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ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Overuse of follow-up chest computed tomography in patients with incidentally identified nodules suspicious for lung cancer

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Abstract

Purpose Although professional societies agreed that CT screening inconsistent with recommendation leads to radiation-related cancer and unexpected cost, many patients still undergo unnecessary Chest CT before treatment. The goal of this study was to assess the overuse of Chest CT in different type of patients.

Methods Data on 1853 patients who underwent pulmonary resection from May 2019 to May 2020 were retrospectively analyzed. Data collected include age, sex, follow-up period, density and size of nodules and frequency of undergoing Chest CT. Pearson χ^2 test and logistic regression were conducted to compare the receipt of CT screening.

Results Among 1853 patients in the study, 689 (37.2%) overused Chest CT during follow-up of the pulmonary nodules. This rate was 16.2% among patients with solid nodules, 57.5% among patients with pure ground glass opacity (pGGO), and 41.4% among patients with mixed ground glass opacity (mGGO) ($P < 0.001$). 50.7% in the "age ≤ 40" group, 39.8% in the "41 ≤ age ≤ 50" group, 38.7% in the "51 ≤ age ≤ 60" group, 32.3% in the "61 ≤ age ≤ 70" group, 27.8% in the "> 70" group underwent unnecessary CT ($P < 0.001$). Female got more unnecessary CT than male (40.6% vs 32.8%, $P < 0.001$). Factors associated with a greater likelihood of overusing Chest CT was the density of nodules [odds ratios (ORs) of 0.53 for mGGO; 0.15 for solid nodule, $P < 0.0001$, vs patients with pGGO].

Conclusion Roughly 37% patients with pulmonary nodules received Chest CT too frequently despite national recommendations against the practice. Closer adherence to clinical guidelines is likely to result in more cost-effective care.

Keywords Non-small cell lung cancer · Lung cancer screening · Safety · Chest CT

Introduction

Lung cancer is the leading cause of cancer death worldwide, with an estimated 1.6 million deaths annually (International Agency for Research on Cancer 2012). As a high range of lung cancer occurs and develops without any symptom until end-stage, screening becomes significant method of spotting lung cancer. As the US National Lung Screening Trial (NLST), Nederlands–Leuvens Longkanker Screenings Onderzoek (NELSON) and other trial revealed that Computed Tomography (CT) can produce more effect compared with X-ray, Chest CT becomes the first choice of lung cancer screening (Aberle et al. 2011; Yousaf-Khan et al. 2017; Pastorino et al. 2019; Koning et al. 2020).

However, CT is not a perfect choice for lung cancer screening. According to John Brodersen, 49% of detected cancers by low-dose CT (LDCT) were overdiagnosed, (Aalst et al. 2016; Brodersen et al. 2020) and researchers also mentioned that risk of radiation-induced cancers could be a potentially harmful effect of Chest CT which is cumulative over a lifetime (Aberle, et al. 2011; Bach et al. 2012; Rampinelli et al. 2017; Kalra et al. 2004; Board on Radiation Effects Research, Division on Earth and Life Studies, National Research Council of the National Academies 2005). Another concern is the cost-effectiveness of CT screening. The NLST results suggested that screening with

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low-dose CT cost $100,000 per QALY gained, but study of William C. Black showed that screening conducted outside the trial might be costlier if patients' counseling and follow-up were properly accounted for the price (Aberle et al. 2011; Black et al. 2014). The cost could become more considerable if the number of unnecessary CT scans increase, making a heavy burden for patients and healthcare economy.

To minimize the risk of radiation and unnecessary cost, multiple specialty societies have issued recommendations against lung cancer screening for patients with suspicious pulmonary nodules (Ettinger et al. 2019; Kazerooni et al. 2015; Wender et al. 2013). Although specific recommendations differ somewhat, all societies agree that CT screening is not an examination which can be experienced without limitation. But even with these numerous guidelines and recommendations, overuse of Chest CT is routinely performed in patients with nodule suspicious for pulmonary tumor. The goal of this study was to assess the use of Chest CT among patients with pulmonary nodules, and identify the demographic and clinical factors associated with receipt of Chest CT.

Materials and methods

Patients and samples

From May 2019 to May 2020, we consecutively procured data of lung cancer patients who underwent pulmonary resection in the Department of Thoracic Surgery, Fudan University Shanghai Cancer Center, Shanghai, China. The frequency of CT screening was collected by telephone follow-up and checking medical history. Subjects eligible for this study had to meet the following criteria: complete follow-up history and clinical data. Patients who received neoadjuvant therapy were excluded from the study because of inconsistencies of the reason they get Chest CT. Patients with recurrent lung cancer, with multiple concurrent cancers, and with former other malignancies were also excluded from the study. Patients who underwent Chest CT because of symptoms related to lung cancer were excluded, since the NCCN guideline could not apply to them. This research was approved by the Institutional Review Board of the Fudan University Shanghai Cancer Center, Shanghai, China. Written informed consent was obtained from all patients.

As different patients needed different strategies of CT screening, we used recommendation written in Non-small Cell Lung Cancer of NCCN Clinical Practice Guidelines (Version 3. 2020) which gave the advice for patients who incidentally found nodules as golden standard (Ettinger et al. 2019). Related descriptions are in page 10–12 of the guideline and then we grouped patients into two groups: abiding by the guideline or not.

Statistical analysis

All the statistical methods were performed using SPSS for Windows (Version 16.0, Chicago, IL). We assessed the baseline characteristics of patients included in our sample, grouped them by following the guideline or not. Age, sex, density and size of nodules were modeled as categorical variables. Variables were reported as counts and percentages, and groups were compared using Chi-square tests for significance. We used the Pearson χ^2 test to compare the lung cancer detection rate. Finally, we performed a multivariable logistic regression for the likelihood of overusing Chest CT for staging. P values were two-tailed for all the tests. Statistical significance was set as $P < 0.05$.

Results

Among 2667 patients with nodules suspicious for lung cancer, a total of 1853 patients met inclusion criteria (Fig. 1). All patients were Chinese. Baseline demographic and clinical characteristics of the cohort are summarized in Table 1.

Overall, during the 12-month study period, around 37.2% of our patients underwent excessive CT. The proportion of females was 56.0%. 40.6% of them ignored the recommendation, while this rate changed to 32.8% among males. The percentage of patients ≤ 40 years, 41–50 years, 51–60 years, 61–70 years and > 70 years were 11.3%, 17.5%, 30.3%, 30.9% and 10.1%, and 50.7%, 39.8%, 38.7%, 32,3%, 27.8% of them received unnecessary examination.

As for density of nodules, 25.8% of patients found pure ground glass opacity (pGGO) nodules, 40.9% found mixed

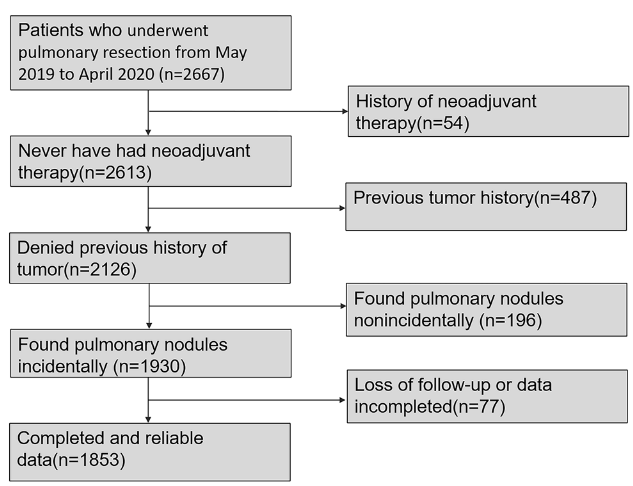

Fig. 1 Study cohort

Table 1 Baseline demographic and clinical characteristics

Variable	Overall cohort *n* (%)	Not abiding by the guideline *n* (%)	Abiding by the guideline *n* (%)	*P* value*
Total, *n*	1853 (100)	689 (37.2)	1164 (62.8)	
Sex				< 0.001
Male	816(44.0)	268 (32.8)	548 (67.2)	
Female	1037 (56.0)	421 (40.6)	618 (59.4)	
Age, years				< 0.001
≤ 40	209 (11.3)	106 (50.7)	103 (49.3)	
41–50	324 (17.5)	129 (39.8)	195 (60.2)	
51–60	561 (30.3)	217 (38.7)	344 (61.3)	
61–70	572 (30.9)	185 (32.3)	387 (67.7)	
> 70	187 (10.1)	52 (27.8)	135 (72.2)	
Nodule density				< 0.001
pGGO	478 (25.8)	275 (57.5)	203(42.5)	
mGGO	759 (40.9)	314 (41.4)	445 (58.6)	
Solid nodule	616(33.2)	100 (16.2)	516 (83.8)	

pGGO pure ground glass opacity, *mGGO* mixed ground glass opacity
*Bold indicates statistically significant *P* values (*P* < 0.05)

Table 2 Required following-up times for different density of nodule

Variable	Overall cohort *n* (%)	Not abiding by the guideline *n* (%)	Abiding by the guideline *n* (%)	*P* value*
pGGO				< 0.001
0	167 (34.9)	93 (55.7)	74 (44.3)	
1	243 (50.8)	125 (51.4)	118 (48.6)	
2	48 (10.0)	39 (81.3)	9 (18.8)	
3	11 (2.3)	10 (90.9)	1 (9.1)	
> 3	9 (1.9)	8(88.9)	1 (10.1)	
mGGO				< 0.001
0	295 (37.3)	144 (50.9)	139 (49.1)	
1	274 (33.9)	62(24.1)	195 (75.9)	
2	84 (10.9)	49 (59.0)	34 (41.0)	
3	71 (9.4)	29 (40.8)	42 (59.2)	
> 3	65 (8.6)	30 (46.2)	35 (53.8)	
Solid nodule				< 0.001
0	440 (56.6)	39 (11.2)	310(88.8)	
1	182 (22.1)	16 (11.8)	120(88.2)	
> 1	152 (21.3)	45 (34.4)	86 (65.6)	

pGGO pure ground glass opacity, *mGGO* mixed ground glass opacity
*Bold indicates statistically significant *P* values (*P* < 0.05)

ground glass opacity (mGGO) nodules, and 32.2% found solid nodules during their screening. 57.5%, 41.4%, and 16.2% of them did not abide by the guideline of NCCN.

Since different density of nodules need different screening strategies, we grouped patients by their density of nodules and assessed how many patients who need different follow-up times were inconsistent with NCCN (Table 2). As a result, for patients with pGGO, 55.7% of patients who need 0 follow-up violated the recommendation, and this rate ranged into 51.4%, 81.3%, 90.9%, 88.9% for who need 1, 2, 3 and more than 3 follow-ups. As for patients with mGGO, 50.9%, 24.1%, 59.0%, 40.8%, 46.2% patients who need 0, 1, 2, 3 and more than 3 follow-ups were not adhere to the guideline, and 11.2%, 11.8%, 34.4% patients with solid nodules who need 0, 1, 2 follow-ups underwent unnecessary Chest CT for screening.

In univariable analysis, factors associated with greater use of CT included younger age [odds ratios (ORs) of 0.64 for 41–50 years, $P = 0.014$; 0.62 for 51–60 years, $P = 0.003$; 0.47 for 61–70 years, $P < 0.001$; and 0.37 for ≥ 71 years, $P < 0.0001$; vs ≤ 40 years], female sex (OR 1.40; $P < 0.001$) and lower nodule density (ORs of 0.52 for mGGO, $P < 0.001$; 0.14 for solid nodule, $P < 0.001$) (Table 3). In terms of the following-up time, patients tended to abide by the guideline when the first follow-up was recommended (ORs of 0.84 for patients with pure GGO, $P = 0.040$; 0.30 for mGGO, $P < 0.001$).

Correlations among patients' unnecessary CT scan with clinical features were further evaluated by multivariable analysis using logistic regression analysis (Table 4). The result suggested that density of the nodules were independent predictors of overusing Chest CT (ORs of 0.53 for mGGO, $P < 0.0001$; 0.15 for solid nodule, $P < 0.0001$, vs patients with pGGO).

Discussion

Despite the mention of risk about overuse of Chest CT by specialty societies, patients are still willing to get the examination as many as possible. In this retrospective cohort study, we found that almost 1 in 3 patients received unnecessary lung cancer screening, and the rate dramatically varied by different characteristics. Previous study suggested the disadvantage of unnecessary Chest CT, and there were studies assessing the rate of community population who underwent lung cancer screening inconsistent with USPSTF (Dull et al. 2017; Richards et al. 2019; Farjah et al. 2021). But to our knowledge, this is the first study to assess the overuse of Chest CT during follow-up after finding nodules suspicious for lung cancer.

Our study finally showed that overuse of CT was likely to happen in patients with less density, and patients with pGGO most tend to undergo CT scan which is inconsistent with recommendation. As a fact, there is no perfect method

Table 3 Univariable analysis of associations with Chest CT

Characteristic	OR	*P* value*
Age, years		
≤40	Ref	
41–50	0.64 (0.45–0.91)	0.014
51–60	0.62 (0.45–0.85)	0.003
61–70	0.47 (0.34–0.64)	< 0.001
≥71	0.37 (0.25–0.57)	< 0.001
Sex		
Male	Ref	
Female	1.40 (1.15–1.70)	< 0.001
Nodule density		
pGGO	Ref	
mGGO	0.52 (0.41–0.65)	< 0.001
Solid nodule	0.14 (0.11–0.19)	< 0.001
Required following-up times for different density of nodule		
pGGO		
0	Ref	
1	0.84 (0.39–0.91)	0.40
2	3.45 (2.27–8.63)	0.002
3	7.96 (1.82–21.82)	0.050
> 3	6..37 (0.78–52.04)	0.084
mGGO		
0	Ref	
1	0.30 (0.21–0.44)	< 0.001
2	1.39 (0.85–2.28)	0.192
3	0.67 (0.39–1.13)	0.132
> 3	0.83 (0.48–1.42)	0.492
Solid nodule		
0	Ref	
1	1.12 (0.61–2.07)	0.70
> 1	4.16 (2.55–6.80)	< 0.001

OR odds ratio, *pGGO* pure ground glass opacity, *mGGO* mixed ground glass opacity

*Bold indicates statistically significant *P* values ($P < 0.05$)

Table 4 Multivariable analysis of associations with Chest CT

Characteristic	OR	*P* value*
Age, years		
41–50	0.83 (0.57–1.20)	0.320
51–60	0.93 (0.66–1.31)	0.658
61–70	0.83 (0.59–1.19)	0.318
≥71	0.80 (0.50–1.26)	0.328
Sex		
Female	0.99 (0.81–1.22)	0.941
Nodule density		
mGGO	0.53 (0.42–0.68)	< 0.001
Solid nodule	0.15 (0.11–0.20)	< 0.001

OR odds ratio, *mGGO* mixed ground glass opacity

*Bold indicates statistically significant *P* values ($P < 0.05$)

to distinguish malignant and benign GGO with accurate certainty. A period of follow-up may be helpful for diagnosis, but the interval of follow-up can be longer than 1 year. Lee et al. reported that pure GGO lesions ≤ 10 mm had a volume-doubling time of more than 400 days, and a study from Japan also suggested that the optimal observation period for patients with multiple GGOs was 36 months (Sato et al. 2017; Oh et al. 2007). According to NCCN guidelines, both pGGO and mGGO < 6 mm do not need any follow up and pure GGO ≥ 6 mm should be followed every 2 years, for up to 5 years (Ettinger et al. 2019).

But as a certain percentage of GGO disappear spontaneously in short term (Lee et al. 2013), some medical workers routinely ask patients to get examination again in 3 months after they found pulmonary nodules to check if the GGO is only an inflammation, leading to a potential risk of radiation overexposure. Another study of Lee et al. suggested that 2 of 90 GGNs (2.2%) followed up for more than 4 years showed significant growth after the 4th year, and whether patients need Chest CT after 5-year follow-up still remains a problem (Huang et al. 2019). These can be reasons for undergoing Chest CT without complying with the recommendation.

Female and younger patients also showed higher rate of inconsistence with NCCN, but this factor may not be the true influencer of unnecessary Chest CT as percentage of GGO was also higher among these groups in our study. 30.8% of females found pGGO during their Chest CT screening, whereas only 14.8% of males found pGGO nodules. This result is in line with those reported by Huang et al. (Balekian et al. 2016). Their study revealed that pGGO was associated with females, and although there was not significance difference, younger age patients got more pGGO in the research.

Given that our analysis relied on data of Fudan University Shanghai Cancer Center and telephone following-up, there are some incumbent limitations to consider. Prior studies have already revealed significant geographic variation about screening and therapy protocol in clinical practice (Milligan et al. 2020). A certain level of recalling bias should be acknowledged, and furthermore, our conclusions only apply to the population analyzed—patients who got pulmonary resection in Fudan University Shanghai Cancer Center. We also excluded patients who had history of other malignant tumors or neoadjuvant therapy, which can lead to selection bias. These patients usually have more advanced disease, and are more likely to get examination for accurate diagnosis, but the purpose of CT for them could be evaluating the therapeutic effect instead of screening, so their examination history shouldn't be judged by the guideline. It would be interest to evaluate the variations among different area and hospitals, and further research in this aspect is warranted.

Conclusion

This retrospective analysis of the data suggested overuse of unnecessary Chest CT in patients with lung nodules suspicious for lung cancer, and this rate vary by radiologic density of the nodules. This dissimilarity may stem from clinical uncertainty, general lack of familiarity with national recommendations and patients' anxious about tumor. Efforts to disseminate evidence-based best practices and adherence to the guidelines will not only spare patients' unnecessary radiation, also curb excessive spending.

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Data availability All data and material is applicable.

Code availability We used SPSS to analyze our data, and the software is applicable.

Declarations

Conflict of interest We declare that there is no professional or other personal interest of any nature or kind in any product.

Ethics approval This research was approved by the Institutional Review Board of the Fudan University Shanghai Cancer Center, Shanghai, China.

Consent to participate Written informed consent was obtained from all patients.

Consent for publication Written informed consent for publication was obtained from all patients.

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