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Three-year survival from diagnosis in surgically treated patients in designated and nondesignated cancer care hospitals in Japan

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Abstract

The Japanese national and prefectural governments have accredited high-capacity, high-experience cancer care hospitals as "designated cancer care hospitals" to standardize cancer care, centralize patients, and improve clinical outcomes, but the performance of these designated hospitals has not been evaluated. We retrospectively compared 3-year patient survival in national, prefectural, and nondesignated cancer care hospitals in 2010-2012 in Osaka using registry-based data of 86 456 surgically treated cancer patients aged 15 years or older. Hazard ratios and 3-year survival probabilities were compared among national, prefectural, and nondesignated hospitals using a Cox proportional hazard regression model. Subgroup analyses for six cancers (stomach, colorectum, lung, breast, uterus, and prostate) and other cancers were carried out. In 2010-2012, 36 634 (42.4%), 38 048 (44.0%), and 11 774 (13.6%) patients were treated at national, prefectural, and nondesignated hospitals, respectively. The mortality hazard for all-site cancer was significantly lower in national and prefectural designated hospitals (adjusted hazard ratio 0.60 [95% confidence interval, 0.53-0.68] and 0.72 [0.66-0.80], respectively) than in nondesignated hospitals. The adjusted 3-year survival probabilities for all-site cancer were 86.6%, 84.2%, and 78.8% in national, prefectural, and nondesignated hospitals, respectively. Site-specific subgroup analyses revealed significantly lower hazard ratios in national and prefectural hospitals than in nondesignated hospitals for stomach, colorectal, lung, breast, and other cancers. To conclude, the majority of cancer patients underwent surgeries at designated hospitals and had higher 3-year survival probabilities than those treated at nondesignated hospitals. Further centralization of patients from nondesignated to designated hospitals could improve population-level survival.

KEYWORDS
cancer care facility, quality of health-care, surgical procedure, survival rate

1 | INTRODUCTION

Cancer has affected individual health and society worldwide, including in Japan. Approximately half of the Japanese population will develop cancer over their life course.[1] Population aging has resulted in an increase of incident cancer cases in Japan.[2] Approximately one million new cancer diagnoses in 2017 and 374 000 cancer deaths in 2018 have been reported.[1] Thus, the reduction of prevalence and mortality rate of cancer is the goal of "the 3rd-term comprehensive 10-year cancer control strategy."[3]

Cancer mortality can be reduced if more patients receive standardized care from qualified care providers at specialized hospitals, namely, through centralization.[4] The concept of centralization has been supported by several studies that report a positive relationship between hospital volume and patient outcome.[5,6] Cancer patients treated at high-volume hospitals showed better short- and long-term survival.[7-9] The centralization policy has been implemented in European and North American countries,[10] and resultant effects of reduced mortality and increased survival have been reported.[11-13]

With the centralization policy, some countries designate specialized medical facilities to promote cancer research and improve clinical practice, which could facilitate the proactive selection of these facilities by cancer patients for their treatment and subsequently promote centralization. In the United States, the National Cancer Institute accredited 71 designated cancer centers in 36 states and in Washington DC to develop and deliver novel and effective prevention, diagnosis, and treatment for cancer.[14] Studies from the United States report a lower mortality rate of patients treated at designated cancer centers, compared to those treated in nondesignated facilities.[15,16] In Korea, in addition to the National Cancer Center, 12 regional cancer centers have been allocated across the country to mitigate the gap in the access to care between patients who are in and outside the capital.[17] In European countries, the cancer center certification program is implemented to develop a professional network and improve the quality of care.[18]

In Japan, 402 medical facilities are designated as cancer care hospitals by the national government (hereinafter referred to as national DCCHs) as of 2020.[19] Notably, the number of national DCCHs is larger in Japan than in the United States and Korea. "The Basic Plan to Promote Cancer Control programs" has been implemented since 2007,[3] and national DCCHs play a central role in the program toward the nationwide standardization of cancer care.[20] Furthermore, the prefectural governments also designate medical facilities specialized for cancer care, which are hereinafter referred to as "prefectural DCCHs," to strengthen the prefectural-level cancer care system in collaboration with national DCCHs and improve the quality of cancer care.[21] For example, 17 national and 49 prefectural DCCHs for adult cancer were operational in Osaka Prefecture in 2020.[22] The national and prefectural DCCH guidelines define their own standards for service delivery system, human resources, case volume, training activity, information service, clinical study, monitoring system, and safety measures to assure the quality of DCCHs. The standard for the national DCCHs is stricter than that for prefectural DCCHs. For example, national and prefectural DCCHs in Osaka need to perform 400 and 200 surgeries, respectively, per year.[23,24]

In the third phase of the cancer control program between 2017 and 2022, the centralization of patients to DCCHs, along with standardization of cancer care and quality improvement, is being addressed to achieve patient-centered medicine.[25] However, to the best of our knowledge, no study has investigated the extent of DCCH centralization and the postoperative survival of patients treated at DCCHs.

Therefore, this study was undertaken to compare the proportion and the 3-year survival since the diagnosis of cancer in patients who underwent surgery in national DCCHs, prefectural DCCHs, and non-DCCHs to assess the extent of centralization and the performance of DCCHs before the third phase of the cancer control program was implemented.

2 | MATERIALS AND METHODS

2.1 | Study design, setting, and data source

This retrospective observational study was carried out in Osaka Prefecture in Japan, which has the third largest population (estimated to be approximately 8.9 million in 2010).[26] A population-based cancer registry system, the Osaka Cancer Registry, was used in this study. The registry regularly collects information of all incident cancer cases from notifications submitted by medical facilities throughout the prefecture or death certificates managed by the prefectural administration and further updates the vital status for all cases at 3, 5, and 10 years from the diagnosis.[27] The registry collects the following basic information of patients: sex, age at cancer diagnosis, date of diagnosis and death, topography, the method of diagnosis, cancer stage, treatment with surgery, chemotherapy, and/or radiotherapy, and the code for the medical facility where the patient first made contact and underwent their initial treatment. The registry database does not have information on patients' socioeconomic characteristics, comorbidities, performance status, or details on treatment for cancer or other diseases. The data of Osaka Cancer Registry has been reported in *Cancer Incidence in Five Continents*, volumes III to XI.[28] Thus, the quality of the registry meets global standards. With regard to the data-quality indicators used in *Cancer Incidence in Five Continents*, the proportion of cases notified by death certificate only was 7.9%, and the proportion of cases verified microscopically was 83.4% for the cohort of patients with new cancer diagnoses in 2012 in the Osaka Cancer Registry.[27]

2.2 | Study sample

Patients who met the following criteria were qualified for inclusion in this study: diagnosed with cancer, were aged 15 years or older, resided in Osaka at the time of diagnosis, and had undergone surgery (ie, open surgery, endoscopic surgery, or endoscopic resection) at medical facilities in Osaka between 2010 and 2012. We defined cancer as codes C00-C96 in ICD-10; thus, cancers in situ were

excluded. Of them, we excluded lymphoma (ICD-10, C81-C85 and C96), multiple myeloma (ICD-10, C88-C90), and leukemia (ICD-10, C91-C95) as surgery is generally not indicated for these cancers. We excluded patients treated at a prefectural pediatric DCCH (n = 1), those with unknown sex (n = 10) or missing information on cancer stage (n = 2), those with unconfirmed death or censorship before completing a 3-year observation (n = 277), and those with unknown survival period (n = 632) or a survival period of 0 days (n = 68). There were no death certificate-only cases. Subsequently, the remaining 86,456 patients were included in the analysis.

2.3 | Outcome variable: 3-year survival from cancer diagnosis

The primary outcome of the study was survival for a 3-year period following a cancer diagnosis. We used the date of diagnosis as the entry point of survival period because the Japanese population-based cancer registry database does not have information on the date of surgery. A death that might have occurred any time within 3 years from diagnosis was considered an event. Thus, the survival period used in this study was the time from diagnosis to event, which is longer than the one used in clinical research, wherein the date of surgery is usually defined as the entry point of the survival period.

2.4 | Independent variable: DCCH type

In 2010-2012, the study participants underwent surgery at 218 medical facilities in Osaka. In the Japanese population-based cancer registry, a patient's record contains a code for the medical facility where he/she underwent the surgery for the new primary cancer. If a patient underwent surgery in more than one facility, his/her record still has one code for the facility with the earliest date of diagnosis. Using the medical facility codes, we categorized these facilities into three types: national DCCH, prefectural DCCH, and non-DCCH. As some non-DCCHs were upgraded to prefectural DCCHs during the study period (n = 7 in 2011, n = 3 in 2012), we checked the DCCH status of the hospitals each year and accordingly categorized the facilities.

2.5 | Potential confounders

We considered the following variables as potential confounders: year of diagnosis (2010, 2011, and 2012), sex (women or men), age group (15-39, 40-49, 50-59, 60-69, 70-79, 80-89, or 90 years or older), cancer site (stomach [C16 in ICD-10], colorectum [C18-C20], lung [C33, C34], breast [C50], uterus [C53-C55], prostate [C61], and others [except for the abovementioned six sites, lymphoma, multiple myeloma, and leukemia]), stage of cancer (localized, regional, adjacent, distant, or unknown), extent of resected tumor (all, partial, or unknown), chemotherapy (received, not received, or unknown), radiotherapy (received, not received, or

unknown), and residential area according to the eight secondary health-care service areas (A–H).

2.6 | Statistical analysis

First, we calculated the number of hospitals and the mean annual surgical volume by the DCCH type and described the distribution of the basic characteristics of patients per DCCH type. Using a multivariable Cox proportional hazard model, HRs for each hospital type (non-DCCHs constituted the reference group) were estimated after adjustment of potential confounders. In the model, 95% CIs of the HR were adjusted using robust estimators of variance because patients who underwent surgery in the same hospital would have cluster correlations. Based on the postestimation of the Cox proportional hazard model, adjusted survival probabilities were estimated.

Subgroup analyses were undertaken for specific cancer sites. We selected six major cancers, stomach, colorectal, lung, breast, uterus, and prostate, because of their high incidence, and each site accounted for 4.0% or more of all cancer cases (Table S1). Patients with the remaining cancer sites were combined as "others" for the analysis. $P < .05$ indicated statistical significance. The Stata 15.1 statistical software package (Stata Corp, College Station, Texas, USA) was used for all analyses in this study.

2.7 | Ethical considerations

This study was approved by the Institutional Review Board of Osaka International Cancer Institute (approval number: 18-0018). The need for informed consent was waived because the dataset had been anonymized before the data were obtained for the study analyses.

3 | RESULTS

3.1 | Basic characteristics of medical facilities

There were 49 and 141, 56 and 128, and 59 and 117 DCCHs and non-DCCHs in 2010, 2011, and 2012, respectively (Table 1). The mean annual surgical volume of national DCCHs was increased from 848.0 (SD 251.5) in 2010 to 902.2 (SD 312.2) in 2012. The mean annual surgical volume of prefectural DCCHs was nearly one-third of that of national DCCHs, and it slightly increased from 306.1 (SD 147.5) in 2010 to 315.0 (SD 170.8) in 2012. The mean annual surgical volume of non-DCCHs was approximately 30, and it showed few changes during the study period.

3.2 | Basic characteristics of patients

This analysis comprised 36 634 (42.4%) patients from national DCCHs, 38 048 (44.0%) from prefectural DCCHs, and 11 774

TABLE 1 Basic characteristics of hospitals and patients among national, prefectural, and non-designated cancer care hospitals

	Total	National DCCHs	Prefectural DCCHs	Non-DCCHs	
Hospitals: n (% by row)					
2010	190 (100.0)	14 (7.4)	35 (18.4)	141 (74.2)	0.559
2011	184 (100.0)	14 (7.6)	42 (22.8)	128 (69.6)	
2012	176 (100.0)	14 (8.0)	45 (25.6)	117 (66.5)	
Annual surgical volume: mean (SD)					
2010	142.9 (249.0)	848.0 (251.5)	306.1 (147.5)	32.3 (61.9)	–
2011	156.6 (262.7)	866.5 (283.2)	313.3 (161.3)	27.6 (48.8)	
2012	173.3 (278.5)	902.2 (312.2)	315.0 (170.8)	31.5 (53.2)	
Patients: n (% by column)	86 456 (100.0)	36 634 (100.0)	38 048 (100.0)	11 774 (100.0)	
Year of diagnosis					
2010	27 146 (31.4)	11 872 (32.4)	10 715 (28.2)	4559 (38.7)	<.0001
2011	28 816 (33.3)	12 131 (33.1)	13 157 (34.6)	3528 (30.0)	
2012	30 494 (35.3)	12 631 (34.5)	14 176 (37.3)	3687 (31.3)	
Sex					
Women	40 138 (46.4)	17 228 (47.0)	17 564 (46.2)	5346 (45.4)	0.003
Men	46 318 (53.6)	19 406 (53.0)	20 484 (53.8)	6428 (54.6)	
Age group					
15-39	2620 (3.0)	1424 (3.9)	911 (2.4)	285 (2.4)	<.0001
40-49	6082 (7.0)	2938 (8.0)	2383 (6.3)	761 (6.5)	
50-59	10 533 (12.2)	4851 (13.2)	4431 (11.7)	1251 (10.6)	
60-69	27 041 (31.3)	11 860 (32.4)	11 748 (30.9)	3433 (29.2)	
70-79	28 482 (32.9)	11 529 (31.5)	12 977 (34.1)	3976 (33.8)	
80-89	10 664 (12.3)	3753 (10.2)	5096 (13.4)	1815 (15.4)	
90+	1034 (1.2)	279 (0.8)	502 (1.3)	253 (2.2)	
Site					
Stomach	17 295 (20.0)	6641 (18.1)	7977 (21.0)	2677 (22.7)	<.0001
Colorectum	19 839 (23.0)	6214 (17.0)	9647 (25.4)	3978 (33.8)	
Lung	6477 (7.5)	2775 (7.6)	3438 (9.0)	264 (2.2)	
Breast	11 159 (12.9)	4811 (13.1)	4880 (12.8)	1468 (12.5)	
Uterus	3474 (4.0)	1917 (5.2)	1233 (3.2)	324 (2.8)	
Prostate	3460 (4.0)	1430 (3.9)	1713 (4.5)	317 (2.7)	
Others	24 752 (28.6)	12 846 (35.1)	9160 (24.1)	2746 (23.3)	
Stage					
Localized	52 090 (60.3)	22 461 (61.3)	23 063 (60.6)	6566 (55.8)	<.0001
Regional	11 776 (13.6)	4819 (13.2)	5211 (13.7)	1746 (14.8)	
Adjacent	13 722 (15.9)	6118 (16.7)	5919 (15.6)	1685 (14.3)	
Distant	7423 (8.6)	2535 (6.9)	3386 (8.9)	1502 (12.8)	
Unknown	1445 (1.7)	701 (1.9)	469 (1.2)	275 (2.3)	
Extent of resection					
All	70 300 (81.3)	29 609 (80.8)	31 687 (83.3)	9004 (76.5)	<.0001
Partial	12 085 (14.0)	4713 (12.9)	4975 (13.1)	2397 (20.4)	
Unknown	4071 (4.7)	2312 (6.3)	1386 (3.6)	373 (3.2)	
Chemotherapy					
Received	24 966 (28.9)	10 860 (29.6)	10 286 (27.0)	3820 (32.4)	<.0001
Not received	61 288 (70.9)	25 764 (70.3)	27 714 (72.8)	7810 (66.3)	
Unknown	202 (0.2)	10 (0.0)	48 (0.1)	144 (1.2)	

(Continues)

TABLE 1 (Continued)

	Total	National DCCHs	Prefectural DCCHs	Non-DCCHs	
Radiation therapy					
Received	7464 (8.6)	3915 (10.7)	2697 (7.1)	852 (7.2)	<.0001
Not received	78 742 (91.1)	32 706 (89.3)	35 298 (92.8)	10 738 (91.2)	
Unknown	250 (0.3)	13 (0.0)	53 (0.1)	184 (1.6)	
Residential area					
Area A	26 716 (30.9)	9309 (25.4)	14 194 (37.3)	3213 (27.3)	<.0001
Area B	9706 (11.2)	4352 (11.9)	5003 (13.2)	351 (3.0)	
Area C	7266 (8.4)	3547 (9.7)	2846 (7.5)	873 (7.4)	
Area D	9676 (11.2)	5134 (14.0)	2481 (6.5)	2061 (17.5)	
Area E	8399 (9.7)	4136 (11.3)	3211 (8.4)	1052 (8.9)	
Area F	6436 (7.4)	3705 (10.1)	1414 (3.7)	1317 (11.2)	
Area G	9069 (10.5)	3839 (10.5)	3663 (9.6)	1567 (13.3)	
Area H	9188 (10.6)	2612 (7.1)	5236 (13.8)	1340 (11.4)	

Abbreviations: DCCH, designated cancer care hospital; –, not applicable.

(13.6%) from non-DCCHs (Table 1). Men accounted for more than half (53.6%) of the study cohort, and the sex distributions were similar across the three DCCH types. The proportion of patients aged 80 years or older was slightly higher in the non-DCCHs (17.6%) than in the national (11.0%) or prefectural DCCHs (14.7%). Among the six selected cancer sites, stomach cancer accounted for the highest proportion in national DCCHs (18.1%), whereas colorectum cancer accounted for the highest proportion in prefectural (25.4%) and non-DCCHs (33.8%). More than 60% of the patients treated at national or prefectural DCCHs had localized cancers at diagnosis, and the proportion of patients with localized cancer was slightly lower in those treated at non-DCCHs (55.8%). Nearly 30% of the patients had chemotherapy, and 10% had radiation therapy with minor difference across the three DCCH types. The annual surgical volume in 2010-2012 per DCCH type are presented in Table S2. The site-specific annual surgical volumes in non-DCCHs ranged between 2.0 (SD 4.0) and 10.0 (SD 13.9) for lung and colorectum cancers, respectively.

3.3 | Distribution of patients per DCCH type and cancer site

Table 2 shows site-specific distributions of patients per DCCH type. The proportion of patients who underwent surgery at either a national or prefectural DCCH was as follows: 86.4% for all cancers and 84.5%, 79.9%, 95.9%, 86.8%, 90.7%, 90.8%, and 88.9% for stomach, colorectal, lung, breast, uterine, prostate, and other cancers, respectively. With regard to the following four cancers, more patients underwent surgery at prefectural DCCHs than at national DCCHs: stomach (38.4% in national DCCHs vs 46.1% in prefectural DCCHs), colorectal (31.3% vs 48.6%), lung (42.8% vs 53.1%), and prostate (41.3% vs 49.5%). In contrast, more patients underwent surgery at national DCCHs than at prefectural DCCHs for the following cancers: uterus (55.2% in national DCCHs vs 35.5% in prefectural

DCCHs) and others (51.9% vs 37.0%). With regard to breast cancer, national and prefectural DCCHs accounted for a similar proportion of surgeries (43.1% vs 43.7%).

3.4 | Adjusted mortality hazards and survival rates by DCCH type

Table 2 presents HRs for 3-year mortality per DCCH type. The mortality hazard for overall cancers was lower in national (aHR 0.60; 95% CI, 0.53-0.68) and prefectural DCCHs (aHR 0.72; 95% CI, 0.66-0.80), compared to non-DCCHs. Similarly, site-specific mortality hazards for the national DCCHs were 0.54-0.65 times lower than for non-DCCHs, and those for prefectural DCCHs were 0.65-0.83 times lower than for non-DCCHs. These HRs showed significant differences in stomach, colorectal, lung, breast, and other cancers.

Table 2 additionally shows the 3-year survival probabilities that were estimated based on the multivariable Cox proportional hazard model. The adjusted survival probabilities of overall cancers were 86.6%, 84.2%, and 78.8% for national DCCHs, prefectural DCCHs, and non-DCCHs, respectively. The survival probabilities varied by the cancer sites and were greater than 80% for stomach, colorectal, and lung cancers in national or prefectural DCCHs, but were 76% or lower in non-DCCHs. The survival probabilities for breast, uterus, and prostate cancers were greater than 90% for all the three DCCH types. The absolute difference in the adjusted survival probability varied by the cancer site and was 1.4%-11.7% points lower in non-DCCHs than that in national DCCHs and 1.0%-8.8% points lower than in prefectural DCCHs.

4 | DISCUSSION

More than 85% of surgically treated cancer patients underwent surgery at national or prefectural DCCHs in Osaka during 2010-2012.

TABLE 2 Distributions of patients, their 3-year mortality hazard, and survival probability

	N	(%)	Crude HRs[a]	(95% CI)	Adjusted HRs[a,b]	(95% CI)	Adjusted survival probability[c]	Absolute difference in survival probability[d]
All sites								
National DCCHs	36,634	(42.4)	0.54	(0.45-0.64)	0.60	(0.53-0.68)	86.6	7.8
Prefectural DCCHs	38,048	(44.0)	0.64	(0.55-0.75)	0.72	(0.66-0.80)	84.2	5.4
Non-DCCHs	11,774	(13.6)	1.00		1.00		78.8	–
Stomach								
National DCCHs	6,641	(38.4)	0.41	(0.32-0.51)	0.59	(0.50-0.70)	85.1	9.0
Prefectural DCCHs	7,977	(46.1)	0.54	(0.45-0.65)	0.72	(0.63-0.83)	82.1	6.0
Non-DCCHs	2,677	(15.5)	1.00		1.00		76.1	–
Colorectum								
National DCCHs	6,214	(31.3)	0.51	(0.44-0.59)	0.60	(0.52-0.68)	84.2	9.2
Prefectural DCCHs	9,647	(48.6)	0.67	(0.59-0.75)	0.72	(0.65-0.81)	81.2	6.2
Non-DCCHs	3,978	(20.1)	1.00		1.00		75.0	–
Lung								
National DCCHs	2,775	(42.8)	0.41	(0.27-0.63)	0.54	(0.39-0.74)	83.5	11.7
Prefectural DCCHs	3,438	(53.1)	0.48	(0.33-0.70)	0.65	(0.49-0.86)	80.6	8.8
Non-DCCHs	264	(4.1)	1.00		1.00		71.8	–
Breast								
National DCCHs	4,811	(43.1)	0.48	(0.27-0.86)	0.54	(0.39-0.73)	97.1	2.5
Prefectural DCCHs	4,880	(43.7)	0.65	(0.37-1.14)	0.69	(0.51-0.94)	96.3	1.7
Non-DCCHs	1,468	(13.2)	1.00		1.00		94.6	–
Uterus								
National DCCHs	1,917	(55.2)	0.69	(0.48-0.99)	0.65	(0.46-0.92)	94.6	2.8
Prefectural DCCHs	1,233	(35.5)	0.92	(0.62-1.35)	0.83	(0.60-1.15)	93.2	1.4
Non-DCCHs	324	(9.3)	1.00		1.00		91.8	–
Prostate								
National DCCHs	1,430	(41.3)	0.52	(0.26-1.04)	0.61	(0.32-1.15)	97.6	1.4
Prefectural DCCHs	1,713	(49.5)	0.68	(0.37-1.24)	0.72	(0.43-1.22)	97.2	1.0
Non-DCCHs	317	(9.2)	1.00		1.00		96.2	–
Others								
National DCCHs	12,846	(51.9)	0.60	(0.51-0.71)	0.64	(0.54-0.75)	75.9	11.1
Prefectural DCCHs	9,160	(37.0)	0.73	(0.62-0.87)	0.75	(0.65-0.86)	72.3	7.5
Non-DCCHs	2,746	(11.1)	1.00		1.00		64.8	–

Abbreviations: DCCH, designated cancer care hospital; HR, hazard ratio; –, not applicable.

[a]Hazard ratios were estimated by Cox proportional hazard model.

[b]The covariates adjusted in the model were sex, age, year of diagnosis, cancer site, cancer stage, extent of resection, receipt of chemotherapy, radiation therapy, and residential area.

[c]Adjusted survival probability was estimated based on the Cox proportional hazard model with adjustment of the covariates.

[d]The absolute difference in the survival probability was calculated by subtracting the survival probability of non-DCCHs from those of national DCCHs and of prefectural DCCHs.

Patients treated at national or prefectural DCCHs showed a significantly lower mortality hazard than those treated at non-DCCHs. The adjusted 3-year survival probabilities for all-site cancers were highest in national DCCHs, followed by prefectural DCCHs and non-DCCHs. Furthermore, the number of patients, mortality hazard, and 3-year survival probabilities among the three DCCH types varied by cancer site. These data described the baseline picture of the centralization of cancer surgery in Osaka before the third phase of the cancer control program was implemented.

The adjusted survival probability of all-site cancers for national and prefectural DCCHs were 7.8% and 5.4% points higher than that for non-DCCHs. These better patient outcomes observed in national and prefectural DCCHs could be attributed to the greater experience of cancer surgeries in DCCHs than of those

in non-DCCHs. For example, our data showed that the average surgical volumes in national and prefectural DCCHs in 2012 were approximately 30 and 10 times higher than those in non-DCCHs. Cancer site-specific surgical volumes in non-DCCHs were 10 or lower, which implies that the surgeons might have insufficient chance to gain experience. Furthermore, hospital characteristics, such as facility infrastructure or human resources that were not measured in this study, might have affected the lower survival probability in the non-DCCHs. The difference in patient survival could also be affected by patient characteristics, because previous studies report that hospital selection is associated with patient characteristics in Japan.[29,30] For example, we observed that the difference in the HR among national, prefectural, and non-DCCHs narrowed after controlling for patient characteristics. A previous study reported that the difference in survival probability among DCCHs was narrowed by adjusting the performance status and comorbidity of patients.[31,32] Thus, the difference in hospital-level patient survival probability should be interpreted with consideration of patient and hospital characteristics.

More than 15% of patients with colorectal and stomach cancers underwent surgery at non-DCCHs. This indicates that the centralization of patients with these cancers was less progressive compared to that of the other selected cancer sites. The reason behind patients opting for surgery at non-DCCHs could be partially because before the DCCH policy was introduced, open surgery for colorectal and stomach cancers was widely performed across hospitals in Osaka to take care of the large number of cancer cases with indications for surgery. After that, the DCCH policy was introduced to provide high-quality care to patients with these major cancers within their residential area,[20] and endoscopic surgeries and resection have become widely available, particularly in DCCHs. Although the centralization of colorectum and stomach cancer patients might progress slowly, the low survival probability observed in patients treated at non-DCCHs suggests that further centralization to DCCHs will be worthwhile to improve the survival rates for these cancer patients.

With regard to lung cancer, patients who underwent surgery at non-DCCHs accounted for only 4%. The difference in the adjusted survival probability between the national DCCHs and non-DCCHs was 11.7%, highlighting the largest difference among the six selected cancer sites. This might indicate that the centralization of lung cancer patients to DCCHs had been already established before the DCCH policy was introduced, and the large gap in the survival probability between the national DCCHs and non-DCCHs could be a result of centralization. This suggests that the centralization of lung cancer patients was effective in improving their survival.

For breast, uterus, and prostate cancers, the 3-year survival probabilities were greater than 90%, and thus, the differences in the adjusted survival probabilities among the three DCCH types were smaller than those for stomach, colorectal, and lung cancers. This finding implies that the potential impact of patient centralization on improved survival might be limited for these types of cancer. However, the centralization approach for these cancers is worthwhile

because the incidence of uterine and prostate cancers was smaller than that of the other four selected cancers, and centralization will allow care providers to practice patient care regularly and maintain their quality of care and improve patient outcomes.[33] Furthermore, breast and prostate cancer patients need long-term follow-up care and treatment after surgery because a small proportion of these patients could develop treatment resistance or a recurrent cancer and die subsequently, as indicated by the lower conditional 5-year survival of breast and prostate cancer patients than those of stomach, colon, and rectum cancer patients.[34] However, breast cancer patients might not necessarily be centralized to DCCHs only because there are clinics specialized for treating specific cancers. For example, a clinic in Osaka carried out an average of 150 surgeries for breast cancer during the study period (data not shown) and offered multidisciplinary treatment. In summary, centralization should not be embedded in a single approach but rather reflect cancer site-specific characteristics, such as the incidence, prognosis, and existing health-care system capabilities.

This study has several limitations. First, the HR and survival probabilities by DCCH types should be interpreted carefully because the Cox proportional hazard model used in this study did not control for several important confounders, such as patient socioeconomic characteristics, comorbidity, performance status, tumor histology, time from diagnosis to surgery, operative procedure, or detailed hospital characteristics (eg, hospital infrastructure, human resources, or surgeon volume). For example, the low survival probability observed in the non-DCCHs might partially be attributed to noncancer mortality in elderly patients with comorbidity. Longer time from diagnosis to surgery could be associated with lower survival probability, as reported by previous studies.[35,36] Furthermore, the survival probability could be biased because we did not control for the effect of surgery when a patient underwent surgery in more than one facility, the effects of treatment that patients received after the initial surgery, or the effects of other diseases that developed after the initial treatment for cancer. Second, the generalizability of the study findings is limited because Osaka is unique in terms of the second smallest prefecture with the third largest population. However, the findings and implications of this study could be applicable to urban areas in other parts of Japan or other countries.

5 | CONCLUSION

The majority of patients underwent surgeries at DCCHs in Osaka before the third phase of the cancer control program was implemented. The 3-year survival probabilities of patients treated at national and prefectural DCCHs were significantly higher than that of patients treated at non-DCCHs. The absolute difference in the survival probability between DCCHs and non-DCCHs varied by the cancer site. Further steering of patients from non-DCCHs to DCCHs with consideration of the site-specific characteristics could improve the population-level survival of cancer patients. The distribution of patients and their postoperative survival rates should be regularly

assessed to evaluate the effect of the cancer control program on centralization and the subsequent patient outcomes.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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