

Research Article

Breast Cancer Screening in Elderly Patients: An Opportunity for Less Aggressive Treatments

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Abstract

In our area, the survival of patients over 70 years did not show changes over time ($p > 0.05$) and keep the same curves and survival rates than patients who were diagnosed and treated during the decades of the 1980s, 1990 and 2000. The percentage of loco-regional recurrence (12.1% vs 18.7%; $p = 0.01$), of multifocal and/or multi centric cases (6.8% vs 13.1%; $p = 0.0001$) are lower in patients with ≥ 70 years old than in those with less than < 70 years. Breast carcinomas in women ≥ 70 years over express HER-2 less frequently than younger women (< 70 years: 23.2%, between 70 and 79 years: 17.3% and ≥ 80 years 9.4%; $p < 0.001$). By contrast, the expression of estrogen receptor increases with age (72% for < 70 years, 78.6% between 70 and 79 years and 84.1% women ≥ 80 years; $p < 0.001$). With the results from this study, we can conclude that the screening for Breast Cancer in women over 70 years should be promoted. Breast carcinomas in women older than 70 years show morphological and clinical characteristics that make it susceptible to respond to tamoxifen and conservative therapies if diagnosed in early stages.

INTRODUCTION

Most of the population breast cancer (BC) screening programs were designed in the early 70s. In this time the shorter life expectancy of older women influence the designs of these screening programs. However, four decades later, life expectancy and quality of life of older women increased significantly.

A significant proportion of women with 70 years and older are in good health and can be expected to live considerably longer than 10 more years. Based on 2010 US Life Tables, approximately 50% of 80-years-old women and 25% of 85-years-old women will live at least more 10 years [1,2]. Thus, the Guideline Update From the American Cancer Society (2015) [3] recommends that

women should continue to perform BC screening as long as their overall health is good and life expectancy is of 10 years or longer. We think that there is scientific evidence [4,5] to recommend screening mammography every two years and opportunistic annual clinical examination to all asymptomatic women between 70 and 84 years, which are fully independent or with a mild dependence (measured by the Katz Index). Actually, in order to make decisions about the type of treatment in older women with BC, it should take into account functional reserve, tolerance to antineoplastic therapies, competing causes of morbidity and death, and patient goals to care [6]. Future research should study the role of geriatric assessment in treatment selection and tolerance, tumor biology, and specific clinical interventions/therapeutics in a clinical trial setting.

MATERIAL AND METHODS

We designed a prospective, retrospective and longitudinal observational study that included a total of 3434 patients who were diagnosed with BC at Vigo University Hospital Complex (Spain) between 1974 and 2009, who were evaluated prospectively for over 10 years. We analyzed the macro features, histopathological, immunohistochemical and BC molecular sub types in patients ≥ 70 years and its relation to prognosis and to age. We study the percentage of in situ carcinomas, multifocal and/or multicentricity, HER-2 over expression HER-2, expression of estrogen receptor, according to age and different times of diagnosis: decade 70s, 80s or 90s. The overall survival analysis was performed using the Kaplan–Meier (log-rank test).

RESULTS

The average age of the total series of BC was 58.19 years (S.D. 13.9), with a range between 21 and 98 years old. The average age of patients with breast cancer has increased ($p < 0.05$) in

the different periods of the study (1974-89, 1990-99 and 2000-09) (Table 1). The percentage of patients with ≥ 70 years Breast Cancer has been increasing: 19.4% (1974 to 1989), 23.0% (1990 to 1999), reaching 26.6% during the years 2000–2009 ($p < 0.0001$). In our area, for several decades BC patients under 70 years were benefiting from prevention campaigns, resulting in a clear improvement in patient survival ($p < 0.0001$). However, the survival of patients over 70 years, unfortunately, did not show changes over time ($p > 0.05$) and keep the same curves and survival rates than patients who were diagnosed and treated during the decades of the 1980s, 1990 and 2000 (Figure 1).

Patients < 70 years increased the percentage of carcinoma in situ from 2.7% (1974-1989) to 13.8% (2000-2009) but, in the patients ≥ 70 the percentage remains low and stable ($< 5\%$) during all this period (1974-2009). The survival curves of BC patients show an inverse relationship with age in relation to different life expectancy (Figure 2) (Table 2).

The pTNM was an excellent prognostic factor at all ages.

PERIOD	N	Mean Age (S.D.) at diagnosis	Minimum Age	Maximum Age	% BC ≥ 70 years
1974-1989	985	56.52 (13.59)	21	96	19.4 %
1990-1999	1059	58.28 (13.76)	26	96	23.0 %
2000-2009	1390	59.31 (14.12)	27	98	26.6 %
Total	3434	58.19 (13.90)	21	98	$p < 0001$

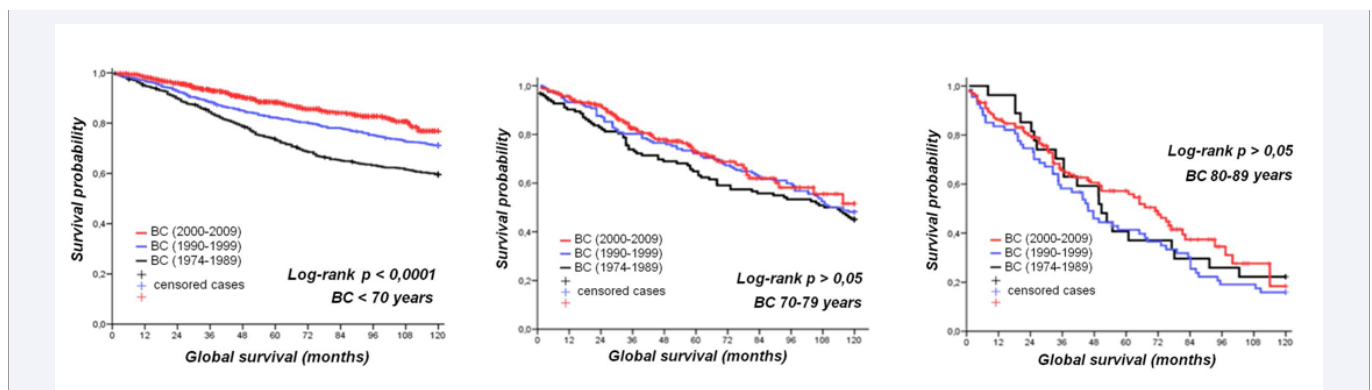


Figure 1 Overall Survival of Breast Cancer in patients with BC in age groups and in the different periods of the study (1974-89, 1990-99 and 2000-09) ($p < 0.0001$).

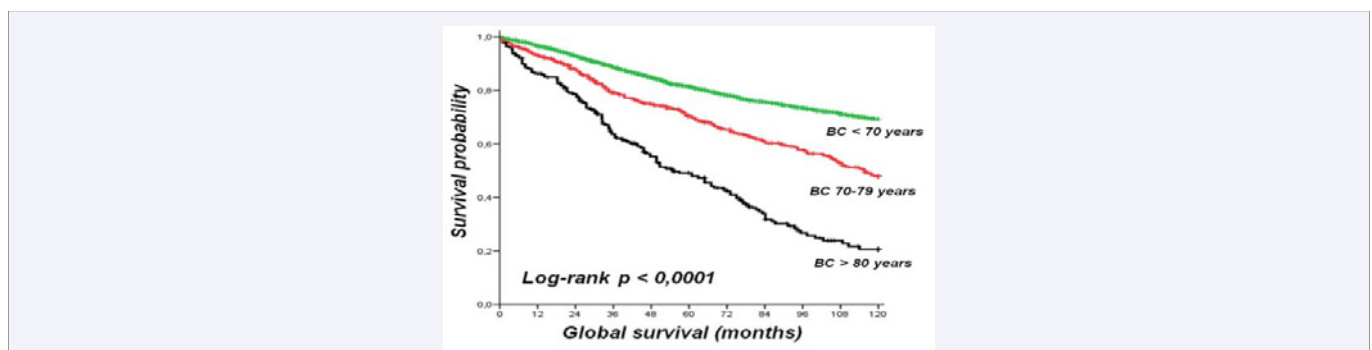


Figure 2 Overall Survival of Breast Cancer by age group: < 70 , 70-79 and > 80 years.

Mean tumor size was 2.6 cm in patients < 70 years versus 3.06 cm in patients ≥ 70 years ($p < 0.001$). Axillary involvement (pN) behaved as an excellent prognostic factor, however the percentage of patients with breast cancer where the breast could not be assessed for different reasons increased significantly ($p < 0.001$): 6.2% those under 70 years, 15.6% in the patients 70 to 79 years and to 44.6% in women ≥ 80 years. The Nottingham Prognostic Index was a good prognostic factor to 79 years old (Figure 3). In women older than 80 years the low percentage of lymphadenectomy underestimates the NPI. The percentage of loco-regional recurrence (12.1% vs 18.7%; $p = 0.01$), of multifocal and/or multi centric cases (6.8% vs 13.1%; $p = 0.0001$) were lower in patients with ≥ 70 years old than in those with less than 70 years. Breast carcinomas in women is ≥ 70 years over express HER-2 less frequently than younger women (< 70 years: 23.2%, between 70 and 79 years: 17.3% and ≥ 80 years: 9.4%; $p < 0.001$). By contrast, the expression of estrogen receptor increases with age (72% for < 70 years, 78.6% between 70 and 79 years and 84.1% women ≥ 80 years; $p < 0.001$) (Table 3).

DISCUSSION

Over the past century, the world has seen unprecedented declines in mortality rates, leading to an accelerated increase in the world population. This century will realize falling fertility rates alongside ageing populations. The 20th century was the century of population ageing; the 21st century will be remembered as the century of ageing.

With the aging of the American population, older women are being diagnosed with breast cancer. With the possible exception of women under 40 years of age, there is no clear evidence of a biologic or clinical difference between breast cancer in younger and older aged groups. Breast cancer is diagnosed at a more advanced stage in older women. Elderly women with breast cancer frequently are treated with less than standard therapy and are less often included in clinical trials. With the exception of specific comorbid conditions that preclude anesthesia and surgery, older women tolerate breast surgery as well as younger women. The results of good surgical and adjuvant therapy for elderly women are as good as those for younger women. Older women with breast cancer deserve the most effective screening, diagnosis, and surgical treatment available [7]. The major risk factor for cancer is progressive age [8]. In our series, the percentage of patients BC over 70 years has been increasing during different decades of the study: 19.4% (80s), 23.0% (90s), reaching 26.6% during the years 2000–2009 ($p < 0.0001$). One of the most intriguing aspects of ageing is how different the ageing process is from person to person; the basis for this variation is largely unknown. Population-based studies and longitudinal surveys have shown that comorbidity and physical and mental functioning are important risk factors; thus, a meaningful assessment of comorbidity and disability should be implemented in clinical practice [9]. There are inadequate numbers of older women enrolled in breast cancer clinical trials. Both physicians and patients should explore and define the barriers to clinical trial

Table 2: Breast carcinoma in situ, with and without micro invasion by age groups in different periods: 1974-1989, 1990-1999 y 2000-2009.

		<i>In situ carcinoma</i>	<i>In situ carcinoma with microinvasion</i>	
PERIOD 1974-1989	< 70 years	2.7 %	1.1 %	$P > 0.05$
	≥ 70 years	0.6 %	0 %	
	Total series	2.3 %	0.9 %	
PERIOD 1990-1999	< 70 years	10.0 %	1.1 %	$p = 0.008$
	≥ 70 years	4.6 %	0 %	
	Total series	8.7 %	0.9 %	
PERIOD 2000-2009	< 70 years	13.8 %	0.8 %	$p < 0.001$
	≥ 70 years	3.8 %	0.1 %	
	Total	11.2 %	0.7 %	

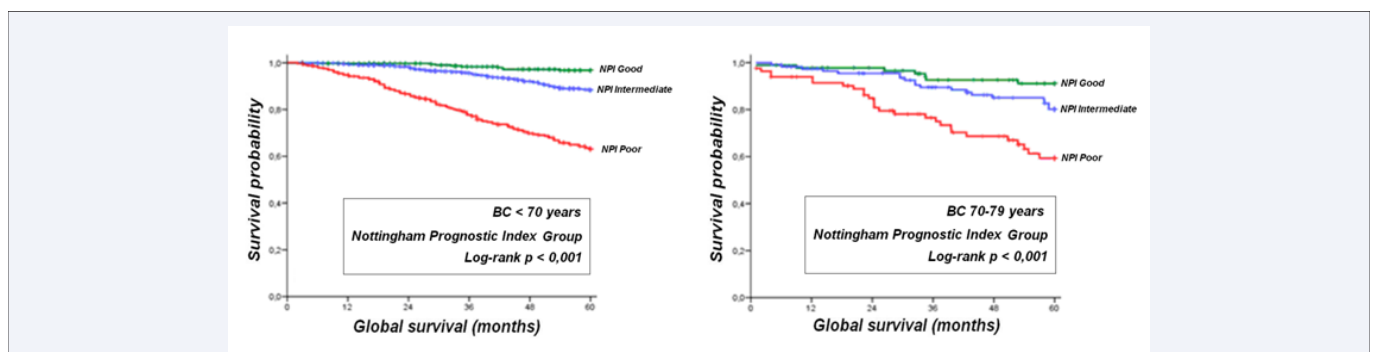


Figure 3 The Nottingham Prognostic Index (NPI) was a good prognostic marker in BC less than 70 years as well as in BC 70-79 years.

Table 3: Multifocal and/or multi centric carcinoma cases or, over expressing of HER-2 and estrogen receptor status by age groups.

	Multifocal and/or Multi centric	HER-2 over expressing	ER Positive
< 70 years	13.1 %	23.2 %	72.0 %
≥ 70 years	6.8 %	14.8 %	80.3 %
	p < 0.0001	p < 0.001	p < 0.001

participation and develop successful interventions to overcome them. The main goal of mammography screening programs is to reduce breast cancer mortality by reducing the incidence rate of advanced breast cancer. Thus, the aim of screening mammography is to detect breast cancer early in its natural history. A screening test that is successful in detecting small invasive cancers also will detect some precursor lesions. We think that there is scientific evidence [4,5] to recommend screening mammography every two years and opportunistic annual clinical examination to all asymptomatic women between 70 and 84 years to be fully independent or with a mild dependence (measured by the Katz Index). With few exceptions, the presence of comorbid conditions is not associated with a decreased rate of screening. In fact, hypertension and the presence of a higher number of comorbid conditions are associated with a higher rate of receipt of cancer screening. This finding may be due to an increase in the frequency of office visits increasing the opportunity for cancer screening [10]. The tumors of older patients are reportedly more often detected by clinical examination rather than imaging techniques. The tumors of older patients were more often detected by clinical examination (38.9% vs. 17.0%, $p < 0.001$) and less often by mammography/sonography (10.4% vs. 29.9%, $p < 0.001$) [11].

The three «big ones» in oncology —breast, prostate and colorectal carcinoma are the most widespread malignant diseases worldwide and, moreover, are characteristic of the elderly. Consequently, the question of whether the elderly should be screened for these entities and how this should be done is essential in reducing the «global impact of cancer» and tumoural disease in Western countries. The inclusion of older ages in screening programs for breast cancer is still inadequate, despite the evidence. In our area, for several decades BC patients under 70 years they are benefiting from prevention campaigns, resulting in a clear improvement in survival ($p < 0,0001$). However, the survival of patients over 70 years, unfortunately, did not show changes over time ($p > 0.05$) and keep the same curves and survival rates than patients who were diagnosed and treated during the decades of the 1980s, 1990 and 2000. We think the main reason that did not increase survival rates in older women is the absence of prevention campaigns in this age group. In fact, in old women percentage of carcinomas in situ has remained low; while for women under 70 years the percentage of in situ carcinomas has come progressively increasing. Adami et al. [12], found that women who were 45 to 49 years old had the best prognosis, with a relative survival exceeding that of the youngest patients (less than 30 years) by 7.6 to 12.9 percent at different periods of observation. Relative survival declined markedly after the age of 49--particularly in women aged 50 to 59--and the oldest women (greater than 75) had the worst rate. Tse et al. [13], conclude that the carcinomas that occur in the elderly do not differ morphologically and molecularly which occurs in other ages. Age

is not considered to be a contraindication for breast-conserving treatment, but retrospective studies have indicated that elderly patients are less likely to be treated conservatively [14]. Older women should offered breast preservation options and should receive breast radiation following lumpectomy. Perhaps an early diagnosis of breast cancer in older women allow less aggressive treatments, based mainly on conserving surgery and tamoxifen. Early diagnosis in older women would offer surgeries that preserve the breast, but should receive breast radiation after lumpectomy. While tamoxifen can be used as initial therapy for the frail women with early breast cancer for late stage, the results are worse than surgery to achieve long-term local control [15]. We think that older women with breast cancer have a lower likelihood of recurrence if diagnosed in early stages. Breast carcinomas older women are less frequently multifocal and multi centric and occur less frequently over expression of HER2. All this reduces the chances of local recurrence and improves outcomes of conservative surgery. In fact, the percentage of loco-regional recurrence in our series was lower among older women BC (12, 1%) than among younger (18.7%) ($p = 0.01$).

Breast cancer is a heterogeneous disease and there is a continual drive to identify markers that will aid in predicting prognosis and response to therapy. To date, relatively few markers have established prognostic power. Oestrogen receptor (ER) is probably the most powerful predictive marker in breast cancer management, both in determining prognosis and in predicting response to hormone therapies. Progesterone receptor (PR) is also a widely used marker, although its value is less well established [16]. Infiltrating ductal carcinoma remains the most common histological sub type of breast cancer diagnosed in older patients and this type of cancer exhibits an overall more favorable biological profile, with a higher percentage of ER-positive tumors that increases with age to 91% in patients aged ≥85 years [17]. In our series, the expression of hormone receptor positive estrogen increases with age: 72% for < 70 years, 78.6% between 70 and 79 years and 84.1% women ≥ 80 years; ($p < 0.001$). Therefore, probably adjuvant tamoxifen therapy should be considered systemic treatment of early breast cancer in older women, and get better benefits. With the results from this study, we can conclude that the screening for Breast Cancer in women over 70 years should be promoted. Breast carcinomas in women older than 70 years show morphological and clinical characteristics that make it susceptible to respond to tamoxifen and conservative therapies if diagnosed in early stages.

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