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Malignant Pleural Mesothelioma: Occupational and Non-Occupational Asbestos Exposures

Abstract

The objectives of this study was to review many epidemiological risk factors on the occurrence of malignant pleural mesothelioma among occupational and non-occupational asbestos-exposed men and women mentioned in several previous studies. Asbestos exposure is a well-documented etiological factor of malignant pleural mesothelioma. The majority of cases are men and only 40% of female cases are occupational exposure. Many western and developing countries are currently suffering malignant pleural mesothelioma epidemic due to their extensive use of asbestos. Exposure to all types of asbestos can induce malignant mesothelioma, including cancer of lung, larynx, ovary, and gastrointestinal organs, particularly, colorectal region. Approximately, 125 million people expose to asbestos in their workplaces worldwide. There are several limitations of the studies on association of the asbestos exposures, both occupational and para-occupational or non-occupational causes, such as inability to take into account confounding by occupational asbestos exposure, difficulties in retrace past exposures, inadequacy of the length of follow-up, various exposure levels at different factories, and unavailability of data regarding the type of asbestos used and measurements of the air-borne asbestos dust concentration in each factory. Currently, there are many governmental asbestos-use-control organizations, including malignant pleural mesothelioma database in many countries, such as The Italian National Institute for Occupational Safety and Health, The Environmental Protection Administration of Taiwan, The French National Mesothelioma Surveillance Program, etc. to protect their people from malignant pleural mesothelioma.

Keywords: Mesothelioma; Pleural; Malignant; Occupational; Non-Occupational

Research Article

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Abbreviations: ARp: population-Attributable Risk; CI: Confidential Interval; CT: Computerized Tomography; EPA: The Environmental Protection Administration of Taiwan; IARC: International Agency for Research on Cancer; ICD: International Classification of Diseases; ISPESL: The Italian National Institute for Occupational Safety and Health; MM: Malignant Mesothelioma; MPM: Malignant Pleural Mesothelioma; NA: Not Available; ORs : Odd Ratios; PNSM: The French National Mesothelioma Surveillance Program; MRI: Magnetic Resonance Imaging; ReNaM: The Italian National Mesothelioma Register; VS: Versus; WHO: World Health Organization

Introduction

Malignant pleural mesothelioma (MPM), a rare tumor that exposure to asbestos is a well-approved etiological factor [1-12]. Particularly, among men, occupational exposure could account for the large group of MPM patients, whereas its attributable risk varies between 30-80% across different populations [13-15]. With adding the para-occupational exposure, such as handling asbestos-contaminated clothes, due to occupational exposure or living near an asbestos factory to the occupational ones, the attributable factor can rise to more than 95% [16]. Only 40% of female cases can be explained by occupational exposure [9], quantifying the risk attributable to such well-demonstrated non-occupational asbestos exposure (para-occupational, domestic or environmental) among female cases is needed [17-19]. Inhalation of asbestos fibers is well-documented etiological relationship with MPM, particularly, dose-response parameters [20, 21]. Asbestos is a group of fibrous silicate minerals are widely used in several industries because of their fire-resistant properties and their strength [22]. Currently, chrysotile is the only type of asbestos in commercial use which accounts for 95% of the asbestos in use globally [23]. Currently, many western countries are suffering the malignant mesothelioma (MM) epidemic due to their extensive use of asbestos between the 1950s and the 1980s various industrial applications and the long latency period since the beginning of exposure that is around 40 years [24]. Asbestos is also widely used in the construction and shipbuilding industries, particularly in acoustic and thermal insulation [24]. Exposure to all types of asbestos fibers can induce MM and cancers of the lung, larynx, and ovaries [25, 26], including gastrointestinal [25], especially colorectal cancer [26]. MM is a tumor originating mainly from the serous membranes of the pleura and, less frequently, of the pericardial and peritoneal cavities and sometimes from the tunica vaginalis [27]. The prognosis of MM is poor [27]. In MPM, the median survival is about 9 months from diagnosis in the population-based studies [27]. Many countries established the forecasts of mesothelioma mortality, such as Spain [28], Japan [29], Italy [30], The Netherlands [31], France [32], Britain [33], and Australia [34]. The World health Organization (WHO) have classified all types of asbestos as carcinogens [34] and the International Agency for Research on Cancer (IARC) have classified them as group I human carcinogens [35]. Recently, the WHO reported that approximately, 125 million individuals globally expose to asbestos in their workplaces, and about 107,000 asbestos-related deaths occurs each year [36]. At the end of the 1980s, Italy was the second largest asbestos producer in Europe, after the Soviet Union, and was the largest in the European Community [24]. The National Mesothelioma Register (ReNaM) that kept at the National Institute for Occupational Safety and Health (ISPESL), was established in 1993 (by force of law since 2002) with investigating occurrences of asbestos exposure, promoting research, identifying any possible unknown source of asbestos contamination, and the remit of estimating MM incidence in Italy [24]. In France, the National Mesothelioma Surveillance Program (PNSM) was established in 1998 to provide relevant information on asbestos-related health effects on its population, relying on the exhaustive recording of all incident primary pleural tumors in specified districts [37]. In the United States, MPM occurs in about 2,500 cases per year, with 20% being female patients [38]. The MPM incidence is expected to increased globally until 2020 [39]. Asbestos use was progressively banned with taking place first in European countries in the 1980s and particularly in 1997 in France [21]. Nevertheless, asbestos is still produced and used in many developing countries [21].

Table 1: Recent Study Results on Asbestos-Exposure Attributable Risk, Odd Ratio, and Incidence Ratio for Malignant Pleural Mesothelioma.

Author(s)	Study Result	Year Published	Reference
Lin *et al*	Standard incidence ratio for male MPM = 5.78 (95% CI : 1.19-16.89)	2015	56
Lacourt *et al*	Occupational asbestos ARp = 83.1% (99% CI : 74.5%-91.7%) for men, 41.7% (99% CI : 25.3%-58.0%) for women, Non-occupational asbestos ARp among Non-occupational- asbestos exposure subjects = 20% (99% CI : 33.5%-73.5%) for men and 38.7% (99% CI : 8.4%-69.0%) for women, ARp for all kinds of asbestos exposure = 87.3% (99% CI : 78.9%-95.7%) for men and 64.8% (99% CI : 45.4%-84.3%) for women	2014	64
Lacourt *et al*	ORs = 17.6 (95% CI : 11.8-26.2) and 9.8 (95% CI : 4.2-23.2) for participants exposed to both asbestos and MW and for participants exposed to both asbestos and silica, respectively, OR = 4.3 (95% CI : 1.9-9.8) occupational asbestos exposure alone	2013	76

Clinical features and diagnosis of malignant pleural mesothelioma

Dyspnea is the most common symptom in the early course of the disease, usually due to the presence of pleural effusion [40]. When the tumor invades the intercostal nerves, chest pain may occur [40]. Finally, the tumor encase the lung contributing to worsening of chest tightness and dyspnea [40]. Computerized tomographic (CT) scan provides much greater sensitivity than the conventional chest roentgenography for visualization of the pleural-based masses [41]. Spiral computerized tomographic scan yields more advantages than the conventional CT scan in minimizing motion artifacts and can reconstruct the three dimensions between pleura, bronchus, lobular septum, artery, and vein [42,43]. Magnetic resonance imaging (MRI) is better CT scan in demonstrating tumor invasion, bony invasion, and tumor spreading [44], but CT scan remains the standard imaging in defining the local extension of the tumor [45]. Positron emission tomography-computed tomographic scan seems to be superior to other imaging modalities in detecting more extensive MPM, including unsuspected occult distant metastases [46]. Thoracoscopic examination can make the diagnosis of the pleural disease definitely and yields almost a 100% success rate [47], while video-assisted thoracoscopy offers the ability to perform biopsies from multiple sites [48]. Open or surgical pleural biopsy yields a sensitivity of 97% and specificity of 56% for identifying epithelial MPM [47]. There are various serum biomarkers for diagnosis of early or asymptomatic MPM, such as mesothelin which yields excellent sensitivity of 84% and specificity of virtually 100% [49].

Discussion

Currently, mesothelioma mortality surveillance is based on territorial cancer registries in Germany [50], on death certificates in Great Britain [9], and on both in the United States [51,52], whereas Italian ReNaM is one of the largest extent system of epidemiological surveillance for MM and also in the field of occupational disease monitoring [24]. By the early 1960s, while in the Great Britain, the United States and Scandinavian countries, asbestos consumption was already decreasing, unfortunately, the Italian consumption rose in the same period and began to decrease only when it was known a ban would be put in place [24]. The development of a complete national cancer incidence registry in the Scandinavian countries contribute to systematic linkage with occupational information archives [53-55]. The Italian ReNaM dataset has some critical limitations because its development has been non-homogeneous [24]. In Taiwan, the majority of asbestos used was imported with the amount peaking at 35,000 tons per year in the mid-1980s, and then significantly falling in the early 1990s because of the Toxic Chemical Substances

Control Act promulgated in 1986 by the Environmental Protection Administration (EPA) of Taiwan [56]. Lin *et al* demonstrated that there was no increase in overall cancer incidence found in their cohort of workers in asbestos-related factories compared to the general population [56]. The term "Healthy Worker Effect" that are the phenomina clearly demonstrated in the current studies' findings was described in 1974 by McMichael AJ in which more vigorous occupations had a relatively lower mortality rate when compared to the death rate among unemployed individuals or in occupations of an easier character [57]. A possible dilution of cancer risk in the whole Taiwanese asbestos-related occupational cohort with heterogeneous exposure levels would be likely to cause substantial underestimation of risk of all cancers due to some industries' application for asbestos use not usually used it according to the report system of the Taiwan EPA [57]. The study conducted by Lin C-K *et al* had a huge gap between expectations and actual results due to not including all asbestos-related facilities by the Taiwan EPA [56], lack of a specific code in ICD-9 [58], and short-form-system basic information collected in a Taiwan population-based cancer registry since 1979 and was changed to a long-form system after 2002 [59]. There is no safety level of asbestos exposure [60] and no evidence of a threshold level [61]. Mesothelioma could be induced by minimal asbestos exposure with long enough latency, and the risk increases exponentially with time since the first exposure after the first 10 to 15 years [22]. The greatest risk with regards to mesothelioma occurring around 20-40 years later [62]. South Korea have begun a nationwide MM surveillance system since 2000 for monitoring pathologically confirmed cases and their exposure histories by interview [63]. The French PNSM was established in 1998 based on continual following up of asbestos-exposure-related MPM among French population [37]. The PNSM relies on the exhaustive recording of all incident primary pleural tumors in the representative districts of France [37]. Recent study conducted by Lacourt *et al* supported the relationship between non-occupational asbestos exposure and the occurrence of MPM [64]. There are several population-based case-control studies that demonstrated an association between para-occupational asbestos exposure including household exposure and the etiology of MPM [65-68]. While an association between geological source of asbestos exposure and the increased incidence of MPM is evidence-based [69], several recent studies have demonstrated an increased risk of MPM associated with environmental exposure related to the proximity with an asbestos plant including residence near asbestos mines [10,70-72]. Currently, there are few weak evidences to support the etiology of MPM and a possible effect of passive exposure in asbestos-contained buildings [18]. A previous French study on spatial distribution of incidence of male and female mesothelioma with or without any identified occupational or non-occupational asbestos exposure indicated the major influence of asbestos among female mesothelioma, likely through unknown environmental exposure [73]. Nevertheless, Lacourt *et al* demonstrated that a possible overestimation of the non-occupational ARp and the overall ARp cannot be excluded due to recall bias if the controls tend to under-report environmental or domestic exposure compared to mesothelioma cases [64]. Among women, this effect might have been extreme, including the observed difference between men and women for the non-occupational ARp_[64]. A study on non-response bias, conducted by Rolland *et al* demonstrated that the sociodemographic characteristics of cases who died before interview or refused to answer questions, did not differ from those of the cases included in study conducted by Lacourt *et al*. [74]. Cases who included in the their study (among men, 80.3% vs 92.3%, respectively; among women, 18.7% vs 45.3%, respectively) were more likely to be more occupationally exposed than cases who had died before the interview [64]. Nevertheless, occupational asbestos exposure mainly was assessed through job titles and derived from simplified questionnaires, contributing to a possible underestimation of occupational exposure among control population in their study [75]. A recent study conducted by Lacourt *et al* revealed that silica and/or mineral wool co-exposures to asbestos were more likely to increase the magnitude of occupational asbestos exposure on increased risk of pleural mesothelioma [76]. They cannot identify any association between silica exposure and pleural mesothelioma despite the significant OR for participants exposed only to silica compared to those not exposed to other studied factors [76]. The main limitations of these recent studies [56,64,76] are difficulties in retrace past exposures, inadequacy of the length of follow-up, inability to take into account confounding by occupational asbestos exposure, various exposure levels at different factories, and unavailability of data regarding the type of asbestos used and measurements of the air-borne asbestos dust concentration in each factory.

Conclusions

There are many evidences that support the minimal asbestos exposure with long latency is enough to increase the risk of MPM occurrence, particularly among male workers. Silica and/or mineral wool co-exposure to asbestos are more likely to increase the risk of MPM.

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Conflict of Interest

No conflict of interest is declared.

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