Asian breast cancer survival in the US: a comparison between Asian immigrants, US-born Asian Americans and Caucasians

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Background
This study examines whether acculturation of Asian American women, assessed by place of birth, is associated with survival after diagnosis of breast cancer. We hypothesized that environmental factors associated with acculturation, such as a high-fat diet, would result in a pattern of better survival for first-generation Asians compared with subsequent-generation Asian Americans.

Methods
Analyses compare survival among women of four ethnic groups (Chinese [n = 1842], Japanese [n = 3319], Filipino [n = 1598] and a random sample of Caucasians [n = 10,000]) who were diagnosed with primary invasive breast carcinoma in three Surveillance, Epidemiology, and End Results Program (SEER) regions (San Francisco/Oakland, Hawaii, Seattle/Puget Sound) between 1973 and 1994. Analyses by birthplace compare first-generation Asian immigrants with subsequent-generation Asian Americans of the same ethnicity. Analyses were based on the Cox proportional hazards model and adjusted for age at diagnosis, stage of disease, year of diagnosis, type of treatment, marital status, and SEER region.

Results
Japanese women had significantly better survival than all other races, but there were no significant differences in survival between Chinese, Filipino, and Caucasian women. There were no significant differences in survival by place of birth within each Asian ethnic group, after adjustment for demographic characteristics, stage of disease, and treatment.

Conclusion
The findings do not support the hypothesis that acculturation of Asian American women is associated with decreased breast cancer survival.

Keywords
Breast cancer survival, Asian Americans, ethnicity, birthplace, acculturation

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that factors associated with acculturation, such as diet, affect breast cancer survival.

Methods

Information about cases of primary invasive breast cancer in three regions (Seattle/Puget Sound, San Francisco/Oakland, and Hawaii) was derived from the Surveillance, Epidemiology, and End Results (SEER) Program. The study subjects were women of Caucasian, Chinese, Japnese, or Filipino ethnicity, who were diagnosed at age 26 or older from 1973 through 1994. Exclusions included non-epithelial cancers and cases with a death certificate or autopsy diagnosis only. The regions selected had the largest number of Asian Americans among the earliest established SEER registries. Caucasians in this study were restricted to non-Latino Whites.

After all exclusions, a total of 1842 Chinese, 3319 Japanese, and 1598 Filipino women were identified, and a sample of 10,000 Caucasians was selected at random.

Stage was defined using information about size of primary tumour and extent of disease according to the American Joint Committee on Cancer criteria. For analysis, stages I, II, and IIB were represented separately, and a fourth group combined the more advanced stages of disease, IIIA, IIIB, and IV. Marital status was categorized into four groups: married, never married, separated or divorced, and widowed. Age at diagnosis was grouped into six categories: 26–44, 45–54, 55–64, 65–74, 75–84, and 85–106 years.

Type of surgery received was categorized as none, lumpectomy, or mastectomy. The lumpectomy grouping included segmental mastectomy, lumpectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, excisional biopsy, or partial mastectomy not otherwise specified, with or without dissection of axillary nodes. The mastectomy grouping included subcutaneous, total simple, modified radical, extended radical surgery, or mastectomy that was not otherwise specified, with or without nodal dissection. For chemotherapy, radiation, and hormone therapy, binary indicators were created for the use of each form of treatment.

The variable for birthplace of ethnic Asian women was dichotomized as either Asia or the US. Because the comparison of interest among the three Asian groups studied was between survival of women born in their Asian homeland and women of the same ethnic background born in the US, Asian birthplace was restricted to countries within East Asia, Southeast Asia, or the Pacific Islands. Missing information about place of birth resulted in the exclusion of 489 Chinese (26.6%), 468 Japanese (14.1%) and 329 Filipinos (20.6%) from analysis.

Survival time was calculated in months from diagnosis to the date of death or to the date last known to be alive. The closure date for follow-up observation was 31 January 1996. The outcome in this analysis was restricted to death due to breast cancer to adjust for competing causes of death, which differed among the ethnic groups. Cases were considered to have experienced the outcome if they had died of primary malignant breast cancer, defined by International Classification of Diseases, Ninth Revision, codes 174.8 or 174.9. Cases who died from other causes or were lost to follow-up were considered ‘withdrawn alive’ at the time of loss or death.

Bivariate relationships between ethnicity and age at diagnosis, stage of disease, type of treatment, year of diagnosis, marital status, and SEER region were evaluated using frequency tables and χ² tests of independence. Survival analysis based on the Cox proportional hazards model compared the survival experience among the four ethnic groups over all, while controlling for covariates. All covariates were coded using indicator variables. A separate analysis within each Asian ethnicity examined the effect of birthplace by comparing the survival of women born in Asia to women born in the US. No violations of the proportional hazards assumption for the covariates were found when examined by plotting the logarithm of the negative logarithm of the survival function over time.

Results

The distributions of characteristics of the cases studied in this analysis, stratified by race, are shown in Table 1. With the exception of the use of hormone therapy, each covariate was significantly associated with race by the χ² test. Japanese women had the largest proportion of cancers diagnosed at the earliest stage of disease. Filipinos were more likely to be diagnosed during later years of the study and at a younger age, a pattern consistent with the demographics of the regions studied in which Filipinos have a lower median age than Chinese, Japanese, and Caucasians. Asian women were more likely to be married at diagnosis than Caucasians, and Caucasians were more likely to be widowed than Asians. Japanese women were less likely to receive radiation, chemotherapy, and hormone therapy compared with Caucasians in bivariate analyses, and all Asians were less likely to have breast-conserving surgery than Caucasians. Differences among ethnic groups in the likelihood of receiving radiation, chemotherapy, and hormone therapy became non-significant after adjustment for stage, age, year of diagnosis, and type of surgery (results not shown).

Stage of disease, age at diagnosis, marital status, and year of diagnosis were associated with death from breast cancer, based on a Cox regression model that included all covariates (Table 1). Relative risk of death increased sharply with the more advanced stages of disease. Risk increased with age only among women aged 75 or older. Women who were married at the time of diagnosis had significantly better survival than women who were separated or divorced or were widowed. Survival improved considerably over time. Radiation and chemotherapy were significantly associated with poorer survival, presumably because they reflect more advanced disease despite adjustment for stage of disease. There was no difference in survival between recipients of lumpectomy compared with mastectomy, but cases that did not receive surgery fared significantly worse. The use of hormone therapy was not associated with survival after adjusting for all other variables and forms of treatment.

Results of Cox models to predict relative risk of death due to breast cancer by race, with and without adjustment for covariates, are shown in Table 2. In all models, Japanese women had the highest survival compared with all other races. Adjusting for demographic factors (age, year of diagnosis, marital status, and SEER region) or for demographic and cancer-related factors (stage, type of treatment) partially explained survival differences, but the survival advantage of Japanese women
persisted. There were no statistically significant differences in survival between Chinese, Filipino and Caucasian women after adjusting for all covariates.

Stage-specific models indicated that Japanese women had improved survival estimates compared with all other races except for the most advanced stages of disease (AJCC Stages IIIA, IIIB, IV; results not shown). An analysis by age found that pre-menopausal (defined as aged <50) Filipinos had significantly poorer survival compared with pre-menopausal Japanese, and that postmenopausal (aged ≥51) Japanese women had significantly better survival than postmenopausal Caucasians (results not shown).

An analysis by place of birth within each Asian ethnic group compared survival of women born in Asia with women born in the US. The distributions of characteristics, stratified by birthplace and ethnicity, are shown in Table 3. Most Japanese
Table 2 Relative risk of death from breast cancer among women with invasive breast cancer by ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>N</th>
<th>RR (95% CI)</th>
<th>sex</th>
<th>Age</th>
<th>marital status</th>
<th>stage, type of treatment, age of diagnosis, marital status, SEER region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>8272</td>
<td>1.00c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>1542</td>
<td>0.95 (0.83–1.08)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>2868</td>
<td>0.68 (0.61–0.76)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filipino</td>
<td>1365</td>
<td>1.09 (0.95–1.25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Variables included in analysis:
- Stage
- Type of treatment
- Age
- Year of diagnosis
- Marital status
- SEER region

a) Surveillance, Epidemiology, and End Results Program.
b) Relative risk of death due to primary malignant breast cancer, estimated by the Cox model.
c) Referent category.

Table 3 Distribution of selected characteristics by ethnicity and place of birth, among Asian American women with invasive breast cancer in three Surveillance, Epidemiology, and End Results (SEER) Program regions, 1973–1994

<table>
<thead>
<tr>
<th>Birthplace</th>
<th>No. of women</th>
<th>AJCCb stage of disease</th>
<th>Age at diagnosis (years)</th>
<th>Marital status</th>
<th>Type of surgery</th>
<th>Other forms of treatment</th>
<th>Year of diagnosis</th>
<th>SEER region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>617</td>
<td>721</td>
<td>2458</td>
<td>385</td>
<td>252</td>
<td>1014</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>19.5</td>
<td>20.9</td>
<td>22.7</td>
<td>25.7</td>
<td>33.7</td>
<td>26.7</td>
<td>35.3</td>
<td>44.5</td>
</tr>
<tr>
<td>Filipino</td>
<td>18.5</td>
<td>22.0</td>
<td>14.1</td>
<td>25.5</td>
<td>10.8</td>
<td>13.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b) American Joint Committee on Cancer 1988 stage grouping.

a) Per cent of women in birthplace category of ethnic group.
women were born in the US and most Filipinos were born in Asia, while Chinese women were about equally represented in the two birthplace groups. US-born Chinese and Japanese women tended to be older at diagnosis, and US-born Filipino women tended to be younger, than their counterparts born in Asia. Table 4 gives the Cox model-predicted relative risks of death from breast cancer for women born in Asia versus those born in the US within each ethnic group, with and without adjustment for covariates. The unadjusted estimates suggest that Chinese and Japanese cases born in Asia had a worse prognosis than cases born in the US. The effect of birthplace diminished and became non-significant after adjustment for demographic factors, stage, and treatment.

Discussion

In this study, Japanese cases had significantly better survival compared with all other races, before and after statistical adjustment for covariates. A survival advantage among other Asian ethnic groups relative to Caucasians was not observed. The improved survival among J Japanese women relative to Caucasians is consistent with other studies comparing ethnic Japanese with mainland Caucasians in the US. Studies in Hawaii of ethnicity and survival from breast cancer found no significant difference between Caucasians and Japanese after adjusting for stage and other covariates. However, the survival rate of Caucasians living in Hawaii was higher than in the US as a whole: 79% compared with 73% 5 years after diagnosis.

Excess risk of death among Filipinos with local stage breast cancer was found in studies in Hawaii and in San Francisco, suggesting that Filipinos may have more aggressive tumors within the same stage. Filipino women with localized disease in San Francisco (diagnosed 1980–1988) had a 5-year relative survival rate of 86%, whereas Japanese women had a significantly higher rate of 95%. In Hawaii, Filipino women with localized disease (diagnosed 1985–1991) had a nearly threefold excess risk of dying than Japanese women. In this analysis, stage-specific models that adjusted for age, year of diagnosis, type of treatment, marital status, and SEER region revealed higher risk of death from breast cancer among Filipinos relative to Japanese within early stages of disease, but the difference was not statistically significant (RR = 1.57, 95% CI : 0.92–2.68 for Stage I disease; RR = 1.28, 95% CI : 0.89–1.84 for Stage II A).

Differences in tumor morphology and host response have been found among Japanese and Caucasian women. Among Japanese women, a more vigorous host response to breast cancer is suggested by more conspicuous sinus histiocytosis within regional lymph nodes and fewer lymph node metastases compared with Caucasian women. A study in Hawaii in 1993 assessed the association of histopathology with breast cancer outcome. Although the survival advantage of Japanese over Caucasians decreased after controlling for stage, in an analysis of histopathological subgroups within stage (nuclear grade, intratumoral lymphocytic infiltration, and sinus histiocytosis), race again emerged as a highly significant prognostic factor. Biological mechanisms may influence the post-induction progression of other types of cancers, and a survival advantage among Japanese over other populations has been observed in studies of gastric and colorectal cancer.

Low dietary fat intake in Japan has been suggested as a partial explanation for the survival advantage of Japanese women. In 1985, dietary fat intake in Japan, as a per cent of total energy, was 25% compared to 37% in the US. Past studies that directly ascertained dietary fat in relation to breast cancer prognosis have not found consistent associations. A recent analysis of dietary components and breast cancer survival among female nurses in the US found that fat consumption before diagnosis was significantly associated with increased mortality, but after diagnosis fat intake had no apparent effect on survival. Although the hypothesis is highly controversial, two randomized clinical trials are underway to test whether dietary fat reduction can improve breast cancer survival.

One limitation of this study is that dietary fat was not measured. Ethnicity may be an indicator of dietary fat, based on international comparisons of dietary fat intake and on studies in Hawaii that confirmed that Asian Americans have lower fat intakes than Caucasians. Place of birth was used as an indicator of acculturation, and one aspect of acculturation is that Asian immigrants tend to increase their consumption of fat in adapting to a western lifestyle. In addition to dietary habits, other lifestyle behaviours may be affected by acculturation, such as physical activity and obesity. One study found that Chinese in China ate less fat, spent more time in vigorous physical activity, and had lower body mass index than North American Chinese. Individuals who have a sedentary lifestyle and consume a high fat diet are prone to obesity, and several studies have found that obesity has an adverse effect on breast cancer survival. Thus, a number of environmental and lifestyle factors associated with acculturation may be expected to have an impact on breast cancer prognosis.
If lifestyle factors as well as host response mechanisms were to improve breast cancer prognosis among Japanese women compared with other ethnic groups, first-generation Japanese women in the US would be expected to have better survival than genetically similar, later-generation Japanese women. No such pattern was observed in any model in this analysis. A study in Hawaii in 1985 examined breast cancer survival of Japanese women by place of birth, among cases diagnosed from 1960–1979. Second-generation Japanese had better breast cancer survival rates than Japanese migrants from Japan, after adjustment for age, stage, and year of diagnosis; the adjusted risk of dying from breast cancer within 5 years of diagnosis, Japanese relative to Hawaii-born, was 1.54 (95% CI: 1.00–2.37). The analogous comparison in this study found a non-significantly increased risk of death from breast cancer among Asian-born relative to US-born Japanese women with breast cancer (RR = 1.16, 95% CI: 0.83–1.63).

Variable proportions of cases by race were missing birthplace information (14.1% of Japanese, 20.6% of Filipinos, and 26.8% of Chinese, and 31.8% of Caucasians). Place of birth was reported more completely among records of deceased subjects. In the analysis by place of birth, neither Caucasians with known birthplace nor all Caucasians regardless of missing birthplace data would have been an appropriate comparison group for Asians having complete place of birth data. Each Asian ethnic group was therefore analysed separately for the effect of birthplace on survival, and records missing birthplace information were excluded from analysis. The loss of the person-time-at-risk that would otherwise have been contributed by cases missing birthplace consequently inflates the hazard rate, but the direction of the bias in the relative risk comparing Asian-born to US-born could not be determined.

Because competitive risk of death varied considerably among the ethnic groups (Table 1), differential mortality from causes other than breast cancer was adjusted internally by using the outcome of death from breast cancer in this study. It was assumed that the proportion of deaths for which the underlying cause might have been misclassified did not differ among ethnic groups. A potential source of bias may result from the tendency for immigrants to return to their country of origin soon after death. Mortality from breast cancer would be underestimated if deaths outside the US were less completely reported to SEER. To detect this potential bias, observation time among subjects lost to follow-up was compared between first- and subsequent-generation Asian Americans within the same ethnicity. With adjustment for age, stage of disease, and year of diagnosis, cases lost to follow-up who were born in Asia had significantly less observation time than cases of the same ethnic group who were born in the US (results not shown). The mean difference ranged, among the ethnic groups, from 3.5 to 10.4 months. This difference could have biased study results if the mortality of those lost to follow-up differed by place of birth.

Although it is well documented that socioeconomic status (SES) is related to survival from cancer, SES was weakly associated with survival among Asian immigrants and unrelated to survival among the ethnic groups studied in Hawaii, despite the fact that SES was highly associated with race in both studies. A limitation to this study was that SES information is not collected in SEER and could not be controlled for in this analysis.

Japanese women had significantly better survival than all other races in this study, but there were no significant differences in survival between Chinese, Filipino, and Caucasian women. There were no differences in survival of Asian American women by place of birth. This is of interest because others have reported differences in diet and body mass index for Asian-born versus US-born Asian Americans that might have been expected to lead to better survival for the Asian-born women.

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**KEY MESSAGES**

- This study examines whether acculturation of Asian American women, assessed by place of birth, is associated with survival after diagnosis of breast cancer.
- We hypothesized that factors associated with acculturation, such as a high-fat diet, would result in better survival among first-generation Asians compared with later-generation Asian Americans.
- Japanese women were found to have significantly better survival than Chinese, Filipino, and Caucasian women.
- There were no significant differences in survival by place of birth within each Asian ethnic group.

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**References**


