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A Comparison of Breast Cancer Treatment Regimens by Demographic Characteristics

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The purpose of this study was to measure ethnic differences in treatment and survival between African American (AA) and European American (EA) women with breast cancer.

We abstracted data on cases of breast cancer diagnosed in members of an HMO in metropolitan Detroit between 1986-1996 (N=886) and followed these cases for survival through April 1997 (N=137 deaths). AA women were diagnosed at a later stage when compared with EA women. Five-year survival was 77% for AAs and 84% for EAs. The crude hazard for AAs relative to EAs was 1.6 (95% confidence interval (CI) 1.1, 2.2). Adjusting only for stage of disease at diagnosis, the hazard ratio was 1.3 (95% CI 0.9, 1.9). Adjusting only for sociodemographics (age, marital status and income), the hazard ratio was 1.2 (95% CI 0.8, 1.9). After adjusting for sociodemographics and stage, the hazard ratio was 1.0 (95% CI 0.7, 1.5). We found no material racial differences in the surgical management of breast cancer. Among women with similar medical care access, we found ethnic differences in stage of breast cancer at diagnosis. Adjusting for this difference and for income, age and marital status, eliminates the effect of race on survival.

The methods used in this study as well as the cohort of women that was assembled for this study has also led to additional analyses contributing to the development of hypotheses that will be investigated in future studies. Preliminary results of one analysis examining ethnicity, stage of detection and mammography use show that among women age 40-49, AA ethnicity was strongly associated with later stage at diagnosis, even after adjustment for screening mammography use (adjusted odds ratio= 2.8, 95% CI 1.2-6.8). These results indicate that factors other than mammography use may explain late stage at diagnosis in the subgroup of younger (age 40-49) African American women.
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INTRODUCTION

In the United States, survival for African American women with breast cancer is inferior to that for European American women. The 1970s and 1980s marked a time of relatively stable rates of mortality among European American women with breast cancer, but increasing rates for African Americans\textsuperscript{1}. However, the decline in mortality observed in the early 1990s for European American with breast cancer was not observed in African Americans\textsuperscript{1,2}. Poorer survival among African Americans has been attributed to biological characteristics of the tumor, advanced stage at diagnosis, lower socioeconomic status (SES), barriers to health care, diagnostic and treatment delays\textsuperscript{3,4} and a higher prevalence of comorbid conditions\textsuperscript{5,6}. Although use of mammography by African American women has been reported to lag behind Caucasian women\textsuperscript{7}, recent research indicates that the racial discrepancy is narrowing\textsuperscript{8}. However, it is too soon to see how increased use of mammography among African Americans will affect survival. The purpose of this study was to examine racial differences in breast cancer treatment and survival.

BODY

The results of our study comparing survival for African American and European American women with breast cancer were reported in detail in our annual report dated October, 1998. These results have been published in the Journal of the National Cancer Institute\textsuperscript{9}. A reprint of this manuscript is included in the Appendix. We have also completed a comparison of surgical treatment for breast cancer by race. These results were published in Surgery\textsuperscript{10}, and a reprint is included in the appendix. The methods used in this study as well as the cohort of women that was assembled for this study has also lead to additional analyses contributing to the development of hypotheses that will be investigated in future studies. Preliminary results of one analysis examining ethnicity, stage of detection and mammography use were presented at the American Association for Cancer Research in March 2000\textsuperscript{11}. 
KEY RESEARCH ACCOMPLISHMENTS

- Found that the 5-year survival for African American women was 77%, compared to 84% for European American women.

- Demonstrated that the effect of race on survival from breast cancer was eliminated after adjusting for sociodemographic characteristics and stage of disease at diagnosis.

- Observed similar patterns of surgical management of breast cancer for African American and European American women, adjusting for stage and sociodemographic characteristics.

- Preliminary results indicate that among women age 40-49, African American ethnicity was strongly associated with breast cancer stage, even after adjusting for screening mammography use. These findings may support the hypothesis that something other than mammography use (e.g. ethnic differences in breast tissue density, and therefore mammography, or ethnic differences in tumor aggressiveness) is related to stage at breast cancer diagnosis in young African American women.

REPORTABLE OUTCOMES

- Two manuscripts and one abstract published (see appendix):


CONCLUSIONS

The results of this study quantify and compare the survival of African American and European American women with breast cancer. These results indicate that in a managed care population, where access to care is equivalent, racial differences in survival are negligible after adjustment for stage, income, age and marital status. These results lend support to the view that the effect of
an intrinsic difference in tumor biology (if any) must be small and exercised mainly through its influence on stage at diagnosis.

We also studied a subset of women with breast cancer covered by HMO as well as other forms of insurance. In this population, we found no material difference in the surgical management of breast cancer after adjusting for sociodemographics and stage.

Finally, results from this study indicate that factors other than mammography use may explain late stage at diagnosis in the subgroup of younger (age 40-49) African American women.

REFERENCES


APPENDICES

- Two manuscripts published:


- Abstract Published:

Race and Differences in Breast Cancer Survival in a Managed Care Population

Marianne Ulcickas Yood, Christine Cole Johnson, Angela Blount, Judith Abrams, Eric Wolman, Bruce D. McCarthy, Usha Raju, David S. Nathanson, Maria Worsham, Sandra R. Wolman

Background: African-American women with breast cancer have poorer survival than European-American women. After adjustment for socioeconomic variables, survival differences diminish but do not disappear, possibly because of residual differences in health care access, biology, or behavior. This study compared breast cancer survival in African-American and European-American women with similar health care access. Methods: We measured survival in women with breast cancer who are served by a large medical group and a metropolitan Detroit health maintenance organization where screening, diagnosis, treatment, and follow-up are based on standard practices and mammography is a covered benefit. We abstracted data on African-American and European-American women who had been diagnosed with breast cancer from January 1986 through April 1996 (n = 886) and followed these women for survival through April 1997 (137 deaths). Results: African-American women were diagnosed at a later stage than were European-American women. Median follow-up was 50 months. Five-year survival was 77% for African-American and 84% for European-American women. The crude hazard ratio for African-American women relative to European-American women was 1.6 (95% confidence interval [CI] = 1.1–2.2). Adjusting only for stage, the hazard ratio was 1.3 (95% CI = 0.9–1.9). Adjusting only for sociodemographic factors (age, marital status, and income), the hazard ratio was 1.2 (95% CI = 0.8–1.9). After adjusting for age, marital status, income, and stage, the hazard ratio was 1.0 (95% CI = 0.7–1.5). Conclusion: Among women with similar medical care access since before their diagnoses, we found ethnic differences in stage of breast cancer at diagnosis. Adjustment for this difference and for income, age, and marital status resulted in a negligible effect of race on survival. [J Natl Cancer Inst 1999;91:1487–91]

In the United States, survival for African-American women with breast cancer is inferior to that for European-American women (1). The 1970s and 1980s marked a time of relatively stable rates of mortality among European-American women with breast cancer but of increasing rates for African-American women (1). The decline in mortality observed in the early 1990s for European-American women with breast cancer was not observed in African-American women (1,2). Poorer survival among African-Americans has been attributed to biologic characteristics of the tumor, advanced stage at diagnosis, lower socioeconomic status (SES), barriers to health care, diagnostic and treatment delays (3,4), and a higher prevalence of comorbid conditions (5,6). Although use of mammography by African-American women has been reported to lag behind use by Caucasian women (7), research (8) indicates that this racial discrepancy is narrowing. However, it is too soon to see how increased use of mammography among African-American women will affect survival.

Most investigations (9–11) have found differences in tumor stage at disease presentation across ethnic groups. Use of multivariate models to control for biologic differences and sociodemographic characteristics has usually reduced but not eliminated the racial differential in survival (6,12–15). Many investigators (16–19) have attributed the mortality differences primarily to racial disparity in SES, by way of its influence on diagnostic delays or even a lag in benefiting from medical advances (20). Others (6,9,10) have perceived an important role for intrinsic differences in tumor aggressiveness.

We present analyses of breast cancer survival in a population of health maintenance organization (HMO) members where screening, diagnosis, treatment, and follow-up patterns are based on practice standards and are similar for all members of the population served within a large, multidisciplinary group practice. We selected this population to minimize heterogeneity in care delivery and to minimize financial barriers to health care.

METHODS

Setting

The setting for this study was the Health Alliance Plan (HAP) HMO. HAP is located in southeastern Michigan and is the largest HMO in Michigan, with more than 450,000 members. Approximately 20% of these members are African-American, 53% are female, and 37% are cared for by physicians in the Henry Ford Medical Group (HFMG). Our study population was drawn from HAP members served by the HFMG. The HFMG is a large group practice that includes an urban medical center in Detroit with primary and specialty care clinics and 26 smaller clinics throughout urban and suburban southeastern Michigan.

The HFMG maintains a comprehensive tumor registry database accredited by the American College of Surgeons. Registry staff use a thorough case-finding system, including review of all pathology and cytology reports, as well as radiology and oncology consultations. The American Joint Commission on Cancer staging system (21)—called "TNM staging"—is used to determine the stage of disease by evaluating tumor size, extent of invasion, microscopic involvement of lymph nodes, and presence of metastases. HFMG registry staff link these data with Detroit area Surveillance, Epidemiology, and End Results (SEER) Program records and conduct annual follow-up for vital status and recurrence. Follow-up information is complete for 94% of the women in the tumor registry.

Ascertainment of Case Patients

By use of the HFMG cancer registry, we identified all African-American and European-American women with incident breast cancer first diagnosed from January 1986 through April 1996. To minimize heterogeneity in clinical practice and access to care just before diagnosis, we limited the study population to women continuously enrolled in HAP for at least 1 year before diagnosis and assigned to a primary care physician within the HFMG at the time of diagnosis. We defined continuous enrollment as no
RESULTS

We identified 1321 African-American and European-American women members of HAP who were diagnosed with breast cancer from January 1986 through April 1996 and for whom mammography was a fully covered benefit. From this group, we excluded 161 women because they were not assigned to HFMG physicians at the time of diagnosis and an additional 274 women because they were not continuously enrolled in HAP for 1 year before diagnosis, for a final sample of 886 women. The proportion of African-Americans (30%) was the same among the women excluded and the study group.

The median follow-up time was 50 months overall and was similar for African-American (49 months) and European-American (50 months) women who were alive at the end of follow-up. A total of 137 deaths occurred during the study period. Table 1 shows the baseline demographic and tumor-specific characteristics of the study population. The multinomial logistic model indicated that European-American women were more likely to have earlier stage disease at diagnosis than were African-American women. When we examined this issue more closely, European-Americans were more likely than African-Americans to have disease of an earlier stage (0 or I), with an absolute difference of 11% (95% CI = 3%–18%). Among women diagnosed with stage II disease (which includes cancers with and without lymph node involvement), we found no material difference between African-American and European-American women in the proportions with positive lymph nodes (difference = 5%; 95% CI = −6% to 17%).

The 5-year survival was 77% for African-Americans and 84% for European-Americans. The crude estimates by race are shown in Fig. 1. African-American women had poorer survival compared with European-American women (hazard ratio = 1.6; 95% CI = 1.1–2.2). Table 2 presents the hazard ratios adjusted for pathologic stage and sociodemographic factors, separately and in combination. When stage was added to the model, the hazard ratio decreased to 1.3 (95% CI = 0.9–1.9). Adjusting only for sociodemographic factors, the hazard ratio was re-
duced to 1.2 (95% CI = 0.8–1.9). When we controlled for both stage and sociodemographic characteristics, the hazard ratio was reduced to 1.0 (95% CI = 0.7–1.5). The survival curves by race, adjusted for sociodemographic characteristics and stage, are shown in Fig. 2 and reflect this equivalent survival pattern. There was no evidence of violation of the proportional hazards assumption in the adjusted model.

**DISCUSSION**

It is well-known that survival after breast cancer diagnosis is poorer for African-American women than for European-American women (13,14,17,19). It is difficult to summarize the pertinent literature because no two studies are precisely comparable, and many papers are quoted differently by the authors who cite them. Nevertheless, some valid generalizations are relevant here. As we found, the difference in distribution of stage at detection has a major influence on differential African-American/European-American survival but does not fully explain it (6,10–15).

By studying only HAP-HFMG patients, we eliminated the issue of lack of insurance coverage for screening and diagnostic services, a factor associated with both later stage at diagnosis and lower SES (4,6,15,23). Even within this equal-coverage population, with its relative homogeneity of health care access and delivery, a large discrepancy in stage remains between African-American and European-American women (Table 1). Our study was not designed to investigate reasons for differences in stage at detection such as mammography use. However, two existing studies, both conducted in HAP-HFMG populations during approximately the same time period as this study, shed some light on this question. These studies measured, respectively, the proportion of women more than 50 years old who received mammography according to guidelines (relatively, 5.6% fewer African-American than European-American women) (24) and the proportion of women more than 50 years old with normal screening mammograms who were screened again within 2 years (relatively, 7.2% fewer African-American than European-American women) (25). These small racial differences in mammography use among women in the same health care system as our sample have two implications: 1) The differences in mammography use are probably too small to explain the racial differences in stage at detection (relatively, 19% fewer African-American women with stage 0 or I disease; Tables 1 and 2) as implied above, uniform insurance coverage and clinical practices are not sufficient to equalize completely African-American and European-American women's use of breast cancer screening services.

Use of health care influences stage at diagnosis and the effectiveness of treatment (4,11,23). The difficulty of obtaining data on populations with even approximate uniformity of care motivates our study. Its detailed results cannot be generalized to different populations or regions, but it constitutes an important addition to the body of work that greatly reduces the influence of race on survival by adjusting for stage and SES.

Wojcicki et al. (26) eliminated the insurance factor by studying women cared for in the Department of Defense system, which also tries to provide equal access. The authors found that, among women with breast cancer, after adjustment for age and stage, European-American women had better survival than African-American women; however, Wojcicki et al. did not control for income, a factor that varied by race in our sample of HMO members.

In our population, sociodemographic variables and stage, taken separately, had comparable confounding effects on the association between race and survival. As noted by Weiss et al. (27) and illustrated in the literature that we cite, SES is difficult to quantify and consists of a constellation of factors, although income plays a primary role. We know of one study besides our own that employs census data at the block group level (28) to improve the precision of SES estimates. Bassett and Krieger (16) do this by using six measures of SES other than income, and they adjust for age and stage. However, they did not study a sample with equivalent health care coverage. Both our study and that of Bassett and Krieger (16) come very close to eliminating race as an independent influence on survival.

The results of our study indicate that factors other than the ability to pay for services affect breast cancer survival. These factors may have some influence on stage at detection in particular. They include various beliefs about cancer risk and the usefulness of early detection, differences in the effects of various outreach and reminder strategies, differences in access mediated by transportation or the ability to get time off work to keep appointments, obesity, comorbidities, and

![Fig. 2. Survival by race, adjusted for age, income, marital status, and stage. Adjusted Kaplan-Meier curves for 886 women with breast cancer seen at the Health Alliance Plan-Henry Ford Medical Group from January 1986 through April 1996. The table under the x-axis gives the numbers of patients at risk at representative time points. CI = confidence interval. Symbols used: ----- = European-American; — = African-American.](image-url)
Table 1. Baseline demographic and tumor characteristics

<table>
<thead>
<tr>
<th></th>
<th>Value (95% CI)</th>
<th>Value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>African-American (n = 273)</td>
<td>European-American (n = 613)</td>
</tr>
<tr>
<td>Socio-demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>54% (48%–60%)</td>
<td>59% (65%–73%)</td>
</tr>
<tr>
<td>Mean age in y at diagnosis</td>
<td>55 (45–57)</td>
<td>56 (55–57)</td>
</tr>
<tr>
<td>Median household income ($1000)</td>
<td>26 (23–27)</td>
<td>44 (42–45)</td>
</tr>
<tr>
<td>Mean HMO enrollment before diagnosis, y</td>
<td>6.9 (6.3–7.5)</td>
<td>5.4 (5.1–5.7)</td>
</tr>
<tr>
<td>Tumor characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#</td>
<td>17% (13%–22%)</td>
<td>21% (17%–26%)</td>
</tr>
<tr>
<td>I</td>
<td>29% (24%–34%)</td>
<td>36% (32%–40%)</td>
</tr>
<tr>
<td>II</td>
<td>41% (34%–46%)</td>
<td>33% (29%–37%)</td>
</tr>
<tr>
<td>III</td>
<td>9% (5%–12%)</td>
<td>7% (5%–10%)</td>
</tr>
<tr>
<td>IV</td>
<td>5% (2%–8%)</td>
<td>3% (1%–4%)</td>
</tr>
<tr>
<td>Mean tumor size, cm</td>
<td>2.4 (2.1–2.6)</td>
<td>2.1 (2.0–2.3)</td>
</tr>
</tbody>
</table>

*CI = confidence interval; HMO = health maintenance organization.
*Stage according to the American Joint Commission on Cancer system (21).

Table 2. Effect of demographic and tumor characteristics on survival estimates

<table>
<thead>
<tr>
<th>Variables in model</th>
<th>Hazard ratio, African-American versus European-American</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race only</td>
<td>1.6</td>
<td>1.1–2.2</td>
</tr>
<tr>
<td>Race + stage*</td>
<td>1.3</td>
<td>0.9–1.9</td>
</tr>
<tr>
<td>Race + sociodemographic factors†</td>
<td>1.2</td>
<td>0.8–1.9</td>
</tr>
<tr>
<td>Race + stage + sociodemographic factors†</td>
<td>1.0</td>
<td>0.7–1.5</td>
</tr>
</tbody>
</table>

*Stage according to the American Joint Commission on Cancer system (21).
†Age, marital status, and median household income.

Differences in breast density that modify the effectiveness of mammograms (4, 11, 23, 29–33).

A fundamental question for us, and for the related studies we cite, is whether African-American women have intrinsically more aggressive tumors than European-American women, thus affecting their survival either directly or by way of stage at detection because of more rapid progression. Our study did not incorporate estrogen receptor status or histologic tumor grade because they were often omitted from the HFMG tumor registry and, when available, had not been evaluated consistently.

The literature can be roughly divided into studies that find intrinsic differences in tumor aggressiveness (higher nuclear and histologic grade, S-phase fraction or mitotic index, and estrogen receptor negativity) to exercise a major influence on differential African-American/European-American survival (6, 9, 10), and the greater number that find no positive evidence for this effect because they attribute a very limited influence to race after adjustment for stage and SES (15–20). In a population with uniform health care coverage, we found that the residual influence of race after adjustment is negligible (hazard ratio = 1.0; 95% CI = 0.7–1.5). This result lends support to the view that the effect of an intrinsic difference in tumor biology (if any) must be small and exercised mainly through its influence on stage at diagnosis.

**References**

23. Lannin DR, Mathews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of...


NOTES

1Editor's note: SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis and the NCI makes the data available to the public for scientific research.

Supported by the Department of Defense's Breast Cancer Program (DAMD17-96-1-6246 and #17-97-1-7302).

Manuscript received November 23, 1998; revised June 14, 1999; accepted July 2, 1999.
Racial differences in the presentation and surgical management of breast cancer

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Background. African American women are seen with more advanced breast cancers, are less likely to be treated with breast-conserving surgery, and generally have poorer prognoses than white women. There are a myriad of potential causes for these phenomena. The purpose of this study was to measure racial differences in the surgical treatment of breast cancer among women with comparable health care access and delivery.

Methods. The Breast Cancer Registry of the Department of Surgery at Henry Ford Hospital was accessed for all patients between January 1, 1990, and December 31, 1997 for whom data on race, tumor characteristics, stage, and treatment specifics were available. Socioeconomic information was collected with use of 1990 census block data. Proportions of women who received each treatment were compared for African Americans and whites with use of the relative risk (RR) and 95% confidence intervals (CI). We used multiple logistic regression to obtain estimates of the relative risk, controlling for potential confounding factors.

Results. Of the 1699 patients in the database, 1250 had sufficient information for analysis. A total of 8.7% of African American women were diagnosed with late-stage disease (ie, stage III or IV) compared with 7.9% of whites. Nevertheless, African American women had a lower frequency of stage I disease (30.5% vs 36.2%) and a higher frequency of stage II disease (36.8% vs 31.4%). Overall and adjusted risk estimates for age, tumor stage, marital status, median income, and type of insurance revealed no substantive or statistically significant differences between African American and white patients. The adjusted RR for local excision was 1.39 (95% CI 0.78 to 2.49), for lumpectomy and axillary dissection RR 0.92 (95% CI 0.66 to 1.29), for simple mastectomy RR 0.84 (95% CI 0.41 to 1.72), and for modified radical mastectomy RR 1.00 (95% CI 0.73 to 1.36).

Conclusions. In this setting of equal access to health care, African American women still have higher frequencies of stage II disease, although the frequencies for late-stage disease are similar. Nevertheless, no surgical differences were found in this population, even after the effects of socioeconomic indicators and stage at diagnosis were controlled for. Survival differences between African American and white women are unlikely to be explained by differences in treatment. (Surgery 1999;125:375-9.)

From the Division of General Surgery, Henry Ford Hospital, and the Josephine Ford Cancer Center, Henry Ford Health System, Detroit, Mich

African American women with breast cancer have been found to be first seen with more advanced disease and tend to have worse prognoses than white women, even when disease stage is controlled for. Data from the National Cancer Data Base from 1995 showed that 37.5% of African Americans were first seen with stage 0 or I disease compared with 54.5% of non-Hispanic whites. Attempts to explain this situation have focused on differences in tumor biologic functions, socioeconomic conditions, cultural influences, and access to health care. Nevertheless, 25% of the difference in survival could not be explained by stage, primary tumor characteristics, treatment, socioeconomic conditions, and demographic factors.

National data show that African American women undergo breast-conserving treatment at a lower rate compared with white women. In the National Cancer Data Base, 49.7% of non-Hispanic whites underwent partial mastectomy compared with 46.8% of African Americans. Some of this difference was explained by level of education and residence in a metropolitan area.
Table I. Distribution of sociodemographic characteristics by race

<table>
<thead>
<tr>
<th></th>
<th>African American</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50</td>
<td>129 (31.0)</td>
<td>263 (31.5)</td>
</tr>
<tr>
<td>51-60</td>
<td>88 (21.2)</td>
<td>213 (25.5)</td>
</tr>
<tr>
<td>61-70</td>
<td>107 (25.7)</td>
<td>188 (22.5)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>92 (22.1)</td>
<td>170 (20.4)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>176 (42.3)</td>
<td>539 (64.6)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>240 (57.7)</td>
<td>295 (35.4)</td>
</tr>
<tr>
<td>Median income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤$20,000</td>
<td>202 (51.4)</td>
<td>48 (6.5)</td>
</tr>
<tr>
<td>$20,000-$35,000</td>
<td>122 (31.0)</td>
<td>182 (24.7)</td>
</tr>
<tr>
<td>$35,001-$50,000</td>
<td>47 (12.0)</td>
<td>281 (38.2)</td>
</tr>
<tr>
<td>&gt;$50,000</td>
<td>22 (5.6)</td>
<td>225 (30.6)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Alliance Plan</td>
<td>189 (45.4)</td>
<td>381 (45.7)</td>
</tr>
<tr>
<td>Blue Cross/Blue Shield</td>
<td>38 (9.1)</td>
<td>108 (13.0)</td>
</tr>
<tr>
<td>Medicare</td>
<td>151 (36.3)</td>
<td>254 (30.5)</td>
</tr>
<tr>
<td>Other</td>
<td>38 (9.1)</td>
<td>91 (10.9)</td>
</tr>
<tr>
<td>Total</td>
<td>416 (100)</td>
<td>834 (100)</td>
</tr>
</tbody>
</table>

Values are number and percent.

It has been documented that low-income patients have higher frequencies of late-stage breast cancer compared with high-income groups. Low-income groups may be underinsured, limiting their ability to obtain adequate health care. This problem with access to health care is reflected in lower rates of screening mammograms, for example. This issue accounts for some of the differences seen between these groups.

The hypothesis of this study is that in a managed care system with equivalent access to health care for whites and African Americans there should be no difference in stage of presentation or surgical treatment if these differences are entirely the result of factors reflecting access to health care.

MATERIAL AND METHODS

Setting. The Henry Ford Health System (HFHS) is an integrated managed care organization serving southeastern Michigan. The tertiary hospital, Henry Ford Hospital, serves not only the system’s health maintenance organization (HMO) patients but also out-of-system referrals (such as fee-for-service insurers). In 1990 the Department of Surgery developed a breast cancer registry as a comprehensive database that includes information on treatments and outcomes for all breast cancer patients evaluated within the HFHS. The registry records data on age, race, tumor size, lymph node status, pathologic stage, surgical treatment, hormonal treatment, cytotoxic chemotherapy, and radiation treatment in addition to other tumor-specific data.

Identification of the study population. From the Breast Cancer Registry we identified all African American and white women seen at HFHS with newly diagnosed breast cancer between January 1, 1990, through December 31, 1997. From this group we excluded those for whom the registry had missing stage, treatment, or nodal status data.

Classification of the stages. Stages were classified in the following manner: stage 0, in situ breast ductal carcinoma (Tis); stage I, invasive ductal, lobular, tubular, or medullary carcinomas ≤ 2 cm (T1) without axillary lymph node metastasis (N0); stage II, invasive ductal, lobular, tubular, or medullary carcinomas > 2 cm (T2 and T3) without lymph node metastasis (N0) or ≤ 5 cm in size without signs of direct extension to the chest wall or skin (i.e., excluding T4 lesions) but with lymph node metastasis; stage III, any tumor with locally invasive lesions to chest wall or skin (T4) or tumor of any size with fixed axillary lymph nodes (N2); and stage IV, metastasis to distant organs (all M1).

Treatment and confounding data. We classified surgical treatment into 4 categories: (1) local excision, removal of mass with or without margins negative for tumor with or without adjuvant radiation therapy; (2) lumpectomy and axillary lymph node dissection, removal of mass with negative margins with axillary lymph node dissection; (3) simple mastectomy, removal of entire breast without axillary lymph node dissection; and (4) modified radical mastectomy, removal of the entire breast with axillary lymph node dissection.
From the HFHS patient registration system we obtained marital status, insurance, and address. We mapped each woman's address to census block groups and estimated household income on the basis of block-group-specific 1990 census data.

Data analysis. Nominal data was analyzed with the chi-square test and randomization test as appropriate with the True Epistat statistical computer program.

For each treatment category we separately calculated the proportion of African American and white women who received each treatment. We compared these proportions with use of relative risks (RR) and corresponding 95\% confidence intervals (CI). We calculated the RR by dividing the proportion of African American women who received each treatment by the proportion of white women who received the treatment.

To control potential confounding, we used SAS statistical software (SAS Institute, Cary, NC) to fit a multiple logistic regression model including tumor stage (0, I, II, III, and IV); age (≤50, 51 to 60, 61 to 70, and >70 years old); marital status (married or unmarried); median income (≤$20,000, $20,001 to $35,000, $35,001 to $50,000, and >$50,000); and insurance (HMO, Blue Cross, Medicare, and other) as indicator terms. From the logistic model we obtained the odds ratio, which approximates the RR when the proportions are small, as they are in this study.

RESULTS

We identified 1699 women with newly diagnosed breast cancer from January 1, 1990, through December 31, 1997. We excluded 78 women who were not African American or white. We also excluded 180 women with missing stage information, 58 women without definitive treatment data, and 138 women with missing nodal status data, leaving a final study population of 1250 women.

The distribution of sociodemographic characteristics by race is shown in Table I. The age distribution was similar for African Americans and whites. African American women were more likely to be unmarried and had lower median household incomes compared with white women. In both groups almost half the women were members of the HFHS HMO, the Health Alliance Plan.

Table II shows the tumor characteristics of the study population. Almost 46\% of African Americans were first seen with regional or distant (stage II, III, and IV) disease compared with 39\% of whites (P = .04). Among those with stage II tumors, for which staging depends on nodal status and size, African Americans were more likely to have tumors >2 cm compared to whites (RR = 1.48, 95\% CI 1.08 to 2.03), whereas African Americans were less likely to have nodal involvement than whites (RR = 0.85, 95\% CI 0.71 to 1.0). Specifically, African Americans had a higher frequency of T2 and T3 tumors compared with whites (P = .014). But, surprisingly, they had also a higher frequency of node-negative disease (P = .04).

The distribution of treatments by race is shown in Table III. We found that overall and after adjustment for age, tumor stage, marital status, estimated
Table III. Distribution of treatments by race and relative risk of receiving specific treatments comparing African Americans with whites

<table>
<thead>
<tr>
<th>Surgical treatment</th>
<th>African American</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative breast surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local excision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>80 (19.2)</td>
<td>156 (18.7)</td>
</tr>
<tr>
<td>No</td>
<td>336 (80.8)</td>
<td>678 (81.3)</td>
</tr>
<tr>
<td>Crude RR (95% CI)</td>
<td>1.03 (0.81-1.31)</td>
<td>1.0</td>
</tr>
<tr>
<td>Adjusted RR (95% CI)*</td>
<td>1.39 (0.78-2.49)</td>
<td>1.0</td>
</tr>
<tr>
<td>Lumpectomy and axillary dissection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>147 (35.3)</td>
<td>321 (38.5)</td>
</tr>
<tr>
<td>No</td>
<td>269 (64.7)</td>
<td>513 (61.5)</td>
</tr>
<tr>
<td>Crude RR (95% CI)</td>
<td>0.92 (0.79-1.07)</td>
<td>1.0</td>
</tr>
<tr>
<td>Adjusted RR (95% CI)*</td>
<td>0.92 (0.66-1.29)</td>
<td>1.0</td>
</tr>
<tr>
<td>Nonconservative breast surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple mastectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (3.6)</td>
<td>31 (3.7)</td>
</tr>
<tr>
<td>No</td>
<td>401 (96.4)</td>
<td>803 (96.3)</td>
</tr>
<tr>
<td>Crude RR (95% CI)</td>
<td>0.97 (0.53-1.78)</td>
<td>1.0</td>
</tr>
<tr>
<td>Adjusted RR (95% CI)*</td>
<td>0.84 (0.41-1.72)</td>
<td>1.0</td>
</tr>
<tr>
<td>Modified radical mastectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>173 (41.6)</td>
<td>225 (40.0)</td>
</tr>
<tr>
<td>No</td>
<td>243 (58.4)</td>
<td>509 (60.0)</td>
</tr>
<tr>
<td>Crude RR (95% CI)</td>
<td>1.07 (0.95-1.29)</td>
<td>1.0</td>
</tr>
<tr>
<td>Adjusted RR (95% CI)*</td>
<td>1.00 (0.73-1.36)</td>
<td>1.0</td>
</tr>
<tr>
<td>Total</td>
<td>416 (100)</td>
<td>834 (100)</td>
</tr>
</tbody>
</table>

*Adjusted for age, tumor stage, marital status, median income, and type of insurance.

household income, and insurance, African Americans and whites received similar treatments. When we dichotomized surgery as nonconserving (simple mastectomy and modified radical mastectomy) or conserving (local excision and lumpectomy with axillary dissection), we found no racial differences in treatment (adjusted RR = 0.97, 95% CI 0.72 to 1.31).

DISCUSSION

Simon and Severson12 with use of the Surveillance, Epidemiology, and End-Results Program data for the metropolitan Detroit area (where most patients treated within the HFHHS reside) found that African American women were more likely to be first seen with regional or distant disease compared with white women. The staging system used by Simon and Severson12 is not strictly analogous to ours because some of our stage II and III patients may not have lymph node metastasis but rather large primary tumors. Nevertheless, if we define stage II, III, and IV patients as those with regional and distant disease, then the rate for African Americans in the Detroit metropolitan area derived from the data of Simon and Severson versus that of the HFHHS for distant disease (44.5% vs 45.5%, respectively) and whites (36.5% vs 39.3%, respectively) are similar. This implies that stage at presentation in a managed care organization is not different than for the regional population as a whole.

Once seen for care, treatment selection is no different between African Americans and whites in our setting. Data from Muss et al7 reported in 1992 that 14% of African American women underwent breast-conserving treatment compared with 27% of white women. In our institution from 1990 to 1997 breast conservation was achieved in >55% for both races. These data also compare favorably with the 35% breast conservation rate published by Lazovich et al9 in 1991, who claimed that breast conservation surgery is underused. Some of these differences between our data and those of Muss et al7 and Lazovich et al9 could be attributed to the general increase in breast conservation after 1992. In addition, others13,14 have shown that failure rates, cosmetic results, and treatment compliance were the same in whites and African Americans. In our managed care system all new breast cancer patients are managed by a breast surgeon, medical oncologist, and a radiation oncologist with a consensus team approach that does not distinguish between African Americans and whites.15

More vexing is the problem of higher-stage presentation for African Americans. Differences in
tumor biology appear to account for a small proportion of this gap.\textsuperscript{3} Differences in mammographic screening also appear to play a limited role.\textsuperscript{16} In a population-based study Jones et al\textsuperscript{16} found that whites were twice as likely as African Americans to undergo screening mammography. However, after adjustment for mammography, the risk of later-stage disease in African Americans was decreased only minimally. Screening compliance in the HFHS is 73%. Patients of lower socioeconomic status are first seen with higher-stage disease and have lower stage-dependent survival.\textsuperscript{4} On the other hand, Frantzini et al\textsuperscript{17} found in their population in Texas that after adjustment for socioeconomic status race was not a significant predictor of breast cancer mortality. Therefore, at best, survival differences can only partially be explained by poorer access to care, even when all other variables are evaluated.

Cultural differences might be implicated. Royal-Schaler et al\textsuperscript{10} have shown that first-degree relatives of African American women with breast cancer significantly underestimate their risk for development of breast cancer and had less knowledge of the symptoms of breast disease. These authors suggested a program of systematic education to enhance African American women’s understanding of breast cancer and its symptoms. Presumably, this would promote early recognition of breast cancer in this group.

In conclusion, we have demonstrated a higher rate of stage II breast cancers in African American women compared with white women but similar rates of advanced (stage III and IV) disease in a managed care environment that provides equal access to health care. However, the choice of treatment between groups is similar, implying that equal counseling to the treatment options will lead to an equal distribution of surgical treatments.

REFERENCES
**#5113 SULFOTRANSFERASE 1A1 (SULT1A1) POLYMORPHISM, ENDOGENOUS ESTROGEN EXPOSURE, WELL-DONE MEAT INTAKE, AND BREAST CANCER RISK.** W Zheng, D W Xie, Z L Deng, J R Cerhan, T A Sellers, W O Wen, and A P Folsom, Univ of South Carolina, Columbia, SC, and University of Minnesota, Minneapolis.

Phenol sulfotransferase 1A1 (SULT1A1) is involved in the inactivation of estrogens and bioactivation of heterocyclic amines. A G→A transition at codon 213 (GCG/Arg to CAC/Pro) of the SULT1A1 gene was recently reported, and individuals homozygous for the His allele have a substantially lower activity of this enzyme than those with other genotypes. We hypothesized that the His allele may be a risk factor for breast cancer, particularly among women who had risk factors related to higher endogenous estrogen exposure. DNA samples and information related to lifestyle factors including meat intake were obtained from breast cancer cases diagnosed during 1992 to 1994 and a random sample of cancer-free control subjects. Multivariate analysis was performed on data from 156 cases and 332 controls who donated a blood sample. The frequency of the His allele was 41.6% in cases and 34.0% in controls, and it was associated with an increased risk of breast cancer (p=0.02). Compared to women with the Arg/Arg genotype, an 80% elevated risk was observed among women homozygous for the His allele (95% CI: 1.0-3.2, P=0.04). This positive association was more pronounced among women who drank alcohol and had high body mass index and late age at menopause, factors related to higher endogenous estrogen exposure, than those who did not have these risk factors.

**#5114 ASSOCIATION OF NAT2, GSTM1, GSTP1, GSTT1, FLAME-BROILED FOOD AND BREAST CANCER RISK IN A NORTHERN INDIANA CONTROL STUDY.** Kala Vishvanathan, Paul Strickland, Doug A Bell, Maria A Watson, Nathaniel Rothman, Sandy Hoffman, and Kathy J Helzlsouer, Johns Hopkins Sch of Hygiene & Public Health, Baltimore, MD, National Cancer Inst, Bethesda, MD, and NIEHS, RTP, NC.

Heterocyclic amines (HCA) are procarcinogens that are produced when meat is cooked in direct heat for long durations. N-Acetyltransferases (NAT2) are involved in the activation of HCA. It was hypothesized that women who consumed flame-broiled foods were rapid acetylators of NAT2 may be at increased risk of breast cancer. The association between NAT2, flame-broiled meat intake and the risk of breast cancer was assessed in a nested case-control study. Genotype information was available for 110 cases and 113 matched controls. 86% of these cases and 89% of the controls also had information on the intake of flame-broiled food in the previous month. The risk of breast cancer was increased among women who ate flame-broiled food greater than two a month compared to those who did not (OR=2.03 95% CI:0.88, 4.68). This risk was further increased among women who also had the rapid acetylator allele of NAT2 and ate flame-broiled food (OR=3.43 95% CI:1.14, 10.35; P trend = 0.021). Glutathione S-transferases may be involved in the detoxification of these carcinogens. Women who had the null genotype for GSTM1 or GSTT1, had higher consumption of flame-broiled food. Women who had the rapid acetylator allele of NAT2, and ate flame-broiled food were at an increased risk of breast cancer. When the four genotypes were assessed in combination, the risk was higher for women who had the rapid acetylator allele of NAT2, null genotype for GSTM1, null genotype for GSTT1 and were flame-broiled food consumers and in combination seemed to significantly increase the risk of breast cancer among women who ate flame-broiled food.

**#5115 GLUTATHIONE S-TRANSFERASE P1 POLYMORPHISM IS ASSOCIATED WITH SURVIVAL AMONG WOMEN TREATED FOR BREAST CANCER.** Carol Sweeney, Gail Y McClure, Manal Y Fares, Patricia A Thompson, Angie Stone, Brian F Coles, Scienia Koruian, Laura F Hutchins, Fred F Kadin, and Christine B Ambrosone, M D Anderson Cancer Ctr, Houston, TX, National Ctr for Toxicological Res, Jefferson, AR, and Univ of Arkansas for Med Sci, Little Rock, AR.

Individual variability in metabolism of therapeutic agents may affect cancer treatment response and survival. Glutathione S-transferases (GSTs) detoxify chemotherapy agents and reactive oxidant molecules produced during radiation therapy. A GST P1 polymorphism (exon 5 G-A) results in an amino acid substitution (Val→Ile) affecting catalytic efficiency of the P1 protein. The effect of this variant allele on breast cancer therapy and survival was evaluated. Survival data according to genotypic GST P1 genotype among women with breast cancer treated by chemotherapy or radiation therapy were examined. Data was extracted from normal tissue (normal lymph node or skin) from paraffin blocks from women with stage I-IV breast cancer diagnosed 1994 to 1999, RFLP analysis of GST P1 exon 5 p.54Val/Val and RFLP were used to detect the GST P1 exon 5 p.54Val/Val genotype. Vital status was determined from cancer registry follow-up. The distribution of GST P1 genotypes among 240 cases was 46.3% Ile/Ile, 44.2% Ile/Val, and 9.6% Val/Val. GST P1 genotype was associated with survival; compared to women with Ile/Ile genotype, there was a trend (p=0.04) of better survival with increased number of GST P1 Val alleles. Hazard ratios (adjusted for stage and age) were 0.8 (95% confidence interval CI 0.5-1.4) for Ile/Val, and 0.3 (95% CI 0.1-1.0) for Val/Val. GST P1 genotype was not associated with age, stage at diagnosis, estrogen or progesterone receptor status, positive nodal involvement, or primary tumor size at diagnosis in GST P1 expression in tumor cells has been associated with poor survival and with drug resistance in vitro, however few studies have addressed genotype and survival. Our results indicate that women with one or two inherited allelic forms of the GST P1 variant may have better outcome with chemotherapy or radiation treatment for breast cancer than women with GST P1 Ile/ile.

**#5116 THE GENOTYPES OF THE 5α-REDUCTASE GENE ARE RELATED WITH PSA EXPRESSION AND RISK IN SPORADIC BREAST CANCER.** Andreas Scarinci, B Bharai, B Hoffman, M Gia, and E P Diamandis, Mount Sinai Hosp, Toronto, ON, Canada, Univ of Toronto, Toronto, ON, Canada, and Univ of Turin, Turin, Italy.

5-alpha-reductase (SRD5A2), an enzyme that is expressed in androgen dependent tissues, catalyzes the reduction of testosterone (T) to its more active form, dihydrotestosterone (DHT), which in turn transactivates a number of genes. The SRD5A2 gene harbors two frequent polymorphic sites, one in the coding region at codon 69 of exon 1, where valine is substituted by leucine (69V); and the other in an untranslated region of the gene, where a single nucleotide substitution outside TA repeat lengths exists. Both polymorphisms are known to affect the activity of this enzyme. We examined 151 sporadic breast tumors from Italian patients for the 69V and TA polymorphisms by sequence and fragment analysis, respectively. Total prostatic specific antigen (PSA) concentration in all samples was measured with an ultrasensitive time-resolved immunofluorometric assay, which utilizes two monoclonal antibodies specific for PSA and has a detection limit of 0.001 ng/ml. The results showed that PSA expression was significantly elevated in tumors with 69V genotype and TA repeat of 8-9 (p=0.008 and p=0.037 respectively). The presence of 69V allele in breast tumors was associated with shorter disease-free (p=0.01) and overall survival (p=0.01) rates. A statistically significant association between high PSA levels and TA repeats of 8-9 was found. Levels of TA repeat longer than 9 were not associated with any significant reduction in the risk of relapse (p=0.04). Our results suggest that the genotype of codon 69 and the TA repeat length of the 5α-reductase gene are associated with sporadic breast cancer aggressiveness and age of onset, likely due to altered androgen metabolism.

**#5117 ETHNICITY, STAGE OF DIAGNOSIS OF BREAST CANCER, AND SCREENING MAMMOGRAPHY IN A HEALTH MAINTENANCE ORGANIZATION.** Christine Cole Johnson, Ulka Bawle, and Marianne Ulcickas Yood, Bristol-Myers Squibb, Wallingford, CT, and Henry Ford Health System, Detroit, MI.

In the United States, an estimated 89% of all breast cancers were diagnosed in women who are white. From 1986-1996, crude 5 year survival for European American women (EA) was better than that for African American (AA) women (OR=1.6; 95%CI 1.1-2.2), with AA women diagnosed at a later stage. We hypothesized that the ethnicity difference in tumor stage at diagnosis could be explained in part by differential use of screening mammography, although in this setting mammography is a covered benefit and strongly emphasized along the health plan stages. To investigate this theory, we obtained information from automated data and medical records on the use of screening mammography during the three years prior to diagnosis. Only women who were continuously enrolled in the HMO during this time period were eligible. The women were classified into two age groups, 40-49 yrs. (n=141) and 50+ yrs. (n=295), based on age differences in screening participation. The 436 women who were diagnosed with stages II-IV (65.9%) more frequently than young EA women (47.0%). This difference was much less striking among women 50+ years. In both age groups, AA women were significantly more likely than their EA counterparts.
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to have not received a screening mammogram (73.2% vs. 40% for younger and 61.2% vs. 31.0% for older women). However, among women 40-49, AA ethnicity was strongly associated with later stage at diagnosis even after adjustment for screening (adjusted OR = 2.8; 95% CI 1.2-6.6). Our data suggest that something other than mammography use (e.g. ethnic difference in breast tissue density and therefore mammography efficacy or ethnic difference in tumor aggressiveness), is related to stage at breast cancer diagnosis in young AA women.

#5118 ADENOMATOUS POLYPS AND EPOXIDE HYDROLYSE POLY-MORPHISMS – RELATION TO SMOKING AND COOKED MEAT CONSUMP-TION. Cornelia M Ulrich, J Bigler, J Whitten, L Fosdick, R Bostick, and J D Potter, Fred Hutchinson Cancer Res Ctr, Seattle, WA

Epoxides are important intermediates in activation and detoxification of xenobiotics particularly polyycyclic aromatic hydrocarbons (PAHs). PAHs are the product of incomplete pyrolysis of organic compounds. They can be activated to reactive metabolites that bind covalently to DNA and form bulky adducts. Some PAHs are known carcinogens. In a study of adenomatous polyps in n cases = 530, n controls = 849), we investigated the role of 2 polymorphisms in exon 3 (71yr13His) and exon 4 (His48Arg) of epoxide hydrolase 1 (Ephx1) – and their interaction with smoking and meat intake. The age- and sex-adjusted ORs (95% CI for exon 3 polymorphisms compared to Tyr/Tyr in tertiles) were: His/His: 1.4 (0.9–2.2). For the exons 4 polymorphisms were all close to 1.0. Current smoking was associated with a 2-fold increase in risk of adenomatous polyps compared to never smokers. The increased risk of colorectal adenoma associated with current smoking was more pronounced among double-drug-metabolizing individuals (Ephx1exon 3 Tyr/Tyr and exon 4 Hepx1 polymorphisms). Excess risk was associated with higher levels of smoking. The increased risk was observed for both men and women. In conclusion, there was evidence that cigarette smoking by men and women increases the risk of colorectal adenoma, and that the risk is related to the amount of smoking.

#5119 HETEROCYCIC AMINES IN COOKING FUMES AND LUNG CANCER RISK AMONG CHINESE WOMEN IN SINGAPORE, Adeline Seow, W T Poh, M Teh, P Eng, Y T Wang, W C Tan, M C Yu, and H P Lee, National Univ of Singapore, Singapore General Hosp, Singapore, Singapore Tan Tock Seng Hosp, Singapore, and Univ of Southern CA, CA

Heterocyclic amines are known carcinogens, which have been identified in cooked meat, and also in fumes generated during frying or grilling of meats. We conducted a case-control study of 303 Chinese women with histopathologically confirmed, primary carcinomas of the lung, and 765 controls to examine the association between exposure to meat cooking and lung cancer risk. Data on demographic background, smoking status and domestic cooking exposure, including fumes from cooking, were obtained by in-person interview while in the home. The proportion of smokers (current or ex-smokers) among cases and controls was 41.7% and 13.1%, respectively. Among smokers, women who reported that they stir-fried daily in the past had a significantly increased risk of lung cancer (adjusted OR = 1.9, 95% CI 1.0–3.7). Among women with a smoking history of less than 1 year, risk was enhanced for those who stir-fried daily, OR 2.5, 95% CI 1.2–4.8. Women who stir-fried daily, but cooked meat less often than daily did not show an elevated risk (OR 1.0, 95% CI 0.4–2.1). Risk was further increased among women who reported that they cooked using high temperatures (OR 3.1, 95% CI 1.5–6.4). Our results suggest that inhalation of carcinogenic carcinogenic amines generated during faying of meat increases risk of lung cancer among smokers. Further studies in different settings are warranted to confirm these findings, which may also help to explain the higher risk observed among women smokers compared with men.

#5120 CIGARETTE COMPOSITION AS A POSSIBLE EXPLANATION OF US-JAPANESE DIFFERENCES IN LUNG CANCER RATES. M V Djordjevic, S D Stellman, T Takezaki, T Kajima, American Health Fdn, Valhalla, NY

US male lung cancer mortality rates greatly exceed those in Japan, despite a much higher prevalence of smoking among Japanese. To find explanations for this anomaly we measured levels of nicotine, "tar", and the carcinogens BaP and NNK in Japanese and US cigarettes and carried out a laboratory study in both countries using comparable designs and data collection instruments. BaP is a representative PAH which causes squamous cell lung cancer while NNK is a tobacco-specific nitrosamine which causes adenocarcinoma of the lung. We found the BaP level to be 27 times higher in Japanese cigarettes than in New York City and Washington, DC, and 411 age-matched controls randomly selected from electoral rolls in Nagoya, Japan. The odds ratio (OR) for lung cancer in current US smokers relative to non-smokers was 2.82 (95% CI 2.1–3.7) and was 1.7 times higher than in Japanese relative to community controls (OR = 3.6, 95% CI = 3.3–3.9). There were no substantial differences in levels of smoking cessation or in inhalation between US and Japanese smokers. Yields of nicotine were similar for leading brands in both countries (± 1.0 mg/ cig). However, yields of "tar", BaP, and NNK were significantly higher in mainstream smoke of US. Smoking behaviors by themselves do not appear to explain US-Japan differences in lung cancer rates, but differences in cigarette carcinogen yields may partly explain observed differences between the two groups.

#5121 H. PYLORI INFECTION, SERUM MICRONUTRITENTS AND SUBSE-QUENT RISK OF GASTRIC DYSPLASIA OR CANCER IN A HIGH-RISK POP-ULATION IN SHANDONG, CHINA. Weicheng You, L Zhang, M H Gail, Y C Chang, J J Frumento Jr., and G W Xu, Beijing Institute for Cancer Res, Beijing China and National Cancer Inst, Bethesda, MD

To determine the risk factors for progression of precancerous gastric lesions in Linqu County, China, an endoscopic screening survey was launched among 3,399 adults in this area in 1989-1990. Antibodies to H. pylori and levels of serum micronutrients were assessed for approximately 2,300 and 900 adults without gastric cancer (GC) at baseline, respectively. Data on cigarette smoking, drinking and other characteristics of the participants were obtained by interview. The cohort was subsequently followed, with endoscopic and histopathologic examination conducted in 1996. A total of 303 bodies to H. pylori infection, levels of serum micronutrients and other characteristics were compared between those with progression from superficial gastritis (SG), chronic atrophic gastritis (CAG), or intestinal metaplasia (IM) to dysplasia (DYS) or GC vs. those with no change or with regression seen in 1994. Infection with H. pylori at baseline (OR = 1.4, 95% CI, 1.0–1.9) was associated with progression to DYS/GC during the 4.5-year follow up. The risk of progression to DYS/GC increased with the number of years of smoking cigarettes and with number of cigarettes smoked. In contrast, risk of progression to DYS/GC decreased by 76% (OR=0.3, 95% CI, 0.1–0.7) among people who reported no smoking in the last 1 year compared to those with lower levels. No such associations were observed between the progression of DYS/GC and other micronutrients including retinol, beta-carotene, alpha-tocopherol, selenium, and copper. Higher intake of dietary vitamin C contribute to the progression of precancerous lesions in leading to GC in this high-risk population.


We conducted a nested case-control, epidemiologic study using subjects drawn from the Life Span Study cohort of approximately 120,000 Hiroshima and Nagasaki residents, who were both exposed and non-exposed to radiation from the 1945 Atomic-bombings. A total of 337 hepatocellular carcinoma (HCC) cases and 897 autopsied controls who died from 1952-1997 were included. Controls were frequency matched to cases on age, sex, year of death, city of residence, and radiation exposure. Archival tissue samples were assessed for hepatitis B virus (HBV) and hepatitis C virus (HCV) status using hybridization and PCR. Reverse transcriptase (RT) PCR was used to determine hepatitis C virus (HCV) status. Radiation exposure estimates were based on physical calculations of yield combined with individual data about location during bombing and shielding by buildings, terrain, and body tissue; liver dose was estimated as a sum of the gamma and neutron dose with the latter multiplied by 10 because of its higher biological effectiveness. Cigarette smoking history was assessed using interviews and mail surveys. Adjusting for confounders, we found a significant interaction between radiation exposure and cigarette smoking. This interaction was not found for HCV infection and cigarette smoking. Our findings suggest a significant interaction between liver irradiation and HCV infection (p = 0.04). Among radiation exposed and non-exposed subjects, the odds ratios for HCC for HCV infection were 23.8 (95% CI: 6.57-97.34) and 3.0 (95% CI: 0.72-11.29, respectively. We found a significant antagonism between HBV and radiation exposure (p = 0.05), which appears to reflect the selective loss from this study of HBV-infected a-bomb survivors who died from HCC too early to be included.

#5123 THE NAD(P)H QUINONE OXIDOREDUCTASE (NQO1) INACTIVATING 699ST POLYMORPHISM IS ASSOCIATED WITH ACUTE LEUKEMIA. Y Wang, G Morgan, J Wiemels, E Kane, E Roman, S Rollinson, R Cartwright, and Martyn T Smith, Univ of CA, Berkeley, CA, and Univ of Leeds, Leeds, United Kingdom

The causes of acute leukemia are largely unknown, although interindividual differences in multiple genetic loci are thought to influence risk of this disease. In this study we examine genetic differences in adult leukemia cases compared to matched controls in NAD(P)H quinone oxidoreductase (NQO1), an enzyme implicated in the detoxification of quinones. A C>T substitution polymorphism at nt 609 of the NQO1 cDNA (NQO1 C609T) results in a proline to serine substitution which is associated with a loss of NQO1 activity. This polymorphism has recently been associated with leukemias secondary to chemotherapy and also infant leukemia. Cases with MLL translocations were 21 times more likely to have activity by the leukemogen, benzene. Peripheral blood DNA samples in a population-based case-control study in England of 555 adult acute leukemia patients and 947 unaffected, age, sex, and geographically matched controls were genotyped for this polymorphism. The frequency of the low NQO1 activity (C allele) (~10% heterozygote) was significantly higher among total acute leukemia cases compared to their matched controls, odds ratio (OR) 1.32, 95% Confidence interval (CI) 1.05–1.65. Acute lymphoblastic leukemia (ALL) cases exhibited a higher ratio.