

# Erectile Dysfunction After Surgical Treatment of Lung Cancer: Real-World Evidence

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Ming-Szu Hung,<sup>1-3</sup> Yi-Chuan Chen,<sup>1,2,4</sup> Tsung-Yu Huang,<sup>5-7</sup> Dong-Ru Ho,<sup>6,8,9</sup> Chuan-Pin Lee,<sup>10</sup> Pau-Chung Chen,<sup>11,12</sup> Yao-Hsu Yang<sup>10,13,14</sup>

<sup>1</sup>Department of Pulmonary and Critical Care Medicine, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, Taiwan; <sup>2</sup>Department of Medicine, College of Medicine, Chang Gung University, Taoyuan, Taiwan; <sup>3</sup>Department of Respiratory Care, Chang Gung University of Science and Technology, Chiayi, Taiwan; <sup>4</sup>Department of Emergency Medicine, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, Taiwan; <sup>5</sup>Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, Taiwan; <sup>6</sup>Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan; <sup>7</sup>Shu-Zen Junior College of Medicine and Management, Kaohsiung, Taiwan; <sup>8</sup>Division of Urology, Department of Surgery, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, Taiwan; <sup>9</sup>Department of Nursing, Chang Gung University of Science and Technology, Chiayi, Taiwan; <sup>10</sup>Health Information and Epidemiology Laboratory, Chang Gung Memorial Hospital, Chiayi, Taiwan; <sup>11</sup>Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taipei, Taiwan; <sup>12</sup>Department of Environmental and Occupational Medicine, National Taiwan University Hospital and National Taiwan University, College of Medicine, Taipei, Taiwan; <sup>13</sup>Department of Traditional Chinese Medicine, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, Taiwan; <sup>14</sup>School of Traditional Chinese Medicine, College of Medicine, Chang Gung University, Taoyuan, Taiwan

Correspondence: Yao-Hsu Yang  
Email r95841012@ntu.edu.tw

**Background:** Sexual problems are common in male lung cancer survivors. However, the development of erectile dysfunction (ED) in lung cancer patients after surgery has been rarely explored. In this study, we aimed to explore the incidence and risk factors of ED after lung cancer surgery.

**Methods:** From 2000 to 2012, 6025 and 24,100 male patients were included in each matched cohort of lung cancer and non-lung cancer patients, respectively. Poisson regression analysis was used to calculate the incidence rate ratio (IRR) and 95% confidence interval (CI).

**Results:** The incidence of ED was higher in the lung cancer cohort compared to the non-lung cancer cohort (38.47 vs 28.28 per 10,000 person-years) with an adjusted IRR (aIRR) of 1.34 (95% CI: 1.06–1.70,  $p=0.014$ ) after the confounders were adjusted for. An increased incidence of ED was observed in the lung cancer cohort aged 40–54 years (aIRR: 5.44, 95% CI: 2.25–13.15,  $p<0.001$ ), 55–64 years (aIRR: 3.62, 95% CI: 1.61–8.17,  $p=0.002$ ) years, and anxiety (aIRR: 2.99, 95% CI: 1.81–4.94,  $p<0.001$ ). In addition, a higher incidence of emergency room (ER) visits (aIRR: 2.19, 95% CI: 1.98–2.42,  $p<0.001$ ) was observed in lung cancer patients with ED compared to those without ED.

**Conclusion:** Our study results suggested that early surveillance and intervention of ED should be advocated in lung cancer patients after surgery.

**Keywords:** lung cancer, surgery, erectile dysfunction

## Introduction

Lung cancer remains the most common cause of cancer deaths worldwide,<sup>1</sup> with a low 5-year survival rate despite treatment.<sup>2</sup> In lung cancer patients, several physical signs and symptoms, including coughing, wheezing, weight loss, insomnia, fatigue, and chest pain, decrease the quality of life. Depressive disorder<sup>3</sup> frequently develops and may result in sexual dysfunction and concerns.<sup>4</sup> Although less than gynecologic or genitourinary cancers, sexual dysfunction is prevalent in lung cancer survivors.<sup>4</sup> In a previous study, it was found that 48% of lung cancer patients experienced sexual problems, and 27% experienced severe sexual problems.<sup>5</sup> The worsening of sexual problems with sexual desire, erectile function, orgasm, frequency of sexual activity, body image, and communication about sex may develop during treatment and after the completion of lung cancer treatment.<sup>4,6,7</sup> In lung cancer patients, more severe sexual concerns were reported in males than in females.<sup>4</sup>

Erectile dysfunction (ED), which is defined as the inability to obtain or maintain an erection sufficient for satisfactory sexual performance, is the most common

sexual dysfunction in men.<sup>8</sup> Risk factors for ED include aging, vascular insufficiency, psychogenic and neural disorders, systemic illness, such as diabetes mellitus, hypertension, and cardiovascular disease, hormonal derangement, and side-effects of medications.<sup>9</sup> ED is associated with negative impacts on the quality of life and men's self-esteem. In clinical practice, ED is often underestimated by physicians. The association of ED and lung cancer has rarely been studied. A study reported that an increased risk of ED was observed in lung cancer patients after thoracotomy.<sup>10</sup> However, further studies with larger patient numbers are still needed to confirm this finding.

In this study, a nationwide population-based real-world database study focusing on the development of ED in male lung cancer patients with surgery was conducted. The incidence rates of ED diagnosed by clinical physicians after lung cancer surgery, the risk factors of ED, and the impact of ED on medical attendance were evaluated.

## Methods

### Data Source

The National Health Insurance Research Database (NHIRD) in Taiwan was used as our data source. National Health Insurance (NHI) is a compulsory universal program for the 23.7 million people in Taiwan. The NHIRD is a comprehensive health-care database that covers nearly the entire population of this country. Admissions and outpatient visits, including information on patient characteristics, such as sex, date of birth, date of admission, date of discharge, dates of visits, and up to five discharge diagnoses or three outpatients visit diagnoses were collected from the database. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes were used for diagnosis. Comprehensive utilization and enrollment information for all patients with "catastrophic illnesses" was also included in this database. With multiple data sources, the NHIRD database could be a powerful research engine for real-world evidence-based medicine in Taiwan.<sup>11</sup> This study was approved by the Ethics Review Board of Chang Gung Memorial Hospital, Chiayi Branch, Taiwan (IRB No. 201900916B1) and the requirement for informed consent was waived by the institutional review board.

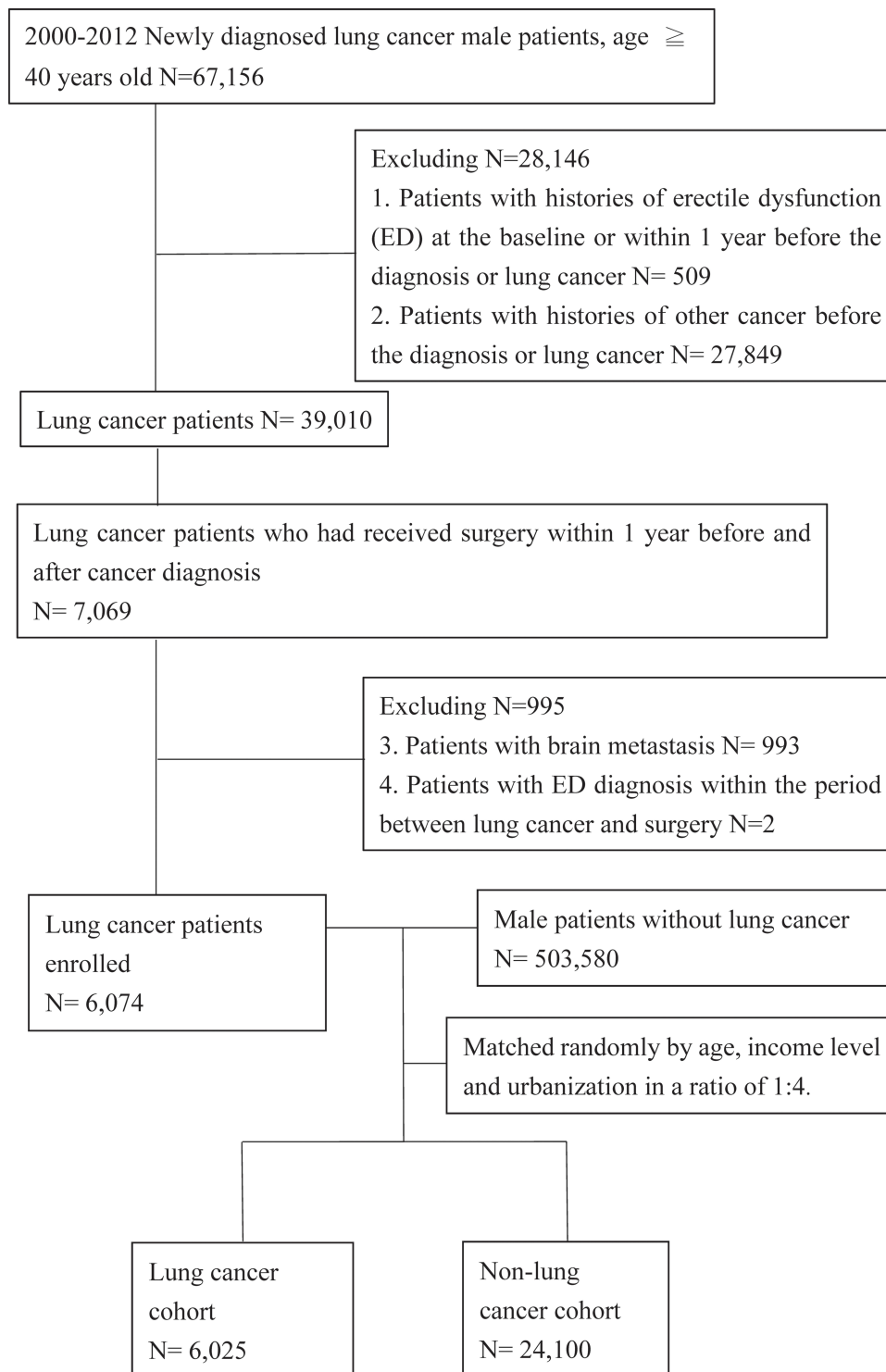
### Study Cohorts

All male patients with a primary diagnosis of lung cancer (ICD-9-CM 162) for the first time between January 1,

2000, and December 31, 2012, from NHIRD were included. Patients were diagnosed to have ED if they had at least one treatment claims for ED in outpatient visits within one year or hospitalization with ED (ICD-9-CM 302.72 and 607.84) during the follow-up period. Patients diagnosed with ED at the baseline or within 1 year before the diagnosis of lung cancer and other cancers were also excluded. Patients who received surgery for lung cancer were further included. A comparison cohort was randomly selected from the remaining insured population without lung cancer. For each lung cancer patient, persons free of lung cancer were selected and matched with age, income, and residential situation. Each non-lung cancer patient was given an index day of lung cancer from the lung cancer cohort with which they were matched. We also excluded patients with brain metastasis and diagnosed with ED before enrollment. To enhance the power of statistical tests, the lung cancer to non-lung cancer ratio was set at 1:4. Finally, we identified 6025 patients with lung cancer and 24,100 subjects in the non-lung cancer cohort for further analysis (Figure 1). All subjects were followed up to the end of 2013 to measure the incidence of ED.

### Demographic Variables and Comorbidities

Age, income for estimating insurance payment, and the urbanization of the subject's residential area were included in the demographic variables in this study. Monthly incomes were determined as New Taiwan Dollar (NT\$): NT\$0, NT\$1–15,840, NT\$15,841–25,000 and  $\geq$ NT\$25,000. Four urbanization levels were determined according to the Taiwan NHRI publications, with level 1 referring to the most-urbanized communities and level 4 to the least urbanized.<sup>12</sup> Coronary artery disease (CAD) (ICD9-CM 414–419), stroke (ICD9-CM 430–438), chronic obstructive pulmonary disease (COPD) (ICD9-CM 496), kidney disease (ICD9-CM 580–589), hypertension (ICD9-CM 401–405), arthritis (ICD9-CM 715, 716.90), peripheral arterial disease (PAD) (ICD9-CM 443.81, 443.9, 440.2, 444.2, 444.89), asthma (ICD9-CM 493), diabetes (ICD9-CM 249–250), smoking-related disorder (ICD9-CM 305.1, 491.2, 492.8, 523.6, and V15.82), obesity (ICD9-CM 278.00–278.02, and 278.1), hyperlipidemia (ICD9-CM 272), depression (ICD9-CM 296.2, 296.3, 300.4, 311), anxiety (ICD9-CM 300.00), Charlson comorbidity index (CCI), chemotherapy (CT), radiotherapy (RT), epidermal growth factor receptor tyrosine



**Figure 1** Flowchart of the patient enrollment process of the lung cancer and matched non-lung cancer cohorts.  
**Abbreviations:** ED, erectile dysfunction; N, number.

kinase inhibitor (EGFR-TKI), antihypertension drugs, nonsteroidal anti-inflammatory drugs and benzodiazepines use were included in the baseline comorbidities for each subject.

## Statistical Analysis

The differences in demographic characteristics and comorbidities between the lung cancer and non-lung cancer cohorts were examined using the  $\chi^2$  test. Poisson

regression analysis was used to obtain the incidence rate ratio (IRR) and related 95% confidence interval (CI) of the lung cancer cohort in relation to the non-lung cancer cohort. Univariate and multivariable models were used to estimate the crude and adjusted IRRs. Multivariable and subgroup analyses using IRR were performed. A Kaplan–Meier estimate was used to plot the survival curve of the cumulative incidence of ED and the difference between these two cohorts was evaluated by the Log rank test. The incidence rates of ED were analyzed as the number of cases per 10,000 person-years (PY) and emergency room (ER) visits, and ward admissions were calculated for each one person-year. These analyses were conducted using SAS statistical software (Version 9.4; SAS Institute, Cary, NC, USA).

## Results

### Demographic Characteristics and Comorbidities Between the Lung Cancer and Non-Lung Cancer Cohorts

A total of 6074 male lung cancer patients who received surgical resection for lung cancer were included in our study from 2000 to 2012. After being matched by age, gender, income, and level of urbanization, 6025 and 24,100 male patients were enrolled in the lung cancer and non-lung cancer cohorts, respectively (Figure 1). In the lung cancer cohort, significantly higher proportions of CAD, COPD, kidney disease, hypertension, arthritis, asthma, diabetes, smoking-related disorder, hyperlipidemia, depression, anxiety, CCI, and nonsteroidal anti-inflammatory drug and benzodiazepine use was also observed in the lung cancer cohort (Table 1). The median follow-up period for the lung cancer matched cohort was 2.79 and 5.16 years for the non-lung cancer cohort (Table 1).

### Incidence of ED Among Lung Cancer and Non-Lung Cancer Cohorts

Of the 6025 lung cancer and 24,100 non-lung cancer cohorts followed up, the development of ED was observed in 91 patients in the lung cancer cohort and 403 patients in the non-lung cancer cohort. After 14 years of follow-up, the cumulative incidence of ED was significantly higher in the lung cancer cohort compared to the non-lung cancer cohort ( $p=0.018$ , Figure 2).

The incidence of ED was also higher in the lung cancer cohort compared to the non-lung cancer cohort (38.47 vs 28.28 per 10,000 person-years) with an IRR of 1.36 (95% CI: 1.08–1.71,  $p=0.008$ ) (Table 2). After adjusting for age, income, urbanization, comorbidities, and the medications listed in Table 1, an increased incidence of ED was still observed in the lung cancer cohort with an adjusted IRR (aIRR) of 1.34 (95% CI: 1.06–1.70,  $p=0.014$ ) (Table 2).

### Comparison of the Incidence Rate of ED Stratified by Age, Gender, and Comorbidities Between the Lung Cancer and Non-Lung Cancer Cohorts

The incidence of ED in the lung cancer and non-lung cancer cohorts was then stratified by age and comorbidities and compared to the non-lung cancer cohort. After adjusting for age, urbanization, income, comorbidities, and medications, an increased aIRR of ED was observed in the lung cancer cohort with an age 40–54 years, COPD, anxiety, depression, smoking-related disorder, with or without obesity, and without asthma, anti-hypertension drugs, and benzodiazepines (Table 3).

### Risk Factors of ED in Lung Cancer Cohort

The risk factors of ED were then analyzed in the lung cancer cohort. In the multivariable analysis, being aged 40–54 years (aIRR: 5.44, 95% CI: 2.25–13.15,  $p<0.001$ ), 55–64 years (aIRR: 3.62, 95% CI: 1.61–8.17,  $p=0.002$ ) years, and anxiety (aIRR: 2.99, 95% CI: 1.81–4.94,  $p<0.001$ ) were independent factors for the increased incidence of ED in the lung cancer cohort (Table 4). Lower aIRRs of ED were observed in patients with nonsteroidal anti-inflammatory drugs, anti-hypertension drugs, benzodiazepines, and CT+RT (Table 4).

### Incidence of ER Visit and Admission in ED and Non-ED Lung Cancer Patients

Of the total of 6025 lung cancer patients, the incidences of ER visits and admissions to hospital were evaluated. After adjusting for age, income level, urbanization, comorbidities, medications, and cancer-related treatments, higher incidences rates of ER visits (aIRR: 2.19, 95% CI: 1.98–2.42,  $p<0.001$ ) were observed in lung cancer patients with ED compared to those without ED (Table 5).

**Table I** Demographic Status and Comorbidity Compared Between Cohorts with and without Lung Cancer

Variables	Lung Cancer			
	With		Without	
Individuals	6025	100.0%	24,100	100.0%
Age				
40–54	990	16.4%	3960	16.4%
55–64	1518	25.2%	6072	25.2%
65–74	2110	35.0%	8440	35.0%
≥75	1407	23.4%	5628	23.4%
Income level (NT\$)				
0	1530	25.4%	6120	25.4%
1~15,840	1290	21.4%	5160	21.4%
15,841~25,000	1905	31.6%	7620	31.6%
≥25,000	1300	21.6%	5200	21.6%
Urbanization				
I	1804	29.9%	7216	29.9%
II	2492	41.4%	9968	41.4%
III	1129	18.7%	4516	18.7%
IV	600	10.0%	2400	10.0%
Comorbidities				
Hypertension	3739	62.1%	14,194	58.9%
Arthritis	2743	45.5%	9619	39.9%
COPD	2408	40.0%	3780	15.7%
Hyperlipidemia	2290	38.0%	8732	36.2%
CAD	2023	33.6%	6991	29.0%
Diabetes	1875	31.1%	7178	29.8%
Smoking-related disorder	1791	29.7%	3456	14.3%
Asthma	1577	26.2%	3595	14.9%
Stroke	1465	24.3%	6633	27.5%
Kidney disease	1209	20.1%	4560	18.9%
Anxiety	995	16.5%	3075	12.8%
Depression	663	11.0%	1863	7.7%
PAD	323	5.4%	1315	5.5%
Obesity	36	0.6%	167	0.7%
CCI (before index date)				
0	181	3.0%	7336	30.4%
1–2	1081	17.9%	8752	36.3%
3–5	3106	51.6%	5817	24.1%
≥6	1657	27.5%	2195	9.1%
Median (Q1-Q3)	4	(3–6)	1	(0–3)
Medications				
Nonsteroidal anti-inflammatory drugs	3563	59.1%	10,878	45.1%
Anti-hypertension drugs	2731	45.3%	10,792	44.8%
Benzodiazepines	2191	36.4%	5792	24.0%
ED diagnosis after index date				
Non-organic ED	91	1.5%	403	1.7%
Organic ED	6	0.1%	36	0.1%
Organic ED	85	1.4%	367	1.5%

(Continued)

**Table I** (Continued).

Variables	Lung Cancer			
	With		Without	
Follow-up duration (year)				
Median (Q1-Q3)	2.79	(1.34–5.46)	5.16	(2.67–8.78)

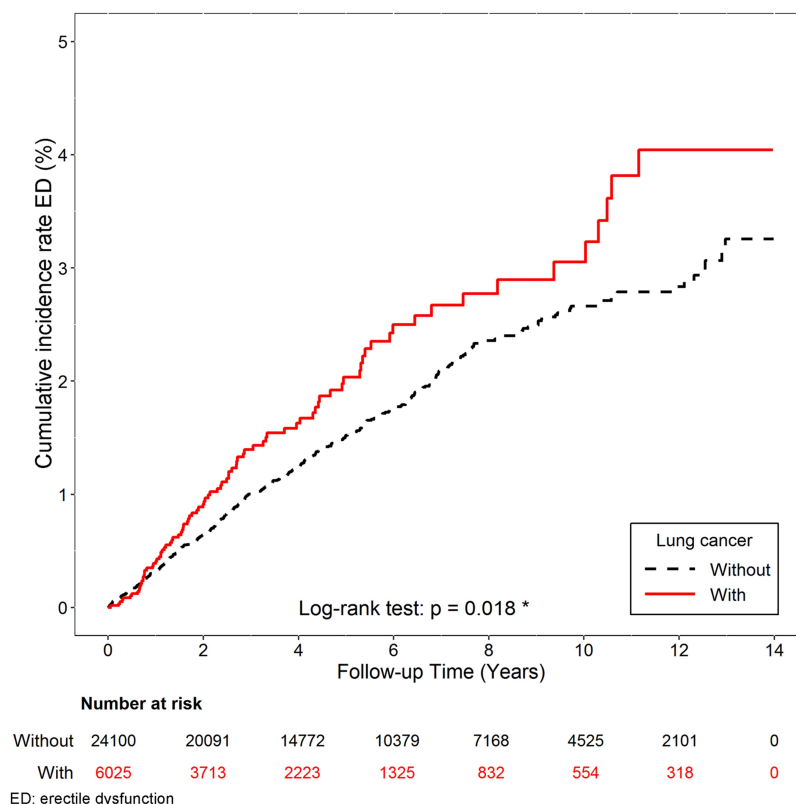
**Abbreviations:** CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; ED, erectile dysfunction; NT\$, New Taiwan Dollar; PAD, peripheral arterial disease.

## Discussion

In this retrospective longitudinal cohort study, we observed higher proportions of comorbidities in lung cancer patients who received surgery. In addition, the incidence of ED was higher after lung cancer surgery compared to the non-lung cancer cohort. Increased risks of ED were associated with a young age and anxiety in lung cancer patients after surgery. Furthermore, a higher incidence of ER visits was observed in lung cancer patients after surgery with ED.

In our study, higher proportions of comorbidities, including CAD, COPD, kidney disease, hypertension, arthritis, PAD, asthma, diabetes, hyperlipidemia, depression, and anxiety were observed in the lung cancer cohort. Similar results have been reported in previous studies. The majority of cancers, including lung cancer, have been reported to increase the risk of CAD.<sup>13</sup> Smoking is a common risk factor for COPD and lung cancer and a diagnosis of COPD is strongly associated with a diagnosis of lung cancer.<sup>14</sup> Hypertension is associated with an increased risk of lung cancer in smoking men.<sup>15</sup> An increased risk of lung cancer and other cancers have been reported in patients with rheumatoid arthritis<sup>16</sup> and PAD.<sup>17</sup> The association of asthma and lung cancer has been inconclusive in the past research; however, a recent meta-analysis showed that asthma may significantly increase the risk of lung cancer.<sup>18</sup> Diabetes has been reported to increase the risk of lung cancer.<sup>19</sup> A high total triglyceride level is positively associated with the risk of lung cancer.<sup>20</sup> Increased incidences of anxiety and depression have been reported after the diagnosis of lung cancer.<sup>21</sup> As a result, the evaluation and management of these comorbidities are important in this group of patients.

Compared to the non-lung cancer cohort, a higher incidence rate of ED was observed in the lung cancer cohort in our study. The mechanisms of ED and lung cancer are less



**Figure 2** The cumulative incidence rate of erectile dysfunction (ED) in the lung cancer (solid line) and non-lung cancer (dashed line) cohorts by the end of the follow-up duration. “\*” denotes  $p < 0.05$ .

**Abbreviation:** ED, erectile dysfunction.

clear and may be explained by several reasons. In our study, we focused on lung cancer patients after surgery. Lung cancer patients after operations have been reported to have a worse quality of life.<sup>22</sup> The surgery for lung cancer may adversely affect the psychogenic status and sexual function due to its intensive nature.<sup>10</sup> The symptoms of lung cancer, such as pain,<sup>23</sup> fatigue, dyspnea, and anorexia,<sup>24</sup> which result in poor physical functioning, poor psychosocial functioning, and a poor quality of life status, may predispose patients to the development of ED.<sup>4</sup>

A higher prevalence of anxiety and depression was observed in lung cancer patients after surgery.<sup>21</sup> Both

anxiety and depression were associated with ED and anxiety had a stronger association.<sup>25</sup> In our study, anxiety was an independent risk factor of ED in the lung cancer cohort. Lung cancer is well known as the leading cause of cancer mortality worldwide. Due to the poor prognosis of lung cancer, patients may have fear and frustration after the diagnosis of lung cancer<sup>26</sup> which may predispose patients to the development of anxiety and then ED. Young patients were also observed to have higher incidence rates of ED after lung cancer surgery in our study. As the diagnosis of ED is based on the clinical diagnosis by physician in our study, we thus

**Table 2** Crude and Adjusted Incidence Rates of ED for Lung Cancer Patients Compared with Non-Lung Cancer Control

	ED Events	Person-Years	IR (95% CI)	IRR (95% CI)	p value	aIRR (95% CI)	p value
Control	403	142,523.7	28.28 (25.65–31.18)	reference		reference	
Lung cancer	91	23,653.4	38.47 (31.33–47.25)	1.36 (1.08–1.71)	0.008*	1.34 (1.06–1.70)	0.014*

**Notes:** aIRR was adjusted for age, income level, urbanization, comorbidities and medications listed in Table 1. “\*” denotes  $p < 0.05$ .

**Abbreviations:** aIRR, adjusted IRR; CI, confidence interval; ED, erectile dysfunction; IR, incidence rate, per 10,000-person-years; IRR, incidence rate ratio.

**Table 3** Subgroup Analysis Based on Different Age and Comorbidity for the Risk of ED in Study Cohort

Clinical Variables	IRR (95% CI)	p value	aIRR (95% CI)	p value
Age (year)				
40–54	2.07 (1.35–3.17)	0.001*	1.93 (1.21–3.06)	0.005*
55–64	1.26 (0.86–1.84)	0.235	1.19 (0.80–1.78)	0.390
65–74	0.84 (0.53–1.35)	0.474	0.96 (0.60–1.56)	0.875
≥75	1.71 (0.82–3.54)	0.150	1.60 (0.74–3.44)	0.231
Comorbidities				
CAD				
No	1.38 (1.05–1.81)	0.022	1.29 (0.97–1.73)	0.081
Yes	1.33 (0.89–2.00)	0.163	1.34 (0.88–2.04)	0.174
Stroke				
No	1.30 (1.01–1.68)	0.042	1.25 (0.96–1.64)	0.097
Yes	1.50 (0.90–2.50)	0.119	1.68 (0.99–2.85)	0.053
COPD				
No	1.30 (0.98–1.73)	0.069	1.19 (0.89–1.59)	0.236
Yes	2.03 (1.31–3.13)	0.002*	1.68 (1.07–2.65)	0.025*
Kidney disease				
No	1.38 (1.08–1.77)	0.009*	1.36 (1.05–1.76)	0.019*
Yes	1.21 (0.65–2.24)	0.553	1.11 (0.59–2.10)	0.751
Hypertension				
No	1.51 (1.06–2.16)	0.024*	1.36 (0.93–1.99)	0.108
Yes	1.27 (0.95–1.71)	0.109	1.26 (0.92–1.70)	0.145
Arthritis				
No	1.45 (1.06–1.99)	0.021*	1.35 (0.97–1.88)	0.079
Yes	1.25 (0.90–1.74)	0.178	1.22 (0.87–1.72)	0.247
PAD				
No	1.36 (1.08–1.72)	0.009*	1.35 (1.06–1.72)	0.015*
Yes	1.27 (0.37–4.39)	0.705	2.04 (0.54–7.65)	0.291
Asthma				
No	1.35 (1.04–1.76)	0.025*	1.32 (1.01–1.74)	0.045*
Yes	1.44 (0.90–2.30)	0.126	1.40 (0.86–2.27)	0.176
Diabetes				
No	1.31 (1.00–1.73)	0.053	1.25 (0.93–1.66)	0.135
Yes	1.47 (0.99–2.20)	0.058	1.53 (1.01–2.33)	0.046*
Hyperlipidemia				
No	1.36 (0.99–1.86)	0.056	1.32 (0.94–1.84)	0.106
Yes	1.33 (0.96–1.85)	0.089	1.29 (0.92–1.82)	0.138
Depression				
No	1.27 (0.99–1.63)	0.065	1.23 (0.95–1.60)	0.119
Yes	1.93 (1.09–3.42)	0.024*	1.84 (1.00–3.39)	0.050*
Anxiety				
No	1.14 (0.87–1.50)	0.343	1.12 (0.84–1.49)	0.448
Yes	2.01 (1.32–3.06)	0.001*	2.18 (1.40–3.40)	0.001*

(Continued)

**Table 3** (Continued).

Clinical Variables	IRR (95% CI)	p value	aIRR (95% CI)	p value
Smoking-related disorder				
No	1.27 (0.97–1.66)	0.087	1.21 (0.92–1.60)	0.171
Yes	2.05 (1.28–3.29)	0.003	1.77 (1.08–2.90)	0.022*
Obesity				
No	1.36 (1.08–1.71)	0.008	1.35 (1.06–1.71)	0.014*
Yes	1.24 (0.15–10.65)	0.842	0.00 (0.00–0.07)	0.001*
Medications				
Nonsteroidal anti-inflammatory drugs				
No use	1.71 (1.21–2.42)	0.003*	1.28 (0.89–1.84)	0.181
Use	1.30 (0.96–1.76)	0.088	1.25 (0.92–1.72)	0.159
Anti-hypertension drugs				
No use	1.60 (1.19–2.16)	0.002*	1.42 (1.04–1.95)	0.028*
Use	1.13 (0.79–1.60)	0.506	1.14 (0.79–1.65)	0.476
Benzodiazepines				
No use	1.49 (1.12–1.98)	0.006*	1.36 (1.01–1.82)	0.042*
Use	1.23 (0.84–1.81)	0.288	1.22 (0.82–1.83)	0.327

**Notes:** aIRR was estimated by competing risk model and adjusted for age, urbanization, income, comorbidities and medications listed in Table 1. "\*" denotes  $p < 0.05$ .

**Abbreviations:** aIRR, adjusted incidence rate ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; ED, erectile dysfunction; IRR, incidence rate ratio; PAD, peripheral arterial disease.

hypothesized that younger patients are in a more sexually active stage and may have a higher motivation to seek medical help.

In our study, the prevalence rate of ED after lung cancer surgery was 1.5% which is lower than previous studies in general populations.<sup>27,28</sup> The discrepancy between our study and other studies may be due to the different methods for the diagnosis of ED or sexual dysfunction, such as questionnaires used in previous studies. A clinical diagnosis for ED by attending physicians after lung cancer surgery was used in our study. Our study may reveal the prevalence rate of clinically significant ED for patients who seek medical intervention from clinical physicians.

Patients with a previous diagnosis of ED before the initiation of follow-up in both lung cancer and non-lung cancer cohorts were excluded in our study, which may have also resulted in a lower prevalence rate of ED in our study. Lower incidence rates of ED were observed in patients with nonsteroidal anti-inflammatory drugs, anti-hypertension drugs, benzodiazepines, and CT+RT. We hypothesized that the aggravated severity of comorbidities and side effects of

treatment may predispose patients to have the associated symptoms and deteriorated physical status, which may mask complaints of ED.

ED is associated with increased emergency and hospital admissions in patients with COPD.<sup>29</sup> Previous studies showed the association of ED with the risk and severity of COPD,<sup>30</sup> CAD,<sup>31</sup> and stroke.<sup>32</sup> A higher incidence of ER visits was observed in lung cancer patients with ED compared to those without ED in our study and we hypothesized that this may be due to the increased associated comorbidities including COPD, CAD, stroke and other diseases in this group of patients. The detailed causes of ER visits were not analyzed in our study due to the study limitations. However, more medical attendance is needed for lung cancer patients with ED.

Certain limitations still exist for this study. Data including the stages, pathology, cancer-related symptoms of lung cancer, physical status, smoking status, personal characteristics, body mass index, or genetic factors were not included in the NHIRD, and these potential confounders may increase the risk of ED. The record of diagnostic tool for ED was also not



**Table 4** Analysis of Risk Factors for Developing ED Among Lung Cancer Patients

Clinical Variables	IRR (95% CI)	p value	aIRR (95% CI)	p value
Age (year, ref: $\geq 75$ )				
40–54	3.69 (1.75–7.80)	0.001*	5.44 (2.25–13.15)	<0.001*
55–64	2.82 (1.35–5.89)	0.006*	3.62 (1.61–8.17)	0.002*
65–74	1.25 (0.57–2.75)	0.576	1.51 (0.67–3.39)	0.316
Income level (ref: 0)				
1–15,840	0.98 (0.50–1.92)	0.946	1.03 (0.52–2.06)	0.930
15,841–25,000	1.11 (0.61–2.02)	0.726	1.19 (0.63–2.25)	0.599
$\geq 25,000$	1.73 (0.97–3.11)	0.065	0.85 (0.44–1.63)	0.616
Urbanization (ref: IV)				
I	1.38 (0.67–2.87)	0.382	1.43 (0.65–3.13)	0.375
II	0.99 (0.48–2.04)	0.969	1.04 (0.48–2.23)	0.923
III	0.49 (0.19–1.27)	0.142	0.50 (0.19–1.31)	0.157
Comorbidities (ref: No)				
CAD	0.90 (0.58–1.40)	0.634	0.99 (0.60–1.63)	0.971
Stroke	0.71 (0.42–1.19)	0.194	0.83 (0.47–1.48)	0.530
COPD	0.93 (0.61–1.41)	0.728	1.40 (0.85–2.30)	0.188
Kidney disease	0.63 (0.34–1.16)	0.137	0.82 (0.44–1.55)	0.547
Hypertension	0.86 (0.56–1.30)	0.469	1.42 (0.81–2.47)	0.217
Arthritis	1.05 (0.70–1.58)	0.818	1.36 (0.85–2.15)	0.196
PAD	0.56 (0.18–1.77)	0.324	0.78 (0.24–2.54)	0.682
Asthma	0.97 (0.61–1.54)	0.906	1.08 (0.66–1.79)	0.752
Diabetes	1.05 (0.68–1.63)	0.824	1.12 (0.69–1.80)	0.645
Hyperlipidemia	1.50 (1.00–2.27)	0.052	1.27 (0.80–2.00)	0.307
Depression	1.80 (1.06–3.05)	0.029*	1.62 (0.90–2.92)	0.107
Anxiety	2.50 (1.62–3.86)	<0.001*	2.99 (1.81–4.94)	<0.001*
Smoking-related disorder	1.05 (0.68–1.64)	0.816	1.22 (0.74–2.00)	0.432
Obesity	1.75 (0.24–12.58)	0.577	1.41 (0.19–10.39)	0.737
Medication (ref: 0–27 days)				
Nonsteroidal anti-inflammatory drugs	0.56 (0.37–0.85)	0.006*	0.59 (0.37–0.95)	0.028*
Anti-hypertension drugs	0.61 (0.40–0.92)	0.020*	0.52 (0.30–0.90)	0.020*
Benzodiazepines	0.74 (0.48–1.13)	0.159	0.60 (0.36–0.98)	0.043*
Cancer related disease/treatment				
CT/RT (ref: without CT/RT)				
CT+RT	0.33 (0.16–0.67)	0.002*	0.40 (0.19–0.84)	0.015*
CT only	0.59 (0.34–1.01)	0.053	0.65 (0.38–1.14)	0.133
RT only	0.65 (0.30–1.42)	0.276	0.72 (0.33–1.59)	0.416
EGFR-TKI (ref: non-user)	0.24 (0.08–0.75)	0.014*	0.33 (0.10–1.08)	0.067

Note: "\*" denotes  $p < 0.05$ .

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; CT, chemotherapy; ED, erectile dysfunction; EGFR-TKI, epidermal growth factor receptor tyrosine kinase inhibitor; NT\$, New Taiwan Dollar; PAD, peripheral arterial disease; RT, radiotherapy; ref, reference.

included. As only clinically diagnosed ED was included, the incidence of ED may be underestimated in our study, and the severity of ED was not identified in the database. Our study was a retrospective study; thus, prospective studies are still recommended in the future.

## Conclusion

In conclusion, our study showed a higher incidence of ED in male lung cancer patients after surgery, especially in young patients and patients with anxiety. The under-diagnosis of ED was also observed in this group of patients. Our study suggested that the surveillance of ED

**Table 5** Incidence of ER Visiting and Admission in ED and Non-ED Lung Cancer Patients

	Patients	Events	Person-Years	IR (95% CI)	IRR (95% CI)	p value	aIRR (95% CI)	p value
ER visiting								
Non-ED	5934	18,680	23,382.1	0.80 (0.79–0.81)	Reference		Reference	
ED	91	403	327.5	1.23 (1.12–1.36)	1.54 (1.40–1.70)	<0.001*	2.19 (1.98–2.42)	<0.001*
Admission								
Non-ED	5934	22,318	23,382.1	0.95 (0.94–0.97)	Reference		Reference	
ED	91	225	327.5	0.69 (0.60–0.78)	0.72 (0.63–0.82)	<0.001*	1.11 (0.97–1.27)	0.119

**Notes:** aIRR was adjusted for age, income level, urbanization, comorbidities, medications and cancer-related treatments listed in Table 4. "\*" denotes  $p < 0.05$ .

**Abbreviations:** aIRR, adjusted IRR; CI, confidence interval; ED, erectile dysfunction; IR, incidence rate, per person-years; IRR, incidence rate ratio.

should be considered during clinical practice in lung cancer patients after surgery.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is 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 no potential conflicts of interest for this article.

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