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TITLE: Is Mammography Useful in Older Women?

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**Abstract:**
Despite the fact that approximately 43% of all breast cancers occur in women over 70 years of age, no previous randomized controlled trial (RCT) addressed women in this age group. Without clear evidence, the usefulness of the mammograms currently performed on 15-36% of women over age 70 is unknown.

We present the use of an administrative utilization database linked to breast cancer outcomes to examine the usefulness of mammography in women age 70 and older. Using the Linked Medicare-SEER Tumor Registry Database, created by the National Cancer Institute and the Health Care Financing Administration, we have created a database of 9767 women diagnosed with breast cancer from January 1, 1987 to December 31, 1993, and compared mammography users versus nonusers on stage of presentation, all cause survival and breast cancer survival.

Women over 70 years who were nonusers of mammography were diagnosed with breast cancer at Stage II or greater more often than regular users (adjusted odds ratio (OR), 3.12 [95% CI, 2.74-3.58]). Nonusers of mammography were at significantly greater risk of dying from their breast cancer than regular users for all women (adjusted hazard ratio (HR), 3.38 [95% CI, 2.65-4.32]) and for women within each age group. Even assuming a lead-time of 1.25 years, nonusers of mammography continued to be at increased risk of dying from breast cancer.

Analyses in the next stage of the study will compare adjusted hazard ratios to data from RCTs, in order to develop an additional adjustment for lead-time bias in observational data.
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(5) INTRODUCTION

Randomized clinical trials

Breast cancer is the second leading cause of cancer-related mortality among women in the United States. Women ages 65 and older bear the greatest burden of disease accounting for more than 43% of newly diagnosed cases of breast cancer (1). Older women are also more commonly diagnosed with advanced stage disease (1-4) and their breast cancer mortality rate is eight times greater than women under age 65 (5). The role of screening mammography in reducing morbidity and mortality from breast cancer in older women is unknown. Randomized controlled trials (RCTs) are inadequate to judge the efficacy of mammography screening, as they did not include sufficient women over age 69 years.

We present our methodology to date and data of retrospective cohort study of 9767 women ages 67 and older with breast cancer, diagnosed and staged from 1987 to 1993, in three geographic areas to estimate benefits from prior mammography use for women aged 67-74, 75-84 and 85 and older. Since our last annual report, we have met the following technical objectives:

Technical Objective 2:
Task 2 Created outcome variables for in situ and unstaged cases.
Task 3 Compared Historical Staging System to American Joint Committee on Cancer Staging System for cases diagnosed from 1988-1993.
Task 4 Finalized categorization of stage at diagnosis using the American Joint Committee on Cancer Staging System.
Task 5 Perform analyses to describe stage at diagnosis for each age group.

Technical Objective 3:
Task 1 Perform analyses to describe the relationship between prior mammography use and stage at diagnosis for each age group.

Technical Objective 4:
Task 1 Construct three outcome measure of survival: all-cause, and breast cancer related, and stage-specific mortality
Task 2 Perform analyses to describe the relationship between prior mammography use and survival for each age group. Repeat analyses for each outcome measure of survival.

This study provides the first large scale population-based evidence of the utility of mammography screening for breast cancer in women over age 70 years.

(5.1) Background

Mammography Use in Older Women

Early detection with mammography has been consistently shown to decrease breast cancer-related mortality by 30% for women age 50-69 years (6-10). Despite this striking reduction in mortality for women age 50-69, there are currently no data to make a statement about the utility of mammography for women age 70 and older. Although one RCT (The Swedish Two County Trial) included women up to age 74 years, there was inadequate power to detect a difference over age 69 years.

There are reasons to expect that older women would benefit from regular mammography despite the lack of scientific data to establish a benefit. First, mammography is a more specific and sensitive test as women age (11,12). Second, the biology of breast cancer in older women is thought to be similar to women age 50-69 years (13). Third, survival times for older women are sufficiently long to benefit from early detection (14,15). Fourth, the cost effectiveness ratio of breast cancer prevention in the elderly is in a reasonable range (16,17).
Given the lack of scientific data on the usefulness of mammography in women age 70 and older, current practice recommendations vary. Annual mammography is recommended by the American Cancer Society (13) and the American Medical Association Council on Scientific Affairs (18) for women after age 50 with no upper age limit. Annual to biennial mammography is recommended for women age 50-74 by the U.S. Preventive Services Task Force (19). The Task Force does not recommend mammography beyond age 74 (19). Annual mammography is recommended for women age 65-74 by the Forum on Breast Cancer Screening in Older Women. The Forum also suggests that mammography "should be encouraged" at regular intervals of approximately every two years for women age 75 and older whose general health and life expectancy are good (20).

Breast Cancer Survival in Older Women

There are several potential explanations for why older women experience poor breast cancer survival. These include suboptimal use of breast cancer screening, advanced stage at diagnosis, less aggressive workup, and more conservative therapy.

A series of national surveys (Behavioral Risk Factor Surveillance System, Mammography Attitudes and Usage Study, National Health Interview Survey) have documented that mammography use decreases with advancing age (11,21,22). In 1993, only 25% of women age 65 and older on Medicare had at least one mammogram. Rates of mammography utilization among women age 65-74, 75-84 and 85+ years were 32%, 21%, and 7%, respectively (23). Factors other than age that influence mammography use in older women include race, income, education, and state of residence (24,25). However, having a regular provider is the most important determinant of mammography use (26-28). We examined mammography utilization among women age 65 and older and found that these sociodemographic factors remained independent predictors of mammography use even after accounting for use of primary care (29).

The stage of breast cancer at diagnosis is the most important predictor of prognosis. Women who are diagnosed while their cancer is localized to the breast experience better 5-year relative survival rate as compared with women diagnosed with more advanced disease (90% versus 64%, respectively) (13). Older women are more likely to be present with advanced disease and are more likely to go unstaged as compared with younger women disease (13,23). Furthermore, age is an independent predictor of advanced stage disease even after adjusting for other important factors (race, marital status, income, education, and source of care) (30-34).

Age has been shown to influence the diagnostic evaluation and treatment offered for breast cancer (35-38). Older women are less likely to receive diagnostic valuations as complete or treatment as aggressive as compared with younger women. However, the poor survival experienced by the older women can primarily be attributed to their advanced stage at diagnosis since stage-specific survival is similar in all age groups and age-related treatment differences do not appear to affect survival (39).

(6) BODY

(6.1) Methods

(6.11) Data Source:

We conducted a retrospective cohort study using the Linked Medicare-Tumor Registry Database (40). The linked database was jointly created by the National Cancer Institute (NCI) and the Health Care Financing Administration (HCFA) to enable researchers to conduct cancer-related health services research. The linked database contains cancer information on patients 65 years of age and older from NCI's SEER Program and Medicare enrollment and utilization information from HCFA's Medicare Statistical System. The linked database contains Medicare data from 1985 to 1994 for breast cancer cases diagnosed between 1973 and 1993.
Two Medicare utilization files are included in the linked database. First is the Medical Provider Analysis and Review (MEDPAR) file, which is a 100 percent utilization file with one record for every inpatient hospitalization or skilled nursing facility stay covered under Medicare Part A. Second is the Physicians' Claims file which is a 100 percent utilization file with one record for every physician claim covered under Medicare Part B. Before 1991, the 100 percent Physicians' Claims file was available for only ten states. Therefore, for our study years, 1987 to 1993, data from the SEER and Medicare Programs overlap in tumor registries for three areas: Connecticut, metropolitan Atlanta, Georgia, and Seattle-Puget Sound, Washington. Specific information describing the linkage between SEER and Medicare has been published elsewhere (40). The match rates for Connecticut, Atlanta, and Seattle were 93.3%, 94.1%, and 91.5%, respectively.

(6.12) Study Sample

Women were eligible for the study sample (n=11,399) if they received a first primary diagnosis of breast cancer between 1 January 1987 and 31 December 1993, were 67 years of age or older, and resided in Connecticut, Atlanta, or Seattle-Puget Sound. Although we selected these areas because physicians' claims were available for all cases, they also represent a geographically diverse population of older women with breast cancer. Women who were enrolled in a health maintenance organization and those with less than two full years of Medicare Part B coverage were not eligible for this study, since their physician claims data (which are required for identifying mammography use) were not available. We restricted our final study sample to women who were 67 years of age and older to ensure that all women had a full two years of Medicare utilization (claims) information before their breast cancer was diagnosed.

(6.13) Measures

We ascertained the following sociodemographic information from SEER: age at diagnosis, marital status, and SEER area. Age at diagnosis (range, 67-107 years) was categorized as 67 to 74, 75 to 84, and 85 and older. Marital status was defined as married or not at diagnosis. SEER area was classified according to the tumor registry of diagnosis: Connecticut, Atlanta, or Seattle. We used 1990 U.S. Census data to define an ecological measure of socioeconomic status: women were assigned to the median household income of their zip code of residence and grouped as < $25,000 or ≥ $25,000.

We obtained information on race from the Medicare beneficiary enrollment file. Enrollees are classified in Medicare files as Black, White, Asian, Native American, Hispanic, or unspecified. We grouped women who were of racial/ethnic backgrounds other than Black or White together because there were too few women to permit separate analyses.

We computed a modified Charlson Comorbidity Index using Deyo's method of classifying ICD-9-CM (International Classification of Diseases, 9th revision, Clinical Modification) diagnosis codes from inpatient claims (41). For each woman, we identified all inpatient hospitalizations beginning two years prior to diagnosis and ending one month after diagnosis. A priori, we extended the observation period to one month past diagnosis because we expected women to have at least one hospitalization around the time of diagnosis. We classified women as 1) non-hospitalized (i.e., comorbidity could not be assessed), 2) having no comorbid conditions (Charlson Index of 0), or 3) having one or more comorbid conditions (Charlson Index ≥ 1).

We measured mammography utilization using Medicare physicians' claims. We identified all bilateral mammograms [CPT (Physicians' Current Procedural Terminology) procedure codes 76091 (mammography, bilateral) or 76092 (screening mammography, bilateral, two films each breast)] within two years prior to the breast cancer diagnosis. We classified women as 1) nonusers (n=2,029) if they had no mammograms during the entire two year period prior to diagnosis, 2) regular users (n=2,383) if they had at least two mammograms within the two years prior to their breast cancer diagnosis that were ten or more months apart, and 3) peri-diagnosis users (n=5,355) if they had their only mammogram(s) within three months before diagnosis. The peri-diagnosis users were a heterogeneous group of women whose
only mammography use was close to their breast cancer diagnosis. This group includes women who had a screening mammogram which led to their breast cancer diagnosis and those whose mammograms were diagnostic. Therefore, analyses relating prior mammography use to breast cancer outcomes considered only nonusers and regular users, as they are clearly distinct groups.

Our first outcome was stage at diagnosis. We developed measures of cancer stage using both the Historical Staging System, and the TNM (tumor, node, metastases) staging system adopted by the American Joint Committee on Cancer. We utilized the latter system as the one most universally used, and providing a greater degree of differentiation across stages. The disadvantage is that we had to drop an additional 844 patients from analyses who did not have this information. We categorized late-stage disease using two classification schemes. First, women diagnosed with carcinoma in situ or Stage I tumors were classified as early-stage; those diagnosed with Stage II or greater tumors were classified as having late-stage disease. Second, we restricted late-stage disease to include only women diagnosed with Stage IIIB or greater; women diagnosed with Stage IIA were reclassified as having had early-stage disease. We repeated our analyses using both classification systems and obtained similar results. We present our analyses classifying late-stage disease as Stage II or greater because they provide a more conservative estimate of the mammography-stage association.

Our second outcome was breast cancer mortality among women with invasive tumors. Women who had carcinoma in situ (n=479) were excluded from this analysis because it is unknown which tumors will progress to invasive disease. We measured survival time as the number of days from date of diagnosis until date of death or 31 December 1994 (end of follow-up). Date of death was obtained from the 1994 Medicare beneficiary enrollment file. Cause of death, obtained from SEER, captures the underlying cause listed on the death certificate. Women who had ICD-O (International Classification of Diseases, Oncology) codes 174.8 and 174.9 were classified as having died from breast cancer. We also calculated and present all cause mortality.

Women whose mammography use could not be categorized (788 women) or whose disease was unstaged (844 women) were excluded from the study. Overall, there were 741 women age 67 to 74 years, 620 women 75 to 84 years, and 271 women 85 and older who met these exclusion criteria.

Follow-up for our final sample (n=9,767) ranged from one to eight years depending on the year of diagnosis. By the end of 1994, 2,332 deaths had occurred; 889 deaths were attributed to breast cancer (385 women 67 to 74 years, 390 women 75 to 84 years, and 114 women 85 years and older).

(6.14) Statistical Analysis

All statistical analyses were performed using SAS statistical software version 6.11 (42). We performed each analysis once for all women and again for women within each age group. We compared women across age groups with respect to sociodemographic factors, comorbidity, stage at diagnosis, and prior mammography use. Chi-square statistics and Students' t-tests were used to identify characteristics at diagnosis that varied significantly with age at diagnosis.

Multivariable logistic regression was used to estimate crude and adjusted odds of late-stage disease for women who failed to undergo mammography compared with women who used regular mammography (43). The odds ratio (OR) for prior mammography use and the corresponding 95 percent confidence intervals (CI) were estimated from the coefficient and standard error from the logistic models (43). Multivariable logistic models adjusted for factors previously found to be related to stage at diagnosis including age at diagnosis, race, marital status, income of zip code of residence, and comorbid conditions (44). For models fit to each age group, we adjusted for age at diagnosis as a continuous variable to account for any residual confounding with age.

To better understand overall survival (i.e., death from all causes) in our study sample, we computed Kaplan-Meier estimates of 5-year survival by age group for each stage at diagnosis. We combined women with Stage III and IV disease to have sufficient numbers for meaningful analysis. Since
this analysis describes survival regardless of cause of death, only women who were alive at the end of follow-up were censored. The Log-rank test was used to identify differences in overall survival by age group within each stage stratum (45).

To further examine the relationship of mammography use and survival, we hypothesize that mammography use should primarily affect breast cancer-related deaths. Therefore, we fit stratified Cox proportional hazards regression models to estimate the crude and adjusted risk of death from breast cancer for women who failed to undergo mammography compared with women who used mammography regularly. All models were stratified by SEER area to account for any lack of proportionality among the three tumor registries by allowing the underlying hazard to differ. In these analyses, women were also censored when they died from causes other than their breast cancer. Each hazard ratio (HR) (i.e., relative risk of mortality) for prior mammography use and its corresponding 95 percent CI was estimated from the coefficient and standard error from a Cox model (45).

Analyses of post-diagnosis survival in relation to cancer screening are subject to lead time bias in which a woman whose disease is diagnosed earlier through screening will live longer “following diagnosis” simply due to earlier detection. Unfortunately, we do not know any individual’s lead time or which women had tumors diagnosed clinically or through screening. We explored the potential effect of lead time bias on our survival results by estimating the risk of dying from breast cancer for nonusers compared with regular users after allowing for a lead time of 1.25 years for each regular user. The number 1.25 years is approximately one-half the mean sojourn time (i.e., on average the maximum lead time achievable) for women 70 to 74 years in the Swedish Two County Trial (46).

(6.2) RESULTS

Characteristics of the study sample (n=9,767) are presented by age group at diagnosis in Table 1. Overall, 47% of women were aged 67 to 74 years at the time of their breast cancer diagnosis, 42% were 75 to 84 years, and 11% were 85 years or older.

Overall, 21% of women had no mammograms within two years prior to their breast cancer diagnosis (nonusers). 24% of women had at least two mammograms within two years preceding diagnosis that were ten or more months apart (regular users), and 55% had their only mammogram(s) within three months prior to their diagnosis (peri-diagnosis users). Figure 1 presents the percentage of women who were nonusers and regular users of mammography according to age at diagnosis. The proportion of women who were peri-diagnosis users was similar across the age groups and is not displayed. Regular mammography use decreased with advancing age at diagnosis such that the women in the oldest age group were substantially less likely to undergo regular mammograms: 29% of women 67 to 74 years, 23% of women 75 to 84 years, and 10% of women 85 years or older were regular users. Although in the two youngest age groups, the proportion of nonusers was similar (18% of women 67 to 74 years and 21% of women 75 to 84 years) and less than the proportion of regular users, the reverse was true for the oldest women. One-third of women 85 years and older did not undergo mammography within two years before their diagnosis.

Figure 2 presents the distribution of stage at diagnosis according to age at diagnosis. Within each age group, most women presented with Stage I or Stage II breast cancers. The distribution of disease among women in the two younger groups is nearly identical, except that fewer women 75 to 84 years presented with carcinoma in situ compared with women 67 to 74 years (8% versus 12%, respectively). However, there is a noticeable shift in the distribution of disease among the oldest women, characterized by the greater frequency of Stage II and Stage III cancers diagnosed in women 85 years and older. Late-stage (i.e., Stage II or greater) breast cancer was diagnosed in 41% and 45% of women 67 to 74 years and 75 to 84 years, respectively, and in 53% of women 85 years or older.

Figure 3 presents the percentage of nonusers and regular users of mammography who were diagnosed with late-stage disease for each age group. Within each age group, nonusers were
significantly more likely to be diagnosed with late-stage disease than regular users. Furthermore, the proportion of nonusers who were diagnosed with late-stage disease increased with advancing age (49% aged 67 to 74 years, 60% aged 75 to 84 years, and 69% aged 85 years or older). In contrast, the proportion of regular users who presented with late-stage disease at diagnosis was substantially lower (28%) and was similar across age groups.

Table 2 presents the odds ratios for late-stage disease comparing nonusers with regular users of mammography for all women and for each age group separately. These analyses were performed to determine whether the relation between prior mammography use and stage at diagnosis is significant for older women of different age groups. Prior mammography use was strongly associated with stage at diagnosis for all women and women in each age group. Even after adjusting for factors that have been found to be associated with late-stage disease at diagnosis, including age at diagnosis, race, marital status, income of zip code of residence, and comorbid conditions, lack of mammography use remained a significant predictor of late-stage at diagnosis in all women (adjusted OR, 3.12 [95% CI, 2.74-3.58]) and within each age group: 67 to 74 years (adjusted OR, 2.46 [95% CI, 2.04-2.98]); 75 to 84 years (adjusted OR, 3.64 [95% CI, 2.96-4.48]); and 85 years or older (adjusted OR, 6.87 [95% CI, 3.97-11.90]).

Table 3 presents overall 5-year survival estimates (i.e., deaths from all causes) following diagnosis by stage at diagnosis and age group. Survival decreased with later stage at diagnosis. Furthermore, survival decreased steadily with advancing age within each cancer stage. Table 4 presents the hazard ratios for breast cancer mortality, comparing nonusers with regular users of mammography for all women and for each age group separately. Table 4 also presents results demonstrating the potential effect of a lead time of 1.25 years. The results in Table 4 focus on breast cancer mortality because one would expect that mammography would primarily impact on deaths from breast cancer. After adjusting for sociodemographic factors and comorbidity, nonusers were at significantly greater risk of death from breast cancer than regular users and had greater risk of dying from breast cancer within each age group. Consideration of lead time somewhat diminished the magnitude of the hazard ratio, but nonusers of mammography continued to be at increased risk of dying from breast cancer. Our findings remained significant for all women and for the two youngest age groups. Although the point estimate remained increased for the oldest women, it no longer achieved statistical significance.
Table 1. Characteristics of the Study Sample by Age at Diagnosis

<table>
<thead>
<tr>
<th>Age at Diagnosis</th>
<th>67 to 74 (n=4,609)</th>
<th>75 to 84 (n=4,072)</th>
<th>≥ 85 (n=1,086)</th>
<th>Total (n=9,767)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>SEER Area</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connecticut</td>
<td>2110 (46)</td>
<td>1992 (49)</td>
<td>536 (50)</td>
<td>4638 (48)</td>
</tr>
<tr>
<td>Seattle</td>
<td>1687 (37)</td>
<td>1392 (34)</td>
<td>384 (35)</td>
<td>3463 (35)</td>
</tr>
<tr>
<td>Atlanta</td>
<td>812 (17)</td>
<td>688 (17)</td>
<td>166 (15)</td>
<td>1666 (17)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4236 (92)</td>
<td>3785 (93)</td>
<td>1020 (94)</td>
<td>9041 (93)</td>
</tr>
<tr>
<td>Black</td>
<td>208 (4)</td>
<td>178 (4)</td>
<td>38 (3)</td>
<td>424 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>165 (4)</td>
<td>109 (3)</td>
<td>28 (3)</td>
<td>302 (3)</td>
</tr>
<tr>
<td><strong>Married at Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2251 (49)</td>
<td>2803 (69)</td>
<td>975 (90)</td>
<td>6029 (62)</td>
</tr>
<tr>
<td>Yes</td>
<td>2358 (51)</td>
<td>1269 (31)</td>
<td>111 (10)</td>
<td>3738 (38)</td>
</tr>
<tr>
<td><strong>Median Income of Zip Code</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ $25,000</td>
<td>4158 (91)</td>
<td>3678 (91)</td>
<td>976 (90)</td>
<td>8812 (91)</td>
</tr>
<tr>
<td>&lt; $25,000</td>
<td>432 (9)</td>
<td>386 (9)</td>
<td>107 (10)</td>
<td>925 (9)</td>
</tr>
<tr>
<td><strong>Comorbidity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Hospitalizations</td>
<td>1174 (25)</td>
<td>1001 (25)</td>
<td>298 (27)</td>
<td>2473 (25)</td>
</tr>
<tr>
<td>0</td>
<td>2559 (56)</td>
<td>2126 (52)</td>
<td>460 (42)</td>
<td>5145 (53)</td>
</tr>
<tr>
<td>1</td>
<td>627 (14)</td>
<td>640 (16)</td>
<td>224 (21)</td>
<td>1491 (15)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>249 (5)</td>
<td>305 (7)</td>
<td>104 (10)</td>
<td>658 (7)</td>
</tr>
</tbody>
</table>

* p = 0.02.
† p < 0.001.
Table 2. Crude and Adjusted Odds Ratios for Late Stage Disease
Nonusers Compared with Regular Users (n = 4,412)

<table>
<thead>
<tr>
<th>Stage ≥ II at Diagnosis</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Women (n=4412)</td>
<td>3.36 (2.96-3.81)</td>
<td>3.12 (2.74-3.58)</td>
</tr>
<tr>
<td>Age 67 to 74 (n=2167)</td>
<td>2.43 (2.03-2.92)</td>
<td>2.46 (2.04-2.98)</td>
</tr>
<tr>
<td>Age 75 to 84 (n=1790)</td>
<td>3.74 (3.07-4.55)</td>
<td>3.64 (2.96-4.48)</td>
</tr>
<tr>
<td>Age ≥ 85 (n=455)</td>
<td>6.25 (3.86-10.12)</td>
<td>6.87 (3.97-11.90)</td>
</tr>
</tbody>
</table>

*Adjusted for age at diagnosis as a continuous variable, race, marital status, income of ZIP Code, and comorbidity.
Table 3. Relation of Stage at Diagnosis to Five-Year Survival Estimates By Age at Diagnosis

Among Nonusers and Regular Users Combined (n = 3,933)*

<table>
<thead>
<tr>
<th>Stage at Diagnosis And Age</th>
<th>n</th>
<th>5-year Estimated Survival (SE)</th>
<th>Log Rank P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67 to 74</td>
<td>1083</td>
<td>0.877 (0.013)</td>
<td></td>
</tr>
<tr>
<td>75 to 84</td>
<td>856</td>
<td>0.842 (0.016)</td>
<td></td>
</tr>
<tr>
<td>≥ 85</td>
<td>168</td>
<td>0.496 (0.052)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stage II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67 to 74</td>
<td>567</td>
<td>0.785 (0.021)</td>
<td></td>
</tr>
<tr>
<td>75 to 84</td>
<td>535</td>
<td>0.620 (0.026)</td>
<td></td>
</tr>
<tr>
<td>≥ 85</td>
<td>185</td>
<td>0.345 (0.043)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stage III/IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67 to 74</td>
<td>217</td>
<td>0.362 (0.040)</td>
<td></td>
</tr>
<tr>
<td>75 to 84</td>
<td>238</td>
<td>0.286 (0.036)</td>
<td></td>
</tr>
<tr>
<td>≥ 85</td>
<td>84</td>
<td>0.225 (0.055)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

* Women with carcinoma in situ were excluded from these analyses.
† Log Rank tests differences in overall survival by age at diagnosis.
Table 4. Crude and Adjusted Risk of Breast Cancer Mortality by Age at Diagnosis

Nonusers Compared with Regular Users (n = 3,933)*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Crude HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
<th>Crude HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Women</td>
<td>3.53 (2.80-4.45)</td>
<td>3.38 (2.65-4.32)</td>
<td>2.36 (1.87-2.98)</td>
<td>2.28 (1.79-2.91)</td>
</tr>
<tr>
<td>Age 67 to 74 (n=1867)</td>
<td>3.18 (2.27-4.46)</td>
<td>2.94 (2.08-4.17)</td>
<td>2.14 (1.52-3.01)</td>
<td>2.14 (1.51-3.02)</td>
</tr>
<tr>
<td>Age 75 to 84 (n=1627)</td>
<td>3.69 (2.58-5.27)</td>
<td>3.95 (2.72-5.74)</td>
<td>2.41 (1.68-3.46)</td>
<td>2.47 (1.70-3.58)</td>
</tr>
<tr>
<td>Age ≥ 85 (n=437)</td>
<td>2.71 (1.22-6.04)</td>
<td>2.29 (1.00-5.26)</td>
<td>1.74 (0.78-3.90)</td>
<td>1.45 (0.63-3.32)</td>
</tr>
</tbody>
</table>

* Women with carcinoma in situ were excluded from these analyses.

† Adjusted for age at diagnosis as a continuous variable, race, marital status, income of ZIP Code, comorbidity, and year of diagnosis. Proportional Hazards models were stratified on SEER area.

‡ Hazard ratio (95% confidence interval)
Figure 1. Prior Mammography Use By Age at Diagnosis

- **Nonusers (n=2029)**
- **Regular Users (n=2383)**
Figure 2. Stage at Diagnosis By Age at Diagnosis

- 67 to 74
- 75 to 84
- 85+

In Situ (n=896) | Stage I (n=4596) | Stage II (n=3310) | Stage III (n=595) | Stage IV (n=406)
Figure 3. Percentage of Women with Stage $\geq$ II Disease By Prior Mammography Use and Age at Diagnosis

*All p-values < 0.001

- Nonusers
- Regular Users
(6.3) DISCUSSION

Our results show a striking association between prior regular mammography use and two outcome 1) early stage of disease, and 2) breast cancer specific mortality. These data are based on a cohort of nearly 10,000 women over seven years in three geographic regions. Data on diagnosis, stage, mortality and comorbidities are collected prospectively and not subject to recall bias. We have controlled for potential confounders including age, race, income, comorbidities.

The major critique of this observational data is its risk of lead time bias. In the initial analyses, we attempted to adjust for this. Therefore in the last stage of this project, we will attempt to formally calculate lead time bias by comparing our findings for women under 70 years with the RCT data for this age group.

(6.4) STATEMENT OF WORK

We have met the objectives for the second 12 months of the project.

Technical Objective 2:
Task 2 Created outcome variables for in situ and unstaged cases.
Task 3 Compared Historical Staging System to American Joint Committee on Cancer Sat System for cases diagnosed from 1988-1993.
Task 4 Finalized categorization of stage at diagnosis using the American Joint Committee on Cancer Staging System.

Technical Objective 3:
Task 1 Perform analyses to describe stage at diagnosis for each age group.
Task 5 Perform analyses to describe the relationship between prior mammography use and stage at diagnosis for each age group.

Technical Objective 4:
Task 1 Construct three outcome measure of survival: all-cause, and breast cancer related, and stage-specific mortality
Task 2 Perform analyses to describe the relationship between prior mammography use and survival for each age group. Repeat analyses for each outcome measure of survival.

(7) KEY RESEARCH ACCOMPLISHMENTS

1. Completed analysis of screening by stage of cancer at presentation
2. Completed analysis of screening by all cause and disease specific survival
3. Submitted publication to the American Journal of Medicine

(8) REPORTABLE OUTCOMES

1. Manuscript submission to the American Journal of Medicine

(9) CONCLUSIONS

Our data are the first to demonstrate a benefit in mammography in women over age 70 years. The final phase of the study will attempt to assess the degree of lead-time bias in this data by comparing our results with data for 65-70 year old women in the RCTs. This analysis should eliminate the concerns of lead time bias in the use of this database, and provide the ability to make estimates of the effectiveness of mammography in women over age 70 years.
REFERENCES:


