Shimane J. Med. Sci., Vol.27 pp.9-16, 2010

# Geographical Analysis of Pancreatic Cancer Mortality in Shimane Prefecture, Japan, 1985 to 2006

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(Received August 27, 2010; Accepted; October 13, 2010)

In this study, we investigated the mortality and localized clusters of deaths from pancreatic cancer in Shimane Prefecture, Japan from 1985 to 2006. The standardized mortality ratio of pancreatic cancer by year in Shimane Prefecture was significantly higher than that of the national population from 1991 to 1997 and from 2000 to 2004 in males, and from 1997 to 2000 in females. The Bayes estimates of standardized mortality ratio of pancreatic cancer by sex and municipality in Shimane Prefecture was high as more than 120 in 5 municipalities in males from 1985 to 1995, and in 4 municipalities in males and 3 municipalities in females from 1996 to 2006. The most likely cluster of pancreatic cancer was located in the central and eastern areas in males between 1985 and 1995 (relative risk=1.09, p=0.011) and between 1996 and 2006 (relative risk=1.27, p=0.004).

Key words: pancreatic cancer, EBSMR, spatial scan statistic, geographical aggregation, Shimane Prefecture

## INTRODUCTION

Pancreatic cancer has high incidence and mortality rates in advanced countries (1). In Japan, the age-adjusted mortality from pancreatic cancer has increased by approximately 9-fold in both sexes between 1950 and 1995 (2), and the number of pancreatic cancer deaths was fifth highest in males and sixth highest in females among the number of deaths from malignant neoplasm in 2006 (3). The mortality from pancreatic cancer is higher in males than females, and the mortality by age increases after the forties in both sexes (3, 4). The age-adjusted mortality from pancreatic cancer in Shimane Prefecture increased remarkably between 1970 and 2005, similar to the national population (Fig. 1)(5).

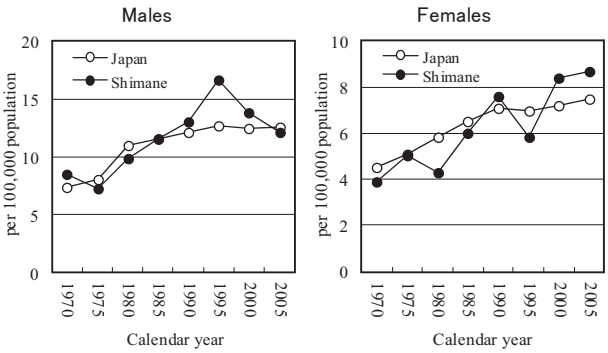


Fig. 1. Time trends of age-adjusted mortality for pancreatic cancer in Shimane Prefecture and Japan, 1970-2005.

Pancreatic cancer is often detected at an advanced stage and has a poor prognosis (4). As risk factors for pancreatic cancer, cigarette smoking is regarded to increase the risk (6, 7). Fernandez *et al*. considered that smoking cessation and improvement of dietary patterns could prevent one fourth of pancreatic cancer deaths (8). In addition, as risk factors associated with other diseases, familial history of pancreatic cancer (9), diabetes (6, 10), chronic pancreatitis (11, 12), and hereditary pancreatitis (13)have been reported. But the etiology of pancreatic cancer remains to be fully elucidated. Descriptions of geographical variation of disease may provide important

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clues about etiology (14). Therefore, epidemiological studies on geographical distribution of pancreatic cancer in Shimane Prefecture, as pancreatic cancer mortality has been increased recently, will be important for prevention measures.

In this study, as descriptive epidemiological study focused on geographical characteristics of pancreatic cancer mortality, we analyzed empirical Bayes estimates of standardized mortality ratio (EBSMR)and localized clusters of death from pancreatic cancer in Shimane Prefecture.

## MATERIALS AND METHODS

Malignant neoplasm of the pancreas has been coded as 157 from 1985 to 1994 according to the International Classification of Diseases (ICD-9th Revision)(15) and changed to C25 in 1995 (ICD 10th Revision)(16). The number of deaths from malignant neoplasm of the pancreas by year (1985-2006) and sex for each municipality in Shimane Prefecture and the total for Japan, as well as the number of deaths from 19 different malignant neoplasms by year (1997-2006) and sex in Shimane Prefecture and the total for Japan were obtained from the National Vital Statistics (17). The population or the estimates by year (1985-2006), sex and age in 21 municipalities in Shimane Prefecture and the total for Japan were obtained from the census or calculated by interpolation method, respectively.

The SMR of pancreatic cancer by year and sex for 22 years (1985-2006) in Shimane Prefecture was calculated on the basis of that of the national population, and shown as a moving average for 5 years (18). Two-sided 95% confidential interval (CI) for SMR was evaluated by multiplying by the coefficient based on Poisson's distribution (19). To examine geographical distribution of pancreatic cancer deaths among 21 municipalities in Shimane Prefecture, as a method to adjust the random fluctuation of SMR in municipalities with small populations, the EBSMR of pancreatic cancer by sex was calculated in the earlier period of 11 years (1985-1995) and the later period of 11 years (1996-2006). EBSMR was calculated according to Tango's method (20) based on Poisson-Gamma model, that assumes Poisson-distribution for deaths and gamma-distribution for prior distribution of the SMR. Moreover, to examine geographical aggregation, the flexible spatial scan statistic (21) of death from pancreatic cancer was conducted for each sex.

Analyses were performed using EB Estimator for Poisson-Gamma Model version 2.1 (22) and FleXScan version 2.0 (23). FleXScan detects all clusters for which p values are less than 1.0 by Monte Carlo Hypothesis testing (with $p<0.05$ as statistical significance).

## RESULTS

The SMRs of 19 malignant neoplasms by sex between 1997 and 2006 in Shimane Prefecture are shown in Table 1. In both sexes, the SMR of malignant neoplasms was significantly lower in Shimane Prefecture than in the national population. Significantly higher SMR was observed for malignant neoplasms of the liver, pancreas and bladder in males and pancreas in females. Although not statistically significant, SMR of esophagous cancer in men tended to be higher. Significantly lower SMR was observed for malignant neoplasms of the stomach and lung in males, and esophagus, colon, gallbladder, lung, breast and uterus in females. In both sexes, the SMR of pancreatic cancer in Shimane Prefecture was significantly higher than in the national population.

Fig. 2 shows the SMR of pancreatic cancer by year and sex for 18 years between 1987 and 2004 in Shimane Prefecture evaluated by moving-average method. The SMR was significantly higher in the 7-year period 1991-1997 and in the 5-year period 2000-2004 than that of the national population in males. In females, the SMR was significantly higher in the 4-year period 1997-2000. In Shimane prefecture, the SMR was higher than that of the national population in the 16-year period 1989-2004 in males.

To investigate the geographical distribution of pancreatic cancer death in Shimane Prefecture, the EBSMRs of pancreatic cancer by sex in 21 municipalities were evaluated for 22 years between 1985 and 2006. As shown in Table 2, there were 5 municipalities with EBSMR >120 for males in the earlier 11-year period 1985-1995. In the later 11-year period 1996-2006, the EBSMR >120 were observed in 4 municipalities for males and 3 municipalities for females (Table 3). The geographical patterns in

Table 1. The SMRs of malignant neoplasms for males and females in Shimane Prefecture, Japan, 1997-2006

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| | Observed deaths | SMR | 95% CI | Observed deaths | SMR | 95% CI |
| Malignant neoplasms | 13,907 | 97.5 * | 95.9 - 99.2 | 9,144 | 91.7 * | 89.9 - 93.6 |
| Oral cavity† | 270 | 98.0 | 87.2 - 110.6 | 116 | 93.5 | 71.0 - 120.6 |
| Esophagus | 704 | 107.2 | 99.6 - 115.4 | 95 | 70.0 * | 50.5 - 94.5 |
| Stomach | 2,383 | 93.8 * | 90.1 - 97.7 | 1,438 | 96.1 | 91.3 - 101.2 |
| Colon | 936 | 95.4 | 89.6 - 101.8 | 936 | 89.5 * | 84.0 - 95.5 |
| Rectum† | 583 | 97.7 | 90.2 - 106.0 | 409 | 105.3 | 95.7 - 116.2 |
| Liver† | 1,833 | 106.0 * | 101.2 - 110.9 | 893 | 99.6 | 93.3 - 106.4 |
| Gallbladder† | 558 | 95.8 | 88.2 - 104.1 | 669 | 89.3 * | 82.8 - 96.4 |
| Pancreas | 912 | 110.0 * | 103.1 - 117.4 | 856 | 108.5 * | 101.5 - 116.1 |
| Larynx | 60 | 79.5 | 48.6 - 122.4 | 5 | 69.9 | 14.4 - 204.0 |
| Lung† | 3,007 | 92.7 * | 89.5 - 96.1 | 1,011 | 78.2 * | 73.5 - 83.2 |
| Skin | 30 | 72.2 | 40.4 - 119.1 | 31 | 68.5 | 39.2 - 111.0 |
| Breast | - | - | - | 546 | 81.3 * | 74.9 - 88.5 |
| Uterus | - | - | - | 286 | 70.9 * | 63.3 - 79.7 |
| Ovary | - | - | - | 280 | 90.0 | 80.2 - 101.4 |
| Prostate | 666 | 96.3 | 89.4 - 104.0 | - | - | - |
| Bladder | 334 | 112.5 * | 101.3 - 125.5 | 135 | 91.5 | 70.9 - 116.1 |
| Central nervous system | 59 | 98.4 | 66.8 - 139.8 | 49 | 98.5 | 66.5 - 140.9 |
| Malignant lymphoma | 331 | 93.2 | 83.9 - 104.0 | 296 | 104.4 | 93.4 - 117.2 |
| Leukemia | 285 | 96.9 | 86.5 - 109.0 | 245 | 110.1 | 97.4 - 125.0 |

Values with an asterisk (*) are significantly different from those of the national population (95%CI>100 or 95%CI<100).
† Oral cavity, lips, oral cavity and phalynx. Rectum, rectosigmoid junction and rectum. Liver, liver and intrahepatic bile ducts. Gallbladder, gallbladder and other unspecified parts of biliary tract. Lung, trachea, bronchus and lung.

Table 2. EBSMR for pancreatic cancer by municipality and sex in Shimane Prefecture, Japan, 1985-1995

| | Males | | Females | |
|---|---|---|---|---|
| | Observed deaths | EBSMR | Observed deaths | EBSMR |
| Matsue | 242 | 119.7 | 120 | 100.6 |
| Hamada | 51 | 87.8 | 54 | 100.9 |
| Izumo | 133 | 119.8 | 93 | 93.7 |
| Masuda | 57 | 111.4 | 38 | 95.1 |
| Oda | 55 | 113.5 | 46 | 102.6 |
| Yasugi | 78 | 137.2 | 35 | 96.7 |
| Gotsu | 41 | 114.6 | 31 | 104.3 |
| Unnan | 32 | 78.2 | 30 | 86.8 |
| Higashiizumo | 16 | 124.1 | 6 | 100.0 |
| Okuizumo | 26 | 111.7 | 13 | 94.6 |
| Iinan | 17 | 134.4 | 6 | 98.5 |
| Hikawa | 36 | 112.9 | 21 | 109.7 |
| Kawamoto | 13 | 115.4 | 7 | 106.5 |
| Misato | 7 | 91.1 | 13 | 113.0 |
| Ohnan | 17 | 95.5 | 21 | 110.4 |
| Tsuwano | 13 | 87.7 | 14 | 106.0 |
| Yoshika | 11 | 102.8 | 8 | 97.6 |
| Ama | 8 | 123.0 | 7 | 113.3 |
| Nishinoshima | 6 | 113.6 | 6 | 106.1 |
| Chibu | 3 | 121.5 | 0 | 98.5 |
| Okinoshima | 18 | 102.5 | 18 | 103.1 |

Table 3. EBSMR for pancreatic cancer by municipality and sex in Shimane Prefecture, Japan, 1996-2006

| | Males | | Females | |
|---|---|---|---|---|
| | Observed deaths | EBSMR | Observed deaths | EBSMR |
| Matsue | 190 | 98.9 | 223 | 120.4 |
| Hamada | 85 | 107.1 | 76 | 103.2 |
| Izumo | 175 | 110.1 | 152 | 103.9 |
| Masuda | 63 | 99.3 | 66 | 109.3 |
| Oda | 54 | 96.9 | 64 | 109.7 |
| Yasugi | 92 | 151.0 | 60 | 111.4 |
| Gotsu | 54 | 132.1 | 30 | 95.5 |
| Unnan | 69 | 109.9 | 59 | 106.0 |
| Higashiizumo | 15 | 117.1 | 17 | 119.5 |
| Okuizumo | 29 | 116.0 | 33 | 121.7 |
| Iinan | 22 | 144.7 | 9 | 107.3 |
| Hikawa | 33 | 115.9 | 26 | 107.6 |
| Kawamoto | 10 | 118.8 | 8 | 110.5 |
| Misato | 15 | 119.2 | 10 | 106.3 |
| Ohnan | 21 | 99.3 | 13 | 92.5 |
| Tsuwano | 20 | 118.3 | 19 | 113.0 |
| Yoshika | 14 | 110.8 | 18 | 116.7 |
| Ama | 4 | 109.8 | 9 | 120.2 |
| Nishinoshima | 9 | 121.5 | 3 | 104.0 |
| Chibu | 0 | 107.8 | 2 | 111.9 |
| Okinoshima | 22 | 103.4 | 27 | 111.6 |

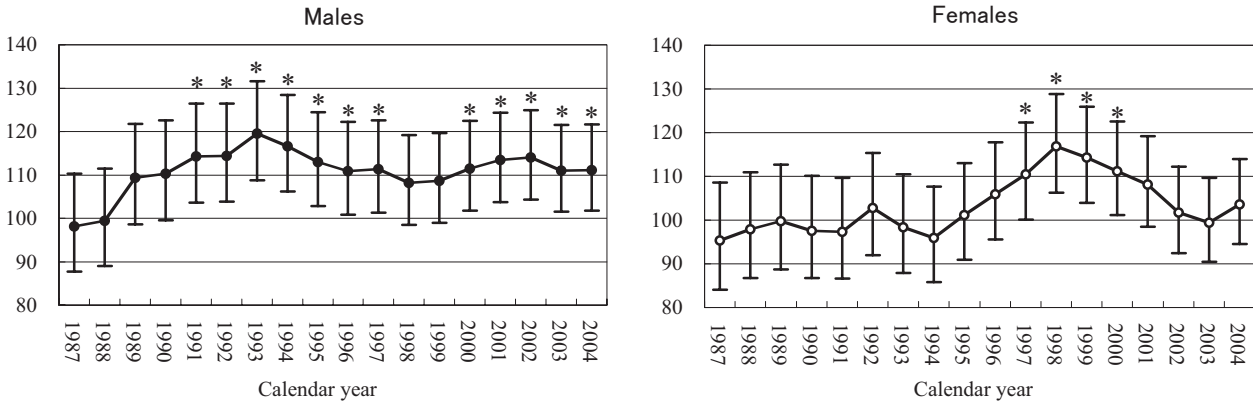


Fig. 2. The SMR of pancreatic cancer by year in Shimane Prefecture, Japan, 1987-2004. Values represent the moving average deviations for every five years. Vertical lines represent 95% CI. Values with an asterisk (*) are significantly different from those of the national population (95%CI>100 or 95%CI<100).

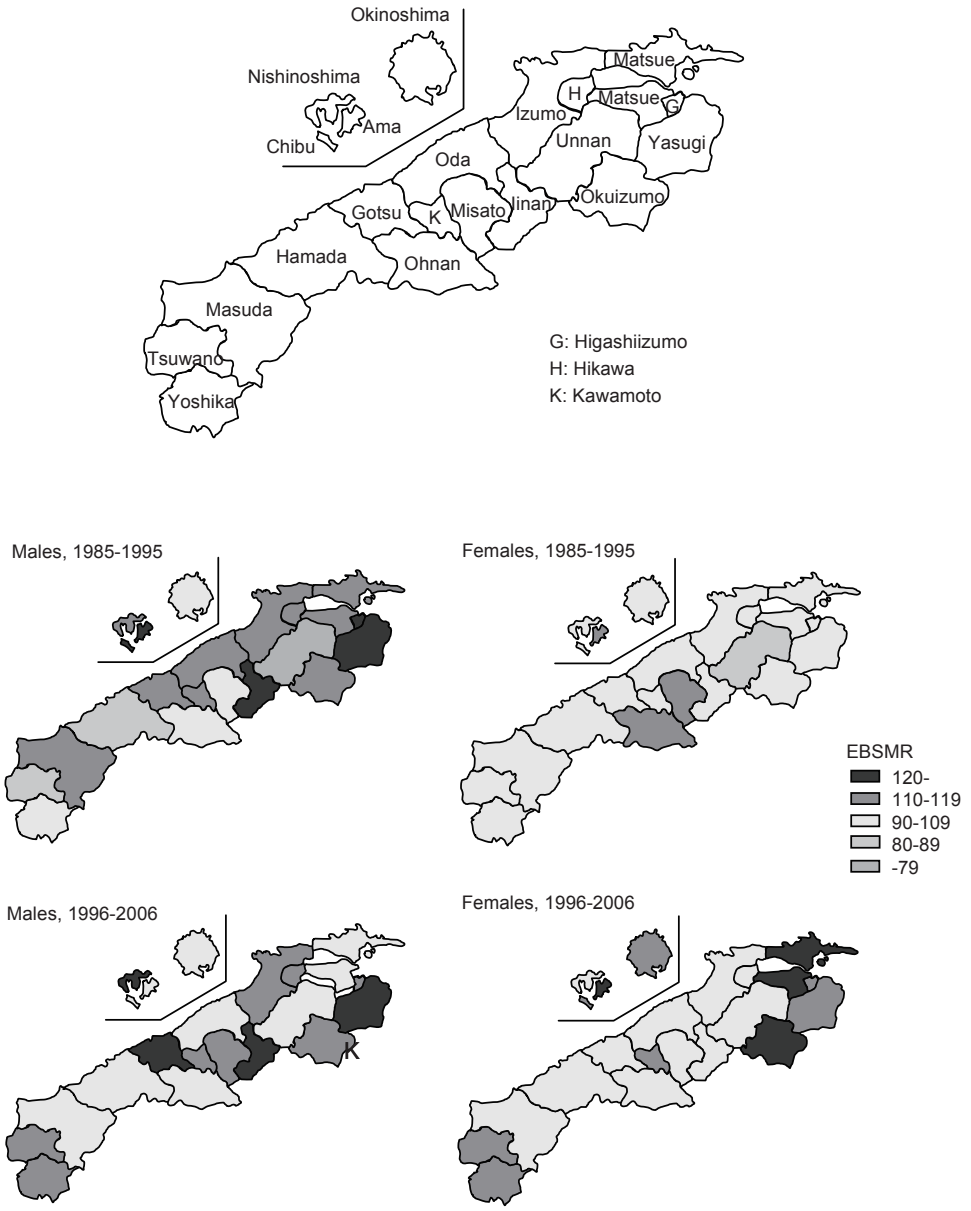


Fig. 3. Geographical distribution of EBSMRs of pancreatic cancer in 21 municipalities in Shimane Prefecture, Japan, 1985-2006.

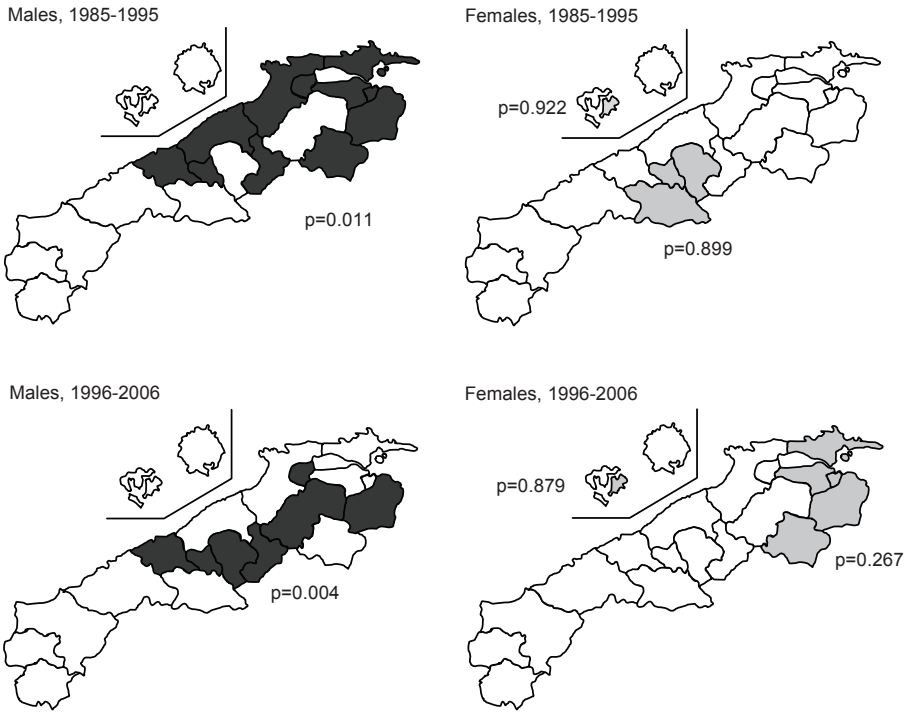


Fig. 4. Clusters of pancreatic cancer deaths detected using flexible spatial scan in 21 municipalities in Shimane Prefecture, Japan, 1985-2006.

EBSMR of pancreatic cancer were shown in Fig. 3. The EBSMR of pancreatic cancer showed high tendency especially in the central and eastern area in Shimane Prefecture for males in both 11-year periods. For females, the EBSMR high tendency was found in the eastern area in Shimane Prefecture in the later 11-year period.

The most likely and second clusters of pancreatic cancer mortality in Shimane Prefecture for 22 years between 1985 and 2006 were detected with the flexible spatial scan statistic (Table 4). For males, there was one statistically significant cluster of pancreatic cancer mortality during both 11-year periods, 1985-1995 and 1996-2006. Fig. 4 indicates, in the earlier 11-year period, the most likely cluster was extended from the central area to eastern area in Shimane Prefecture for males (relative risk (RR)=1.09, p=0.011). In the later 11-year period, the most likely cluster was found in from central to eastern area including mainly intermediate and mountainous area (RR=1.27, p=0.004). For females, 2 clusters, which were not statistically significant,

Table 4. Spatial clusters of mortality for pancreatic cancer using flexible spatial scan statistic for males and females in Shimane Prefecture, Japan, 1985-2006

| Cluster | Approximate cluster location | Number of municipalities | Expected cases | Observed cases | Relative risk | p value |
|---|---|---|---|---|---|---|
| Males (n=880), 1985-1995 | | | | | | |
| Most likely cluster | East of Shimane Prefecture (Yasugi to Gotsu) | 10 | 600.4 | 657 | 1.09 | 0.011 |
| Second cluster | - | - | - | - | - | - |
| Females (n=587), 1985-1995 | | 3 | | | | |
| Most likely cluster | Central region of Shimane Prefecture (Misato to Ohnan) | 3 | 30.4 | 41 | 1.35 | 0.899 |
| Second cluster | Ama | 1 | 3.2 | 7 | 2.17 | 0.922 |
| Males (n=996), 1996-2006 | | 7 | | | | |
| Most likely cluster | East of Shimane Prefecture (Yasugi to Gotsu) | 7 | 218.9 | 277 | 1.27 | 0.004 |
| Second cluster | - | - | - | - | - | - |
| Females (n=924), 1996-2006 | | | | | | |
| Most likely cluster | East of Shimane Prefecture (Yasugi to Okuizumo) | 4 | 291.2 | 333 | 1.14 | 0.267 |
| Second cluster | Ama | 1 | 4.4 | 9 | 1.83 | 0.879 |

were observed during each 11-year period (Table 4). As shown in Fig. 4, in the earlier 11-year period, the most likely cluster for females was located in the intermediate and mountainous part in the central area of Shimane Prefecture (RR=1.35, p=0.899). In the later 11-year period, the most likely cluster for females was found in the eastern area in the Shimane Prefecture (RR=1.14, p=0.267).

## DISCUSSION

In Shimane Prefecture, the SMR of pancreatic cancer was significantly higher than that of the national population in both sexes in the last decade between 1997 and 2006. The SMR of pancreatic cancer in Shimane Prefecture in males continued to be high from 1987 to 2004. The EBSMR of pancreatic cancer by municipality showed tendency to be high especially in the central and eastern area in Shimane Prefecture for both sexes between 1985 and 2006. The flexible spatial scan statistic detected the statistically significant cluster of pancreatic cancer mortality in the central and eastern area in Shimane Prefecture for males.

In previous studies about geographical distribution of the mortality of pancreatic cancer, Kato *et al*. reported that the age-adjusted mortality from cancer of the pancreatic head by prefecture was high in Hokkaido and Tohoku, the northern part of Japan, between 1979 and 1987 (24). Then, Seino *et al*. reported that the age-adjusted mortality from pancreatic cancer by prefecture was high in Hokkaido and Tohoku during 1968 and 2002 (25). Moreover, Seino *et al*. observed that in addition to these areas, the Sea of Japan areas including Niigata Prefecture and Shimane Prefecture tended to have high SMR of pancreatic cancer during 1998 and 2002 (26). In accordance with the report, our study revealed that SMR of pancreatic cancer for males in Shimane Prefecture has continued to be significantly high since 1989. In addition, the SMR in both sexes showed a significant increase during the last decade from 1997 to 2006.

In our study, geographical distribution of the EBSMR of pancreatic cancer by 21 municipalities in Shimane Prefecture tended to be high in municipalities located in the central and eastern area of Shimane Prefecture in both sexes between 1996 and 2006. In addition, the geographical clustering of pancreatic cancer mortality detected the statistically significant cluster in the central and eastern area for male between 1985 and 2006. The geographical patterns of pancreatic cancer provide a valuable source of information that can help in formulating etiological hypothesis. As the study of all of Japan, a significant positive correlation between the smoking rate by prefecture during the decade between 1986 and 1995 and the mortality from pancreatic cancer in 1995 in Japan was reported (27). Besides, Kinoshita *et al.* (28) examined the correlation between the SMR of pancreatic cancer by prefecture from 1998 to 2002 and the amount of global solar radiation and the daily maximum temperature in 2006. The results showed an inverse correlation between the SMR of pancreatic cancer and the amount of global solar radiation and the daily maximum temperature, suggesting that climatic factors might be related to pancreatic cancer risk. In Shimane Prefecture, however, the smoking rate was comparable with the national average for males and far lower than the national averages for females (27), therefore smoking is unlikely to be a main reason of the high mortality of pancreatic cancer in Shimane Prefecture. The area with low global solar radiation and low daily maximum temperature does not necessarily correspond to the area with high morality of pancreatic cancer in Shimane Prefecture.

It is very difficult to detect pancreatic cancer in the early stage by general health examination because of the low incidence rate and lack of typical early symptoms. However, defining a high-risk group of pancreatic cancer may enable effective early detection and treatment. As risk factors for pancreatic cancer, smoking (6, 7), incidence rate of diabetes (6, 10) and pancreatitis (11-13), familial history of pancreatic cancer (9) and lifestyle such as high cholesterol intake (29), dietary fat of animal origin (30, 31) and alcohol consumption (32) have been reported. To elucidate the etiology and pathogenic mechanism of pancreatic cancer in Shimane Prefecture, it is necessary to evaluate the association with various suspected factors in more detail. Elucidation of the characteristic risk factors associated with pancreatic cancer in Shimane Prefecture may

enable prevention and early detection by targeting those risk factors effectively in each area. In Shimane Prefecture, a population-based cancer registry has just been started, and this upgrading and utilization may enable more detailed analysis.

In conclusion, our study revealed that the SMR of pancreatic cancer for both sexes in Shimane Prefecture was significantly higher than that of the national population. In Shimane Prefecture, areas with significantly higher mortality of pancreatic cancer were detected. With these results, it is anticipated that risk factors of pancreatic cancer characteristic of Shimane Prefecture may be elucidated for prevention and early detection of pancreatic cancer. Additionally, because some municipalities with high EBSMR of pancreatic cancer and geographical clusters of the mortality were detected along the prefecture's border with Shimane Prefecture, more investigations are needed to elucidate geographical aggregation by comparing the geographical distribution of the EBSMRs of pancreatic cancer and the geographical clustering in neighboring prefectures.

## REFERENCES


1) Michaud DS (2004) Epidemiology of pancreatic cancer. *Minerva Chir* 59: 99-111.

2) Lin Y, Tamakoshi A, Wakai K, Kawamura T, Aoki R, Kojima M and Ohno Y (1998) Descriptive epidemiology of pancreatic cancer in Japan. *J Epidemiol* 8: 52-59.

3) The Editorial Board of Cancer Statistics in Japan. Cancer Statistics in Japan 2008. (Cited 5 Nov 2008) Available from URL: ganjoho.ncc.go.jp/public/statistics/backnumber/2008_jp.html (in Japanese).

4) Tanaka M (2007) Pancreatic Cancer Registry Report 2007, *Suizo* 22: e1-427 (in Japanese).

5) Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare, Japan (2007) Age-adjusted death rates by prefecture, Specified Report of Vital Statistics, 2005. Tokyo: Health and Welfare Statistics Association (in Japanese).

6) Luo J, Iwasaki M, Inoue M, Sasazuki S, Otani T, Ye W and Tsugane S; JPHC Study Group (2007) Body mass index, physical activity and the risk of pancreatic cancer in relation to smoking status and history of diabetes: a large-scale population-based cohort study in Japan--the JPHC study. *Cancer Causes Control* 18: 603-612.

7) Lin Y, Tamakoshi A, Kawamura T, Inaba Y, Kikuchi S, Motohashi Y and Kurosawa M; JACC Study Group. Japan Collaborative Cohort (2002) A prospective cohort study of cigarette smoking and pancreatic cancer in Japan. *Cancer Causes Control* 13: 249-54.

8) Fernandez E, La Vecchia C and Decarli A (1996) Attributable risks for pancreatic cancer in northern Italy. *Cancer Epidemiol Biomarkers Prev* 5: 23-27.

9) Klein AP, Brune KA, Petersen GM, Goggins M, Tersmette AC, Offerhaus GJ, Griffin C, Cameron JL, Yeo CJ, Kern S and Hruban RH (2004) Prospective risk of pancreatic cancer in familial pancreatic cancer kindreds. *Cancer Res* 64: 2634-2638.

10) Lin Y, Tamakoshi A, Kawamura T, Inaba Y, Kikuchi S, Motohashi Y, Kurosawa M and Ohno Y (2002) Risk of pancreatic cancer in relation to alcohol drinking, coffee consumption and medical history: findings from the Japan collaborative cohort study for evaluation of cancer risk. *Int J Cancer* 99: 742-746.

11) Kitagawa M (2004) Pancreatic cancer and chronic pancreatitis. *KAN-TAN-SUI* 48:591-597 (in Japanese).

12) Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, Dimagno EP, Andrén-Sandberg A and Domellöf L (1993) Pancreatitis and the risk of pancreatic cancer. International Pancreatitis Study Group. *N Engl J Med* 328: 1433-1437.

13) Whitcomb DC, Applebaum S and Martin SP (1999) Hereditary pancreatitis and pancreatic carcinoma. *Ann N Y Acad Sci* 880: 201-209.

14) Lawson AB and Kulldorff M (1999) A review of cluster detection methods. In: Disease Mapping and Risk Assessment for Pablic Health. (Lawson AB, Biggeri A, Bohning D, Lesaffre E, Viel JF and Bertollini R, ed.) pp. 99-110, John Wiley & Sons, New York.

15) World Health Organization. (1977) Manual of international statistical classification of diseases,

injuries, and causes of death. Based on the recommendations of the ninth revision conference, 1975, adopted by twenty-nine World Health Assembly. World Health Organization, Geneva.

16) World Health Organization (1992) International statistical classification of diseases and related health problems, 10th revision (ICD-10), volume 1. World Health Organization, Geneva.

17) Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare, Japan (1985-2005) Vital Statistics of Japan 1985-2005. Health and Welfare Statistics Association, Tokyo (in Japanese).

18) Fukutomi K and Hashimoto S (2008) Health statistics-Epidemiology, 4th revision. Nanzando, Tokyo.

19) Schoenberg BS (1983) Calculating confidence intervals for rates and ratios. *Neuroepidemiology* 2: 257-265.

20) Tango T (1999) Disease mapping and spatial disease clustering. J Natl Inst Public Health 48: 84-93 (in Japanese).

21) Tango T and Takahashi K (2005) A flexibly shaped spatial scan statistic for detecting clusters. *Int J Health Geogr* 4: 11.

22) Takahashi K (2009) EB estimator for Poisson-Gamma model. National Institute of Public Health, Japan. Available from: http://www.niph.go.jp/soshiki/gijutsu/download/ebpoig/index_j.html

23) Takahashi K, Yokoyama T and Tango T (2009) FleXScan v3.0: Software for the Flexible Scan Statistic. National Institute of Public Health, Japan. Available from: http://www.niph.go.jp/soshiki/gijutsu/download/flexscan/index_j.html

24) Kato I, Kuroishi T and Tominaga S (1990) Descriptive epidemiology of subsites of cancers of the liver, biliary tract and pancreas in Japan. *Jpn J Clin Oncol* 20: 232-237.

25) Seino T, Nakadaira H, Endoh K and Yamamoto M (2008) Changes in pancreatic cancer mortality, period patterns, and birth cohort patterns in Japan: analysis of mortality data in the period 1968-2002. *Environ Health Prev Med* 13: 234-242.

26) Seino T, Nakadaira H, Endoh K and Yamamoto M (2006) Descriptive epidemiologic studies on geographical clusterings of pancreatic cancer mortality and incidence. *Jpn J Hyg* 61: 366-74 (in Japanese).

27) Asahi S, Oki I, Tanihara S, Ojima T, Nakamura Y, Okayama A, Matsumura Y and Yanagawa H (2001) Relationship between smoking rates and mortality rate from diseases by prefecture. *J Health Welfare Stat* 48: 11-15 (in Japanese).

28) Kinoshita S, Wagatsuma Y and Okada M (2007) Geographical distribution for malignant neoplasm of the pancreas in relation to selected climatic factors in Japan. *Int J Health Geogr* 6: 34.

29) Lin Y, Tamakoshi A, Hayakawa T, Naruse S, Kitagawa M and Ohno Y (2005) Nutritional factors and risk of pancreatic cancer: a population-based case-control study based on direct interview in Japan. *J Gastroenterol* 40: 297-301.

30) Thiébaut AC, Jiao L, Silverman DT, Cross AJ, Thompson FE, Subar AF, Hollenbeck AR, Schatzkin A and Stolzenberg-Solomon RZ (2009) Dietary fatty acids and pancreatic cancer in the NIH-AARP diet and health study. *J Natl Cancer Inst* 101: 1001-1111.

31) Heinen MM, Verhage BA, Goldbohm RA and van den Brandt PA (2009) Meat and fat intake and pancreatic cancer risk in the Netherlands Cohort Study. *Int J Cancer* 125: 1118-1126.

32) Silverman DT, Brown LM, Hoover RN, Schiffman M, Lillemoe KD, Schoenberg JB, Swanson GM, Hayes RB, Greenberg RS, Benichou J, Schwartz AG, Liff JM and Pottern LM (1995) Alcohol and pancreatic cancer in blacks and whites in the United States. *Cancer Res* 55: 4899-4905.