Metabolic Syndrome Components and the Risk of Pulmonary Nodules: A Cross-sectional Study in Northern China

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Abstract

Objective: The components of metabolic syndrome have been shown to be associated with lung cancer. Pulmonary nodules (PNs), early predictors of lung cancer, have become common incidental findings with the widespread use of low-dose computed tomography (LDCT) but few epidemiological studies have been performed. The present study aimed to determine the association between MetS and/or its components with PNs in Chinese adults.

Methods:A total of 3,340 participants (51.4% women) aged 18 years or older were included from the Jidong communities. MetS was defined by the criteria from the American Heart Association, and National Heart, Lung, and Blood Institute (AHA/NHLBI). PNs were detected using LDCT.

Results: The prevalence rate of PNs was 19.2% in participants with MetS, while 12.8% in healthy controls (P<0.001). The odds ratio (OR) and 95% confidence internal (CI) for PNs in participants with elevated blood pressure (≥130/85 mmHg or on drugs for treatment of hypertension) was OR = 1.23, 95% CI: 1.01–1.51. Compared to individuals without MetS components, the ORs (95% CI) for PNs development among those with 1, 2, and ≥3 MetS components were 1.25 (0.94–1.67), 1.10 (0.82–1.48), and 1.43 (1.08–1.89), respectively (P for trend =0.04). Moreover, individuals with MetS had an approximately 30% increased risk of PNs than those who did not meet the MetS diagnostic criteria (number of MetS components<3) (OR = 1.29, 95% CI: 1.03–1.61).

Conclusion: The present study suggested that PNs was associated with abnormal MetS components in Chinese adults. Individuals with MetS might have a higher PNs risk than those without MetS.

Introduction

Globally, lung cancer has become the leading cause of cancer-related morbidity and mortality, with an estimated 2.1 million (11.6%) new lung cancer cases and 1.8 million deaths in 2018, representing 1 in 5 (18.4%) cancer deaths[1]. In China, it has also been the major malignancy and the leading cause of cancer death, of which China contributed 35.8% of new cases and 37.6% of deaths worldwide. In addition, the incidence of lung cancer in China is increasing, especially with accumulating number of young lung cancer patients, which is not consistent with the status quo in most western countries[1]. Despite improvements in the treatment of lung cancer, the 5-year survival rate in Chinese population is only 19.7%[2]. However, early detection of pulmonary nodules is very critical for patient care, which will increase the overall 5-year survival rate to 52%[3]. Theore, the prevention of lung cancer is particularly important and urgent.

Pulmonary nodules (PNs), defined as predominantly peripheral solitary or multiple small (≤3cm in diameter), focal radiographic opacities that may be early predictors of lung cancer[4, 5]. Given the widespread application of low-dose computed tomography (LDCT), PNs have become common incidental findings in recent years. About 30% of all chest computed tomography (CT) scans contain one or more pulmonary nodules. By extrapolation, over 1.5 million Americans are expected to have an

incidental pulmonary nodule each year[6]. As compared to chest X-ray, it' s reported a 20% reduction of lung cancer-related mortality after routine screen by LDCT according to the National Lung Cancer Screening Trial (NLST), and emphasized the importance of nodule early detection and evaluation[5, 7]. A multicentre prospective cohort study with 16078 adults in Spain indicated that 51 cases of the 413 patients with SPN detected through CT were diagnosed with lung cancer (12.4 %; 95 % CI 9.3, 15.9), while only 0.85 % of the patients without an abnormality in CT developed lung cancer[8]. Additionally, most existing epidemiologic studies demonstrated that size, location, shape, composition, density, and enhancement of intrapulmonary nodules were strongly associated with the increased risk of malignancy[9]. Recent studies have reported that new pulmonary nodules, although mostly benign, may have a higher odds of being lung cancer than do nodules diagnosed at baseline[10]. Consequently, given early detection and prevention of the occurrence or development of lung nodules, it would be of great significance to reduce the risk of lung cancer.

Metabolic syndrome (MetS) has been used to describe a multifactorial pathological condition characterized by the presence of more than any 3 of 5 risk factors: elevated triglyceride (TG), reduced high-density lipoproteion cholesterol (HDLC), elevated blood pressure (BP), elevated fasting blood glucose (FBG), and an enlarged waist circumference (WC)[11, 12]. Individuals with MetS had increased risks of cardiovascular disease[13], type 2 diabetes mellitus (T2DM)[14], total cancer mortality and all-cause mortality[15, 16]. Furthermore, epidemiologic evidence suggested that the MetS may play a significant role in the development of certain types of neoplasia such as colon, prostate, and breast cancer[17-20]. A link between MetS and lung diseases has also been observed in several cross-sectional and longitudinal studies[21].

Previous studies reported a robust association between lung cancer and each of the 5 MetS components. In these studies, patients with high WC, hypertension, hyperlipidaemia or reduced high-density lipoproteion cholesterol were more likely to have lung cancer, whereas risk with fasting blood glucose was was inconsistent yet[22-25]. Most researches focused on the risk factors for lung cancer, including tobacco smoking, air pollution, occupational exposures and genetic risk factors[26], but few on pulonary nodules[6]. Only He et al comprehensively evaluated a wide range of epidemiological risk factors, assessed their impact on pulmonary nodules in Chinese, and reported that smoking, exposure to second-hand smoke (SHS), eating preserved foods, lung disease and family history of cancer positively correlate with PNs, while eating vegetables, beans and tea does the opposite[27]. However, to our knowledge, the extent that MetS predicting risk of PNs have not been described.

Despite guidelines for the management of pulmonary nodules were published by Fleischner Society and the American College of Chest Physicians (ACCP), few practical methods are accessible for patients with lung nodules apart from regular follow-up and operation treatment[9, 28]. Thus, it is critically urgent to identify modifiable risk factors for prevention and control of pulmonary nodules. With the increasing female patients and non-smokers in Asia[1, 29], it is urgent to identify other unknown risk factors, which can be used in to evaluate the occurrence and development of PNs from the perspective of clinical and biochemical indicators, and give early predication. Taken together, we hypothesized that pulmonary

nodule risk might be correlated with the number of abnormal MetS components. A cross-sectional study with a large sample size from North China was conducted to explore the association between pulmonary nodules and metabolic syndrome components.

Patients And Methods

Study design and population

The study recruited 9078 participants from the Jidong communities (Tangshan City, northern China) from 2013 to 2014[30]. Participants were excluded when they did not meet the inclusion criteria as follows: 1) individuals aged 18 years or older; 2) complete diagnostic history of LDCT; 3) all necessary data are completed and available such as baseline information on MetS components, medical history and family history.

The study was performed according to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Jidong Oilfield Inc Medical Centers. Written informed consent was obtained from each of the participants.

Assessment of Metabolic Syndrome

MetS was defined as the presence of any three of the following five risk factors: 1) elevated waist circumference (≥90 cm for men and ≥80 cm for women); 2) elevated TG levels (≥1.7 mmol/L or on drug for treatment of hypertriglyceridemia); 3) reduced HDL-C (< 1.0 mmol/L in males and < 1.3 mmol/L in females); 4) hypertension (systolic blood pressure(SBP) ≥130 or diastolic blood pressure(DBP) ≥85 mmHg or on drugs for treatment of hypertension); 5) elevated FBG levels (≥5.6 mmol/L or on drugs for treatment of hyperglycemia)[12].

Diagnosis of PNs

Diagnosis of PNs was based on the presence of following abnormal findings according to the guidelines of Fleischner Society and the clinical practice consensus guidelines for Asia[4, 9]: peripheral solitary or multiple small (≤3cm in diameter) detected by medical imaging. LDCT was performed by 3 experienced radiologists who were blinded to the clinical presentation and laboratory findings, using a 64-Slice CT scanner(Sensation 64, Siemens,Germany) (120 KVP, 30 mAs, 5-mm slice thickness, 1.0-1.25mm reconstruction thickness). The images were displayed using the fixed lung window setting (window width 1600-2000 Hu; window level - 600–700 Hu) and mediastinal window (window width 350-380 Hu; window level 10-15 Hu). The subjects were supine and at suspended full inspiration.

Assessment of potential covariates

In this study, details of all participants came from standard questionnaires, clinical examination and laboratory tests. Clinical characteristics and biochemical indicators were assessed at Jidong Oilfield Inc Medical Centers[30]. Smoking status was classified as “never”, “current”or “former”, and drinking status was classified as “never”, “moderate” or “heavy”. The average monthly income per person was categorized as “≤¥1,000”, “¥1,001-3,000” or “>¥3,000”. Salt intake was classified as “low (salt: <6 g/day)” , “medium (salt: 6–10 g/day)” or “high (salt: >10 g/day)”. Education degree was categorized as “illiteracy or primary,” “middle school” or “college graduate or higher.” Physical activity was classified as “very active (exercise ≥150 min/week of moderate intensity or ≥75 min/week of vigorous intensity)” , “moderately active (exercise: 1–149 min/week of moderate intensity or 1–74 min/week of vigorous intensity)” or “inactive (exercise: none)”

Blood samples were collected from the antecubital vein of all participants in the morning under fasting conditions, then centrifuged at a speed of 3000 r/min at room temperature. Within four hours, the serum were measured using an autoanalyzer (Hitachi 747; Hitachi, Tokyo, Japan) at the central laboratory of the Staff Hospital of Jidong oil-field of Chinese National Petroleum. Biochemical indicators included FBG, TG and HDL-c levels[31].

Statistical analysis

Continuous variables were presented as the mean ± standard deviation [32] and were compared by T-test. Categorical variables were presented as frequencies and percentages and were compared using chi-squared tests.

Logistic regression analysis was used to estimate the association between MetS and MetS components with PNs by calculating the odds ratios (OR) and 95% confidence interval (CI). Model 1 was unadjusted. Model 2 was adjusted for age, income, education level , frequency of tobacco smoking, degree of drinking, frequency of physical activity and frequency of salt intake. First, we examined associations of PNs with each of the five MetS components separately using logistic regression analysis. We also estimated the PNs risk based on the number of MetS components by logistic regression analysis. Finally, estimate the correlation between PNs risk and MetS overall.

All statistical analyses were performed using SAS , version 9.4 (SAS Institute Inc, Cary, NC, USA). The statistical tests were two-sided, and the significance level was $P < 0.05$.

Results

Characteristics of participants

The final analyses included 3340 participants after excluding 5629 persons with missing information on MetS Components, LDCT or questionnaire survey, 127 participants with at least one history or current lung diseases and 32 individuals with the family history of lung cancer (Figure1).

Table 1 shows the characteristics of participants according to PNs status. The prevalence of PNs was 13.7% (456/3340). The prevalence rates of PNs in individuals with and without MetS were 19.17% and 12.76% (Figure 2). The mean age of the participants was 52.9 ± 8.9 years and 51.3% of participants were female. The mean values of WC, TG, SBP, DBP, HDL-C, and FBG were 86.2cm, 1.7 mmol/L, 131.0 mmHg, 83.6 mmHg, 1.2mmol/L, and 5.5 mmol/L, respectively.

Compared to participants without PNs, PNs cases were more likely to be older, have lower education levels (illiterate or primary school), lower income (≤¥1,000/month), less physical activity (inactive) and were more inclined to smoking ($P < 0.05$). The levels of WC ($P < 0.001$), SBP ($P < 0.001$) and FBG ($P = 0.05$) were higher among participants with PNs than among those without PNs. However, the levels of TG ($P = 0.178$), DBP ($P = 0.753$), and HDL-C ($P = 0.78$) were similar between the two groups (Table 1).

Table 1
Baseline characteristics of participants by PNs

		PNs:Pulmonary Nodules	NPNs:Non-Pulmonary Nodules	
Characteristics	Total (n=3340)	PNs (n=456)	NPNs(n=2884)	P value
WC	86.2 ± 10.3	87.9± 9.5	86 ± 10.4	<0.001
TG	1.7 ± 1.4	1.6 ± 1.2	1.7 ± 1.4	0.178
SBP	131 ± 20.0	134.3 ± 19.8	130.8 ± 20.0	<0.001
DBP	83.6 ± 13.4	83.4 ± 12.5	83.6 ± 13.5	0.753
HDL	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	0.78
FBG	5.5 ± 1.3	5.6 ± 1.5	5.5 ± 1.3	0.029
Age (years)	53 ± 8.92	58.1 ± 7.5	52.2± 8.9	<0.001
Sex, n (%)				0.908
Male	1625 (48.7)	223 (48.9)	1402 (48.6)	
Female	1715 (51.4)	233 (51.1)	1482 (51.4)	
Smoking history, n (%)				0.045
Never	2359 (70.6)	317 (69.5)	2042 (70.8)	
Current	791 (23.7)	102 (22.4)	689 (23.9)	
Former (>12m)	156 (4.7)	33 (7.2)	123 (4.3)	
Former (<12m)	34 (1.0)	4 (0.9)	30 (1.0)	
Drinking history, n (%)				0.271
Never	2338 (70.0)	333 (73.0)	2005 (69.5)	
Moderate	440 (13.2)	57 (12.5)	383 (13.3)	
Heavy	562 (16.8)	66 (14.5)	496 (17.2)	
Income,/month, n (%)				<0.001
≤1000	1638 (49.6)	277 (61.4)	1361 (47.8)	
1000-3000	1449 (43.9)	153 (33.9)	1296 (45.5)	
≥3000	213 (6.5)	21 (4.7)	192 (6.7)	

Salt intake, n (%)				0.510
Low	757 (22.7)	98 (21.5)	659 (22.9)	
Medium	1724 (51.6)	231 (50.7)	1493 (51.8)	
High	859 (25.7)	127 (27.9)	732 (25.4)	
Level of education, n (%)				<0.001
Illiteracy/Primary school	238 (7.1)	59 (12.9)	179 (6.2)	
Middle school	1873 (56.1)	302 (66.2)	1571 (54.5)	
University and above	1229 (36.8)	95 (20.8)	1134 (39.3)	
Physical activity, n (%)				0.025
Inactive	928 (27.8)	114 (25.0)	814 (28.2)	
Moderately	343 (10.3)	35 (7.68)	308 (10.7)	
Very active	2069 (62.0)	307 (67.3)	1762 (61.1)	
Note.PNs, pulmonary nodules; WC, waist circumference; FBG, fasting blood glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.				

Associations Between Individual Components of MetS and PNs Risk

The associations between each components of MetS and PNs Risk was calculated in multivariable-adjusted models. Compared to the participants with normal BP (SBP < 130 or DBP < 85 mm Hg), those with a high BP (SBP ≥ 130 or DBP ≥ 85 mm Hg) had a higher risk of PNs development (OR = 1.234, 95% CI: 1.007–1.511). Paticipants with raised WC (≥90 cm for men or ≥80 cm for women) had an incresaed risk of PNs with borderline significance (OR=1.170, 95% CI: 1.003–1.437). Participants with raised FBG (≥5.6 mmol/l or antidiabetic medication for the treatment of previously raised glucose) and low HDLC (<1.0 mmol/L in males and < 1.3 mmol/L in females) had an higer but not statistically significant risk of developing PNs (OR=1.052, 95% CI: 0.783–1.413; OR = 1.098, 95% CI: 0.875–1.379, respectively). No increased risk was found for individuals with decreased TG (<1.7 mmol/l) (OR = 0.944, 95% CI: 0.762–1.169; Table 2).

Association Between MetS and PNs Risk

Multivariate analysis presented the association between MetS or number of MetS components and PNs risk. Compared to individuals without MetS components, the ORs (95% CI) for PNs development among those with 1, 2, and ≥3 MetS components were 1.254 (0.941–1.672), 1.101 (0.819–1.481), and 1.431 (1.082–1.893), respectively, which showed a statistically significant trend (P for trend=0.033) of increased PNs risk with an increasing number of abnormal MetS components. Additionally, when compared to those with no MetS, participants with MetS had a higher risk of PNs which reaching significance from a statistical standpoint (OR = 1.286, 95% CI: 1.028–1.609; Table 3).

Table 2
Associations between individual components of MetS and PNs risk in participants

Group	Case	OR (95% CI)	
		Model 1	Model 2
WC (cm)[a]			
Normal	2102	1	1
High	1238	1.238 (1.013-1.514)	1.170 (1.003-1.437)
TG (mmol/l)			
<1.7	2210	1	1
≥1.7	1130	0.964 (0.781-1.188)	0.944 (0.762-1.169
BP (mmHg)[b]			
Normal	1864	1	1
High	1476	1.352 (1.109-1.647)	1.234 (1.007-1.511)
HDL (mmol/l)[c]			
Low	908	1.066 (0.856-1.328)	1.098 (0.875-1.379)
Normal	2432	1	1
FBG (mmol/l)			
<5.6	2406	1	1
≥5.6	934	1.552 (1.150-2.016)	1.052 (0.783-1.413)

Note. PNs, pulmonary nodules; MetS, metabolic syndrome; WC, waist circumference; TG, triglyceride; BP , blood pressure; HDL-C, high-density lipoprotein cholesterol; FBG, fasting blood glucose; Model 1: unadjusted; Model 2: adjusted for age, income, education level , smoking, drinking, physical activity and salt intake. [a] High was defined as ≥90cm for men and ≥80cm for women. Normal was defined as <90cm for men and <80cm for women. [b] High was defined as ≥130/85 mmHg or on drugs for treatment of hypertension. Normal was defined as < 130/85 mm Hg. [c] Low was defined as < 1.0 mmol/L in men and < 1.3 mmol/L in women. Normal was defined as ≥ 1.0 mmol/L in men and ≥ 1.3 mmol/L in women.

Table 3
Associations between MetS and PNs risk in participants

Group	Case	OR (95%CI)	
		Model 1	Model 2
Num.of MetS componentsa			
0	955 (28.6)	1	1
1	800 (24.0)	1.344 (1.014-1.783)	1.254 (0.941-1.672)
2	776 (23.2)	1.212 (0.907-1.620)	1.101 (0.819-1.481)
≥3	809 (24.2)	1.576 (1.198-2.073)	1.431 (1.082-1.893)
P for trend		0.004	0.033
Dichotomously defined			
No MetS	2531 (75.8)	1	1
MetS	809 (24.2)	1.345 (1.080-1.675)	1.286 (1.028-1.609)

Note. PNs, pulmonary nodules; MetS, metabolic syndrome; Num., number; Model 1: unadjusted; Model 2: adjusted for age, income, education level , smoking, drinking, physical activity and salt intake. a Cut-off points were based on previously published criteria from the American Heart Association, and National Heart, Lung, and Blood Institute (AHA/NHLBI): (a) central obesity (waist circumference≥90 cm for men and ≥80cm for women) (b) raised FBG levels (≥5.6 mmol/L or previously diagnosed type 2 diabetes mellitus), (c) rasied BP levels (≥ 130/85 mm Hg or treatment of previously diagnosed hypertension), (d) elevated TG levels (≥1.7 mmol/L), (e) low HDL-C levels (< 1.0 mmol/L in males and < 1.3 mmol/L in females). MetS was defined as the presence of ≥ 3 of the necessary 5 criteria.

Discussion

Based on this large, population-based, cross-sectional study, we recognized that elevated SBP and high WC was associated with PNs development. When considered jointly, the number of abnormal MetS components was linearly associated with increased PNS risk. Remarkably, individuals with ≥3 MetS components had an approximately 40% increased risk of PNs than those with no MetS components. In addition, individuals with MetS had an approximately 30% increased risk of PNs than those who did not meet the MetS diagnostic criteria (number of MetS components<3). To the best of our knowledge, this is the first large-scale cross-sectional study to demonstrate the relationship between MetS components and PNs risk in china. The results provide strong evidence to support the potential impact of MetS components on the increased risk of PNs.

Previous studies have reported that some components of MetS were associated with lung cancer. The increased risk of PNs in individuals with high WC in our study was consistent with that observed in

previous. The European Investigation Into Cancer and Nutrition (EPIC) showed that compared with individuals with similar BMIs and normal WC, those with a greatly higher WC (≥94 cm for men, ≥88 cm for women) had a HR of 1.25 (95% CI: 1.05, 1.50)[33]. A pooled analysis of 12 cohort studies involving more than 1.6 million individuals globally with an average 12-year follow-up found that WC and WHR were associated with increased lung cancer risk, regardless of sex, smoking status, follow-up time, and tumor histology. Even when considering BMIs, participants with BMIs of less than 25 kg/m^2 but higher WC had a 40% greater risk (HR = 1.40, 95% CI: 1.26 - 1.56) than those with BMIs of 25 kg/m^2 or greater but normal/moderate WC[34]. Consequently, abdominal obesity is a part of MetS, which requires us to improve diet and increasing physical exercise.

A follow-up study in Finland provided evidence that both SBP and DBP were weighty predictors of lung cancer, with a 10% increase in risk every 10-mmHg rise in blood pressure. Among smokers, the age-adjusted hazard ratios for blood pressure increment of 10 mmHg are: SBP 1.11 (95% CI: 1.05, 1.17)), DBP 1.17 (95% CI: 1.05, 1.29), respectively[23]. Similarly, a meta-analysis of 7 prospective cohort studies in Europe revealed that In men, significant linear associations in analysis per 10-mm Hg increment of mid-BP were found among men for cancers of lung (*P* for trend□0.05, HR=1.09 (95% CI: 1.03 –1.16). Futher, a positive association by quintiles and 10-mm Hg increments of BP was also found for lung cancer mortality among men (p for trend□0.05, HR=1.09 (95% CI: 1.02 –1.16)[35]. This association is basically consistent with what we found in lung nodules. After adjustment for confounders, results indicated that a positive association of high BP with PNs (OR = 1.23 (1.01–1.51), which reminds us to constantly adhere to the detection and control of blood pressure, reduce salt intake and other risk factors of hypertension.

However, inconsistent to previous studies, we did not find the significant correlation between the remaining other components and pulmonary nodules. Zhang and his collegues found that compared with males with normal TG (75-100 mg/dL), both low TG (HR=1.24, 95%CI: 0.99-1.54) and high TG (HR =1.27, 95%CI: 1.01-1.59) were correlated with increased lung cancer risk[24]. Several longtitude prospective cohort studies indicated that the inverse association of HDL cholesterol was evident for cancers of lung despite of different explanation on the role of reverse causation[36, 37]. Regarding blood glucose, although there is no clear evidence that it is related to increased risk, it's well known that cancer cells prefer to metabolize glucose by Warburg effect[38]. Additionally, a study showed that low FBG levels and diabetes were associated wth poor survival in patientsits with lung cancer[39]. Moreover, a case-cohort study of Finnish men inferred that higher fasting serum insulin concentrations, as well as the presence of insulin resistance, appear to be associated with an elevated risk of lung cancer development[25]. Diabetes was also confirmed to be an independent predictor of the risk of recurrence following resection of NSCLC[40]. Compared with non-diabetic controls limiting the analysis to studies adjusting for smoking status, diabetes was independently associated with the increased risk of lung cancer (RR, 1.11; 95% CI, 1.02–1.20; I2= 46.1%)[41]. Differences in race, definitions of major variables, and adjusted confounders might possibly explain these discrepancie.

The association of lung cancer risk with MetS is currently controversial. Some studies suggested there were no obvious association between MetS and lung cancer[16, 17]. In contrast, some studies indicated

that MetS and/or its components are somewhat associated with a higher risk of lung cancer incidence and believed the mechanism of MetS promotes the cancer development/growth is not well defined, especially for lung cancers[42]. Interestingly, rencent epidemiological analysis indicated that the prevalence of MeS in survivors of lung cancer showed higher prevalence of MeS compared with that of the controls without chronic disease (OR = 2.11; 95% CI = 1.33–3.36)[43]. From a genetic perspective, a review showed that genes associated with metabolic syndrome were present among genes related to susceptibility to lung adenocarcinoma in never smokers. Epidermal growth factor receptor (*EGFR*), vesicle transport through interaction with t-SNAREs homologue 1A gene (VTI1A), tumor necrosis factor receptor superfamily member 10C (TNFRSF10C), Chromosome 3 open reading frame 21 (C3ORF21) and hyper methylation of TNFSF10C, Basic helix-loop-helix transcription factor 5 (BHLHB5), and boule-like RNA-binding protein (BOLL) are involved in the metabolic pathways of metabolic syndrome[44]. Our observations on the association of PNs risk with MetS yielded similar and interesting conclusions.

In addition to the genetic perspective, several potential mechanisms might explain the associations between MetS and PNs including several processes such insulin resistance, dyslipidemia, endothelial dysfunction, abnormal glucose utilization, and oxidative stress, DNA damage, Low-grade systemic inflammation, asabnormal cell proliferation etc[23, 34, 41, 42, 45]. An index case also highlighted the emerging interaction between MetS and tuberculosis[46]. Central obesity, hypertension, hyperglycemia and the rest work together to increase risk. Hence, it need to confirm the degree of the correlation of factors that might be mediated by MetS. It need further investigations to explain the intrinsic biological mechanism underlying the correlation between MetS components and PNs.

Potential limitations of our study ought to be discussed. First, due to its observational nature, our discoveries might be influenced by measurement errors in anthropometric variables and residual confounding in covariates such as smoking exposure. Second, all participants in this study recruited from the Jidong communities in northern China, which restricts the generalization of the finding. Finally, the design of this cross-sectional study made it difficult to evaluate the causality between MetS and PNs. In the future, we need to increase the sample size and perform a longtime follow-up examinations to compare the change of MetS components while clarifying the diagnosis of benign and malignant lung nodules.

Conclusion

In summary, our community-based study indicates PNs risk is related with abnormal MetS components. Additionally, elevated SBP and high WC are of both public and clinical healthy significances for recognizing subjects with high PNs risk. Consequently, performing health education in the population, controlling the risk factors of MetS, especially keeping SBP and WC within an proper range, might be a efficiently preventive strategy to control the occurrence and development of PNs in China.

Abbreviations

PNs: Pulmonary Nodules; LDCT: Low-dose Computed Tomography; AHA/NHLBI: American Heart Association, and National Heart, Lung, and Blood Institute; CI: Confidence Internal; OR: Odds Ratio; MetS: Metabolic Syndrome; NLST: National Lung Cancer Screening Trial; TG: Triglyceride; HDLC: High-Density Lipoproteion Cholesterol; BP: Blood Pressure; FBG: Fasting Blood Glucose; WC: Waist Circumference; T2DM: Type 2 Diabetes Mellitus; SHS: Second-hand Smoke; ACCP: American College of Chest Physicians; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; EPIC: European Investigation Into Cancer and Nutrition; EGFR: Epidermal Growth Factor Receptor; VTI1A: Vesicle Transport Through Interaction with t-SNAREs Homologue 1A Gene; TNFRSF10C: Tumor Necrosis Factor Receptor Superfamily Member 10C; C3ORF21: Chromosome 3 Open Reading Frame 21; BHLHB5: Basic Helix-loop-helix Transcription Factor 5; BOLL: Boule-like RNA-binding Protein.

Declarations

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Authors’contributions

MYZ and XYC drafted the manuscript and interpreted the data. XCZ, QQS, TFZ and YRH helped with the acquisition and analyses of the data. YZ helped coordinate the study within the communities. JJC and CSC reviewed the manuscript and made suggestions. All authors read and approved the manuscript.

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Availability of data and materials

The datasets analysed during this study are available from corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Jidong Oilfield Inc Medical Centers (NO.1). Written informed consent was obtained from each of the participants.

Consent for publication

Not applicable.

Competing interests

Authors have no conflict of interests.

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Figures

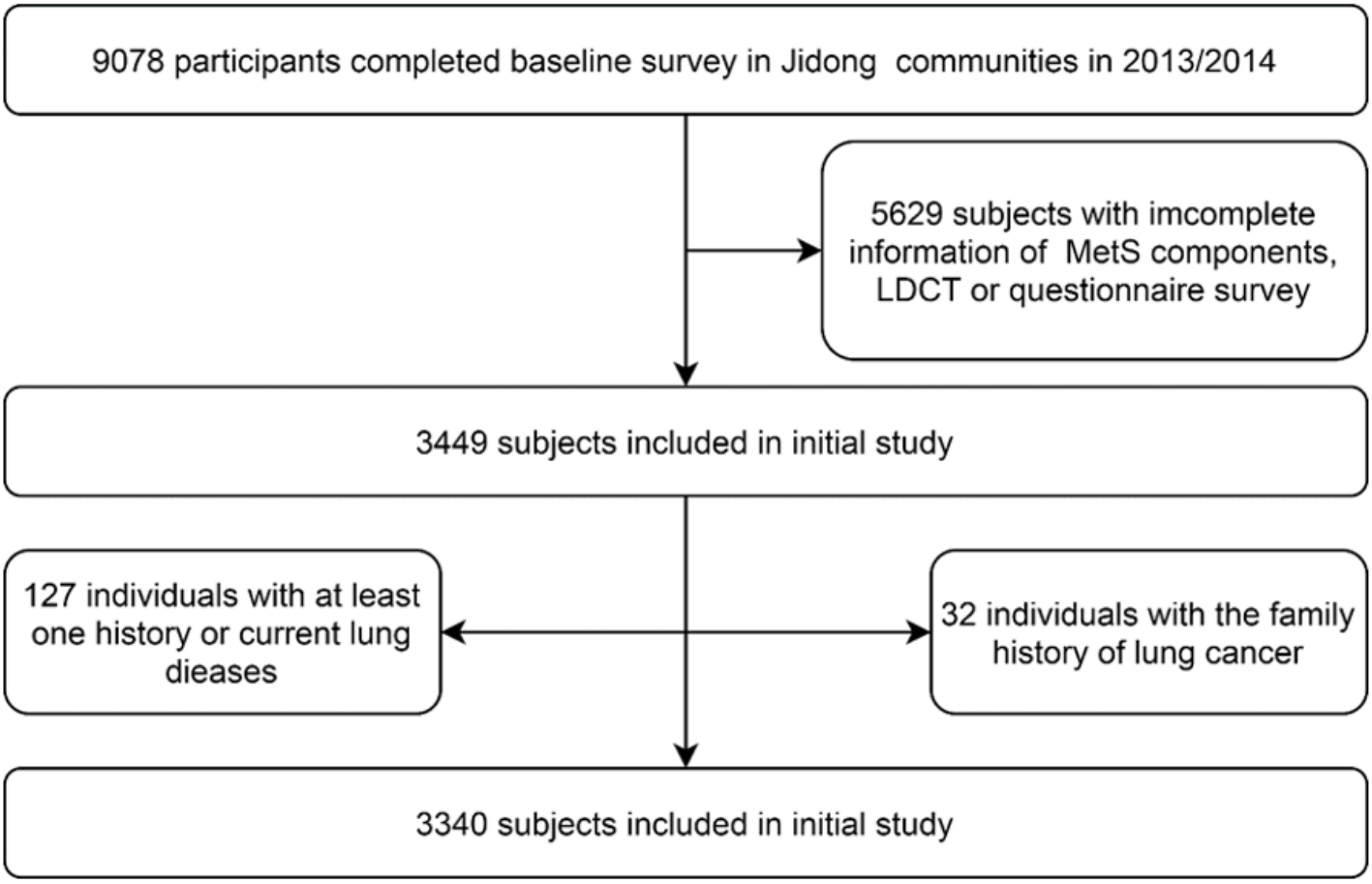

Figure 1

Flow chart of this study

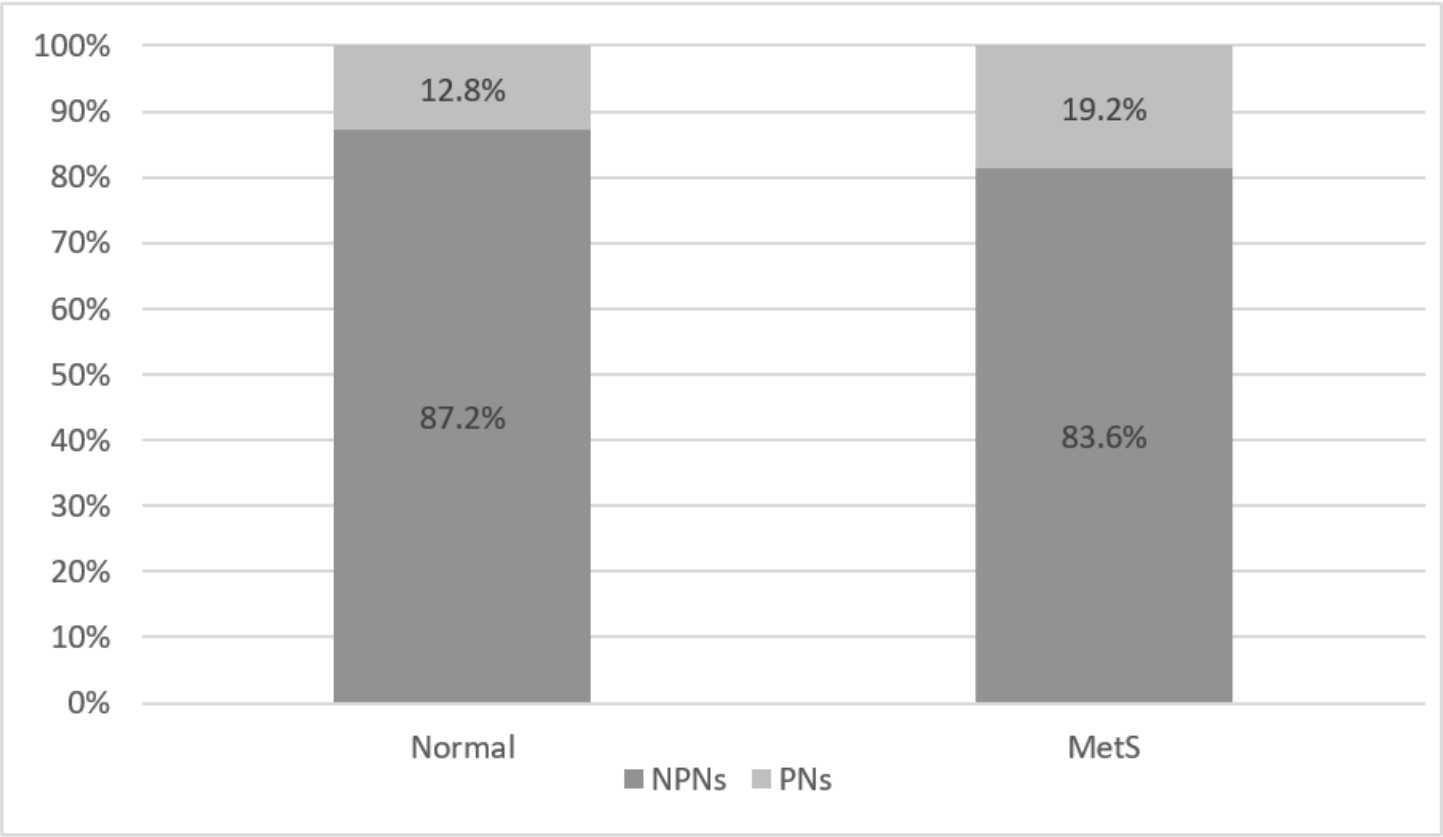

Figure 2

Prevalence of PNs in participants with or without MetS Note.PNs, pulmonary nodules; NPNs, Non-Pulmonary nodules.