screened group. Because of the retrospective design, lead time bias is possible when we compare SDLC and NSDLC; thus, our data could not show the survival benefit of screening.

While poor adherence in the real world is a big issue, the recently published study by Silvestri *et al.* showed that 23.2% of the 70–77-year-old The U.S. Preventive Services Task Force (USPSTF)-eligible population underwent follow-up LDCT (31). We think that the relatively high adherence rate to follow-up CT in our study is a strength considering real-world data. Even though our adherence rate is lower than the rates reported in powered RCTs, comparing other real-world data with our data (63.4% of the participants in round 2) showed that our adherence rate was higher than that reported in previous studies (23–66% of the adherence rate) (31,32).

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Conclusions

This study provides valuable insights into the detection of LC in the older population through LCS with LDCT. The findings highlight the comparable role of LCS with LDCT in identifying LC in patients in their early and late 70s, with LC detection rates comparable to those reported in previous studies. Moreover, a substantial proportion of the detected LCs was at an early stage, indicating potentially favorable treatment outcomes. Importantly, the majority of older patients diagnosed with LC through screening received appropriate treatment based on their individual LC stage. Further research on the survival benefits of LCS with LDCT in this older population is warranted.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-23-266/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form. HRK received research grants from VHS Medical Center for this study and another project. JHS received a research grant from VHS Medical Center unrelated to this study. KBC received a consultant fee from KOLON PHARMA and honoraria for lectures from GSK and Hanmi Pharmaceutical. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the Veterans Health Service Medical Center (No. BOHUN 2023-02-004-001), and the requirement for written informed consent was waived due to the retrospective nature of the study.

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Supplementary

Table S1 Lung cancer detection according to subgroups at baseline low-dose chest computed tomography

Variables	No. of patients with cancer/total No. (%)			P value
	Total participants	Early 70s	Late 70s	
Total	37 of 1,281 (2.8)	27 of 1,020 (2.7)	9 of 261 (3.5)	0.485
Sex				
Male	35 of 1,212 (2.9)	27 of 973 (2.8)	8 of 239 (3.4)	0.636
Female	1 of 69 (1.5)	0 of 47 (0.0)	1 of 22 (4.6)	0.141
Smoking history				
Current smoker	20 of 419 (4.8)	15 of 354 (4.2)	5 of 65 (7.7)*	0.230
Former smoker	14 of 704 (2.0)	11 of 551 (2.0)	3 of 153 (2.0)*	0.978
Never smoker	2 of 135 (1.5)	1 of 97 (1.0)	1 of 38 (2.6)*	0.489
COPD	19 of 510 (3.7)	15 of 398 (3.8)	4 of 112 (3.6)	0.922
Non-COPD	17 of 771 (2.2)	12 of 622 (1.9)	5 of 149 (3.4)	0.287
Emphysema	25 of 665 (3.8)	21 of 522 (4.0)	4 of 143 (2.8)	0.495
Non-emphysema	11 of 616 (1.8)	6 of 498 (1.2)	5 of 118 (4.2)	0.025

*, P value for the three groups: 0.104. COPD, chronic obstructive pulmonary disease.

Table S2 Lung cancer detection rate according to person-year and relative lung cancer detection risk

Variables	Total participants		Early 70s		Late 70s		P value*
	Lung cancer detection per 1,000 person-year†	Multivariable-adjusted rate ratios (95% CI)‡	Lung cancer detection per 1,000 person-year†	Multivariable-adjusted rate ratios (95% CI)‡	Lung cancer detection per 1,000 person-year†	Multivariable-adjusted rate ratios (95% CI)‡	
Total participants	6.5		6.1		8.3		0.428
Sex							
Female	2.7	1.0	0	1.0	8.0	1.0	0.334
Male	6.8	1.14 (0.11–12.02)	6.5	Non-calculable	8.3	0.50 (0.34–7.35)	0.525
Smoking history							
Never smoker	3.0	1.0	2.2	1.0	5.1	1.0	0.704
Former smoker	4.8	1.03 (0.18–5.91)	4.8	0.90 (0.11–7.21)	4.8	1.1 (0.06–18.74)	0.770
Current smoker	11.4	2.52 (0.45–14.17)	9.8	1.90 (0.24–14.97)	21.7	4.30 (0.28–66.38)	0.149
Non-COPD	5.1	1.0	4.5		8.2		0.272
COPD	8.7	1.59 (0.80–3.16)	8.5	1.72 (0.77–3.83)	8.7	1.22 (0.32–4.60)	0.794
Non-emphysema	4.3	1.0	3.0		9.3		0.077
Emphysema	8.4	0.5 (0.1–2.09)	8.7	2.66 (1.03–6.86)	7.1	0.50 (0.11–2.09)	0.702

*, P values were presented for statistically significant differences in lung cancer detection per 1,000 person-year between participants aged 70–74 years and those aged 75–80 years; †, lung cancer detection rates were not adjusted; ‡, rate ratios were adjusted for sex, BMI, and smoking history. COPD, chronic obstructive pulmonary disease; CI, confidence interval.

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