available at www.sciencedirect.com

ScienceDirect

Impact of older age on presentation, management and outcome of breast cancer in the multi-ethnic Asian population of Singapore

Nakul Saxena[a], *Mikael Hartman*[a,b,*], *Zakir Hussain*[a], *Nirmala Bhoo Pathy*[c,d], *Philip Iau*[b], *Soo Chin Lee*[e], *Khai Mun Lee*[f], *Siew Eng Lim*[e], *John E.L. Wong*[e], *Helena M. Verkooijen*[a,c]

[a] *Department of Epidemiology and Public Health, National University of Singapore, Block MD3, 16 Medical Drive, Singapore 117597, Singapore*
[b] *Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore, c/o National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074, Singapore*
[c] *Division of Radiology, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, The Netherlands*
[d] *Julius Centre University of Malaya, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia*
[e] *Department of Hematology Oncology, National University Cancer Institute, National University of Singapore 119074, Singapore*
[f] *Department of Radiation Oncology, National University Cancer Institute, National University of Singapore 119074, Singapore*

ARTICLE INFO

Article history:
Received 22 June 2010
Received in revised form 23 July 2010
Accepted 10 August 2010
Available online 6 September 2010

Keywords:
Breast cancer
Elderly patients
Relative survival
Treatment
Diagnosis

ABSTRACT

Aim: This study aims to improve insight in breast cancer characteristics and outcome in the understudied population of elderly Asian women with breast cancer.
Patients and methods: We identified 2195 women, ≥40 years, diagnosed with breast cancer between 1990–2007 at the National University Hospital in Singapore. Patient and tumor characteristics, treatment and outcome were compared between women diagnosed at age <65 years and ≥65 years.
Results: Older women were more often diagnosed with advanced stages and estrogen receptor positive tumors. They were less likely to have undergone axillary clearance, radiotherapy post breast conserving surgery and chemotherapy for lymph node positive disease. Older women had poorer relative survival than younger women; however these differences largely disappeared after stage stratification.
Conclusion: Similar to Western populations, older Asian breast cancer patients present with more advanced stages and are less likely to receive standard treatment. Older age was not associated with worse survival within different stage strata.

1. Introduction

Breast cancer is the most common type of cancer and the most common cause of cancer death among women worldwide.[1] Breast cancer is a disease of the elderly [2,3] with a majority of Caucasian patients being over 65 years of age at diagnosis.[4,5] In contrast to Europe and the US, where breast cancer incidence rates have stabilized or even decreased, Asian breast cancer rates are increasing dramatically.[6–8] With the Westernization of Asian countries, one can expect this trend

* *Corresponding author*. Department of Epidemiology and Public Health, National University of Singapore, Block MD3, 16 Medical Drive, Singapore 117597, Singapore. Fax: +65 67791489.
E-mail address: ephbamh@nus.edu.sg (M. Hartman).

1879-4068/$ – see front matter
doi:10.1016/j.jgo.2010.08.002

to continue. In Singapore, breast cancer incidence rates have tripled over the past three decades [9] and today a Singaporean woman has a lifetime risk of 1 in 20 to develop breast cancer.[10] Singapore has seen a shift in peak age of incidence from the mid forties to late fifties.[11] With the increasing incidence of breast cancer in general, the shift towards the older age groups and the aging population, it is crucial to have a good understanding of breast cancer in older Asian women.

Elderly patients are more likely to receive non-standard treatment.[12] Reasons for this include the higher prevalence of co-morbid conditions, the assumption among clinicians that breast cancer is less aggressive in older women than in younger women and their limited life expectancy, thereby decreasing the perceived benefit of adequate treatment. Since older women are less likely to participate in clinical trials,[13] little evidence exists on optimal treatment for elderly women. Several observational studies have suggested that non standard treatment of older breast cancer patients strongly impairs their outcome.[14–16] Until now, characteristics of older patients, the degree of non-standard treatment and the impact on outcome have hardly been studied in an Asian setting. The purpose of this study was to examine differences in tumor characteristics, treatment and survival among older and younger female breast cancer patients in Singapore.

2. Patients and methods

For this study we used data from the Breast Cancer Registry of the National University Hospital (NUH), one of two tertiary teaching hospitals in Singapore.[10] The Breast Cancer Registry was established in 1995, through prospective data collection on demographics, tumor characteristics, treatment and follow up of all patients presenting with invasive or *in situ* breast cancer. Data from 1990 to 1995 was collected retrospectively from medical records. The Breast Cancer Registry has been approved by the NUH Institutional Ethics Review Board. NUH followed a standard management protocol, based on international guidelines, throughout the study period.

In this study we included all women diagnosed with primary invasive or *in situ* (ductal carcinoma in situ only) breast cancer between 1990 and 2007 aged 40 years or above ($N=2195$). Variables of interest included age at diagnosis (continuous), year of diagnosis (1990–1995, 1996–2000, 2001–2005, 2006–2007), ethnicity (Chinese, Malay, Indian, others), stage (0, 1, 2, 3, 4, unknown),[17] estrogen receptor (ER) and progesterone receptor (PR) status (positive, i.e., >10% of the tumor cells expressing ERs or PRs, negative or unknown), lymphovascular invasion (LVI) (yes, no, unknown), histology (ductal, lobular, mucinous, others, unknown), tumor grade (good, moderate, poor, unknown), number of lymph nodes excised and number of positive lymph nodes (0, 1–3, 4–9, ≥10 nodes in accordance with the TNM nodal staging classification).[17] Tumor characteristics were based on surgical specimens. For patients not undergoing surgery, tumor characteristics were determined from core biopsy specimens. Treatment variables in the study were surgery (mastectomy, breast conserving surgery, no surgery) radiotherapy (yes, no), chemotherapy (yes, no) and hormone therapy (yes, no).

We divided patients into two age categories <65 years and ≥65 years at diagnosis and compared sociodemographic and tumor characteristics and treatments received. To assess the level of standard treatment we compared (1) proportions of breast cancer patients treated with surgery, (2) proportion receiving radiotherapy following breast conserving surgery (BCS), (3) proportion of estrogen receptor (ER) positive patients receiving hormonal therapy, (4) proportion of ER negative and lymph node (LN) positive patients receiving chemotherapy and (5) proportion of women with invasive breast cancer who underwent axillary clearance. These analyses were repeated after excluding stage 4 patients in order to separate patients receiving treatment for adjuvant vs. metastatic disease.

2.1. Statistical methods

We performed univariate logistic regression analysis to identify sociodemographic, tumor and treatment characteristics that were significantly associated with older age. Subsequently we applied multivariate logistic regression analysis to identify which factors were independently and significantly associated with older age.

We calculated relative survival rates (RSRs) to estimate the excess mortality among the patient population due to breast cancer.[18] Population mortality data for Singapore was used to compute these estimates. Relative survival is defined as the ratio of the proportion of observed survivors in a cohort of cancer patients to the proportion of expected survivors in the background population with same age and period distribution.[19] The formulation is based on the assumption of independent competing causes of death. The relative survival adjusts for the general survival of the Singapore population for that race, sex, age and year. Thus the relative survival is a net survival measure representing cancer survival in the absence of other causes of death.

With Cox proportional hazard analysis we determined the association between type of locoregional treatment (i.e. BCS plus radiotherapy, mastectomy, BCS alone or no surgery) and overall risk of death for younger and older age groups with stage 1–3 breast cancer adjusting for other prognostic factors and after testing for proportionality.

Relative survival analyses were carried out using STATA (version 10) and all other analyses were carried out using SPSS (version 16).

3. Results

Of the 2195 patients in our study, 1869 (85.1%) patients were 40 to 64 years old and 326 (14.9%) patients were 65 years or older. In general, older patients had more missing information on the various patient and tumor characteristics than younger patients (Table 1a).

3.1. Patient and tumor characteristics and treatment

In univariate analysis, ethnicity, stage, LVI, ER status, number of lymph nodes excised were associated with older age. In multivariate analysis, older age appeared to be independently and significantly associated with disease stage, i.e., older