Table 2. Characteristics of corpus cancer patients by area-based socioeconomic status (SES)

Factor	Percentage of male unemployment in each municipality				Percentage of college or graduate school graduates in each municipality			
	Low	Middle	High	*P*-value	High	Middle	Low	*P*-value
No. of patients	906	1225	982		1127	1292	694	
Mean age (years)	55	56	58	0.357	56	56	57	0.385
Age (years)				<0.0001				0.039
Under 40	64 (7.1)	60 (4.9)	37 (3.8)		60 (5.3)	66 (5.1)	35 (5.0)	
40–49	188 (20.8)	233 (19.0)	162 (16.5)		219 (19.4)	245 (19.0)	119 (17.2)	
50–59	355 (39.2)	527 (43.0)	374 (38.1)		449 (39.9)	539 (41.7)	268 (38.6)	
60–69	196 (21.6)	271 (22.1)	243 (24.7)		258 (22.9)	292 (22.6)	160 (23.0)	
70–79	81 (8.9)	103 (8.4)	133 (13.5)		108 (9.6)	119 (9.2)	90 (13.0)	
80+	22 (2.4)	31 (2.6)	33 (3.4)		33 (2.9)	31 (2.4)	22 (3.2)	
Cancer stage				0.005				0.009
Localized	623 (68.7)	749 (61.1)	599 (61.0)		756 (67.1)	803 (62.1)	412 (59.4)	
Regional	148 (16.3)	256 (20.9)	190 (19.3)		200 (17.8)	261 (20.2)	133 (19.1)	
Distant	63 (7.0)	104 (8.5)	85 (8.7)		77 (6.8)	102 (7.9)	73 (10.5)	
Unknown	72 (8.0)	116 (9.5)	108 (11.0)		94 (8.3)	126 (9.8)	76 (11.0)	
Histology				0.401				0.994
Squamous carcinomas	12 (1.3)	23 (1.9)	12 (1.2)		16 (1.4)	20 (1.6)	11 (1.6)	
Adenocarcinomas	712 (78.6)	963 (79.0)	747 (76.1)		887 (78.7)	1002 (78.0)	532 (76.7)	
Other specific carcinomas	40 (4.4)	51 (4.2)	38 (3.9)		46 (4.1)	50 (3.9)	32 (4.6)	
Sarcomas	39 (4.3)	50 (4.1)	52 (5.3)		48 (4.3)	83 (4.6)	34 (4.9)	
Other	103 (11.4)	133 (10.8)	133 (13.5)		130 (11.5)	137 (11.9)	85 (12.2)	
Treatment				0.005				<0.0001
Surgery alone	324 (35.8)	399 (32.6)	364 (37.1)		403 (35.8)	443 (34.3)	241 (34.7)	
Radiation alone	16 (1.8)	27 (2.2)	26 (2.7)		23 (2.0)	23 (1.8)	23 (3.3)	
Chemotherapy alone	15 (1.7)	39 (3.2)	24 (2.4)		19 (1.7)	40 (3.1)	19 (2.7)	
Surgery + radiation	59 (6.5)	108 (8.8)	84 (8.6)		79 (7.0)	122 (9.4)	50 (7.2)	
Surgery + chemotherapy	364 (40.2)	454 (37.1)	318 (32.4)		438 (38.9)	456 (35.3)	242 (34.9)	
Radiation + chemotherapy	7 (0.8)	10 (0.8)	14 (1.4)		9 (0.8)	14 (1.1)	8 (1.2)	
Surgery, radiation + chemotherapy	66 (7.3)	111 (9.1)	71 (7.2)		88 (7.8)	107 (8.3)	53 (7.6)	
Other treatments	8 (0.9)	7 (0.6)	5 (0.5)		8 (0.7)	6 (0.5)	6 (0.9)	
Unknown	47 (5.2)	70 (5.7)	76 (7.7)		60 (5.3)	81 (6.3)	52 (7.5)	

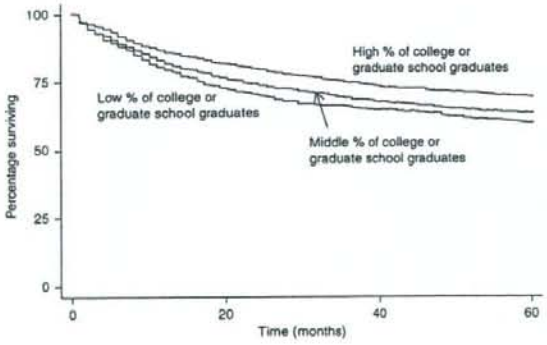

Fig. 4. Kaplan–Meier survival curves by socioeconomic status (SES) (education) for corpus cancer patients.

Table 4 shows cumulative 5-year survival by cancer stage and SES for cervical cancer patients. Survival differences by area SES were apparent for localized and regional stage cancers. However, SES differences were not seen for survival following distant stage tumors. In contrast, cumulative 5-year survival differences by SES (education) were not apparent for corpus cancer (Table 4).

Prognostic factors may confound the association between area SES and survival. Table 5 shows the univariate and multivariate analyses for the effects of area-based SES on cumulative 5-year survival for cervical cancer patients. In models 1, 2 and 3, area-based SES (both unemployment and education) was significantly related to cumulative 5-year survival for cervical cancer patients, although the effect of SES came with the addition of control variables. However, even after controlling for age, cancer stage, histology and treatment, survival differences between high and low SES still remained (model 3). For example, in model 3 cervical cancer patients in high unemployment municipalities had a 31% higher hazard ratio for mortality compared with patients in low unemployment municipalities. Cervical cancer patients in low education municipalities had a 17% higher hazard ratio compared with patients in high education municipalities. Table 6 shows the univariate and multivariate analyses for the effects of area-based SES on cumulative 5-year survival among corpus cancer patients. We did not enter histology as a covariate in models 2 and 3 because the distribution of histology for corpus cancer patients did not vary by area-based SES. Differences in survival for corpus cancer patients between low and high unemployment municipalities still remained after controlling for age and cancer stage (model 2) as well as after control for age, cancer stage and treatment (model 3).

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Table 3. Cumulative 5-year percentage survival by clinical factors for cervical and corpus cancer patients

Factor	Cervical cancer			Corpus cancer		
	5-year survival (%)	95% CI	*P*-value	5-year survival (%)	95% CI	*P*-value
Age (years)			<0.0001			<0.0001
Under 40	81.7	(79.6–83.5)		81.4	(73.6–87.0)	
40–49	73.0	(71.3–74.7)		77.5	(73.6–81.0)	
50–59	62.5	(60.7–64.2)		72.8	(70.0–75.4)	
60–69	56.3	(54.4–58.2)		54.2	(50.3–58.0)	
70–79	41.3	(38.9–43.7)		39.1	(33.6–44.6)	
80+	21.8	(18.1–25.8)		21.0	(12.9–30.4)	
Cancer stage			<0.0001			<0.0001
Localized	82.0	(81.0–82.9)		81.6	(79.6–83.3)	
Regional	38.6	(37.1–40.1)		41.8	(37.6–45.9)	
Distant	7.3	(5.3–9.7)		11.3	(7.8–15.6)	
Unknown	53.4	(50.5–56.2)		51.9	(4.5–5.8)	
Histology			<0.0001			<0.0001
Squamous carcinomas	65.1	(64.2–66.1)		48.9	(33.1–63.0)	
Adenocarcinomas	54.8	(51.0–58.2)		69.7	(67.6–71.6)	
Other specific carcinomas	63.6	(57.2–69.2)		67.1	(58.0–74.7)	
Sarcomas	–	–		29.5	(21.8–37.5)	
Other	28.1	(25.2–31.0)		45.0	(39.5–50.4)	
Treatment			<0.0001			<0.0001
Surgery alone	91.4	(90.3–92.3)		81.6	(78.9–84.0)	
Radiation alone	44.4	(42.4–46.5)		36.4	(25.0–47.9)	
Chemotherapy alone	7.2	(4.2–11.1)		6.5	(2.4–13.5)	
Surgery + radiation	66.4	(64.2–68.4)		61.6	(54.7–67.8)	
Surgery + chemotherapy	73.3	(70.1–76.2)		65.4	(62.3–68.2)	
Radiation + chemotherapy	31.5	(29.0–34.2)		24.3	(10.7–40.7)	
Surgery, radiation + chemotherapy	50.9	(48.3–53.5)		45.5	(38.9–51.8)	
Other treatments	72.2	(62.2–80.1)		55.9	(30.8–75.0)	
Unknown	50.1	(46.0–54.0)		42.0	(34.4–49.4)	

CI, confidence interval.

Table 4. Cervical and corpus cancer cumulative 5-year percentage survival by cancer stage and area-based socioeconomic status (SES)

	Percentage of male unemployment in each municipality				Percentage of college or graduate school graduates in each municipality			
	Low	Middle	High	*P*-value	High	Middle	Low	*P*-value
Cervical cancer stage								
Localized	86.2	83.3	73.9	<0.0001	84.5	81.3	79.5	0.0004
Regional	44.3	40.1	32.9	<0.0001	41.3	39.3	34.5	0.0002
Distant	7.7	8.9	5.4	0.503	7.9	9.1	4.4	0.297
Unknown	56.3	56.7	48.0	0.027	51.3	56.4	51.7	0.239
All stages	68.9	64.3	50.9	<0.0001	65.1	62.2	56.1	<0.0001
Corpus cancer stage								
Localized	85.8	83.7	71.8	<0.0001	83.8	81.1	78.0	0.075
Regional	44.9	48.4	29.4	0.0002	44.8	39.1	42.4	0.447
Distant	17.5	11.7	6.2	0.063	14.3	12.2	7.0	0.117
Unknown	62.2	54.8	38.6	0.022	53.0	49.9	54.1	0.400
All stages	72.4	66.7	51.7	<0.0001	69.2	62.9	59.2	0.0001

Discussion

In this population-based analysis of a metropolitan representative sample in Japan, we have shown substantial socioeconomic disparities in survival following cervical and corpus cancer, which remained statistically significant even after controlling for age, cancer stage, histology and treatment. We have also shown differences in the distribution of cancer stage, histology and treatment by SES in cervical cancer, as well as differences in the distribution of cancer stage and treatment following corpus cancer.

Many studies have indicated a significant association between low SES and poorer cancer survival in Western countries,[3] including the well-established socioeconomic disparities in survival among breast cancer patients in the USA.[20] The association between low SES and poorer survival

Table 5. Effects of area-based socioeconomic status (SES) on cervical cancer cumulative 5-year survival estimated by Cox proportional hazards regression models

Independent variable	Unemployment Univariate Hazard ratio (95%CI)	Model 1 Hazard ratio (95%CI)	Model 2 Hazard ratio (95%CI)	Model 3 Hazard ratio (95%CI)	Education Univariate Hazard ratio (95%CI)	Model 1 Hazard ratio (95%CI)	Model 2 Hazard ratio (95%CI)	Model 3 Hazard ratio (95%CI)
Area-based SES[†]								
High	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Middle	1.19 (1.10–1.29)	1.15 (1.07–1.24)	1.11 (1.23–1.20)	1.08 (0.99–1.17)	1.10 (1.03–1.18)	1.09 (1.02–1.17)	1.06 (0.99–1.13)	1.05 (0.95–1.12)
Low	1.80 (1.67–1.95)	1.59 (1.47–1.72)	1.39 (1.28–1.50)	1.31 (1.21–1.42)	1.36 (1.26–1.47)	1.29 (1.20–1.40)	1.21 (1.12–1.31)	1.17 (1.09–1.27)
Age (years)								
Under 40	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
40–49	1.56 (1.35–1.79)	1.56 (1.36–1.79)	1.31 (1.14–1.50)	1.24 (1.08–1.43)	1.56 (1.35–1.79)	1.55 (1.35–1.78)	1.31 (1.14–1.50)	1.24 (1.08–1.43)
50–59	2.32 (2.03–2.65)	2.25 (1.97–2.56)	1.56 (1.36–1.78)	1.31 (1.15–1.50)	2.32 (2.03–2.65)	2.30 (2.02–2.63)	1.58 (1.38–1.80)	1.32 (1.16–1.51)
60–69	2.80 (2.46–3.20)	2.66 (2.33–3.03)	1.82 (1.59–2.08)	1.39 (1.22–1.60)	2.80 (2.46–3.20)	2.77 (2.43–3.16)	1.85 (1.62–2.11)	1.40 (1.23–1.61)
70–79	4.29 (3.75–4.90)	4.61 (3.56–4.65)	2.57 (2.21–2.90)	1.75 (2.28–3.17)	4.29 (3.75–4.90)	4.24 (3.71–4.85)	2.58 (2.25–2.95)	1.77 (1.53–2.03)
80+	7.85 (6.71–9.19)	7.42 (6.34–8.69)	4.06 (3.46–4.76)	2.69 (2.77–3.22)	7.85 (6.71–9.19)	7.76 (6.63–9.08)	4.16 (3.54–4.88)	2.72 (2.31–3.21)
Cancer stage								
Localized	1.00		1.00	1.00	1.00		1.00	1.00
Regional	4.82 (4.49–5.18)		4.02 (3.74–4.32)	2.99 (2.77–3.22)	4.82 (4.49–5.18)		4.09 (3.80–4.40)	3.01 (2.79–3.24)
Distant	14.94 (13.42–16.63)		11.25 (10.09–12.55)	8.06 (7.21–9.01)	14.94 (13.42–16.63)		11.44 (10.25–12.76)	8.10 (7.25–9.06)
Unknown	3.25 (2.93–3.60)		2.43 (2.19–2.70)	1.89 (1.70–2.10)	3.25 (2.93–3.60)		2.48 (2.23–2.75)	1.91 (1.71–2.12)
Histology								
Squamous carcinomas	1.00		1.00	1.00	1.00		1.00	1.00
Adenocarcinomas	1.43 (1.28–1.60)		1.61 (1.44–1.80)	1.62 (1.45–1.81)	1.43 (1.28–1.60)		1.61 (1.44–1.79)	1.62 (1.45–1.81)
Other specific Carcinomas	1.05 (0.86–1.30)		1.27 (1.03–1.56)	1.28 (1.04–1.58)	1.05 (0.86–1.30)		1.25 (1.01–1.54)	1.26 (1.02–1.56)
Other	3.10 (2.85–3.38)		2.56 (2.35–2.79)	2.43 (2.22–2.65)	3.10 (2.85–3.38)		2.58 (2.36–2.81)	2.44 (2.24–2.67)
Treatment								
Surgery alone	1.00			1.00	1.00			1.00
Surgery combined with either radiation, chemotherapy, or both	4.95 (4.36–5.63)			2.84 (2.49–3.25)	4.95 (4.36–5.63)			2.87 (2.51–3.28)
No surgery (radiation alone, chemo alone, or combined radiation + chemotherapy)	10.27 (9.07–11.63)			4.04 (3.52–4.63)	10.27 (9.07–11.63)			4.121 (3.59–4.73)
Other treatments and unknown	9.31 (7.96–10.88)			4.48 (3.79–5.28)	9.31 (7.96–10.88)			4.501 (3.82–5.31)

[†]In the case of 'unemployment', high area-based SES means a low percentage of male unemployment in each municipality. In the case of 'education', high area-based SES means a high percentage of college or graduate school graduates in each municipality. In model 1 we controlled for age; in model 2 we controlled for age plus biological factors (cancer stage and histology); in model 3 we controlled for all of the variables in model 2, plus treatment type. CI, confidence interval.

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Table 6. Effects of area-based socioeconomic status (SES) on corpus cancer cumulative 5-year survival estimated by Cox proportional hazards regression models

Independent variable	Unemployment Univariate Hazard ratio (95%CI)	Model 1 Hazard ratio (95%CI)	Model 2 Hazard ratio (95%CI)	Model 3 Hazard ratio (95%CI)	Education Univariate Hazard ratio (95%CI)	Model 1 Hazard ratio (95%CI)	Model 2 Hazard ratio (95%CI)	Model 3 Hazard ratio (95%CI)
Area-based SES†								
High	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Middle	1.27 (1.08–1.49)	1.26 (1.08–1.49)	1.10 (0.94–1.30)	1.10 (0.94–1.30)	1.26 (1.09–1.46)	1.30 (1.13–1.51)	1.15 (0.99–1.33)	1.17 (1.01–1.36)
Low	1.99 (1.69–2.35)	1.72 (1.46–2.03)	1.54 (1.31–1.82)	1.56 (1.32–1.84)	1.43 (1.21–1.69)	1.36 (1.15–1.61)	1.17 (0.99–1.39)	1.17 (0.99–1.39)
Age under 40	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
40–49	1.18 (0.76–1.82)	1.14 (0.74–1.76)	1.09 (0.71–1.68)	1.10 (0.72–1.71)	1.18 (0.76–1.82)	1.17 (0.76–1.81)	1.11 (0.72–1.72)	1.14 (0.74–1.75)
50–59	1.46 (0.97–2.19)	1.37 (0.91–2.07)	1.25 (0.83–1.89)	1.26 (0.84–1.90)	1.46 (0.97–2.19)	1.44 (0.95–2.16)	1.28 (0.85–1.92)	1.29 (0.86–1.95)
60–69	2.73 (1.81–4.10)	2.50 (1.66–3.77)	2.14 (1.42–3.22)	2.12 (1.41–3.20)	2.73 (1.81–4.10)	2.70 (1.79–4.05)	2.26 (1.50–3.41)	2.26 (1.50–3.40)
70–79	4.20 (2.77–6.38)	3.71 (2.44–5.65)	3.27 (2.15–4.99)	2.95 (1.93–4.48)	4.20 (2.77–6.38)	4.12 (2.71–6.27)	3.59 (2.36–5.47)	3.24 (2.13–4.93)
80+	8.07 (5.09–12.81)	7.38 (4.65–11.72)	6.61 (4.26–10.51)	4.88 (3.05–7.81)	8.07 (5.09–12.81)	8.13 (5.13–12.91)	6.86 (4.32–10.91)	5.07 (3.17–8.11)
Cancer stage								
Localized	1.00		1.00	1.00	1.00		1.00	1.00
Regional	4.50 (3.85–5.27)		4.51 (3.85–5.38)	3.93 (3.33–4.64)	4.50 (3.85–5.27)		4.51 (3.85–5.28)	3.98 (3.37–4.70)
Distant	12.78 (10.71–15.26)		11.84 (9.91–14.27)	9.44 (7.82–11.39)	12.78 (10.71–15.26)		11.82 (9.88–14.14)	9.50 (7.86–11.47)
Unknown	3.50 (2.83–4.32)		3.12 (2.52–3.86)	2.43 (1.93–3.06)	3.50 (2.83–4.32)		3.16 (2.55–3.91)	2.45 (1.94–3.09)
Treatment								
Surgery alone	1.00			1.00	1.00			1.00
Surgery combined with either radiation, chemotherapy, or both	2.31 (1.94–2.74)			1.41 (1.17–1.70)	2.31 (1.94–2.74)			1.36 (1.13–1.64)
No surgery (radiation alone, chemotherapy alone, or combined radiation + chemotherapy)	8.33 (6.64–10.47)			2.74 (2.15–3.50)	8.33 (6.64–10.47)			2.721 (2.13–3.48)
Other treatments and unknown	5.15 (4.04–6.56)			2.35 (1.80–3.07)	5.15 (4.04–6.56)			2.321 (1.78–3.03)

†In the case of 'unemployment', high area-based SES means a low percentage of male unemployment in each municipality. In the case of 'education', high area-based SES means a high percentage of college or graduate school graduates in each municipality. In model 1 we controlled for age; in model 2 we controlled for age plus biological factors (cancer stage); in model 3 we controlled for all of the variables in model 2, plus treatment type. CI, confidence interval.

among cervical/corpus cancer patients has also been examined in previous studies outside of Japan, using different measures of SES, for example, education,[5,7,21] occupation,[8–11] housing tenure,[11] income,[21] poverty,[5] and composite measure.[4,12,13] In these studies, stage of cancer at diagnosis has been found to be the most important explanatory factor in the association between cancer survival and SES.[2,4,13,22] We additionally controlled for type of treatment, although we did not have information on the quality of treatment. Choice of treatment depends on histological type, cancer stage, age and the health status of patients, among other things. Importantly, even after controlling for these prognostic factors, disparities in survival by SES still remained. Several explanations can be offered for our findings.

First, our use of survival as an end-point reflects mortality from all causes of death, which might have overestimated SES differences. According to a population-based study by Auvinen *et al.*, the difference between all-cause mortality and cancer-specific mortality following cervical and corpus cancer was about 5%, but the impact on the estimated magnitude of SES differences was relatively small.[11] In order to address this issue, analyses of cancer-cause specific survival are needed.

Another data issue is that we excluded 'part unspecified' uterus cancer cases (ICD, 10th revision, code C55) which may have affected survival differences by SES. However, reanalysis of cervical cancer including 929 cases with ICD, 10th revision, code C55 also indicated residual SES differences after adjustment for prognostic factors. The reanalyzed results of the fully adjusted regression models were almost identical to the results shown in Table 5. Hazard ratios for patients from middle and high unemployment areas compared to patients from low unemployment areas were 1.09 (95% confidence interval [CI] 1.02–1.18) and 1.30 (95%CI 1.21–1.40), respectively. Hazard ratios for middle and low education SES were 1.05 (95%CI 0.98–1.12) and 1.16 (95%CI 1.08–1.25).

The vital status of several patients (out of the 4708 cervical cancer and 812 corpus cancer patients who originally resided in Osaka City from 1975–1992) were not ascertained by the registers in Osaka City office 5 years after the diagnosis, but via matching to the cancer death certificate file. This may have overestimated cancer survival. However, if this source of potential misclassification was corrected, the survival differences by SES could become larger because such cases occurred only among patients from the middle and low SES strata.

A second issue in interpreting our findings is that other explanatory factors may have been related to both patient and tumor characteristics.[6,11,23,24] Complications of treatment and psychosocial factors might be important as explanatory factors related to patient survival. Low SES patients tend to suffer from more comorbidity.[25–27] Differences in susceptibility to complications might be closely related to general health status, including nutrition status or lifestyle factors such as smoking, drinking and exercise. Health care seeking behavior prior to diagnosis as well as compliance with treatment after diagnosis also vary between SES groups.[28] In turn, these factors depend on knowledge and awareness at the individual level, as well as social networks and social ties at the interpersonal level.[29] Tumor characteristics similarly vary across SES,[30] including histology[21] and exposure to different risk factors.[31,32] Exposure to risk factors, such as infection with the papillomavirus, fertility history, cigarette smoking and diet for cervical cancer,[33–35] as well as obesity, age at menopause, lower parity, smoking, use of estrogen replacement therapy and oral contraceptive use for corpus cancer[36–40] vary across SES groups, and may in turn contribute to differences in tumor characteristics.

In the present study, we used area-based SES measurements as a proxy for individual-level SES because we lacked information on the latter. Accordingly, our findings need to be interpreted with caution. For example, we were unable to determine which SES groups were at increased risk of lower survival within low SES areas. Conversely, our findings have suggested the existence of substantial disparities in survival following cervical and corpus cancer. Our study suggest that socioeconomic data at the ecological level, which are available from routine government sources, can serve as effective tools for assessing and monitoring cancer survival inequalities.

In conclusion, our study has demonstrated, for the first time in Japan, SES differences in survival following cervical and corpus cancer. We also indicated differences in the distribution of prognostic factors by SES. The Japan Ministry of Health, Labor and Welfare recommends cervical cancer screening to be carried out every other year for females aged over 20 years and increased health education efforts targeting the prevention of cervical and corpus cancer. Only 20% of Japanese women have received cervical cancer screening within the past year.[41] Our findings point to the need for appropriate interventions including health education, screening, and improvement of access to care and treatment to ameliorate the survival difference across SES groups.

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Population-based study of the relationship between hospital surgical volume and 10-year survival of breast cancer patients in Osaka, Japan

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Breast cancer is the most prevalent cancer among Japanese women; however, its outcome has never been analyzed in relation to hospital volume in Japan. We utilized data from the Osaka Cancer Registry for investigating correlations between hospital volume and 10-year survival of breast cancer patients. According to the total number of surgical procedures of breast cancer in each hospital during the period 1985–1991, we classified reporting hospitals in Osaka into four categories (high, medium, low, very low). The survival analysis was restricted to the 4333 female patients reported who were 30–64 years old, living in Osaka Prefecture (except for Osaka City), and for whom active follow up was available more than 10 years after diagnosis. In total, the relative 10-year survival was 79.7% in the high-volume, 80.3% in the medium-volume, 78.2% in the low-volume, and 68.2% in the very low-volume hospitals. After adjustment for age at diagnosis, clinical stage and clues for detection with the Cox regression model, the patients who received care in the very low-volume hospitals had a significantly higher risk of death than those in the high-volume hospitals. Meanwhile, no significant differences in risk were observed for the other two categories. These findings led us to conclude that the surgical volume of the hospitals did not affect the 10-year survival rate significantly, except for the very low-volume hospitals in Osaka, Japan. However, the study of these relationships should be continued and expanded in future to include quality of life. (*Cancer Sci* 2006; 97: 618–622)

Relationships between hospital surgical volume and outcome of cancer treatments are of great concern. This is because hospital volume is often regarded as an index of technical skill for cancer treatments. In a previous study,[1] we reported that the relationship between hospital surgical volume and 5-year survival for stomach cancer diminished in the 1990s, except in very low-volume hospitals, according to data provided by the Osaka Cancer Registry (OCR). Ioka *et al.* reported that ovarian cancer patients who received treatment in Japanese hospitals with higher surgery volumes showed better survival rates.[2] Relationships between hospital procedure volumes and the outcome of cancer treatments are, thus, likely to differ and change according to cancer site, stage and time. It is very important to analyze and monitor these relationships regularly and extensively.

In the present paper, we assess whether hospital surgical volume is related to long-term survival of breast cancer patients in Osaka, Japan, where breast cancer became the most prevalent cancer among women in 1996.[3,4] Although surgery for breast cancer is neither complex nor risky, its treatment needs multidisciplinary approaches: adjuvant chemotherapy, hormonal therapy and radiotherapy after breast surgery for better quality of life and long-term survival. We therefore focused on 10-year survival to assess the effect of multidisciplinary treatment for breast cancer in Japan.

Subjects and Methods

Data from the OCR were used for this study. The registry work is described elsewhere.[5] According to the data provided by OCR, we identified 8656 newly reported cases of breast cancer (ICD Tenth Revision, C50) that were diagnosed and treated at hospitals in Osaka Prefecture during the period 1985–1991. Of these 8656 cases, 8439 patients (97.5%) underwent surgery. Relative to the number of surgeries carried out between 1985 and 1991, each hospital was divided into four categories (high, medium, low, very low) so that each would have an approximately equal number of surgeries. In the OCR, the vital status of the registered patients was confirmed by referring to the inhabitant's registry in local municipalities, 5 and 10 years after diagnosis. However, in Osaka City active follow-up information was not available until 1993. Survival analysis was therefore restricted to those patients who lived in Osaka Prefecture, except Osaka City where 3065 cases were identified. Furthermore, to increase the internal validity of the study, the following subjects were excluded: male breast cancers (57 cases), subsequent primary cases (223 cases) and cases aged less than 30 years (90 cases) or 65 years and over (1712 cases). Therefore in the present study, the 10-year survival analysis was conducted for the remaining 4333 cases. The clinical stage of cancer was classified into the following three categories: (1) localized, where cancer was confined to the original organ; (2) regional, where cancer had spread to regional lymph nodes or to tissues immediately adjacent; and (3) distant, where cancer had metastasized to distant organs.

The cumulative observed survival rate was estimated using the Kaplan–Meier method relative to the hospital surgical volume. The relative 5-year and 10-year survival rates were calculated by the ratio of observed to expected survival, the

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Table 1. The number of hospitals, range of breast cancer surgical procedures per hospital and the number of patients by cancer stage

	Hospital volume			
	High	Medium	Low	Very low
No. hospitals	3	6	14	177
Total no. patients	1987	2161	2134	2157
Range of surgeries per hospital	562–736	283–475	99–212	1–88
Range of surgeries per hospital per year	94–123	47–79	16–36	<15
Cancer stage				
Localized	1126 (56.7%)	1220 (56.5%)	1139 (53.4%)	1090 (50.5%)
Regional	694 (34.9%)	805 (37.3%)	800 (37.5%)	790 (36.6%)
Distant	114 (5.7%)	114 (5.3%)	158 (7.4%)	211 (9.8%)
Unknown	53 (2.7%)	22 (1.0%)	37 (1.7%)	66 (3.1%)

Table 2. Characteristics of patients analyzed by hospital volume

Characteristics	Hospital volume			
	High	Medium	Low	Very low
No. patients	810	1281	1192	1050
Mean age				
Years	48.4	48.0	48.3	48.3
90% confidence interval	47.8–48.9	47.5–48.4	47.9–48.8	47.8–48.8
Screening detected	58 (7.2%)	134 (10.5%)	28 (2.3%)	16 (1.5%)
Not screening detected	663 (81.8%)	1079 (84.2%)	1100 (92.3%)	972 (92.6%)
Unknown	89 (11.0%)	68 (5.3%)	64 (5.4%)	62 (5.9%)

latter being estimated with the survival probability of a Japanese population of subjects similar with respect to age, sex and calendar year at diagnosis. Here the Ederer II method was used.[6] Survival differences were analyzed by Cox's proportional hazards model adjusting for age at diagnosis and clue for detection (screening detected or not detected). The statistical software STATA (Stata Corporation, College Station, TX, USA) was used for statistical analysis. Statistical significance and 95% confidence intervals (CI) of the hazard rate ratio were obtained and judged using a two-sided test. Use of data from the OCR was approved by the Ethical Committee of Osaka Medical Center for Cancer and Cardiovascular Diseases.

Results

Table 1 shows the number of hospitals in each surgical volume range, the number of breast cancer surgical procedures per hospital in each range and the number of patients by clinical stage. A total of 8439 cases were newly diagnosed patients who underwent surgical treatment in the 200 hospitals in Osaka Prefecture during 1985–1991. Three hospitals fell into the high-volume range and they conducted a total of 1987 surgeries, six were categorized into the medium-volume range with a total of 2161 surgeries, 14 were categorized into the low-volume range with a total of 2134 surgeries, and 177 were categorized into the very low-volume range with a total of 2157 surgeries. The average number of surgeries per hospital in the high-volume category was 1.8 times larger than that in the medium-volume category, 4.3 times larger than that in the low-volume category, and 54.4 times larger than that in the very low-volume category. The proportion of localized cases was somewhat larger in the high-volume category than in the low-volume category, whereas the proportion of cases in which it was unknown where the cancer was localized was minute (1–3%) in each category.

Table 2 shows the mean ages of the patients analyzed for survival and the distributions of the clues for detection (screening detected or not detected) by hospital volume. The mean age was 48 years, and differences in mean age were small among the four hospital volume categories. The proportion of cases detected through screening was higher in the high-volume and medium-volume categories than in the lower-volume categories.

Table 3 shows relative 5-year and 10-year survival rates together with hazard ratios using the high-volume hospitals as a base with respect to clinical stage. Figure 1 shows relative survival curves of cases whose cancers were localized, according to hospital volume. Differences of relative 5-year survival among the hospital surgical volume categories were very small: 95.3% in the high-volume category, 95.3% in the medium-volume category, 94.9% in the low-volume category, and 95.1% in the very low-volume category. However, the decrease in survival after 5 years was larger in the very low-volume category. Although the difference was not statistically significant, relative 10-year survival in the very low-volume category was somewhat lower (88.7%) than that in the other categories: 90.5% for high volume, 90.2% for medium volume, and 90.4% for low volume. Figure 2 shows the relative survival curves of cases whose cancer was regional, according to hospital surgical volume. The relative survival curves were similar among the three categories high, medium and low volume, whereas relative survival in the very low category was much lower. In the very low-volume category, 5-year survival was lower than in the other categories, and there was a greater decrease in survival after 5 years. Patients who had undergone care in the

Table 3. Relative 10-year survival and hazard ratio (HR) by cancer stage and hospital volume groups

	Hospital volume			
	High	Medium	Low	Very low
Localized				
n	457	708	618	527
5-year survival (SE)	95.3 (1.1)	95.3 (0.9)	94.9 (1.0)	95.1 (1.1)
10-year survival (SE)	90.5 (1.6)	90.2 (1.3)	90.4 (1.4)	88.7 (1.6)
HR[1] (95% CI)	1.00	1.03 (0.74–1.44)	1.00 (0.71–1.42)	1.14 (0.80–1.62)
Regional				
n	315	534	512	429
5-year survival (SE)	79.9 (2.3)	80.6 (1.8)	79.0 (1.9)	68.5 (2.3)
10-year survival (SE)	68.4 (2.7)	71.1 (2.1)	69.0 (2.2)	54.7 (2.5)
HR[1] (95% CI)	1.00	0.89 (0.70–1.14)	0.99 (0.78–1.26)	1.55 (1.22–1.96)
Distant				
n	17	28	45	66
5-year survival (SE)	23.9 (10.4)	18.8 (7.6)	22.5 (6.3)	15.4 (4.5)
10-year survival (SE)	12.3 (8.2)	7.7 (5.3)	18.3 (5.9)	3.1 (2.2)
HR[1] (95% CI)	1.00	1.44 (0.76–2.74)	0.98 (0.54–1.79)	1.50 (0.85–2.64)
All stages				
n	810	1281	1192	1050
5-year survival (SE)	87.4 (1.2)	87.5 (1.0)	85.0 (1.1)	78.2 (1.3)
10-year survival (SE)	79.7 (1.5)	80.3 (1.2)	78.2 (1.3)	68.2 (1.5)
HR[2] (95% CI)	1.00	0.98 (0.82–1.18)	1.10 (0.92–1.33)	1.65 (1.38–1.98)

[1]HR adjusted for age at diagnosis and screening detected or not detected. [2]HR adjusted for stage, age at diagnosis and screening detected or not detected. CI, confidence interval.

very low-volume hospitals had a higher risk of death than those who had received treatment in the other higher-volume hospitals, but the risk of death in the other three categories was approximately equal.

As shown in Table 3, multivariate analysis with Cox's proportional hazards model confirmed the above-mentioned findings. That is, in the localized cases, hazard ratios were not significantly different among the four volume categories, whereas it was suggested that there was a slightly higher risk for the very low-volume category. For the regional cases, hazard ratios were not different among the three higher-volume categories; however, it was shown that there was a significantly higher risk for the very low-volume category.

For the distant cases, the relative 5-year survival rates were 23.9%, 18.8%, 22.5% and 15.4% for the high-volume, medium-volume, low-volume and very low-volume categories, respectively, and the relative 10-year survival rates were 12.3%, 7.7%, 18.3% and 3.1%, respectively. The 10-year survival rate was lower in the very low-volume category than in the other categories, but the difference was not significant because of the relatively few number of patients analyzed. For all stages, relative 5-year and 10-year survival rates were higher in the three higher-volume categories than in the very low-volume category. After adjustment for age at diagnosis, clinical stage and clues for detection with the Cox regression model, patients receiving care in the very low-volume hospitals had a significantly higher risk of death than those in the high-volume hospitals.

Discussion

The findings of the present study suggest that there is no relationship between relative 10-year survival for breast cancer and hospital volume, although lower survival was observed for the very low-volume category. A significantly higher risk was found only in cases whose cancer had spread to the regional lymph nodes or adjacent tissues and in all stages of cancer.

Several studies from the USA have reported on the survival of breast cancer in relation to hospital volume. Roohan *et al.* reported that breast cancer patients treated in very low-volume hospitals (less than 10 surgeries per year) had a greater risk of mortality than patients in high-volume hospitals (more than 150 surgeries per year), based on the New York State hospital discharge database between 1984 and 1989.[7] Their risk ratio of very low volume against high volume (1.60) was comparable to our study (1.65). However, they also found that patients treated in hospitals with low (11–50) and moderate (51–150) volumes had a higher risk of dying (30% and 19%, respectively) than patients in high-volume hospitals. Skinner *et al.* evaluated 5-year survival by annual hospital volume using the Cancer Surveillance Program database for Los Angeles County, which shows 84% in high-volume (>125), 82% in medium-volume (71–125), 78% in small-volume (36–70) and 75% in very small-volume hospitals (<35).[8] They calculated the hazard ratio for each hospital category compared to the very small-volume category: 0.77 in high-volume hospitals, 0.78 in medium-volume hospitals and 0.92 in small-volume hospitals. They also reported that patients who had undergone surgery at hospitals where >125 breast cancer surgeries were carried out each year were more likely to achieve long-term survival. In contrast, Harcourt and Hicks reported that survival for breast cancer between 1980 and 1994 did not correlate with hospital case volume ($P = 0.40$), based on the Blue Mountain Regional Tumor Registry.[9]

In our previous study on stomach cancer, there were no clear relationships between hospital volume and 5-year survival except for in very low-volume hospitals, after adjusting for age

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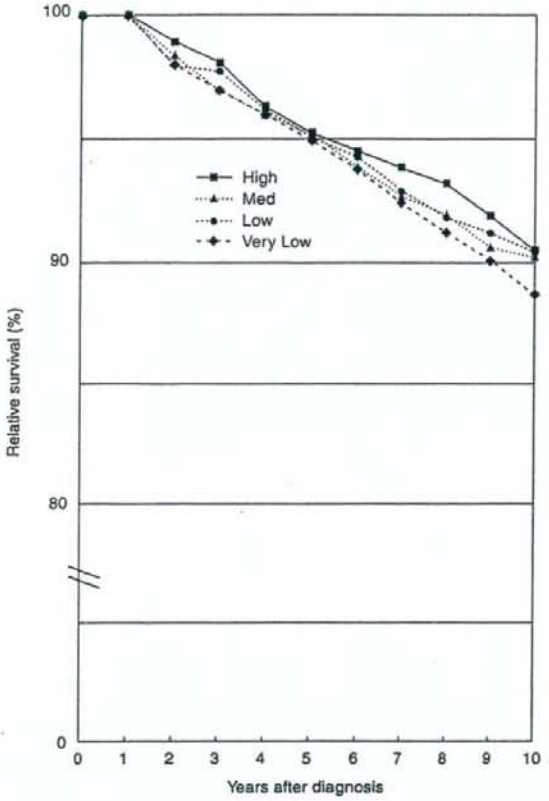

Fig. 1. Relative survival of cases whose cancer was confined to the original organ (localized).

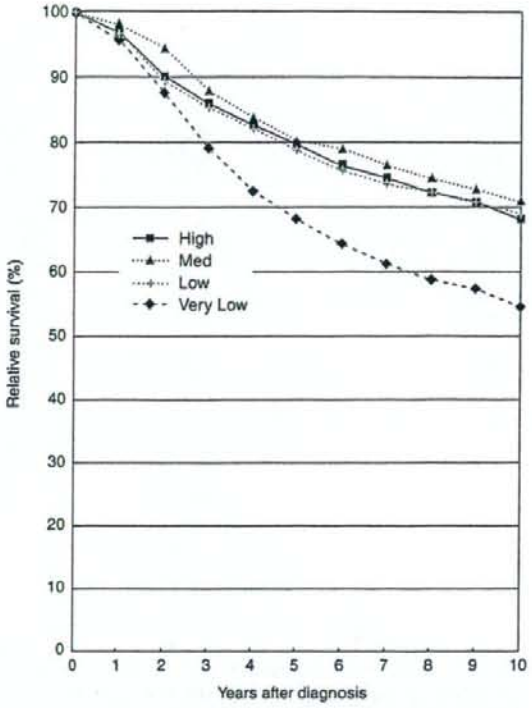

Fig. 2. Relative survival of cases whose cancer spread to regional lymph nodes and/or immediately adjacent tissues (regional).

at diagnosis, sex and the extent of disease. These studies were carried out in Osaka Prefecture where the population density was high (4569 people/km) and the population was 8.7 million for 537 hospitals, including five university hospitals, as of the year 2000. Stomach and breast cancers are the most common forms of cancer in Japan, and surgeries for these cancers are not considered risky. Under these conditions there would be many opportunities for surgeons to carry out these operations, and medical technology and equipment is improving, in general. Standard treatments for these cancers might have been widely adopted across hospitals in Osaka Prefecture, so that hospital volume had no great influence on patient survival.

Several limitations inherent in this study should be considered before accepting any of our conclusions. First, survival differences were not analyzed with consideration of comorbidity. Satariano and Ragland reported that comorbidity in patients with breast cancer appeared to be a strong predictor of 3-year survival.[10] We restricted study patients aged less than 65 years in order to minimize the influence of comorbidity. Furthermore, the patients analyzed were young (mean age 48 years) and differences in patient age were small among the four hospital volumes. Differences in comorbid conditions among hospital volume groups therefore seemed to be small. Second, we must consider the possibility of stage migration. High-volume hospitals might have carried out more detailed inspections and found minute infiltrations or metastases. In this case, however, survival according to the extent of disease should be higher in the high-volume category than in the other categories. Third, the data quality of the OCR should be considered. Hospitals with poor notification completeness might have under-reported patients who were still alive, thus underestimating survival. In this study period, the proportion of death certificate only cases was 3% for female breast cancer in the OCR, which might not have affected the result seriously. Finally, our study period fell during a time when the surgical procedure for breast cancer was changing from broad dissection to reduced dissection. In 1985 the proportions of radical mastectomy of Halsted, extended mastectomy, total mastectomy and breast-conserving surgery were 41.1%, 23.6%, 33.2% and 0.4%, respectively, in Japan. In 1991, the proportions of the former two were reduced to 16.0% and 6.5%, whereas the latter two were increased to 64.2% and 12.7%, respectively.[11] It was also reported that differences in surgical procedures did not affect survival significantly.[12–14] Thus, our study might not reflect the level of treatment for breast cancer in terms of quality of life.

In conclusion, our study results suggest that hospital surgical volume did not affect 10-year survival, except in very low-volume hospitals in Osaka, Japan. However, we should continue to study these relationships and expand their scope in the future to include quality of life.

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Trend in Incidence of Adenocarcinoma of the Esophagus in Japan, 1993–2001

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Background: Several studies with population-based cancer registry data have suggested that incidence of adenocarcinoma of the esophagus has been increasing since 1970 in some European and North American countries and Australia. However, data from Asian countries with regard to the incidence of esophageal cancer by histological type based on the population-based cancer registry are lacking. The aim of this study was to describe the incidence of esophageal cancer by histological type in a Japanese population.
Methods: Cancer incidence data for 1993–2001 from 15 population-based cancer registries were collected by the Japan Cancer Surveillance Research Group in 2005. We used data from eight registries corresponding to inclusion criteria for data quality.
Results: Squamous cell carcinoma remains the predominant type in all esophageal cancers in Japan. The ratio of squamous cell carcinoma to adenocarcinoma is 26:1. For adenocarcinoma, estimated average annual percentage change was 4.7% (95% confidence interval: 0.7, 8.9) in men and 6.0% (2.4, 9.8) in women. Age-adjusted incidence rate (the world standard population) per 100 000 for 2001 was 0.3 in men and 0.05 in women. Incidence of squamous cell carcinoma was increasing slightly in men and nearly constant in women. Age-adjusted incidence rate for 2001 was 8.2 in men and 1.0 in women.
Conclusion: No dramatic increase in adenocarcinoma has occurred, and absolute incidence remains low in Japan.

Key words: esophagus adenocarcinoma incidence

A rising trend of incidence of adenocarcinomas of the esophagus was first reported from the USA in 1991 (1). Several subsequent reports on the incidence of esophageal cancer by histological type based on population-based cancer registries have revealed dramatic increases in the incidence of adenocarcinomas of the esophagus in the USA, Canada, Australia and some European countries over the last three decades (2–7). Some studies have investigated the associations between this increasing trend and factors, such as misclassification of tumor sites (lower esophagus versus gastric cardia) or overdiagnosis resulting from increased use of upper endoscopy (8,9), and concluded that the rising trend was unlikely to be explained by such information bias.

Recent studies suggest that being a white male, high body-mass index (BMI), Barrett's esophagus, gastro-esophageal reflux disease (GERD) and absence of *Helicobacter pylori* (*H. pylori*) infection represent substantial risk factors for adenocarcinomas of the esophagus (10). In Japan, risk factors such as obesity and absence of *H. pylori* infection seem to be increasing (11,12), and we thus need to start monitoring trends in the incidence of adenocarcinoma of the esophagus. A previous study based on the data collected from a lot of hospitals throughout Japan has reported that no increase in the relative proportion of adenocarcinomas among all reported esophageal cancers was identified over the period 1980–94 (13). International Agency for Research on Cancer provides incidence rates of esophageal cancer by histological type from Osaka, Miyagi and Nagasaki cancer registries up to 1997, respectively (14). However, incidence rates of esophageal cancer by histological type throughout Japan have not been available.

In 2005, a research group supported by the Ministry of Health, Labor and Welfare started collecting cumulative

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incidence data from several population-based cancer registries in Japan that met various criteria for data quality, and included the data into a database. The purpose of this study was to describe the trends in the incidence of esophageal cancer by histological type in Japan during 1993–2001.

MATERIALS AND METHODS

We used cancer incidence data for 1993–2001 from 15 population-based cancer registries collected by the Japan Cancer Surveillance Research Group in 2005. Since 1975, national estimates of cancer incidence in Japan have been provided and published by this research group (15,16).

All primary malignant neoplasms of the esophagus (International Classification of Diseases for Oncology, Third Edition: ICD-O-3) topography codes C15.0–C15.9, morphology codes 8000–9581 and behavior code 3, excluding lymphomas, were included in this study. Seven registries were excluded from the analysis because the percentage of histologically verified diagnosis (%HV) of esophageal cancers comprised <70% registered cases. Finally, this analysis was performed using the data from the following eight registries: Miyagi, Yamagata, Niigata, Fukui, Shiga, Osaka, Saga and Nagasaki. Mean proportion of death certificate only (DCO) cases was 15.6% and %HV was 79.1% in these registries between 1993 and 2001. The population covered by the eight registries totaled 19 400 747, corresponding to 15% of the total population of Japan in 1997. Mortality data were obtained from the Japanese Ministry of Health, Labor and Welfare using the National Vital Statistics.

Esophageal cancers were divided into the following histological categories: squamous cell carcinoma (ICD-O-3 codes 8050–8084), adenocarcinoma (ICD-O-3 codes 8140–8384), other specified malignant neoplasm (ICD-O-3 codes 8011–8046, 8090–8131 and 8380–9581) and neoplasm not otherwise specified (NOS) (ICD-O-3 codes 8000–8010). Esophageal cancers were also classified according to one of the following subtypes: upper third or cervical area (ICD-O-3 codes C15.0 and C15.3), middle third or thoracic (ICD-O-3 codes C15.1 and C15.4), lower third or abdominal (ICD-O-3 codes C15.2 and C15.5) and origin intermediate or NOS (ICD-O-3 codes C15.8 and C15.9). Cancer cases were classified according to age (5-year age groups up to +85 years) and sex.

Statistical Methods

Incidence and mortality rates were estimated and age-adjusted to the 1985 Japanese model population or the world model population using direct adjustment. Point estimates and 95% confidence intervals (CIs) of estimated average annual percentage change (EAPC) in incidence and mortality rates during the study period were estimated by fitting a log-linear regression model to the standardized incidence using the least squares method. The model was of the form $\log Y = a + bx$, where Y is the estimated standardized incidence rate and x is the year of incidence. The expression $100\ (10^b - 1)$ is an estimate of the annual percentage change in this rate. All statistical analyses were performed using Intercooled Stata 8.0 for Windows software (StataCorp LP, College Station, TX, USA).

RESULTS

During the period from 1993 to 2001, a total of 20 093 patients were diagnosed with esophageal cancer in the eight regional cancer registries in Japan. Proportions of esophageal cancer by histological type, sub-site, calendar year of diagnosis and sex are shown in Table 1. Squamous cell carcinoma was the predominant histological type during the study period (mean percentage: 73.3% for men; 66.0% for women). Mean percentage of adenocarcinomas was <3% and the ratio of squamous cell carcinomas to adenocarcinomas was 26:1. The distribution of cases with histology of 'other types and unspecified' was almost constant throughout 9 years and mean percentage was 25.3%. Since sub-sites belonging to 'origin intermediate or NOS' accounted for 60.1%, we could not perform further analysis of sub-sites.

Age-standardized (the 1985 Japanese model population) incidence rates (ASIRs) and mortality rates (ASMRs) per 100 000 person-years of esophageal carcinoma between 1993 and 2001 are shown in Fig. 1. For men, incidence rates were slowly increasing, with an EAPC of 1.68% (95% CI: +0.73, +2.63) and a point-estimated ASIR (the world model population) for 2001 of 11.5. For women, incidence rates were nearly constant, and point-estimated ASIR (the world model population) for 2001 was 1.5. Mortality rates increased slightly for men (EAPC: 1.22; 95% CI: 0.13, 2.33) and declined gradually for women (EAPC: −1.09; 95% CI: −2.55, 0.08).

Figure 2 shows the trends in ASIR by the histological types of esophageal cancer. Incidence rates were 7- to 8-fold higher in men than in women irrespective of histological type. Risk of squamous cell carcinoma was over 20-fold greater than that of adenocarcinoma, regardless of sex. Incidence of squamous cell carcinoma increased slightly during the period for men, but was nearly constant in women. Table 2 shows the incidence trends of esophageal cancer by histological types expressed as EAPC over the interval. For men, we observed annual increases in the incidence of all esophageal cancers and all histological subtypes. Point-estimated ASIRs (world population) in 2001 for adenocarcinoma and squamous cell carcinoma were 0.3 and 8.2, respectively. For women, annual changes were not significant in the incidence of all esophageal cancers, squamous cell carcinomas and other types and NOS carcinomas, with only adenocarcinomas showing an annual increasing trend. Point-estimated ASIRs (world population) in 2001 for adenocarcinoma and squamous cell carcinoma were 0.05 and 1.0, respectively.

Table 1. Cases of esophageal cancer by sex, year of diagnosis, histology and anatomic site

	Males						Females					
	1993–95		1996–98		1999–2001		1993–95		1996–98		1999–2001	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Total number	4819	100.0	5734	100.0	6360	100.0	990	100.0	1033	100.0	1157	100.0
Carcinoma subtype												
Squamous cell carcinoma	3496	72.5	4277	74.6	4629	72.8	661	66.8	686	66.4	750	64.8
Adenocarcinoma	125	2.6	146	2.5	192	3.0	19	1.9	28	2.7	41	3.5
Other types of carcinoma	87	1.8	120	2.1	140	2.2	21	2.1	23	2.2	33	2.9
Unspecified carcinoma	1111	23.1	1191	20.8	1399	22.0	289	29.2	296	28.7	333	28.8
Subsite of origin												
C 15.0, C 15.3	154	3.2	162	2.8	220	3.5	53	5.4	58	5.6	77	6.7
C 15.1, C 15.4	1348	28.0	1668	29.1	1749	27.5	220	22.2	237	22.9	251	21.7
C 15.2, C 15.5	470	9.8	498	8.7	605	9.5	78	7.9	84	8.1	84	7.3
C 15.8, C 15.9	2847	59.1	3406	59.4	3786	59.5	639	64.5	654	63.3	745	64.4

C15.0–C15.9, topography codes.

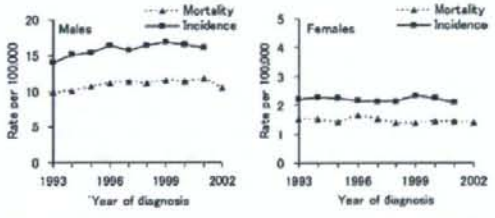

Figure 1. Trends in age-adjusted incidence and mortality rate (the 1985 Japanese model population) of esophageal cancers by sex.

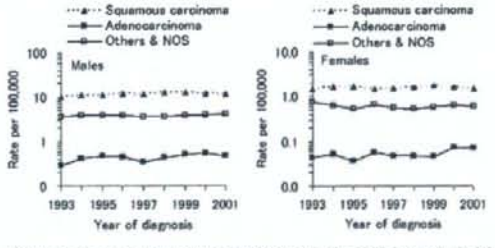

Figure 2. Trends in age-adjusted incidence rate (the 1985 Japanese model population) of esophageal cancers by histological subtypes and sex.

DISCUSSION

Our data demonstrate that no dramatic increase in adenocarcinoma of the esophagus has occurred in Japan. Although incidence rates of adenocarcinoma of the esophagus are gradually increasing in both sexes, absolute incidence rates remain much lower than those of squamous cell carcinoma and those of most Western countries (1,3–6).

Table 2. Estimated annual percentage change (EAPC) in incidence of esophageal cancer by histological subtypes and all esophageal cancers

	EAPC (95% CI)	
	Males	Females
All esophageal cancer	1.68 (0.73, 2.63)	−0.34 (−1.22, 0.54)
Squamous cell carcinoma	1.78 (0.41, 3.17)	0.07 (−1.67, 1.84)
Adenocarcinoma	4.73 (0.74, 8.88)	6.03 (2.37, 9.82)
Other types and NOS	1.02 (0.03, 2.02)	−1.63 (−4.41, 1.23)

CI, confidence interval; NOS, not otherwise specified.

Vizcaino et al. (6) described the time-trend of the incidence of both major histological types of esophageal carcinomas in selected countries worldwide. According to that description, Western countries, with some exceptions, are displaying increasing incidence rates of adenocarcinoma and relatively stable or decreasing rates of squamous cell carcinoma. In most countries in 1970s, the rates of squamous cell carcinoma among men were over one per 100 000 person-years (the world population model) and those of adenocarcinoma were below one per 100 000 person-years. However, in the USA (white), Canada, Australia, Scotland, Denmark and Iceland, the incidence rates of adenocarcinoma among men have caught up with or surpassed those of squamous cell carcinoma up to 1995 and rates of adenocarcinoma reached over one per 100 000 person-years. Reliable incidence data for esophageal cancer

by histological types are limited. Fernandes et al. (7) reported that the incidence rate of squamous cell carcinoma among men had decreased to 3.9 per 100 000 person-years and those of adenocarcinoma was increasing gradually up to 0.5 per 100 000 person-years in 2002 in Singapore. For the current study in Japan, the incidence rate of squamous cell carcinoma among men was still 8.2 per 100 000 person-years (world population), whereas the rate of adenocarcinoma was 0.3 per 100 000 person-years in 2001. With regard to adenocarcinoma, the incidence trends in Japan resemble those in Singapore.

The most potent risk factors for adenocarcinomas of the esophagus appear to be obesity and the absence of *H. pylori* infection (10). The association between high BMI and adenocarcinoma of the esophagus has been investigated in numerous studies, and a meta-analysis eventually supported a positive association in 2006 (17). In Japan, although the proportion of overweight adults (BMI $\geq$ 25) increased from 19.0 to 22.4% ($\times$1.23) between 1980 and 1995, that percentage is still only half the level of many Western and Oceanian countries (WHO: Global Database on Body Mass Index. http://www.who.int/bmi/index.jsp). Another possible risk factor for adenocarcinoma of the esophagus is the absence of *H. pylori* infection. However, previous study results regarding this inverse association have been inconsistent, and many investigators have speculated that *H. pylori* infections causing severe pangastritis could decrease gastric acid secretion and protect against the development of GERD, Barrett's esophagus and adenocarcinoma of the esophagus (10). In Japan, more than 80% of the population born before 1950 is positive for *H. pylori* (12,18), and an active recommendation for eradication of *H. pylori* in patients with gastric ulcer was just started in 2000. The majority of individuals covered in this study were thus still likely to be *H. pylori* positive. The insignificant increase in the incidence of adenocarcinoma is likely to have resulted from a lower prevalence of overweight adults and higher prevalence of *H. pylori* positive individuals in the Japanese population compared with Western countries.

For squamous cell carcinoma of the esophagus, incidences are stable or decreasing slowly in both sexes in most countries (6). As an exception, the incidence of squamous cell carcinoma among females increased rapidly in Switzerland between 1980 and 1995. Conversely, incidence of squamous cell carcinoma decreased progressively in Singapore between 1968 and 2002 (7).

The strongest risk factors for squamous cell carcinoma of the esophagus are smoking and drinking (19). According to the Japanese National Survey, the proportion of daily smokers decreased by 12% among men and increased by 2.6% among women between 1989 and 2004, and 43% of the male population and 12% of the female population remained daily smokers as of 2004 (20). In the same way, the proportion of daily drinkers decreased by 3.1% among men and increased by 2.2% among women between 1989 and 2002, and 49% of the male population and 8.5% of the female population were still daily drinkers as of 2002. Considering the higher prevalence of these risk factors in the Japanese population, the high absolute incidence of squamous cell carcinoma is likely.

The present study displays some limitations. First, despite using combined data from multiple regional cancer registries offering better quality data, DCO was 15.6%. This is considerably inferior to the international standard level (6). However, we consider our data trustworthy enough to evaluate the trends of incidence rate for esophageal cancer by histological subtype, as 5-year relative survival rate for esophageal cancer remains poor in Japan, at 26% in 1993–96, and the trends in the incidence and mortality of all esophageal cancers have been changing in parallel during the study period (21).

Secondly, our data included ~25% of the cases with unspecified histology, 10-fold greater than the cases with adenocarcinoma. However, we consider that our data were sufficient to allow the observation of the incidence trends for esophageal cancer by major histological subtype, since the proportion of histologically unspecified carcinomas was stable throughout the study period. And these data are the only available measures to discuss incidence rate of esophageal cancer by histological type throughout Japan.

In conclusion, we identified that no dramatic increase in adenocarcinoma of the esophagus has occurred and the absolute incidence remained low in Japan. The incidence trends for esophageal cancer by histological type in Asia appear to differ from those of many Western countries. This fact could be useful in identifying risk factors for adenocarcinomas of the esophagus.

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Conflict of interest statement
None declared.

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総説

がん検診と地域がん登録

Cancer screening and population-based cancer registry

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Abstract

Cancer screening aims to reduce the mortality of cancer and to improve the quality of life of cancer patients through the systemic implementation of evidenced-based interventions in early diagnosis. Cancer screening is an important part of cancer control. In the context of a systemic cancer control program, cancer statistics build around a population-based cancer registry is an essential element. Data on the size and evolution of the cancer burden in the population are essential to evaluation of the current situation, to setting objectives for cancer control, and defining priorities. The population-based cancer registry can provide not only statistical data on incidence, stage distribution and survival in the local situation but also information about the prevalence of cancer in the population. In Japan, 35 prefectures and 1 city implement population-based cancer registries in August 2007, but the completeness and quality of registrations are insufficient in general. High completeness and quality of registration is necessary to use cancer registry data for cancer control including cancer screening.

Keywords: cancer screening incidence

はじめに

本講演で使う「がん検診」とは、市町村のがん対策として地域住民に対して実施される「対策型検診」と定義する[1]。久道は、がん検診について実施条件を提唱している[2]。そのうちの4つの条件は登録精度の高い地域がん登録があってはじめて効率的、継続的に把握できる。その4つとは、罹患率・有病率・死亡率の高いがんであること、早期発見による早期治療効果があること、検診精度が高いこと、集団のがん死亡率を下げること、である。地域がん登録は、当該地域住民を分母とするがん罹患率を知る唯一の仕組みであり、以下、がん検診の実施条件とがん罹患率のかかわりについて記述する。

がん検診とがん罹患率

がんの集団検診は、罹患率、有病率、死亡率の高いがんに実施してこそ、目に見える効果を期待できる。目安として、1万人に1人くらいの稀ながんの集団検診は重要といえないともいわれている。罹患の動向と死亡の動向は異なるため、死亡の動向だけで罹患を類推することは難しい[3]。日本では、がんの死亡率は、人口動態統計令に基づき把握されている。一方、がんの罹患を把握するための法令はなく、一部の地方自治体が健康増進事業の一環として地域のがん罹患率の把握に努めている。

がん検診の質的評価と地域がん登録

がん検診は、早期がんを発見し、余計な精密検査

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を受けさせることなく、見落としの少ない手段で実施されなければならない。がん検診の質的精度を測る主な指標は、感度、特異度、陽性反応適中度である。陽性反応適中度は、検診の回報書等を使って求めることができる。しかし、感度と特異度は、一定期間中の偽陰性例、いわゆる見逃し数がわからないと計算できない。偽陰性例を知るには、全検診受診者を追跡調査するか、精度のよい地域がん登録と照合するという方法がある。きわめて多数の全検診受診者を追跡するのは困難な作業であると想像できる。しかし、検診受診者ファイルと地域がん登録データベースを照合できれば、効率よく検診受診者中のがん診断患者を見つけだせる。ただし、精度のよくない地域がん登録と照合すると、偽陰性例を把握漏れすることになり、感度が高く見積もられることに注意しなくてはならない。

がん検診が集団の死亡率を下げるということ

集団のがん死亡率を下げること、という条件を満たしているかを知るには、がん死亡率の推移を追うだけでは十分ではない。がん、すなわち死という時代ではなく、全がんにおいても5年生存率50％を達成している[4]。死亡率の増減には、罹患の増減、診断技術の進歩による早期発見の効果、治療技術の進歩やその水準が複合的に関与しており、少なくとも、罹患の増減をとらえずして死亡率の増減の理由を類推することはできない。

がん検診が早期のがんを見つけているか

地域がん登録では、標準的に進展度と発見経緯という情報も収集しており、これらの項目からがん検診が着実に早期のがんを発見しているかをある程度把握できる。地域がん登録では、これらの項目を罹患の増減の原因を類推する材料の一つとして収集している。たとえば、急激ながん罹患率の増加を見た場合、同時に上皮内がんや検診発見の割合も増加していれば、検診の動向が罹患率の動向に影響していると類推できる。

地域がん登録とは

山形県地域がん登録は、人口約120万人の山形県で新規に発生するがんについて情報の収集に努め、登録する作業を行っている。毎年約60の医療機関から延べ200人前後の医師の協力を得て、電子媒体による届出も含めて年間8,000件を超える届出を処理している。地域がん登録では、医療機関からの届出情報のほかに県内4か所の保健所から毎月届けられる、年間約12,000件の死亡小票転写票の処理も行う。これらの膨大な情報を、中央登録室事務職員2名と地域がん登録担当医師1名で、ルールにしたがって罹患数を推計できるように処理している。

地域がん登録について、こんな収集項目では協力する意味がない（自分の役に立たない）、データが古すぎて役に立たない、なぜ患者の氏名・住所まで必要なのか、などの意見を耳にする。以下、これらの意見について地域がん登録の視点にたって解説を試みる。

社会医学としての地域がん登録

医学は、個人と向き合う臨床医学と集団を単位とする社会医学に大別される。社会医学である公衆衛生学は、共同社会の組織的な努力を通じて、疾病を予防し、寿命を延長し、身体的・精神的健康と能率の増進を図る科学・技術、と定義され、がん検診や地域がん登録はこの科学技術分野として発達してきた。さらに、地域がん登録は、人間集団において疾病の発生頻度を時、場所ごとに記述し、特徴・傾向をつかむという記述疫学という分野に属する。記述疫学は、取り組むべき対象を把握し、対策をたて、対策の優先順位をつけるのに役立つ。このような集団単位の医学の考え方は、一般に馴染みが薄いかもしれないが、地域がん登録はこのような観点から都道府県事業として運営されているのである。

また、地域がん登録の標準登録項目は、個人のがんのカルテを作るためでなく、日本、世界の地域がん登録間で比較可能ながん統計を作成することを意図して決められている。比較可能ながん罹患統計のためには、罹患日の定義、登録・集計する腫瘍の定義、病期の定義が最低限必要で、これらには、World Health Organization（WHO）の下部組織である国際がん登録学会（IACR）、国際対がん連合（UICC）や米国

のがん登録の仕組みの一つであるSurveillance, Epidemiology and End Results (SEER) などの定義が用いられている。たとえば、がん罹患数を決定する国際ルールはIACRが決めており、現在、悪性腫瘍と考える腫瘍として、「国際疾病分類　腫瘍学第3版」において性状2、3の組織コードを持つ腫瘍と定義されている。また、IACRは多重がんとして計上する範囲も定義している。もし、多重がんの判定基準がなかったら、肝臓に次々に発生する肝細胞がんをそれぞれ独立したがんとする登録と、初回のみ集計する登録では、肝臓がんの罹患数が異なってしまうことは容易に想像できる。

なぜ最新罹患統計が4、5年前なのか

がんの死亡統計が死亡年から3年目には公表されているのに対して、がんの罹患統計の多くは罹患年から4、5年目に公表されている。なぜ、罹患統計の作成には時間がかかるのか。第1に、人の死亡は人口動態統計令という法律に基づき届出義務があり、届出に一つの医療機関しか関与しないので確実に把握できるが、がんの罹患数の把握は地方自治体による健康増進事業であり届出義務はないことがあげられる。第2に、がん罹患には通常複数の医療機関が関与し、一人で複数部位の罹患もあるので情報の整理が難しい、という点がある。第3に、がん罹患数の推計方法による。届出義務がないので必ず報告漏れで、かつ生存しているがん患者が存在するので、真の罹患数の把握はほぼ不可能であり、がん罹患数は実測値でなく推計値である。推計罹患数を求める国際ルールがあり、その推計値の確からしさを示す指標も同時に示す。その推計値の確からしさを示す指標として、Death Certificate Notification (DCN；死亡診断書によってはじめてがん登録された者の割合) やDeath Certificate Only (DCO；死亡診断書からがん罹患が把握された者で、それ以外にがん罹患情報がない者の割合)、IM比 (Incidence mortality ratio) 等がある。

たとえば、2007年1年間のがんの罹患数を数えるとする。地域がん登録室には、まず、2007年の死亡者の情報が死亡月の1～2か月後に死亡小票転写票として届き、実務者は死亡小票転写票にがんの記載のある患者さんから順次登録する。この時点では、DCO、DCNが100％である。死亡小票転写票を登録しているうちに、2007年に診断された患者の届出が医療機関から少しずつよせられる。2007年に診断された患者の情報が2008年12月ころまでに推定罹患数の80％以上集まるのが理想的だが、現実には罹患年から数えて最低3年以上かかる。さらに、正確な罹患情報を追加するために、死亡小票転写票にがんの記載があって、届出情報のない者について死亡診断医療機関に情報提供をお願いする遡り調査をする登録室もあり、その調査回答を待ってようやく罹患数推計のための情報が確定する。地域がん登録室では、登録精度の指標であるDCOやDCNを小さくしたいので、集計報告のタイミングを遅くする傾向がある。2007年11月、IACRによって「5大陸のがん」第9巻が公表されたが、そのデータの採用基準はDCOが20％未満であった[5]。罹患統計の公表時期を早めるためには、がん罹患情報を迅速に地域がん登録室に届出いただくことが最善の方策である。

なぜ姓名や住所情報が必要なのか

地域がん登録では、日本には国民背番号制がないので、正確に新発生数を把握するために、経験と実験に基づくもっとも名寄せ漏れの少ないと方法として、漢字姓・漢字名・生年月の組み合わせ4パターンを基本とする名寄せを推奨している。死亡小票転写票と複数の医療機関から届けられる届出情報を適切に名寄せしなければ、罹患数の増減にかかわる。登録室ではまず、既登録患者かどうかを判断し、そうでなければ新規登録する。名寄せによって既登録腫瘍があると判明すれば、多重がんとして登録する、同じ腫瘍の重複届出として情報を追加する、などの判断と登録を随時ルールにしたがって行っている。

日本の地域がん登録の現状

2007年において、日本で地域がん登録を実施している県は35県である。そのうち、国立がんセンターがん対策・情報センターが推計し、公表している日本全体のがんの罹患推計に使用できる登録精度であった県は10県であり、国際水準のDCO10％未満の県

は福井県と岡山県の2件のみである。日本の地域がん登録の抱える最大の問題は登録精度が悪いことであり、登録精度が悪いので統計資料として信用されず、使われず、認知されず、理解されないという悪循環が続いている。市民にとっては、自分のがんのカルテではないので自分に役立たない仕組みに思え、医師にとっては、がん罹患の法的な届出義務はないので面倒な書類仕事に思える。各県にとっては、新たに地域がん登録事業を実施するには地方公共団体ごとに個人情報保護審議会に諮問し、答申を受けなければならず根気強い作業を要する。しかし、いったん県を実施主体とする地域がん登録事業が開始されれば、国に申請して人口動態統計死亡小票を利用してがん患者の死亡日を把握する、市町村に協力をお願いして住民基本台帳の照会等で最終生存日を確認するなどが、一医療機関がそれぞれ試みるよりも公的機関どうしとして手続きが進みやすいよい側面もある。死亡日や最終生存日がわかれば正確な生存率を計測することができ、罹患率と生存率がわかれば有病率推計も可能になり、生存率や有病率のような市民に身近ながん統計資料を提供することができる。

また、登録精度のよい地域がん登録があれば、自県のがん患者の台帳として利用することも可能である。たとえば、市町村の住民検診受診者台帳やコホート研究の登録者のリストと地域がん登録データベースを照合することで、がん検診の精度指標を求める、コホートのがん罹患状況やその後の生存状況を追跡する、などが可能になる。

筆者らは、2002年から2003年にかけて、地域がん登録を利用して、山形県の視触診による乳がん検診の精度を評価した[6]。1997年4月1日から1998年12月31日の期間に県内29市町村による住民検診を受診した延べ51,700人について、偽陰性の定義を追跡期間1年で、検診受診日から追跡期間内にがん登録された者と次年度の検診で要精密検査とされ、がん登録に登録された者として偽陰性例を把握し、感度と特異度を推計した。この調査を実施するために、29市町村から調査に対する同意を得て、また、山形県地域がん登録の利用申請条件に基づき、倫理委員会による研究審査と承認を事前に得た。地域がん登録と検診受診者の照合によって作成された同一人物候補者リストを目視で確認し、偽陰性例31例を見つけ、視触診による乳がん検診の感度は46.6%、特異度は97.3%という結果を得た。わずか31例の偽陰性例を発見するために、51,700人の検診受診者を地域がん登録データベースと照合して同一人物を確定する作業も時間がかかるが、全検診受診者を郵便・電話を利用して追跡するよりは作業量が少ないと考える。

まとめ

以上、がん検診と地域がん登録の関係について、地域がん登録からの視点で記述した。平成16年から継続している厚生労働省の第3次対がん10カ年総合戦略事業に「がん罹患・死亡同行の実態把握の研究」班があり、10年計画で日本の地域がん登録の標準化を進めている。興味をお持ちの方はインターネットで"地域がん登録"で検索していただくと、地域がん登録技術支援のページや地域がん登録全国協議会のページがあるので、ご覧頂ければ幸いである。自県が地域がん登録事業をしているかどうかは、地域がん登録全国協議会のホームページで確認できる。自県が地域がん登録を未実施の場合、県の健康福祉部系、がん対策担当課系にご相談いただきたい。地域がん登録を実施しているが登録精度が悪い場合は、いますぐ地域がん登録届出票を取り寄せてご協力いただくか、院内がん登録にご協力いただきたい。地域がん登録を実施していて、登録精度もよい場合は、がん検精度管理に利用できるかもしれないので、自県の地域がん登録室にご相談いただければ幸いである。

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