ABSTRACT

Background: Asbestos is an occupational and environmental hazard, which has been responsible for millions of deaths worldwide. In addition to causing asbestosis, asbestos is a known human carcinogen. Although use of amphibole asbestos has been banned decades ago, chrysotile asbestos has continued to be mined, manufactured and used in many countries. To provide more convincing evidence for cancerous outcomes resulting from exposure to chrysotile, we conducted a 37-year prospective cohort study (two years longer than we originally proposed) in a group of asbestos workers and a 26-year historical cohort study (six years longer than we initially proposed) in asbestos miners from mainland China. These workers were exposed relatively pure chrysotile in their work. The primary objective of the study was to evaluate the relationship between cause-specific mortality, in particular lung cancer mortality, and exposure to chrysotile asbestos.

Study subjects and methods: *Asbestos worker cohort:* We followed 577 male asbestos workers from January 1972 to December 2008 (37 years in total), who worked in an asbestos product manufactory. Meanwhile, we followed 435 male workers in original cohorts from an electronic equipment plant located in the same city of China, as *external control*. The follow-up rate was 99% in the asbestos worker cohort and 73% in the control cohort. We further categorized asbestos workers into high, medium and low exposure levels based on their job titles and workshops, where asbestos dust/fibre measurements were available.

Asbestos miner cohort: Another cohort consisting of 1539 male workers who worked in the largest chrysotile asbestos mine in China was established and followed from January 1981 to December 2006, making up 26 years. We divided these workers into two groups based on their job titles: *miner group*, consisting of 1080 workers who were directly engaged in asbestos mining and milling; *internal control group*, including 459 workers who were not directly exposed to asbestos in their job.

We collected employment data from plants and smoking information from workers and their family members. Workers' vital status was ascertained from plant personnel

records and the municipal death registry. We calculated mortality rates of lung cancer and other selected causes based on person-years of observation, and constructed Cox proportional hazard model to estimate hazard ratios (HR) of cause-specific mortality associated with asbestos exposure (namely, asbestos workers *vs.* external controls; miners vs. internal controls), while taking into account age, smoking and asbestos exposure level (in the asbestos worker cohort). In addition, we estimated standardized mortality ratios (SMR) in both miner group and internal control group using national mortality rates in males.

Major results: *Asbestos worker cohort study*: we identified 259 (45%) deaths in the asbestos cohort and 96 died of all cancers. Lung cancer (n = 53) and nonmalignant respiratory diseases (n = 81) were major causes of deaths in asbestos workers, in contrast to 9 lung cancers and 11 respiratory diseases in the controls. Age and smoking adjusted HRs for mortality for all causes and all cancers in asbestos workers were 2.05 (95% CI, 1.56, 2.68) and 1.89 (1.25, 2.87), respectively. The risks for lung cancer and respiratory disease deaths in asbestos workers were over threefold that in the controls (HR = 3.31, 1.60, 6.87; HR= 3.23, 1.68, 6.22, respectively). There was a clear exposure-response trend of lung cancer mortality with asbestos exposure level in both smokers and nonsmokers.

In the stratifying analysis by three exposure levels, the greatest cancer mortality was observed in the high exposure level, with 1.5-fold age-adjusted mortality from all cancers and 2-fold from lung cancer compared to the low exposure level. Age and smoking adjusted hazard ratio in the high exposure group was 2.99 (95%CI, 1.30, 6.91) for lung cancer and 2.04 (1.12, 3.71) for all cancers. Both smokers and nonsmokers at the high exposure level had a high risk for lung cancer death, with a clearer exposure-response trend seen in smokers. The results indicated an increased mortality from lung cancer and all cancers in asbestos workers, and the cancer mortality was associated with asbestos exposure level.

Asbestos miner cohort study: All mortality rates of selected causes, particularly lung cancer, were substantially higher in the miner group than in the internal controls. SMRs

for lung cancer and nonmalignant respiratory diseases in the miners were 4.71 (95%CI, 3.57, 6.21) and 3.53 (2.78, 4.48), respectively. When compared to the national level (an external comparison), the controls had similar mortality rates of all causes, lung cancer, all cancers as national rates, but a higher mortality from non-malignant respiratory diseases. Asbestos exposure was related to a 4.6-fold mortality risk for lung cancer and over 3-fold risk for all cancers and respiratory diseases, after smoking and age were adjusted. There was a trend that SMRs of all selected causes were increased with exposure years, especially at entry. SMR of lung cancer was 7.46 for those with exposure years of 20 or more at entry, in contrast to 4.92 and 1.40 for those with less than 20 and less than 10 years, respectively. The greatest SMR of lung cancer (7.05) was observed in those with total exposure between 20 and 30 years. A similar trend was seen in respiratory diseases.

In the stratifying analysis by smoking status, greater SMRs for lung cancer were found in the miner group, regardless of smoking, though the greatest rate (5.45; 95% CI 4.11, 7.22) was observed in smoking miners. Synergy index of asbestos exposure and smoking was 3.26 with a statistical significance, indicating a significant interaction between the two factors, which was more than additive.

Conclusions: The data from the 37-yr prospective cohort of asbestos workers and 26-yr historical cohort of asbestos miners provided consistent results, showing substantially excessive cause-specific mortality, in particular for lung cancer and respiratory diseases, in asbestos exposed workers/miners. The study provides additionally strong and valuable evidence for the association between mortality of lung cancer (and all cancers and non-malignant respiratory diseases) and exposure to chrysotile asbestos.

This study has a strong implication to the current and future practice in Hong Kong and mainland. Chrysotile has not yet banned in Hong Kong, as well as in the mainland, although amphibole has been banned for more than a decade. The central and local government and public health agencies should take fast and active steps toward the ban of using all types of asbestos, so to achieve the goal of protecting the health of workers from occupational exposure and of general population from environmental exposure.