Original Article

Epidemiology and trend analysis on malignant mesothelioma in China

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Abstract

Objective: Population-based cancer registration data were used to analyze the epidemiology and trend of malignant mesothelioma in China, and the result would provide basic data for its prevention and control.

Methods: Malignant mesothelioma data in 2013 were retrieved from the database of National Cancer Registry. Malignant mesothelioma incidence and mortality were estimated using age-specific rate by urban/rural and gender according to the national population in 2013. Malignant mesothelioma data from 22 cancer registries were used for trend analysis during 2000–2013.

Results: It is estimated that there were 2,041 new malignant mesothelioma cases and 1,659 malignant mesothelioma deaths occurred in 2013. The crude incidence rate in China were 1.50/10^6 (males 1.67/10^6, females 1.32/10^6), age-standardized incidence rates by Chinese standard population (ASIRC) and by world standard population (ASIRW) were 1.03/10^6 and 1.02/10^6, respectively. The crude mortality rate in China was 1.22/10^6 (males 1.67/10^6, females 1.32/10^6), age-standardized mortality rates by Chinese standard population (ASMRC) and by world standard population (ASMRW) were 0.83/10^6 and 0.81/10^6, respectively. There was an increasing trend of incidence rate for malignant mesothelioma in registration areas of China during 2000–2013 with annual percentage change (APC) of 2.5% [95% confidence interval (95% CI): 0.6%–4.5%]. After age standardization, no significant differences were observed. No matter for crude mortality rates or age-standardized mortality rates, no significant differences were observed during 2000–2013.

Conclusions: Malignant mesothelioma is the major occupational and environmental neoplasm associated with asbestos exposure. The increasing incidence trend suggests that more attention should be paid on this disease.

Keywords: Malignant mesothelioma; incidence; mortality; trend; cancer registry

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Introduction

Malignant mesothelioma, a rare cancer, is highly correlated with asbestos exposure. The latency period from exposure to disease-related risk factors and clinical symptoms were about 20–40 years (1). According to the cancer site, the disease comprises two major types, pleural and peritoneal mesothelioma. Researches identified that knowledge gaps are barriers to preventing and treating malignant mesothelioma (2). In China, few researches reported on malignant mesothelioma incidence and mortality situation. In this study, we use the most update data from National Central Cancer Registry (NCCR) to analyze the malignant mesothelioma epidemiology and its trend, and the results would help health-related staff to know more about this disease and provide basic information for policy-makers.

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Materials and methods

Data source

The NCCR is in charge of population-based cancer registry with responsibility of data collection, evaluation and publication from local cancer registries in China (3). By 1st June 2016, 347 cancer registries (126 cities and 221 counties) from 32 provinces submitted 2013 data to the NCCR. After quality control, 255 cancer registries (88 cities and 167 counties) meet the requirements. Data covered about 226,494,490 people (114,860,339 males and 111,634,151 females), accounting for about 16.65% of the national population at the end of 2013. Invasive cases of malignant mesothelioma (ICD10: C45) were extracted and analyzed from the overall cancer database.

Population data

We use the fifth and the sixth National Population Census data provided by the National Statistics Bureau of China to estimate the national population in 2013, taking into account changes in age structure, gender ratio, and the proportion of urban and rural transformation released by the National Bureau of Statistics (http://data.stats.gov.cn/). The 2013 national population was stratified by area (urban/rural), gender, and 19 age groups (0–, 1–4, 5–84 by 5 years, 85+ years). Changes in age-specific death probability were also adjusted when calculating the population. Linear changes were assumed in each age group between the fifth and sixth population censuses.

Quality control

Data submitted to the NCCR were evaluated according to "Guideline for Chinese Cancer Registration" (4) and referring to relevant data quality criterion of "Cancer Incidence in Five Continents Volume IX" by International Agency for Research on Cancer/International Association of Cancer Registries (IARC/IACR) (5). The percentage of morphological verification (MV%), the percentage of death certificate-only cases (DCO%), mortality to incidence (M/I) ratio, and the percentage of unknown basis of diagnosis (UB%) were used to evaluate the completeness, validity and reliability of cancer statistics (6,7).

Statistical analysis

Incidence and mortality, proportions, crude, age-standardized, accumulated, truncated, and age-specific incidence and mortality rates were calculated by area, gender and age groups. The number of new cases and deaths were estimated using the 5-year age-specific cancer incidence/mortality rates and the corresponding populations. The Chinese population in 2000 and Segi's world population were used to calculate age-standardized rates. The cumulative risk of developing or dying from cancer before 75 years of age (in the absence of competing causes of death) was calculated and presented as a percentage. Truncated age-standardized rate was calculated among the cases aged between 35 and 64 years old. Software including MS-Excel, IARCcrgTools 2.05 issued by IARC/IACR were used for data checking and evaluation. SAS (version 9.2; SAS Institute, Cary, NC, USA) was used to calculate incidence and mortality rates. Trend analysis were conducted using Joinpoint Regression Program 3.4.3 software (Version 3.4.3; National Cancer Institute, USA) (8). Linear model was used to calculate the crude and age-standardized rates of annual percentage change (APC) and its 95% confidential interval (95% CI).

Results

Data quality

There were 255 qualified cancer registries included in the final analysis. The data quality indicators of MV%, DCO%, M/I and UB% were 94.59%, 0.00%, 0.82 and 0.28, respectively. In urban areas, they were 95.20%, 0.00%, 0.84 and 0.44, respectively. In rural areas, they were 93.44%, 0.00%, 0.79 and 0.00, respectively (*Table 1*).

Table 1 Quality control index of malignant mesothelioma in China in 2013

Areas	Sex	M/I	MV%	DCO%	UB%
All	Both sexes	0.82	94.59	0.00	0.28
	Male	0.89	93.47	0.00	0.50
	Female	0.74	96.05	0.00	0.00
Urban areas	Both sexes	0.84	95.20	0.00	0.44
	Male	0.89	94.07	0.00	0.74
	Female	0.78	96.81	0.00	0.00
Rural areas	Both sexes	0.79	93.44	0.00	0.00
	Male	0.89	92.19	0.00	0.00
	Female	0.67	94.83	0.00	0.00

M/I, mortality to incidence ratio; MV%, the percentage of morphological verification; DCO%, the percentage of death certificate-only cases; UB%, the percentage of unknown basis of diagnosis.

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Incidence

There was an estimated of 2,041 new malignant mesothelioma cases occurred in China in 2013, accounting for 0.06% of all new cancer cases. The crude incidence, age-standardized rate of incidence by Chinese standard population (ASIRC), and age-standardized rate of incidence by world standard population (ASIRW) of breast cancer were 1.50/10^6, 1.03/10^6, and 1.02/10^6, respectively. In patients aged 0–74 years, the cumulative incidence rate was 0.01%, while for those aged 35–64 years, the truncated age-standardized rate (TASR) was 1.95/10^6 (*Table 2*).

The estimated number of new malignant mesothelioma cases in urban areas in 2013 was about 1,384, accounting for 0.07% of all new cancer cases. The crude incidence, ASIRC and ASIRW in urban areas were 1.89/10^6, 1.25/10^6 and 1.24/10^6, respectively. The cumulative incidence rate was 0.02% and the TASR was 2.27/10^6. The estimated number of new malignant mesothelioma cases in rural areas in 2013 was about 657, accounting for 0.04% of all new cancer cases. The crude incidence, ASIRC and ASIRW in rural areas were 1.04/10^6, 0.75/10^6 and 0.74/10^6, respectively. The cumulative incidence rate was 0.01% and the TASR was 1.52/10^6. The incidence rate was higher in urban than in rural areas (*Table 2*).

In 2013, the age-specific incidence of malignant mesothelioma was increased after 35 years old with fluctuated incidence rates (*Figure 1*).

Mortality

There was an estimated of 1,659 malignant mesothelioma deaths occurred in China in 2013, accounting for 0.07% of all cancer deaths. The crude mortality, age-standardized rate of mortality by Chinese standard population (ASMRC), and age-standardized rate of mortality by world standard population (ASMRW) of breast cancer were 1.22/10^6, 0.83/10^6, and 0.81/10^6, respectively. In patients aged 0–74 years, the cumulative mortality rate was 0.01%, while for those aged 35–64 years, the truncated age-standardized rate (TASR) was 1.25/10^6 (*Table 3*).

The estimated number of malignant mesothelioma deaths in urban areas in 2013 was about 1,149, accounting for 0.10% of all cancer deaths. The crude mortality, ASMRC and ASMRW in urban areas were 1.57/10^6, 1.03/10^6 and 1.00/10^6, respectively. The cumulative mortality rate was 0.01% and the TASR was 1.56/10^6. The estimated number of malignant mesothelioma deaths in rural areas in 2013 was about 510, accounting for 0.05% of all cancer deaths. The crude mortality, ASMRC and ASMRW in rural areas were 0.81/10^6, 0.58/10^6 and 0.58/10^6, respectively. The cumulative mortality rate was 0.01% and the TASR was 0.86/10^6. The mortality rate was higher in urban than in rural areas (*Table 3*).

In 2013, the age-specific mortality of malignant mesothelioma was increased after 40 years old with fluctuated mortality rates, and males had higher mortality rates than females (*Figure 2*).

Trend

Incidence trend

During 2000–2013, the incidence rate of 22 cancer registries was 2.14/10^6 in 2000 and increased to 3.14/10^6 in 2013. In males, it increased from 2.01/10^6 to 3.81//10^6, while in females, it increased from 2.28/10^6 to 2.47/10^6.

Table 2 Malignant mesothelioma incidence in China in 2013

Areas	Sex	Case No.	Crude rate (1/10^6)	Ratio (%)	ASIRC (1/10^6)	ASIRW (1/10^6)	Cumulative rate 0–74 (%)	TASR 35–64 (1/10^6)
All	Both sexes	2,041	1.50	0.06	1.03	1.02	0.01	1.95
	Male	1,163	1.67	0.06	1.18	1.19	0.01	2.24
	Female	878	1.32	0.05	0.88	0.87	0.01	1.65
Urban areas	Both sexes	1,384	1.89	0.07	1.25	1.24	0.02	2.27
	Male	819	2.19	0.07	1.50	1.49	0.02	2.72
	Female	565	1.58	0.06	1.01	1.00	0.01	1.81
Rural areas	Both sexes	657	1.04	0.04	0.75	0.74	0.01	1.52
	Male	344	1.06	0.04	0.79	0.80	0.01	1.61
	Female	313	1.02	0.05	0.72	0.70	0.01	1.42

ASIRC, age-standardized incidence rate by Chinese standard population; ASIRW, age-standardized incidence rate by world standard population; TASR, truncated age-standardized rate by world standard population.

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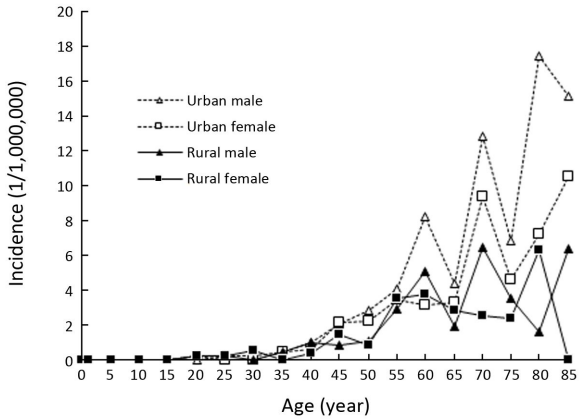

Figure 1 Malignant mesothelioma incidence in China in 2013.

After age standardization, the incidence rate was 1.72/10^6 in 2000 and decreased to 1.71/10^6. It increased from 1.71/10^6 to 2.17/10^6 for males, while decreased from 1.76/10^6 to 1.28/10^6 for females. The Joinpoint trend analysis showed that there was an increasing trend of incidence rate of malignant mesothelioma in registration areas of China during 2000–2013 with an APC of 2.5% (95% CI: 0.6%–4.5%); the same increasing trend was observed in males with an APC of 3.9% (95% CI: 1.4%–6.5%); and no significant differences were observed in females. After age standardization, no significant differences were observed in both sexes (*Table 4*, *5*).

Mortality trend

During 2000–2013, the mortality rates of 22 cancer registries increased from 1.24/10^6 in 2000 to 2.44/10^6 in 2013. It increased from 1.34/10^6 to 3.24/10^6 for males, and for females, it increased from 1.14/10^6 to 1.63/10^6. After age standardization, the mortality rate was 0.97/10^6 in 2000 and increased to 1.31/10^6. In both sexes, they showed increasing trends. It increased from 1.14/10^6 in 2000 to 1.81/10^6 in 2013 in males and 0.79/10^6 to 0.84/10^6 in females. The Joinpoint trend analysis showed that no significant differences were observed in both sexes, while an increasing trend of mortality rate was observed in males during 2003–2013 with an APC of 3.9% (95% CI: 1.2%–6.6%). In females, during 2000–2009, we also see an increasing trend with an APC of 7.6% (95% CI: 3.1%–12.4%). After age standardization, no significant differences were observed, except for females during 2000–2007 with an APC of 7.6% (95% CI: 0.3%–15.4%) (*Table 5*, *6*).

Discussion

Malignant mesothelioma is an environment and occupation-related cancer with poor survival. With the rapid development of Chinese economy, progressing industrialization may result in a series of problems which need to be concerned. Asbestos is an important industrial mineral which can lead to asbestos-related diseases. Malignant mesothelioma is one of major diseases induced by asbestos. Almost all of the asbestos consumption concentrated in developing economies. In 2010, Asian accounted for 60% of the global chrysotile consumption, compared with 30% for China (9). More attention should be attached on monitoring, diagnosis, treatment and registration of malignant mesothelioma and make data regards to its incidence and mortality accessible for researchers.

The incidence or mortality rates varied across the

Table 3 Malignant mesothelioma mortality in China in 2013

Areas	Sex	Case No.	Crude rate (1/10^6)	Ratio (%)	ASMRC (1/10^6)	ASMRW (1/10^6)	Cumulative rate 0–74 (%)	TASR 35–64 (1/10^6)
All	Both sexes	1,659	1.22	0.07	0.83	0.81	0.010	1.25
	Male	1,018	1.46	0.07	1.05	1.02	0.012	1.53
	Female	641	0.97	0.08	0.62	0.61	0.007	0.97
Urban areas	Both sexes	1,149	1.57	0.10	1.03	1.00	0.011	1.56
	Male	715	1.92	0.10	1.32	1.27	0.014	1.86
	Female	434	1.21	0.10	0.75	0.73	0.008	1.24
Rural areas	Both sexes	510	0.81	0.05	0.58	0.58	0.008	0.86
	Male	303	0.93	0.05	0.70	0.71	0.010	1.08
	Female	207	0.68	0.05	0.45	0.46	0.006	0.64

ASMRC, age-standardized mortality rate by Chinese standard population; ASMRW, age-standardized mortality rate by world standard population; TASR, truncated age-standardized rate by world standard population.

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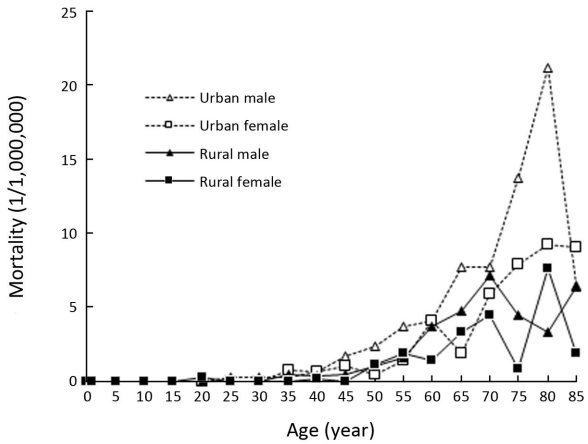

Figure 2 Malignant mesothelioma mortality in China in 2013.

regions of the world. The incidence rates were higher in some European countries (UK, the Netherlands, Malta, Belgium) and some Oceanian countries (Australia, New Zealand), Japan and countries from central Europe had relatively low incidence/mortality rates (10). According to the Surveillance, Epidemiology, and End Results (SEER) Cancer Statistics Review figures, the age-adjusted incidence rate was $0.92/10^5$ in 2014, $1.59/10^5$ in males and $0.42/10^5$ in females. And 5-year relative survival was 9.1% during 2007–2013 (11). In the USA, deaths with malignant mesothelioma were increasing from 2,479 deaths in 1999 to 2,597 in 2015 with age-adjusted death rates decreased from $1.40/10^5$ in 1999 to $1.09/10^5$ in 2015 (12). The UK has been conducting researches on malignant mesothelioma deaths since 1968. According to the latest statistics of the UK, there were 2,515 mesothelioma deaths due to past asbestos exposures in 2014 (13). During 1993–2014, the European age-standardized incidence rates in the UK increased from $5.1/10^5$ to $8.9/10^5$ in males, and from $0.7/10^5$ to $1.3/10^5$ in females (14). In Australia, the ASIRW was $0.9/10^5$ in 1982 and increased to $1.5/10^5$ in 2013, while the ASMRW was $1.5/10^5$ in 1997 and decreased to $1.3/10^5$ in 2014 (12). According to the report from Hong Kong, China, the estimated annual incidence rate was $1.0/10^6$ (15). When compared with western countries, the incidence rate in Eastern Asia is very low (16). The reasons to explain the discrepancy may be complex, such as underdiagnosis or underregistration of malignant mesothelioma, and not developing into malignant tumors for the long latency periods of the disease. Besides, genetic susceptibility, environmental exposures, occupational exposures may play as co-factors in the development of malignant mesothelioma. The incidence and mortality rates in China were relatively low. There is a big concern that most Chinese physicians do not have experience to diagnose the rare disease. Malignant mesothelioma, especially peritoneal malignant mesothelioma, is often misdiagnosed in eastern China (17), and more and more professional training on diagnosis procedure of the disease

Table 4 Malignant mesothelioma incidence in 22 cancer registries during 2000–2013 ($1/10^6$)

Period	Both sexes		Male		Female	
	CR	ASR	CR	ASR	CR	ASR
2000	2.14	1.72	2.01	1.71	2.28	1.76
2001	1.99	1.62	1.91	1.69	2.06	1.55
2002	2.49	1.96	2.61	2.19	2.36	1.82
2003	2.66	1.97	2.50	1.96	2.81	2.01
2004	2.68	1.93	3.24	2.43	2.11	1.51
2005	2.75	1.85	3.10	2.17	2.39	1.58
2006	2.90	2.01	3.00	2.20	2.80	1.83
2007	2.57	1.75	2.92	2.06	2.21	1.47
2008	2.66	1.79	2.72	1.89	2.59	1.70
2009	2.95	1.85	3.41	2.17	2.49	1.55
2010	3.20	1.93	3.68	2.23	2.73	1.67
2011	2.11	1.18	2.23	1.20	1.98	1.19
2012	3.49	1.97	3.98	2.27	2.99	1.69
2013	3.14	1.71	3.81	2.17	2.47	1.28

CR, crude rate; ASR, age-standardized rate (using World standard population).

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Table 5 Trend analysis in 22 cancer registries during 2000–2013 by Joinpoint (%)

Sex	Trend 1			Trend 2		
	Year	APC	95% CI	Year	APC	95% CI
Crude Incidence						
Total	2000–2013	2.5*	0.6–4.5			
Male	2000–2013	3.9*	1.4–6.5			
Female	2000–2013	0.9	–0.9–2.8			
ASIRW						
Total	2000–2013	–0.7	–2.6–1.3			
Male	2000–2013	0.2	–2.5–2.9			
Female	2000–2013	–1.8	–3.5–0.0			
Crude Mortality						
Total	2000–2013	18.7	–2.6–44.7			
Male	2000–2003	1.3	–1.8–4.5	2003–2013	3.9*	1.2–6.6
Female	2000–2009	7.6*	3.1–12.4	2009–2013	–7.8	–20.6–7.1
ASMRW						
Total	2000–2003	15.4	–7.4–43.7	2003–2013	–1.7	–5.0–1.7
Male	2000–2013	0.5	–2.1–3.2			
Female	2000–2007	7.6*	0.3–15.4	2007–2013	–6.8	–14.7–1.8

APC, annual percentage change; 95% CI, 95% confidence interval; ASIRW, age-standardized incidence rate by world standard population; ASMRW, age-standardized mortality rate by world standard population; *, P<0.05.

Table 6 Malignant mesothelioma mortality in 22 cancer registries during 2000–2013 ($1/10^6$)

Period	Both sexes		Male		Female	
	CR	ASR	CR	ASR	CR	ASR
2000	1.24	0.97	1.34	1.14	1.14	0.79
2001	1.62	1.27	2.03	1.70	1.19	0.88
2002	1.67	1.29	1.90	1.57	1.43	1.04
2003	2.34	1.69	2.81	2.22	1.84	1.20
2004	1.98	1.37	2.57	1.89	1.38	0.92
2005	2.05	1.35	2.45	1.69	1.63	1.04
2006	2.17	1.49	2.23	1.62	2.10	1.38
2007	2.41	1.66	2.69	1.95	2.12	1.40
2008	2.18	1.39	2.45	1.61	1.91	1.19
2009	2.37	1.38	2.53	1.60	2.21	1.18
2010	2.98	1.83	3.50	2.19	2.45	1.51
2011	1.88	1.13	2.19	1.41	1.58	0.85
2012	2.36	1.25	2.66	1.45	2.05	1.06
2013	2.44	1.31	3.24	1.81	1.63	0.84

CR, crude rate; ASR, age-standardized rate (using World standard population).

should be enhanced. The incidence trend of malignant mesothelioma was increasing in China, while its mortality trend was stable. The changes in trend were similar to that of more developed countries.

Malignant tumors are a kind of multi-factor and multi-stage disease, and there are many factors associated with malignant mesothelioma. Occupational asbestos exposure is the major factor in developing the aggressive disease.

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Workers could exposure to asbestos through a variety of industrial operations, including mining and milling, manufacturing, shipbuilding and repair, and construction (18). In addition, environmental exposure to asbestos could also contribute to malignant mesothelioma, including naturally occurring asbestos exposure, neighborhood or household exposure to occupationally exposed subjects, and one major feature found in this kind of causes was that a higher disease burden was observed in females than in males (19). Asbestos-related diseases are of big threat to lives that result in heavy disease burden. Based on the estimation of National Center for Health Statistics mortality data, during 1999–2010, a total of 427,005 years of potential life lost to life expectancy (YPLL) and 55,184 years of potential life lost to life expectancy to age 65 (YPLL65) were attributed to asbestosis (56,907 YPLL and 2,167 YPLL65) and malignant mesothelioma (370,098 YPLL and 53,017 YPLL65) (20).

This study provided the latest data on the epidemiology of malignant mesothelioma and further analyzed its trends in China. The results will be helpful in deep understand of the current situation of malignant mesothelioma and provide basic information for health-related staff to monitor and control the disease. Although the incidence or mortality rate of malignant mesothelioma in China was relatively low compared with western countries, the incidence rate of malignant mesothelioma showed an increasing trend which should be paid more attention. Therefore, strengthening supervision laws to restricted asbestos use and further enhancing primary and secondary prevention of high risk subjects would be put in the first place.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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