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Original Research

Familial risk of pleural mesothelioma increased drastically in certain occupations: A nationwide prospective cohort study



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KEYWORDS

Mesothelioma; Familial risk; First-degree relatives; Occupation **Abstract** *Objective:* We aimed to explore the effect of occupation on familial risk of pleural mesothelioma in a nationwide cohort study design.

Method: The nationwide Swedish Family-Cancer Database includes all Swedes born after 1931 and their biological parents, totalling 16.1 million individuals with about 2.3 million cancer patients. Hazards ratios (HRs) were calculated adjusting for age, sex and region of residence.

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Results: Having asbestos-related occupation in the absence of family history of mesothelioma increased risk of mesothelioma more than threefold (adjusted HR = 3.2, 95% confidence interval [CI]: 3.0-3.5). In those who had a history of mesothelioma in their first-degree relatives and an asbestos-related occupation, risk of mesothelioma dramatically increased compared with individuals without such occupations and family history (without chronic obstructive pulmonary disease [COPD] HR = 24, 95% CI: 15-39; with COPD 45, 95% CI: 15-141). In those who had a family history of mesothelioma and no history of an asbestos-related occupation, risk of mesothelioma and no history of an asbestos-related occupation, risk of mesothelioma and no history of an asbestos-related occupation, risk of mesothelioma did not show significant increase compared with those who had no family history of mesothelioma and no asbestos-related occupation (HR = 1.6; 95% CI: 0.7-3.8).

Conclusion: First-degree relatives of patients with pleural mesothelioma had a drastic risk of developing this malignancy in case of certain occupations, which shows a gene–environment interaction is probable in risk of mesothelioma.

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1. Introduction

Mesothelioma is an aggressive cancer, for which no curative oncological treatment currently exists [1]. As the median survival of this malignancy is less than 1 year, there is a dire necessity to find out methods for early detection and therapeutic strategies for this rare cancer.

Asbestos exposure is well established as the primary risk factor and cause of mesothelioma. Mediterranean regions, such as Greece and Turkey, have experienced epidemics of malignant mesothelioma as a result of nonoccupational, 'domestic' exposure to tremolite asbestos and fibrous erionite [2]. In the Turkish region of Cappadocia, a large proportion of deaths have been due to mesothelioma because of erionite containing building material [3]. Even immigrants from Turkey have higher risk of mesothelioma [4]. The use of asbestos in Sweden was at a fairly low level until after the Second World War when it rapidly increased, and a decrease was seen only after the prohibition of installation of asbestos cement products in 1976, which resulted in a dramatic decrease in the import of raw asbestos. This was followed by a general prohibition (albeit with exceptions) of asbestos processing and machining in 1982, thus drastically reducing the number of exposed workers [5].

Researchers have found that individuals with germ line mutation in several genes and in particular BAP1 and CDKN2A are at increased risk of developing mesothelioma [6], particularly in the presence of asbestos exposure [7-10]. However, the prevalence of germ line BAP1 mutations in sporadic pleural mesothelioma patients is low, which suggests a minor role of germ line BAP1 mutation in the pathogenesis of sporadic pleural mesothelioma [10,11]. Some studies showed that risk of mesothelioma is increased when relatives are diagnosed with mesothelioma [12–14]. A comprehensive study showed an increased risk of mesothelioma in specific occupations [15]. In Sweden, as in the other Nordic countries, asbestos-related occupations such as plumbers, mechanics, welders, electrical workers, insulators, seamen, smelter workers and engine operators showed typically the highest incidence of mesothelioma [15]. Pre-existing lung disease is also considered a risk factor for mesothelioma [16].

Although having a family history of mesothelioma is not modifiable, it is possible that a genetic/environmental/life style predisposition to mesothelioma, which is represented by a positive family history, is modifiable through alteration of known environmental factors or by adequate intervention strategies. A better understanding of family history within the population is a key factor to improve our understanding of cancer aetiology and to provide appropriate advice for clinical counselling and early detection.

A population-based study that could clarify the effect of occupation on familial risk of mesothelioma is lacking. Therefore, we investigated this effect in the Swedish Family-Cancer Database (FCD), which is the world's largest of its kind. Our database is registerbased, thus avoiding biases of the interview studies, where participants report cancers in their family members [17,18]. Apart from medically verified data on diagnosis of mesothelioma in our database, family structures and occupation of subjects in several decades were derived from registered sources. Our aim was to elucidate the effect of occupation on familial risk of pleural mesothelioma.

2. Material and methods

The Swedish FCD was created in the 1990s by linking information from the Multi-generation Register, national censuses, Swedish Cancer Registry, and death notifications [19]. Data on family relationships were obtained from the Multi-generation Register, where children born in Sweden in 1932 and later are registered with their biological parents as families. Thus, the Download English Version:

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