2) Nomura E, Tsukum H, Ajiki W, et al. Population-based study of relationship between hospital surgical volume and 5-year survival of stomach cancer patients in Osaka, Japan. Cancer Sci, 94, 998-1002, 2003.

3) Ioka A, Tsukuma H, Ajiki W, et al. Influence of hospital procedure volume on ovarian cancer survival in Japan, a country with low incidence of ovarian cancer. Cancer Sci, 95, 233-7, 2004.

4) Ioka A, Tsukuma H, Ajiki W, et al. Influence of hospital procedure volume on uterine cancer survival in Osaka, Japan. Cancer Sci, 96, 689-94, 2005.

5) Peter BB, Laura DC, Deborah S, et al. The influence of hospital volume on survival after resection for lung cancer. N Engl J Med, 345, 181-8,2001.

6) Romano PS, Mark DH. Patient and hospital characteristics related to in-hospital mortality after lung cancer resection. Chest, 101, 1332-7, 1992.

7) Begg CB, Cramer LD, Hoskins WJ, et al. Impact of hospital volume on operative mortality for major cancer surgery. JAMA , 280, 1747-51, 1998.

8) Birkmeyer JD, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. N Engl J Med, 349, 2117-27, 2003.

9) Metzger R, Bollschweiler E, Vallbohmer D, et al. the number needed to achieve low postoperative mortality? Dis Esophagus, 17, 310-4, 2004.

10) Sosa JA, Bowman HM, Gordon TA, et al. Importance of hospital volume in the overall management of pancreatic cancer. Ann Surg, 228, 429-38, 1998.

11) Roohan PJ, Bickell NA, Baptiste MS, et al. Hospital volume differences and five-year survival from breast cancer. Am J Public Health, 88, 454-7, 1998.

12) Stefoski MJ, Haward RA, Johnston C, et al. Surgeon workload and survival from breast cancer. Br J Cancer, 89, 487-91, 2003.

13) Schrag D, Cramer LD, Bach PB, et al. Influence of hospital procedure volume on outcomes following surgery for colon cancer. JAMA, 284, 3028-35, 2000.

14) Yao SL, Lu-Yao G. Population-based study of relationships between hospital volume of prostatectomies, patient outcomes, and length of hospital stay. J Natl Cancer Inst, 91, 1950-6, 1999.

15) Dimick JB, Pronovost PJ, Cowan JA, et al. Surgical volume and quality of care for esophageal resection: do high-volume hospitals have fewer complications? Ann Thorac Surg, 75, 337-41, 2003.

16) Osaka Cancer Registry (ed). Survival of cancer patients in Osaka, 1975-89, The Shinohara Publishers Inc, Tokyo, 1998.

17) Osaka Prefecural Department of Public Health and Welfare, Osaka Medical Association, Osaka Medical Center for Cancer and Cardiovascular Diseases: Annual Report of Osaka Cancer Registy No.68 - Cancer Incidence and Medical Care in Osaka 2001 and the Survival in 1997. OPDPHW, 2005.

18) Matsuo K, Hamajima N, Morishima Y, et al. Hospital capacity and post-transplant survival after allogeneic bone marrow transplantation: analysis of data from the Japan Society for Hematopoietic Cell Transplantation. Bone Marrow Transplant, 26, 1061-67, 2000.

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胃がん、肺がんにおける術後5年までの外科手術技術集積性に関する検討

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目　　的：がんの外科手術の成果に関する技術集積性の検討を行うため、1986年から1995年に大阪府地域がん登録に登録された胃がんと肺がんの患者の術後予後を検討した。

対象・方法：解析条件を満たす胃がん（18,582例）と非小細胞肺がん（2,819例）とした。目的変数を術後一定期間までの生死、説明変数を治療医療機関の年平均手術件数（連続値）、性別、年齢、進行度、化学療法と放射線療法の有無（化学療法のみ、放射線療法のみ、化学療法と放射線療法の併用）、病院種別（大学特定病院、大病院、中病院、小病院）として、ロジスティック回帰分析を術後5年まで30日間隔で繰り返し行った。

結果・考察：治療医療機関の年平均手術件数は、術後5年まで30日ごとのどの時点でも、胃がん、肺がんともに予後と有意な関連を示した。胃がんでは、術後60日でもっとも高く（OR = 0.990）、肺がんでは、術後90日（OR = 0.974）がもっとも高かった。

和文キーワード

外科手術予後、技術集積性、肺がん、胃がん、大阪府地域がん登録

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Hospital Procedure Volume and Survival of Cancer Patients in Osaka, Japan: A Population-based Study with Latest Cases

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Epidemiology Report

Hospital Procedure Volume and Survival of Cancer Patients in Osaka, Japan: A Population-based Study with Latest Cases

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Background: Recent studies reported that hospital procedure volume (i.e. volume of patients per hospital receiving a particular treatment)was directly proportional to cancer survival; however the degree of association might be different according to the primary tumor site, extent of disease and year of diagnosis. We performed a systematical examination of survi vals by hospital procedure volume according to the primary site with inclusion of latest cases in Osaka, Japan.

Methods: Individual data on reported cancer cases with active follow-up information and diagnosis between 1994 and 1998 were retrieved from Osaka Cancer Registry's database. The analysed primary sites included oesophagus, stomach, large bowel, liver, gall bladder, pancreas, lung, breast, uterus, ovary, prostate, bladder and lymphoma. Hospitals were ranked as high-, medium-, low- and very low-volume hospitals for every primary site by dividing the number of cancer patients who received treatment in hospitals into four quartiles.

Results: The primary sites could be classified into three categories based on the association between hospital procedure volume and cancer survival: In type 1, a better survival was associated with a higher procedure volume as for oesophagus, liver, lung, ovary, prostate, or lymphoma; in type 2, a better survival was associated with a higher procedure volume but there was no significant difference in survival between high- and medium-volume hospitals as for uterus; and in type 3, there was no significant difference in survival among high-, medium- and low-volume hospitals as for stomach, large bowel, gall bladder, pancreas, breast, or bladder sites.

Conclusions: A higher procedure volume was generally associated with a better survival; however, this association could be classified into three types according to the primary site.

Key words: hospital procedure volume – survival – cancer – primary site

INTRODUCTION

Recent studies have suggested that hospital procedure volume is directly proportional to cancer survival (1–4) however, the degree of association might be different according to the primary site, extent of disease and year of diagnosis as suggested partly in our studies (5–8). We have thus tried to clarify the association between hospital procedure volume (i.e. the number of patients who received treatment) and survival systematically according to the primary site using the latest data of the Osaka Cancer Registry (OCR).

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METHODS

Data Sources

Individual data on reported cancer cases with active follow-up information and a diagnosis during 1994–98 were retrieved from the database of the OCR, which has been operating since December 1962 and covers Osaka Prefecture with a population of 8.8 million (2000 census) (9,10). Criteria for the analysis were as follows:

i) In the case of multiple tumors, only the first was included.
ii) Cases diagnosed as carcinoma *in situ* or mucosal cancer of colon and rectum were excluded.
iii) Primary sites were oesophagus (C15, ICD Tenth Revision), stomach (C16), large bowel (C18–C21), liver (C22), gall bladder, etc. (C23–C24), pancreas (C25), trachea, bronchus and lung (C33–C34), breast (C50), uterus (C53–C55), ovary (C56), prostate (C61), bladder (C67) and lymphoma (C81–C90, C96).

In the processing of OCR's data for cancer statistics, primary facilities for treatment of each cancer were determined and coded in the following order: surgery, radiotherapy, transarterial embolization, ethanol injection, chemotherapy, immunotherapy, hormone therapy, laser therapy and thermotherapy. Hospitals were ranked as high-, medium-, low- and very low-volume hospitals for every site by dividing the number of cancer patients who received treatment in hospitals, excluding clinics and unknown, into four quartiles. The cancer stage at diagnosis was classified into the following three categories:

i) Localized: cancer is confined to the original organ.
ii) Regional: cancer has spread to regional lymph nodes and/or to immediately adjacent tissues.
iii) Distant: cancer has metastases to distant organs.

Statistical Analysis

A cumulative survival was estimated using the Kaplan–Meier method for each category of hospital procedure volume. Survival time was computed from the date of first diagnosis to the end-point, defined as death from any cause. Closing date was defined as the date 5 years after the first diagnosis. The relative 5-year survival (11,12) was calculated as the ratio of the observed survival to the expected survival estimated using the survival probability of similar subjects in the general population of Japan with respect to sex, age and calendar year at diagnosis. The prognostic factors were adjusted using the Cox proportional hazards regression model during the 5 years following diagnosis. In this analysis, independent variables were sex, age, cancer stage (localized, regional, distant and unknown), and hospital procedure volume (high-, medium-, low- and very low-procedure volume). Differences were considered as statistically significant if P values were less than 0.05 by two-sided test. The statistical package software STATA (13) was used for data management and statistical analysis.

RESULTS

Tables 1–13 illustrate the relative 5-year survival by hospital procedure volume according to the primary site. In stomach,

Table 1. The relative 5-year survival by hospital procedure volume for oesophagus cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage												All[3]				Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant									
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	716	(24.2)	45.7	2.1	1440	(48.6)	13.3	0.9	533	(18.0)	3.5	0.8	2961	(100.0)	20.0	0.8	–	–
High-volume hospital	3	3.6	172	(26.3)	56.0	4.3	340	(51.9)	22.4	2.4	118	(18.0)	11.0	3.0	655	(100.0)	29.3	1.9	1.0	–
Medium-volume hospital	6	1.6	179	(30.3)	46.4	4.1	314	(53.2)	12.6	2.0	74	(12.5)	4.3	2.4	590	(100.0)	21.9	1.8	1.3	1.2–1.5
Low-volume hospital	17	0.6	161	(27.4)	52.1	4.4	306	(52.0)	11.5	1.9	102	(17.3)	1.1	1.1	588	(100.0)	21.1	1.8	1.3	1.2–1.5
Very-low-volume hospital	117	0.1	134	(22.4)	32.2	4.4	316	(52.9)	9.8	1.8	112	(18.8)	1.0	1.0	597	(100.0)	13.0	1.5	1.6	1.4–1.9

CI, confidence interval.
[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 2. The relative 5-year survival by hospital procedure volume for stomach cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All*[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	8817	(41.7)	89.0	0.5	6510	(30.8)	30.7	0.6	3815	(18.1)	1.1	0.2	21 119	(100.0)	50.1	0.4	–	–
High-volume hospital	8	9.5	2541	(55.8)	93.5	0.8	1467	(32.2)	40.8	1.4	484	(10.6)	2.5	0.7	4556	(100.0)	66.1	0.8	1.0	–
Medium-volume hospital	12	5.4	1899	(48.6)	92.5	0.9	1222	(31.2)	37.3	1.5	556	(14.2)	1.4	0.5	3911	(100.0)	59.6	0.9	1.1	1.0–1.2
Low-volume hospital	26	2.8	2100	(48.9)	93.3	0.9	1424	(33.2)	37.4	1.4	582	(13.6)	2.0	0.6	4292	(100.0)	60.5	0.9	1.1	1.0–1.1
Very-low-volume hospital	242	0.3	1391	(33.0)	79.9	1.4	1697	(40.3)	18.7	1.0	946	(22.4)	0.7	0.3	4214	(100.0)	34.3	0.8	1.6	1.5–1.7

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 3. The relative 5-year survival by hospital procedure volume for large bowel cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	6172	(41.0)	89.1	0.6	4771	(31.7)	51.3	0.8	2736	(18.2)	5.6	0.5	15 045	(100.0)	58.0	0.5	–	–
High-volume hospital	8	7.1	1712	(50.3)	93.4	1.1	1203	(35.4)	59.0	1.6	432	(12.7)	10.4	1.6	3402	(100.0)	69.7	1.0	1.0	–
Medium-volume hospital	14	3.8	1418	(44.4)	92.3	1.2	1086	(34.0)	62.2	1.7	482	(15.1)	7.1	1.2	3197	(100.0)	66.7	1.0	1.0	1.0–1.1
Low-volume hospital	27	2.1	1565	(47.1)	92.7	1.1	1079	(32.5)	57.0	1.7	498	(15.0)	8.1	1.3	3325	(100.0)	66.9	1.0	1.1	1.0–1.2
Very-low-volume hospital	212	0.3	1073	(33.0)	76.2	1.7	1202	(37.0)	31.7	1.5	835	(25.7)	3.1	0.6	3253	(100.0)	38.4	1.0	1.8	1.7–1.9

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 4. The relative 5-year survival by hospital procedure volume for liver cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	5956	(50.1)	26.9	0.6	1541	(13.0)	7.0	0.7	1337	(11.3)	1.9	0.4	11 880	(100.0)	16.8	0.4	–	–
High-volume hospital	5	6.4	1389	(72.8)	41.4	1.4	280	(14.7)	19.9	2.6	163	(8.5)	6.7	2.1	1907	(100.0)	34.4	1.2	1.0	
Medium-volume hospital	13	2.6	1383	(69.0)	33.1	1.4	207	(10.3)	11.3	2.3	157	(7.8)	2.9	1.4	2003	(100.0)	25.7	1.1	1.3	1.2–1.4
Low-volume hospital	24	1.3	1203	(62.8)	26.4	1.4	152	(7.9)	4.4	1.7	162	(8.5)	2.1	1.2	1915	(100.0)	19.4	1.0	1.5	1.4–1.6
Very-low-volume hospital	189	0.2	921	(48.2)	17.3	1.3	283	(14.8)	2.9	1.1	243	(12.7)	0.9	0.6	1909	(100.0)	10.4	0.7	1.9	1.8–2.1

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 5. The relative 5-year survival by hospital procedure volume for gall bladder cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	557	(20.2)	46.1	2.4	1167	(42.2)	6.7	0.8	597	(21.6)	0.4	0.3	2763	(100.0)	12.8	0.7	–	–
High-volume hospital	8	0.8	124	(33.2)	66.7	5.0	164	(43.9)	16.3	3.1	66	(17.6)	1.6	1.6	374	(100.0)	29.3	2.6	1.0	
Medium-volume hospital	14	0.4	114	(31.4)	68.2	5.1	167	(46.0)	7.9	2.2	54	(14.9)	2.1	2.0	363	(100.0)	26.0	2.5	1.1	0.9–1.3
Low-volume hospital	29	0.2	98	(26.8)	49.8	5.8	173	(47.4)	11.1	2.6	79	(21.6)	0.0	0.0	365	(100.0)	18.5	2.2	1.2	1.0–1.4
Very-low-volume hospital	126	0.0	66	(18.2)	39.6	6.9	183	(50.6)	2.4	1.2	57	(15.7)	0.0	0.0	362	(100.0)	8.9	1.6	1.6	1.4–1.9

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 6. The relative 5-year survival by hospital procedure volume for pancreas cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	314	(9.2)	28.8	2.8	1312	(38.6)	3.3	0.5	1314	(38.7)	0.6	0.2	3395	(100.0)	4.7	0.4	–	–
High-volume hospital	5	1.3	86	(21.3)	48.3	6.0	194	(48.1)	10.0	2.2	108	(26.8)	0.0	1.0	403	(100.0)	15.0	1.9	1.0	–
Medium-volume hospital	14	0.5	64	(14.3)	38.8	6.5	206	(46.2)	3.7	1.4	148	(33.2)	2.8	1.4	446	(100.0)	8.5	1.4	1.2	1.0–1.3
Low-volume hospital	27	0.3	39	(9.4)	33.8	8.1	187	(45.3)	5.9	1.8	152	(36.8)	1.4	1.0	413	(100.0)	7.0	1.3	1.1	0.9–1.2
Very-low-volume hospital	140	0.0	33	(8.0)	6.4	4.4	209	(50.5)	1.6	0.9	143	(34.5)	0.0	0.0	414	(100.0)	1.3	0.6	1.5	1.3–1.7

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 7. The relative 5-year survival by hospital procedure volume for lung cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	2482	(18.2)	55.3	1.2	5036	(37.0)	11.8	0.5	4819	(35.4)	1.7	0.2	13 609	(100.0)	15.6	0.3	–	–
High-volume hospital	3	13.5	661	(27.1)	78.6	2.0	1037	(42.6)	21.5	1.4	720	(29.5)	3.5	0.7	2437	(100.0)	31.7	1.0	1.0	–
Medium-volume hospital	4	8.4	355	(17.6)	65.8	3.0	1006	(49.8)	12.7	1.1	631	(31.2)	2.9	0.7	2022	(100.0)	18.8	0.9	1.3	1.2–1.4
Low-volume hospital	13	3.2	616	(25.0)	59.3	2.3	901	(36.6)	14.0	1.2	882	(35.9)	2.1	0.5	2460	(100.0)	21.0	0.9	1.3	1.3–1.4
Very-low-volume hospital	196	0.2	374	(16.1)	43.9	2.9	848	(36.6)	8.2	1.0	929	(40.1)	1.0	0.3	2316	(100.0)	10.7	0.7	1.8	1.6–1.9

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 8. The relative 5-year survival by hospital procedure volume for breast cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	4525	(52.8)	95.8	0.4	3148	(36.7)	74.8	0.8	496	(5.8)	19.7	1.9	8575	(100.0)	82.9	0.5	–	–
High-volume hospital	4	8.6	1191	(58.0)	97.2	0.7	747	(36.4)	78.6	1.6	89	(4.3)	22.6	4.6	2055	(100.0)	87.1	0.8	1.0	–
Medium-volume hospital	7	4.6	1041	(53.9)	96.4	0.9	732	(37.9)	76.0	1.7	75	(3.9)	24.3	5.2	1931	(100.0)	85.1	0.9	1.1	1.0–1.3
Low-volume hospital	17	2.0	1097	(52.9)	96.8	0.9	834	(40.2)	77.7	1.6	96	(4.6)	27.5	4.7	2073	(100.0)	85.7	0.9	1.1	0.9–1.2
Very-low-volume hospital	154	0.2	1031	(52.1)	93.8	1.1	729	(36.9)	67.4	1.9	181	(9.2)	17.0	2.9	1978	(100.0)	76.5	1.1	1.6	1.4–1.8

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 9. The relative 5-year survival by hospital procedure volume for uterine cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	1705	(53.7)	89.8	0.9	1084	(34.2)	48.2	1.6	219	(6.9)	10.2	2.1	3173	(100.0)	67.7	0.9	–	–
High-volume hospital	2	6.4	500	(65.0)	92.4	1.4	221	(28.7)	64.6	3.5	34	(4.4)	12.4	5.8	769	(100.0)	80.6	1.6	1.0	–
Medium-volume hospital	2	5.2	386	(61.5)	95.3	1.4	210	(33.4)	59.1	3.6	32	(5.1)	32.2	8.4	628	(100.0)	80.0	1.7	0.9	0.7–1.1
Low-volume hospital	6	2.2	389	(49.2)	88.4	2.0	318	(40.3)	50.5	3.0	56	(7.1)	9.6	4.1	790	(100.0)	66.7	1.8	1.3	1.1–1.6
Very-low-volume hospital	77	0.2	370	(52.6)	83.8	2.2	244	(34.7)	34.3	3.2	52	(7.4)	4.1	2.8	704	(100.0)	57.6	2.0	2.1	1.7–2.5

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 10. The relative 5-year survival by hospital procedure volume for ovarian cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	356	(28.6)	81.2	2.2	439	(35.3)	30.1	2.2	329	(26.4)	13.8	2.0	1245	(100.0)	40.5	1.4	–	–
High-volume hospital	3	1.5	112	(42.9)	85.0	3.7	93	(35.6)	48.7	5.3	51	(19.5)	28.2	6.4	261	(100.0)	60.3	3.1	1.0	–
Medium-volume hospital	9	0.5	99	(34.7)	90.3	3.3	107	(37.5)	41.8	4.9	63	(22.1)	11.8	4.2	285	(100.0)	52.4	3.1	1.3	1.0–1.7
Low-volume hospital	16	0.3	76	(28.6)	76.9	5.1	105	(39.5)	23.6	4.2	67	(25.2)	15.4	4.5	266	(100.0)	37.0	3.0	1.7	1.4–2.2
Very-low-volume hospital	84	0.05	55	(20.6)	76.7	6.3	104	(39.0)	14.0	3.5	85	(31.8)	12.5	3.7	267	(100.0)	27.0	2.8	2.0	1.6–2.5

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 11. The relative 5-year survival by hospital procedure volume for prostate cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	892	(44.0)	94.2	1.9	267	(13.2)	68.5	4.0	677	(33.4)	31.6	2.2	2027	(100.0)	66.6	1.4	–	–
High-volume hospital	3	2.4	262	(61.6)	100.0	2.4	72	(16.9)	82.8	6.7	84	(19.8)	50.9	6.4	425	(100.0)	90.9	2.5	1.0	–
Medium-volume hospital	7	1.1	249	(53.7)	91.1	3.6	63	(13.6)	71.9	8.2	139	(30.0)	52.6	5.6	464	(100.0)	76.5	3.0	1.4	1.1–1.8
Low-volume hospital	13	0.6	197	(45.1)	94.2	4.2	64	(14.6)	80.7	8.3	148	(33.9)	31.2	4.5	437	(100.0)	69.5	3.1	1.7	1.3–2.1
Very-low-volume hospital	98	0.08	121	(27.4)	74.6	5.9	49	(11.1)	40.2	9.1	222	(50.2)	15.6	2.9	442	(100.0)	39.2	2.9	2.7	2.1–3.3

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 12. The relative 5-year survival by hospital procedure volume for bladder cancer

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	1428	(73.0)	86.6	1.4	239	(12.2)	22.2	3.0	132	(6.8)	4.9	2.2	1955	(100.0)	70.5	1.3	–	–
High-volume hospital	3	2.3	346	(83.8)	92.6	2.6	46	(11.1)	39.7	8.0	11	(2.7)	9.8	9.3	413	(100.0)	83.7	2.6	1.0	–
Medium-volume hospital	6	1.3	418	(87.3)	86.4	2.5	36	(7.5)	35.7	9.6	19	(4.0)	13.8	9.2	479	(100.0)	79.2	2.5	1.2	1.0–1.5
Low-volume hospital	10	0.7	356	(82.6)	92.4	2.6	38	(8.8)	16.0	6.7	22	(5.1)	5.7	5.6	431	(100.0)	81.0	2.7	1.1	0.8–1.4
Very-low-volume hospital	70	0.10	260	(61.2)	76.5	3.6	83	(19.5)	15.7	4.4	46	(10.8)	2.9	2.9	425	(100.0)	53.6	2.9	1.6	1.3–2.0

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

Table 13. The relative 5-year survival by hospital procedure volume for lymphoma

	No. of hospitals	No. of patients/ hospital-month	Cancer stage																Adjusted hazard ratio[4]	95% CI
			Localized				Regional				Distant				All[3]					
			No.	(%)	RSR[1]	SE[2]	No.	(%)	RSR	SE	No.	(%)	RSR	SE	No.	(%)	RSR	SE		
Osaka prefecture	–	–	537	(18.4)	65.1	2.3	470	(16.1)	43.4	2.5	1213	(41.5)	26.8	1.4	2920	(100.0)	37.7	1.0	–	–
High-volume hospital	4	2.6	140	(22.4)	69.7	4.4	110	(17.6)	69.4	4.8	344	(55.1)	42.0	2.8	624	(100.0)	53.7	2.1	1.0	–
Medium-volume hospital	8	1.2	126	(22.3)	71.3	4.5	94	(16.6)	47.7	5.5	204	(36.0)	32.7	3.5	566	(100.0)	47.8	2.3	1.2	1.0–1.4
Low-volume hospital	18	0.6	138	(22.5)	64.0	4.6	94	(15.3)	49.5	5.7	250	(40.8)	22.9	2.8	613	(100.0)	36.3	2.1	1.5	1.3–1.8
Very-low-volume hospital	142	0.1	81	(13.3)	53.8	6.2	118	(19.3)	23.2	4.1	249	(40.8)	11.6	2.2	610	(100.0)	20.9	1.8	2.2	1.9–2.5

[1]Relative 5-year survival. [2]Standard error. [3]All including cases with unknown stage. [4]Adjustment for sex, age and cancer stage.

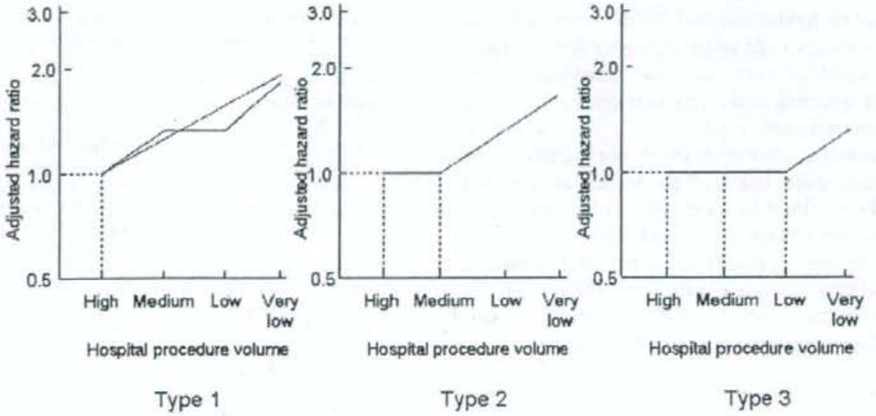

Figure 1. Three types of associations between hospital procedure volume and adjusted hazard ratios (HRs). In type 1, a lower HR was associated with a higher procedure volume; in type 2, a lower HR was associated with a higher procedure volume but there were equivalent HRs between high- and medium-volume hospitals; and in type 3, there were almost equivalent HRs among high-, medium- and low-volume hospitals.

large bowel and breast cancer, the survival in medium-/low-volume hospitals was almost the same as that in high-volume hospitals, however, in other cancers, the survival increased with increasing hospital procedure volume. The associations between the hospital procedure volume and adjusted hazard ratio (HR) were classified into three types (Fig. 1): type 1 showed a higher procedure volume–lower HR association for oesophagus, liver, lung, ovary, prostate and lymphoma; type 2 showed a higher procedure volume–lower HR association but equivalent HRs between high- and medium-volume hospitals for the uterus; and type 3 showed almost equivalent HRs among high-, medium- and low-volume hospitals for stomach, large bowel, gall bladder, pancreas, breast and bladder.

DISCUSSION

A population-based study with recent data from OCR suggested a significant association between hospital procedure volume and survival. Three types of association were observed according to the primary site. This study is unique and valuable for the use of population-based data with active follow-ups, although several limitations were inherent.

These relationships might have been confounded by treatment modalities: operable cases might have been treated by higher volume hospitals even in the same stage and primary site, which lead to spurious associations. We have already examined relationships between hospital surgical volume and survival for cancers of the stomach, breast, uterus and ovary, which all showed findings similar to the present study. Because treatment procedures closely correlate with cancer stage, we analysed the associations according to the stage and/or with adjustment for the stage. However, the observed associations might be still confounded by treatment modalities.

Hospitals were classified into four categories by dividing the number of cancer patients who received treatments in hospitals into four quartiles, as high-, medium-, low- and very low-volume hospitals based on a bigger number of patients per hospital-month. In this study however, the number of patients per hospital-month was very few in several primary sites even in high-volume hospitals. Therefore, the interpretation of the high-volume category should be made carefully because it may not necessarily mean physicians and medical teams belonging to high-volume hospitals had lots of experience of cancer treatments.

We suggested that the primary sites were classified into three categories based on the association between hospital procedure volume and cancer survival, which was supported by partition clustering method of medians: when a high-volume hospital was taken as a reference, adjusted HRs were categorized into four clusters (i.e. almost the same HRs as 1.0 with median 1.0, much higher HRs than 1.0 with median 2.1, and lower/higher intermediate HRs between these with median 1.3/1.6) using this method. The primary sites were, then, reasonably classifiable into types 1–3 when we considered combinations of these clusters of HRs and 95% CI of HRs.

In lung, liver and prostate cancers belonging to type1, a much higher survival in high-volume hospitals might have been influenced by stage migration as well as insufficient adjustment for cancer stage distribution: for example, in lung cancer at the localized stage, the survival in high-volume hospitals was double that in very low-volume hospitals. In gall bladder and pancreas cancers belonging to type3, the 5-year survival might have been too long to evaluate associations between hospital procedure volume and survival, as well as in the other cancers with distant metastases.

Some other limitations should be kept in mind in this study. Among the patients' characteristics, we only took sex and age into consideration. We should have also considered the prevalence of co-morbidities and difference of socioeconomic factors, and so on. In addition, as we mentioned in prior studies, we should have taken into consideration the completeness of reporting to the cancer registry and quality of information on treatment.

Despite the limitations mentioned above, our analysis is now one of the few approaches to clarify the association between hospital procedure volume and survival. The study results suggest that there were three types of relationships between hospital procedure volume and cancer survival. The authors consider that epidemiology data like this would be very important for the planning and execution of effective cancer control programs in Osaka where there are many hospitals.

Conflict of interest statement

None declared.

References

1. Killeen SD, O'Sullivan MJ, Coffey JC, Kirwan WO, Redmond HP. Provider volume and outcomes for oncological procedures. *Br J Surg* 2005;92:389–402.
2. Hillner BE. Is cancer care best at high-volume providers? *Curr Oncol Rep* 2001;3:404–9.
3. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002;346:1128–37.
4. Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. *JAMA* 1998;280:1747–51.
5. Ioka A, Tsukuma H, Ajiki W, Oshima A. Influence of hospital procedure volume on uterine cancer survival in Osaka, Japan. *Cancer Sci* 2005;96:689–94.
6. Ioka A, Tsukuma H, Ajiki W, Oshima A. Influence of hospital procedure volume on ovarian cancer survival in Japan, a country with low incidence of ovarian cancer. *Cancer Sci* 2004;95:233–7.
7. Nomura E, Tsukuma H, Ajiki W, Oshima A. Population-based study of relationship between hospital surgical volume and 5-year survival of stomach cancer patients in Osaka, Japan. *Cancer Sci* 2003;94: 998–1002.
8. Nomura E, Tsukuma H, Ajiki W, Ishikawa O, Oshima A. Population-based study of the relationship between hospital surgical volume and 10-year survival of breast cancer patients in Osaka, Japan. *Cancer Sci* 2006;97:618–22.
9. Ajiki W, Tsukuma H, Oshima A. Trends in cancer incidence and survival in Osaka. In: Tajima K, Oshima A, Kuroishi T, editors. *Cancer Mortality and Morbidity Statistics: Japan and the World—2004*, Gann Monograph on Cancer Research No. 51. Tokyo: Japan Sci Soc Press 2004; 137–63.
10. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB. Cancer Incidence in Five Continents, Vol. VIII. IARC Scientific Publ. No. 155. Lyon, France: International Agency for Research on Cancer 2002.
11. Ajiki W, Matsuda T, Sato Y, Fujita M, Yamazaki S, Murakami R, et al. Standard method of calculating relative survival rates in population-based cancer registries—an investigation using stomach cancer patients. *Jpn J Cancer Cli* 1997;43:1005–14.
12. Estev J, Benhamou E, Raymond L. Statistical Methods in Cancer Research, Vol. IV: Descriptive Epidemiology. IARC Scientific Publ. No. 128. Lyon, France: International Agency for Research on Cancer 1994; 231–45.
13. StataCorp. Stata Statistical Software: Release 8.0. Texas, US Stata Corporation 2003.

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Cancer Survival Trends in Osaka, Japan: the Influence of Age and Stage at Diagnosis

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Background: Five-year survival is an important index for evaluating the overall effectiveness of cancer diagnosis and treatment. The aim of this study was to monitor trends in 5-year cancer survival in Osaka, Japan, during 1975–94, with adjustment for trends in age and stage at diagnosis.
Methods: Five-year crude survival was estimated for cancers of the stomach (39 697 patients), lung (17 400 patients) and breast (11 988 women) in four consecutive 5-year periods, with adjustment for age and/or stage, using the age and stage distribution of cases diagnosed during 1975–79 as standard weights. We estimated the impact of adjusting for either age or stage alone by their proportionate impact on the trend in fully (age- and stage-) adjusted survival.
Results: The absolute increase in unadjusted 5-year survival over 20 years was about 20% for stomach cancer, 14% for breast cancer and 5% for lung cancer. Lack of age adjustment would have caused proportionate under-estimation of these trends by 13–14% (stomach), 7% (breast), 14% (lung, men) and 4% (lung, women). Lack of adjustment for the trend toward earlier stage would have caused proportionate over-estimation (152%, men: 133%, women) of stomach cancer survival trends, which seemed more influenced by earlier diagnosis than more effective treatment. For breast cancer, the 31% over-estimation of trend from lack of stage adjustment suggests the impact of earlier diagnosis, while the improvement of survival after additional adjustment for age may be due to more effective treatment. Failure to adjust for stage led to a proportionate 21% under-estimation of lung cancer survival trends for men, and 4% over-estimation for women.
Conclusion: This study confirms the importance of adjusting for trends in age and stage distribution when evaluating time trends in cancer survival.

Key words: Survival analysis – cancer registries – risk adjustment – early diagnosis – ageing

INTRODUCTION

Five-year survival is an important index to evaluate the overall effectiveness of cancer diagnosis and treatment. An increase of 20% in 5-year cancer survival has been proposed as a possible objective for the Japanese government's 'Strategy of Healthy Frontier' between 2005 and 2015 (1). When the objective is finally agreed, it will be necessary to monitor progress towards the target figure. Progress should be evaluated with data from the seven population-based prefectural cancer registries that have already published survival data, which can be used as a baseline (2). The cancer population will change over the next decade, however, with an increase in the average age at diagnosis and a shift toward earlier stage at diagnosis, both of which will influence trends in overall survival. Stratification or adjustment for these variables will be necessary for valid comparison of cancer survival over time (3).

The aim of this study was to monitor time trends in 5-year survival while adjusting for the influence of trends in the distribution of stage and age at diagnosis. Previous studies using population-based cancer registry data have shown time trends in cancer survival adjusted either for age or for stage at diagnosis (4). In this study, we have adjusted

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simultaneously for both age and stage, and compared the impact of this joint adjustment with the impact of adjusting for each variable separately.

MATERIALS AND METHODS

We have examined survival trends among residents of Osaka Prefecture who were diagnosed with cancer of the stomach, lung or breast (women only) during the 20-year period 1975–94 and registered in Osaka Cancer Registry. All patients were followed up for at least 5 years to determine their vital status.

Data Sources

Osaka Cancer Registry has collected population-based data on all residents of Osaka Prefecture diagnosed with a first primary malignancy since 1962. The prefectural population is approximately 8.8 million, of whom 2.6 million live in Osaka City. The registry has actively followed up each patient to ascertain their vital status (4). Active follow-up was not conducted for patients residing in Osaka City during the period 1975–92, however, so the analysis reported here was restricted to residents of Osaka Prefecture other than Osaka City itself. Data were retrieved from the registry database on patients resident outside Osaka City who were registered as newly diagnosed with a first primary malignancy of the stomach (ICD-10 code C16, 45 444 patients), lung (C33–34, 20 023 patients) or breast (C50, 12 727 women) during the 20-year period 1975–94. We were able to analyse data for 39 697 patients with stomach cancer, 17 400 with lung cancer and 11 988 women with breast cancer, for all of whom the stage at diagnosis was known. We estimated separately the survival for patients with unknown stage at diagnosis (9098 cases, 11.6% of total). A small proportion of cases were not followed up for 5 years after diagnosis (stomach, 1.7%; breast 3.0%; lung 0.6%). Sixteen patients (0.02%) diagnosed under 15 years of age were excluded from analysis.

Statistical Analysis

We calculated the absolute 5-year survival with the actuarial method for patients diagnosed in each of four calendar periods (1975–79, 1980–84, 1985–89, 1990–94). Survival estimates were also adjusted for age at diagnosis (five categories: 15–44, 45–54, 55–64, 65–74, 75+ years), stage (four categories: localized, involvement of regional lymph nodes, direct invasion of adjacent organs or tissue and distant metastasis) and age and stage combined (20 categories). Adjustment was made with a method proposed by Brenner et al. (5–10). Using this approach for age adjustment, for example, age-specific weights are first assigned to each patient in a given age group, and conventional survival analysis is then carried out with the 'weighted individual data', in which weights are applied to the contributions of each patient to the number of persons at risk of death. Thus if r_i is the proportion of patients in the ith age group in a particular patient group (e.g. those diagnosed in 1980–84, 1985–89 and 1990–94), and s_i is the corresponding proportion in the standard population (patients diagnosed in 1975–79), then the weight assigned to each patient in the ith age group is s_i/r_i. This method overcomes a problem that arises with the traditional approach (11) to direct standardization, when data are sparse in some or all of the categories for which we wish to adjust the survival estimate. Although our data set was large, data were still sparse in some of the 20 categories of age and stage combined, in that we extended the single-factor approach to deal with two factors.

Interpreting trends in survival as a guide to progress, without adjustment for stage or age, would be complicated by the combined effect on survival of trends in the distribution of age and stage among cancer patients diagnosed in successive calendar periods. We therefore defined the reference value for the trend in survival as the difference between the survival estimate for patients diagnosed in 1975–79 (baseline) and the survival estimate for patients diagnosed in 1990–94, after adjustment for changes in the distribution of age and stage since 1975–79. The impact of adjusting for stage or age was quantified by the proportionate difference from the reference trend obtained by adjusting only for age or for stage (see Appendix).

RESULTS

The proportion of patients diagnosed with stomach cancer at localized stage increased substantially from about 25% in the late 1970s to over 40% in the early 1990s, even though the age distribution has shifted toward more elderly patients (Table 1). The age distribution of women with breast cancer also shifted slightly toward the elderly, and the stage distribution has shifted towards earlier stage at diagnosis: more than half the women with known stage diagnosed during the early 1990s had localized disease. The shift toward more elderly patients was more marked for lung cancer, but the stage distribution has not changed much since the early 1980s: more than 40% of patients still present with metastatic disease; the proportion was actually lower in the late 1970s.

Stomach

Five-year survival from stomach cancer increased rapidly in both sexes, from about 25% for patients diagnosed during 1975–79 to 45% for those diagnosed during 1990–94 (Fig. 1a,b). For men, the estimate of the trend in survival without adjustment (raw trend), a 19% increase, was hardly altered by adjustment for age (21% increase). By contrast, adjustment for stage substantially altered the estimate of trend in survival (only a 7% increase since 1975–79, and 8% increase when fully adjusted). Thus fully adjusted

Table 1. Trends in the distribution (%) of patients by sex, age and stage: selected cancers, Osaka, Japan, 1975–94

	Men				Women			
Period of diagnosis	1975–79	1980–84	1985–89	1990–94	1975–79	1980–84	1985–89	1990–94
Stomach								
No. of patients	4286	6100	7328	7595	2751	3588	4173	3876
age								
15–44	13.0	12.0	9.8	7.1	21.7	20.2	17.2	12.7
45–54	19.1	19.7	20.6	17.5	16.8	16.8	18.4	18.0
55–64	24.7	24.4	29.7	32.1	22.1	21.0	21.6	22.2
65–74	30.9	29.7	25.0	26.7	26.5	27.0	24.5	24.4
75+	12.3	14.1	14.9	16.6	13.0	15.0	18.3	22.7
stage								
Localized	25.3	30.2	39.1	43.1	23.2	28.7	35.8	41.8
Regional lymph nodes	27.7	26.0	23.2	23.8	27.2	27.3	24.9	23.0
Adjacent organs	25.6	21.2	15.8	13.1	26.3	20.8	16.4	13.7
Distant metastasis	21.5	22.6	21.9	20.1	23.3	23.1	22.9	21.6
Breast								
No. of patients	–	–	–	–	1567	2542	3495	4384
age								
15–44	–	–	–	–	37.8	35.5	32.8	25.5
45–54	–	–	–	–	30.1	31.7	32.1	35.4
55–64	–	–	–	–	16.2	18.0	19.1	20.9
65–74	–	–	–	–	12.4	10.3	10.7	11.9
75+	–	–	–	–	3.5	4.4	5.3	6.2
stage								
Localized	–	–	–	–	43.1	49.3	51.7	55.5
Regional lymph nodes	–	–	–	–	46.1	41.2	39.7	36.1
Adjacent organs	–	–	–	–	3.4	3.0	2.9	2.8
Distant metastasis	–	–	–	–	7.3	6.5	5.7	5.6
Lung								
No. of patients	1846	2718	3900	4402	652	938	1325	1619
age								
15–44	5.9	4.2	4.2	3.9	8.0	6.9	6.3	6.1
45–54	13.7	12.8	11.6	10.4	15.2	12.8	13.2	12.4
55–64	24.6	23.9	27.1	26.7	24.4	21.0	22.0	22.8
65–74	39.8	38.3	34.2	34.5	34.4	36.1	33.8	28.9
75+	16.0	20.9	22.8	24.5	18.1	23.1	24.7	29.9
stage								
Localized	19.2	16.3	15.6	16.1	17.6	15.6	15.8	17.3
Regional lymph nodes	25.9	21.0	21.0	21.2	23.2	20.0	19.4	19.3
Adjacent organs	22.5	22.5	21.6	23.3	25.2	20.5	19.1	20.1
Distant metastasis	32.4	40.1	41.9	39.3	34.0	43.9	45.7	43.2

survival only increased from 26 to 34% and little change occurred after the early 1980s.

Compared with the fully adjusted trend in survival between 1975–79 and 1990–94, taken as the standard, the trend would have been under-estimated by a proportionate 13–14% if age adjustment had not been done (I_{age}, −0.139 for men and −0.134 for women, Table 2). More seriously, failure to adjust for the marked shift toward earlier stage at

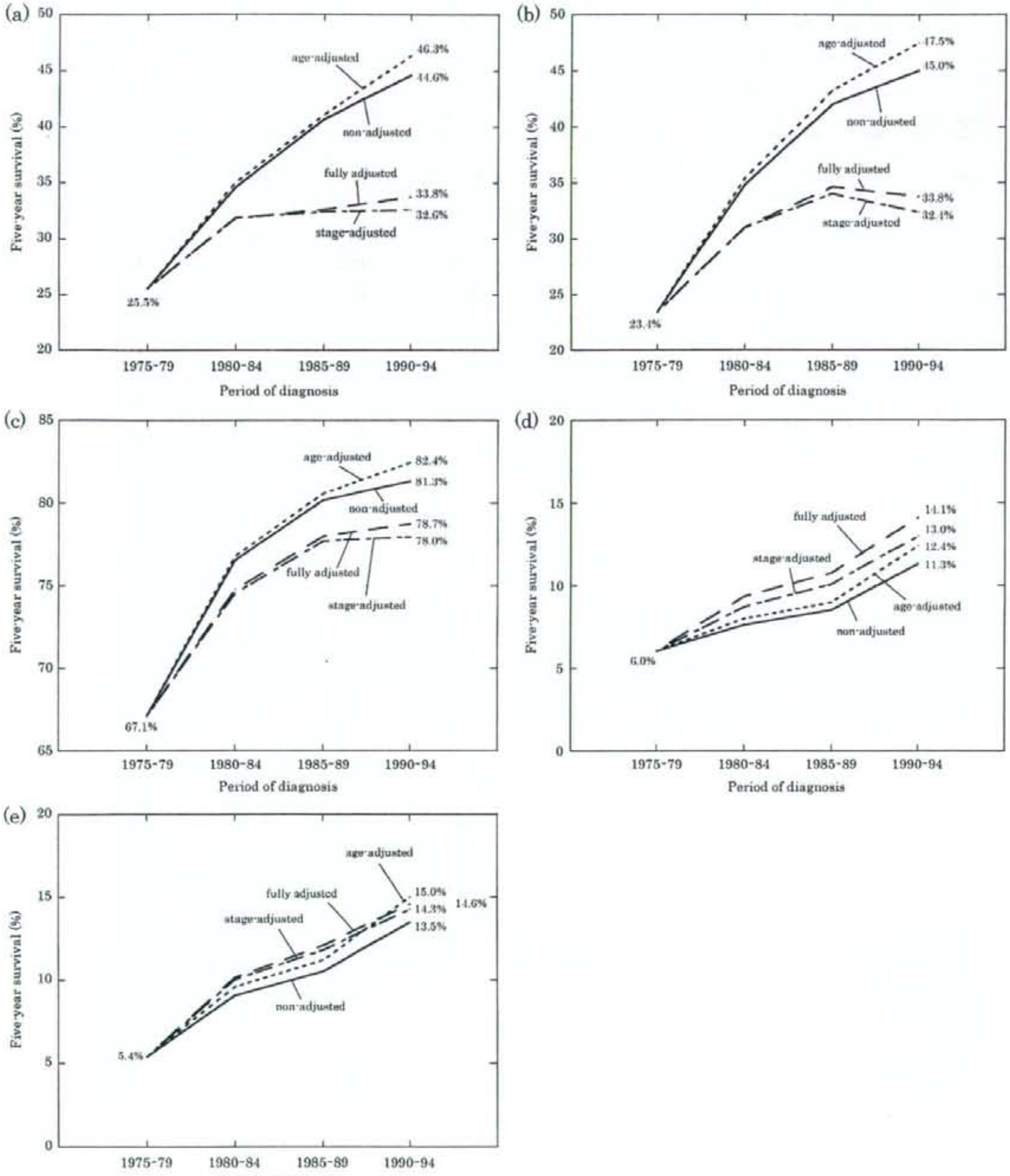

Figure 1. Time trend in 5-year survival, from 1975–79 to 1990–94: selected cancers, Osaka, Japan. (a) stomach, men (b) stomach, women (c) breast, women (d) lung, men (e) lung, women.

diagnosis would have led to a greater than two-fold overestimation of the increase in survival (152.4% too high for men and 132.5% for women, corresponding to I_{stage} 1.524, 1.325; Table 2).

Breast

Five-year survival from breast cancer also increased, from about 67% for women diagnosed during 1975–79 to the

Table 2. Summary of change in 5-year survival (%) from 1975–79 to 1990–94, selected cancers, Osaka, Japan

		Absolute difference between 1975–79 and 1990–94 (%)				Impact of adjustment by age		Impact of adjustment by stage	
		Raw (1)	Age (2)	Stage (3)	Full (4)	(3)/(4)	I_{age}	(2)/(4)	I_{stage}
Stomach	Men	19.1	20.8	7.1	8.2	0.861	−0.139	2.524	1.524
	Women	21.6	24.1	9.0	10.4	0.866	−0.134	2.325	1.325
Breast	Women	14.2	15.3	10.9	11.6	0.934	−0.066	1.319	0.319
Lung	Men	5.3	6.4	7.0	8.1	0.861	−0.139	0.788	−0.212
	Women	8.1	9.6	8.8	9.2	0.965	−0.035	1.044	0.044

(1) = $S_{raw}(t_1) - S(t_0)$; (2) = $S_{age}(t_1) - S(t_0)$; (3) = $S_{stage}(t_1) - S(t_0)$; (4) = $S_{full}(t_1) - S(t_0)$.

fully adjusted figure of 79% for women diagnosed during 1990–94 (Fig. 1c). The estimate of the fully adjusted trend (12% increase) was similar to the unadjusted raw trend (14% increase), with 15% and 11% increases after adjustment for age or stage, respectively. Little change in the fully adjusted survival occurred between 1985–89 and 1990–94.

The overall 12% increase in fully adjusted breast cancer survival between 1975–79 and 1990–94 would have been slightly under-estimated if age adjustment had not been done (a proportionate 6.6%, I_{age}, −0.066; Table 2). More importantly, lack of adjustment for the shift toward earlier stage at diagnosis would have led to over-estimation of the increase in survival by almost a third (31.9%, I_{stage}, 0.319).

Lung

Five-year survival from lung cancer increased from 6.0% in men and 5.4% in women diagnosed 1975–79 to the fully adjusted figure of 14.1% in men and 14.6% in women for 1990–94, overall increases of 8.1 and 9.2%, respectively (Fig. 1d,e). These overall increases would have been under-estimated by a proportion of 13.9% for men and 3.5% for women if age adjustment had not been done (I_{age}, −0.139, −0.035; Table 2). Failure to adjust for stage would have caused proportionate under-estimation of the trend by 21.2% for men, and a slight over-estimation of 4.4% for women (I_{stage}, −0.212, 0.044; Table 2).

The proportion of cases of unknown stage at diagnosis fell from 20% in 1975–79 to less than 10% in 1990–94: this trend was similar for all three cancers examined (data not shown). Five-year survival for unstaged cases was lower than the overall survival for all cases of known stage (data not shown): the difference was largest in stomach cancer (all staged cases 37%, unstaged 20%). For each cancer, however, the overall 5-year survival for all cases combined, both staged and unstaged, was not markedly different from survival for cases with known stage, about 2% lower for stomach cancer and less than 1% lower for cancers of the breast and lung: this is because only about 12% of tumours were of unknown stage (data not shown).

DISCUSSION

Monitoring long-term trends in survival will often require adjustment for changes in the characteristics of patients diagnosed in successive calendar periods. Age and stage are perhaps the most important of these characteristics. When we sub-divide patient populations into many categories defined by such variables, sparse data may complicate the adjustment. Brenner's approach resolves this problem and it enabled us to quantify the impact of changes in the distribution of age and stage at diagnosis on observed survival trends in Osaka, by comparing survival trends adjusted by either age or stage alone with the fully adjusted trend.

For stomach cancer, both unadjusted and age-adjusted survivals rose continuously from 1975–79 to 1990–94, but stage-adjusted and fully adjusted survival levelled off in the 1980s. This seems to result from a trend to progressively earlier diagnosis. Awareness of the importance of early detection of stomach cancer in daily clinical practice and the spread of screening programmes, commonly provided by local communities or employers in Japan, has probably contributed to an increase in early detection (12,13). The trends we report here suggest that, after adjustment for a trend toward earlier diagnosis, treatment did not lead to much improvement in 5-year survival between the early 1980s and the early 1990s.

For women with breast cancer, 5-year survival increased substantially even after adjustment for age and stage. Earlier diagnosis and improved treatment would both seem to have contributed to the improvement. Mass screening with mammography for women aged 50 and over was only introduced in 2000 (40 years and over from 2004), but opportunistic mammography began to be widely used from the 1990s and it has been credited with earlier diagnosis of breast cancer (14). Additionally, breast-conserving surgery, combined with pre-operative or post-operative chemotherapy, and with radiotherapy, also became more widely used between the 1980s and the 1990s (15).

For lung cancer, stage-adjusted and fully adjusted 5-year survival increased more than the unadjusted trend. The higher proportion of cases diagnosed with distant metastases from 1980 onwards is probably due to improved diagnostic procedures. Some patients who would not have been diagnosed as metastatic in 1975–79 might have been so diagnosed with the techniques that became available later, especially after the introduction and widespread use of computerized tomography (16). This 'stage migration' is probably responsible for the increase in stage-specific and stage-adjusted survival (data not shown) (17).

In this study, we used the same age categories (15–44, 45–54, 55–64, 65–74 and 75+) for each cancer. Gondos et al. (9) have examined many methods to categorize age groups because the age distribution differs between cancers, e.g. prostate cancer patients are older. Further examination of how to categorize age in respect to the size of sample and the balance between age groups will be required.

The influence of stage migration needs to be borne in mind when we examine trends in fully adjusted survival. Stage migration may also affect time trends in stage-specific survival, as with lung cancer in this study.

The survival of patients with unknown stage at diagnosis is generally lower than that of patients with known stage, so their exclusion will tend to over-estimate survival in the population as a whole. Ideally, overall survival estimates used for public health evaluation of cancer control should include all cancer patients, even those for whom stage at diagnosis is unknown. The effect on overall survival estimates of excluding unstaged cases was not large in these data, however, since stage was known for a high proportion of cases.

This study suggests that adjustment for changes in the distribution of age and stage at diagnosis of cancer patients diagnosed in successive calendar periods may provide a very different picture of trends in survival than that obtained from unadjusted trends. It follows that Government policy to improve cancer survival—and the surveillance of progress toward any 'target' survival rate—should incorporate the impact of trends in the distribution of age and stage, in order to avoid spurious claims about success or failure of the policy.

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APPENDIX

Estimating the Impact on Survival Trends of Adjusting for Age and Stage

The overall proportionate change in 5-year survival (τ) between patients diagnosed during 1975–79 and those diagnosed during 1990–94 was defined as follows, where $S(t)$ is the 5-year survival rate at time t, with baseline time period t_0 as 1975–79 and t_1 as 1990–94.

$$\tau = \frac{S(t_1) - S(t_0)}{S(t_0)} \quad (1)$$

The proportionate change in survival between 1975–79 and 1990–94 was estimated for unadjusted, age-adjusted, stage-adjusted and fully (age- and stage-) adjusted survival. The impact of adjustment by age I_{age} can then be taken as the proportionate difference between the impact of full adjustment and the impact of adjusting only for stage:

$$I_{age} = \frac{\tau_{stage}}{\tau_{full}} - 1 = \frac{S_{stage}(t_1) - S(t_0)}{S_{full}(t_1) - S(t_0)} - 1. \quad (2)$$

If I_{age} is positive, it reflects the extent to which the change in survival is over-estimated when we adjust only for stage and not also for age. Conversely, if I_{age} is negative, it reflects the extent to which the change in survival is under-estimated when we adjust for stage but not also for age.

The impact of adjusting the survival trend for stage I_{stage} can be written as follows, and the values interpreted equivalently:

$$I_{stage} = \frac{\tau_{age}}{\tau_{full}} - 1 = \frac{S_{age}(t_1) - S(t_0)}{S_{full}(t_1) - S(t_0)} - 1 \quad (3)$$

Conflict of interest statement

None declared.

References

1. Ministry of Health, Labour and Welfare. Commission of screening and health guidance for life-style related disease, the first meeting document, [in Japanese]. http://www.mhlw.go.jp/shingi/2005/07/s0725-7h.html
2. Tsukuma H, Ajiki W, Ioka A, Oshima A. Survival of cancer patients diagnosed between 1993 and 1996: a collaborative study of population-based cancer registries in Japan. *Jpn J Clin Oncol* 2006;36:602–7.
3. Parkin DM, Hakulinen T. Analysis of survival. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet R editors. Cancer Registration: Principles and Methods. IARC Scientific Publications No. 95. Lyon: International Agency for Research on Cancer 1991; 159–76.
4. Ajiki W, Tsukuma H, Oshima A. Trends in cancer incidence and survival in Osaka. *Gann Monogr Cancer Res* 2004;51:137–63.
5. Brenner H, Hakulinen T. On crude and age-adjusted relative survival rates. *J Clin Epidemiol* 2003;56:1185–91.
6. Brenner H, Arndt V, Geffeller O, Hakulinen H. An alternative approach to age adjustment of survival rates. *Eur J Cancer* 2004;40:2317–22.
7. Brenner H, Hakulinen T. Reduction in selective under-ascertainment bias in population-based estimates of cancer patient survival by age adjustment. *Eur J Cancer* 2005;41:1788–93.
8. Brenner H, Hakulinen T. Age adjustment of cancer survival rates: methods, point estimates and standard error. *Br J Cancer* 2005;93:372–5.
9. Gondos A, Parkin DM, Chokunonga E, Brenner H. Calculating age-adjusted cancer survival estimates when age-specific data are