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RESEARCH ARTICLE

The effect of $PM_{2.5}$ exposure on the mortality of patients with hepatocellular carcinoma in Tianjin, China

Hao Cui[1,2,3] · Ye Qi[1,3,4,5,6] · Chunyue Guo[1,3] · Naijun Tang[4,5,6]

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Abstract

Several studies have shown the effects of $PM_{2.5}$ exposure on respiratory and cardiovascular systems. However, there is no cohort study evidence of adverse effects of $PM_{2.5}$ exposure on survival in patients with hepatocellular carcinoma (HCC) in China. This study is aimed at evaluating this association. This cohort study included 1440 HCC patients treated at the Third Central Clinical College of Tianjin Medical University from September 2013 to December 2018. We collected patient information, including demographic data, medical history, lifestyle characteristics, and disease characteristics. Based on $PM_{2.5}$ concentrations measured at monitoring stations, the inverse distance weighted (IDW) method was used to assess the individuals' exposure during their survival period. Survival status was analysed by the Kaplan–Meier method. Restricted cubic splines and Cox proportional hazards models were used to estimate the relationship between $PM_{2.5}$ and mortality, and potential confounders were adjusted for. The mortality rate of HCC patients exposed to $PM_{2.5} \geq 58.56$ μg/m^3 was significantly higher than that of HCC patients living in environments with $PM_{2.5} < 58.56$ μg/m^3 (79.0% *vs* 50.7%, $P < 0.001$). The restricted cubic spline model showed a linear relationship between the $PM_{2.5}$ concentration and mortality risk (P overall-association < 0.0001 and P nonlinear-association $= 0.3568$). Cox regression analysis showed that after adjusting for confounding factors, for every 10-μg/m^3 increase in atmospheric $PM_{2.5}$, the risk of death for HCC patients increased by 44% [hazard ratio (HR) = 1.44, 95% confidence interval (CI) 1.34, 1.56; $P < 0.001$]. Compared with patients exposed to $PM_{2.5}$ <58.56 μg/m^3, those exposed to $PM_{2.5} \geq 58.56$ μg/m^3 had a 1.55-fold increased risk of death. Stratified analysis results showed that the effects of $PM_{2.5}$ on HCC mortality were more significant in patients aged ≥60 years or patients living in central urban areas. We found that exposure to elevated $PM_{2.5}$ after HCC diagnosis may affect survival, with a higher concentration corresponding to a greater effect.

Keywords $PM_{2.5}$ · Air pollution · Hepatocellular carcinoma · Particulate matter · Cohort · Mortality

Introduction

In recent years, the potential health risks of air pollution have become a research hotspot. Many studies have shown that air pollution is closely related to various adverse health

Hao Cui and Ye Qi contributed equally.

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✉ Naijun Tang
tangnaijun@tmu.edu.cn

[1] The Third Central Clinical College of Tianjin Medical University, 83 Jintang Road, Hedong District, Tianjin 300170, China

[2] Department of Hepatology and Gastroenterology, The Third Central Hospital of Tianjin, 83 Jintang Road, Hedong District, Tianjin 300170, China

[3] Tianjin Institute of Hepatobiliary Disease, Tianjin 300170, China

[4] Department of Occupational and Environmental Health, School of Public Health, Tianjin Medical University, Tianjin 300070, China

[5] Tianjin Key Laboratory of Environment, Nutrition, and Public Health, Tianjin Medical University, No. 22 Meteorological Station Road, Heping District, Tianjin 300070, China

[6] Center for International Collaborative Research on Environment, Nutrition and Public Health, Tianjin 300070, China

outcomes, such as respiratory, cardiovascular, and cerebrovascular diseases (Liu et al. 2019; Strak et al. 2021; Yin et al. 2020). Particulate matter with a diameter of 2.5 μm or less ($PM_{2.5}$), also known as fine particulate matter, is the main component of air pollution. It can be suspended in the air for long periods of time and can contain or adsorb heavy metals, polycyclic aromatic hydrocarbons, toxic gases, bacterial viruses, and other harmful substances (Luo et al. 2022). The International Agency for Research on Cancer (IARC) listed particulate matter (PM) in air pollution as a Class I carcinogen, mainly based on evidence of a positive correlation between PM and lung cancer in epidemiological and experimental studies; however, few studies have explored the effects of PM on other malignant tumours that threaten human health (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans 2016).

Liver cancer has become a growing concern worldwide. According to the 2020 IARC Global Cancer Statistics, primary liver cancer was the sixth most commonly diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 960,000 new cases and 830,000 deaths (Sung et al. 2021). Hepatocellular carcinoma (HCC) is the most common histological type of primary liver cancer, accounting for 75% to 85% of primary liver cancer cases (Harris et al. 2019; Rumgay et al. 2022). Prevention of HCC is crucial because of the low 5-year survival rate (Sun et al. 2021; Villanueva 2019). Therefore, identifying risk factors that affect the survival of HCC patients and implementing effective prevention and control measures are very important. Recent studies have investigated the health effects of exposure to $PM_{2.5}$ on cancer mortality, especially HCC. A study from Wong CM et al. confirmed that the risk of death from upper gastrointestinal, liver, and other digestive system cancers is associated with long-term $PM_{2.5}$ exposure in the elderly population in Hong Kong, China (Wong et al. 2016). Lee et al. revealed the relationship between HCC-related mortality and $PM_{2.5}$; that is, the risk of HCC death is higher with exposure to higher environmental concentrations of $PM_{2.5}$ (>36 μg/m^3) (Lee et al. 2019). In addition, every 10-μg/m^3 increase in $PM_{2.5}$ is associated with an OR=1.292 and 95% confidence interval (CI) of 1.030 and 1.598. In a US study, Deng et al. found that exposure to high concentrations of $PM_{2.5}$ (≥ 30 μg/m^3) after HCC diagnosis may shorten survival time, with a higher concentration corresponding to a greater effect (Deng et al. 2017). $PM_{2.5}$ has also been reported to induce the metastasis of SMMC-7721 and HuH-7 liver cancer cells (Gores 2014), and tumour metastasis is considered one of the important causes of liver cancer death.

Although the pathogenic mechanisms of $PM_{2.5}$ are unknown, due to the wide range of sources and complex components of $PM_{2.5}$, its pathogenic mechanism may be to induce a series of reactions, such as liver oxidative damage, inflammatory response, immune disorder, and genotoxicity, and to promote the invasion and migration of HCC cells (Kim et al. 2014; Schneider et al. 2022; Zhang et al. 2017; Zheng et al. 2015).

With rapid industrial development and increases in energy consumption, air pollution, especially $PM_{2.5}$ pollution, has become a serious environmental problem in China. In addition, China is an endemic area for liver disease and liver cancer. Long-term exposure to air pollution particles is a well-known risk factor for cardiopulmonary disease and lung cancer death. However, few studies have reported the effects of $PM_{2.5}$ on cancer mortality, except for lung cancer mortality, and studies focusing on the long-term health effects of $PM_{2.5}$ on HCC are especially limited. Therefore, this study enrolled patients with liver cancer from a liver disease hospital in Tianjin as the research subjects and explored the long-term impact of environmental $PM_{2.5}$ exposure on the mortality of this sensitive population.

Methods

Enrolment of the research subjects

A total of 1987 patients with primary HCC (International Classification of Diseases Oncology Special Edition (ICD-O-3), HCC: code C22.0 and morphology codes 8170–8175) treated at the Third Central Clinical College of Tianjin Medical University from September 2013 to December 2018 were identified. We excluded HCC patients under the age of 18, those with liver transplantation, those with incomplete clinical information, those without a residential address, those not living in Tianjin, those with other malignant tumours, those who died within one month, and those reject to follow-up. Finally, a total of 1440 eligible HCC patients were included in the analysis. Patients were divided into two groups using the median of the annual average ambient $PM_{2.5}$ concentration as the cut-off point: the $PM_{2.5}$ < 58.56 μg/m^3 group (n = 720) or $PM_{2.5}$ ≥ 58.56 μg/m^3 group (n = 720). The patient inclusion and exclusion criteria are detailed in Fig. 1.

Data collection

Electronic medical record systems were reviewed to collect information including sex, age, ethnicity, marital status, occupation, smoking, drinking, disease aetiology, diabetes, hypertension, liver function stage (Child-Turcotte-Pugh, CTP), treatment times, liver function indexes (albumin, alanine aminotransferase, aspartate transaminase, total bilirubin, and international normalised ratio), initial treatment method, tumour number, tumour diameter, Barcelona Clinic Liver Cancer (BCLC) staging, urban area of

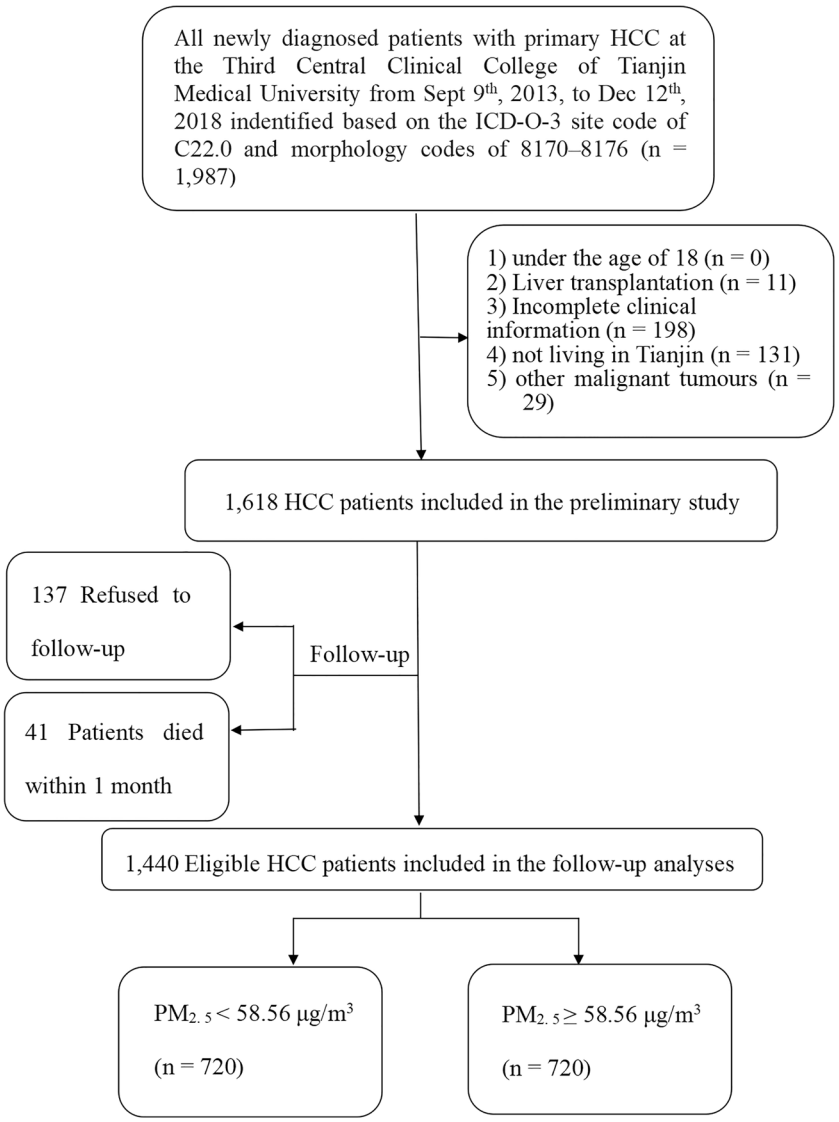

Fig. 1 Flowchart of the study population with inclusion and exclusion criteria

residence, $PM_{2.5}$ concentration at the place of residence, vascular invasion, date of hospitalisation, and last follow-up or date of death.

Related diagnostic criteria

HCC was clinically diagnosed based on alpha-fetoprotein measurement, imaging evidence such as ultrasonography, enhanced three-dimensional dynamic computed tomography, magnetic resonance imaging, angiography, and/or documented histopathology (Shiina et al. 2012).

Liver function staging

Liver function grading standards were based on the CTP grading method (Pugh et al. 1973).

BCLC staging

HCC patients were staged according to the Barcelona Liver Cancer Clinical Staging Criteria (Llovet et al. 1999).

Assessment of individual exposure to atmospheric $PM_{2.5}$

The daily concentration of $PM_{2.5}$ was collected from the historical monitoring data of Tianjin ambient air quality monitoring stations. We collected the daily average $PM_{2.5}$ concentration data from monitoring stations from 2013 to 2021 and calculated the annual average concentration for each year. The longitude and latitude coordinates of patients' home addresses and those of monitoring stations were queried in batches from Baidu Maps, and the annual mean $PM_{2.5}$ concentration for each patient during the survival period

was estimated using the inverse distance weighting (IDW) method. Individual exposure concentrations in the survival period were calculated as the annual mean $PM_{2.5}$ from diagnosis to death or to the end of the study.

Follow-up

Patients were followed up once every 2–6 months in the outpatient clinic, and a complete medical history and physical examination were performed at each follow-up visit. The follow-up started from the diagnosis of HCC, the endpoint was death or the last follow-up outcome, and overall survival was recorded. The results for deceased HCC patients were confirmed from hospital electronic databases or by telephone. The last follow-up date was December 31, 2021.

Statistical analyses

To compare baseline characteristics between groups, normally distributed continuous variables are expressed as the mean and standard deviation and were analysed using the *t*-test; nonnormally distributed variables are expressed as the median (interquartile range (IQR)), and the Mann–Whitney *U* test was used for group comparisons. Categorical variables are expressed as frequencies and percentages in brackets, and chi-square tests were used for comparisons between groups. Survival data were analysed by the Kaplan–Meier method, and the log-rank test was used for significance testing. HCC death was the dependent variable, and $PM_{2.5}$ concentration was the independent variable after adjusting for basic information (age, sex, and ethnicity), medical history (diabetes, hypertension), lifestyle characteristics (smoking, drinking, occupation, marriage, and urban centre of residence) and disease factors (liver function indexes, disease aetiology, CTP, treatment times, initial treatment method, tumour number, tumour diameter, BCLC staging, and vascular invasion). A multivariate Cox regression proportional risk model was used to analyse the association between $PM_{2.5}$ and mortality risk in HCC patients. The dose–response relationship between atmospheric $PM_{2.5}$ and the risk of HCC patient mortality was assessed using restricted cubic splines. Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc.) and R version 4.0.2 (http://www.R-project.org). A P value < 0.05 was considered statistically significant.

Results

Distribution of the baseline characteristics of HCC patients

The baseline characteristics of the enrolled patients are shown in Table 1. A total of 720 patients were exposed to environments with $PM_{2.5} < 58.56$ μg/m^3, while the other 720 patients were exposed to environments with $PM_{2.5} \geq 58.56$ μg/m^3. The group exposed to $PM_{2.5} < 58.56$ μg/m^3 had higher albumin levels and higher proportions of patients with CTP grade A, radiofrequency ablation at the first treatment, and BCLC grade A. In contrast, the group exposed to $PM_{2.5} \geq 58.56$ μg/m^3 had higher levels of aspartate transaminase and total bilirubin and higher proportions of patients with CTP grades B and C, multiple tumours, central urban area residence, vascular invasion, and BCLC grades C and D ($P < 0.01$). In addition, the average tumour diameter and mortality rate of HCC patients exposed to $PM_{2.5} \geq 58.56$ μg/m^3 were significantly greater than those of HCC patients exposed to $PM_{2.5} < 58.56$ μg/m^3 ($P < 0.001$).

Survival analysis

The median follow-up time for the HCC patients was 27 (8–50) months. The median survival time was 57 months in the $PM_{2.5}$ <58.56 μg/m^3 group and 23 months in the $PM_{2.5} \geq 58.56$ μg/m^3 group. Kaplan–Meier survival analysis showed that the cumulative survival rate of patients exposed to $PM_{2.5} \geq 58.56$ μg/m^3 was significantly lower than that of patients exposed to $PM_{2.5}$ <5 8.56 μg/m^3 (log-rank test, $P < 0.0001$, Fig. 2).

Association between $PM_{2.5}$ exposure and HCC mortality risk

Cox analysis showed that after adjusting for confounding factors, compared with patients exposed to $PM_{2.5} <$ 58.56 μg/m^3, those exposed to $PM_{2.5} \geq$58.56 μg/m^3 had an increased risk of death [hazard ratio (HR) = 1.55, 95% CI: 1.38, 1.79]. In addition, for every 10-μg/m^3 increase in environmental $PM_{2.5}$ exposure, the risk of liver cancer death increased by 44% [adjusted HR = 1.44, 95% CI: 1.34, 1.56; $P < 0.001$]. The details are listed in Table 2.

In Fig. 3, we analysed the relationship between $PM_{2.5}$ concentration and the risk of death using restricted cubic spline curves (RCS). The RCS analysis indicated that there was a linear dose-response association between $PM_{2.5}$ concentration and the risk of death with 3 knots (10th, 50th, and 90th) after multivariable adjustment (P for overall association test < 0.0001 and P for nonlinear association test = 0.3568). Akaike information criterion(AIC) was the minimum (AIC = 10,836.295). After adjusting for confounding factors, the risk of all-cause death increased with increasing $PM_{2.5}$ concentration. When $PM_{2.5}$ increased to > 58.57 μg/m^3 [$PM_{2.5}$ reference ratio: $PM_{2.5} = 58.57$ μg/m^3, HR = 1.00], the curve became steeper.

Table 1 Comparison of baseline characteristics of patients with HCC

Characteristic	$PM_{2.5}$ < 58.56 μg/m^3 (n = 720)	$PM_{2.5}$ ≥ 58.56 μg/m^3 (n = 720)	P value
Age (y)	60.69 ± 9.00	60.45 ± 10.24	0.637
Male sex, *n* (%)	541 (75.1)	525 (72.9)	0.336
Han nationality, *n* (%)	695 (96.5)	697 (96.8)	0.769
Marital status, *n* (%)			0.198
Married	631 (87.6)	612 (85.0)	
Unmarried	6 (0.8)	12 (1.7)	
Widowed or divorced	83 (11.5)	96 (13.3)	
Occupation, *n* (%)			0.307
Office worker/service worker/self-employed	468 (65.0)	485 (67.4)	
Manual worker	210 (29.2)	205 (28.5)	
Unemployed	42 (5.8)	30 (4.2)	
Smoking, *n* (%)	397 (55.1)	365 (50.7)	0.091
Drinking, *n* (%)	358 (49.7)	333 (46.3)	0.187
Disease aetiology, *n* (%)			0.043
HBV	468 (65.0)	465 (65.0)	
HCV	73 (10.1)	72 (10.0)	
AC	107 (14.9)	88 (12.2)	
PBC	11 (1.5)	11 (1.5)	
AIH	14 (1.9)	6 (0.8)	
Others[a]	47 (6.5)	75 (10.4)	
Diabetes, *n* (%)	182 (25.3)	166 (23.1)	0.325
Hypertension, *n* (%)	190 (26.4)	172 (23.9)	0.274
Treatment times ≥2, *n* (%)	176 (24.4)	188 (26.1)	0.467
ALT (U/L)	31 (22,53)	34 (22,55)	0.553
AST (U/L)	41 (28,72)	48 (29,83)	0.013
TBiL (μmol/L)	20 (14,32)	23 (15,38)	0.001
Albumin (g/L)	36.75 ± 6.98	35.06 ± 6.41	<0.001
INR	1.27 ± 0.37	1.29 ± 0.32	0.458
CTP (%)			<0.001
A	456 (63.3)	346 (48.1)	
B	209 (29.0)	278 (38.6)	
C	55 (7.6)	96 (13.3)	
Tumour diameter (mm)	37(24,50)	38 (27.62)	<0.001
Initial treatment method, *n* (%)			<0.001
Supportive	141 (19.6)	161 (22.4)	
Transarterial chemoembolization	339 (47.1)	341 (47.4)	
Radiofrequency ablation	201 (27.9)	114 (15.8)	
Others[b]	39 (5.4)	104 (14.4)	
Tumour number ≥2, *n* (%)	371 (51.5)	454 (63.1)	<0.001
BCLC, *n* (%)			<0.001
A	422 (58.6)	281 (39.0)	
B	145 (20.1)	178 (24.7)	
C	103 (14.3)	175 (24.3)	
D	50 (6.9)	86 (11.9)	
Vascular invasion, *n* (%)	109 (15.1)	188 (26.1)	<0.001
Urban area of residence, *n* (%)	308 (42.8)	380 (52.8)	<0.001
Mortality, *n* (%)	365 (50.7)	569 (79.0)	<0.001

ALT alanine aminotransferase, *AST* aspartate transaminase, *TBiL* total bilirubin, *INR* international normalised ratio

[a]Acute hepatitis of unknown cause, drug-induced liver injury, nonalcoholic steatohepatitis, acute icteric hepatitis, and schistosomiasis

[b]Resection, biological therapy, chemoradiotherapy, immunotherapy, targeted therapy, and Chinese medicine

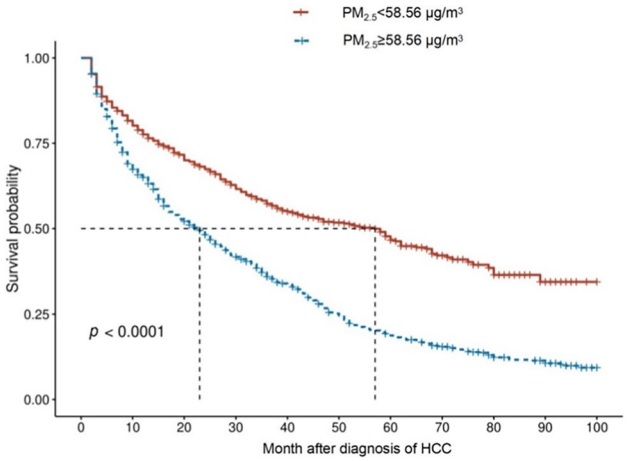

Fig. 2 Kaplan–Meier survival curve analysis

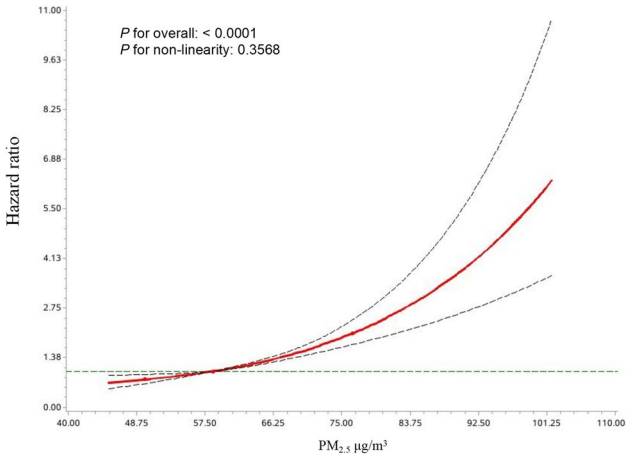

Fig. 3 Restricted cubic spline association of atmospheric $PM_{2.5}$ exposure with HCC mortality risk. Association adjusted for basic information (age, sex, and ethnicity), medical history (diabetes, hypertension), lifestyle characteristics (smoking, drinking, marital status, occupation, and urban area of residence), and disease-related factors (liver function indexes, disease aetiology, CTP, treatment times, initial treatment, tumour number, tumour diameter, BCLC, and vascular invasion)

Table 2 Cox proportional hazards regression model analysis of the associations between $PM_{2.5}$ exposure and mortality in HCC

Type	Hazard ratio[a] (95% confidence interval)	*P* value
Categorized $PM_{2.5}$ (μg/m^3)		
< 58.56	Ref	
≥ 58.56	1.55 (1.38, 1.79)	< 0.001
Continuous $PM_{2.5}$[b]	1.44 (1.34, 1.56)	< 0.001

[a]Adjusted for age, sex, ethnicity, marital status, occupation, smoking, drinking, disease aetiology, diabetes, hypertension, liver function indexes, CTP, treatment times, initial treatment, tumour number, tumour diameter, BCLC, urban area of residence, and vascular invasion

[b]Hazard ratios for mortality per 10.0-μg/m^3 increase in $PM_{2.5}$

Stratified analysis of $PM_{2.5}$ exposure and HCC death

As shown in Fig. 4, the results of the multivariate stratified analysis confirmed the association of exposure to high-level $PM_{2.5}$ with the risk of HCC death, including in patients aged 60 years or older (HR = 2.01, 95% CI: 1.62, 2.50) or younger than 60 years (HR = 1.26, 95% CI: 1.01, 1.56) and in those who living in central urban areas (HR = 1.83, 95% CI: 1.47, 2.28) or not living in central urban areas (HR = 1.45, 95% CI: 1.18, 1.78). The factors of age, smoking, and living in central urban areas showed significant differences between patient subgroups.

Sensitivity analysis

To further verify the relationship between $PM_{2.5}$ and HCC death, patients with HCC complications (gastrointestinal bleeding, infection, hepatic coma, hepatic encephalopathy, and ascites) were excluded for sensitivity analysis to reduce the impact on the relationship. After screening out these diseases, 1213 HCC patients were included in the analysis. After adjusting for demographic data, medical history, lifestyle characteristics, and disease characteristics, the risk of death increased by 1.35 times for every increase in $PM_{2.5}$ concentration of 10 μg/m^3 (95% CI: 1.08, 1.68). The analysis results were consistent with the above studies, and the association between the two was significantly different ($P = 0.008$).

Discussion

Few studies in the literature report the health effects of $PM_{2.5}$ on HCC patients, especially in relation to the hypothesis that $PM_{2.5}$ exposure adversely affects survival after HCC diagnosis. Based on a large patient population ($n = 1440$), this study showed that $PM_{2.5}$ exposure is associated with mortality after HCC diagnosis and that there is a linear relationship between the two. Higher $PM_{2.5}$ levels led to greater adverse effects; that is, for every 10-μg/m^3 increase in $PM_{2.5}$, the possibility of death increased by 44% [HR = 1.44, 95% CI: 1.34, 1.56; $P < 0.001$]. When exposed to a $PM_{2.5}$ concentration ≥ 58.56 μg/m^3, the mortality risk of HCC patients was 1.55 times that of HCC patients exposed to a $PM_{2.5}$ concentration < 58.56 μg/m^3. To date, this is the first clinical study in China to investigate the relationship between environmental $PM_{2.5}$ exposure and the risk of liver cancer death.

$PM_{2.5}$ induces liver oxidative damage, inflammation, and genotoxicity and promotes HCC invasion and migration (Deng et al. 2017; Kim et al. 2014; Zhang et al. 2017; Zheng

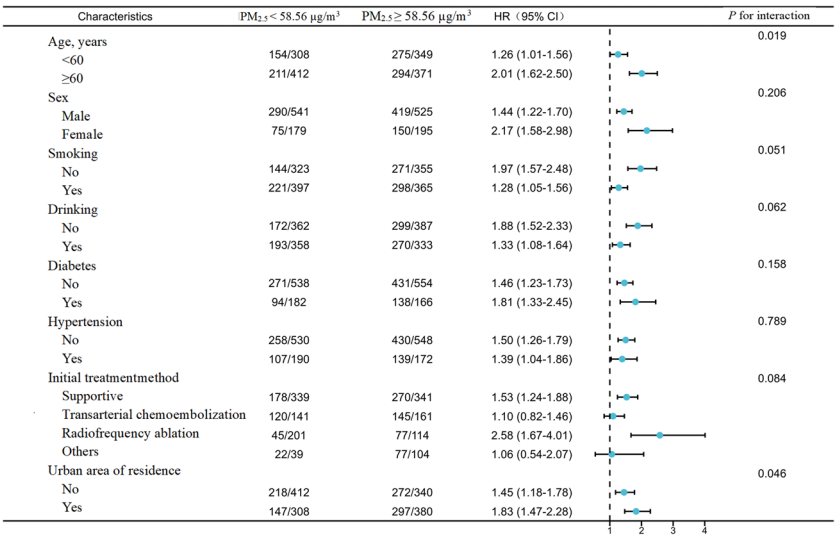

Fig. 4 Multivariate stratified analyses of the association between $PM_{2.5}$ and HCC mortality. Adjusted for basic information (age, sex, and ethnicity), medical history (diabetes, hypertension), lifestyle characteristics (smoking, drinking, marital status, occupation, and urban area of residence), disease-related factors (liver function indexes, disease aetiology, CTP, treatment times, initial treatment, tumour number, tumour diameter, BCLC, and vascular invasion)

et al. 2015). Studies have shown that $PM_{2.5}$ can stimulate cells to produce a large amount of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Based on the body's antioxidant mechanisms, increased ROS generation may lead to oxidative stress, which subsequently induces adverse effects such as DNA damage, lipid peroxidation, and protein modification (Schneider et al. 2022; Thangavel et al. 2022; Wang et al. 2016). Another theory is that $PM_{2.5}$ induces inflammation, activates the release of pro-inflammatory factors and chemokines, promotes angiogenesis and malignant cell proliferation and metastasis, and induces the epithelial-mesenchymal transition (EMT) process (Zhang and Li 2019; Zhang et al. 2021).

Deng H et al. showed that exposure to elevated $PM_{2.5}$ after HCC diagnosis shortened the survival time of patients, with a higher concentration producing a greater effect (Deng et al. 2017). This study provides evidence supporting potential adverse health effects caused by high pollution levels. Similarly, a linear relationship between HRs and $PM_{2.5}$ was observed in our study, and the risk of death increased with the concentration of pollutants. Although this study is consistent with the analysis by Deng et al., our study differs from the other in that we adjusted for confounding individual disease-related factors to confirm this finding.

We adjusted for age, sex, race, and daily living conditions at the individual level, which are known or suspected to be HCC risk factors, including heavy alcohol consumption, smoking, hypertension, diabetes, occupation, marital status, and place of residence. In our analysis, we also adjusted for individual disease factors, which may be major risk factors for HCC. In the study by Lee et al., 1003 HCC patients treated at Chang Gung Memorial Hospital from 2000 to 2009 were included, and Cox regression analysis of the risk of death showed that $PM_{2.5}$ ($\geq$36 μg/m^3) (P= 0.004), Child–Pugh score ($P < 0.001$), macrovascular invasion ($P < 0.001$), tumour number ($P< 0.001$), and tumour size ($P < 0.001$) were key risk factors for death (Lee et al. 2019). This observation has also been further verified in our study. After adjusting for the above indicators, exposure to a polluted environment with high-concentration $PM_{2.5}$ ($\geq$ 58.56 μg/m^3) increased the risk of death for HCC patients [HR = 1.55, 95% CI: 1.38, 1.79; $P < 0.001$]. The results of this study are basically consistent with the conclusions of related studies, but the critical value for the $PM_{2.5}$ concentration differed, which may be related to differences in the main sources of atmospheric $PM_{2.5}$, exposure levels, individual exposure estimation methods, and the selection of research objects.

Identifying susceptible populations is a key node in the prevention and control of adverse health effects caused by air pollution. This study found that $PM_{2.5}$ has a greater impact on patients aged $\geq$ 60 years and those living in central urban areas. The possible reason is that with ageing and the gradual weakening of regulatory functions, the human body is more prone to adverse outcomes. In addition, the population density of central urban areas is higher, and higher population density is associated with an increased risk of liver cancer death. VoPham et al. concluded that $PM_{2.5}$ exposure in high-population-density areas was positively associated with HCC risk [adjusted incidence rate ratio (IRR) = 1.32, 95% CI: 1.11, 1.58] (VoPham et al. 2018). Notably, the $PM_{2.5}$concentration is higher in areas with high population densities, which is related to the sources of $PM_{2.5}$, including motor vehicle exhaust emissions and other anthropogenic factors (power generation, fossil fuel combustion, etc.) (Wu et al. 2020). Overpopulated areas are characterised by high traffic intensity, reduced traffic speeds, and increased vehicle emissions (Su et al. 2021).

This study has certain limitations. First, the research subjects were from only one medical institution, and the exposure level did not cover a wide range. Second, we were unable to collect sufficient confounding factors, such as BMI and

socioeconomic status, which may have impacted the analysis of the relationship between $PM_{2.5}$ and death. Finally, the level of pollutant exposure was assessed only based on data from environmental monitoring stations, and factors affecting $PM_{2.5}$ exposure at the individual level, such as time outdoors, were lacking.

In summary, this study suggests that exposure to atmospheric $PM_{2.5}$ can increase the risk of death in HCC patients. Adding to the previously reported negative impact of air pollution on common diseases such as cardiac, brain, and respiratory diseases, we provide relevant evidence for the adverse effects of air pollution on the survival of liver cancer patients and reveal clues for exploring the relationship between liver cancer survival and air pollution.

Author contribution Conceptualization, writing—original draft, and resources were performed by Hao Cui. Conceptualization and writing—original draft—were performed by Ye Qi. Visualisation and formal analysis were performed by Chunyue Guo. Writing-review and editing and supervision were performed by Naijun Tang.

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Availability of data and materials All the data used to support the findings of this study are available on reasonable request from the corresponding author.

Declarations

Ethics approval This retrospective cohort study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of the Third Central Clinical College of Tianjin Medical University.

Consent to participate We obtained participants' informed consent before we began data collection.

Consent for publication The authors give their consent to publish all submitted material.

Conflict of interest The authors declare no competing interests.

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