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Factors Influencing Treatment Patterns in Breast Cancer Patients Age 75 and Over

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Factors influencing treatment patterns of breast cancer patients age 75 and older

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Contents

Abstract

Purposes: To retrospectively determine the factors influencing treatment decisions in older breast cancer patients at a single center. *Experimental design*: 216 patients age $\geqslant 75$ seen in post-treatment follow-up between January, 1997 and June, 2000 were identified in the Memorial Sloan–Kettering breast cancer database. Eligible patients were $\geqslant 75$ years old at diagnosis, had a diagnosis of stage I, II, or III breast cancer, and received their follow-up care at Memorial Sloan Kettering Cancer Center. A retrospective chart review was performed. Patients were stratified by: (1) prognostic factors (age (75–79 or $\geqslant 80$), Charlson comorbidity score, tumor size, nodal status, stage, ER, PR, creatinine, albumin, hemoglobin, and liver function tests), (2) local treatment (lumpectomy, axillary lymph node dissection (AxLND), radiation (XRT), modified radical mastectomy (MRM)) and (3) systemic treatment (tamoxifen, chemotherapy). Combined local treatment was defined as (a) lumpectomy, AxLND, XRT or (b) MRM, AxLND, XRT (if tumor $\geqslant 5$ cm or $\geqslant 4+$ lymph nodes). *Results*: 96 patients were eligible for this study: 46 patients (75–79 years); 50 patients ($\geqslant 80$ years). The majority of patients (74%) were treated with lumpectomy but those $\geqslant 80$ were less likely to receive XRT (94% age 75–80; 45% age >80; $P < 0.01$). Patients $\geqslant 80$ were also less likely to receive AxLND (94% age 75–79; 62% age $\geqslant 80$; $P < 0.01$). A logistic regression model identified two independent prognostic variables for not receiving combined local treatment: increased age ($P < 0.01$) and increased comorbidity score ($P = 0.01$). Increased age did not correlate with increased comorbidity ($P = 0.48$). 5.2% of patients received adjuvant chemotherapy (all age <80). 83% of ER positive patients received tamoxifen (89% age 75–79; 79% age >80). *Conclusion*: We hypothesize that both comorbidity and age play a significant role in influencing treatment decisions in the older breast cancer patient but these two variables are not necessarily correlated. Prospective studies are needed to determine the relative impact of these variables.

Keywords: Breast cancer; Older patient

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1. Introduction

Age is the dominant risk factor for breast cancer [1]. The number of older cancer patients is rapidly increasing as our population is aging. In 1900 there were 3.1 million people age 65 and older. Presently there are approximately 33.2 million people age 65 and older. This number is continuing to grow, so that in 2030, an estimated 70.2 million people will be over the age of 65 [2]. Despite the large number of older cancer patients, few clinical trials have focused on this patient population. The under-representation of older patients is particularly notable in breast cancer treatment trials. In a study of 164 Southwest Oncology Group treatment trials between 1993 and 1996, only 9% of patients enrolled in breast cancer studies were 65 or older; however, approximately half of all breast cancers occur in this age group [3].

Previous studies describe a pattern of less aggressive care in the older breast cancer patients: older women less likely to receive breast conservation therapy, less likely to receive radiation, and less likely to receive chemotherapy. [4–13] It is unclear whether physicians made these treatment decisions based on age alone, or whether other factors play a role in decision-making. In this study, we examined the treatment patterns of women age $\geqslant 75$ with early stage breast cancer at a large single institution cancer center. This age cut-off was chosen, rather than the traditional age $\geqslant 65$, in order to gain more information about treatment patterns in this older age group, which has not been as widely studied. In addition, treatment decisions in this age group are often more complex secondary to competing comorbid medical conditions. The goal of this study is to determine local and systemic treatment patterns in women age $\geqslant$ 75 and to understand factors influencing these treatment decisions. In addition, we sought to determine whether there is a significant difference in treatment patterns in patients age 75–79, in comparison to patients older than age 80.

2. Methods

The Memorial Sloan-Kettering Breast Cancer Database was searched to identify all patients age 75 and older that were seen in post-treatment follow-up between January, 1997 and June, 2000. Inclusion criteria were: (1) patients $\geqslant 75$ years old at diagnosis (2) diagnosis of stage I, II, or III breast cancer and (3) patients must have received their follow-up care at Memorial Sloan-Kettering Cancer Center. Patients with bilateral or recurrent breast cancer were excluded. A retrospective chart review was performed to gather the data.

The following data was gathered: age (75–79 or $\geqslant$ 80), other comorbid medical conditions, tumor size, nodal status, stage, ER/PR, creatinine, albumin, hemoglobin, and liver function tests, local treatment (lumpectomy or modified radical mastectomy (MRM), axillary lymph node dissection (AxLND), and radiation (XRT) and systemic treatment (tamoxifen or chemotherapy). A separate category entitled 'combined local treatment' was defined as (a) lumpectomy, AxLND, and XRT or (b) MRM, AxLND, and XRT, (if tumor $\geqslant 5$ cm or $\geqslant 4+$ lymph nodes).

The Charlson comorbidity score was used to assess the impact of comorbid medical conditions. Charlson et al. developed this scale in 1987, using data from patients on an internal medicine inpatient service [16]. Patients were analyzed with respect to 1-year mortality as a function of other comorbid medical conditions. As a result, a comorbidity scale was developed consisting of 19 items. The scale has been validated in numerous studies including studies of breast cancer patients and studies in the older patient [17].

Univariate association of the following factors with local treatment (lumpectomy or MRM, AxLND, and XRT) and systemic treatment (tamoxifen or chemotherapy) patterns was performed: age (75–79 or $\geqslant 80$),

Table 1
No significant difference in patient tumor characteristics or laboratory values by age

Variables	Age 75–79	Age > 80	*P* value
T stage			
1	34 (74%)	28 (56%)	0.13
2	7 (16%)	18 (36%)	
3	1 (2%)	2 (4%)	
4	3 (7%)	2 (4%)	
Biopsy only	1 (2%)	0 (0%)	
N stage			
0	33 (72%)	22 (44%)	0.22
1	10 (22%)	13 (26%)	
Nx	3 (7%)	15 (30%)	
ER			
(+)	37 (80%)	47 (94%)	0.14
(−)	6 (13%)	2 (4%)	
NA	3 (7%)	1 (2%)	
PR			
(+)	28 (61%)	36 (72%)	0.50
(−)	15 (33%)	13 (26%)	
Nx	3 (7%)	1 (2%)	
Laboratory values			
Creatinine	1.0 (SD 0.24)	1.0 (SD 0.21)	
Albumin	4.3 (SD 0.31)	4.3 (SD 0.28)	
Hemoglobin	13.4 (SD 1.2)	13.5 (SD 1.1)	
Liver function tests			
Normal	43 (93%)	40 (80%)	0.36
Abnormal	1 (2%)	3 (6%)	
NA	2 (4%)	7 (14%)	

Charlson comorbidity score, tumor size, nodal status, stage, ER/PR, creatinine, albumin, hemoglobin, and liver function tests. A χ^2-test or Fisher's exact test was used to describe the association of categorical factors to treatment patterns. Continuous data were analyzed using a t-test. The independent prognostic values of these factors in determining treatment decisions were evaluated using logistic regressions. In all analyses, a two tailed P value <0.05 was considered significant.

3. Results

A total of 216 patients age $\geqslant 75$ were identified in the Memorial Sloan–Kettering follow-up breast cancer database between January, 1997 and June, 2000. Of these, 96 patients were eligible for study. The majority of those who were ineligible had not received their follow-up care at MSKCC. Patient characteristics are detailed in Table 1. Patients were stratified into two age groups: age 75–79 (range 75–79, mean age 76.9) and age $\geqslant 80$ (range 80–96, mean age 84.5). There was no significant difference in tumor and nodal stage between the two patient groups. Seventy-five percent of patients had stage I or II breast cancer. There was no significant difference in hormone receptor status between patients age 75–79 and patient age $\geqslant 80$. Eighty-eight percent of patients had tumors that were hormone receptor positive.

Baseline laboratory values including hemoglobin, creatinine (as a measure of renal function), albumin (as a measure of nutritional status), and liver function tests were recorded. There was no significant difference in laboratory values between the two groups. The mean creatinine of patients in both groups was 1.0 (SD 0.24 for age 75–79 and SD 0.21 for age $\geqslant 80$). The mean albumin of patients in both groups was 4.3 (SD 0.31 for age 75–79 and SD 0.28 for age $\geqslant 80$). The mean hemoglobin for patients age 75–79 was 13.4 (SD 1.2) and for patient age $\geqslant 80$ was 13.5 (SD 1.1). Eighty-seven percent of patients had normal liver function tests.

Patient comorbidity was measured by the Charlson comorbidity score (Table 2). The majority of patients had a comorbidity score of 0 or 1 (94% age 75–79; 92% age $\geqslant 80$). There was no significant difference in comorbidity score with age. Increased comorbidity score did not correlate with increased age either as a continuous variable or when stratified by age 75–79 vs. age $\geqslant 80$.

Table 2
Charlson comorbidity score does not increase with age

Charlson comorbidity	Age 75–79	Age > 80	P value
0	33/46 (72%)	32/50 (64%)	0.48
1	10/46 (22%)	14/50 (28%)	
2	2/46 (4%)	2/50 (4%)	
3	0/46 (0%)	2/50 (4%)	
4	1/46 (2%)	0/50 (0%)	

Table 3
Surgical treatment patterns by age

Variables	Age 75–79	Age > 80	P value
Local surgery			
Lumpectomy	34 (74%)	37 (74%)	0.9
MRM	11 (24%)	13 (26%)	
Biopsy	1 (2%)	0 (0%)	
Axillary dissection			
Yes	43 (93%)	35 (70%)	0.01
No	3 (7%)	15 (30%)	

Patients age $\geqslant 80$ are less likely to receive axillary dissection.

Table 4
Treatment patterns among patients with lumpectomy

Variables	Age 75–79	Age > 80	P value
XRT	32/34 (94%)	14/31 (45%)	$P < 0.01$
AxLND	32/34 (94%)	23/37 (62%)	$P < 0.01$

Patients age $\geqslant 80$ are less likely to receive XRT or AxLND.

Table 5
Increased Charlson comorbidity score and decreased likelihood to receive XRT

Comorbidity score	Radiation		Total
	No	Yes	
0	9	38	47
1	6	6	12
2	1	2	3
3	2		2
4	1		1
Total	19	46	65

χ^2 $P = 0.02$.

Surgical treatment patterns are detailed in Table 3. Patients were stratified by whether they received lumpectomy or MRM and whether they received AxLND. The majority of patients received a lumpectomy (74% of both age groups). A significantly lower number of patients age $\geqslant 80$ received AxLND (93% age 75–79 and 70% age $\geqslant 80$; $P < 0.01$). Of the patients who received a lumpectomy, significantly fewer patients $\geqslant$ age 80 received radiation therapy (94% age 75–79 and 45% age $\geqslant 80$; $P < 0.01$) and AxLND (94% age 75–70 and 62% age $\geqslant 80$; $P < 0.01$) (Table 4). There is no significant association between comorbidity score and whether AxLND was performed; however there are few patients with comorbidity score >1. Patients with increased comorbidity score were significantly less likely to receive radiation (Table 5).

Table 6
Prognostic factors predict for lack of local treatment

Prognostic factors	Univariate (P value)	Multivariate (P value)	Odds ratio
Age > 80	**< 0.01**	**< 0.01**	**10**
Comorbidity ⩾ 1	**0.02**	**0.01**	**2.5**
T	0.38	NS	
N	**0.03**	NS	
ER	0.71	NS	
PR	> 0.9	NS	
CR	**0.02**	NS	
Albumin	0.45	NS	
Hemoglobin	0.85	NS	
LFT	> 0.9	NS	
Stage	0.12	NS	

Only 38% of patients age 80 and older received combined local treatment ('combined local treatment' was defined as (a) lumpectomy, AxLND, and XRT or (b) MRM, AxLND, and XRT, (if tumor ⩾ 5 cm or ⩾ 4+ lymph nodes)) in comparison to 87% of patients age 75–79 ($P < 0.01$). This data illustrates that a significant number of patients age 80 and older do not undergo axillary dissection or receive radiation after lumpectomy or after treatment of high risk tumors by mastectomy.

In order to determine why women over the age of 80 were not receiving combined local treatment, patients were stratified by the following prognostic factors: age (75–79 or ⩾ 80), Charlson comorbidity score, tumor size, nodal status, stage, ER/PR, creatinine, albumin, hemoglobin, and liver function tests (Table 6). Two factors independently predicted for lack of complete local treatment: age ⩾ 80 ($P < 0.01$; odds ratio 10) and comorbidity ($P = 0.01$; odds ratio 2.5).

Systemic treatment patterns were also determined. Patients were stratified as to whether they received chemotherapy or tamoxifen (Table 7). A minority of patients age 75 and older received adjuvant chemotherapy: 5% of patients received adjuvant chemotherapy, all in the 75–79 age group (mean age 75.8). No patients older than 80 received adjuvant chemotherapy. In contrast, a majority of patients with hormone receptor positive tumors received tamoxifen: 89% of patients age 75–79 and 79% of patients age ⩾ 80. There is a trend for patients ⩾ age 80 with ER positive tumors to receive less tamoxifen but this was not statistically significant.

Table 7
Systemic treatment by age

	No	Yes	Total
Tamoxifen[a]			
Age 75–79	4 (11%)	31 (89%)	35
Age ⩾ 80	9 (21%)	33 (79%)	42
Total	13 (17%)	64 (83%)	77
Chemotherapy[b]			
Age 75–79	41 (89%)	5 (11%)	46
Age ⩾ 80	46 (100%)	0 (0%)	46
Total	87 (95%)	5 (5%)	92

[a] χ^2 $P = 0.24$; Fisher's exact test $P = 0.36$.
[b] χ^2 $P = 0.02$; Fisher's exact test $P = 0.06$.

4. Conclusions

In this study, we examined the treatment patterns of women ⩾ age 75 with early stage breast cancer at a large single cancer center. The goal of this study is to determine local and systemic treatment patterns in women with breast cancer ⩾ age 75, to understand factors influencing these treatment decisions, and to determine if there is a difference in treatment patterns in patients age 75–79 in comparison to patients age ⩾ 80.

In this study, there was a difference in treatment patterns in women with breast cancer age 75–79 in comparison to age ⩾ 80. Patients age ⩾ 80 were significantly less likely to receive an AxLND and XRT in comparison to patients age 75–79. There was no significant association between comorbidity score and whether AxLND was performed; however there were few patients with Charlson comorbidity score > 1. Patients with increased comorbidity score were significantly less likely to receive radiation. A study by the Cancer and Leukemia Group B demonstrated the importance of radiation in decreasing the risk of locoregional recurrence in older women who underwent a lumpectomy. In this study, women, age 70 and older, with clinical stage I, estrogen receptor positive disease were randomized to lumpectomy alone or lumpectomy plus radiation. With a median follow-up of 24 months, women receiving lumpectomy alone had an increase in locoregional recurrence in comparison to those treated with lumpectomy and radiation [19].

In this study, ten prognostic factors were examined to determine which variables would independently predict for patients to not receive combined local treatment (defined as (a) lumpectomy, AxLND, and XRT or (b) MRM, AxLND, and XRT, (if tumor ⩾ 5 cm or ⩾ 4+ lymph nodes)). We identified two independent prognostic variables predicting which individuals would not receive combined local treatment: age ⩾ 80 and comorbidity score ⩾ 1. Increased age was the strongest predictor of lesser treatment. Interestingly, increasing age did not correlate with increased Charlson comorbidity score and patients older than age 80 did not have increased comorbidity in comparison to those younger than age 80. This may be a reflection of a healthier older patient population seen in this large single institution cancer center.

There was no significant difference in likelihood of receiving hormonal therapy. Among patients with

hormone receptor positive tumors, there was a trend for patients age $\geqslant 80$ (89% age 75–79 vs. 79% age $\geqslant 80$) to receive less tamoxifen but this was not statistically significant. It therefore appears that for less toxic therapies, such as hormonal treatment, older women were almost as likely as younger women to be treated. However, for treatments that carry greater risk and toxicity, such as chemotherapy or AxLND, older women were less likely to be so treated.

In this study, very few patients were treated with chemotherapy. The benefit of adjuvant chemotherapy in early stage breast cancer was assessed in the worldwide overview, published by the Early Breast Cancer Trialist's Collaborative Group in 1998. Prolonged multiagent chemotherapy, in women under the age of 50, decreased the annual odds of relapse by 35% and mortality by 27%. The benefits were smaller but still significant for women older than age 50: decreased the annual odds of relapse by 20% and mortality by 11%. For women age 60–69 years, the proportional risk reduction for recurrence and mortality were 18 and 8%, respectively. There were not enough women over the age of 70 to allow for subset analysis of these patients [14]. The etiology of the decreased benefit of chemotherapy with increasing age is not known; however, one possible explanation is that older women have a different tumor biology secondary to more hormone receptor positive tumors. Another possible explanation is that the older women represented in the meta-analysis were referred for treatment on a clinical trial because they had a more aggressive tumor histology. Lastly, older patients may have been given decreased chemotherapy dose intensity in comparison to younger patients, accounting for the decreased benefit with age.

Given the decreased benefit of adjuvant chemotherapy in the older population in comparison to the younger population, the decision to give adjuvant chemotherapy needs to be based on the individual patient's risk of relapse, absolute benefit from chemotherapy, and comorbid conditions which might limit the ability to tolerate chemotherapy [14]. Extermann et al. examined the threshold 10 year risk of relapse from breast cancer needed for adjuvant chemotherapy to produce a 1% absolute decrease in relapse or mortality, taking into account the patient's other comorbid medical conditions that may be a competing source of mortality. This information is valuable in considering the absolute benefit of adjuvant treatment for an individual patient [18].

In making treatment decisions with an older patient, it is important to consider that, there may be some patients who are functionally much younger than their chronologic age who may derive greater benefit from this treatment than would be suggested based on chronological age alone. In addition, previous studies have suggested that less definitive therapy may be associated with a poorer outcome, although the results of these limited studies are inconsistent [10–12,15].

For therapies that carry a higher risk to benefit ratio, prognostic variables may help to define appropriate candidates for treatment. In this study, comorbidity and age were independent prognostic factors predicting for treatment decisions. Factors other than comorbidity, such as functional status and cognition might also be helpful in distinguishing two individuals of the same age.

Limitations of our study include its retrospective design, modest number of patients, and inability to determine whether the treatment decisions were secondary to patient preference verses physician recommendation. In addition, the data presented in this study was derived from a large tertiary care cancer center on the East Coast. Previous studies have noted substantial variability in patterns of care based on geographic variation, with a greater likelihood to receive breast conservation in a large city or if treatment was received in a cancer center [7]. The differential in treatment patterns of older cancer patients may be even greater in other geographic locations. This data suggests that we need further research regarding the risk, benefits, and determinants of treatment patterns in older patients, with a particular focus on the impact of treatment decisions in patients age $\geqslant 80$. Prospective studies are underway to address these questions.

Reviewers

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Biography

Arti Hurria is a geriatrician and oncologist, focusing on care of the older cancer patient. She completed an internal medicine residency at Beth Israel Medical Center in Boston in 1998. Following this, Dr Hurria completed a geriatric fellowship in the Harvard Geriatric Fellowship Program, followed by a hematology–oncology fellowship at Memorial Sloan-Kettering Cancer Center. Dr Hurria presently serves as Clinical Assistant Physician on the Breast Cancer Medicine Service at Memorial Sloan-Kettering Cancer Center. Her clinic and research focus is on care of the older breast cancer patient.