

## Cancer Incidence in Hawaiian Japanese: Migrants from Okinawa Compared with Those from Other Prefectures

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Japanese men in Hawaii whose ancestral roots were in Okinawa were compared to Japanese migrants from all other prefectures. The Okinawan migrants have acquired fewer cancers than men from other prefectures ( $P=0.12$ ). No one primary site accounts for this difference. Stomach cancer rates showed the largest difference between the two migrant groups. This replicates the experience of Okinawans and non-Okinawans in Japan itself. Lymphosarcoma mortality rates are much higher in Okinawa than in all Japan, but this difference is not reproduced in Hawaiian migrants. This could be explained by a post migrational decrease in HTLV-I-related acute T-cell lymphoma/leukemia. Cancer of the mouth, pharynx and esophagus has decreased in all Japanese migrants, but the decrease is much greater among Okinawan migrants, suggesting they have escaped exposure to risk factors peculiar to the Okinawan environment. Colon cancer is more common in migrant Japanese than in U.S. whites. The dramatic increase in the frequency of this tumor affects Okinawan and non-Okinawan migrants to an equal degree.

Key words: Okinawa — Migrant studies — Lymphosarcoma — Oropharyngeal cancer — Stomach cancer

The disease experience of the Japanese in Hawaii is distinctly different from that of the people living in Japan. They have lower rates of gastric and biliary tract cancer<sup>1)</sup> and of stroke<sup>2)</sup> than do indigenous Japanese. In contrast, they show higher rates of colon cancer, breast cancer<sup>2)</sup> and myocardial infarction.<sup>2)</sup> The fall in gastric cancer and stroke rates may be due to qualitative changes in nutrient intake (increased fresh vegetable and animal protein consumption).<sup>3,4)</sup> Correlational studies suggest that the rise in frequency of myocardial infarction and colon cancer is due to increased consumption of fat<sup>5)</sup> and sedentary lifestyle.<sup>6)</sup> Case-control studies and prospective cohort studies have not consistently reproduced the findings of the correlational studies in respect to the colon cancer-fat association<sup>7)</sup>; and changes in disease frequency have not been uniform in degree. For example, myocardial infarction rates among Hawaii Japanese are stable<sup>8)</sup> at a level midway between the experience of indigenous Japanese and U.S. whites, while their colon cancer rates are rising and now exceed those of U.S. whites.<sup>9)</sup> These observations suggest that subsets of Hawaiian Japanese men could acquire different diseases while sharing similar lifestyles.

One group of Japanese immigrants may be separated from the remainder. These are the migrants from Okinawa. Okinawa was an independent kingdom until

1879 when it became a prefecture of the Japanese empire.<sup>10)</sup> Okinawan ethnic cultural patterns and dietary practices differ from those of other Japanese.

The period of migration from Okinawa also differs from that of other Japanese migrants. The first large contingent of Japanese arrived in Hawaii in 1885, and migration continued until 1924 when it was ended abruptly by restrictive legislation.<sup>11)</sup> The first Okinawans did not reach Hawaii until 1900, by which time the majority of the immigrants from other prefectures had already arrived. The migrants who came to Hawaii were hired as contract laborers in the sugar and pineapple industries. Those that remained after the termination of their contracts gained employment as artisans, small merchants and independent farmers. The long-term result, affecting all migrants regardless of their prefecture of origin, has been increasing affluence and employment in less physically demanding occupations.

The Honolulu Heart Study (HHS) assembled a cohort of men of Japanese ancestry for a prospective study of heart disease and stroke.<sup>12)</sup> It was found that 14% of the men were of Okinawan ancestry when these men were examined in the years 1965-68.<sup>13)</sup> The percentages of men from other prefectures were as follows: Hiroshima, 25%; Yamaguchi, 23%; Kumamoto, 14%, Fukuoka, 6%; Niigata, 5%; Fukushima, 4%; all others, 9%.

The HHS cohort has been followed for 20 or more years after baseline examination. The present study was

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undertaken in order to determine whether the cancer experience of Okinawan men has been different from that of other Japanese migrants.

## MATERIALS AND METHODS

The 8006 men in the HHS were originally identified as living on the island of Oahu and as having registered for military service in the years 1940–42.<sup>12)</sup> They were interviewed and examined during the years 1965–68.<sup>13)</sup> The cohort was divided into two groups: those of Okinawan origin and those who came from other prefectures. A man was classified as Okinawan if he, or his father, had been born in Okinawa. The prefecture of origin was not identified for 223 subjects. Removal of these men from the analysis left 7783 men. There remained 1109 Okinawan men and 6674 non-Okinawan men. The men were also classified as to generational status: issei=first generation, kibeï = second generation men born in Hawaii, but educated in Japan, nisei=second generation men who were Hawaii-born and educated. Previous studies have shown that issei and kibeï more closely resemble indigenous Japanese than do men of the nisei generation.<sup>14)</sup> Kibeï and issei were therefore combined in studies of generational differences in cancer frequency.

The Japan-Hawaii Cancer Study (JHCS) maintains daily surveillance of all hospital deaths and discharges on the island of Oahu. This study is confined to histologically confirmed cancers. Linkage is maintained with the Hawaii Tumor Registry and the Hawaii Department of Health to identify cancers missed by our surveillance (e.g., diagnosis made on outpatients). Based on a separate 19-year follow-up survey of study subjects since their 1965–1968 exam, only 1.3% of the men could not be

located on Oahu. As a result, the surveillance for incidence of cancer should be nearly complete.

Age-adjusted mean values of selected continuous risk factors (e.g., diastolic blood pressure) taken at initial examination were calculated for Okinawan and for non-Okinawan men. The adjustment for age was done using

Table Ib. Group Differences on Selected Categorical Variables Measured at Baseline in Okinawan and Non-Okinawan Japanese Migrants

	Okinawan		Non-Okinawan		P-Value <sup>a)</sup>
	No.	(%)	No.	(%)	
<b>Education</b>					
None	1	(0.1)	2	(0.03)	
Primary	127	(11.5)	340	(5.1)	
Inter/Jr High	619	(55.9)	2852	(42.8)	
Sr High	275	(24.8)	2432	(36.5)	
Tech School	31	(2.8)	285	(4.3)	
University	55	(5.0)	761	(11.4)	<0.001
<b>Usual Occupation</b>					
Retired	0	(0.0)	3	(0.04)	
Not working	1	(0.1)	7	(0.1)	
Unskilled	94	(8.5)	214	(3.2)	
Semi-skilled	228	(20.6)	737	(11.1)	
Skilled	453	(40.9)	2920	(43.8)	
Farmer	64	(5.8)	91	(1.4)	
Clerical-Sales	154	(13.9)	1436	(21.5)	
Foreman-Supervisor	73	(6.6)	660	(9.9)	
Professional/Managerial	42	(3.8)	602	(9.0)	<0.001

a) Categorical group differences assessed by the chi-square test.

Table Ia. Age-adjusted Means for Selected Cancer Risk Factors Measured at Baseline in Okinawan and Non-Okinawan Japanese Migrants

	Okinawan		Non-Okinawan		P-Value <sup>a)</sup>
	No.	Mean ( $\pm$ SE)	No.	Mean ( $\pm$ SE)	
Diastolic blood pressure (mm Hg)	1109	81.8 (0.4)	6674	82.3 (0.1)	0.18
Systolic blood pressure (mm Hg)	1109	134.9 (0.6)	6674	133.9 (0.3)	0.15
Serum cholesterol (mg%)	1104	220.5 (1.2)	6634	218.2 (0.5)	0.06
Body mass index (kg/m <sup>2</sup> )	1108	24.4 (0.1)	6670	23.8 (0.04)	<0.0001
Serum glucose (mg%)	1107	158.9 (1.7)	6647	161.9 (0.7)	0.12
Serum uric acid (mg%)	1105	6.1 (0.4)	6643	6.0 (0.02)	0.06
Serum triglyceride (mg%)	1061	249.1 (6.4)	6379	235.2 (2.6)	<0.05
Cigarettes per day	1103	10.3 (0.4)	6657	10.2 (0.2)	0.99
Alcohol (oz/mo)	1095	15.1 (0.7)	6574	13.5 (0.3)	<0.05

a) Test for difference between age-adjusted means, by analysis of covariance.

one-way unbalanced analyses of covariance,<sup>15)</sup> with age at initial exam as the single continuous covariate. In addition, the differences in the percent of selected categorical variables (e.g., level of education) in the Okinawan versus non-Okinawan Japanese were also determined using a chi-square test.

Site-specific and total cancer incidence rates for Okinawan and mainland Japanese were adjusted for age at initial examination via the direct method of standardization, with the entire cohort serving as the reference population. Mantel-Haenszel chi-square test with one degree of freedom was used to test for significance ( $P \leq 0.05$ ) of rate differences.<sup>16)</sup> The age-adjusted mortality rates for major sites of cancer in all Japan and in Okinawa Prefecture between 1983-87 were calculated based on vital statistics of Japan by the direct method, standardized on the world population.

RESULTS

Tables Ia and Ib compare the Okinawan and non-Okinawan men in respect to several epidemiologic variables. The Okinawan men are characterized by higher body mass index, higher serum triglyceride, higher alcohol consumption, fewer university graduates, and fewer men employed at the professional/managerial level.

The age-adjusted incidence rates/1000 men among Okinawan and non-Okinawan Japanese in Hawaii are shown in Table II. The overall age-adjusted cancer incidence was greater for non-Okinawan men than those from Okinawa but the difference was not statistically significant ( $P=0.12$ ). No individual tumor site showed a significant difference in age-adjusted cancer incidence between Okinawans and non-Okinawans, but there were notable differences in the rates of gastric and prostate cancer.

Table III compares the age-adjusted incidence rates among Okinawan and non-Okinawan Japanese for the nisei generation and for the combined issei-kibei generations. A larger proportion of Okinawan migrants were members of the issei-kibei generation than were non-Okinawan migrants (37.5% vs. 16.9%). Okinawan and non-Okinawan men in the issei-kibei generation had almost identical overall cancer incidence rates. The age-adjusted overall cancer incidence rate of nisei Okinawans is lower than that of nisei from other prefectures, but the difference is not statistically significant ( $P=0.18$ ).

DISCUSSION

Previous studies of cardiovascular disease in this cohort have indicated that the prefecture of ancestral origin did not play a major role in the incidence of CHD

Table II. Age-adjusted Cancer Incidence Rates/1000 Men Derived from Okinawa vs. Those from Other Japanese Prefectures

Cancer site	Okinawan (n=1109)		Non-Okinawan (n=6674)		P-value <sup>a)</sup>
	No.	(%)	No.	(%)	
All cancer					
Cases	183	(16.5)	1295	(19.4)	0.12
Rate	170.9		193.5		
Mouth-esophagus					
Cases	7	(0.6)	39	(0.6)	0.98
Rate	7.9		7.2		
Stomach					
Cases	21	(1.9)	184	(2.8)	0.18
Rate	24.4		33.5		
Colon					
Cases	35	(3.2)	216	(3.2)	0.94
Rate	40.4		39		
Rectum					
Cases	9	(0.8)	91	(1.4)	0.21
Rate	11.2		16.9		
Lung					
Cases	32	(2.9)	185	(2.8)	0.89
Rate	33.9		33.5		
Prostate					
Cases	30	(2.7)	240	(3.6)	0.25
Rate	32.8		43.3		
Bladder					
Cases	10	(0.9)	75	(1.1)	0.63
Rate	11.5		13.8		
Lymphosarcoma/leukemia					
Cases	6	(0.5)	37	(0.6)	0.97
Rate	6.5		7.1		
Other					
Cases	33	(3.0)	228	(3.4)	0.71
Rate	35.0		40.6		

a) Test for significance using the Mantel-Haenszel chi-square method.

Table III. Age-adjusted Cancer Incidence Rates/1000 Men Derived from Okinawa vs. Those from other Japanese Prefectures

Cancer site	Okinawa No.=1109	Non-Okinawan No.=6674	P-value <sup>a)</sup>
All cancer			
Nisei	No.=693	No.=5543	
Cases	98	1054	0.18
Noncases	595	4489	
Rate	173.0	197.2	
All cancer			
Issei & Kibei	No.=416	No.=1131	
Cases	85	241	0.78
Noncases	331	890	
Rate	183.7	184.3	

a) Test for significance using the Mantel-Haenszel chi-square method.

Table IV. Age-adjusted Cancer Mortality Rates<sup>a)</sup> (per 100,000) in Japan (1983-87)

Site of cancer	Okinawa	All Japan	Ratio
All sites	131.8	149.9	0.9
Mouth-esophagus <sup>b)</sup>	14.5	8.5	1.7
Stomach	21.5	40.9	0.5
Colon	6.1	7.5	0.8
Rectum	4.8	6.2	0.8
Lung	34.3	27.7	1.2
Prostate	2.5	3.3	0.7
Urothelium <sup>c)</sup>	1.6	2.5	0.6
Lymphoid tissue	11.6	6.0	1.9
Population	578,531	59,105,600	

a) Standard population is Segi-Doll's World Population.

b) Excluding salivary glands and nasopharynx.

c) Includes urinary bladder, ureters and renal pelvis.

and stroke following immigration, in spite of regional differences in many epidemiologic variables.<sup>17)</sup> The same observation may apply to cancer. Migrants from Okinawa have acquired fewer cancers than men of other prefectures, but the difference was not statistically significant ( $P=0.12$ ). The small prefectural difference in overall cancer rates is limited to the nisei generation. Okinawan nisei are younger than those from other prefectures, as might be expected from the temporal differences in migration from Japan (see above). It is possible that the small nisei differences in cancer rates may be erased as more Okinawan nisei enter the high risk age groups.

Table IV summarizes the cancer mortality data for Japan in the years 1983-87. The differences in total cancer risk among indigenous Okinawan and other Japanese are similar to those among Japanese migrants. Different patterns emerge when specific tumor sites are assessed. Okinawan descendants, like indigenous Okinawans, appear to have a lower risk of gastric cancer than do men from other Japanese prefectures, but they do not show the excess of lymphosarcoma observed when comparing Okinawa with other prefectures. Okinawa is one of the southern prefectures where acute T-cell leukemia/lymphoma constitutes as least three-fourths of all

lymphomas.<sup>18)</sup> In Hawaii, however, B-cell lymphomas predominate among all Japanese.<sup>19)</sup> The similarity of lymphoma rates among Okinawan and non-Okinawan Japanese migrants could be due to a decreasing trend for T-cell tumors among Okinawans in Hawaii. HTLV-I infection persists among Okinawan nisei in Hawaii, but at lower frequencies than in Okinawa itself.<sup>20)</sup>

Okinawan men show higher mortality rates for cancer of the mouth, pharynx and esophagus than do men from other prefectures (Table IV). If we assume that the proportion of mortality to incidence is the same in Hawaii and Japan, there has been a greater decrease in the frequency of these tumors among Okinawan than non-Okinawan Japanese migrants (Table II). This suggests that migration has removed exposure to cancer risks that are peculiar to the Okinawan environment. At least two possible risk factors can be considered. 1) The parallel decrease in acute T-cell leukemia/lymphoma and cancer of the mouth, pharynx and esophagus raises the possibility that HTLV-I might sensitize cells of the upper digestive tract to the actions of known carcinogens (tobacco, alcohol). The virus has been identified in small cell carcinoma of the lung<sup>21)</sup> and should be looked for in Okinawans with tumors of the upper aerodigestive tract. 2) Okinawan people have used flour from the cycad nut (*sotetsu*) as a starch substitute during periods of food shortage.<sup>22)</sup> This contains cycasin, a carcinogen after hydrolysis to its aglycon, methylazoxymethanol.<sup>23)</sup> This is a less likely mechanism since very little of this food product has been consumed in the period of over 40 years since World War II, and animal experiments with cycasin have produced tumors at sites other than the aerodigestive tract (colon, liver and kidney).<sup>23)</sup>

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