Ethnic Differences and Factors Related to Breast Cancer Survival in Hawaii

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Breast cancer is the most common cancer among women of Hawaii, with approximately 700 cases diagnosed annually from 1990 to 1993. The incidence rate for Hawaii, age-adjusted to the United States 1970 standard population, has increased from 40 per 100 000 women in 1960 to 110 per 100 000 women in 1990. Although the incidence rate has increased progressively, the mortality rate has remained relatively stable.

Breast cancer survival rates have been found to vary among different communities and geographical areas, but factors related to breast cancer survival are not fully understood. Previous investigations have found the following to be related to survival: stage at diagnosis, age at diagnosis, ethnicity, socioeconomic status (SES), histology, marital status, obesity, oestrogen receptor status, treatment received, and nutritional and hormonal status. Differences in lifestyle, culture and environment may explain the difference in cancer survival among ethnic groups. The prognostic factors mentioned above have been found to account for the observed differences in breast cancer survival between African-Americans and Caucasians. Similarly, factors such as treatment and age are related to breast cancer survival discrepancies between Japanese and Caucasians. Hawaii offers a unique setting to study ethnic differences in breast cancer survival because of its multi-ethnic population and a fairly uniform health care environment. The survival experience of invasive breast carcinoma cases diagnosed between 1960 and 1979 varied among Hawaii’s five major ethnic groups, after adjustment for stage of disease at diagnosis, age at diagnosis and SES. Native Hawaiian women had the lowest survival, followed by Filipino, Caucasian, Chinese and Japanese women. It was suggested that the observed ethnic differences in breast cancer survival were more likely due to environmental than to genetic factors.

With the increase in early detection and the introduction of new treatments, it is time to take another look at the effect of previously identified and additional factors on Hawaii’s breast cancer survival pattern. To explain the differences in survival among ethnic groups, we examined the survival experience of women...
from the five major ethnic groups who were diagnosed between 1980 and 1988.

METHODS

Study Population

The Hawaii Tumor Registry (HTR) is a state-wide, population-based cancer registry, which is part of the Surveillance, Epidemiology and End Results (SEER) program. A total of 3682 newly diagnosed and microscopically confirmed invasive breast cancer cases were identified among Hawaii residents by the HTR from 1 January 1980 to 31 December 1988. Women with ethnic backgrounds other than the five major groups (African-American, Native Americans, Korean, Vietnamese, Samoans, etc.) were excluded (N = 213), as well as 124 women with missing information. As a result, 3345 cases were included for analysis, of whom 35.6% were Caucasian, 33.8% Japanese, 16.4% native Hawaiian (of which more than 90% are part-Hawaiian), 7.2% Chinese and 7.0% Filipino.

Variables

To investigate the effect of covariates, we computed survival curves by ethnicity, stage of disease at diagnosis, menopausal status, geographical residence and marital status. All tumour and covariate information was collected by the HTR through hospital records and by the Hawaii Department of Health through death certificates. Assignment of socioeconomic status further used data from the 1990 US Census.

Ethnicity classification was based on the patient’s self-identification at the time of hospitalization. A breast cancer case with any Hawaiian ancestry was counted as native Hawaiian. Caucasians were a pure group, in that any Caucasian admixtures were included in the other ethnic group. Japanese, Chinese and Filipino groups included cases where only that race was cited in addition to admixtures.

Stage at diagnosis was categorized into three levels: ‘localized’; ‘regional’, including regional by direct extension and/or spread to the lymph nodes; and ‘distant’ or metastatic.

Menopausal status was defined as follows: premenopausal (≤50 years old at diagnosis) and postmenopausal (>50 years old at diagnosis). This definition was found to be a reasonable surrogate for menopausal status when reproductive history information was unavailable.15 Marital status was categorized into four groups: married, never married, separated or divorced, and widowed. Since patients living in rural areas or islands other than Oahu might have less access to high quality medical services than women in Honolulu and since the ethnic distribution varies by geographical region within state, geographical residence was included in the study and was classified as Honolulu, other Oahu, or other islands. The findings may help to understand the geographical variation of breast cancer survival in the state.

Each case was assigned an SES index based on the census tract of her residence at diagnosis. This index was computed for each census tract as an equal weighting of the mean years of education completed by people 25 years of age and older and the mean income of households living in that tract.16 Because individuals living in most census tracts in Hawaii are relatively homogeneous in social characteristics, this indirect measure of SES index is acceptable.16 Cases were assigned SES scores based on 1990 census tracts (87%) when available and 1980 census tract (13%) otherwise. Census tracts comprising ships at sea or with more than 70% military residents were excluded because the transient nature of the population makes their census information unreliable.16 The SES scores were divided into tertiles for this analysis. The mean income of households and mean years of education (for people over 24 years) for the three SES tertiles were respectively: $38 301 and 11.9, $47 958 and 12.8, $63 819 and 13.9.

Survival time was calculated as months from the date of diagnosis to the date of death or to the date last known to be alive. Follow-up information was available through 31 December 1993. The HTR obtains cause of death for all fatalities via linkage with state and national death registries. Patients with International Classification of Diseases, 9th Revision, codes 174.8 or 174.9 as the underlying cause were classified as having died of breast cancer. Patients were considered as ‘dead’ only if they died of breast cancer, or ‘alive’ if they were still alive after diagnosis until the closure date 31 December 1993. Cases who were lost-to-follow-up or who died from causes other than breast cancer were considered ‘withdrawn alive’ at the time of their loss or death, i.e. they were censored. The rationale for censoring other causes of death is that it adjusts for competitive risks of death, which vary considerably among the five ethnic groups. The quality of reporting causes of death is high in Hawaii and misclassification of cancer deaths should be very small. The average follow-up was 46.4 months (range 0–169) for breast cancer deaths, and 101.2 months (range 0–183) for other cases.

Statistical Analysis

Bivariate relationships between ethnicity and other covariates were evaluated using frequency tables and \( \chi^2 \) tests of independence. In order to compare the survival distribution by subgroups, the Kaplan-Meier product
limit method\textsuperscript{17} was applied to estimate the 60-month actuarial survival functions.

The Cox regression model\textsuperscript{17,18} was used to determine the simultaneous influence of the covariates, adjusting for age at diagnosis. The addition of age to the model did not change any of the results for the covariates. All covariates were coded using indicator variables. No violations of the proportional hazards assumption for the covariates were found when tested by plotting the logarithm of the negative logarithm of the survival function over time.\textsuperscript{17} All analyses were performed using the SAS statistical package.\textsuperscript{19}

The significance of a covariate in models was tested by the log-rank test, i.e. by comparing twice the log likelihoods for a model without and with the covariate. Estimated risk ratios of death and 95% confidence intervals (CI) were obtained by exponentiating the appropriate parameters.

\textbf{RESULTS}

\textit{Relationship between Ethnicity and Other Covariates}

The distribution of characteristics of the breast cancer cases studied in this analysis, stratified by ethnicity, is summarized in Table 1. Each covariate is significantly associated with ethnicity by the $\chi^2$ test. Filipinos have the largest proportion of regional and distant cancers at diagnosis, followed by native Hawaiians. Japanese and Chinese patients are generally diagnosed with less advanced disease. Overall, a greater proportion of cases are diagnosed with localized cancers than with regional and distant cancers.

Filipino and native Hawaiian women are more likely to be diagnosed before age 51, compared to women of other ethnic groups. This pattern is consistent with the age structure in Hawaii, where Filipinos and native Hawaiians have a lower mean age than Japanese and Caucasians.\textsuperscript{20}

Marital status is distributed quite differently among the ethnic groups. Native Hawaiian and Caucasian women are more likely to be divorced, separated or never married at diagnosis, while Chinese, Filipino and Japanese cases are more likely to be married. A larger proportion of Filipino and native Hawaiian breast cancer cases are in the low SES group when compared to Chinese, Japanese and Caucasians. This distribution corresponds to the State’s distribution.\textsuperscript{1}

Almost three-quarters of Chinese patients reside in Honolulu compared to less than half in all other groups; Filipino and native Hawaiian patients are more likely to live on Oahu outside of Honolulu.

\begin{table}[h]
\centering
\caption{Per cent distribution of selected characteristics for breast cancer cases by ethnicity, Hawaii, 1980–1988}
\begin{tabular}{lccccccc}
\hline
Characteristics & Japanese & Chinese & Caucasian & Filipino & Hawaiian & Total & \textit{p}^a \\
\hline
N & 1130 & 242 & 1191 & 233 & 549 & 3345 & \\
\hline
\multicolumn{7}{l}{Stage:} \\
localized & 63.7 & 68.6 & 62.6 & 54.5 & 56.3 & 61.8 & <0.002 \\
regional & 32.0 & 26.9 & 31.3 & 39.1 & 35.9 & 32.5 & \\
distant & 4.3 & 4.5 & 6.1 & 6.4 & 7.8 & 5.7 & \\
\hline
\multicolumn{7}{l}{Menopausal status:} \\
pre-menopausal & 25.4 & 22.7 & 26.6 & 49.8 & 31.0 & 28.2 & <0.001 \\
post-menopausal & 74.6 & 77.3 & 73.4 & 50.2 & 69.0 & 71.8 & \\
\hline
\multicolumn{7}{l}{Marital status:} \\
marrried & 67.6 & 61.2 & 57.4 & 70.8 & 52.6 & 61.3 & <0.001 \\
widowed & 15.4 & 20.7 & 22.8 & 12.9 & 24.9 & 19.8 & \\
never married & 10.6 & 13.6 & 8.7 & 9.0 & 10.0 & 9.9 & \\
divorced/separated & 6.4 & 4.5 & 11.2 & 7.3 & 12.4 & 9.0 & \\
\hline
\multicolumn{7}{l}{Census tract SES:} \\
low & 30.9 & 22.3 & 22.6 & 53.2 & 43.9 & 31.0 & <0.001 \\
middle & 30.6 & 32.2 & 31.0 & 29.6 & 31.3 & 30.9 & \\
high & 38.5 & 45.5 & 46.4 & 17.2 & 24.8 & 38.1 & \\
\hline
\multicolumn{7}{l}{Residence:} \\
Honolulu & 49.2 & 72.7 & 45.8 & 34.3 & 32.8 & 46.0 & \\
Other Oahu & 28.9 & 21.9 & 27.9 & 39.1 & 39.9 & 30.6 & \\
Other islands & 21.9 & 5.4 & 26.3 & 26.6 & 27.3 & 23.4 & \\
\hline
\end{tabular}
\textsuperscript{a} Comparison among ethnic groups based on $\chi^2$ test for independence.
\textsuperscript{b} Pre-menopausal is diagnosed at age 50 or younger; post-menopausal is diagnosed after age 50.
Relationships between Survival Probability and Covariates

The ethnic differences in overall actuarial survival are shown as a function of time since diagnosis in Figure 1. Japanese patients have the highest survival at each of the 60 months; the survival curves of Chinese and Caucasians are below but numerically close to the Japanese curve. The survival of Filipinos follows the same pattern as that of Caucasians until 30 months after diagnosis, when survival drops off rapidly. Native Hawaiians have the lowest survival for all months. When the actuarial 5-year survival rates are tested by the log-rank test (Table 2), the differences of survival functions among ethnic groups are statistically significant.

As expected, women with distant breast cancer at diagnosis have the worst survival at 5 years while localized tumours lead to the best prognosis ($P = 0.0001$) (Table 3). Women married at the time of diagnosis have a better survival rate than unmarried women whose survival at 5 years is about 83% regardless of category, i.e. widowed, divorced, separated and never married.

![Figure 1 Actuarial survival of women with invasive breast cancer, Hawaii, 1980–1988](image)

### Table 2  Actuarial$^a$ and model-predicted$^b$ five-year survival rates for breast cancer cases by ethnicity, Hawaii, 1980–1988

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Actuarial</th>
<th>Model-predicted adjusted for covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Stage</td>
</tr>
<tr>
<td>Japanese</td>
<td>0.8834</td>
<td>0.8839</td>
</tr>
<tr>
<td>Chinese</td>
<td>0.8591</td>
<td>0.8596</td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.8556</td>
<td>0.8551</td>
</tr>
<tr>
<td>Filipino</td>
<td>0.8016</td>
<td>0.8042</td>
</tr>
<tr>
<td>Hawaiian</td>
<td>0.7783</td>
<td>0.7758</td>
</tr>
</tbody>
</table>

$^a$ Computed by the Kaplan-Meier method.
$^b$ Computed by Cox regression.

### Table 3 Effects of patient characteristics on breast cancer survival, Hawaii, 1980–1988

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Actuarial$^a$ survival probability</th>
<th>Risk ratio$^b$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>0.9091</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>Chinese</td>
<td>0.8845</td>
<td>1.3 (0.9–1.9)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>0.8964</td>
<td>1.1 (0.9–1.5)</td>
</tr>
<tr>
<td>Filipino</td>
<td>0.8609</td>
<td>1.6 (1.1–2.3)</td>
</tr>
<tr>
<td>Hawaiian</td>
<td>0.8502</td>
<td>1.7 (1.3–2.2)</td>
</tr>
<tr>
<td>Stage at first diagnosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>localized</td>
<td>0.9415</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>regional</td>
<td>0.7682</td>
<td>4.3 (3.5–5.4)</td>
</tr>
<tr>
<td>distant</td>
<td>0.2423</td>
<td>25.5 (19.7–33.1)</td>
</tr>
<tr>
<td>Menopausal status:$^c$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre-menopausal</td>
<td>0.8393</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>post-menopausal</td>
<td>0.8533</td>
<td>0.9 (0.7–1.3)</td>
</tr>
<tr>
<td>Marital status:$^d$</td>
<td></td>
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</tr>
<tr>
<td>married</td>
<td>0.8627</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>widowed</td>
<td>0.8280</td>
<td>1.3 (1.0–1.6)</td>
</tr>
<tr>
<td>never married</td>
<td>0.8294</td>
<td>1.1 (0.8–1.6)</td>
</tr>
<tr>
<td>divorced/separated</td>
<td>0.8290</td>
<td>1.3 (1.0–1.8)</td>
</tr>
<tr>
<td>Census tract SES:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>low</td>
<td>0.8422</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>middle</td>
<td>0.8471</td>
<td>1.0 (0.8–1.3)</td>
</tr>
<tr>
<td>high</td>
<td>0.8565</td>
<td>1.0 (0.8–1.3)</td>
</tr>
<tr>
<td>Geographical residence:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Honolulu</td>
<td>0.8567</td>
<td>1.0 (Ref.)</td>
</tr>
<tr>
<td>Other Oahu</td>
<td>0.8342</td>
<td>1.0 (0.8–1.3)</td>
</tr>
<tr>
<td>Other islands</td>
<td>0.8545</td>
<td>1.0 (0.8–1.3)</td>
</tr>
</tbody>
</table>

$^a$ Computed by the Kaplan-Meier method.
$^b$ Estimated by the Cox model adjusted for age and all other covariates in Table.
$^c$ Pre-menopausal is diagnosed at age 50 or younger; post-menopausal is diagnosed after age 50.
$^d$ 0.01 < $P$ < 0.05.
$^e$ $P < 0.001$. 
No significant differences in survival are found by geographical residence, menopausal status or census tract SES.

**Ethnic Differences and Effects of Other Covariates on Survival**

Filipino and native Hawaiian women have a significantly higher risk of dying in 5 years than Japanese women, whose survival was similar to that of Chinese and Caucasian women (Table 4). Cox models to predict survival functions for ethnicity with and without adjustment for stage, marital status and other covariates, are summarized in the last four columns of Table 2. The overall 5-year survival rates for each ethnic group estimated from the model without any adjustment are very close to the results from actuarial calculation. The predicted survival rates for all ethnic groups increase after controlling for stage. In all models, the Japanese have the highest survival, followed by Chinese and Caucasians. Native Hawaiians and Filipinos have the lowest and next-to-lowest survival rates in all models (Figure 2). Compared to the curves for the unadjusted model (Figure 1), the ethnic differences become much smaller after statistically controlling for the effects of other covariates. The range between the highest and lowest survival rates changes from 0.1081 in the unadjusted rates to 0.0589 after adjusting for all covariates. Comparing the initial model for only ethnicity to the models containing ethnicity and selected covariates (Table 4) indicates that ratios become smaller, meaning that the introduced covariates partially explain survival differences among ethnic groups. Stage explains a large portion of survival difference between Japanese and Caucasians, as well as between Filipinos and native Hawaiians. Marital status has only a small effect on the differences between Japanese and any other ethnic group. The combination of stage and marital status accounts for approximately 45% of the ethnic difference in survival. Stage at diagnosis is the most important factor for breast cancer survival. Generally, distant cases have a 25-fold risk of death compared to women with localized cancer (Table 3). Married patients have the longest survival, and this difference is significant when compared to widows and borderline significant when compared to divorced or separated women. Menopausal status, census tract SES and geographical residence were not important for prediction of prognosis.

Stage-specific models (Table 5) suggest that for localized disease, Filipino women have a dramatically greater risk of dying (nearly threefold), while Caucasian and native Hawaiian women have an almost twofold higher risk of dying than Japanese women. For advanced disease (i.e. regional and distant disease), native Hawaiians have a twofold higher risk of dying than Japanese.

**DISCUSSION**

Significant ethnic differences in survival rates for invasive breast cancer were found among Hawaii cases diagnosed from 1980 to 1988. Before and after statistical adjustment for covariates, Japanese patients had the highest survival rate, followed by Chinese and Caucasians. Native Hawaiians and Filipinos had a higher risk of dying from breast cancer than the other ethnic groups. About 40% of the difference between the ethnic groups with the lowest and highest in survival probability can be explained by stage at diagnosis. Marital status had a modest influence on survival, accounting for an additional 5% in the ethnic range differences in survival. Meanwhile, menopausal status, SES, and geographical residence were not related to survival.

Compared to the previous study of survival among Hawaii breast cancer patients diagnosed from 1960 to 1979, the overall survival rates for all ethnic groups...
have much improved. This phenomenon was also found in another study. The 5-year survival rates increased from 65% to 78% in native Hawaiians and from 84% to 88% in Japanese. Although the same ethnic variation in survival was found, the differences were larger in the previous study. One reason for this is probably the concurrent reduction in SES differences among ethnic groups. Census tract SES was found to be positively related to survival in the previous study. According to 1980 and 1990 census information, ethnic differences have declined both in the level of poverty and years of education. Another reason might be that health care has become more widely accessible.

The SEER program found a survival rate of 80% for US mainland Caucasians diagnosed with breast cancer in the 1980s. Caucasian patients in Hawaii have a higher survival rate of 86%, which is closer to the rate of Japanese in Hawaii (88%) than to the rate of Caucasians on the mainland. This result is also supported by a previous study that found no significant difference in breast cancer survival between Japanese and Caucasians in Hawaii, diagnosed in 1960–1979 and part of an
aetiology study of breast cancer.\textsuperscript{23} It is possible that Caucasians in Hawaii have a combined Western and Oriental lifestyle leading to a prognosis similar to Japanese in Hawaii. Therefore, to study ethnic differences related to breast cancer, it would be useful to explore environmental risk factors such as diet. In fact, high fat diets were associated with a worse prognosis among Caucasian breast cancer cases in Hawaii.\textsuperscript{23}

The strong effect of stage at diagnosis on survival was shown in many other studies.\textsuperscript{1-5} The current study found the stage of disease at diagnosis to be the most important prognostic factor for invasive breast cancer survival. The difference in survival rates between Japanese cases and native Hawaiian and Filipino cases declined after controlling for stage. Stage of diagnosis appeared to explain more of the ethnic variation in survival in the present study than in the previous time period,\textsuperscript{1} probably because the influence of other factors, such as SES, has declined.

It is noteworthy that marital status produced an effect on breast cancer survival in the current series, a result not found in the previous study.\textsuperscript{1} Married women had better survival than unmarried women, with the survival of widows significantly lower and the survival of divorced or separated women slightly lower. Past studies have suggested that widowed cases were at greater risk of cancer death (breast cancer and other sites) than married cases.\textsuperscript{24-26} Widowed people have been found to experience deterioration in physical health following bereavement and more episodes of psychiatric disturbances.\textsuperscript{27-28} Wilkinson \textit{et al.} found that married women had longer survival after the diagnosis of breast cancer than unmarried women.\textsuperscript{29} The marital effect partially explained the difference between native Hawaiian and Japanese patients since Japanese patients were more likely to be married and less likely to be widowed than native Hawaiians. Although divorced and separated women had a similar survival experience as widowed cases, the difference between them and married women was not significant because of small numbers.

In accordance with previous studies in Hawaii, no association of survival with geographical residence was found, suggesting that demographic, socioeconomic factors and health care utilization were rather uniform among these areas. Menopausal status was also not a significant prognostic factor. Although age group classification was found to be an adequate surrogate for menopause,\textsuperscript{15} perhaps it was not accurate enough to describe the critical period of menopause. However, a previous study on breast cancer survival in Hawaii also found no association for menopausal status defined as cessation of menstruation. The patterns of the previous study\textsuperscript{1} were not reproduced for SES. However, as mentioned previously, the differences in SES among the ethnic groups have decreased from 1980 to 1990. Because the SES of patients was assigned based on their census tract of residence, misclassification would have occurred for cases whose individual SES was markedly different than the average of the census tract.

Since the Hawaii Tumor Registry is a population-based registry and the Hawaii population has a small emigration rate, this study had the advantage of studying ethnic and residential survival differences in a geographically well-defined area, where access to medical care is fairly homogeneous. The case-finding and follow-up activities involved frequent quality-control evaluations. Case and death ascertainment were virtually complete.\textsuperscript{4} Misclassification on ethnicity was minimal based on an unpublished report comparing the race from the Hawaii Tumor Registry with more detailed interviewer-elicited race information from aetiology studies on the same set of cases.

The rate of loss-to-follow-up is 9.9% in this series of cases. With such low loss-to-follow-up rate, the error in the results would be acceptably small.

The survival curve for Filipino women declined much faster at 2 years post-diagnosis than the curves for other ethnic groups. It is unclear why this happens as the stage distribution for Filipino patients parallels that for native Hawaiians. Perhaps, Filipino patients have more aggressive tumours within the same stage. In fact, in stage-specific analyses, Filipinos had the highest risk of dying with localized breast cancer (1.5-fold the risk in native Hawaiians with localized disease). Further study is needed to determine if Filipino women are not getting appropriate screening or treatment, or if there is a genetic component to their poorer prognosis. More information is also needed to investigate why native Hawaiians have the poorest survival, overall and with metastatic disease. Possible explanations include the lack of appropriate treatment, genetics and comorbidities, such as obesity, diabetes and heart disease.

A limitation of this study is that no detailed clinical information was available although it might explain the remaining ethnic differences. It has been suggested that histopathological differences partially explain the ethnic disparity in breast cancer mortality in Hawaii.\textsuperscript{2}

This study investigated ethnicity and other factors related to the survival patterns among breast cancer patients diagnosed in Hawaii from 1980 to 1988. There were significant ethnic differences in breast cancer survival in Hawaii. The improved survival rates among all ethnic groups observed since 1983 might be due to increased mammography utilization, which increased the incidence of cases at early stage. Early diagnosis allows treatment to prolong survival, thereby reducing the
differences in breast cancer survival among ethnic groups, and increasing survival rates for native Hawaiian and Filipino breast cancer patients. Some of the ethnic differences remain unclear. Oestrogen receptor status, dietary habits, genetic differences, obesity, treatment variations, and comorbidities should be explored in future study.1–12,23,30

REFERENCES


(Revised version received May 1997)