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Association of Nonalcoholic Fatty Liver Disease with Risk of Pulmonary Nodule in Patients with Intestinal Polyp

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Abstract

Objective: Associations of the metabolic risk factors with lung cancer remain to be elusive, and little evidence is available on the association between nonalcoholic fatty liver disease (NAFLD) and pulmonary nodules. We aimed to examine the independent association of NAFLD with the risk of pulmonary nodules.

Methods: Cross-sectional analyses of 1119 patients with intestinal polyp hospitalized in the Department of Gastroenterology, Minhang District Central Hospital of Shanghai, China were conducted. NAFLD was identified by hepatic ultrasonography or hepatic CT scanning diagnosis of hepatic steatosis without excessive alcohol consumption, viral or autoimmune liver disease. Pulmonary nodules were defined as focal, quasi circular, high-density solid or sub solid pulmonary shadows with a diameter $\leq$ 3cm using chest computer tomography test. Multivariable logistic regression analyses were used to calculate the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of NAFLD and clinical characteristics with the risk of pulmonary nodule.

Results: Among the 979 patients with intestinal polyp, prevalence of NAFLD and pulmonary nodule was 25.9% and 32.8%, respectively. Patients with pulmonary nodule, compared to those without, showed significantly higher prevalence of NAFLD (31.5% vs. 23.3%, p=0.006) and obesity (41.4% vs. 32.5%, p=0.006). After adjusting for potential confounding factors, NAFLD was significantly associated with increased risk of pulmonary nodule, and the adjusted odds ratio (OR) (95% confidence intervals (CI)) was 1.370 (1.006-1.867, p=0.046). Besides, old age, ever smoking and obesity were also significantly associated with higher risk of pulmonary nodules, with the adjusted ORs (95%CIs) of 1.022 (1.010-1.033), 1.599 (1.033-2.475) and 1.410 (1.057-1.880) (all p=values<0.05), respectively.

Conclusion: NAFLD was independently associated with increased risk of pulmonary nodules in patients with intestinal polyp. Our findings imply that screening and management of NAFLD and pulmonary nodules are important for lung cancer prevention in patients with intestinal polyp.

Keywords: NAFLD; Pulmonary nodules; Obesity; Lung cancer; Intestinal polyp

Introduction

Nonalcoholic Fatty Liver Disease (NAFLD) comprises a spectrum of pathological conditions, such as simple steatosis, nonalcoholic steatohepatitis and cirrhosis due to fat accumulation in the liver [1]. The prevalence rate of NAFLD among general populations was estimated to be approximately 20-30% in Western countries and 5-18% in Asia [2]. NAFLD has been becoming a heavy public health burden due to its consequences not only for chronic liver disease, hepatocellular carcinoma but also for extra-hepatic diseases, such as Type 2 Diabetes Mellitus (T2DM), Cardiovascular Disease (CVD), and Chronic Kidney Disease (CKD) [3,4]. Furthermore, NAFLD has also been found to be associated with variety types of cancer, including not only hepatocellular carcinoma but also extra-hepatic cancer, such as esophageal, gastric, colorectal, pancreatic, renal, breast and prostate cancers [5-8]. Both incidence and prevalence rates of lung cancer is increasing worldwide, which has been acknowledged as an epidemic with variabilities across countries due to differences in smoking patterns and socio-economic prerequisites [9,10]. Lung cancer is the most frequent malignant neoplasm and the main cancer-related cause of mortality in most developed countries [11]. Important characteristics of lung cancer, compared with other types of cancer, include shorter onset time, higher malignancy, and more difficult to diagnose accurately in the early stage [12]. With increasing development and utility of Computer Tomography (CT) in most countries, the detection of pulmonary nodules has been becoming the most important early clinical manifestation of lung cancer [13,14]. Smoking and genetic risk factors have been well documented as risk factors of lung cancer [15,16]. Zhu et al found that NAFLD and obesity were independently and positively associated with risk of pulmonary adenocarcinoma, but associations of the metabolic risk factors with lung cancer remain to be elusive [17]. Furthermore, little evidence is available on the association between NAFLD and pulmonary nodules. In the present study of 1119 patients with intestinal polyp, we firstly aimed to determine the independent associations between NAFLD and risk of pulmonary nodules. Secondly, we aimed to explore the independent associations of other clinical risk factors with risk of pulmonary nodules.

Methods

Study Population

From January 1, 2020 to April 30, 2021, all patients with intestinal polyp hospitalized in the Department of Gastroenterology, Minhang District Central Hospital of Shanghai, China were recruited into the present study. Of them, 1119 patients with complete data on clinical measurements were included in the present analysis. The inclusion criteria were: (1) intestinal polyp, (2) successfully complete examinations on chest Computer Tomography (CT) plain scanning, hepatic ultrasonography scanning and thyroid ultrasonography scanning, (3) serum biochemical and other laboratory measurements. The exclusion criteria included: (1) age <18 years old, (2) without colonoscopy examination, (3) colorectal cancer, inflammatory bowel disease, ischemic enteritis, non-specific enteritis; lung cancer, familial adenomatous polyposis, colonectomy, other types of cancer, (4) excessive alcohol consumption (total ethanol >30 g/day for men or > 20 g/day for women), viral, drug, autoimmune or other liver diseases, (5) patients with total parenteral nutrition, coeliac disease, hypothyroidism, Cushing's syndrome, β lipoprotein deficiency, (6) uncomplete clinical data or unwillingness to participate in the study. This study was approved by the Human Research Ethics Committee of Minhang District Central Hospital of Shanghai, China. All the participants provided written informed consent.

Measurements

Face-to-face interviews were conducted to collect sociodemographic data, lifestyle habits, present and previous history of health, and medications with each patient. After removal of shoes and heavy clothing, each subject underwent body weight and height measurements using a calibrated scale. Body Mass Index (BMI) was calculated as weight in kilograms divided by height squared in squared meters. Subjects were classified as obesity if BMI equal to or more than 25.0 kg/m^2 according to WHO guidelines for the Asian Pacific population **[18].** Arterial Blood Pressure (BP) was measured with a mercury sphygmomanometer after sitting for at least 15 minutes. Blood pressure measurements were taken according to the National guideline for hypertension management in China (2019), and hypertension was diagnosed as systolic BP ≥ 140 or diastolic BP ≥ 90 mmHg, or treatment of previously diagnosed hypertension **[19].** Venous blood samples were collected in the morning after at least 8-hour fast. All biochemical measurements were tested in the clinical laboratory of Minhang District Central Hospital of Shanghai, China. Blood routine examination, C-Reactive Protein (CRP), Fasting Plasma Glucose (FPG), glycosylated Hemoglobin A1c (HbA1c), liver function (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Gamma-Glutamyl Transpeptidase (GGT), Alkaline Phosphatase (AKP), total bilirubin, direct- and indirect-bilirubin), lipid profiles (Triglyceride (TG), Total Cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c)) and serum Uric Acid (UA) were determined using an automatic biochemical analyzer (Roche Cobas 8000). According to Chinese Diabetes Society Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020), diabetes was defined as (1) a self-reported history of diabetes previously diagnosed by health care professionals; (2) FGP ≥126 mg/dL (7.0 mmol/L); (3) 2-hour plasma glucose (2-h PG, OGTT) ≥200 mg/dL (11.1 mmol/L) **[13].** According to the same guideline, for a person to be defined as metabolic syndrome, they must have at least 3 of the following 4 conditions: (1) overweight or obesity (BMI ≥ 25.0 kg/m^2); (2) hyperglycemia (FPG ≥ 110 mg/dL (6.1 mmol/L), 2-h PG ≥ 140 mg/dL (7.8 mmol/L) or previously diagnosed type 2 diabetes); (3) hypertension (systolic BP ≥ 140 or diastolic BP ≥ 90 mmHg, or treatment of previously diagnosed hypertension); (4) dyslipidemia (TG level ≥ 150 mg/dL (1.7 mmol/L), or HDL-cholesterol < 35 mg/dL (0.9 mmol/L) in males and < 39 mg/dL (1.0 mmol/L) in females) **[20].**

Imaging, ultrasonography and colonoscopy examinations

Hepatic ultrasonography scanning was performed by an experienced radiologist using Philips_iE_Elite / Canon_Aplio_500 / Mindray_DC8_pro / Mindray_Resona7S / Canon_Xario_200/Sonoscape_S50 scanner with a 4-MHz probe, and hepatic steatosis was diagnosed on the basis of characteristic sonographic features, including hepatorenal echo contrast, liver parenchymal brightness, deep beam attenuation, and vessel blurring **[21].** Hepatic CT scanning was also applied and hepatic steatosis was diagnosed on the basis of widely reduced liver density or CT ratio of liver/ spleen <1.0 **[22].** Other abdominal organs (gallbladder, pancreas, spleen and kidney), carotid and thyroid ultrasonography scanning as well as CT tests in chest and abdomen were conducted using standard protocols and techniques. Chest CT plain scanning was conducted using a 32 row CT scanner, and the scanning parameters were as following: total radiation exposure dose ≤ 5 mSv; KVp=120, mAs<60; frame rotation speed ≤ 0.5; detector quasi diameter ≤ 1.5 mm; scanning layer thickness=7 mm; scanning spacing ≤ layer thickness; scanning range: from the tip of the lung to the costal septal angle (including all lungs), with a scanning sampling time of ≤ 10 seconds and a breathing phase of deep inspiratory end.

Definitions of NAFLD and pulmonary nodule

The definition of NAFLD was based on hepatic ultrasonography or hepatic CT diagnosis of hepatic steatosis without excessive alcohol consumption, viral or autoimmune liver disease **[21,23].** Pulmonary nodules were defined as focal, quasi circular, high-density solid or sub solid pulmonary shadows with a diameter ≤ 3cm **[24].**

Statistical analyses

Data are presented as mean ± Standard Deviation (SD) for continuous variables followed the approximation of normal distributions or number and percentage for categorical variables. Differences between subjects with pulmonary nodule (yes vs. no) were analyzed using t-test for normally distributed continuous variables and the chi-square test for categorical variables. Univariable and multivariable logistic regression analyses were used to calculate the unadjusted and adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of NAFLD and clinical characteristics with the risk of pulmonary nodule. All p-values were two-sided, and statistical significance was set at p <0.05. All analyses were performed using SPSS 26.0 software (IBM Corporation).

Results

Of the 979 patients with intestinal polyp, 433 were women and 546 were men with the means (±SDs) of ages of 61.3±0.5 and 61.0±0.6 years, respectively (p-value=0.948).

Demographic and clinical characteristics stratified across pulmonary nodule

Among them, 143 (33.0%) women and 178 (32.6%) men were identified to have pulmonary nodule (p-value=0.888). And the total prevalence rate of pulmonary nodule among the 979 patients with intestinal polyp was 32.8%. **Table 1** showed the differences in the demographic and clinical characteristics stratified by pulmonary nodule (yes vs. no) in all patients. Generally, patients with pulmonary nodule showed significantly higher levels of age, body weight, BMI and were more likely to smoking, prevalence of obesity, compared with their controls (all p-values<0.05). Prevalence of NAFLD in subjects with pulmonary nodule (31.5%) was significantly higher than that in subjects without pulmonary nodule (23.3%, p=0.006).

Table 1: Demographic and clinical characteristics of subjects stratified across pulmonarynodule.

Pulmonary Nodule			
Variables	No	Yes	P value
Demographics			
N (%)	658 (67.2%)	321 (32.8%)	0.888
Sex (n, %)			
Men	368 (55.9%)	178 (55.5%)	

Women	290 (44.1%)	143 (44.5%)	
Age (years)	60.2±0.5	63.4±0.6	<0.001‡
Ever smoking (n, %)	55 (8.4%)	40 (12.5%)	0.043*
Clinical characteristics			
Weight (kg)	64.9±0.4	66.4±0.7	0.049*
BMI (kg/m2)	23.8±0.2	24.4±0.2	0.016*
Obesity (>=25.0) (n, %)	214 (32.5%)	133 (41.4%)	0.006†
Fasting plasma glucose (mmol/L)	5.45±0.06	5.58±0.10	0.207
GGT (U/L)	35.3±2.7	35.1±2.9	0.959
Triglyceride (mmol/L)	1.70±0.07	1.73±0.09	0.81
Total cholesterol (mmol/L)	4.25±0.04	4.32±0.06	0.305
HDL-cholesterol (mmol/L)	1.16±0.02	1.13±0.02	0.237
LDL-cholesterol (mmol/L)	2.83±0.04	2.89±0.05	0.339
NAFLD (n, %)	153 (23.3%)	101 (31.5%)	0.006†

* p<0.05, †p<0.01, ‡p<0.001

All percentages are column percentage; except for percentages, all values are mean±s.d.

Abbreviations: BMI: body mass index; GGT: gamma-glutamyl transpeptidase; HDL: high-density lipoprotein; HDL: high-density lipoprotein; LDL: low-density lipoproteincholesterol

Demographic and clinical characteristics stratified across NAFLD

Table 2 showed the differences in demographic and clinical characteristics stratified by NAFLD (yes vs. no) for all patients. Among the 979 patients, 254 (25.9%) were identified to be NAFLD. Generally, patients with NAFLD, compared to those without, showed significantly higher levels of body weight, BMI, fasting plasma glucose, gamma-glutamyl transpeptidase, TG, TC and LDL-cholesterol and were more likely to be obese and significantly lower level of HDL-cholesterol (all p-values<0.05). Furthermore, prevalence of pulmonary nodule in those with NAFLD (39.8%) was significantly higher than that in subjects without NAFLD (30.3%, p=0.006).

Table 2: Demographic and clinical characteristics of subjects stratified across NAFLD.

NAFLD			
Variables	No	Yes	P value
Demographics			
N (%)	725 (74.1%)	254 (25.9%)	
Sex (n, %)			0.696
Men	407	139 (54.7%)	

	(56.1%)		
Women	318 (43.9%)	115 (45.3%)	
Age (years)	61.1±0.5	61.8±0.8	0.462
Ever smoking (n, %)	66 (9.1%)	29 (11.4%)	0.278
Clinical characteristics			
Weight (kg)	63.7±0.4	70.1±0.7	<0.001‡
BMI (kg/m2)	23.5±0.1	25.6±0.2	<0.001‡
Obesity (>=25.0) (n, %)	206 (28.4%)	141 (55.5%)	<0.001‡
Fasting plasma glucose (mmol/L)	5.35±0.06	5.86±0.10	<0.001‡
GGT (U/L)	32.6±2.4	41.9±3.5	0.037*
Triglyceride (mmol/L)	1.50±0.06	2.20±0.12	<0.001‡
Total cholesterol (mmol/L)	4.20±0.04	4.44±0.07	0.002†
HDL-cholesterol (mmol/L)	1.18±0.01	1.05±0.02	<0.001‡
LDL-cholesterol (mmol/L)	2.80±0.04	2.96±0.06	0.017*
Pulmonary nodule (n, %)	220 (30.3%)	101 (39.8%)	0.006†

p<0.05, †p<0.01, ‡p<0.001

All percentages are column percentage; except for percentages, all values are mean ±s.d.

Abbreviations: BMI, body mass index; GGT, gamma-glutamyl transpeptidase; HDL,high-density lipoprotein; HDL, high-density lipoprotein; LDL, low-density lipoprotein cholesterol

Univariable unadjusted ORs with 95% CI for risk of pulmonary nodule in all patients

Table 3 showed the unadjusted ORs and 95% CIs of NAFLD and other clinical risk factors associated with risk of pulmonary nodule using univariable logistic regression analyses for all subjects. Increasing age, BMI, ever smoking and obesity were all significantly associated with increasing risk of pulmonary nodule (all p-values<0.05). NAFLD (yes vs. no) was significantly associated with elevated risk of pulmonary nodule, and the unadjusted OR (95% CI) was 1.515 (1.126-2.039, p=0.006).

Table 3: Univariable logistic regression analysis for pulmonarynodule.

Pulmonary Nodule			
Variables	OR	95%CI	P-value
Age (years)	1.021	1.010 - 1.032	<0.001*
Ever smoking (yes vs. no)	1.555	1.011 - 2.394	0.047*
BMI (kg/m2) †	1.048	1.008 -	0.017*

		1.089	
Obesity (>=25.0) (yes vs. no)	1.468	1.114 - 1.933	0.007*
NAFLD (yes vs. no)	1.515	1.126 - 2.039	0.006*

* p<0.05

Multivariable adjusted ORs with 95% CI for risk of pulmonary nodule in all patients

The adjusted ORs and 95% CIs of NAFLD and other clinical risk factors with risk of pulmonary nodule using multivariable logistic regression analyses for all subject were shown in **Table 4.** With adjustment for confounding variables in the multivariable logistic regression models, increasing age, ever smoking and obesity were still significantly associated with increased risk of pulmonary nodule (all p-values<0.05). And NAFLD (yes vs. no) was still significantly associated with higher risk of pulmonary nodule with the adjusted OR (95% CI) of 1.370 (1.006-1.867, p=0.046).

Table 4: Multivariable logistic regression analysis for pulmonarynodule.

Pulmonary Nodule			
Variables	OR	95%CI	P-value
Age (years)	1.022	1.010 - 1.033	<0.001*
Ever smoking (yes vs. no)	1.599	1.033 - 2.475	0.035*
Obesity (>=25.0) (yes vs. no)	1.41	1.057 - 1.880	0.019*
NAFLD (yes vs. no)	1.37	1.006 - 1.867	0.046*

* p<0.05

Discussion

In the present study of 979 patients with intestinal polyp, the prevalence rates of NAFLD and pulmonary nodules were 25.9% and 32.8%, respectively. Patients with pulmonary nodules showed significantly higher prevalence of NAFLD and obesity. With adjustment for all potential confounding factors in the multivariable logistic regression analyses, we found NAFLD was independently associated with increased risk of pulmonary nodules. Furthermore, older age, smoking and obesity were also independently associated with higher risk of pulmonary nodules. Both NAFLD and lung cancer has been becoming heavy threats on public health worldwide with their rapidly increasing prevalence, incidence and related economic cost burdens. NAFLD is associated with not only hepatocellular carcinoma but also extra-hepatic cancer. Lung cancer has been becoming the leading cause of cancer death worldwide **[25].** Pulmonary adenocarcinoma is the most common type of lung cancer, which is characterized by gland and/or duct formation and/or significant amounts of mucus production and usually is considered as the most frequently diagnosed histological subtype of non-small-cell lung cancer with dramatically increasing incidence over the past few decades **[26].** Although pulmonary adenocarcinoma has relatively the better prognosis of all type of lung cancer, the overall 5-year survival for lung cancer is frustrating even with extensive therapeutic intervention **[27,28].** Based on a retrospective study of 3664 lung cancer patients, Zhu found that NAFLD and obesity were independently associated with increased risk of pulmonary adenocarcinoma, especially in nonsmoking females, and underscore the need for further study of mechanisms underlying the association of NAFLD with pulmonary adenocarcinoma **[17].** Based on a meta-analysis of 10 cohort studies with a total sample of 182202 middle-aged individuals (24.8% with NAFLD) and a median follow-up period of 5.8 years, Mantovani et al. **[29]** found that NAFLD was associated with 30% increased incidence risk of lung cancer (HR (95%CI): 1.30 (1.14-1.48)). However, little evidence is available on the association between NAFLD and risk of pulmonary nodules. In the present study, to the best of our knowledge, we found that NAFLD was independently associated with increased risk of pulmonary nodules for patients with intestinal polyp, and the adjusted OR (95%CI) was 1.370 (1.006-1.867). To the best of us knowledge, this is the first study to report the independent associations of NAFLD with risk of pulmonary nodules in patients with intestinal polyp. The "two-hit" hypothesis was proposed for the development of NAFLD **[30].** Hyperinsulinemia, production of free radicals and inflammatory mediators play important roles in the two hits. Metabolic syndrome, hypertension and type 2 diabetes mellitus have been shown to be associated with NAFLD, and insulin resistance plays a central etiology role of metabolic syndrome and promotes NAFLD development **[31].** Chronic inflammation was found to be involved in the development of lung cancer **[32].** Therefore, we inferred that these factors may also involve in the associations between NAFLD and pulmonary nodule in patients with intestinal polyp, but future studies on the mechanisms between them are need. Obesity is associated with risk of pulmonary disease, such as asthma and Chronic Obstructive Pulmonary Disease (COPD), and affects lung function adversely. But evidence on the association of obesity with risk of pulmonary nodule is limited **[33].** In the present study, we found that obesity was significantly associated with increased risk of pulmonary nodule, with adjusted OR of about 1.41. Obesity is highly correlated with NAFLD. However, in the present study, we found both NAFLD and obesity were independently associated with risk of pulmonary nodule. Besides of hyperinsulinemia, insulin resistance, chronic inflammation, other potential pathophysiological mechanism underlying the independent associations among NAFLD, obesity and pulmonary nodule need to clarified in future studies. However, our study still had several limitations. First, it was based on cross-sectional analyses, and we could not determine the temporal sequences of the associations of NAFLD, obesity with pulmonary nodules. Second, the sample size was small, and all 979 participants were patients with intestinal polyp sampled from one hospital in Shanghai, China; therefore, selection bias in the present study was inevitable, and we could not generalize the present findings to other populations with limited power. Third, NAFLD was diagnosed using hepatic ultrasonography or hepatic CT scanning with only data on description of hepatic steatosis diagnoses but not quantitative data. Therefore, future studies with larger sample sizes and more accurate and severities of NAFLD, particularly based on prospective cohort study design, are needed.

Conclusion

In the present study, NAFLD and pulmonary nodules was common in patients with intestinal polyp. NAFLD was independently associated with increased risk of pulmonary nodules. Besides, older age, smoking and obesity were also independently associated with risk of pulmonary nodules for all. Therefore, our findings imply that screening and management of NAFLD and pulmonary nodules are important for patients with intestinal polyp from the perspective of lung cancer prevention.

Ethical Approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and the Helsinki Declaration and its later amendments or comparable ethical standards.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no conflicting of interest.

References

1. Angulo P. Nonalcoholic fatty liver disease. N Engl J Med. 2002;346:1221-31.
2. Masarone M, Federico A, Abenavoli L, Loguercio C, Persico M. Non alcoholic fatty liver: epidemiology and natural history. Rev Recent Clin Trials. 2014;9(3):126-33.
3. Targher G, Byrne CD. Clinical Review: Nonalcoholic fatty liver disease: a novel cardiometabolic risk factor for type 2 diabetes and its complications. J Clin Endocrinol Metab. 2013;98(2):483-95.
4. Byrne CD, Targher G. NAFLD: a multisystem disease. J Hepatol. 2015;62(1):S47-64.
5. Sanna C, Rosso C, Marietti M, Bugianesi E. Non-Alcoholic Fatty Liver Disease and Extra-Hepatic Cancers. Int J Mol Sci. 2016;17(5):717.
6. Veracruz N, Hameed B, Saab S, Wong RJ. The Association Between Nonalcoholic Fatty Liver Disease and Risk of Cardiovascular Disease, Stroke, and Extrahepatic Cancers. J Clin Exp Hepatol. 2021;11(1):45-81.
7. Wegermann K, Hyun J, Diehl AM. Molecular Mechanisms Linking Nonalcoholic Steatohepatitis to Cancer. Clin Liver Dis (Hoboken). 2021;17(1):6-10.
8. Mantovani A, Petracca G, Beatrice G, Csermely A, Tilg H, Byrne CD, et al. Non-alcoholic fatty liver disease and increased risk of incident extrahepatic cancers: a meta-analysis of observational cohort studies. Gut. 2022;71(4):778-88.
9. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69-90.
10. Hovanec J, Siemiatycki J, Conway DI, Olsson A, Stücker I, Guida F, et al. Lung cancer and

socioeconomic status in a pooled analysis of case-control studies. PLoS One. 2018;13(2):e0192999.
11. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48(3):889-902.
12. Jakobsen E, Olsen KE, Bliddal M, Hornbak M, Persson GF, Green A. Forecasting lung cancer incidence, mortality, and prevalence to year 2030. BMC Cancer. 2021;21(1):985.
13. Zhao Y, Wang Z, Liu X, Chen Q, Li C, Zhao H, et al. Pulmonary Nodule Detection Based on Multiscale Feature Fusion. Comput Math Methods Med. 2022;2022:8903037.
14. Ding J, Li A, Hu Z. Accurate pulmonary nodule detection in computed tomography images using deep convolutional neural networks. Computer Methods Programs Biomed. 2017;11(3):559-67.
15. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. BMJ. 2000;321(7257):323-9.
16. Parikh AR. Lung Cancer Genomics. Acta Med Acad. 2019;48(1):78-83.
17. Zhu CY, Qu JC, Cao HX, Chen GY, Shi YH, Fan JG. Obesity and nonalcoholic fatty liver disease associated with adenocarcinoma in patients with lung cancer. Medicine (Baltimore). 2019;98(37):e17098.
18. World Health Organization, International Obesity Task Force, International Association for the Study of Obesity. WHO/IOTF/IASO The Asia-Pacific perspective: Redefining Obesity and its Treatment, Hong Kong. 2000.
19. Bureau of Disease Prevention and Control, National Health Commission of People′s Republic of China; National Center for Cardiovascular Diseases; Chinese Academy of Medical Science & Peking Union Medical College, Fuwai Hospital; Chinese Center for Control and Prevention; Chinese Society of Cardiology; Chinese Medical Doctor Association Hypertension Committee; China Sport Science Society; Chinese Nutrition Society; Chinese Stroke Association; Editorial Board of Chinese Journal of Cardiology. [National guideline for hypertension management in China (2019)]. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48(1):10-46. Chinese.
20. Chinese Diabetes Society. Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020 edition). Chin J Diabetes Mellitus. 2021;13(4):315-409.
21. Jian-gao F. Chinese Liver Disease Association: Guidelines for management of nonalcoholic fatty liver disease. An updated and revised edition. Zhonghua Gan Zang Bing Za Zhi 2010;18:163-6. In Chinese.
22. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008;246(3):697-22.
23. Zeng MD, Fan JG, Lu LG, Li YM, Chen CW, Wang BY, et al. Chinese National Consensus Workshop on Nonalcoholic Fatty Liver Disease. Guidelines for the diagnosis and treatment of nonalcoholic fatty liver diseases. J Dig Dis. 2008;9(2):108-12.
24. MacMahon H, Naidich DP, Goo JM, Lee KS, Leung ANC, Mayo JR, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43.
25. Devarakonda S, Morgensztern D, Govindan R. Genomic alterations in lung adenocarcinoma. Lancet Oncol. 2015;16(7):e342-51.

26. Travis WD. Pathology of lung cancer. Clin Chest Med. 2011;32(4):669-92.
27. Motono N, Funasaki A, Sekimura A, Usuda K, Uramoto H. Prognostic value of epidermal growth factor receptor mutations and histologic subtypes with lung adenocarcinoma. Med Oncol. 2018;35(3):22.
28. Tseng CH, Chiang CJ, Tseng JS, Yang TY, Hsu KH, Chen KC, et al. EGFR mutation, smoking, and gender in advanced lung adenocarcinoma. Oncotarget. 2017;8(58):98384-93.
29. Mantovani A, Petracca G, Beatrice G, Csermely A, Tilg H, Byrne CD, et al. Non-alcoholic fatty liver disease and increased risk of incident extrahepatic cancers: a meta-analysis of observational cohort studies. Gut. 2022;71(4):778-88.
30. Day CP, James OF. Steatohepatitis: a tale of two "hits"? Gastroenterology. 1998;114:842-5.
31. Bugianesi E, McCullough AJ, Marchesini G. Insulin resistance: a metabolic pathway to chronic liver disease. Hepatology. 2005;42:987-1000.
32. Lee G, Walser TC, Dubinett SM. Chronic inflammation, chronic obstructive pulmonary disease, and lung cancer. Curr Opin Pulm Med. 2009;15(4):303-307.
33. Brock JM, Billeter A, Müller-Stich BP, Herth F. Obesity and the Lung: What We Know Today. Respiration. 2020;99(10):856-66.

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