Effect of PM2.5 on Mortality, Tumor Recurrence, and Postoperative Complications in Resectable Non-Small Cell Lung Carcinoma: A Retrospective Cohort Study

Bongkotmas Kosanpipat
Chiang Mai University
Thanida Wongwut
Chiang Mai University
Natthawat Norrasan
Chiang Mai University
Parada Watthanawongsa
Chiang Mai University
Phichayut Phinyo
Chiang Mai University
Somcharoen Saeteng
Chiang Mai University
Sophon Siwachat
Chiang Mai University
Busayamas Chewaskulyong
Chiang Mai University
Apichat Tantraworasin
apichat.t@cmu.ac.th
Chiang Mai University

Article

Keywords: Particular matter, long-term survival, In-hospital mortality, Lung cancer, Air pollution

Posted Date: February 23rd, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3943336/v1

Additional Declarations: No competing interests reported.

Abstract

This study aimed to explore the impact of PM 2.5 exposure on survival, post-operative outcomes, and tumor recurrence in resectable non-small cell lung cancer (NSCLC) patients. The study cohort comprised 587 patients at Chiang Mai University Hospital between January 1, 2010, and December 31, 2017. Patients were categorized based on their residents' average PM 2.5 concentration into two groups: exposed (PM 2.5 ≥ 25 μg/m3 annual mean) and unexposed (PM 2.5 < 25 μg/m3 annual mean). The exposed group had 278 patients, while the unexposed group had 309 patients. Baseline differences in gender and surgical approach were observed between the groups. Multivariable regression analysis revealed that patients in the exposed group had a higher risk of death (HR 1.44, 95% CI, 1.08-1.89, p=0.012). However, no significant associations were found between PM 2.5 and post-operative pulmonary complications (RR 1.12, 95% CI, 0.60-2.11, p=0.718), in-hospital mortality (RR 1.98, 95% CI, 0.40-9.77, p=0.401), and tumor recurrence (HR 1.12, 95% CI, 0.82-1.51, p=0.483). In conclusion, a PM 2.5 concentration ≥ 25 μg/m3 annual mean was associated with decreased overall survival and a potential increase in in-hospital mortality among resectable NSCLC patients. Larger studies with extended follow-up periods are required to validate these findings.

Introduction

Particulate matter (PM) in outdoor air pollution was recently designated as a Group I carcinogen by the International Agency for Research on Cancer (IARC)[1]. Elevated concentrations of PM 2.5 (ranging between 100 and 200 μg/m3) pose a significant concern in Thailand, particularly during the burning seasons in the northern region, as they have been linked to lung injury and cancer, a leading cause of cancer-related mortality [2]. Thailand's national air quality standards, as indicated by the World Health Organization (WHO) guidelines and Greenpeace's City Rankings for MP2.5, fall below WHO recommendations. The annual standard for PM2.5, the most harmful pollutant, is set at 25 micrograms per cubic meter ($\mu g/m^3$), which is 2.5 times higher than the WHO guideline. Similarly, the daily standard of 50 $\mu g/m^3$ and annual mean of 25 $\mu g/m^3$ are double the WHO's recommendations [3, 4]. Exposure to PM2.5 levels exceeding these thresholds significantly increases the mortality rate from lung cancer [5]. Additionally, reports indicate that Northern Thai women have the highest incidence of lung cancer in Asia [6].

Pulmonary resection is the standard treatment for early-stage non-small cell lung cancer (NSCLC) [7]. However, postoperative complications can lead to prolonged hospital stays, increased medical costs, and higher mortality rates [8]. In Chiang Mai, Thailand, known for its hazardous levels of PM2.5, the potential relationship between in-hospital mortality, post-operative pulmonary complications, and PM2.5 concentration in surgically treated NSCLC patients remains largely unexplored at the individual-data level within our region and nation. Therefore, the objective of this study is to investigate the association between PM 2.5 exposure and short- and long-term outcomes following pulmonary resection in NSCLC patients.

Methods

Study design and data collection

This is a retrospective cohort study that investigates the effect of PM2.5 on overall survival, in-hospital mortality, postoperative pulmonary complications, and disease-free survival in resectable NSCLC. We obtained approval from the Institutional Review Board (Research Ethics Committee Faculty of Medicine, Chiang Mai University No: 354/2021, Research ID 07877) with a waiver for written informed consent due to the retrospective nature of the study. All data were maintained confidentially following the Helsinki Declaration.

We collected annual concentrations of PM2.5 at background stations divided by patient residence by requesting data from the Chiang Mai Air Quality Health Index (CMAQH) (Website: https://cmaqh.org) from 2007–2017). We also review the medical records of adult patients (age > 18 years old) diagnosed with NSCLC who underwent surgical resection in the General Thoracic Surgery Unit, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, between January 1, 2007, and December 31, 2017. Patients' lifestyle modifications were also reviewed.

The patient characteristics such as age, gender, address, smoking status, comorbid disease, stage of NSCLC, operative data, postoperative outcomes, pathologic results, follow-up time, treatment modalities, and patient status, were obtained from the medical recording systems. The primary outcome of this study is overall survival. The secondary outcomes include disease-free survival (recurrent-free survival), in-hospital mortality, and postoperative pulmonary complications such as pneumonia, lung atelectasis requiring bronchoscopy, and re-intubation.

According to previous studies, we divided all patients into two groups based on the upper concentration truncation of PM2.5 at 25 μg/m^3 annual mean: the exposed group (≥ 25 μg/m^3 annual mean) and the non-exposed group (< 25 μg/m^3 annual mean)[9]. The average concentration of PM 2.5 in the month of surgery was used to investigate the association between PM 2.5 and post-operative pulmonary complications.

We calculated the required sample sizes for a two-sample comparison of survivor functions using an exponential test, hazard difference, and a significance level (alpha) of 0.05 and a power (beta) of 0.20. Our calculations were based on the study by Lepeule et al (2012), which used overall survival (i.e., overall mortality) as the primary endpoint. The calculated sample size for deceased patients was 97 cases, while for surviving patients it was 1,333 cases, with a ratio of 12.8:1 and a Hazard ratio of 1.37.

Statistical analysis

Categorical variables were presented as count and percent and analyzed by using Fisher's exact test. Continuous variables were presented as mean and standard deviation (SD), or median and interquartile range (IQR) depending on data distribution and analyzed by using Student's *t*-test or Wilcoxon rank-sum

test as appropriate. The recurrence-free survival and overall survival curves were estimated using the Kaplan–Meier methods. The relationship between PM2.5 exposure (across two study groups) and postoperative pulmonary complications, as well as in-hospital mortality, was examined using a multivariable risk regression model. This model was adjusted for potential confounding factors, including age, gender, Charlson comorbidity index, disease stage, annual PM10 exposure levels, concentrations of CO, SO2, NO2, and O3, as well as average temperature and humidity, all based on patient residency. Additionally, the type of pulmonary resection was taken into account. The estimated values are presented as risk ratios (RR) along with their corresponding 95% confidence intervals (CI) The association between PM 2.5 and recurrence-free survival and long-term survival were analyzed by multivariable Cox's regression model adjusted by other confounding factors such as age, gender, Charlson comorbidity index, stage of disease, pathologic result, procedures, concentrations of CO, SO2, NO2, and O3, average temperature and humidity, all based on patient residency, and adjuvant chemotherapy, presented as hazard ratio (HR) with 95% CI. A multiple imputation method for variables with ≥ 10% missing values [10] was performed. A modest amount of missing formation is recommended for three to five multiple imputations (< 30%) and then estimate the whole model. After that, the results from a complete-case analysis were compared to those from a multiple imputations analysis. If the final model by multiple imputations gave the same results or had only a slightly different results, we decided to report the result from the complete-case analysis. All tests were two-tailed and performed with Stata 16.0 (StataCorp LP, College Station, TX, USA), with $p < 0.05$ indicating a statistically significant difference.

Results

The results of this study show that a total of 587 patients diagnosed with NSCLC underwent surgical resection, with 278 patients in the exposed group and 309 patients in the unexposed group. The mean age of the exposed group was 62.51 ± 10.52 years, while the exposed group had a mean age of 62.32 ± 10.39 years. Demographic data, preoperative characteristics, and pathologic results are presented in Table 1. Differences in gender and surgical approaches were observed at baseline, while there were no statistically significant differences in age, smoking status, co-morbidity, insurance type, pathologic stage, cell type, pathologic findings, procedures, occupation, air purifier used in household, and PM2.5 mask use between the two groups.

Table 1
patient characteristics between groups (587 patients)

Variable	Exposed group N = 278	Unexposed group N = 309	p-value
Age (years)	62.51 ± 10.52	62.32 ± 10.39	0.920
Gender, n (%)			0.029
male	149 (53.60)	193 (62.66)	
female	129 (46.40)	115 (37.34)	
Smoking Status, n (%)			0.835
Nonsmoker	67 (24.10)	68 (22.01)	
Former smoker	185 (66.55)	210 (67.96)	
Current smoker	8 (2.88)	7 (2.27)	
Passive smoker	18 (6.47)	24 (7.77)	
Co-Morbidity, n (%)			
COPD	38 (13.67)	54 (17.48)	0.213
Hypertension	107 (38.49)	123 (39.81)	0.800
Diabetes Mellitus	35 (12.59)	37 (11.97)	0.900
Dyslipidemia	58 (20.86)	54 (17.48)	0.344
Family history of cancer	19 (6.83)	18 (5.83)	0.734
Charlson comorbidity index (Median (IQR))	0 (0–1)	0 (0–1)	0.425
Insurance type, n (%)			0.070
UCS (, .)	142 (51.08)	173 (55.99)	
CSMBS ( )	111 (39.93)	124 (40.13)	
SSS ( )	22 (7.91)	11 (3.56)	
Private insurance or self-paid	3 (1.08)	1 (0.32)	
Occupation, n (%)			0.129
Indoor work environment	158 (56.83)	195 (63.11)	
Outdoor work environment	120 (43.17)	114 (36.89)	

CSMBS; Civil servant medical benefit scheme, SSS; Social security scheme, UCS; Universal coverage scheme

Variable	Exposed group N = 278	Unexposed group N = 309	p-value
Cell type			0.447
Adenocarcinoma	182 (65.47)	192 (62.14)	
Squamous cell carcinoma	57 (20.50)	77 (24.92)	
Others	39 (14.03)	40 (12.94)	
Pathological stage (8th edition)			0.645
I	104 (37.55)	99 (32.04)	
II	64 (23.10)	83 (26.86)	
IIIA	70 (25.27)	83 (26.86)	
IIIB or IIIC	20 (7.22)	25 (8.09)	
IV	19 (6.86)	19 (6.15)	
Procedures, N (%)			0.310
Wedge resection	54 (19.57)	45 (14.66)	
Segmentectomy	9 (3.26)	8 (2.61)	
Lobectomy	209 (75.72)	246 (80.13)	
Pneumonectomy	4 (1.45)	8 (2.61)	
Approach, n (%)			< 0.001
Open thoracotomy	206 (74.10)	271 (88.56)	
VATS	72 (25.90)	35 (11.44)	
Cell differentiation			0.449
Well differentiated	85 (36.64)	90 (34.75)	
Moderately differentiated	93 (40.09)	105 (40.54)	
Poorly differentiated	50 (21.55)	53 (20.46)	
Undifferentiated	4 (1.72)	11 (4.25)	
Mediastinal lymph node management, n (%)			0.154
No mediastinal LN sampling or dissection	47 (16.91)	37 (11.97)	

CSMBS; Civil servant medical benefit scheme, SSS; Social security scheme, UCS; Universal coverage scheme

Variable	Exposed group N = 278	Unexposed group N = 309	p-value
Mediastinal lymph node sampling	40 (14.39)	39 (12.62)	
Mediastinal lymph node dissection	191 (68.71)	233 (75.40)	
Intratumoral vascular invasion, n (%)	114 (40.01)	111 (35.92)	0.234
Intratumoral lymphatic invasion, n (%)	198 (71.22)	222 (71.84)	0.927
Visceral pleural invasion, n (%)	53 (19.06)	53 (17.15)	0.592
Chemotherapy			0.311
No chemotherapy	141 (50.72)	148 (47.90)	
Adjuvant chemotherapy	87 (31.29)	115 (37.22)	
Induction chemotherapy	21 (7.55)	24 (7.77)	
First-line chemotherapy	29 (10.43)	22 (7.12)	
Air purifier used in household, n (%)	18 (6.47)	15 (4.85)	0.544
PM2.5 mask used, n (%)	25 (8.99)	24 (7.77)	0.608
CSMBS; Civil servant medical benefit scheme, SSS; Social security scheme, UCS; Universal coverage scheme			

When comparing between groups and considering other particles, gas concentrations, temperature, and humidity per year based on patient residency, it was observed that the average amount of PM10 and the concentration of CO and NO2 were significantly higher in the exposed group. However, there were no significant differences in terms of SO2 and O3. The mean temperature and humidity per year were also found to be similar between the two groups, as illustrated in Table 2.

Table 2
Other particles, gas concentration, temperature, and humidity per year between groups

Variable	Exposed group N = 278	Unexposed group N = 309	p-value
PM 10 ($\mu g/m^{3)}$, Mean ± SD	74.08 ± 11.76	71.80 ± 11.91	0.020
CO (ppm), Mean ± SD	0.67 ± 0.29	0.63 ± 0.23	0.042
SO_2 (ppb), Mean ± SD	1.54 ± 0.89	1.64 ± 0.90	0.199
NO_2 (ppb), Mean ± SD	12.17 ± 5.29	10.99 ± 5.32	0.008
O_3 (ppb), Mean ± SD	22.09 ± 5.33	22.73 ± 5.88	0.170
Temperature (C)	25.59 ± 1.45	25.82 ± 1.62	0.080
Humidity	75.24 ± 3.14	75.06 ± 3.52	0.519
PM = Particulate matter, CO = Carbon monoxide, SO_2 = sulfur dioxide, NO_2 = Nitrogen dioxide, O_3 = Ozone, ppm = parts per million, ppb = parts per billion			

The postoperative treatment outcomes are presented in Table 3. There was no statistically significant difference in terms of postoperative complications, postoperative pulmonary complications, and length of hospital stayed between the two groups. Although there was no statistically significant difference in terms of in-hospital mortality, patients in the exposed group had a higher in-hospital mortality than those in the unexposed group (2.88% vs 0.97%). In multivariable analysis (Table 4), there was no statistically significant difference in terms of postoperative pulmonary complication and in-hospital mortality. However, patients in the exposed group showed a trend towards higher in-hospital mortality than those in the unexposed group (adjusted HR 1.98, 95%CI = 0.40–9.77).

Table 3
Outcomes of treatment between groups

Outcomes	Exposed group N = 278	Unexposed group N = 309	p-value
Postoperative complications, n (%)			
Pneumonia	8 (2.88)	11 (3.56)	0.816
Atelectasis needed bronchoscopy	9 (3.24)	6 (1.94)	0.434
Re-intubation	8 (2.88)	7 (2.27)	0.795
Postoperative bleeding	13 (4.68)	10 (3.24)	0.401
Surgical site infection	3 (1.08)	1 (0.32)	0.349
Postoperative air leakage	23 (8.27)	23 (7.44)	0.759
In-hospital mortality	8 (2.88)	3 (0.97)	0.127
Postoperative pulmonary complication**, n(%)	20 (7.19)	21 (6.80)	0.872
Length of hospital stayed (days), Median (IQR)	7 (5–10)	7 (6–11)	0.438
Tumor recurrence, n (%)	83 (30.63)	88 (29.14)	0.368*
Time to recurrence (month), Median (IQR)	19 (9–40)	16 (9–39)	0.446
Long-term mortality, n (%)	111 (40.96)	96 (31.37)	0.012*
Total follow-up time (month), Median (IQR)	93 (26–132)	124 (56–166)	< 0.001
*analyzed by logrank test			
**Postoperative pulmonary complications included pneumonia, lung atelectasis requiring bronchoscopy, and re-intubation.			

Table 4
Univariable and multivariable analysis of effect of PM2.5 (exposed group versus non-exposed group) on clinical outcomes.

Outcomes (Exposed versus Unexposed)	Univariable analysis			Multivariable analysis		
	Estimate	95% CI	p-value	Estimate	95% CI	p-value
Postoperative pulmonary complication*	RR 1.06	0.57–1.95	0.855	1.12#	0.60–2.11	0.718
In-hospital mortality	RR 2.96	0.79–11.17	0.109	1.98#	0.40–9.77	0.401
Tumor recurrence	HR 1.14	0.85–1.54	0.381	1.12Ƀ	0.82–1.51	0.483
Long-term mortality	HR 1.42	1.08–1.87	0.012	1.44@	1.08–1.89	0.012

*Pneumonia, lung atelectasis needed bronchoscopy, and re-intubation

#Analyzed by risk regression analysis, reported with risk ratio (RR). Adjusted with age, gender, Charlson comorbidity index, occupation, stage of disease, type of pulmonary resection, average per year of PM10, CO, SO_2, NO_2, O_3 concentration, temperature, and humidity in multivariable analysis model.

Analyzed by risk regression analysis, reported with risk ratio (RR). Adjusted with age, gender, Charlson comorbidity index, occupation, stage of disease, postoperative respiratory complications, type of pulmonary resection, average per year of PM10, CO, SO_2, NO_2, O_3 concentration, temperature, and humidity in multivariable analysis model.

Ƀ Analyzed by cox regression analysis, reported with hazard ratio (HR). Adjusted with age, gender, Charlson comorbidity index, occupation, stage of disease, type of pulmonary resection, histology, insurance type, pathologic characteristic, adjuvant chemotherapy, average per year of PM10, CO, SO_2, NO_2, O_3 concentration, temperature, and humidity in multivariable analysis model.

@ Analyzed by cox regression analysis, reported with hazard ratio (HR). Adjusted with age, gender, Charlson comorbidity index, stage of disease, type of pulmonary resection, histology, insurance type, adjuvant chemotherapy, pathologic characteristic, average per year of PM10, CO, SO_2, NO_2, O_3 concentration, temperature, and humidity in multivariable analysis model.

In long-term outcomes, patients in the exposed group were more likely to have lower overall survival. The median total follow-up time in the exposed group was shorter than that in the unexposed group (93 months (IQR = 26–132) vs 124 months (IQR = 56–166), $p < 0.001$). Figure 1 shows the Kaplan-Meier curve of overall survival, comparing between the two groups. In multivariable analysis (Table 4), patients in the exposed group had a higher risk of long-term mortality (adjusted HR 1.44, 95% CI = 1.08–1.89). Patients in the unexposed group were more likely to survive than those in the exposed group ($p = 0.012$). There was no statistically significant difference in recurrent-free survival between the two groups, however, patients in exposed group have trend towards higher in tumor recurrence than those in unexposed group

(adjusted HR 1.12, 95% CI = 0.82–1.51). The incidence of overall mortality in each month of the year is presented in Fig. 2, where the highest incidence occurred in October and the lowest in September. There was no correlation found between the incidence of overall mortality in each month of the year (r = -0.277, p-value = 0.383).

Discussion

PM2.5 can penetrate deeply into the lungs and irritate the alveolar wall[11]. It can also cause epigenetic and microenvironmental alterations in lung cancer, including the activation of tumor-associated signaling pathway mediated by microRNA dysregulation, DNA methylation, and increased levels of cytokines and inflammatory cells[5]. These mechanisms increase the risk of recurrence, disease progression, and postoperative complications in lung cancer patients. Additionally, PM2.5 can affect autophagy and apoptosis of tumor cells, further exacerbating the negative impact on patient outcomes[12]. We hypothesize that PM2.5 may influence these outcomes, especially respiratory complications.

In multivariable analysis of this study revealed that the exposed group had an increased risk of long-term mortality, while there was no significant association observed between PM2.5 exposure and postoperative pulmonary complications or tumor recurrence. However, we observed a trend towards an increase in in-hospital mortality among exposed patients.

Previous studies have shown that PM2.5 is associated with the incidence and survival of lung cancer [13–15], and can promote its progression [12, 16]. Some studies have also shown that limited exposure to PM2.5 can decrease the risk of lung cancer and mortality rates in lung cancer patients [13].

A recent study by Liu et al[17] examined the effect of ambient PM2.5 exposure on the survival of lung cancer patients after lobectomy and found that every 10 μg/m^3 increase in monthly PM2.5 concentration in the first and second months after lobectomy increased the risk of death (HR = 1.043, 95%CI = 1.02–1.07) and HR = 1.036, 95% CI = 1.01–1.06, respectively. Although we did not find a statistically significant difference between PM2.5 and postoperative pulmonary complications, in-hospital mortality, and tumor recurrence, patients in the exposed group had a trend toward a higher risk of postoperative pulmonary complications (adjusted HR = 1.12, 95%CI = 0.60–2.11), in-hospital mortality (adjusted HR = 1.98, 95%CI = 0.40–9.77), and tumor recurrence (adjusted HR = 1.12, 95%CI = 0.82–1.51) compared to the unexposed group.

Based on our data, we found that only 8.3% (49/587 patients) and 5.6% (33/587 patients) of the patients reported using masks and air purifiers at home, respectively. Therefore, we recommend that Thailand, particularly in the northern region, should revise its health promotion and policy strategies to prevent forest fires and improve air quality. Economic growth is important, but it should be balanced with environmental protection to ensure sustainable development. Additionally, public health education and promotion campaigns are essential.

There are some limitations to this study. Firstly, the retrospective nature of the study design may have introduced selection bias in surgical cases. Secondly, the number of patients who used masks or air purifiers was too small to be used for further data analysis. We attempted to explore the association between mortality and the seasonal high values of PM2.5, but we did not find any association. The available sample size was not powered enough to detect any significant associations among PM2.5, recurrent-free survival, postoperative pulmonary complication, and in-hospital mortality. Therefore, larger studies with longer follow-up periods are required to validate the findings of this study.

Conclusions

In conclusion, our study suggests that high PM 2.5 concentration is associated with increased long-term mortality in resectable NSCLC patients and may also affect in-hospital mortality. Further investigations with larger sample sizes and longer follow-up periods are needed to confirm these findings.

Declarations

Acknowledgements

This study was partially supported by Chiang Mai University, Chiang Mai, Thailand.

Author contributions

A.T. designed study, checked quality of collected data and quality assurance, performed the statistical analyses, evaluated the results, and revised the manuscript. B.K., T.W., N.N., and P.W. collected the data and contributed substantially to data preparation and first draft of manuscript. P.P., B.K., T.W., N.N., P.W., S.S., S.S., and B.C. participated in the conception and design of the study. S.S., S.S., and B.C. revised the manuscript for important intellectual content. All authors have read and approved the final manuscript.

Data Availability

All data are fully available without restriction. All relevant data are available upon request from Effect of PM2.5 on Mortality, Tumor Recurrence, and Postoperative Complications in Resectable Non-Small Cell Lung Carcinoma: A Retrospective Cohort Study should be sent to apichat.t@cmu.ac.th and are subject to approval by the Faculty of Medicine, Chiang Mai University Ethics Committee.

Fundings

The author(s) received no specific funding for this work.

Conflict of interest

The authors have no conflicts of interest to declare.

References

1. Poirier, A. E., Grundy, A., Khandwala, F., Friedenreich, C. M. & Brenner, D. R. Cancer incidence attributable to air pollution in Alberta in 2012. *CMAJ Open* **5**, E524-E528, doi:10.9778/cmajo.20160040 (2017).
2. Siegel, R. L., Miller, K. D. & Jemal, A. Cancer statistics, 2020. *CA Cancer J Clin* **70**, 7-30, doi:10.3322/caac.21590 (2020).
3. Greenpeace's City Rankings for PM2.5 in Thailand. <https://greenpeace.or.th/s/right-to-clean-air/PM2.5CityRankingsREV.pdf>.
4. *WHO Air Quality Guidelines*, <https://www.c40knowledgehub.org/s/article/WHO-Air-Quality-Guidelines?language=en_US> (
5. Li, R., Zhou, R. & Zhang, J. Function of PM2.5 in the pathogenesis of lung cancer and chronic airway inflammatory diseases. *Oncol Lett* **15**, 7506-7514, doi:10.3892/ol.2018.8355 (2018).
6. Pongpiachan, S. *et al.* Chemical characterisation of organic functional group compositions in PM2.5 collected at nine administrative provinces in northern Thailand during the Haze Episode in 2013. *Asian Pac J Cancer Prev* **14**, 3653-3661, doi:10.7314/apjcp.2013.14.6.3653 (2013).
7. Wu, C. F. *et al.* Recurrence Risk Factors Analysis for Stage I Non-small Cell Lung Cancer. *Medicine (Baltimore)* **94**, e1337, doi:10.1097/MD.0000000000001337 (2015).
8. Nakada, T. *et al.* Risk factors and cancer recurrence associated with postoperative complications after thoracoscopic lobectomy for clinical stage I non-small cell lung cancer. *Thorac Cancer* **10**, 1945-1952, doi:10.1111/1759-7714.13173 (2019).
9. West, S. C. A. a. J. J. The Global Burden of Air Pollution on Mortality: Anenberg et al. Respond. *Environ Health Perspect* **119**, 158-159, doi:10.1289/ehp.1003276R (2011).
10. Shrive, F. M., Stuart, H., Quan, H. & Ghali, W. A. Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. *BMC Med Res Methodol* **6**, 57, doi:10.1186/1471-2288-6-57 (2006).
11. Pun, V. C., Kazemiparkouhi, F., Manjourides, J. & Suh, H. H. Long-Term PM2.5 Exposure and Respiratory, Cancer, and Cardiovascular Mortality in Older US Adults. *Am J Epidemiol* **186**, 961-969, doi:10.1093/aje/kwx166 (2017).
12. Chao, X., Yi, L., Lan, L. L., Wei, H. Y. & Wei, D. Long-term PM(2.5) exposure increases the risk of non-small cell lung cancer (NSCLC) progression by enhancing interleukin-17a (IL-17a)-regulated proliferation and metastasis. *Aging (Albany NY)* **12**, 11579-11602, doi:10.18632/aging.103319 (2020).
13. Yang, L. *et al.* The PM(2.5) concentration reduction improves survival rate of lung cancer in Beijing. *Sci Total Environ* **858**, 159857, doi:10.1016/j.scitotenv.2022.159857 (2023).
14. Wen, J., Chuai, X., Gao, R. & Pang, B. Regional interaction of lung cancer incidence influenced by PM(2.5) in China. *Sci Total Environ* **803**, 149979, doi:10.1016/j.scitotenv.2021.149979 (2022).

15. Liu, Y. *et al.* Short-term association of PM 2.5 /PM 10 on lung cancer mortality in Wuhai city, China (2015-2019): a time series analysis. *Eur J Cancer Prev* **31**, 530-539, doi:10.1097/CEJ.0000000000000764 (2022).
16. Chen, Z. *et al.* Fine Particulate Matter (PM(2.5)) Promoted the Invasion of Lung Cancer Cells via an ARNT2/PP2A/STAT3/MMP2 Pathway. *J Biomed Nanotechnol* **14**, 2172-2184, doi:10.1166/jbn.2018.2645 (2018).
17. Liu, C. *et al.* The effect of ambient PM(2.5) exposure on survival of lung cancer patients after lobectomy. *Environ Health* **22**, 23, doi:10.1186/s12940-023-00976-x (2023).

Figures

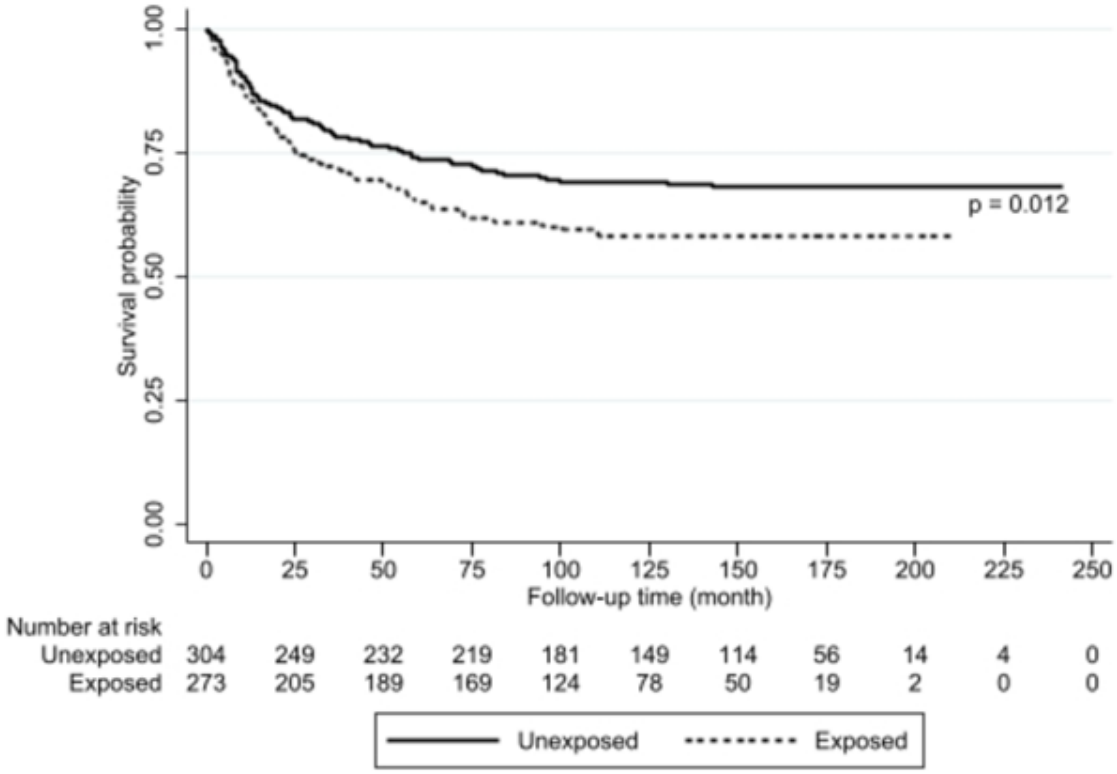

Figure 1

Kaplan-Meier curve demonstrated long-term survival comparing between two groups.

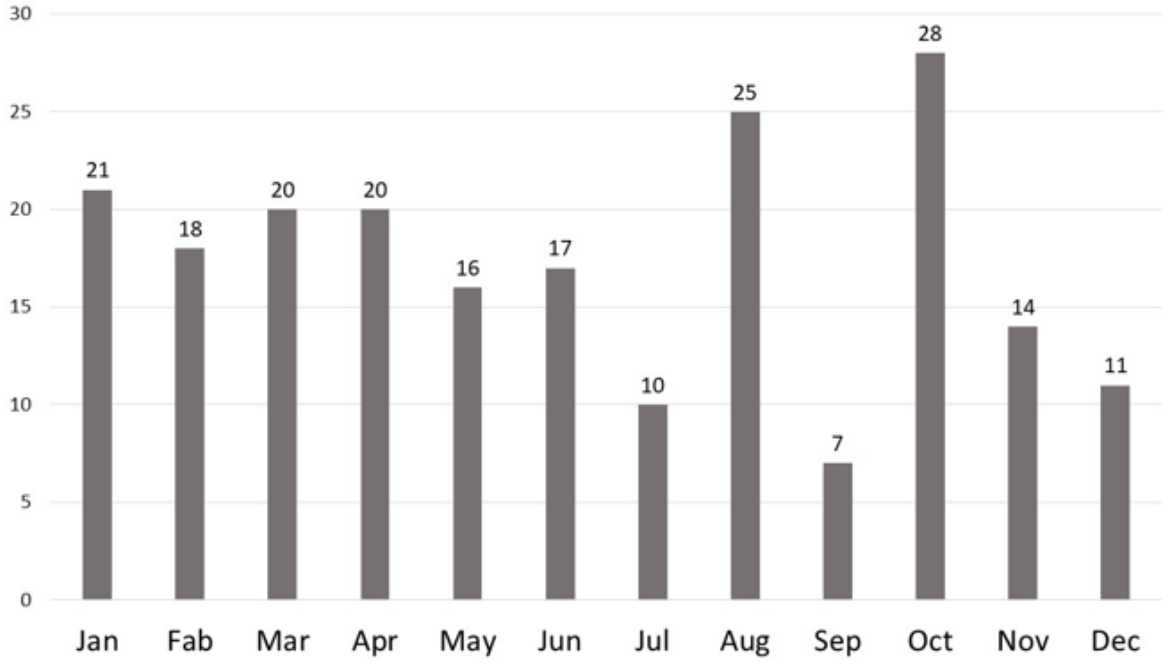

Figure 2

demonstrate number of dead patients in each month of the year.