Lung Cancer xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Impact of malignant mesothelioma in Taiwan: A 27-year review of population-based cancer registry data

Lukas Jyuhn-Hsiarn Lee[a,b], Yu-Yin Chang[b], Jung-Der Wang[a,b,c,*]

[a] Department of Environmental and Occupational Medicine, National Taiwan University Hospital, Taipei, Taiwan
[b] Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei, Taiwan
[c] Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

ARTICLE INFO

Article history:
Received 1 February 2009
Received in revised form 1 May 2009
Accepted 21 May 2009

Keywords:
Mesothelioma
Asbestos
Survival
Expected years of life lost (EYLL)
Occupational cancer
Outcome research

ABSTRACT

Purpose: To describe the epidemiologic characteristics of malignant mesothelioma (MM) in Taiwan; to evaluate the impact of the condition.
Methods: The Taiwan Cancer Registry Database was used to retrieve the cases of MM registered from 1979 to 2005. Only cases of histopathologically verified MM were included. For evaluating the impact of MM, the cancer sites of the pleura and peritoneum (ICD-O codes 163 and 158, respectively) were used for statistical analysis and estimation of the expected years of life lost (EYLL). Their survival was calculated by Kaplan–Meier analysis and extrapolated to obtain the EYLL using the Monte Carlo simulation by borrowing information from gender- and age-matched populations in Taiwan.
Results: A total of 423 cases of MM were included; MM of the pleura and peritoneum accounted for 91% of all cases (387/423). The median survival of pleural and peritoneal MM was 7.6 and 13.5 months for males and females, respectively. The incidence of MM increased during the observation period. A total of 232 males and 155 females diagnosed with MM were used for estimation of EYLL: 14.8 [95% Confidence Interval: 13.1–16.6] life years for males and 13.7 [11.2–16.2] life years for females.
Conclusion: The increasing incidence and significant EYLL for MM were observed for both males and females during 1979–2005 in Taiwan, although under-diagnosis and under-estimation were likely.

1. Introduction

Malignant mesothelioma (MM) is the primary tumour of the serosal membranes (mesothelium), which line the thoracic and abdominal cavities [1]. It was a rare malignancy in the past, with background incidence of around 1–2 per million persons annually [2], but significantly increasing incidences in many developed countries have been demonstrated to closely reflect previous asbestos usage [3–6].

MM is an aggressive malignancy with a dismal prognosis and most of those affected die within one year of diagnosis [3,7], resulting in a loss of life expectancy. The survival time for pleural MM was reported in the range of 8–14 months [8]. Even with advanced treatment, only three additional months are gained with participation in the phase III clinical trial using advanced chemotherapy [9]. Since MM is primarily caused by exposure to asbestos [8], it can be prevented by banning asbestos use or by implementing comprehensive controls to avoid asbestos exposure. In fact, asbestos has been banned successfully in more than 40 developed countries worldwide [10], but the "magic minerals" are still imported and in use in most Asian countries, including China, India, Thailand, and Taiwan. Thus, it is important to quantify the disease burden or expected years of life lost for a case of MM to facilitate the outcome research and cost-effectiveness analysis for prevention. We conducted this study to evaluate the impact of MM in Taiwan and to estimate the median survival time and expected years of life lost in comparison with the general population.

2. Methods

The major sources of data in this study are the Taiwan Cancer Registry from 1979 to 2005, which was linked with the Database of Death Registry to verify the vital status for every case up to the end of 2007. The Taiwan Cancer Registry, a population-based cancer registry, was founded in 1979. All hospitals with a capacity of greater than 50-bed are recruited to participate in reporting all newly diagnosed malignant neoplasms to the registry [11]. The database has been used in many cancer epidemiological studies [12,13]. The variables recorded in the cancer registry include personal identification number, age, date of diagnosis, location of tumours, geographic

* Corresponding author at: Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Room 719, No. 17, Xuzhou Road, Taipei 100, Taiwan. Tel.: +886 2 33668080; fax: +886 2 23224660.
E-mail address: jdwang@ntu.edu.tw (J.-D. Wang).

0169-5002/$ – see front matter.
doi:10.1016/j.lungcan.2009.05.016

location of the hospital that reported the case, and histopathological information in terms of morphology code.

We analysed information on the cases registered in the Taiwan Cancer Registry Database between January 1979 and December 2005. We identified all cases of histopathologically verified malignant mesothelioma (MM), coded according to the International Classification of Disease for Oncology (ICD-O) [14], i.e., ICD-O codes 163 and 158 for cancer sites of the pleura and peritoneum, respectively, and morphology codes 9050/3, 9051/3, 9052/3, and 9053/3. The incidence of a particular cancer site was analysed after careful identification of possible duplicate reported cases from different hospitals. The earlier date of diagnosis was selected for further survival analysis when duplicated cases were found. In fact, there were a total of 24 such cases for pleura and peritoneum.

The age-standardised incidence rates (ASIRs) for malignant mesothelioma were calculated according to the age distribution based on world standard population statistics reported by the World Health Organisation for the year 2000. We also obtained data on asbestos imports and domestic production from the Ministry of Economic Affairs, Taiwan [15], to plot the total amount of manufacturing for each year.

The survival for MM was followed up to 2007 and calculated by Kaplan–Meier analysis, which was then extrapolated to estimate the expected years of life lost (EYLL) and defined as the lifetime survival difference between the cancer cohort and an age- and sex-matched reference population. The details of the estimation method were described elsewhere for 17 types of major cancer in Taiwan [16]. Briefly, the survival function for an age- and gender-matched reference population was generated by the Monte Carlo method from the life-table of the Taiwanese general population in the year 2000. A constant excess hazard model was used to project long-term survival of the patients with MM, with linear extrapolation of a logit-transformed curve of survival ratio between MM patients and the reference population. We estimated the average EYLL by calculating the difference in under-curve areas between long-term survival curves for the MM cohort and the age- and gender-matched reference Taiwanese population [16–18]. EYLL provides us with an estimation of the magnitude to which a patient's life is shortened by the malignancy and therefore it can be regarded as an indicator of the total cancer burden as experienced by the society as a whole [19]. To facilitate the estimation, we used a free software program, MC-QAS, from the R statistical package, which can be downloaded from http://www.stat.sinica.edu.tw/jshwang. For analysis of descriptive data and Kaplan–Meier analysis, SAS 9.1 software was used.

3. Results

A total of 423 cases of MM were included in this study. There were 387 cases of MM of the pleura and peritoneum, which accounted for 91% of all MM. The epidemiological features were summarised in Table 1. The male-to-female ratio was about 1.5:1. The mean age at diagnosis was 57.9 ± 15.3 years. The median survival was 9 months for all cases, 7.6 and 13.5 months for males and females, respectively. The average expected years of life lost (EYLL) due to malignant mesothelioma was 14.2 years (Table 1), which was calculated from subtraction of the estimated life expectancy from the gender- and age-matched general population of Taiwan, as shown in Fig. 1.

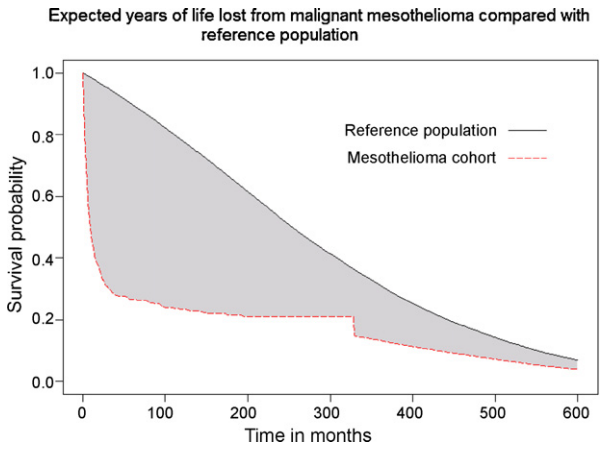

Fig. 1. The shaded area shows the expected years of life lost (EYLL) from malignant mesothelioma of the pleura and peritoneum compared with the gender- and age-matched reference population.

Fig. 2 illustrates the three-year moving average of asbestos imports, domestic production in Taiwan, and the trends of age-standardised incidence rates (ASIR) of malignant mesothelioma of the pleura and peritoneum from 1979 to 2005. The majority of asbestos used in Taiwan was imported, with an increasing trend in the mid-1970 s, which climbed further to a peak of 35,000 tons per year in the mid-1980 s, and then dropped in the early 1990's due to the promulgation of the Toxic Substance Control Act by the Environmental Protection Administration of Taiwan; less than 5000 tons per year were imported by 2001. The incidence of MM increased over the observation period. When the data were stratified by age into subjects less than 35 years of age and those that were 35 and over, there was a significant increase in the incidence of MM in the latter age group.

4. Discussion

The burden of MM can be expressed in terms of numbers of deaths, mortality, and incidence in the society. Although there have been numerous studies conducted on the impact of asbestos-related diseases, few reports have focused on the real quantification of total years of life lost. The calculation of disability-adjusted life year (DALY) loss was estimated based on universal assumptions regarding life expectancy and quality of life, a practice which is very useful for international comparison. However, such estimations in developing countries with much shorter life expectancies appear less realistic or useful. Programs for the treatment of each disease must compete for resources allocation; the comparative assessment must be based on real life expectancy for a specific

Table 1
The epidemiological features of malignant mesothelioma of the pleura and peritoneum, median survival months, and expected years of life lost based on the Taiwan Cancer Registry Database from 1979 to 2005.

	All (N = 387)	Male (N = 232)	Female (N = 155)
Age at diagnosis [years]			
Mean ± S.D. (median, range)	57.9 ± 15.3 (60, 11–97)	58.3 ± 15.1 (61, 18–97)	57.3 ± 15.6 (60, 11–89)
Median survival [months][a]	9.0	7.6	13.5
Expected years of life lost[b] (95% Confidence Interval)	14.2 (12.8–15.7)	14.8 (13.1–16.6)	13.7 (11.2–16.2)

[a] Kaplan–Meier (KM) survival analysis.
[b] The reference population was obtained from the general population and matched with regard to gender and age, as based on Taiwan vital statistics in 2000.

Please cite this article in press as: Lee LJ-H, et al. Impact of malignant mesothelioma in Taiwan: A 27-year review of population-based cancer registry data. Lung Cancer (2009), doi:10.1016/j.lungcan.2009.05.016

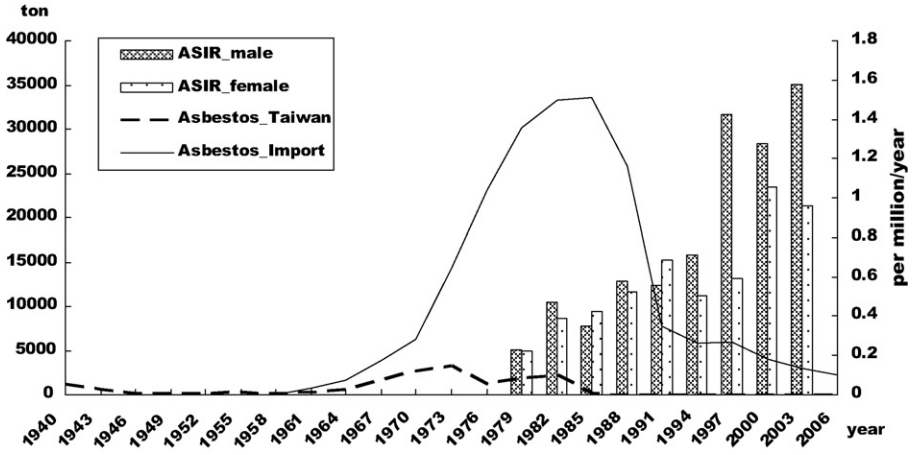

Fig. 2. Time-trends of asbestos imports, domestic production in Taiwan, and age-standardised incidence rates of malignant mesothelioma of the pleura and peritoneum from 1979 to 2005.

country. The analysis in this study quantifies the gain of life years from successful prevention of a case of MM and can be directly used in outcome evaluation. However, it is still limited by the lack of quality of life data to comprehensively calculate the quality-adjusted life year (QALY) loss, and future studies need to be conducted to investigate the measurement of quality of life for patients with MM.

There appears to be a temporal relationship between the past uses of asbestos and the increasing incidence of MM in Taiwan, as illustrated in Fig. 2. These findings seem to corroborate the ecological association between increased risk of mesothelioma and population exposure to asbestos over the past 3–4 decades [20]. For a case of MM, there would be 14.2 expected years of life lost (EYLL) based on the estimation in this study. Such figures can be used for comparative assessment of outcome research of prevention and new therapeutic agents [21] in the context of decision-making regarding health policies in Taiwan.

The incidence of MM is low as compared with those of other countries [22]. Since all hospitals with a capacity of greater than 50-bed have been recruited to participate in reporting all newly diagnosed malignant neoplasms to the registry, the coverage seems acceptable. After 1995 when the National Health Insurance began, the registry has been even more comprehensive because the co-payments of registered cancer patients can be waived. In fact, there are additional 242 cases of pleural or peritoneal cancer without histopathological proof in the registry. Thus, our data are a lower bound of real incidence cases for MM because of potential underestimation and possible misdiagnosis.

There is no data of exposure history in the cancer registry, and so we are unable to calculate the latent period for our cases. But in the early 1970s our workers usually began their career as early as 15–18, or after their junior or senior high school. We conducted a general survey in 33 registered asbestos factories during 1986–1987 and found that all of them employed less than 100 workers with the average age of 41.6 (range 16–67) years and average duration of 8.1 years, or a high turn-over rate, a low awareness of hazard, and only about 42% of them provided regular medical screening [23,24]. According to the industrial hygiene survey, chrysotile was in use in the majority of the factories (31/33, 94%), one factory used amosite, and a mixture of chrysotile, amosite, and crocidolite was used in one factory [23]. Thus, many workers probably died of malignant mesothelioma without detecting their real cause of death until 1995 when the National Health Insurance started and coverage extended to all people and we may be able to detect the disease earlier.

The male-to-female ratio was about 1.5:1, which is low compared with Western countries. The probable explanations include one or more of following factors: although the male-to-female ratio among asbestos workers was about 487:80 in a general survey during 1986–1987 [23], female workers were mainly employed in asbestos textile factories where the concentration of airborne asbestos was the highest, or 6.25 fibres/mL [25]. In addition, women may have paraoccupational or domestic exposure to asbestos fibres brought home by male workers on their clothing. The median survival of pleural and peritoneal malignant mesothelioma was 7.6 and 13.5 months for males and females, respectively. Although the major reasons remain to be elucidated, the average age at diagnosis in females seems to be one year earlier than that of males, which may account for the similar finding that females tend to have better prognosis than males in other studies [26,27].

Asbestos-related disease burden is an emerging public health issue worldwide. Asbestos is the primary cause of mesothelioma, and a recent study in the UK estimated the attributable fraction of asbestos among male cases of mesothelioma from occupational, paraoccupational and environmental sources to be 98% [28]. Even though asbestos has been banned in more than 40 countries, large amounts of asbestos are used for many industrial purposes in the developing world. More than half of the asbestos consumed is used by Asian countries [6], apparently due to a lack of awareness and the paucity of data on the comparative assessment of health benefits related to different prevention strategies. Thus, it is not surprising that the Taiwanese government has failed to completely ban the use of asbestos. The Collegium Ramazzini, the International Commission on Occupational Health, the International Labour Organisation, and the World Health Organisation have all called for a global ban on mining and the use of all forms of asbestos, including chrysotile [10]. Therefore, the governments in developing countries should take account of the significant burden from asbestos exposure and increase the awareness of the general public in order to reduce this preventable loss of life years by appropriate regulatory action.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We wish to thank the Bureau of Health Promotion at Taiwan's Department of Health for providing the dataset from the Taiwan Cancer Registry with links to the mortality certificate data. We thank that the National Health Research Institutes (NHRI) of Taiwan funded this research on occupationally related cancer (NHRI-97A1-PDCO-01-0811-2).

Please cite this article in press as: Lee LJ-H, et al. Impact of malignant mesothelioma in Taiwan: A 27-year review of population-based cancer registry data. Lung Cancer (2009), doi:10.1016/j.lungcan.2009.05.016

References

[1] King JE, Hasleton PS. The epidemiology and aetiology of malignant mesothelioma. In: Kenneth O'Byrne K, Valerie Rusch V, editors. Malignant pleural mesothelioma. Oxford: Oxford University Press; 2006. p. 1–18.
[2] McDonald JC, McDonald AD. The epidemiology of mesothelioma in historical context. Eur Respir J 1996;9:1932–42.
[3] Peto J, Hodgson JT, Matthews FE, Jones JR. Continuing increase in mesothelioma mortality in Britain. Lancet 1995;345:535–9.
[4] Peto J, Decarli A, La Vecchia C, Levi F, Negri E. The European mesothelioma epidemic. Br J Cancer 1999;79:666–72.
[5] Hodgson JT, McElvenny DM, Darnton AJ, Price MJ, Peto J. The expected burden of mesothelioma mortality in Great Britain from 2002 to 2050. Br J Cancer 2005;92:587–93.
[6] Takahashi K. Asbestos-related diseases: time for technology sharing. Occup Med (Lond) 2008;58:384–5.
[7] Robinson BW, Lake RA. Advances in malignant mesothelioma. N Engl J Med 2005;353:1591–603.
[8] British Thoracic Society Standards of Care Committee. BTS statement on malignant mesothelioma in the UK, 2007. Thorax 2007;62(Suppl. 2):ii1–19.
[9] Vogelzang NJ, Rusthoven JJ, Symanowski J, Denham C, Kaukel E, Ruffie P, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 2003;21:2636–44.
[10] Collegium R. An appeal to delegates to the 4th conference of the parties to the Rotterdam convention re: chrysotile asbestos, endosulfan and tributyl tin. News on 27 October 2008. Available at: http://www.collegiumramazzini.org/news.asp [accessed on 01.12.08].
[11] Taiwan Cancer Registry, with summary information at the website available at http://crs.cph.ntu.edu.tw/main.php?Page=N1 [accessed on 23.04.09].
[12] Hsu C, Shen Y-C, Cheng C-C, Hong R-L, Chang C-J, Cheng A-L. Difference in the incidence trend of nasopharyngeal and oropharyngeal carcinomas in Taiwan: implication from age-period-cohort analysis. Cancer Epidemiol Biomarkers Prev 2006;15:856–61.
[13] Chen CJ, You SL, Lin LH, Hsu WL, Yang YW. Cancer epidemiology and control in Taiwan: a brief review. Jpn J Clin Oncol 2002;32:S66–81.
[14] Department of Health of Taiwan. Chinese translation version of the International Classification of Disease for Oncology. 2nd edn World Health Organization; 1997 [June].
[15] Ministry of Economic Affairs. Mineral statistic yearbook Taiwan area, the Republic of China. Taipei: Ministry of Economic Affairs; 1962–2007 [in Chinese].
[16] Chu PC, Wang JD, Hwang JS, Chang YY. Estimation of life expectancy and the expected years of life lost in patients with major cancers: extrapolation of survival curves under high-censored rates. Value Health 2008;11:1102–9.
[17] Fang CT, Chang YY, Hsu HM, Twu SJ, Chen KT, Lin CC, et al. Life expectancy of patients with newly-diagnosed HIV infection in the era of highly active antiretroviral therapy. QJM—An Int J Med 2007;100:97–105.
[18] Hwang JS, Wang JD. Monte Carlo estimation of extrapolation of quality-adjusted survival for follow-up studies. Stat Med 1999;18:1627–40.
[19] Brown ML, Lipscomb J, Snyder C. The burden of illness of cancer: economic cost and quality of life. Annu Rev Public Health 2001;22:91–113.
[20] Lin RT, Takahashi K, Karjalainen A, Hoshuyama T, Wilson D, Kameda T, et al. Ecological association between asbestos-related diseases and historical asbestos consumption: an international analysis. Lancet 2007;369:844–9.
[21] Cordony A, Le Reun C, Smala A, Symanowski JT, Watkins J. Cost-effectiveness of pemetrexed plus cisplatin: malignant pleural mesothelioma treatment in UK clinical practice. Value Health 2008;11:4–12.
[22] Bianchi C, Bianchi T. Malignant mesothelioma: global incidence and relationship with asbestos. Ind Health 2007;45:379–87.
[23] Chang HY, Wang JD, Chang JW, Chen CR, Suoo R, Wu MC. Industrial hygiene survey for asbestos-related factories in Taiwan. J Natl Public Health Assoc (ROC) 1988;8:161–71 [in Chinese].
[24] Chen CR, Chang HY, Suo J, Wang JD. Occupational exposure and respiratory morbidity among asbestos workers in Taiwan. J Formosan Med Assoc 1992;91:1138–42.
[25] Chang HY, Wang JD, Chang JW, Chen CR, Wu MC. Airborne asbestos concentration in asbestos-related factories in Taiwan. J Natl Public Health Assoc (ROC) 1988;8:28–35 [in Chinese].
[26] Edwards JG, Abrams KR, Leverment JN, Spyt TJ, Waller DA, O'Byrne KJ. Prognostic factors for malignant mesothelioma in 142 patients: validation of CALGB and EORTC prognostic scoring systems. Thorax 2000;55:731–5.
[27] Rusch VW, Venkatraman ES. Important prognostic factors in patients with malignant pleural mesothelioma, managed surgically. Ann Thorac Surg 1999;68:1799–804.
[28] Rushton L, Hutchings S, Brown TP. The Burden of cancer at work: estimation as the first step to prevention. Occup Environ Med 2008;65:789–800.

Please cite this article in press as: Lee LJ-H, et al. Impact of malignant mesothelioma in Taiwan: A 27-year review of population-based cancer registry data. Lung Cancer (2009), doi:10.1016/j.lungcan.2009.05.016