Association between metabolic overweight/obesity phenotypes and readmission risk in patients with lung cancer: A retrospective cohort study

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Summary

Background Increased body mass index (BMI) and metabolic abnormalities are controversial prognostic factors of lung cancer. However, the relationship between metabolic overweight/obesity phenotypes and hospital readmission in patients with lung cancer is rarely reported.

Methods We established a retrospective cohort using the United States (US) Nationwide Readmissions Database (NRD). We included adult patients diagnosed with lung cancer from January 1, 2018 to November 30, 2018 and excluded patients combined with other cancers, pregnancy, died during hospitalization, low body weight, and those with missing data. The cohort was observed for hospital readmission until December 31, 2018. We defined and distinguished four metabolic overweight/obesity phenotypes: metabolically healthy with normal weight (MHNW), metabolically unhealthy with normal weight (MUNW), metabolically healthy with overweight or obesity (MHO), and metabolically unhealthy with overweight or obesity (MUO). The relationship between metabolic overweight/obesity phenotypes and 30-day readmission risk was assessed by multivariable Cox regression analysis.

Findings Of the 115,393 patients included from the NRD 2018 (MHNW [58214, 50.4%], MUNW [44980, 39.0%], MHO [5044, 4.4%], and MUO [7155, 6.2%]), patients with the phenotype MUNW (6531, 14.5%), MHO (771, 15.3%), and MUO (1155, 16.1%) had a higher readmission rate compared to those with MHNW (7901, 13.6%). Compared with patients with the MHNW phenotype, those with the MUNW (hazard ratio [HR], 1.10; 95% CI, 1.06−1.14), MHO (HR, 1.15; 95% CI, 1.07−1.24), and MUO (HR, 1.28; 95% CI, 1.20−1.36) phenotypes had a higher risk of readmission, especially in men, those without surgical intervention, or those aged >60 years. In women, similar results with respect to readmission were observed in people aged >60 years (MUNW [HR, 1.07; 95% CI, 1.01−1.13], MHO [HR, 1.19; 95% CI, 1.06−1.35], and MUO [HR, 1.28; 95% CI, 1.16−1.41]). We also found increased costs for 30-day readmission in patients with MHO (OR, 1.18; 95% CI, 1.07−1.29) and MUO (OR, 1.11; 95% CI, 1.02−1.20).

Interpretation Increased BMI and metabolic abnormalities are independently associated with higher readmission risks in patients with lung cancer, whereas increased BMI also increases the readmission costs. Follow-up and intervention method targeting increased BMI and metabolic abnormalities should be considered for patients with lung cancer.

Abbreviations: NRD, Nationwide Readmissions Database; MS, metabolic syndrome; HCUP, Healthcare Cost and Utilization Project; ICD-10, International Classification of Diseases, 10th Revision; PCS, Procedure Coding System; HR, hazard ratio; OR, odds ratio; CI, confidence interval; BMI, body mass index; MHNW, metabolically healthy with normal weight; MUNW, metabolically unhealthy with normal weight; MHO, metabolically healthy with overweight or obesity; MUO, metabolically unhealthy with overweight or obesity; LOS, length of stay

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Keywords: Lung cancer; Readmission; Body mass index; Metabolic abnormality; Phenotype

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Research in context

Evidence before this study

We searched PubMed for studies published in English until Mar 30, 2022, using combinations of "readmission", "phenotype" and "lung cancer". We only identified one meta-analysis but it was not related to our study. There was no study exploring the relationship between metabolic overweight/obesity phenotype and readmission risk in patients with lung cancer. We also used combinations of "BMI" and "lung cancer", "metabolic syndrome" and "lung cancer". We found that patients with overweight or obesity had a lower risk of death, which was known as the "obesity paradox". The relationship between metabolic syndrome and lung cancer was controversial.

Added value of this study

This study was the first to make an exploration of the relationship between metabolically defined overweight/obesity and readmission risk in patients with lung cancer using the large national retrospective cohort study.

Implications of all the available evidence

We found increased BMI and metabolic abnormalities are independently associated with higher readmission risks in patients with lung cancer, whereas increased BMI also increases the 30-day readmission costs in patients with lung cancer. Follow-up and intervention method targeting increased BMI and metabolic abnormalities could be considered for patients with lung cancer to reduce hospital readmission and disease burden.

Introduction

Hospital readmission is an important predictor of resource utilization and a metric used to improve nursing quality and cut down costs associated with patient care.[1] Identifying readmission factors can help design more personalized follow-up plans to reduce readmission for patients and decrease the disease burden according to the Hospital Readmissions Reduction Program (HRRP), although cancer is not currently included in this program.[2]

Lung cancer is the leading cause of cancer-related death with 18.4% mortality, which is the first in males and the second in females around the world.[3] It has a lower five-year survival rate than other cancers. The numbers of incident cases and deaths from lung cancer increased globally during the past decade which makes patients with lung cancer have a high disease burden.[4] As the global data show, the burden of lung cancer worldwide will remain substantial for the foreseeable future.[5] Therefore, identifying readmission factors for lung cancer is necessary to decrease this constant burden.

Obesity is a risk factor and a negative prognostic factor for cancers.[6] In America alone, people with obesity account for more than one-third of adults and another one-third are patients with overweight.[7] To this trend, the global incidence of obesity is expected to reach about 20% by 2025.[8] However, epidemiological studies of lung cancer have shown that patients with overweight or obesity have a lower risk of death, which is known as the "obesity paradox".[9] The reasons for this confounding phenomenon remain unclear. Obesity, especially central obesity, is also an important constituent part of metabolic syndrome (MS) which also includes hypertension, hyperlipidemia, and hyperglycemia.[10] Due to its high incidence all around the world, MS has become a noteworthy public health problem and significant comorbidity.[11] Studies have found that MS is associated with the risk of lung cancer and the reason may be their shared pathophysiological mechanisms, such as low-grade chronic inflammation.[12] However, other reports indicated that MS didn't increase the risk of lung cancer.[13] Considering these contradictory opinions, it seems to be more fitting to consider overweight/obesity or metabolic status separately or in combination to identify novel risk factors for readmission in patients with lung cancer.

To our knowledge, few studies have explored the relationship between metabolically defined overweight/obesity and the readmission risk in patients with lung cancer. It is not clear whether the effect of overweight/obesity on readmission risk is influenced by metabolic abnormalities. Therefore, we used the Nationwide Readmissions Database (NRD) to investigate the relationship between different metabolic overweight/obesity phenotypes and readmission risk in patients with lung cancer in this study to address this important knowledge gap.

Methods

Study design and data source

In this retrospective cohort study, we used data from the United States (US) NRD 2018 which has a large sample size and provides sufficient data for various types of analyses of national readmission rates for all patients, regardless of the expected payer (method of payment: Medicare, Medicaid, private insurance, self-pay, no charge or others) for the hospital stay.[14] This nationally representative database is part of the Healthcare Cost and Utilization Project (HCUP), which was built by the Agency for Healthcare Research and Quality to conduct national readmission estimations. Depending on a unique linkage number, it allows to track of patients between hospitals within a state but does not allow patients to be tracked across years. It contains clinical and non-clinical variables to support readmission analysis and provides safeguards to protect the privacy of patients, doctors, and hospitals.[14] The NRD 2018, containing data from 28 states and representing 60% of the US population, makes diagnoses with the International Classification of Diseases, 10th Revision (ICD-10) codes to give a maximum of 40 diagnoses, and with Procedure Coding System (PCS) codes to give up to 25 procedures per patient. The study was based on STROBE reporting guidelines and complied with the United States Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project Data Use Agreement and was exempt from research ethics board review. Data from the NRD 2018 was de-identified; therefore, consent to participate was not applicable.

Study population

We included adults with discharge diagnoses of lung cancer from January 1, 2018 to November 30, 2018 using the ICD-10 codes from the NRD 2018. We excluded (1) patients aged < 18 or with pregnancy for the first hospitalization, (2) patients combined with other cancers (malignant skin tumor, thyroid cancer, prostatic cancer, bladder cancer, breast cancer, endometrial cancer, colorectal cancer, cervical cancer, ovarian cancer, esophagus cancer, gastric cancer, carcinoma of small intestine, liver cancer, and pancreatic cancer), (3) patients discharged in December 2018, allowing a follow-up period of 30 days, (4) missing data for baseline characteristics for analyzing, (5) patients with body mass index (BMI) 19.9 or less (Z681 based) which was considered low body weight according to ICD-10 codes, (6) patients died during the first hospitalization. In addition, we excluded planned readmissions. The study population was followed until December 31, 2018. The details of the inclusion and exclusion criteria and the

ICD-10 codes used are given in Supplementary Figure 1, Supplementary Table 1, respectively.

Data collection

We collected the following patients' characteristics using NRD variables: age, sex, disposition of the patient, admission types (whether unplanned), length of stay (LOS), total charges, expected primary payer (Medicare, Medicaid, private insurance, self-pay, no charge or others), patient location, emergency record, resident (identify patient as a resident of the State in which he or she received hospital care), median household income, risk mortality, severity, same day events (same-day stay collapsed records), rehab transfer (transfer to rehabilitation, evaluation, or other aftercare). We also collected data on surgery (lobectomy or pneumonectomy) using the ICD-10 PCS. According to Charlson's comorbidity index and assigned weights for diseases,[15] we calculated comorbidity score in our study. The comorbidities included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, hemiplegia, moderate/severe renal disease, leukemia, lymphoma, moderate/severe liver disease, Acquired Immune Deficiency Syndrome (AIDS). All the ICD-10 codes used to identify comorbidities were shown in Supplementary Table 2.

Definitions and outcomes

Patients were classified into BMI categories: normal weight (BMI <25 kg/m²), and overweight/obesity (BMI ≥25 kg/m²). Metabolic status was defined by the components of MS except for waist circumference (WC) which was collinear with BMI: (1) hyperlipidemia: high serum triglyceride (TGs) levels or high high-density lipoprotein (HDL)-cholesterol levels, etc.; (2) hypertension; (3) hyperglycemia. We defined the metabolically unhealthy as the appearance of ≥ 2 of these components according to the Adult Treatment Panel-III (ATP-III) criteria.[16] Based on BMI categories and metabolic status, we distinguished four metabolic overweight/obesity phenotypes: (1) metabolically healthy with normal weight (MHNW); (2) metabolically unhealthy with normal weight (MUNW); (3) metabolically healthy with overweight or obesity (MHO); and (4) metabolically unhealthy with overweight or obesity (MUO). All the above diagnoses were determined using ICD-10 codes (Supplementary Table 3).

We also divided the patients in our study into 8 groups based on BMI categories and simple metabolic abnormality types: (1) normal weight with no metabolic abnormality; (2) normal weight only with hyperlipidemia; (3) normal weight only with hypertension; (4) normal weight only with hyperglycemia; (5) overweight/obesity with no

metabolic abnormality; (6) overweight/obesity only with hyperlipidemia; (7) overweight/obesity only with hypertension; (8) overweight/obesity only with hyperglycemia. In addition, we divided the population into another 8 groups based on BMI categories and the number of metabolic abnormalities: (1) normal weight with no metabolic abnormality; (2) normal weight with one metabolic abnormality; (3) normal weight with two metabolic abnormalities; (4) normal weight with three metabolic abnormalities; (5) overweight/obesity with no metabolic abnormality; (6) overweight/obesity with one metabolic abnormality; (7) overweight/obesity with two metabolic abnormalities; (8) overweight/obesity with three metabolic abnormalities.

Our primary outcome was 30-day readmission. We defined the readmission as diagnoses with lung cancer and unplanned hospital readmissions from the discharge which did not include planned readmission like regular treatment. To reduce the impact of other diseases, we adjusted the comorbidities of patients. With regard to the patients who had more than one readmission, we only included the first record. The secondary outcome was readmission cost which was divided into quartiles to be ordinal variables.

Statistical analysis

The baseline characteristics in patients with different metabolic overweight/obesity phenotypes were described. Continuous variables were evaluated by the one-way ANOVA and denoted as mean and standard deviation, while categorical variables by the chi-square test and denoted as frequency counts and percentages. Two-sided tests were used in all hypothesis tests with a significance level of $p < 0.050$. 30-day readmission of lung cancer and readmission cost were analyzed using multivariable Cox regression model and ordered logistic regression model, respectively. Relevant variables were selected as covariates if $p < 0.050$ in univariate analysis. Results in the regression model were represented by hazard ratios (HRs) or odds ratios (ORs) with an accompanying 95% confidence interval (CI). Additionally, stratified analyses were performed based on: (1) age at first hospitalization (< 46 years; 46−60 years; > 60 years), (2) sex (male, female), (3) surgery (with or without lobectomy or pneumonectomy). The SPSS (Statistical Product Service Solutions) 26.0 software was used to conduct all statistical analyses in our study.

Sensitivity analysis

(1) We used another cutoff (30 kg/m^2) of BMI to classify metabolic obesity phenotype for sensitivity analysis to demonstrate the reliability of our results (Supplementary Text 1). (2) Lung cancer related readmission was defined as 30-day readmission with diagnoses of lung cancer in top five diagnoses and it was analyzed with Fine and Gray competitive risk model (Supplementary Text 2).

Role of funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation or writing of this report. ZY, XF and JZ had access to dataset and had final responsibility for the decision to submit for publication.

Results

Baseline characteristics of patients with lung cancer with metabolic overweight/obesity phenotypes

Table 1 shows the baseline characteristics of each study group. Among 17,686,511 patients with discharge records in NRD 2018, we identified 115,393 records for analysis of which 50.4% (n = 58,214) were MHNW, 39.0% (n = 44,980) were MUNW, 4.4% (n = 5044) were MHO, and 6.2% (n = 7155) were MUO, respectively. The average age was 70 years and females accounted for 50.1%.

Patients with MUNW or MUO were older on average compared to the patients with MHNW or MHO, which meant metabolically unhealthy patients were older ($p < 0.050$). Patients with MHO or MUO representing patients with overweight or obesity had a longer length of stay, cost more, and seemed to be at a higher severity level. In addition, patients with overweight or obesity were more likely to require surgery compared to patients without overweight or obesity (all $p < 0.050$). Compared to the MHNW phenotype, patients with MUNW, MHO, and MUO were more likely to transfer to other institutions, less likely to be routinely discharged and had higher comorbidity score ($p < 0.050$). Regarding readmission (Figure 1), patients with MUNW (6531, 14.5%), MHO (771, 15.3%), and MUO (1155, 16.1%) had a higher risk compared to the patients with MHNW (7901, 13.6%), which meant overweight/obesity and metabolic abnormality both increased 30-day readmission in patients with lung cancer, especially in males, patients without previous surgery, and those aged >60 years group (all $p < 0.050$). Moreover, in the general population, females, patients without previous surgery and age >60 years group, and even patients with MUO had a higher prevalence than those with MUNW ($p < 0.050$). Interestingly, no differences in 30-day readmission were observed between the MHNW and MHO groups in females. Namely, overweight/obesity increased 30-day readmission in patients with lung cancer, irrespective of metabolic status.

Readmission risk of patients with lung cancer with metabolic overweight/obesity phenotypes

Compared with MHNW, we found that MUNW (HR, 1.10; 95% CI, 1.06−1.14), MHO (HR, 1.15; 95% CI, 1.07−1.24), and MUO (HR, 1.28; 95% CI, 1.20−1.36) had higher 30-day readmission risk after adjusting the

	Normal weight (*n*=103,194)		Overweight/obesity (*n*=12,199)		Total (*N*=115,393)	*P* value
	Metabolically healthy (MHNW) *n*=58,214	Metabolically unhealthy (MUNW) *n*=44,980	Metabolically healthy (MHO) *n*=5044	Metabolically unhealthy (MUO) *n*=7155		
Age (years), mean (SE)	68 (11) a	73 (9) b	66 (11) c	70 (9) d	70 (10)	< 0.0001
LOS	6 (6) a	6 (6) b	7 (7) c	7 (7) c	6 (6)	< 0.0001
Total charge	71,759 (88,608) a	74,236 (84,727) b	87,156 (102,522) c	83,876 (92,128) c	74,149 (88,095)	< 0.0001
Comorbidity score	1.35 (1.37) a	1.92 (1.56) b	1.46 (1.38) c	2.00 (1.52) d	1.62 (1.49)	< 0.0001
Age groups						< 0.0001
< 46 years, *n* (%)	1250 (2.1) a	78 (0.2) b	156 (3.1) c	35 (0.5) d	1519 (1.3)	
46–60 years, *n* (%)	13,384 (23.0) a	4296 (9.6) b	1385 (27.5) c	1106 (15.5) d	20,171 (17.5)	
>60 years, *n* (%)	43,580 (74.9) a	40,606 (90.3) b	3503 (69.4) c	6014 (84.1) d	93,703 (81.2)	
Sex						< 0.0001
Male, *n* (%)	28,056 (48.2) a	23,935 (53.2) b	2145 (42.5) c	3454 (48.3) a	57,590 (49.9)	
Female, *n* (%)	30,158 (51.8) a	21,045 (46.8) b	2899 (57.5) c	3701 (51.7) a	57,803 (50.1)	
Weekend, *n* (%)	10,247 (17.6) a	8014 (17.8) a	871 (17.3) a	1198 (16.7) a	20,330 (17.6)	0.14
Rehab transfer, *n* (%)	426 (0.7) a	490 (1.1) b	55 (1.1) b	89 (1.2) b	1060 (0.9)	< 0.0001
Resident, *n* (%)	54,788 (94.1) a	42,626 (94.8) b	4761 (94.4) a, b	6781 (94.8) a, b	108,956 (94.4)	< 0.0001
Same day events, *n* (%)	1522 (2.6) a	1530 (3.4) b	214 (4.2) c	321 (4.5) c	3587 (3.1)	< 0.0001
Nonelective, *n* (%)	44,086 (75.7) a	34,185 (76.0) a	3662 (72.6) b	5036 (70.4) c	86,969 (75.4)	< 0.0001
Emergency record, *n* (%)	37,575 (64.5) a	30,129 (67.0) b	3206 (63.6) a, c	4466 (62.4) c	75,376 (65.3)	< 0.0001
Surgery, *n* (%)	9453 (16.2) a	7508 (16.7) a	998 (19.8) b	1586 (22.2) c	19,545 (16.9)	< 0.0001
Readmission						< 0.0001
Total, *n* (%)	7901 (13.6) a	6531 (14.5) b	771 (15.3) b, c	1155 (16.1) c	16,358 (14.2)	
Male, *n* (%)	4016 (14.3) a	3706 (15.5) b	354 (16.5) b	580 (16.8) b	8656 (15.0)	
Female, *n* (%)	3885 (12.9) a	2825 (13.4) a	417 (14.4) a, b	575 (15.5) b	7702 (13.3)	
Without surgery	7495 (15.4) a	6154 (16.4) b	735 (18.2) c	1073 (19.3) c	15,457 (16.1)	
With surgery	406 (4.3) a	377 (5.0) a	36 (3.6) a	82 (5.2) a	901 (4.6)	
< 46 years, *n* (%)	198 (15.8) a	5 (6.4) a	23 (14.7) a	7 (20.0) a	233 (15.3)	
46 to 60 years, *n* (%)	2063 (15.4) a	725 (16.9) a	220 (15.9) a	193 (17.5) a	3201 (15.9)	
> 60 years, *n* (%)	5640 (12.9) a	5801 (14.3) b	528 (15.1) b, c	955 (15.9) c	12,924 (13.8)	
Disposition of the patient						< 0.0001
Routine, *n* (%)	32,465 (55.8) a	22,870 (50.8) b	2710 (53.7) c	3773 (52.7) c	61,818 (53.6)	
Transfer to Short-term Hospital, *n* (%)	612 (1.1) a	450 (1.0) a	57 (1.1) a	56 (0.8) a	1175 (1.0)	
Transfer Other: Includes SNF, ICF, Another Type of Facility, *n* (%)	9179 (15.8) a	7882 (17.5) b	822 (16.3) a, b	1211 (16.9) a, b	19,094 (16.5)	
HHC, *n* (%)	15,257 (26.2) a	13,442 (29.9) b	1420 (28.2) b	2078 (29.0) b	32,197 (27.9)	

Table 1 (Continued)

	Normal weight (*n*=103,194)		Overweight/obesity (*n*=12,199)		Total (*N*=115,393)	*P* value
	Metabolically healthy (MHNW) *n*=58,214	**Metabolically unhealthy (MUNW) *n*=44,980**	**Metabolically healthy (MHO) *n*=5044**	**Metabolically unhealthy (MUO) *n*=7155**		
AMA, *n* (%)	630 (1.1) a	298 (0.7) b	31 (0.6) b	34 (0.5) b	993 (0.9)	
Discharge alive, destination unknown, *n* (%)	71 (0.1) a	38 (0.1) a	4 (0.1) a	3 (0.0) a	116 (0.1)	
Primary expected payer						< 0.0001
Medicare, *n* (%)	36,739 (63.1) a	35,606 (79.2) b	3046 (60.4) c	5350 (74.8) d	80,741 (70.0)	
Medicaid, *n* (%)	6287 (10.8) a	2245 (5.0) b	565 (11.2) a	438 (6.1) c	9535 (8.3)	
Private insurance, *n* (%)	12,536 (21.5) a	5803 (12.9) b	1194 (23.7) c	1162 (16.2) d	20,695 (17.9)	
Self-pay, *n* (%)	1104 (1.9) a	305 (0.7) b	93 (1.8) a	66 (0.9) b	1568 (1.4)	
No charge, *n* (%)	119 (0.2) a	39 (0.1) b	11 (0.2) a	7 (0.1) a, b	176 (0.2)	
Other, *n* (%)	1429 (2.5) a	982 (2.2) b, c	135 (2.7) a, c	132 (1.8) b	2678 (2.3)	
Patient Location: NCHS Urban-Rural Code						< 0.0001
"Central" counties of metro areas of >=1 million population, *n* (%)	14,062 (24.2) a	11,499 (25.6) b	1188 (23.6) a	1753 (24.5) a, b	28,502 (24.7)	
"Fringe" counties of metro areas of >=1 million population, *n* (%)	15,377 (26.4) a	12,496 (27.8) b	1390 (27.6) a, b	1955 (27.3) a, b	31,218 (27.1)	
Counties in metro areas of 250,000−999,999 population, n (%)	13,097 (22.5) a	9892 (22.0) a	1110 (22.0) a	1597 (22.3) a	25,696 (22.3)	
Counties in metro areas of 50,000−249,999 population, *n* (%)	5935 (10.2) a	4465 (9.9) a	522 (10.3) a	753 (10.5) a	11,675 (10.1)	
Micropolitan counties, *n* (%)	5358 (9.2) a	3616 (8.0) b	462 (9.2) a, c	590 (8.2) b, c	10,026 (8.7)	
Not metropolitan or micropolitan counties, *n* (%)	4385 (7.5) a	3012 (6.7) b	372 (7.4) a, b	507 (7.1) a, b	8276 (7.2)	
Median household income for patient's ZIP Code						< 0.0001
0-25th percentile, *n* (%)	15,827 (27.2) a	12,035 (26.8) a	1353 (26.8) a	1877 (26.2) a	31,092 (26.9)	
26th to 50th percentile (median), *n* (%)	16,448 (28.3) a	12,293 (27.3) b	1499 (29.7) a	2091 (29.2) a	32,331 (28.0)	
51st to 75th percentile, *n* (%)	14,312 (24.6) a	11,197 (24.9) a	1294 (25.7) a, b	1905 (26.6) b	28,708 (24.9)	
76th to 100th percentile, *n* (%)	11,627 (20.0) a	9455 (21.0) b	898 (17.8) c	1282 (17.9) c	23,262 (20.2)	
Risk Mortality						< 0.0001
No class specified, *n* (%)	0 (0.0) a	1 (0.0) a	0 (0.0) a	0 (0.0) a	1 (0.0)	
Minor likelihood of dying, *n* (%)	7732 (13.3) a	4383 (9.7) b	692 (13.7) a	716 (10.0) b	13,523 (11.7)	

Table 1 (Continued)

	Normal weight (*n*=103,194)		Overweight/obesity (*n*=12,199)		Total (*N*=115,393)	*P* value
	Metabolically healthy (MHNW) *n*=58,214	**Metabolically unhealthy (MUNW)** *n*=44,980	**Metabolically healthy (MHO)** *n*=5044	**Metabolically unhealthy (MUO)** *n*=7155		
Moderate likelihood of dying, *n* (%)	16,882 (29.0) a	11,014 (24.5) b	1273 (25.2) b	1773 (24.8) b	30,942 (26.8)	
Major likelihood of dying, *n* (%)	25,818 (44.4) a	22,911 (50.9) b	2367 (46.9) c	3625 (50.7) b	54,721 (47.4)	
Extreme likelihood of dying, *n* (%)	7782 (13.4) a	6671 (14.8) b	712 (14.1) a, b	1041 (14.5) b	16,206 (14.0)	
Severity						< 0.0001
No class specified, *n* (%)	0 (0.0) a	1 (0.0) a	0 (0.0) a	0 (0.0) a	1 (0.0)	
Minor loss of function, *n* (%)	5254 (9.0) a	2780 (6.2) b	312 (6.2) b	292 (4.1) c	8638 (7.5)	
Moderate loss of function, *n* (%)	19,453 (33.4) a	14,397 (32.0) b	1374 (27.2) c	2040 (28.5) c	37,264 (32.3)	
Major loss of function, *n* (%)	22,704 (39.0) a	19,442 (43.2) b	2164 (42.9) b	3262 (45.6) c	47,572 (41.2)	
Extreme loss of function, *n* (%)	10,803 (18.6) a	8360 (18.6) a	1194 (23.7) b	1561 (21.8) b	21,918 (19.0)	
Comorbidity						
Myocardial infarction	3187 (5.5) a	5932 (13.2) b	269 (5.3) a	854 (11.9) c	10,242 (8.9)	< 0.0001
Congestive heart failure	5945 (10.2) a	9275 (20.6) b	732 (14.5) c	1887 (26.4) d	17,839 (15.5)	< 0.0001
Peripheral vascular disease	4314 (7.4) a	5822 (12.9) b	335 (6.6) a	730 (10.2) c	11,201 (9.7)	< 0.0001
Cerebrovascular disease	3162 (5.4) a	3766 (8.4) b	200 (4.0) c	401 (5.6) a	7529 (6.5)	< 0.0001
Dementia	2358 (4.1) a	2634 (5.9) b	131 (2.6) c	215 (3.0) c	5338 (4.6)	< 0.0001
Chronic pulmonary disease	29,265 (50.3) a	24,608 (54.7) b	2702 (53.6) b	4215 (58.9) c	60,790 (52.7)	< 0.0001
Connective tissue disease	1884 (3.2) a	1461 (3.2) a	194 (3.8) a	242 (3.4) a	3781 (3.3)	0.12
Ulcer disease	699 (1.2) a	626 (1.4) b	60 (1.2) a, b	92 (1.3) a, b	1477 (1.3)	0.053
Mild liver disease	2609 (4.5) a	1711 (3.8) b	277 (5.5) c	326 (4.6) a, c	4923 (4.3)	< 0.0001
Hemiplegia	1486 (2.6) a	1079 (2.4) a, b	95 (1.9) b	137 (1.9) b	2797 (2.4)	< 0.0001
Moderate/severe renal disease	9339 (16.0) a	13,067 (29.1) b	978 (19.4) c	2362 (33.0) d	25,746 (22.3)	< 0.0001
Leukemia	407 (0.7) a	315 (0.7) a	26 (0.5) a	54 (0.8) a	802 (0.7)	0.43
Lymphoma	445 (0.8) a	379 (0.8) a	33 (0.7) a	62 (0.9) a	919 (0.8)	0.30
Moderate/severe liver disease	325 (0.6) a, b	174 (0.4) c	40 (0.8) b	30 (0.4) a, c	569 (0.5)	< 0.0001
AIDS	157 (0.3) a	68 (0.2) b	11 (0.2) a, b	6 (0.1) b	242 (0.2)	< 0.0001

Table 1: **Baseline characteristics of patients with lung cancer with metabolic overweight/obesity phenotypes.**

The small letters (a, b, c, d) in this table refer to comparisons between groups. There is no statistical difference between groups with the same small letters. LOS, length of stay; SNF, Skilled Nursing Facility; ICF, Intermediate Care Facility; HHC, Home Health Care; AMA, Against Medical Advice; NCHS, National Center for Health Statistics; AIDS, Acquired Immune Deficiency Syndrome.
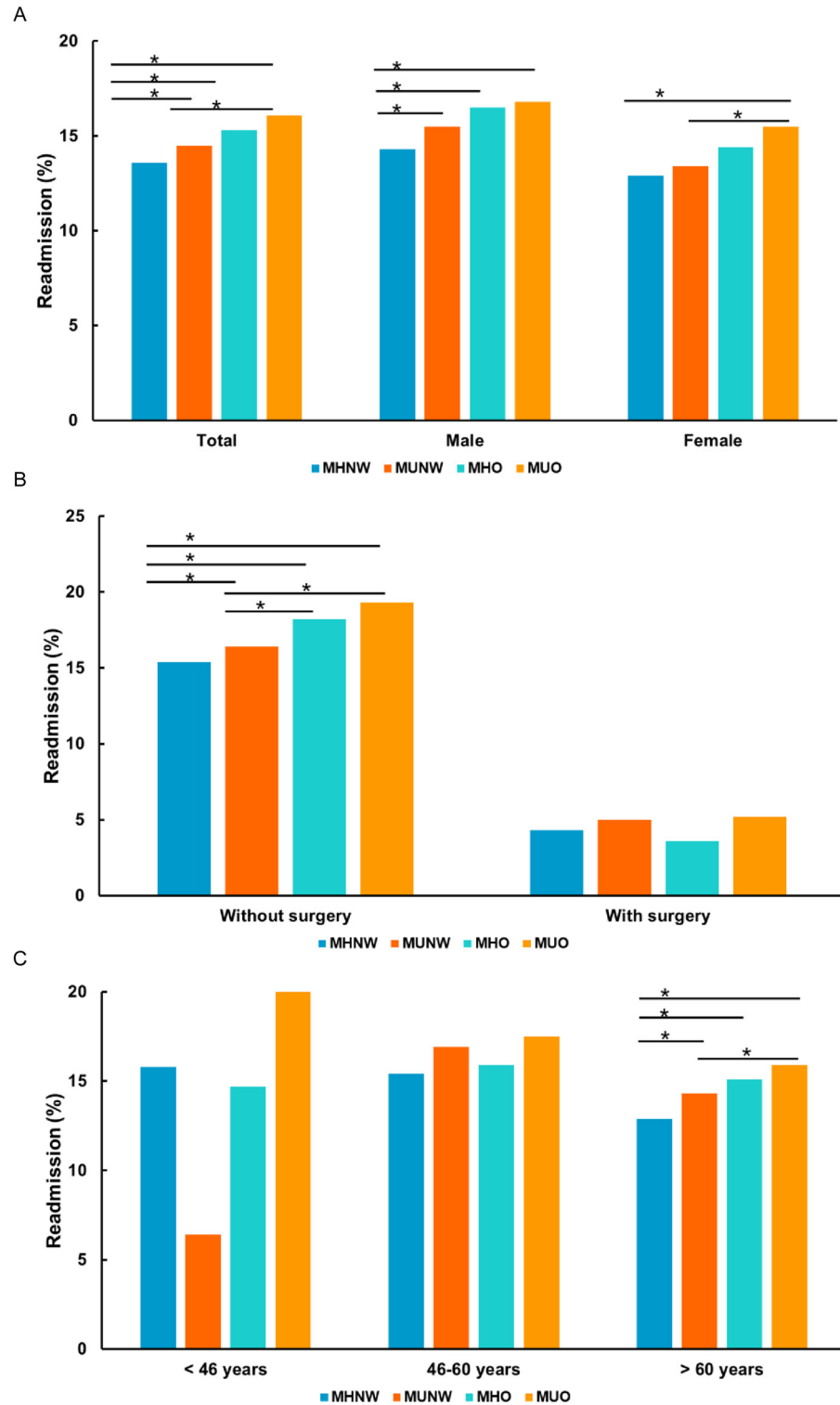
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Figure 1. Readmission in patients with lung cancer with metabolic overweight/obesity phenotypes. (A) In total population and by sex. (B) By surgery. (C) By age. *, The *p* value of inter-group comparison was less than 0.050. MHNW, metabolically healthy with normal weight; MUNW, metabolically unhealthy with normal weight; MHO, metabolically healthy with overweight or obesity; MUO, metabolically unhealthy with overweight or obesity.

covariates of age, sex, disposition of the patient, LOS, admission types, expected primary payer, patient location, emergency record, resident, median household income, same day events, lobectomy or pneumonectomy, comorbidity score and rehab transfer (Table 2, Figure 2A). Male patients with MUNW, MHO, and MUO had 1.15-fold ($p < 0.0001$), 1.17-fold ($p = 0.0050$) and 1.28-fold ($p < 0.0001$) increased readmission risk compared to the MHNW phenotype. Similarly, in all patients without previous surgery at baseline, the MUNW, MHO, and MUO phenotypes had 1.13-fold, 1.15-fold, and 1.29-fold increased risk to readmit compared to patients with MHNW (all $p < 0.0001$) (Table 2). No differences were found in patients with surgery and females with MHO. However, we found a higher

readmission risk in the age >60 years females with MHO (HR, 1.19; 95% CI, 1.06−1.35; $p = 0.0040$) and age 46 to 60 years male with MUNW (HR, 1.17; 95% CI, 1.04−1.31; $p = 0.010$) (Table 3).

Separately, in all age > 60 years patients, the MUNW (HR, 1.10; 95% CI, 1.06−1.15), MHO (HR, 1.21; 95% CI, 1.10−1.32), and MUO (HR, 1.30; 95% CI, 1.22 −1.40) phenotypes had increased readmission risks than the MHNW (all $p < 0.0001$). Whereas in the age 46 to 60 years group, only metabolically unhealthy groups had a higher readmission risk compared to the MHNW phenotype (MUNW: HR, 1.10; 95% CI, 1.01 −1.20; $p = 0.029$; MUO: HR, 1.17; 95% CI, 1.01−1.36; $p = 0.035$). Conversely, there was a decreased readmission risk in MUNW with the age < 46 years group (HR,

		Variable Metabolic overweight/ obesity phenotypes	Population (n)	Hazard Ratio (95% CI)[a]	P value
Total		MHNW	58,214	1(reference)	
		MUNW	**44,980**	**1.10(1.06,1.14)**	**< 0.0001**
		MHO	**5044**	**1.15(1.07,1.24)**	**< 0.0001**
		MUO	**7155**	**1.28(1.20,1.36)**	**< 0.0001**
Sex	**Male**	MHNW	28,059	1(reference)	
		MUNW	**23,935**	**1.15(1.10,1.21)**	**< 0.0001**
		MHO	**2145**	**1.17(1.05,1.31)**	**0.0050**
		MUO	**3454**	**1.28(1.18,1.40)**	**< 0.001**
	Female	MHNW	30,158	1(reference)	
		MUNW	**21,045**	**1.09(1.04,1.15)**	**0.0010**
		MHO	2899	1.09(0.98,1.20)	0.10
		MUO	**3701**	**1.26(1.15,1.37)**	**< 0.0001**
Surgery	**Without Lobectomy or pneumonectomy**	MHNW	48,761	1(reference)	
		MUNW	**37,472**	**1.13(1.09,1.17)**	**< 0.0001**
		MHO	**4046**	**1.15(1.07,1.24)**	**< 0.0001**
		MUO	**5569**	**1.29(1.21,1.37)**	**< 0.0001**
	With Lobectomy or pneumonectomy	MHNW	9453	1(reference)	
		MUNW	7508	1.03(0.89,1.19)	0.72
		MHO	998	0.81(0.57,1.13)	0.21
		MUO	1586	1.01(0.80,1.29)	0.93
Age	**< 46 years**	MHNW	1250	1(reference)	
		MUNW	**78**	**0.38(0.15,0.95)**	**0.038**
		MHO	156	1.01(0.66,1.57)	0.95
		MUO	35	1.47(0.68,3.20)	0.33
	46−60 years	MHNW	13,384	1(reference)	
		MUNW	**4296**	**1.10(1.01,1.20)**	**0.029**
		MHO	1385	1.05(0.92,1.21)	0.46
		MUO	**1106**	**1.17(1.01,1.36)**	**0.035**
	> 60 years	MHNW	43,580	1(reference)	
		MUNW	**40,606**	**1.10(1.06,1.15)**	**< 0.0001**
		MHO	**3503**	**1.21(1.10,1.32)**	**< 0.0001**
		MUO	**6014**	**1.30(1.22,1.40)**	**< 0.0001**

Table 2: 30-day readmission risk in patients with lung cancer as compared with MHNW.
   [a] Adjustment for age, sex, disposition of the patient, LOS, admission types, expected primary payer, patient location, emergency record, resident, median household income, same day events, lobectomy or pneumonectomy, comorbidity score and rehab transfer.
MHNW, metabolically healthy with normal weight; MUNW, metabolically unhealthy with normal weight; MHO, metabolically healthy with overweight or obesity; MUO, metabolically unhealthy with overweight or obesity; CI, confidence interval.
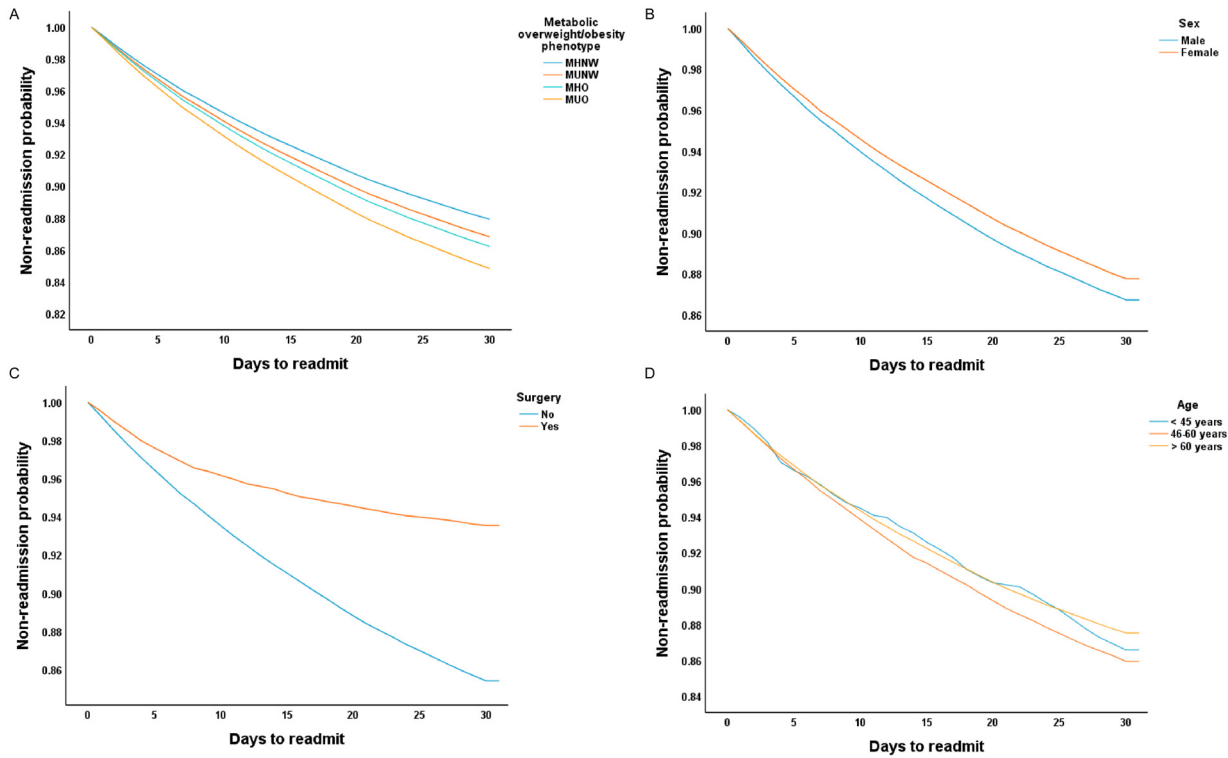
Figure 2. **Cox survival curve of 30-day readmission in patients with lung cancer**. (A) By metabolic overweight/obesity phenotype. (B) By sex. (C) By surgery. (D) By age. MHNW, metabolically healthy with normal weight; MUNW, metabolically unhealthy with normal weight; MHO, metabolically healthy with overweight or obesity; MUO, metabolically unhealthy with overweight or obesity.

	Variable	Female		Male	
		Hazard Ratio (95% CI)[a]	P value	Hazard Ratio (95% CI)[a]	P value
< 46 years	Metabolic overweight/obesity phenotypes				
	MHNW	1(reference)		1(reference)	
	MUNW	0.68(0.21,2.16)	0.51	0.32(0.08,1.32)	0.12
	MHO	1.21(0.69,2.10)	0.51	0.75(0.36,1.57)	0.45
	MUO	1.70(0.67,4.29)	0.26	0.82(0.18,3.76)	0.80
46−60 years	MHNW	1(reference)		1(reference)	
	MUNW	1.04(0.91,1.18)	0.60	**1.17(1.04,1.31)**	**0.010**
	MHO	0.96(0.79,1.16)	0.64	1.19(0.97,1.46)	0.099
	MUO	1.21(0.99,1.48)	0.066	1.14(0.91,1.42)	0.25
> 60 years	MHNW	1(reference)		1(reference)	
	MUNW	**1.07(1.01,1.13)**	**0.019**	**1.13(1.08,1.19)**	**< 0.0001**
	MHO	**1.19(1.06,1.35)**	**0.0040**	**1.21(1.06,1.38)**	**0.0040**
	MUO	**1.28(1.16,1.41)**	**< 0.0001**	**1.32(1.19,1.45)**	**< 0.0001**

Table 3: 30-day readmission risk in patients with lung cancer.

[a] Adjustment for disposition of the patient, LOS, admission types, expected primary payer, patient location, emergency record, resident, median household income, same day events, lobectomy or pneumonectomy, comorbidity score and rehab transfer.

MHNW, metabolically healthy with normal weight; MUNW, metabolically unhealthy with normal weight; MHO, metabolically healthy with overweight or obesity; MUO, metabolically unhealthy with overweight or obesity; LOS, length of stay; CI, confidence interval.

0.38; 95% CI, 0.15−0.95; p = 0.038) (Table 2). Overall, there were higher readmission risks in males, patients without surgery, and patients aged 46 to 60 years (Figure 2B, C, and D).

Readmission risk of patients with lung cancer in further metabolic overweight/obesity analysis

With respect to overweight/obesity with simple metabolic abnormality groups, we only observed a higher risk of readmission in patients with overweight/obesity but no metabolic abnormality (HR, 1.21; 95% CI, 1.07−1.37; p = 0.0030) and overweight/obesity only with hypertension (HR, 1.14; 95% CI, 1.02−1.27; p = 0.018) group (Supplementary Table 4). Moreover, overweight/obesity only with hyperlipidemia group in males had a higher readmission risk (HR, 1.49; 95% CI, 1.07−2.06; p = 0.018) and overweight/obesity with no metabolic abnormality only increased the risk in females (HR, 1.19; 95% CI, 1.01−1.41; p = 0.041). In addition, our overweight/obesity and abnormality number groups found that more than one metabolic abnormality was associated with a higher readmission risk in both females and males, while overweight/obesity with no metabolic abnormality only increased the readmission risk of females (HR, 1.18; 95% CI, 1.00−1.40; p = 0.049) (Supplementary Table 5).

Readmission costs of patients with lung cancer with metabolic overweight/obesity phenotypes

We found increased costs for 30-day readmission after adjusting for sex, disposition of the patient, LOS, admission types, expected primary payer, patient location, emergency record, resident, median household income, same day events, lobectomy or pneumonectomy, comorbidity score and rehab transfer in patients with MHO (OR, 1.18; 95% CI, 1.07−1.29; p = 0.0010) and MUO (OR, 1.11; 95% CI, 1.02−1.20; p = 0.013). Only phenotype MHO in males (OR, 1.16; 95% CI, 1.01−1.34; p = 0.034), MUNW in all patients with surgery (OR, 1.22; 95% CI, 1.03−1.46; p = 0.025) and MHO in age >60 years group (OR, 1.18; 95% CI, 1.06−1.33; p = 0.0040) had significantly higher costs compared to MHNW (Supplementary Table 6). No significant difference was found in patients aged <46 years.

Discussion

As stated in the NRD overview,[14] it has a large sample size, which provides sufficient data for analysis across hospital types and the study of readmissions for relatively uncommon disorders and procedures. The NRD is designed to support various types of analyses of national readmission rates for all patients, regardless of the expected payer for the hospital stay which ensures the cohort in our study is representative for the wider population of patients with lung cancer. Based on the NRD 2018, the association between metabolic overweight/obesity phenotypes and the 30-day readmission risk in patients with lung cancer was evaluated. We found that the risk increased by 1.10-fold, 1.15-fold, and 1.28-fold in patients with MUNW, MHO, and MUO compared to patients with MHNW, respectively. There were similar trends in males, patients without surgery at baseline, and the oldest age group (>60 years) in our

study. In addition, we documented that overweight/obesity seemed to increase the readmission risk in older females and the readmission costs. Further analyses indicated that the number of metabolic abnormalities was associated with the readmission risk in patients with lung cancer as well. For all we know, this study was the first to make an exploration of the relationship between metabolically defined overweight/obesity and readmission risk in patients with lung cancer using the large national retrospective cohort study.

Hospital readmission, especially within 30 days, has already attracted public attention and is used as an indicator of health care because of its accompanying heavy burden and resource utilization.[17] Using Medicare claims data from 2003 to 2004, a study denoted that about one-fifth of the discharged patients were readmitted to the hospital within 30 days.[1] There were complex reasons associated with readmission like biological, social, or surgical factors.[18] However, it is common knowledge that reducing readmission and identifying relevant factors were of great importance to the public welfare.

Increased BMI had long been considered a protective prognostic factor for lung cancer. Petrelli et al. had shown that the mortality risk of lung cancer with obesity was lower than patients without obesity.[19] A meta-analysis also confirmed that patients with lung cancer with overweight or obesity had better survival rates and outcomes, and omentin may serve as a prognostic factor explaining the obesity paradox.[20] However, some research had also found that there were confounders between increased BMI and lung cancer which may be physical fitness, muscle-fat crosstalk, endocrinal changes or smoking.[21] The existing study had shown that MS and its components were associated with several cancers, especially cancers of the digestive system. The mechanism for that was not entirely clear, one explanation was that MS was a substitution for other risk factors like reduced physical activity, high fat intake, or oxidative stress.[22] Circadian rhythms and the gut microbiota may play a role as well.[23] However, previous studies have shown that MS did not affect the morbidity, survival, or outcomes of lung cancer.[13,24] In our further 8-group exploration, we found that more than one metabolic abnormality was a risk factor for readmission risk in patients with lung cancer. If metabolic abnormality was regarded as comorbidity, consistent with our view, Zhu et al. would show that the readmission risk in patients with lung cancer who combined with comorbidities was significantly higher and the readmission risk increased with the number of comorbidities.[5] The effects of metabolic status on overweight or obesity-associated risk assessments were not considered in previous clinical studies. In our study, we reduced the interaction of two factors by using the metabolic overweight/obesity phenotypes and observed that increased BMI and metabolic abnormalities were independent risk factors for readmission in patients with lung cancer, and illustrated the need to take targeted measures on these patients after discharge.

To analyse whether sex or age influenced the relationship between metabolic overweight/obesity phenotypes and readmission risk in patients with lung cancer, we divided the population accordingly and suggested that overweight/obesity in total females did not increase the readmission risk in patients with lung cancer, but it did in females over 60 years. In addition, our further analyses of 8 groups identified that overweight/obesity with no metabolic abnormality only increased readmission risk in females, not males. This finding further reflected the modification of metabolic status on overweight/obesity and sex difference. As a previous study found, in chemotherapy-treated non-small cell lung cancer (NSCLC), females exhibited longer progression-free survival than males, indicating that female was a favorable prognostic factor for lung cancer, which may explain our results.[25] As another study showed, the potential mechanism of obesity affecting lung cancer was through the endogenous estrogen which appeared protection via the combination of estrogen receptors on lung tissue which reduced exposure to other risk factors.[26] In females over 60 years, most in menopause, the protective effects of estrogen diminished and even disappeared, which caused a higher readmission risk. Age difference also showed up across the total population in our study, which was reflected as the increased readmission risk induced by overweight/obesity and metabolic abnormality focused on older patients. Metabolic abnormality even showed a protective effect in patients <46 years. A current review reported that the survival between younger and older patients with lung cancer was significantly different.[27] Yet another possible explanation was that lung cancer was most likely to occur in elderly people, making the population difference in patient number,[28] and the population <46 years, really small in our study. Though specific reasons needed to be further explored and with certain limitations, elderly patients with lung cancer, especially females, were required to be given close attention and further methods should be identified to reduce rehospitalization in this population.

To the best of our knowledge, this was the first study to assess the readmission risk in patients with lung cancer with metabolic overweight/obesity phenotype. Our study had the strength that we used the national representative database to establish a retrospective cohort study, ensuring the size and range of our sample. Moreover, unlike most institutional or other data sets with only a specific insurance class, the NRD includes all payers. Despite the many strengths, there were several limitations to our study. First, we used the ICD-10 and PCS codes to make diagnoses and there were potential coding errors because of selection bias. Nevertheless, HCUP quality control procedures are carried out to

ensure the reliability and validity of the NRD data.[29] Second, the database lacks the death information of patients after discharge, which acted as an important role in the analysis. We limited the analysis of readmission to 30 days according to the recommendations of HCUP to reduce the bias due to patient mortality and future research should take this into account.[14] Third, the NRD lacks personal medication data, personalized therapeutic interventions and pathologic information like histological types and stages of lung cancer. However, it was inconsistent in the impact of drugs like aspirin and metformin on metabolic status or bodyweight.[21,30] Fourth, the sensitivity of BMI defined by ICD-10 codes rather than exact value was low. Finally, we could not confirm the exact cause of the admission. But we limited the readmission with the lung cancer diagnosis and we adjusted the comorbidities to make the readmission related to lung cancer as far as possible. We also conducted sensitivity analysis to validate our findings. Considering our results were not completely generalizable, further research using actual calculated BMI and specifical laboratory data would be necessary to verify our findings.

In conclusion, we found that increased BMI and metabolic abnormalities were independently associated with the increased 30-day readmission risk in patients with lung cancer. Increased BMI also enhanced the risk when having unhealthy metabolic status, especially in women. Increased BMI, not metabolic abnormalities, increased the costs for 30-day readmission. Follow-up and intervention method targeting increased BMI and metabolic abnormalities should be considered for patients with lung cancer.

Contributors
JZ created the study protocol. XF contributed to the analysis plan. ZY wrote the first draft of the manuscript. JH, YC, YS, DW and KLP revised the manuscript to create the final version. ZY, XF and HD contributed to the data analysis. ZY and XF have accessed and verified the underlying data. All authors have approved the manuscript and agreed with the submission and publication.

Data sharing statement
The data that support the findings of this study are available from the Nationwide Readmissions Database (NRD) of Healthcare Cost and Utilization Project (HCUP) site, subject to registration and application process. Further details can be found at https://www.hcup-us.ahrq.gov/db/nation/nrd/nrddbdocumentation.jsp and https://www.hcup-us.ahrq.gov/tech_assist/centdist.jsp.

Declaration of interests
All authors declare no competing interests.

References
1 Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the medicare fee-for-service program. *N Engl J Med*. 2009;360(14):1418–1428.
2 Hospital Readmissions Reduction Program (HRRP). https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program. Accessed 4 April 2022.
3 Torre LA, Siegel RL, Jemal A. Lung cancer statistics. *Adv Exp Med Biol*. 2016;893:1–19.
4 Huang J, Deng Y, Tin MS, et al. Distribution, risk factors, and temporal trends for lung cancer incidence and mortality: a global analysis. *Chest*. 2022;161(4):1101–1111.
5 Zhu D, Ding R, Ma Y, Chen Z, Shi X, He P. Comorbidity in lung cancer patients and its association with hospital readmission and fatality in China. *BMC Cancer*. 2021;21(1):557.
6 Ligibel JA, Alfano CM, Courneya KS, et al. American society of clinical oncology position statement on obesity and cancer. *J Clin Oncol*. 2014;32(31):3568–3574.
7 Quail DF, Dannenberg AJ. The obese adipose tissue microenvironment in cancer development and progression. *Nat Rev Endocrinol*. 2019;15(3):139–154.
8 NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet*. 2016;387(10026):1377–1396.
9 Jiang M, Fares AF, Shepshelovich D, et al. The relationship between body-mass index and overall survival in non-small cell lung cancer by sex, smoking status, and race: a pooled analysis of 20,937 International lung Cancer consortium (ILCCO) patients. *Lung Cancer*. 2021;152:58–65.
10 Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet*. 2005;365(9468):1415–1428.
11 Saklayen MG. The global epidemic of the metabolic syndrome. *Curr Hypertens Rep*. 2018;20(2):12.
12 Hursting SD, Hursting MJ. Growth signals, inflammation, and vascular perturbations: mechanistic links between obesity, metabolic syndrome, and cancer. *Arterioscler Thromb Vasc Biol*. 2012;32(8):1766–1770.
13 Qiao L, Ma D, Lv H, et al. Metabolic syndrome and the incidence of lung cancer: a meta-analysis of cohort studies. *Diabetol Metab Syndr*. 2020;12:95.
14 NRD Overview. Healthcare cost and utilization project (HCUP). https://www.hcup-us.ahrq.gov/nrdoverview.jsp. Accessed 30 March 2022.
15 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.
16 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA*. 2001;285(19):2486–2497.
17 Chirapongsathorn S, Poovorawan K, Soonthornworasiri N, Pan-Ngum W, Phaosawasdi K, Treeprasertsuk S. Thirty-day readmission and cost analysis in patients with cirrhosis: a nationwide population-based data. *Hepatol Commun*. 2020;4(3):453–460.
18 Wahl TS, Hawn MT. How to predict 30-day readmission. *Adv Surg*. 2018;52(1):101–111.

19 Petrelli F, Cortellini A, Indini A, et al. Association of obesity with survival outcomes in patients with cancer: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(3):e213520.

20 Parida S, Siddharth S, Sharma D. Role of omentin in obesity paradox in lung cancer. *Cancers (Basel)*. 2021;13(2):275.

21 Zhang X, Liu Y, Shao H, Zheng X. Obesity paradox in lung cancer prognosis: evolving biological insights and clinical implications. *J Thorac Oncol*. 2017;12(10):1478–1488.

22 Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. *Diabetes Care*. 2012;35(11):2402–2411.

23 Bishehsari F, Voigt RM, Keshavarzian A. Circadian rhythms and the gut microbiota: from the metabolic syndrome to cancer. *Nat Rev Endocrinol*. 2020;16(12):731–739.

24 Wen YS, Zhang XW, Qin RQ, Zhang LJ. Effect of metabolic syndrome and its components on recurrence and survival in early-stage non-small cell lung cancer. *Med Oncol*. 2015;32(1):423.

25 Wheatley-Price P, Le Maître A, Ding K, et al. The influence of sex on efficacy, adverse events, quality of life, and delivery of treatment in National cancer institute of Canada clinical trials group non-small cell lung cancer chemotherapy trials. *J Thorac Oncol*. 2010;5 (5):640–648.

26 Bethea TN, Rosenberg L, Charlot M, O'Connor GT, Adams-Campbell LL, Palmer JR. Obesity in relation to lung cancer incidence in African American women. *Cancer Causes Control*. 2013;24 (9):1695–1703.

27 Pilleron S, Gower H, Janssen-Heijnen M, et al. Patterns of age disparities in colon and lung cancer survival: a systematic narrative literature review. *BMJ Open*. 2021;11(3):e044239.

28 SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. https://seer.cancer.gov/archive/csr/1975_2009_pops09/. Accessed 13 April 2022.

29 HCUP Quality Control Procedures. Published February 23, 2021. https://hcup-us.ahrq.gov/db/quality.pdf. Accessed 10 April 2022.

30 Brancher S, Støer NC, Weiderpass E, et al. Metformin use and lung cancer survival: a population-based study in Norway. *Br J Cancer*. 2021;124(5):1018–1025.