

Epidemiology Note

Incidence and Survival of Mesothelioma in Osaka, Japan

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Background: Mortality statistics show rapid increase in the number of deaths from mesothelioma. However, population-based study of the incidence and the survival has never been conducted. Time-trends and regional differences in the incidence of mesothelioma in Osaka were examined together with their 5-year survival.

Methods: Individual data for mesothelioma were retrieved from Osaka Cancer Registry during the period 1966–2001. Annual incidence rates were calculated for every 3 years from 1975 to 2001, and age-standardized rates were calculated with the Japanese model population of 1985. Standardized incidence ratios were also calculated by age-specific number of population of each municipality and the corresponding age-specific incidence rates of mesothelioma in Osaka Prefecture during the period 1981–2001. The survival analysis was performed with the Kaplan–Meier method, based on the newly reported cases diagnosed during the period 1975–1997.

Results: Incidence rates of mesothelioma have increased rapidly both among males and females in Osaka during the past few decades. Geographical differences in the standardized incidence ratios were found to be remarkable in Osaka Prefecture. The result shows that the survival of malignant mesothelioma was very poor (5-year survival and median survival time: 5.1% and 6 months for males, 10.2% and 5 months for females).

Conclusions: Incidence of mesothelioma has increased remarkably in Osaka, Japan, during past few decades. Geographical variations in the incidence were also suggested. Five-year survival of the patients was very poor.

Key words: mesothelioma – incidence – survival – time-trends

INTRODUCTION

National mortality statistics show rapid increase in the number of deaths from mesothelioma in Japan since 1995, when ICD 10th revision had just assigned unique codes to this tumor. It was 500 in 1995, and it increased to 953 in 2004 (1). Such remarkable increase suggests that it is closely related to the increase in the asbestos import and the use of their products in Japan (2). Osaka is one of the prefectures with the highest mortality from mesothelioma (<http://www.mhlw.go.jp/toukei/saikin/hw/jinkou/tokusyu/chuuhsy05/index.html>). Population-based study of the incidence and the survival has, however, not been conducted systematically so far in Japan. In this article, we describe the time-trends and regional

differences in the incidence of mesothelioma in Osaka, Japan, together with their 5-year survival, based on the data from the Osaka Cancer Registry (OCR), one of the oldest Japanese cancer registries with largest population.

SUBJECTS AND METHODS

Details of the OCR were described elsewhere (3). Briefly, it has operated since 1962, covering all Osaka Prefecture (population: 8.8 millions in 2000 census). Active follow-ups for vital status 5 years after diagnosis have been conducted for patients diagnosed since 1975 except for residents in Osaka city during the period 1975–1992. Individual data for mesothelioma were retrieved from the OCR database. Incidence data of 1966–2001 was used for time-trends analysis. Annual incidence rates were calculated for every 3 years from 1975

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to 2001, and age-standardized rates were calculated with the Japanese model population of 1985. Asbestos imports in Japan were calculated every 3 years from 1930 to 2001 through the Japan trade statistics from Japan Asbestos Association (2).

Regional differences in the incidence for mesothelioma were evaluated with standardized incidence ratios (SIRs), which were calculated by age-specific number of population of each municipality and the corresponding age-specific incidence rates of mesothelioma in Osaka prefecture during the period 1981–2001. To minimize random variations of SIRs, the regions were restricted to the municipalities with at least five incident cases of mesothelioma.

Five-year survival of mesothelioma in Osaka was calculated using the Kaplan–Meier method, based on the newly reported cases, whose cancer information at the initial diagnosis was notified, diagnosed during the period 1975–1997 (male = 298, female = 122).

Statistical analyses were conducted with STATA (4). Statistical difference for the incidence rate ratio (IRR) was tested by Poisson regression model after adjustment for covariates. Statistical significance of SIR was judged based on the Poisson distribution. Difference in the survival curves was evaluated with Log-rank test. Cox regression models were also employed for the survival analysis. Ninety-five percent confidence interval and statistical significance were all based on two-sided test.

RESULTS

Table 1 shows basic figures for the incidence of mesothelioma in Osaka, 1966–2001. Total number of the incidence was 686 for males and 263 for females. Male to female ratio was 2.61. Age was distributed somewhat younger for males than for females (mean age: 64.6 for males, 66.4 for females, $P = 0.055$). Most mesothelioma originated from pleura, while proportion of cases originated from peritoneum was larger for females than for males ($P < 0.001$). Newly reported cases were 71.0% of the total incidence, and death certificate only cases (DCOs) were 22.7%. If the study was divided into three periods with almost equal number of the incidence, proportion of DCOs was 17.5% in 1966–1992, 25.8% in 1993–1997 and 24.8% in 1998–2001. Proportion of histologically verified cases was 100, 100 and 99.7%, respectively. Mortality statistics showed that annual number of deaths from mesothelioma closely resembled the incidence in Osaka. The total number of deaths was 332 for males and 111 for females during the period 1995–2001, while the incidence to mortality ratio was 1.20 for males and 1.06 for females in this period.

Figure 1 shows time-trends in the amount of asbestos imports in Japan and the number of incidence cases for mesothelioma by sex in Osaka (5). The amount of asbestos imports increased substantially from the beginning of 1950s to the early 1970s, and after showing a biphasic fluctuation, it turned to decrease in 1988. Asbestos imports in Japan diminished to 0 in

Table 1. Basic figures for the incidence of mesothelioma in Osaka, 1966–2001

	Male N = 686 (%)	Female N = 263 (%)
Age (years)		
0–39	25 (3.6)	10 (3.8)
40–49	51 (7.4)	32 (12.2)
50–59	141 (20.6)	31 (11.8)
60–69	219 (31.9)	69 (26.2)
70–79	178 (25.9)	76 (28.9)
80+	73 (10.6)	45 (17.1)
Primary Site (ICD-0-T)		
Pleura (C45.0)	575 (83.8)	194 (73.8)
Peritoneum (C45.1)	47 (6.9)	43 (16.3)
Pericardium (C45.2)	11 (1.6)	4 (1.5)
Others (C45.7)	13 (1.9)	2 (0.8)
Unknown (C45.9)	40 (5.8)	20 (7.6)
Type of registration		
Newly reported	501 (73.0)	173 (65.8)
Recurrence only	42 (6.1)	18 (6.8)
Death certificate only	143 (20.9)	72 (27.4)

November 2004. The number of incidence started to increase remarkably for both sexes in the late 1970s. Interval was around 30–40 years between the times of exponential increase in the amount of asbestos imports and the times of exponential increase in the number of incidence for malignant mesothelioma.

Figure 2 shows age-specific incidence rates for mesothelioma by sex in Osaka, 1992–2001. The rates began to increase in the group of 40–49 for males and 50–59 for females, and then went up exponentially with getting older although showing down in the 80s and over. IRR for females was 0.287, significantly lower than that for males after adjustment for age ($P < 0.0005$).

Age-standardized incidence rates per 1000 000 also increased remarkably among both males (from 0.8 in 1975–1977 to 12.5 in 1999–2001) and females (from 0.30 to 3.0), while the increase among males was more prominent (Fig. 3).

Figure 4 showed geographical distributions of SIRs for mesothelioma (both sexes). The SIRs were grouped into 5 categories after excluding 14 municipalities with the number of incidence <5: SIR <0.70 (7 municipalities), <0.90 (16 municipalities), <1.2 (14 municipalities) <1.50 (6 municipalities), and 1.50 and over (10 municipalities). Significantly higher SIRs than 1.0 were observed in Nishiyodogawa-ward, Nishinari-ward, Yodogawa-ward and Hirano-ward.

Cumulative 5-year survival of mesothelioma is presented according to gender in Fig. 5. The median survival for females was 5 months, while that for males was 6 months. The 5-year survival was estimated to be 5.1% for males and 10.2% for females (Log-rank test for equality of survivor functions 2.73,

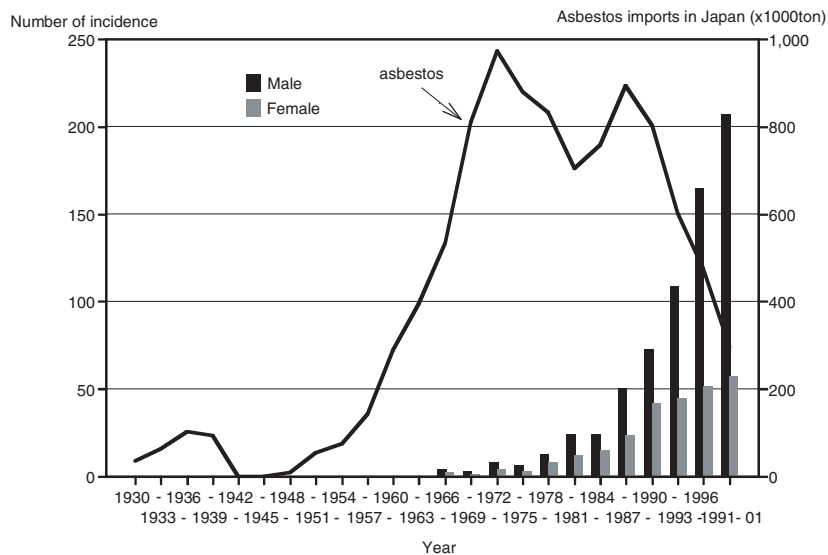


Figure 1. Time-trends in the amount of asbestos imports in Japan and the number of incidence cases for mesothelioma by sex in Osaka.

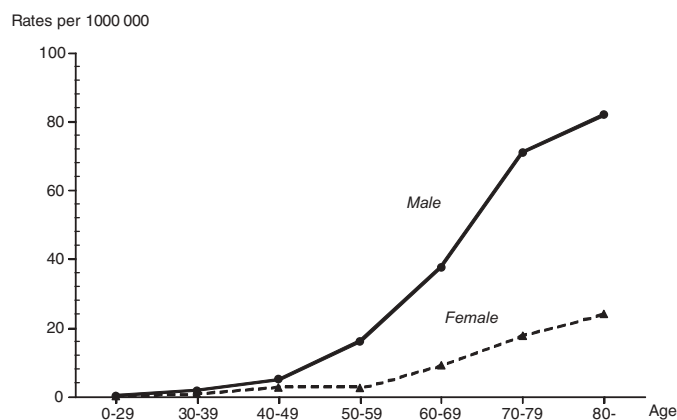


Figure 2. Age-specific incidence rates of mesothelioma by sex in Osaka, 1992–2001.

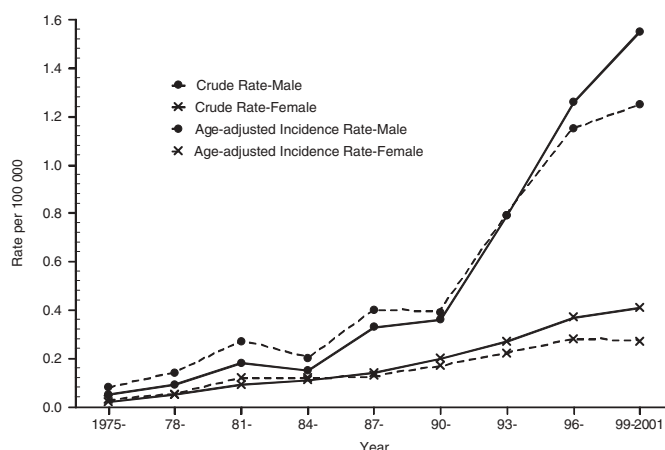


Figure 3. Time-trends of incidence rates for mesothelioma by sex in Osaka.

$P = 0.098$). Cox’s regression analysis indicated that age and primary site adjusted hazard rate ratio (HRR) was 0.828 for females (95% CI 0.658–1.042, $P = 0.109$) as compared with males. The cumulative 5-year survival was 5.4% for males and 6.0% for females if excluded for patients whose origin of mesothelioma was peritoneum.

DISCUSSION

The present study indicated that incidence rates of mesothelioma increased rapidly both among males and females in Osaka during past few decades, with 30–40 years time-lag after the rapid increase in asbestos import into Japan. Weill et al. (6) reported that age adjusted male incidence rates (2000 US standard population, per 100 000) of mesothelioma rose from 0.73 in 1973 to over 2.0 in the early 1990s in the US, and the rates have declined thereafter. Meanwhile the pattern of

asbestos use in the US indicated a relatively steep increase in the early 1970s, followed by a subsequent, relatively steep decline. They consider that the overall burden of asbestos health effects in the US is waning. Asbestos regulations and controls were delayed in Japan compared with those in the US. Assuming that Japan follows the same course as the US, the rates will continue to rise for some time.

Geographical differences in the SIRs were found to be remarkable even in Osaka Prefecture, which would be related to asbestos exposures in the municipalities. Japanese Ministry of Health, Labour and Welfare made an official announcement of the locations of the Labour Standard Inspection Offices which had jurisdiction over factories manufacturing asbestos products, having had made compensation for asbestos-related accidents. Significantly higher SIRs than 1.0 might be related to the locations of those factories, but we could not identify the locations of those factories, nor obtain any information on

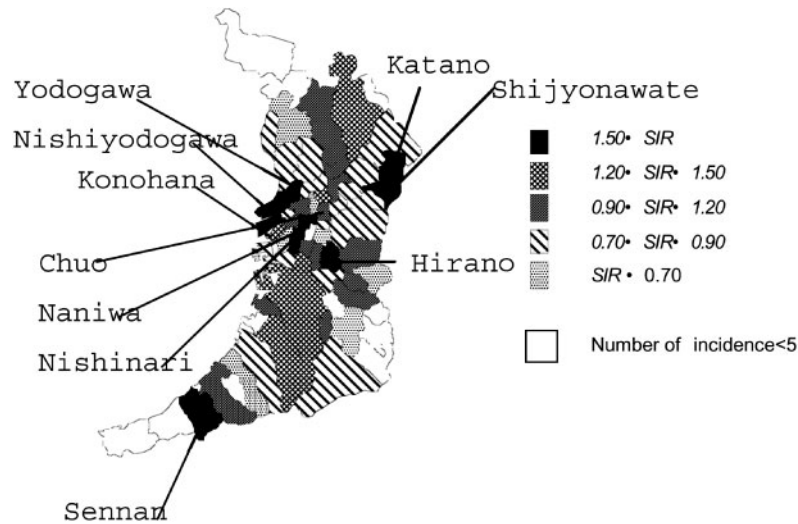


Figure 4. Geographical distributions of standardized incidence ratios for mesothelioma (both sexes) in Osaka, 1981–2001.

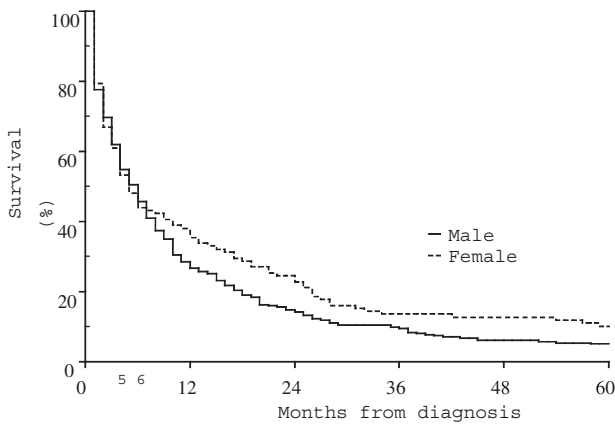


Figure 5. Cumulative 5-year survival of mesothelioma by sex in Osaka, 1975–1997.

what kind of asbestos was manufactured, and when, how long and how much asbestos were handled. Such information will be essential to evaluate the geographical distribution properly.

Significantly higher proportion of peritoneal mesothelioma was shown among females than among males. One of the reasons might be the possible misclassifications between the dissemination of ovarian epithelial cancer to the surface of the peritoneal cavity and peritoneal mesothelioma, since

differential diagnosis between them is said to be very difficult even for experienced pathologists (7).

Survival of mesothelioma was very poor for both sexes, while females showed slightly better 5-year survival than males. Such difference, however, diminished after exclusion of cases whose origins were peritoneum. Thus, it might be explained in part by misclassifications between the dissemination of ovarian epithelial cancer with better survival and peritoneal mesothelioma.

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