Journal of the Egyptian National Cancer Institute (2014) **26**, 23–30

Cairo University

Journal of the Egyptian National Cancer Institute

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www.sciencedirect.com

Full Length Article

Age at diagnosis in women with non-metastatic breast cancer: Is it related to prognosis?

Nelly H. Alieldin [a,*], Omnia M. Abo-Elazm [a], Dalia Bilal [a], Salem Eid Salem [b], Eman Gouda [c], Magda Elmongy [d], Amal S. Ibrahim [a]

[a] *Department of Biostatistics and Cancer Epidemiology, National Cancer Institute NCI, Cairo University, Fom Elkhalig Sq, Cairo, Egypt*
[b] *Department of Medical Oncology, NCI, Cairo University, Fom Elkhalig Sq, Cairo, Egypt*
[c] *Department of Pathology, NCI, Cairo University, Fom Elkhalig Sq, Cairo, Egypt*
[d] *Department of radiotherapy, NCI, Cairo University, Fom Elkhalig Sq, Cairo, Egypt*

Received 22 June 2013; accepted 28 August 2013
Available online 21 October 2013

KEYWORDS

Breast cancer;
Young age;
Disease-free survival;
Prognostic factors

Abstract *Objective:* Primary objective was to verify whether breast cancer patients aged less than 40 years at diagnosis have poorer prognosis than older patients. Secondary to assess prognostic factors influencing disease free survival.
Methods: 941 women were diagnosed with non-metastatic breast cancer at NCI, Cairo in 2003. Epidemiologic, clinico-pathological characteristics, treatment modalities and disease free survival were compared among the two age groups. Prognostic factors were evaluated for association with disease-free survival.
Results: One hundred-eighty-one patients (19.2%) were younger than 40 years and 760 (80.8%) were older. Older women presented with higher rates of comorbidities and younger women presented with more hormone non-responsive tumors. Young women presented with larger tumors pT4 = 13.8% compared to 8.6% in older women, yet not significant. Young women were treated with more conservative surgery, more adjuvant chemotherapy and radiotherapy while older women with more radical mastectomies and more hormonal treatment. Recurrence rates were significantly higher among young women 44.2% compared to 34.5% in older women. Five year disease free

* Corresponding author. Tel.: +20 2 2364 1772.
E-mail address: nelly26660@gmail.com (N.H. Alieldin).
Peer review under responsibility of The National Cancer Institute, Cairo University.

ELSEVIER Production and hosting by Elsevier

 http://dx.doi.org/10.1016/j.jnci.2013.08.005

survival in young women was 38.9% ± 4.6% compared to 48.6% ± 2.5% with adjusted hazard ratio of 1.22 95% CI (0.91–1.64), $p = 0.19$. Multivariate analyses identified positive axillary lymph nodes (pN2-pN3), larger tumor size (pT3-pT4), hypertension, lobular carcinoma type and lack of adjuvant systemic treatment as independent factors associated with poor DFS.

Conclusion: Young women were not found to have poorer prognosis, yet they presented with more ER negative tumors. Most of women presented with advanced stage and young women had higher recurrence rates.

Introduction

Among women in Egypt, breast cancer is a challenging health problem coming on top of all malignancies [1] with a poor outcome compared to international figures [2]. Many studies showed that age at diagnosis of breast cancer in Arab countries is a decade younger than that in Western countries [3–5]. In the US median age at presentation for breast cancer is 61 years [5], compared to 50–54 years in Egypt [1]. A 10-year survey of breast cancer treatment at the United States showed that 6.4–7.8% of women are diagnosed younger than 40 years of age [6]. Several studies investigating breast cancer in young women have shown that it is more aggressive, with higher mortality and recurrence rates compared with older women [3,7–9]. Chung and colleagues [8] have found that women who were diagnosed with invasive breast cancer at 40 years of age and younger had a poor 5 year disease free survival of 60.8% second only to women older than 80 years of age. Though a population-based study in Switzerland showed that young women presented with larger tumors and more aggressive tumors, it found no effect of age on survival [10]. Results of a study in 1992 in Saudi Arabia and another study in 2004 in Singapore did not report an adverse effect of age on survival [11,12]. A recent study in Japan aimed at identifying the prognostic value of age in premenopausal women younger than 40 years of age, found that age at diagnosis was not an independent prognostic factor on survival [13]. Although the negative prognostic impact of young age has been substantiated in numerous studies, the mystery of young age at diagnosis has not been resolved in Egypt. The primary aim of the present study is to verify whether breast cancer patients aged less than 40 years old at diagnosis have poorer prognoses than those aged 40 years or more. The secondary objective is to assess prognostic factors influencing disease free survival in patients with breast cancer.

Patients and methods

Patients and treatment

From the database of cancer registry system at National Cancer Institute Hospital, Cairo, Egypt, women who were diagnosed with primary breast cancer in the period between January and December 2003 with stage I–III disease were included. The medical records of the patients included in the study were reviewed. Information derived from the database and medical records included epidemiologic, clinical and histological variables. Epidemiologic variables included age; residence, and marital status. Age was dichotomized (younger than 40 years and 40 years of age and older). Women younger than 40 years of age were grouped together, as they represent a special high-risk population. Clinicopathologic data included menopausal status, family history of breast cancer; history of diabetes mellitus, hypertension, laterality of the lesion, pathologic types, pathologic grade, T stage (primary tumor), N stage (regional lymph node); estrogen receptor (ER) and progesterone receptor (PR) status; operative procedures; radiation therapy; adjuvant systemic therapy (chemotherapy and hormonal therapy).

In all cases, T and N stages were assessed according to the UICC TNM classification (6^{th} edition). ER and PR expression were determined as positive or negative by enzyme immunoassay or immunohistochemistry (IHC).

Regular schedule of patients' follow up at NCI, Cairo is every 3–6 months during the first 5 years and every 6–12 months from the 5^{th} to 10^{th} year. Physical examination, mammography with or without breast ultrasound, chest X-ray, abdominal ultrasonography and bone scintigraphy are performed when the patients complain of any symptoms and/or tumor recurrence is suspected. Approval of Institutional Review Board was achieved for the current study.

Statistical methods

Chi-square test was used to assess differences in clinical and pathological factors between the two age groups of patients. A p value $\leqslant 0.05$ was considered statistically significant. Disease-free survival (DFS) was defined as the time from surgical resection to the date of any of the following events: locoregional relapse, distant relapse, or death. Locoregional relapse was defined as the reappearance of cancer in the ipsilateral breast, chest wall or regional lymph nodes. Distant relapse included metastasis in nonvisceral sites (soft-tissue and/or bone) or visceral (including lung, liver, brain and other organs). DFS time was estimated by the Kaplan–Meier method and compared among patient subsets using the log-rank test. In univariate analyses, the following prognostic factors were evaluated for their potential associations with DFS: age at the time of diagnosis, family history of breast cancer, hypertension and diabetes (as commonest co-morbidities), pT stage, pN stage, histological type, histological grade, ER and PR receptor status, operative procedure, administration of adjuvant systemic therapy and radiation therapy. Multivariate analysis of potential prognostic factors was performed to generate a Cox proportional hazards model. Multivariate models were created using age at diagnosis and other variables that either showed significant or borderline association or believed to confound the effect of other prognostic variables on DFS. All tests were two-tailed, with p value set significant at 0.05 level. The statistical software SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses.