Population-based study of relationship between hospital surgical volume and 5-year survival of stomach cancer patients in Osaka, Japan

Etsuko Nomura, Hideaki Tsukuma, Wakiko Ajiki and Akira Oshima

Department of Cancer Control and Statistics, Osaka Medical Center for Cancer and Cardiovascular Diseases, 1-3-3 Nakamichi, Higashinari-ku, Osaka 537-8511

(Received June 24, 2003/Revised September 4, 2003/Accepted September 5, 2003)

Despite the large number of surgical operations for stomach cancer in Japan, no study based on data from population-based cancer registries has been conducted regarding the relationship between hospital surgical volume for stomach cancer and patients' survival. Using data from the Osaka Cancer Registry (OCR), we performed survival analyses on 28,608 patients aged 35–79 years old who underwent surgery for stomach cancer, according to the extent of disease at diagnosis (localized: cancer is confined to the original organ; regional: cancer spreads to regional lymph nodes; adjacent: cancer infiltrates to adjacent tissue; distant: cancer metastasizes to distant organs). The study was divided into four periods; 1975–79, 1980–84, 1985–89 and 1990–94, according to year of diagnosis. Hospitals were stratified into four groups by total number of stomach cancer operations during each of the study periods, so that the numbers of operations in each group would be approximately equal. Cox's proportional hazards model was used to examine the relationships between hospital volume and 5-year survival according to the extent of disease, after adjustment for age at diagnosis and sex. Positive relationships between hospital volume and 5-year survival were seen in the localized and regional groups during the period 1975–79. These associations, however, decreased in later periods and disappeared in 1990–94 except for the very-low-volume hospitals. Stomach cancer patients treated in these hospitals remained at significantly higher risk of death than in the high-volume hospitals. In the case of the distant group, there was no clear relationship between hospital volume and 5-year survival during the study periods. (Cancer Sci 2003; 94: 998–1002)

Knowledge of the relationship between hospital surgical volume and long-term survival for cancer is of great concern not only for patients and their families, but also for health care providers, since hospital volume is often regarded as an index of technical skill in cancer therapy. Recently, based on data from population-based cancer registries in the US, several studies have documented a significant relationship between hospital volume and survival.[1–3] In these studies, hospital volume is defined as the number of surgical operations for cancer performed at a hospital. However, no study has been conducted regarding the relationship between hospital volume of operations for cancer and survival using population-based data in Japan. Tanaka *et al.*[4] analyzed survivals of stomach cancer, lung cancer and breast cancer according to hospital types in Osaka. Oshima *et al.*[5] compared survival of testicular cancer patients treated in a cancer center with that recorded in the population-based cancer registry in Osaka. However, these analyses were restricted to relationships between survival and hospital bed number or teaching status, and not directed to hospital volume. Hospital bed number might not be related to volume and quality of surgery, or to quality of patient care for some cancers. In the present study, we used data from the Osaka Cancer Registry (OCR) to analyze relationships between hospital volume and survival according to the extent of disease, after adjustment for age at diagnosis and sex.

Subjects and Methods

The OCR has been operating since December 1962, covering Osaka Prefecture, which has a population of 8.8 million (2000 census). Cancer incidence data in Osaka have been reported in Cancer Incidence in Five Continents through volumes III to VIII.[6] The quality of the data, therefore, seems to meet the standard level of the International Association of Cancer Registries at least during the past 3 decades. In 1993–97, the proportion of death certificate-only cases was 11%, and the mortality to incidence (M/I) ratio was 0.58 for stomach cancer.[6]

In the OCR's data processing for cancer statistics, primary facilities for treatment of each cancer were determined and coded according to the following categories: surgery, radiotherapy, transarterial embolization, ethanol injection, chemotherapy, immunotherapy, hormone therapy, laser therapy, and thermotherapy.

From the OCR's data base, 55,782 cases were retrieved for this study. They were all notified cases diagnosed as stomach cancer during 1975–94, and had undergone surgery at hospitals in Osaka Prefecture. Based on these registry data, hospital volumes for surgical procedures on stomach cancer could be counted. The average annual number of stomach cancer cases who underwent surgery for that condition was calculated per hospital.

Since active follow-ups for vital status by searching residential registers were not conducted for patients living in Osaka City during the periods 1975–92, survival analysis in this study was restricted to those who lived in Osaka Prefecture except for Osaka City (where 20,079 cases lived). Furthermore, to increase the validity of the study, the following subjects were excluded from the survival analysis; cases that had been detected by routine screening (3211 cases), patients aged less than 35 years or 80 years and over at diagnosis (2086 cases), cases whose stomach cancer was a subsequent primary (726 cases), and cases whose extent of disease at diagnosis was unknown (1074 cases). A total of 28,608 cases were thus included for survival analysis. Follow-up procedures in the OCR are described elsewhere.[7] Confirmation of vital status by referring to residential registers of municipalities was conducted 5 years after diagnosis. The starting date in this study was set as the date of diagnosis and the closing date was 5 years after that. The proportion of cases of unknown vital status was 4.27% in 1975–79, 1.73% in 1980–84, 1.16% in 1985–89 and 0.96% in 1990–94.

In the OCR, the stage of the disease is classified according to the extent of disease at diagnosis, i.e., 1) localized: cancer is confined to the original organ, 2) regional: cancer spreads to re-

E-mail: NomuraE@mbox.pref.osaka.jp

gional lymph nodes, 3) adjacent: cancer infiltrates adjacent tissue, 4) distant: cancer metastasizes to distant organs.

The total study period was divided into the periods of 1975–79, 1980–84, 1985–89 and 1990–94 according to the year of diagnosis. All hospitals in Osaka which reported at least one case with surgical treatment for stomach cancer were divided into 4 categories of hospital volume with almost equal sizes: high, medium, low, and very low, according to the total number of surgical procedures in each study period.

Observed 5-year survival was calculated by the Kaplan-Meier method. Survival differences were analyzed by Cox's proportional hazards model adjusting for age at diagnosis and sex. The statistical package software STATA (Stata Corp., College Station, TX) was used for statistical analysis. Statistical significance and 95% confidence intervals (CI) of hazard rate ratio were obtained and judged by using a 2-sided test.

Results

Table 1 shows the number of hospitals and number and range of stomach cancer surgical procedures per hospital, according to study period and category of hospital volume. Only 2% (5–7 hospitals) of all hospitals belonged to the high-volume group, and their procedures accounted for a quarter of the stomach cancer operations in Osaka Prefecture. The medium-volume group consisted of 4% of all hospitals. Thus, 6% of hospitals in Osaka Prefecture provided a half of the stomach cancer procedures in Osaka Prefecture. In contrast, more than 83% of the hospitals belonged to the very-low-volume group where the annual number of procedures was less than 25.

Table 2 shows the mean age (with 95% CI) of analyzed patients at diagnosis according to the hospital volume and the study period. Overall, the mean age increased as the study period became more recent. A weak inverse relationship was observed between mean age and hospital volume, although the differences were small.

Table 3 shows the observed 5-year survival of the cases whose cancer was confined to the original organ (localized), together with their age- and sex-adjusted hazard rate ratios compared by hospital volume. In the period 1975–79, a positive association was observed between 5-year survival and hospital volume. The association however decreased during the period 1980–84 because the 5-year survival rates in the medium- and the low-volume hospitals improved. In the very-low-volume group the survival rate remained lower than the others during the entire study period, although the difference decreased with time. These findings were confirmed by Cox's proportional hazards model after adjustment for age and sex.

Table 4 shows the results for the cases whose cancer had spread to the regional lymph nodes. A positive relationship between 5-year survival and hospital volume was seen in 1975–79. In the period 1980–84, the relationship had disappeared except for the very-low-volume group. These findings were also

Table 1. Numbers of hospitals and stomach cancer surgeries with range of the surgical operations per hospital, according to study period and hospital volume

Year of diagnosis		Hospital volume			
		High	Medium	Low	Very low
1975–79	Number of hospitals	5	9	22	173
	Number of operations	2475	2401	2492	2533
	Range of operations per hospital	386–678	178–370	72–174	1–70
1980–84	Number of hospitals	6	10	20	231
	Number of operations	3568	3380	3467	3532
	Range of operations per hospital	494–819	284–471	113–256	1–112
1985–89	Number of hospitals	7	11	25	260
	Number of operations	4254	4057	4033	4177
	Range of operations per hospital	487–740	237–468	113–232	1–112
1990–94	Number of hospitals	7	13	26	250
	Number of operations	3844	3878	3850	3841
	Range of operations per hospital	487–644	231–421	96–223	1–84

Table 2. Mean age with 95% CI of analyzed patients at diagnosis, by hospital volume and study period

Extent of disease	Year of diagnosis	Hospital volume			
		High	Medium	Low	Very low
Localized	1975–79	56.9 (55.6–58.3)	57.3 (56.2–58.5)	57.4 (56.2–58.6)	58.7 (57.4–60.1)
	1980–84	57.3 (56.5–58.1)	58.0 (57.2–58.9)	58.0 (57.1–58.9)	59.7 (58.7–60.7)
	1985–89	58.5 (57.8–59.2)	58.6 (57.9–59.3)	59.2 (58.4–60.0)	60.1 (59.2–60.9)
	1990–94	59.9 (59.3–60.5)	59.7 (59.1–60.4)	60.5 (59.8–61.2)	61.6 (60.7–62.4)
Regional	1975–79	56.5 (55.0–57.9)	58.0 (57.1–58.9)	59.2 (58.2–60.2)	59.7 (58.5–60.8)
	1980–84	59.2 (58.2–60.1)	59.9 (59.0–60.8)	59.6 (58.6–60.5)	60.4 (59.5–61.2)
	1985–89	59.3 (58.4–60.1)	60.0 (59.1–60.9)	60.6 (59.7–61.5)	60.8 (59.9–61.6)
	1990–94	61.3 (60.5–62.2)	61.0 (60.2–61.9)	61.7 (60.9–62.6)	62.6 (61.7–63.5)
Adjacent	1975–79	58.0 (55.7–60.2)	58.8 (57.6–60.0)	59.5 (58.2–60.8)	61.0 (59.8–62.1)
	1980–84	58.4 (56.9–59.8)	58.6 (57.3–59.9)	60.4 (59.2–61.5)	61.8 (60.7–62.8)
	1985–89	59.4 (58.0–60.8)	60.1 (58.9–61.4)	61.7 (60.5–63.0)	61.2 (60.1–62.3)
	1990–94	61.4 (60.0–62.8)	63.0 (61.7–64.3)	61.0 (59.6–62.4)	63.2 (62.1–64.3)
Distant	1975–79	58.9 (56.9–61.0)	58.0 (56.7–59.3)	59.6 (58.2–61.0)	57.4 (55.7–59.0)
	1980–84	58.9 (57.3–60.4)	60.4 (59.1–61.6)	58.5 (57.2–59.8)	60.5 (59.3–61.6)
	1985–89	57.5 (56.0–58.9)	59.3 (58.3–60.4)	61.1 (60.0–62.3)	59.7 (58.6–60.8)
	1990–94	60.9 (59.4–62.3)	60.0 (58.4–61.6)	61.7 (60.4–63.0)	61.4 (60.3–62.4)

Table 3. Cumulative 5-year survival of cases whose cancer was confined to the original organ (localized) and adjusted hazard rate ratio

Year of diagnosis		Hospital volume			
		High	Medium	Low	Very low
1975–79	*n*	244	389	342	252
	5-year survival	89	77	73	63
	95% CI	84–92	72–81	68–77	56–69
	HR	1.0	2.2	2.7	3.8
	95% CI		1.4–3.4	1.7–4.2	2.5–5.9
1980–84	*n*	673	635	670	524
	5-year survival	85	82	83	74
	95% CI	82–87	78–85	80–86	70–78
	HR	1.0	1.2	1.1	1.6
	95% CI		0.9–1.5	0.8–1.4	1.3–2.1
1985–89	*n*	918	1041	806	703
	5-year survival	85	85	81	72
	95% CI	82–87	82–87	78–83	69–76
	HR	1.0	1.0	1.3	1.9
	95% CI		0.8–1.3	1.0–1.6	1.5–2.4
1990–94	*n*	1185	1077	878	616
	5-year survival	84	86	82	76
	95% CI	82–86	83–88	79–84	72–79
	HR	1.0	0.9	1.2	1.5
	95% CI		0.7–1.1	0.9–1.4	1.2–1.9

HR, age and sex-adjusted hazard rate ratio; CI, confidence interval.

Table 4. Cumulative 5-year survival of cases whose cancer spread to the regional lymph nodes and adjusted hazard rate ratio

Year of diagnosis		Hospital volume			
		High	Medium	Low	Very low
1975–79	*n*	199	545	519	366
	5-year survival	63	56	36	23
	95% CI	56–69	48–62	32–40	19–27
	HR	1.0	1.7	1.8	2.5
	95% CI		1.3–2.2	1.4–2.3	1.9–3.1
1980–84	*n*	476	599	606	609
	5-year survival	44	44	47	31
	95% CI	40–49	40–48	43–51	27–34
	HR	1.0	1.0	0.9	1.5
	95% CI		0.9–1.2	0.8–1.1	1.3–1.8
1985–89	*n*	552	592	616	639
	5-year survival	45	47	41	28
	95% CI	41–49	42–51	37–45	25–32
	HR	1.0	1.0	1.1	1.6
	95% CI		0.8–1.1	0.9–1.2	1.3–1.8
1990–94	*n*	570	587	557	521
	5-year survival	43	47	41	24
	95% CI	39–47	43–51	37–45	21–28
	HR	1.0	0.9	1.0	1.7
	95% CI		0.7–1.0	0.9–1.2	1.4–1.9

HR, age and sex-adjusted hazard rate ratio; CI, confidence interval.

confirmed by Cox's proportional hazards model after adjustment for age and sex.

Table 5 shows the 5-year survival for the cases whose cancer had spread to immediately adjacent tissue. Differences in survival rates between the high-, medium- and low-volume groups were not seen in the period 1975–79. In the very-low-volume group, however, the survival rate was lower than in the others during the entire study period. Multivariate analysis by means of Cox's proportional hazards model confirmed these findings.

Table 6 shows the results for the cases whose cancer had metastasized to distant organs. The 5-year survival was very low and the differences by hospital volume were trivial during the entire period.

Discussion

This study suggests that the positive relationship between hospital volume and 5-year survival for stomach cancer patients observed in Osaka Prefecture during 1975–79 had decreased in the two decades of the study, becoming modest during 1990–1994. Our results are consistent with those recently reported by Schrag *et al.*[1] They analyzed survival for colon cancer patients aged 65 years and over, diagnosed in the US during 1991–96, and found that the association between hospital volume and 5-year mortality was greatest among patients with stage II and stage III disease, although the differences were modest. Several authors[2, 3] reported that higher-volume hospitals showed a bet-

Table 5. Cumulative 5-year survival of cases whose cancer spread to immediately adjacent tissue and adjusted hazard rate ratio

Year of diagnosis		Hospital volume			
		High	Medium	Low	Very low
1975–79	*n*	79	303	279	339
	5-year survival	11	16	10	6
	95% CI	6–20	12–20	7–14	4–9
	HR	1.0	0.9	1.2	1.4
	95% CI		0.7–1.2	1.0–1.6	1.1–1.9
1980–84	*n*	243	297	334	430
	5-year survival	20	16	15	8
	95% CI	15–25	12–20	12–20	6–11
	HR	1.0	1.1	1.1	1.7
	95% CI		0.9–1.3	0.9–1.4	1.4–2.0
1985–89	*n*	271	309	296	380
	5-year survival	17	23	14	8
	95% CI	13–22	19–28	10–18	6–11
	HR	1.0	0.7	1.0	1.4
	95% CI		0.6–0.9	0.8–1.2	1.2–1.6
1990–94	*n*	209	268	213	319
	5-year survival	12	13	12	5
	95% CI	8–16	9–17	8–17	3–8
	HR	1.0	0.8	0.9	1.2
	95% CI		0.7–1.0	0.8–1.1	1.0–1.5

HR, age and sex-adjusted hazard rate ratio; CI, confidence interval.

Table 6. Cumulative 5-year survival of cases whose cancer metastasized to distant organs and adjusted hazard rate ratio

Year of diagnosis		Hospital volume			
		High	Medium	Low	Very low
1975–79	*n*	112	329	235	199
	5-year survival	3	4	1	2
	95% CI	1–7	2–6	0–3	0–4
	HR	1.0	1.1	1.2	1.2
	95% CI		0.9–1.4	1.0–1.5	0.9–1.5
1980–84	*n*	215	320	310	359
	5-year survival	3	2	3	1
	95% CI	1–6	1–4	1–5	0–2
	HR	1.0	1.1	1.0	1.2
	95% CI		0.9–1.3	0.8–1.2	1.0–1.4
1985–89	*n*	226	421	352	409
	5-year survival	7	4	4	2
	95% CI	4–10	2–6	3–7	1–3
	HR	1.0	1.2	1.1	1.5
	95% CI		1.0–1.4	1.0–1.4	1.2–1.7
1990–94	*n*	196	192	283	375
	5-year survival	4	4	2	2
	95% CI	2–7	2–7	1–4	1–4
	HR	1.0	1.0	1.1	1.1
	95% CI		0.9–1.3	0.9–1.3	0.9–1.3

HR, age and sex-adjusted hazard rate ratio; CI, confidence interval.

ter outcome for cancers that needed technologically complex surgical procedures. However, it might be possible that the relationships were modest for cancers primarily treated with low-risk surgery. Stomach cancer is the most common cancer in Japan and the annual incidence in Osaka Prefecture was recently estimated to be about 60 per 100,000.[8, 9] Our study results suggest that in the case of surgery for a common cancer such as stomach cancer, where improved medical technology and cancer care have been widely adopted among various types of hospitals in Osaka Prefecture, the influence of hospital volume on survival rate might have become small. Although the results are not presented here, similar findings were obtained for 1-year survival and hospital volume for stomach cancer.

Several limitations of this study should be considered. Firstly, survival differences were analyzed by using Cox's proportional hazards model adjusting for age at diagnosis and sex, but not for co-morbidities. More patients with co-morbidities might have been referred to the high-volume hospitals than to the low-volume hospitals. As a result, survival might have been lower in the high-volume hospitals. The mean age of the study patients, however, was less in high-volume hospitals than in others; thus, the probability of performing operations on stomach cancer patients with other complications would be lower.

Secondly, 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, survival according to the extent of disease should be higher in high-volume hospitals than in others. This, however, does not explain the result that the survival differences by extent of the disease have diminished or disappeared. Thirdly, we need to take into consideration the data quality of the OCR. As mentioned in "Subjects and Methods," the proportion of cases of unknown vital status at 5 years after diagnosis is small, but the proportion of death certificate-only cases is not small if compared with North American and North/West European registries' data.[6] Hospitals with poor completeness of notification show tendencies of underreporting of patients who are still alive, thus underestimating survival rates. Although there is no actual index of this factor, completeness of notification might be better in high-volume hospitals than in others. This, however, does not explain the fact that the differences in survival by hospital volume have decreased or disappeared. Thus, it seems very likely that survival differences by hospital volume reflected the levels of technological skill for stomach cancer surgery.

This study also suggests that the differences in effectiveness of techniques for stomach cancer surgery have leveled off recently in almost all hospitals in Osaka Prefecture except for very-low-volume hospitals. We focused here on the association between surgical volume and 5-year survival of stomach cancer patients, but we did not consider other factors in hospital treatment which are directly associated with the outcomes, such as the technical expertise of surgeons and the availability of experienced pathologists and oncologists. Furthermore, we were not able to examine other factors associated with hospital volume, for example, frequency of post-operative complications, short-term outcome, length of stay and quality of life, since the OCR did not have such information. It will be necessary extend the development of hospital-based cancer registration systems in Japan in order to make further and wider analyses.

This study was done in Osaka Prefecture, where the population is 8.8 million and there are 366 hospitals, including 7 university hospitals. It is questionable whether the associations between survival and hospital volume observed here are true in other prefectures in Japan, where the population is generally smaller. Furthermore, the associations between survival and hospital volume must be different by cancer type and treatment type. Thus, for a better understanding of relationships between hospital volume and long-term survival, it is essential to establish high-quality population-based cancer registries in every region and prefecture, together with hospital-based registries.

1. Schrag D, Cramer LD, Bach PB, Cohen AM, Warren JL, Begg CB. Influence of hospital procedure volume on outcomes following surgery for colon cancer. *JAMA* 2000; **284**: 3028–35.
2. Bach PB, Cramer LD, Schrag D, Downey RJ, Gelfand SE, Begg CB. The influence of hospital volume on survival after resection for lung cancer. *N Engl J Med* 2001; **345**: 81–8.
3. Birkmeyer JD, Warshaw Al, Finlayson SRG, Grove MR, Tosteson ANA. Relationship between hospital volume and late survival after pancreaticoduodectomy. *Surgery* 1999; **126**: 78–83.
4. Tanaka H, Hiyama T, Hanai A, Fujimoto I. Interhospital differences in cancer survival: magnitude and trend in 1975–1987 in Osaka, Japan, *Jpn J Cancer Res* 1994; **85**: 680–5.
5. Oshima A, Kitagawa T, Ajiki W, Tsukuma H, Takenaka S, Iura A. Survival of testicular cancer patients in Osaka, Japan. *Jpn J Clin Oncol* 2001; **31**: 438–43.
6. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (eds). Cancer incidence in five continents. vol. VIII. IARC Scientific Publications No. 155. Lyon: IARC; 2002.
7. Osaka Cancer Registry (ed). Survival of cancer patients in Osaka, 1975–89. Tokyo: The Shinohara Publishers Inc; 1998.
8. Osaka Prefectural Department of Public Health and Welfare, Osaka Medical Association, Osaka Medical Center for Cancer and Cardiovascular Diseases. *Annual report of Osaka cancer registry No. 65—Cancer incidence and medical care in Osaka in 1999 and the survival in 1995—*. OPDPHW, 2002 (in Japanese).
9. Ajiki W, Tsukuma H, Oshima A. Trends in cancer incidence and survival in Osaka. In: Tominaga S, Oshima A, editors. Cancer mortality and morbidity statistics Japan and the World—1998. Gann Monogr. on Cancer Res. No. 47. Tokyo; Japanese Cancer Association; 1999. p.145–151.