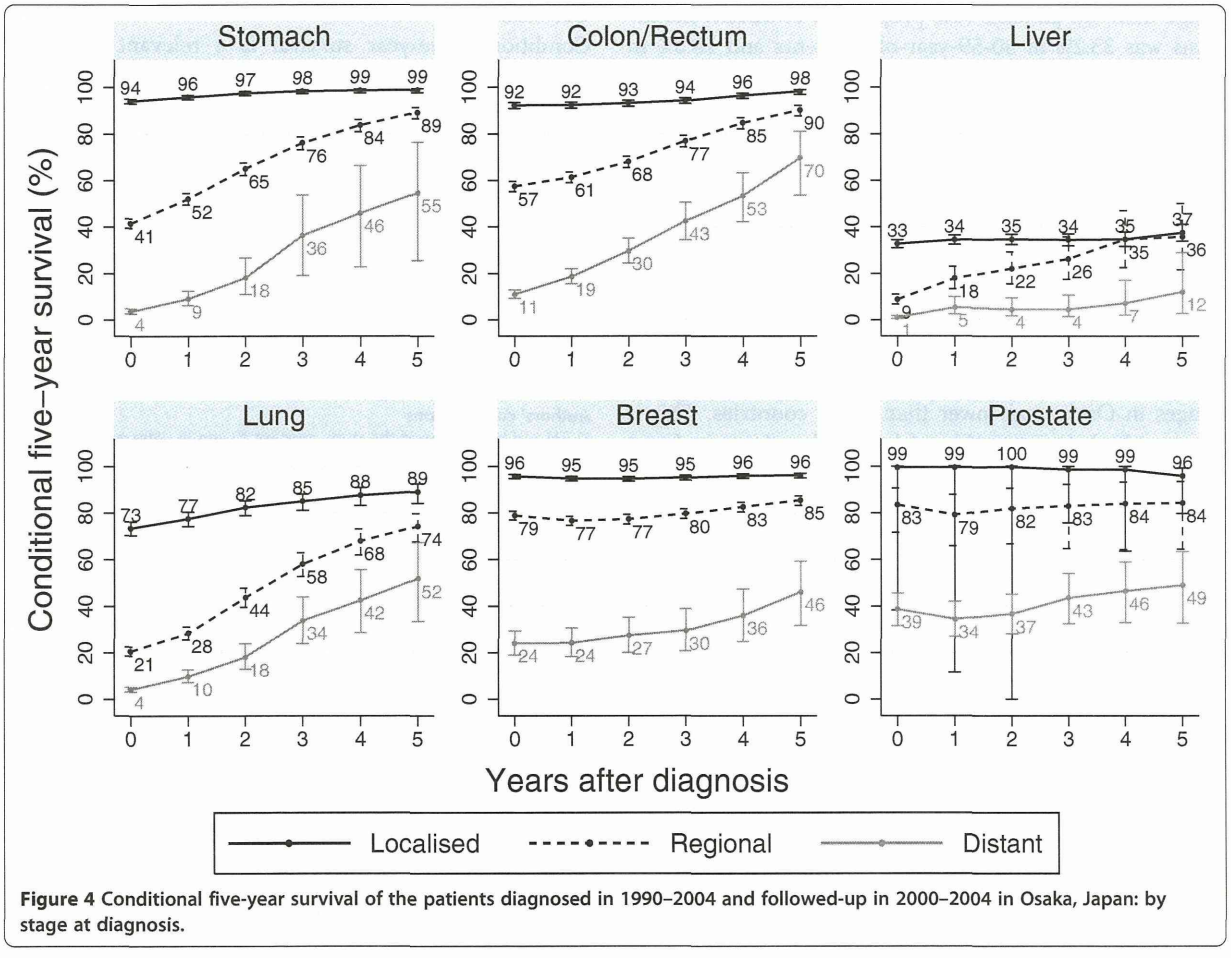

Figure 4 Conditional five-year survival of the patients diagnosed in 1990–2004 and followed-up in 2000–2004 in Osaka, Japan: by stage at diagnosis.

However, the figures were lower than those for stomach and colorectal cancer. This was because lung cancer patients have a higher risk of death due to complications related to cancer or cancer risk (smoking), such as ischemic heart disease.

Breast and prostate cancer

Conditional five-year survival rates for all cases of both breast and prostate cancer were around 80-90%, due to the higher proportion of localised patients in all cases. Conditional five-year survival for localised prostate cancer patients slightly decreased five years after diagnosis. This could be partly explained by the recurrence or progression of tumours during long-term follow-up. For these cancers, we need to follow-up patients for a longer period.

Liver cancer

Conditional survival for liver cancer was much lower than for other cancers at any stage or age after several years. Even in localised patients, conditional five-year survival was less than 40% after five years. This is probably because many liver cancer patients experienced a recurrence of cancer, or died from liver cirrhosis or liver failure related to the hepatitis B or C virus.

Effect of age and stage at diagnosis

Trends in conditional survival by age group were quite similar except for liver and prostate cancer. For most cancers, age did not significantly affect conditional survival. In the case of liver cancer, conditional survival for young patients (15–49 years old) was higher than for old patients (60–69 years old) after several years. This could be explained by the fact that the old patients had been exposed to hepatitis viruses for long time; as a result, they tended to develop liver cirrhosis and liver failure more than young patients. Conditional survival of young prostate cancer patients (50–59 years old) was lower than old patients (60–69 years old). This is probably because young patients are diagnosed at a more advanced

stage than old patients (the proportion of distant metastasis was 35.2% in 50-59-year-old patients and 28.3% in 60-69-year-old patients).

The conditional survival curve was different by stage; stage at diagnosis was an important prognostic factor. Conditional survival for localised patients was stable at 85-95%, while for regional and distant metastasis patients it increased after several years of diagnosis.

Trends in conditional survival for breast and colorectal cancer patients in Osaka were similar to other countries (shown in Additional file 1: Figures S1-S4 from Australia [2,6], US [8], Canada [5,11] and European countries [3,9]). Conditional survival for prostate cancer at all stages in Osaka was lower than other countries. This is due to the low proportion of localised patients in Japan compared to other countries. Conditional survival of stomach cancer for all stage and localised in Osaka was higher than in Australia [2]. Stomach cancer patients in Osaka were diagnosed at an earlier stage than in Australia (e.g. 51% patients diagnosed at localised stage in Osaka, 28% in Australia). In addition, approximately half of the stomach cancer patients in Japan were diagnosed at T1 (UICC TNM classification) [23]. Therefore we can estimate a higher proportion of T1 in localised patients in Osaka than in Australia. Higher conditional survival for localised patients can be partly explained by differences in tumour. This may be due to stomach cancer screening programmes [24] and wide use of endoscopy in clinical settings in Japan. Conditional survival of localised lung cancer in Osaka was higher than in other countries. This could be explained by differences in tumour size and histology [25,26]. Conditional survival for liver cancer patients in Canada increased some years after diagnosis [11], while in Osaka it was stable at low survival. This can be explained by the differences in etiological factor among these countries. In the US and Canada, prevalence of hepatitis B or C viruses in liver cancer cases was lower than in Japan [27]. Liver cancer patients in Japan might have greater likelihood of liver failure or hepatitis-related cirrhosis than those in the US and Canada.

Conditional five-year survival for stomach and colorectal cancer patients who were alive five years after diagnosis was about 100%; this means those patients have similar survival probability to the general population. Therefore those patients can be considered as 'cured'. For other sites of cancer, further long-term follow-up time may be needed to estimate 'cured' time.

Conditional survival is an important statistic for planning long-term life after diagnosis, not only for cancer patients and their families, but also patients with other diseases. However, a population-based disease registry system, such as the population-based cancer registry, is essential to estimate this type of statistic.

Conclusion

Conditional five-year survival is a relevant figure for long-term cancer survivors in Japan. It is important for population-based cancer registries to provide figures which cancer patients and oncologists really need.

Additional file

Additional file 1: Figure S1-S4. Comparison of conditional survival between countries, by site and stage.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

YI, TN and HT developed the study concept. YI and IA were responsible for data management and statistical analysis. TN, IM and HT reviewed the clinical background of the results. YI wrote the draft of the report. All authors critically reviewed and revised the manuscript.

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Descriptive Epidemiology of Bile Duct Carcinoma in Osaka

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Objective: An outbreak of bile duct carcinoma has been reported among workers in a certain printing company in Osaka, Japan, where there was no descriptive epidemiological study. We conducted descriptive studies of bile duct carcinoma in Osaka.
Methods: Based on the data from the Osaka Cancer Registry, the incidence and survival rate of intrahepatic and extrahepatic bile duct carcinomas, gallbladder carcinomas and hepatocellular carcinomas were analyzed. The study period was between 1975 and 2007, and total 108 407 incidents were retrieved from the Osaka Cancer Registry. Age- and sex-specific incidence rates and age-standardized incidence rates were calculated. Standardized incidence ratios were evaluated for each municipality in Osaka prefecture. Relative 5-year survival rates were also calculated for the cases diagnosed between 1993 and 2005.
Results: Age-standardized incidence rates of bile duct carcinomas increased distinctly from the middle of the 1970s to the early 1980s in males and the 1990s in females. However, no distinct increase in the incidence rates was observed in 2000. Standardized incidence ratios of those did not exceed the unity significantly in males between 1992 and 2007. In females, standardized incidence ratios exceeded the unity significantly in a few regions without any relation to the location of the printing company where the outbreak was reported. The relative 5-year survival rate is generally poor; however, patients who were diagnosed with localized disease at the age of 25–49 years showed a better survival.
Conclusion: Neither change in trend nor regional accumulation of bile duct carcinoma was confirmed in Osaka, corresponding to the outbreak reported in the printing company.

Key words: bile duct carcinoma – incidence – relative survival rate – cancer registry

INTRODUCTION

An outbreak of bile duct carcinoma has been reported among workers in a certain printing company in Osaka (1). There have been neither descriptive epidemiological studies nor reports of relative survival of patients with intrahepatic and/or extrahepatic bile duct carcinomas in Osaka, Japan. This study describes characteristics of bile duct carcinoma in Osaka, Japan, and examined whether any change in the time trend and disproportional geographical distribution was recognized in relation to the outbreak.

PATIENTS AND METHODS

The analysis was made using the data from the Osaka Cancer Registry between 1975 and 2007. Totally, 108 407 incidence data were retrieved; coded ICD-10 C22.1 (Intrahepatic bile duct carcinoma), C23 (malignant neoplasm of gallbladder), C24.0 (extrahepatic bile duct carcinoma) and C22.0 (hepatocellular carcinoma). Among those 108 407 cases, newly reported cases were 78 762. C22.9 (Malignant neoplasm of liver, unspecified) were 1.1% of C22 (malignant neoplasm of liver and intrahepatic bile ducts), while C24.1 (malignant

Table 1. Outlines of the newly reported cases with hepatocellular, intrahepatic, gallbladder and extrahepatic bile duct carcinomas, Osaka 1975–2007

		Hepatocellular n = 61315				Intrahepatic bile duct n = 3095				Gallbladder n= 7836				Extrahepatic bile duct n = 6516			
		Male		Female		Male		Female		Male		Female		Male		Female	
		n = 45898		n = 15417		n = 1797		n = 1298		n = 2801		n = 5035		n = 3638		n = 2878	
Age	Mean ± SE	63.7 ± 0.05		68.9 ± 0.08		66.5 ± 0.21		68.0 ± 0.34		69.2 ± 0.21		70.9 ± 0.16		68.9 ± 0.19		72.0 ± 0.22	
			%		%		%		%		%		%		%		%
	0–24	38	0.1	23	0.1	0	0.0	2	0.2	1	0.04	1	0.02	1	0.03	7	0.2
	25–29	38	0.1	14	0.1	1	0.1	3	0.2	5	0.2	4	0.1	4	0.1	1	0.0
	30–34	102	0.2	25	0.2	5	0.3	7	0.5	6	0.2	6	0.1	8	0.2	5	0.2
	35–39	315	0.7	53	0.3	16	0.9	10	0.8	20	0.7	23	0.5	19	0.5	9	0.3
	40–44	826	1.8	149	1.0	37	2.1	24	1.8	40	1.4	53	1.1	44	1.2	33	1.1
	45–49	2148	4.7	296	1.9	78	4.3	47	3.6	77	2.7	137	2.7	98	2.7	71	2.5
	50–54	4591	10.0	618	4.0	155	8.6	91	7.0	140	5.0	244	4.8	200	5.5	128	4.4
	55–59	7277	15.9	1314	8.5	225	12.5	125	9.6	246	8.8	354	7.0	342	9.4	193	6.7
	60–64	8630	18.8	2210	14.3	259	14.4	156	12.0	329	11.7	535	10.6	512	14.1	253	8.8
	65–69	8772	19.1	3082	20.0	339	18.9	203	15.6	466	16.6	745	14.8	588	16.2	406	14.1
	70–74	6789	14.8	3114	20.2	309	17.2	217	16.7	519	18.5	855	17.0	615	16.9	441	15.3
	75–79	3905	8.5	2359	15.3	222	12.4	190	14.6	459	16.4	873	17.3	537	14.8	496	17.2
	80–84	1736	3.8	1338	8.7	99	5.5	122	9.4	295	10.5	663	13.2	419	11.5	430	14.9
	85 +	1462	3.2	822	5.3	52	2.9	101	7.8	198	7.1	542	10.8	251	6.9	405	14.1
Year of diagnosis	1975–1991	18548	40.4	5116	33.2	443	24.7	352	27.1	1048	37.4	2073	41.2	1164	32.0	933	32.4
	1992–2007	27350	59.6	10301	66.8	1354	75.3	946	72.9	1753	62.6	2962	58.8	2474	68.0	1945	67.6
Age 25–45	Total	1565	3.4	285	1.8	74	4.1	49	3.8	78	2.8	103	2.0	94	2.6	53	1.8
Year of diagnosis	1975–1991	979	(5.3)	169	(3.3)	39	(8.8)	23	(6.5)	47	(4.5)	60	(2.9)	55	(4.7)	28	(3.0)
	1992–2007	586	(2.1)	116	(1.1)	35	(2.6)	26	(2.7)	31	(1.8)	43	(2.1)	39	(1.6)	25	(1.3)
Extent of disease																	
Stage	Localized	21578	47.0	7655	49.7	441	24.5	312	24.0	403	14.4	691	13.7	699	19.2	490	17.0
	Regional	6420	14.0	1938	12.6	602	33.5	434	33.4	1220	43.6	2183	43.4	1487	40.9	1175	40.8
	Distant	5779	12.6	1635	10.6	448	24.9	326	25.1	801	28.6	1531	30.4	595	16.4	528	18.3
	Unknown	12121	26.4	4189	27.2	306	17.0	226	17.4	377	13.5	630	12.5	857	23.6	685	23.8
Surgery	Yes	7522	16.4	1953	12.7	624	34.7	439	33.8	1158	41.3	2077	41.3	1477	40.6	954	33.1
	No	35494	77.3	12405	80.5	1099	61.2	805	62.0	1525	54.4	2776	55.1	2004	55.1	1804	62.7
	Unknown	2882	6.3	1059	6.9	74	4.1	54	4.2	118	4.2	182	3.6	157	4.3	120	4.2

neoplasm of ampulla of Vater), C24.8 (malignant neoplasm of overlapping lesion of biliary tract) and C24.9 (malignant neoplasm of biliary tract, unspecified) were 16.8, 0.1 and 5.8% of C24 (malignant neoplasm of other and unspecified parts of biliary tract), respectively.

The age of diagnosis was grouped by 5-year range for those who were between 25 and 84 and those data were obtained every 3-year interval. The age-standardized incidence rates (ASRs) were calculated by using Japanese 1985 model population as a standard. Standardized incidence rates (SIRs) of each municipality in Osaka were calculated using the age-specific incidence rates of Osaka as unity, and tested whether statistically significant differences existed with a 0.05 significance level, on Poisson's distribution.

Relative 5-year survival time and median survival time (MST) were calculated for each group (25–49, 50–74 and 75–99), and the extent of disease (localized, regional and distant) (2) for the cases was diagnosed between 1993 and 2005, who were followed up for at least 5 years after the diagnosis.

RESULTS

Outlines of the Study Subjects

Outlines of the newly reported cases are shown in Table 1. The proportion of the cases between 25 and 45 years, the same age range at which workers in the printing company in Osaka were diagnosed with bile duct carcinomas, was 3.0% for hepatocellular carcinoma (males 3.4%, females 1.8%), 4.0% for intrahepatic bile duct carcinoma (males 4.1%, females 3.8%), 2.3% for gallbladder carcinoma (males 2.8%, females 2.0%) and 2.3% for extrahepatic bile duct carcinoma (males 2.6% females 1.8%). The female-to-male ratios were 0.34, 0.72, 1.80 and 0.79, respectively.

Trends of ASRs and Age-specific Incidence Rates

ASRs of the intrahepatic bile duct carcinoma in both males and females rapidly increased from the year 1975 to the 1990s, and turned to decrease in the beginning of 2000 (Figure 1). ASRs of the extrahepatic bile duct carcinoma increased remarkably until the early 1980s, and then has become almost plateau from the beginning of 1990s in males. In females, the ASR increased until the early 1980s, and plateaued or decreased slightly thereafter (Figure 1). For the gallbladder carcinoma, ASRs had increased since 1975, plateaued in the 1980s and then decreased later. Age-specific incidence rates of both the intrahepatic and extrahepatic bile duct carcinomas have never increased since around 2000 (Figure 2). Incidence rates of intrahepatic and extrahepatic bile duct carcinomas were higher in males than in females (Figure 2).

SIR of Each Municipality in Osaka

SIRs of the bile duct carcinomas combined with intrahepatic and extrahepatic bile duct carcinomas did not exceed the unity significantly in males between 1992 and 2007 (Figure 3). SIRs

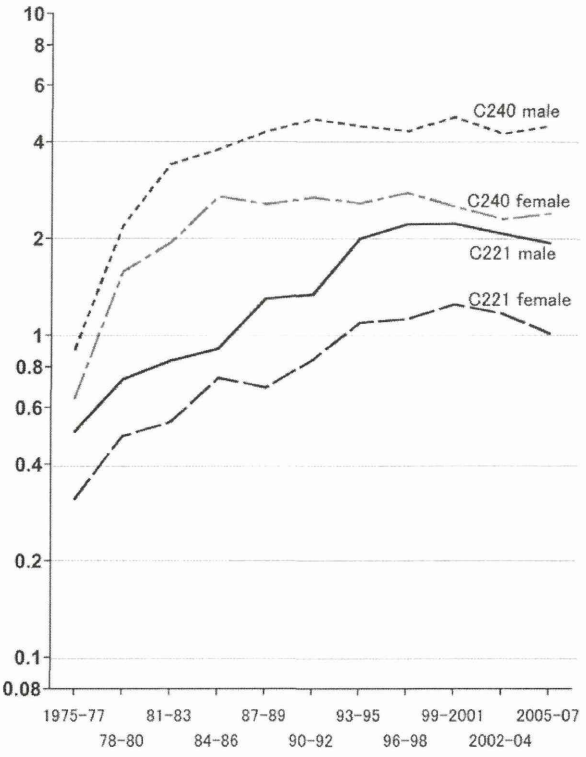

Figure 1. Age-standardized incidence rates (ASRs per 100 000 Japanese 1985 model population) of intrahepatic and extrahepatic bile duct carcinomas in Osaka, 1975–2007.

in females were significantly higher than the unity in Higashi-yodogawa-ku (ward) and Suminoe-ku. In Chuo-ku, where that printing company is located, SIRs of the bile duct carcinoma were 1.11 (95%CI 0.79–1.44) in males and 1.10 (95%CI 0.75–1.44) in females. Any SIR (not shown) never exceeded significantly than the unity.

Relative 5-year Survival and MST

Relative 5-year survival is generally poor among patients who are diagnosed with bile duct carcinoma in Osaka between 1993 and 2005. Some patients who were 25–49 years old with localized disease showed a better survival: 52.7% for the intrahepatic bile duct carcinoma and 76.4% for the gallbladder carcinoma, although they show a poor survival: 26.9% for the extrahepatic bile duct carcinoma. The difference in the relative survival of patients with localized disease between the age groups 25–49 and 50–74 was getting smaller, in the order of intrahepatic bile duct carcinoma, gallbladder carcinoma and extrahepatic bile duct carcinoma. There was no remarkable difference in relative survival among the age groups for regional and distant diseases, except regional cases of the extrahepatic bile duct carcinoma. In the age group of 25–49, the MST of the patients with intrahepatic bile duct carcinoma was 8.0 months for the regional and 6.0 months for the distant, while the MST of the patients with extrahepatic bile duct carcinoma was 16.4 months for the regional and 6.0 months for the distant (Figure 4).

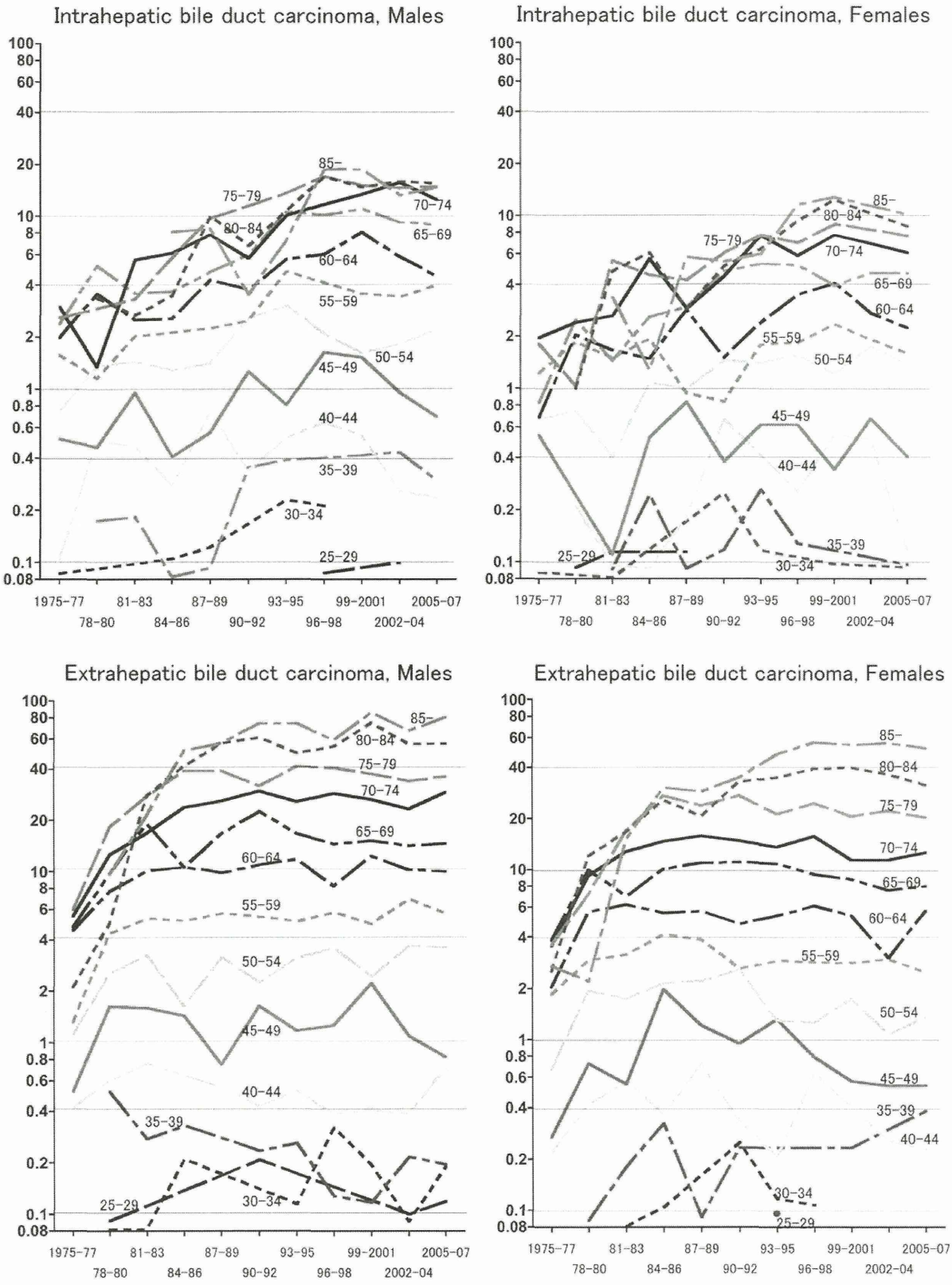

Figure 2. Age-specific incidence rates (per 100 000 population) of intrahepatic and extrahepatic bile duct carcinomas in Osaka, 1975–2007.

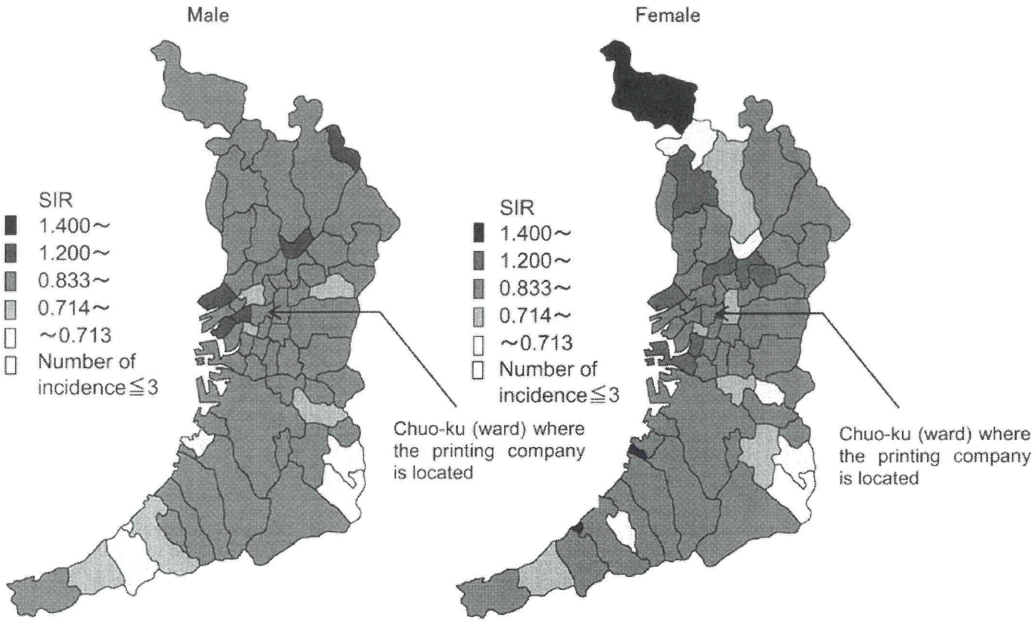

Figure 3. Standardized incidence ratios (SIRs) of bile duct carcinomas (C22.1 + C24.0) by municipality in Osaka, 1992–2007.

DISCUSSION

This study presented descriptive epidemiological profiles of bile duct carcinoma in Osaka, Japan, where the outbreak of bile duct carcinoma has been reported among workers in a printing company. Observed findings did not support any change in the time trend and disproportional geographical distribution related to the outbreak.

Advantages and Limitations of This Study

Osaka Cancer Registry has provided reliable and high-quality incidence data for a long period. This enabled us to examine incidence and survival of bile duct carcinoma in Osaka for over 30 years. Possible underreporting to the Osaka Cancer Registry may lead to lower estimation of cancer incidence and survival; however, cancers with poor survival are not caused by this bias. Therefore, we consider that our findings are reliable.

Our study did not support that any change in the time trend and disproportional geographical distribution was recognized in relation to the outbreak; however, this does not mean that such outbreak has never affected the environment. Exposure must be widely distributed and more people might have been exposed to some extent, according to the exert impact of the incidence rate. Although this study has some limitations to evaluate the effect of the outbreak, the geographical cluster analysis may be a suitable procedure to approach this problem.

Reason of the High Incidence of Bile Duct Carcinoma

ASRs of biliary tract cancer had increased since 1975, and reached peak or plateau in the 1980s to 1990s. These increases starting in 1975 were considered to be caused mainly by the improved diagnostic image techniques, such as endoscopic retrograde cholangiopancreatography (3), ultrasonography, computed tomography and magnetic resonance cholangiopancreatography (MRCP) (4,5). The detection rate for bile duct carcinoma by MRCP has been reported to be over 90% (6). In the USA, the increased incidence of the intrahepatic bile duct carcinoma between 1973 and 1997 was reported (7), and they have suggested that this might be related to increase in metabolic syndrome. However, this explanation is unlikely in Japan.

Survival of Bile Duct Carcinoma

Relative 5-year survival is generally poor among patients with bile duct carcinoma in Osaka. However, patients aged 25–49 years with localized disease showed a better survival: 52.7% for the intrahepatic bile duct carcinoma and 76.4% for the gallbladder carcinoma. The Biliary Tract Cancer Statistics Registry (8) in Japan reported that 5-year survival of extrahepatic biliary tract cancer patients with Stage I was >60% after surgical resection. These results suggest the importance of early detection and surgical resection for a better prognosis in the biliary tract cancer. To detect this cancer in the early stage, it will be necessary to build a screening system for high-risk workers by skilled clinical staffs.

Funding

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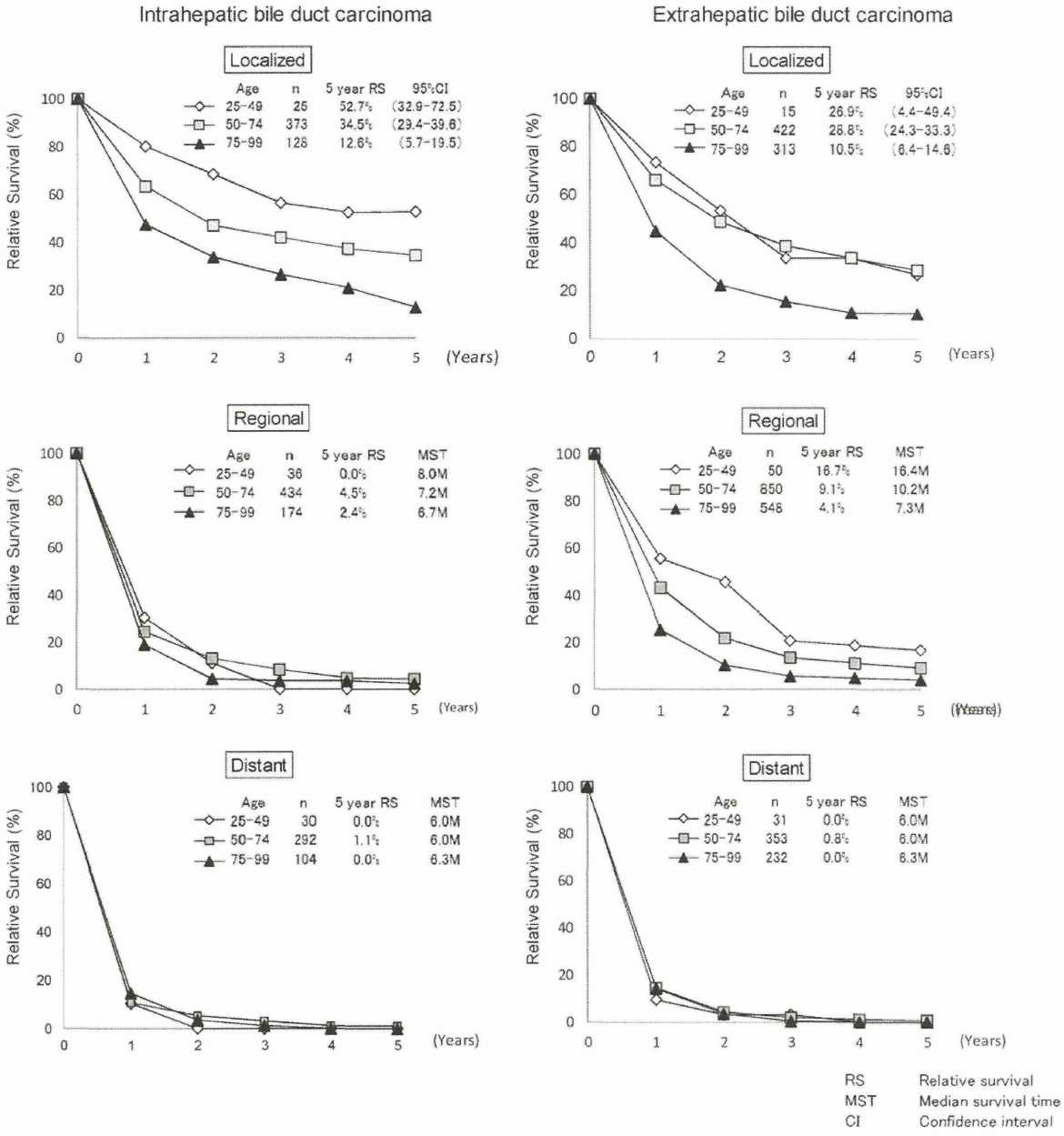

Figure 4. Relative survival of intrahepatic and extrahepatic bile duct carcinomas in Osaka, cases, 1993–2005.

Conflict of interest statement

None declared.

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Epidemiology Note

Incidence of Soft Tissue Sarcoma Focusing on Gastrointestinal Stromal Sarcoma in Osaka, Japan, During 1978–2007

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To clarify the incidence of soft tissue sarcoma and gastrointestinal stromal sarcoma in Osaka, Japan, we analyzed Osaka Cancer Registry's data. We identified a total of 6998 cases, except for those of bones and joints, during 1978–2007. The age-adjusted incidence rate of those sarcomas was 2.7 per 100 000 (male 2.8, female 2.6) person-years. The trend in the incidence for the last 10-year period (1998–2007) increased significantly overall and for females, while it was not significant for males. Except for cases not otherwise specified, the most prevalent histological subtype was leiomyosarcoma in digestive organs and gastrointestinal stromal sarcoma, followed by leiomyosarcoma excluding that in digestive organs and liposarcoma. Gastrointestinal stromal sarcomas were registered for the first time in 1988 and have increased since 1999, while leiomyosarcomas in digestive organs have decreased. Gastrointestinal stromal sarcoma might have been diagnosed as leiomyosarcoma in digestive organs before using immunohistochemistry.

Key words: soft tissue sarcoma – gastrointestinal stromal sarcoma – incidence – population-based cancer registry

INTRODUCTION

Soft tissue sarcomas (STSs) are rare mesenchymal neoplasms with heterogeneous differentiation and those may arise in various organs. In the last two decades, diagnosis of subtyping for STSs advanced significantly, because of the accumulating knowledge of molecular mechanisms of the oncogenic mutations as well as the application of immunohistochemical techniques, especially for leiomyosarcomas. Hirota et al. at Osaka University Medical School first found that a large proportion of gastrointestinal stromal tumors (GISTs) were positive for a c-kit gene product, KIT receptor tyrosine kinase (KT) and had gain-of-function mutation of the c-kit gene (1,2). In this study, we examined the incidence rates of STSs in Osaka prefecture, and clarified whether the diagnosis with the new techniques reflected their trends by histological group.

SUBJECTS AND METHODS

We employed data from Osaka Cancer Registry (OCR), which started in 1962 and covered all Osaka Prefecture (2010 Census population 8.7 millions, 7% of Japanese population). Details of the registration procedures and the methods were described elsewhere (3). Data quality and reliability have been fairly satisfactory, and cancer incidence data in Osaka have been accepted for publication in Cancer Incidence in five continents from volume 3 in 1976 to volume 9 in 2007 (4).

We retrieved all incident cases of STS during 1978–2007, except for those of bones and joints. In OCR, topography and morphology of the neoplasm are corded according to third edition of the International Classification of Diseases for Oncology (ICD-O) (5). Its histological classification of STS is in accordance with the WHO classification of STS, 2002 (6)