



Occupational exposure to asbestos and cardiovascular related diseases: A meta-analysis

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ABSTRACT

Asbestos has become one of the leading causes of death among occupational workers in the world. The association between asbestos and cardiovascular disease is less reported. We performed a meta-analysis to quantify the association between asbestos exposure and the mortality of cardiovascular related diseases. We performed a systematic review in the PubMed database before December 2014. All cohort studies citing the standardized mortality ratio (SMR) of cardiovascular related diseases in workers exposed to asbestos were collected. We then calculated the pooled standardized mortality ratios of such diseases. Sixteen studies were included. The combined results from all studies indicated the pooled SMR estimate for cardiovascular related diseases was 1.11 (95% CI, 1.01–1.22). This meta-analysis showed that asbestos exposure significantly increased the risk of cardiovascular related diseases in exposed workers.

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Introduction

Asbestos designates a group of naturally occurring silicate minerals used commercially for their desirable physical properties. The harmful effects of asbestos, however, have made it one of the world's leading

causes of death among occupational workers. For example, asbestos is one the most important occupational carcinogens, causing about one half of all deaths from cancer linked to workplace exposure (Driscoll et al., 2005). Currently, approximately 125 million workers are exposed to asbestos worldwide and at least 107,000 of them die from asbestos-related diseases every year (Burki, 2009). Despite progressively more stringent regulations controlling occupational exposure to asbestos, the asbestos-related disease epidemic has not eased. It is well accepted that occupational exposure to asbestos predicts incidence of various diseases such as lung cancer, asbestosis, or mesothelioma (Selikoff & Seidman, 1991; Lotti, 2010) but the association

Abbreviations: SMR, Standard mortality ratio; SEs, Standard errors; CI, Confidence interval; CD, Circulatory diseases; IHD, Ischemic heart disease; ODH, Other diseases of the heart; PHD, Pulmonary heart diseases; AHD, All heart diseases.

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between asbestos and non-respiratory diseases such as cardiovascular disease is less clear.

Chronic inflammation processes plays an important role in the pathogenesis of cardiovascular diseases (Libby, 2006). A growing body of evidence suggests that long-term exposure to combustion particles is associated with atherosclerosis and cardiovascular diseases (Hassing et al., 2009; Hoek et al., 2013). In addition, silica, a non-combustion particle, has also been reported to increase mortality from cardiovascular diseases in a cohort study of 74,040 workers. The standardized mortality ratios of ischemic heart disease (1.65, 1.35–1.99) were significantly elevated among workers exposed to respirable silica concentrations equal to or lower than 0.1 mg/m³ (Chen et al., 2012). Asbestos, a kind of silicate, can also induce a strong inflammatory reaction in animal models and promotes atherogenesis (Gardner et al., 1986; Dogra & Donaldson, 1995; Dostert & Petrilli, 2008; Cyphert et al., 2012). However, little attention has been given to adverse health effects of asbestos exposure on cardiovascular system. It could be hypothesized that asbestos may be a risk factor of cardiovascular events. Certainly, some cohort studies have suggested an association between the increased risk of cardiovascular diseases and exposure to asbestos (Loomis et al., 2009; Harding et al., 2012) but there are also quite a number of studies which provide negative results (Battista et al., 1999; Sichelidis et al., 2009). The mortality of cardiovascular events in these studies which focus on the major asbestos-related diseases, namely lung cancer or mesothelioma, was not studied in depth. The potential role of chance, confounding factors, and other forms of bias were not taken into account. For this reason, this meta-analysis of the epidemiologic evidence was conducted. Our objective was to quantify the association between asbestos exposure and the mortality of cardiovascular related diseases.

Materials and methods

Search strategy

All published studies citing the SMR of cardiovascular diseases in workers exposed to asbestos were collected by conducting a search on PubMed before December 2014. The following key words were used: “cardiovascular diseases,” “heart diseases,” “mortality,” “incidence,” “asbestos,” “crocidolite,” “chrysotile,” “amphibole,” and “amosite.” In addition, we searched all the references of collected studies to identify additional relevant reports. Individual studies and the data extracted were reviewed independently by two authors using a standardized form. We screened titles first and then a second screening on abstracts and full-text was considered. Only English language full-text papers were included that reported either SMR or observed and expected deaths in cohort study. The studies were excluded if there were not sufficient data to provide for the determination of standardized mortality ratio and confidence interval. If different opinions on including or excluding one paper appeared, the disagreement was resolved by voting among all authors. If a study made a stratified analysis based on gender, type of cardiovascular related diseases or kind of asbestos exposed, the results of stratification analysis were set as new literatures to be included. Each study was reviewed critically and the following data was extracted: (1) Author of the paper and year of publication, (2) Type of cardiovascular related disease, (3) Country of origin, (4) Type of industry and asbestos exposed in the study, (5) Number of the cohort and the information of gender, (6) Follow-up of study participants, (7) The SMR and the confidence interval for the SMR, (8) Assessment of asbestos exposure and (9) All-cause mortality. Details of the papers were summarized in Table 1.

Statistical analysis

Statistical analysis was conducted on natural logarithm of the SMR, the ln-SMR, because its sampling distribution more closely

approximates a normal distribution proves more useful analyzing a combination of papers on different participants. Based on the reported confidence interval, we calculated the standard errors (SEs) for the ln(SMR) given by the formula $SE = [\ln(\text{upper limit}) - \ln(\text{lower limit})] / 3.92$. Overall pooled SMR estimates and corresponding 95% CIs were calculated using fixed-effects (Mantel–Haenszel method) and random-effects (DerSimonian and Laird method) methods (Harris, 2008). Because of the significant amount of heterogeneity, we only presented the random-effects estimates. Meta-regression techniques were used to determine the extent to which variables following might explain heterogeneity: gender (male, female, or gender mixed), geographic region (United States vs. Europe), type of industry (textiles, mining, cement, mixed, or others) magnitude of the SMR for all causes (≤ 1.0 or > 1.0), type of asbestos (crocidolite, chrysotile, amphibole, amosite, or mixed), type of cardiovascular diseases (circulatory diseases, ischemic disease, pulmonary heart disease, all heart diseases, or others), and follow-up period (< 35 or ≥ 35 years). To assess heterogeneity not only among studies but also between sub groups, we used the I^2 and Q statistics. For I^2 , a value $> 25\%$ was considered a measure of heterogeneity; for the Q statistic, $P_Q < 0.10$ indicated significant heterogeneity (Higgins & Thompson, 2002). Paper bias was assessed by visual inspection of Begg's funnel plots and investigated using Egger's regression asymmetry method formally. We defined statistical significance as p -value < 0.05 for all analyses except for the heterogeneity. All meta-analyses were completed with Stata software (Version 10.0; StataCorp, College Station, TX).

Results

Literature search

A total 1124 unique citations were initially retrieved from the PubMed database. The majority of these were excluded after the first screening on titles or abstracts, mainly because they were not cohort studies or not English papers, no SMR of cardiovascular related diseases reported, or not relevant to our research. After review of 29 full-text papers, 10 studies were excluded because of incomplete confidence interval information. For three studies in which the data analysis of the cohort was updated, we chose the most recent (Musk et al., 2008; Pira et al., 2009; Harding et al., 2012) and excluded 3 papers from the previous report. Finally, 16 studies were included in our analysis (Fig. 1).

Study characteristics

The characteristics of the 16 studies included are given in Table 1. Nine of the studies were conducted in European countries (United Kingdom, Denmark, Italy, Lithuania, Greece), four in North America (United States, Canada), and one was carried out in China, Australia and South Africa respectively. Five of the sixteen studies included data stratified by gender (Gardner et al., 1986; Smailyte et al., 2004; Hein et al., 2007; Harding et al., 2012; Wang et al., 2013). Six cohorts only included female workers and eight cohorts only were conducted on male workers, seven included both males and females. Of the sixteen papers analyzed, nine reported circulatory diseases (CD), seven reported ischemic heart disease (IHD), two reported pulmonary heart diseases (PHD), four reported all heart diseases (AHD), and three reported other diseases of the heart (ODH). The industries of asbestos exposure involved in analysis included mining, manufacture of textiles, cement production and construction.

Meta-analysis

Fig. 2 presents the SMR and 95% CIs of individual studies and the pooled SMR results from the random-effects model. The average pooled SMR for cardiovascular related diseases among asbestos exposed

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