Impact of Mammography Detection on the Course of Breast Cancer in Women Aged 40–49 Years¹

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Purpose:

To analyze trends in detection method related to breast cancer stage at diagnosis, treatments, and outcomes over time among 40–49-year-old women.

Materials and Methods:

This study was institutional review board approved, with a waiver of informed consent, and HIPAA compliant. A longitudinal prospective cohort study was conducted of women aged 40–49 years who had primary breast cancer, during 1990–2008, and were identified and tracked by a dedicated registry database ($n = 1977$). Method of detection—patient detected (PtD), physician detected (PhysD), or mammography detected (MamD)—was chart abstracted. Disease-specific survival and relapse-free survival statistics were calculated by using the Kaplan-Meier method for stage I–IV breast cancer.

Results:

A significant increase in the percentage of MamD breast cancer over time (28%–58%) and a concurrent decline in patient and physician detected (Pt/PhysD) breast cancer (73%–42%) (Pearson $\chi^2 = 72.72$, $P < .001$) were observed over time from 1990 to 2008, with an overall increase in lower-stage disease detection and a decrease in higher-stage disease. MamD breast cancer patients were more likely to undergo lumpectomy (67% vs 48% of Pt/PhysD breast cancer patients) and less likely to undergo modified radical mastectomy (25% vs 47% of the Pt/PhysD breast cancer patients) ($P < .001$). Uncorrected for stage, 13% of MamD breast cancer patients underwent surgery and chemotherapy versus 22% of Pt/PhysD breast cancer patients ($P < .001$), and 31% of MamD breast cancer patients underwent surgery, radiation therapy, and chemotherapy versus 59% of Pt/PhysD breast cancer patients ($\chi^2 = 305.13$, $P < .001$). Analyzing invasive cancers only, 5-year relapse-free survival for MamD breast cancer patients was 92% versus 88% for Pt/PhysD patients (log-rank test, 12.47; $P < .001$).

Conclusion:

Increased mammography-detected breast cancer over time coincided with lower-stage disease detection resulting in reduced treatment and lower rates of recurrence, adding factors to consider when evaluating the benefits of mammography screening of women aged 40–49 years.

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Supplemental material: <http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.1111734/-/DC1>

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In the United States, breast cancer is the most common type of non-skin-related type of malignancy in women and is the second leading cause of cancer death in women (1). For 1990–2007, the percentage of breast cancer cases, in situ and malignant, diagnosed in the United States and reported to Surveillance Epidemiology and End Results (2) for 40–49-year-old women was 18% of the total for women aged 20–85 years and older.

Substantial debate currently exists between organizations and medical societies regarding the benefit of screening mammography for women aged 40–49 years. In 2009, the U.S. Preventive Services Task Force (3) did not recommend routine mammography screening for 40–49-year-old women, concluding the net benefit is small for women aged 40–49 years compared with older women. The “C” rating, in which the U.S. Preventive Services Task Force found at least fair evidence that mammography screening can improve health outcomes but concluded that the balance of benefits and harms is too close to justify a general recommendation, was based on a computer modeling analysis of randomized controlled trials carried out predominantly in the past century (4–12). Some older analyses of randomized controlled trial studies lacked statistical power to

evaluate the utility of mammography screening programs to reduce mortality for women aged 40–49 years (13). While the U.S. Preventive Services Task Force analysis confirmed mortality reduction from current studies of mammography screening in the 40–49-year-old age group, their risk-benefit analysis suggested that the benefits of screening were potentially outweighed by the harms of screening, including false-positive results. The U.S. Preventive Services Task Force 2009 guidelines represented a substantial change from the 2002 U.S. Preventive Services Task Force guidelines (14) that recommended mammography screening every 1–2 years for women aged 40–49 years. Medical Societies such as the American Cancer Society, American College of Radiology, and Society of Breast Imaging (15,16) did not change their recommendations for women to begin undergoing annual mammography screening at age 40 years.

In addition to randomized controlled trials, other approaches are being utilized to evaluate the potential benefit of screening mammography. Service screening data for women aged 40–49 years from Sweden repeatedly have demonstrated a shift to earlier stage of detection, with a reduction in breast cancer mortality (17–20). Specifically, a recently published large prospective trial in Sweden demonstrated a 29% reduction in mortality (21). Other measures to evaluate efficacy of screening mammography are related to survival benefit, with downstaging of malignancy

accompanied by reduced treatment and related toxicity (22–28).

The purpose of this study was to analyze trends in detection method related to breast cancer stage at diagnosis, treatments, and outcomes over time among 40–49-year-old women.

Materials and Methods

This project was Health Insurance Portability and Accountability Act compliant and was approved by the institutional review board at our community-based regional cancer center (Swedish Cancer Institute, Seattle, Wash), with a waiver of consent.

We conducted a retrospective review of prospectively acquired data from women aged 40–49 years in whom primary breast cancer biopsy confirmed stage 0–IV from 1990–2008. These women were identified and tracked with our dedicated breast cancer registry database. A breast cancer registry of all patients seen at our institution was created in 1990 and contains detailed information on method of diagnosis, patient characteristics, and stage at diagnosis. Clinical presentation characteristics, including age, race, tumor staging system category, family and pregnancy

Advances in Knowledge

- Our study shows a real and significant shift to mammography-detected (MamD) breast cancer from 28% to 50% of the annual total over an 18-year period, with fewer patient-detected cases in a large carefully followed up cohort of patients from a community institution.
- The shift to more mammography-detected breast cancer cases was accompanied by a shift to diagnosis at a lower stage of disease (diagnosis at stage 0 increased 66% and diagnosis at stage III decreased 66%) and disease that requires less treatment.

Implication for Patient Care

- Our prospective study empowers physicians and patients with data demonstrating the reduction in morbidity associated with MamD breast cancer in the 40–49-year age group, including substantial reduction in number of mastectomies, treatment with chemotherapy, and decreased recurrence, with higher rates of disease-free survival.

Published online

10.1148/radiol.11111734 Content code: MO

Radiology 2012; 262:797–806

Abbreviations:

DCIS = ductal carcinoma in situ
MamD = mammography detected
PhysD = physician detected
Pt = patient
PtD = Pt detected
Pt/PhysD = Pt and PhysD

Author contributions:

Guarantors of integrity of entire study, J.A.M., H.G.K.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, J.A.M., J.P., H.G.K.; clinical studies, J.P., H.G.K.; statistical analysis, J.A.M.; and manuscript editing, J.A.M., J.P., H.G.K.

Potential conflicts of interest are listed at the end of this article.

history, histologic type, and method of detection—patient detected (PtD), physician detected (PhysD), or mammography detected (MamD), were chart abstracted at the time of diagnosis.

Registry follow-up is updated on an annual basis by a certified cancer registrar with information on recurrence, subsequent treatment, and vital status, current through 2008. Vital and disease status information is obtained from chart review if the patient is still seen at our institution or through physician-directed follow-up letter if follow-up care is provided elsewhere. Patients who are not receiving the care of a managing physician are contacted by mail by using an institutional review board–approved letter from their diagnosing physician requesting annual follow-up information. If no response is received, the institution's cancer registry and the Surveillance Epidemiology and End Results 9 Seattle–Puget Sound Registry are reviewed for the patient's vital and disease status (29).

Cases with unknown or other method of detection were removed ($n = 25$), and one case lost to follow-up was also removed. The analytic cohort of 40–49-year-old patients was $n = 1977$. Tumor size was assigned by the pathologist if surgery was performed before chemotherapy. For cases with neoadjuvant chemotherapy, tumor size was determined by physician estimation. In the case of a multifocal tumor, the largest tumor was used to assign tumor size. The *AJCC Cancer Staging Manual* (sixth edition) categories and definitions were used for cancer staging for all years (30).

All cases are patients diagnosed with breast cancer presenting or referred to our high-volume community-based cancer care center in a major urban area. Because the Swedish Cancer Institute is not a screening center, all patients, with MamD, PtD, and PhysD breast cancer cases, are referrals. Initial breast cancer detection method information was obtained by review of patient medical records by a certified cancer registrar. The three detection methods were mammography

Figure 1

Figure 1: Flow diagram.

(MamD), physician examination (PhysD), or patient detection (PtD). A mammography-detected breast cancer refers to disease discovered by using routine mammography in the absence of complaints or known physical findings. The mammogram could have been obtained as part of a screening program or as a repeat mammogram to verify a previous equivocal mammography finding. A mammography-detected breast cancer was not prompted by an initial physical finding. Physician detection is defined as initiation of a work-up for breast cancer by physical findings discovered by the physician at a routine visit or a visit for other problems. Patient detection was assigned if the patient detected breast symptoms, such as a palpable lump, pain, swelling, or bleeding, that prompted her to schedule a doctor's visit. Patients with self-detected tumors may have subsequently undergone mammography or ultrasonography, but such tumors would still be labeled as patient-detected breast cancers. The detection method designation was only made when it was certain from the record. If the detection method was ambiguous or incomplete, the tumor detection method was marked as unknown, and the patients in whom the tumor detection method was unknown were excluded from the analysis.

Statistical Analysis

Software (IBM SPSS Statistics 18.0.0, formerly PASW Statistics 18.0.0, August 2009; SPSS, Chicago, Ill) was used for

all statistical analysis. The two main comparison groups were mammography-detected breast cancer compared with manually detected breast cancer, combining the PtD and PhysD breast cancers into one group (patient and physician detected [Pt/PhysD]). Pearson χ^2 tests were used for bivariate analysis of dichotomous variables, and the F statistic was used for mean comparisons. All P values were two tailed, with $P = .05$ indicative of a significant difference. Forward stepwise logistic regression was used for multivariate modeling with MamD compared with manually detected breast cancer by patient (PtD) or physician (PhysD) as the outcome of interest with order of entry into the model according to significance level equal to .05.

The cohort for the survival analysis was truncated at diagnosis year 2006 to allow for a minimum of 2 years of follow-up through 2008 for recurrence and mortality ($n = 1627$) (Fig 1). Survival analysis by using the Kaplan-Meier method was conducted by using "died of any cause" as the outcome for overall survival, breast cancer-specific mortality for disease-specific survival, and recurrence of breast cancer—local, regional, or distant—for the relapse-free survival by using the log-rank test for comparison of survival curves. Survival analysis was run with and without ductal carcinoma in situ (DCIS) to include analyses restricted to invasive cancers. Patients with stage IV disease (never disease free) ($n = 28$) and patients with cancer status unknown at follow-up ($n = 16$) were excluded from the relapse-free survival analysis.

Table 1

Patient and Tumor Characteristics according to Detection Method in Women Aged 40–49 Years (*n* = 1977)

Variable	No. of Pt/PhysD breast cancer patients (<i>n</i> = 1112)*	No. of MamD breast cancer patients (<i>n</i> = 865)*	<i>P</i> Value
Age (y)			<.001
40–49	1112 (56.0)	865 (44.0)	
40–44	523 (62.5)	314 (37.5)	
45–49	589 (51.7)	551 (48.3)	
Race			<.001
White	901 (54.4)	756 (45.6)	
Asian	114 (68.3)	53 (31.7)	
Black	48 (71.6)	19 (28.4)	
Other	52 (58.4)	37 (41.6)	
Diagnosis year			<.001
1990	37 (72.5)	14 (27.5)	
1991	40 (58.8)	28 (41.2)	
1992	42 (58.3)	30 (41.7)	
1993	45 (67.2)	22 (32.8)	
1994	56 (71.8)	22 (28.2)	
1995	47 (65.3)	25 (34.7)	
1996	53 (61.6)	33 (38.4)	
1997	63 (68.5)	29 (31.5)	
1998	63 (68.5)	41 (39.4)	
1999	47 (56.6)	36 (43.4)	
2000	55 (62.5)	33 (37.5)	
2001	50 (50.0)	50 (50.0)	
2002	61 (60.4)	40 (39.6)	
2003	61 (59.2)	42 (40.8)	
2004	93 (56.0)	73 (44.0)	
2005	74 (49.7)	75 (50.3)	
2006	73 (48.7)	77 (51.3)	
2007	89 (46.1)	104 (53.9)	
2008	66 (42.0)	91 (58.0)	
Tumor stage			<.001
0	57 (17.0)	278 (83.0)	
I	322 (47.8)	351 (52.2)	
II	457 (70.3)	193 (29.7)	
III	247 (86.4)	39 (13.6)	
IV	32 (88.9)	4 (11.1)	
Mean tumor size (cm)	2.98	1.80	<.001
Family history of first-degree relative with breast cancer			.003
Yes	197 (49.6)	200 (50.4)	
No	881 (57.9)	641 (42.1)	

* Numbers in parentheses are percentages.

Results

From 1990 to 2008, 1977 breast cancer cases in women aged 40–49 years were diagnosed, and the patients were treated at our institution, representing 24% of our registry cohort population of

8306 patients in that time. Mean age at diagnosis was 45 years, with significantly more MamD cases in patients aged 45–49 years (65% [551 of 865] of the MamD breast cancer patients were 45–49 years of age and 53% [589 of 1112] of the Pt/PhysD patients were 45–49

years of age) ($P < .001$; Table 1). The racial composition of our cohort was 83.7% white, with 8.4% Asian, 3.4% black, 1.7% Hispanic, 0.7% Native American, and 2.2% other or unknown race. Significantly more of the Pt/PhysD cases were in nonwhite patients ($P < .001$) and significantly more of the MamD cases were in women who had a first-degree relative with a history of breast cancer ($P = .003$). Among PtD and PhysD cases with a mammogram obtained after initial presentation, 27% (PtD) and 39% (PhysD) of breast cancers were not visible on the mammogram, totaling 278 false-negative results (occult).

From 1990 to 2000, the percentage of MamD breast cancer cases ranged from 28% to 43%. From 2001 to 2004, the percentage of MamD cases increased to 40% or greater, and from 2005 to 2008, the percentage was consistently 50% or more ($P < .001$) (Fig 2). The relative percentage of PhysD cases ranged from a low of 1.5% in 1991 to a high of 12.8% in 1996 but was below 10% from 1997 to 2008, averaging seven cases per year (Fig 3). A significant increase in percentage of MamD breast cancers over time (1990–2008) was present in both the 40–44-year age group (MamD breast cancers increased from 27% [six of 22] to 56% [39 of 70], $P < .001$) and the 45–49-year age group (MamD breast cancers increased from 28% [eight of 29] to 60% [52 of 87], $P < .001$).

Including all detection methods, the relative percentage of stage 0 cases averaged approximately 10% of the total cases per year until 2002, when the percentage steadily increased to approximately 30% in 2008 (Fig 4). Stage I and II cases fluctuated from 30% to 40% over time, with stage I at 30% from 2004 to 2008 and stage II below 30% from 2005 to 2008. Percentage of stage III cases declined over time from 24% in 1990 to 8% in 2008 ($P < .001$) (Fig 4). The increase in stage 0 cancers was exclusively among MamD cases (Fig 5).

Stage 0 cases comprised 17% of our total cohort (335 of 1977), with 89% DCIS, 10% lobular carcinoma in situ,

Figure 2

Figure 2: Proportional change in detection method in women aged 40–49 years over time for years 1990–2008 ($n = 1977$).

Figure 3

Figure 3: Number of cases according to detection method in women aged 40–49 years over time for years 1990–2008 ($n = 1977$).

Figure 4

Figure 4: Change in tumor stage for breast cancers diagnosed with all detection methods according to year of diagnosis over time for years 1990–2008 ($n = 1977$).

Figure 5

Figure 5: Change in tumor stage for MamD breast cancer cases according to year of diagnosis over time for years 1990–2008 ($n = 865$).

and 1% other, and 83% were MamD and 17% were Pt/PhysD cases. Sixty-three percent of the women with DCIS were treated with lumpectomy and radiation therapy, and the remainder underwent surgery without radiation therapy. Twenty-six percent of DCIS cases had subcutaneous or modified radical mastectomies.

Among women with tumor size recorded, 1890 of 1977 patients (96%), the mean tumor size of the MamD tumors was 1.80 cm, with a range of 0.1 to 13 cm (95% confidence interval: 1.70, 1.93), and the mean tumor size of the Pt/PhysD tumors was 2.98 cm, with a range of 0.1 to 20 cm (95% confidence interval: 2.92, 3.32) ($P < .001$) (Table 1).

Uncorrected for stage, MamD breast cancer patients were more likely to have undergone lumpectomy, 67%

versus 48% of the Pt/PhysD breast cancer patients, and less likely to have undergone modified radical mastectomy, 25% versus 47% of the Pt/PhysD breast cancer patients (Table 2). Thirteen percent of the MamD breast cancer patients underwent surgery and chemotherapy versus 22% of the Pt/PhysD breast cancer patients, and 32% of the MamD breast cancer patients underwent surgery, radiation therapy, and chemotherapy versus 60% of the Pt/PhysD breast cancer patients ($P < .001$) (Table 2).

Results were similar when the analysis was conducted without the stage 0 cases (DCIS and lobular carcinoma in situ), as there was no difference between the 40–44-year age group and the 45–49-year age group, or by race according to detection method. Tumor size was significantly different according

to detection method, with average size equal to 3.02 cm for Pt/PhysD tumors and equal to 1.63 cm for MamD tumors ($P < .001$) (Table E1 [online]). MamD breast cancer patients were more likely to undergo lumpectomy, 62%, versus 47% of Pt/PhysD breast cancer patients and were less likely to undergo a modified radical mastectomy, 31%, versus 49% of the Pt/PhysD breast cancer patients ($P < .001$). More of the MamD breast cancer patients underwent surgery followed by radiation therapy (25% versus 10%), and fewer patients underwent surgery, radiation therapy, and chemotherapy (46% versus 63%) than the Pt/PhysD breast cancer patients ($P < .001$) (Table E2 [online]).

In forward stepwise logistic regression analysis, with mammography detection as the outcome of interest, the variable order of entry into the model

Table 2

Treatment and Outcome Characteristics according to Detection Method in Women Aged 40–49 Years (*n* = 1977)

	No. of MamD breast cancer		
Variable	No. of Pt/PhysD breast cancer patients patients (<i>n</i> = 1112)*	(<i>n</i> = 865)*	<i>P</i> Value
Treatment			
Surgery			<.001
None	16 (88.9)	2 (11.1)	
Lumpectomy	532 (48.0)	577 (52.0)	
Skin-sparing mastectomy	37 (33.9)	72 (66.1)	
Modified radical mastectomy	526 (71.1)	214 (28.9)	
Combined therapy			<.001
Surgery only	56 (28.0)	144 (72.0)	
Surgery and radiation therapy	137 (29.2)	332 (70.8)	
Surgery and chemotherapy	243 (68.1)	114 (31.9)	
Surgery, radiation therapy, and chemotherapy	660 (70.9)	271 (29.1)	
Outcome characteristics			<.001
Alive, no evidence of disease	913 (53.4)	796 (46.6)	
Alive with this cancer	38 (74.5)	13 (25.5)	
Alive with other cancer	8 (53.3)	7 (46.7)	
Died, no evidence of disease	12 (75.0)	4 (25.0)	
Died from this cancer	119 (78.3)	33 (21.7)	
Died from other cancer	6 (60.0)	4 (40.0)	
Recurrence type			<.001
None	923 (53.3)	810 (46.7)	
Local	20 (66.7)	10 (33.3)	
Regional	13 (81.3)	3 (18.8)	
Distant	128 (79.0)	34 (21.0)	
Combination	7 (58.3)	5 (41.7)	
Never disease free	19 (86.4)	3 (13.6)	

* Numbers in parentheses are percentages.

Table 3

Logistic Regression Model for MamD Breast Cancer in Women Aged 40–49 Years (*n* = 1977)

Variable	Odds Ratio*
Tumor stage	
0	29.20 (18.86, 45.19)
I	6.93 (4.84, 9.92)
II	2.68 (1.86, 3.86)
III and IV	Reference category
Ages 45–49 vs 40–44 y	1.61 (1.31, 1.97)
Race, white vs nonwhite	1.69 (1.27, 2.25)
Diagnosis year	
2005–2008	1.55 (1.19, 2.01)
1998–2004	1.29 (1.01, 1.65)
1990–1997	Reference category
First-degree relative with breast cancer	1.35 (1.05, 1.73)

* Numbers in parentheses are the 95% confidence intervals.

was (1) tumor stage; (2) age; (3) race; (4) diagnosis year of 1990–1997, 1998–2004, and 2005–2008; and (5) family history of first-degree relative with breast cancer (Table 3). MamD breast cancer was more likely to be in situ breast cancer (stage 0), among women aged 45–49 years, who were of the white race, diagnosed in years 2005–2008, and with a family history of a first-degree relative with breast cancer.

MamD breast cancer patients were less likely to die of disease (4% vs 11%, $P < .001$) and less likely to have recurrences (6% vs 17%, $P < .001$) compared with Pt/PhysD breast cancer patients (Table 2). Mean length of follow-up for patients diagnosed with breast cancer prior to 2007 was 8.87 years, with a

range of 1.13–20.25 years. There was a significant difference among relapse-free, disease-free, and overall survival experience between MamD and Pt/PhysD breast cancer cases, including stage 0 (Figs 6–8), with $P < .001$. At 5 years, the estimated relapse-free survival rates were 94% for MamD breast cancer cases versus 88% for Pt/PhysD breast cancer cases, and at 10 years, the rates were 91% for MamD breast cancer cases versus 82% for Pt/PhysD breast cancer cases (Fig 6). At 5 years the estimated disease-specific survival rates were 98% for MamD breast cancer cases versus 93% for Pt/PhysD breast cancer cases, and at 10 years, the rates were 94% for MamD breast cancer cases versus 87% for Pt/PhysD

breast cancer cases (Fig 7). At 5 years, the estimated overall survival rates were 97% for MamD breast cancer cases versus 93% for Pt/PhysD breast cancer cases, and at 10 years, the rates were 93% for MamD breast cancer cases versus 86% for Pt/PhysD breast cancer cases (Fig 8). Likewise, when the population was restricted to invasive cancer only, there was a significant difference among relapse-free, disease-free, and overall survival experience between MamD breast cancer cases and Pt/PhysD breast cancer cases ($P < .001$). At 5 years, the estimated relapse-free survival rate was 92% for MamD breast cancer cases versus 88% for Pt/PhysD breast cancer cases, and at 10 years, the rates were 89% for MamD breast cancer cases versus 81% for Pt/PhysD breast cancer cases. At 5 years, the disease-specific survival rates were 95% for MamD breast cancer cases versus 91% for Pt/PhysD breast cancer cases, and at 10 years, the rates were 93% for MamD breast cancer cases versus 88% for Pt/PhysD breast cancer cases. At 5 years, the overall survival rates were 97% for MamD breast cancer cases

Figure 6

Figure 6: Relapse-free survival after diagnosis according to detection method ($n = 1583$).

Figure 7

Figure 7: Disease-specific survival after diagnosis according to detection method ($n = 1610$).

versus 93% for Pt/PhysD cases, and at 10 years, the rates were 91% for patients with MamD cases versus 85% for patients with Pt/PhysD cases.

Discussion

The purpose of our research was to assess the differences between mammography- and nonmammography-detected breast cancer, with the hypothesis that earlier detection confers a treatment and mortality advantage related to earlier stage at diagnosis. We evaluated patient factors associated with mammography detection and change in rate of presentation according to diagnosis method over time. Approximately 20% of breast cancer patients at our institution are 40–49 years of age, and by 2008, more than 50% had mammography-detected breast cancer at presentation. In this age group, MamD breast cancer patients were more likely to have a first-degree relative with breast cancer, as seen in another study (31).

We observed a stage shift over time, with an overall decrease in higher-stage tumors in our population and an

Figure 8

Figure 8: Overall survival after diagnosis according to detection method ($n = 1627$).

increase in lower-stage cancer with the increase in stage 0 cancers exclusively among patients with MamD cancer. Researchers in numerous studies (32–35) have found a consistent downstaging of disease to earlier more treatable disease among mammography-screened populations, more so in older than younger women. Because we were not studying a mammography-screened population and most patients of our cohort were patient or physician detected, 56% over all years, the magnitude of downstaging observed may be less than in a screened population.

A higher percentage of the MamD patients compared with the Pt/PhysD patients were treated with breast-conserving surgery (lumpectomy with radiation therapy), with fewer mastectomies and less chemotherapeutic treatment. Stage is a critical factor in the decision-making process as to whether or not to administer chemotherapy, and patients with MamD breast cancer have more favorable prognostic factors, such as estrogen receptor positivity and proportionally lower-stage disease, resulting in the receipt of significantly less surgical and chemotherapy treatment (36).

An increase in breast-conserving surgery rates related to screening mammography in women aged 40–49 years has been demonstrated in other retrospective studies (24–26). Women who are able to choose a breast-preservation option have more positive attitudes about body image, avoiding the more disfiguring option of mastectomy (37,38).

Likewise, in our cohort analysis, we observed significantly less chemotherapeutic treatment among the MamD breast cancer patients compared with the Pt/PhysD breast cancer patients. In two retrospective studies, Barth et al (26) and Coldman et al (28) found less toxic therapy was used to treat early-stage mammography screening-detected breast cancer compared with later-stage physical examination-detected breast cancer. The consistent demonstration of reduction in potentially toxic treatments with lower-stage mammography-detected tumors is important in avoiding potentially life-threatening and life-altering side effects and costly

treatment and should be included in evaluation of screening mammography studies (39–43).

In our survival analysis, MamD breast cancer patients were significantly less likely to have a disease-related recurrence or death at 5 and 10 years after diagnosis compared with patients with PtD and PhysD breast cancer cases. Evaluation of the relationship of mammography screening to mortality reduction in women aged 40–49 years has yielded statistically significant results in many studies (17–21). Our results are not directly comparable to mortality reduction assessments measured in randomized clinical trials of screening mammography, but the consistency in results between studies supports a probable mortality advantage from mammography detection in this age group.

The strengths of our study are the large number of women aged 40–49 years in our cohort ($n = 1977$), the prospective cohort design, collection of data over 18 years, and extensive follow-up (mean, 8.87 years). From a prospective cohort study, we cannot directly comment on causal relationships. Our study is not an evaluation of a mammography screening program, and the method of detection is from chart review as reported by the treating physician. Women with MamD breast cancers did not present with a palpable mass or physical irregularity discovered by the patient or her doctor. We do not know whether patients had undergone routine breast examination by a physician or they regularly examined their own breasts. Our study population was relatively homogeneous with respect to sociodemographic factors such as ethnicity and may not be generalizable to a more diverse population.

DCIS and perhaps some invasive breast cancers may not always hold a mortal threat of disease if untreated at an early stage (44,45). However, we are currently unable to determine which patients within the early-stage groups will do well regardless of treatment. Therefore, until we have the ability to distinguish between the two,

it is incumbent on us to use the tools available to us to diagnose early disease and treat it accordingly.

The shift over time in our cohort to increasing incidence of mammography-detected breast cancer has the same trajectory as national self-reported rates of participation in screening programs (46,47). Women aged 40–49 years whose breast cancer was detected with mammography received a diagnosis at an earlier stage than would be possible without mammography, allowing for less invasive surgery and less toxic chemotherapeutic treatment and accompanied by a lower rate of recurrence and disease-related mortality. The objective of screening is to detect disease at an earlier more treatable phase, which, from our review, mammography accomplishes; therefore, the evaluation of mammographic screening should include treatment reduction and not concentrate solely on mortality reduction.

The decision to undergo screening mammography by women aged 40–49 years is multifactorial. The decision should be made by empowering patients with information and data from knowledgeable providers, counseling patients in regard to the benefits and harms of screening mammography. Our study results indicate that patients should be informed that screening mammography can help reduce morbidity and mortality associated with a more advanced-stage breast cancer diagnosis and treatment.

Disclosures of Potential Conflicts of Interest:

J.A.M. No potential conflicts of interest to disclose. **J.P.** Financial activities related to the present article: none to disclose. Financial activities not related to the present article: was paid as a consultant and to serve on the Scientific Advisory Board by Hologic; was paid for expert testimony in medical malpractice litigation by plaintiff and defense; and received payment for lectures including service on speakers bureaus by World Class CME, MTMI. Other relationships: none to disclose. **M.K.A.** No potential conflicts of interest to disclose. **H.G.K.** No potential conflicts of interest to disclose.

Acknowledgments: This research was supported by the Kaplan Cancer Research Fund and the Cancer Surveillance System of the Fred Hutchinson Cancer Research Center, which is funded by Contract No. N01-PC-35142 from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute with

additional support from the Fred Hutchinson Cancer Research Center and the State of Washington.

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