Clinico-Pathological Features of Breast Cancer and Impact on Survival in Elderly Patients

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Abstract:

Background: Breast carcinoma is one of the most commonly identified cancers in women worldwide, the 5th reason of cancer-related deaths and commonly affecting older Egyptian females.

Aim: To explore the clinical and pathological characteristics of breast cancer in elderly women and impact on survival.

Methods: A retrospective study was performed based on medical records of females who were treated in National Cancer Institute, Cairo University, Zagazig University Hospitals, and Meet-Ghamr Oncology Center in the period between January 2012 and December 2016.

Results: The study included 343 breast cancer patients whose age ranging between 65 and 80 years with mean age 68.8 years. About 85.1% of the studied cases had no family history of breast carcinoma and 82.8% of them had negative history of taking oral contraceptive pills (OCP). Associated co-morbidities were noticed in 57.4% of this group. Our group tends to present with clinical stage II and III (44.8%), (34%) respectively, with lymph node involvement in (56.6%) of cases and high percentage of hormone expression [ER-positive (79.6%), PR-positive (76.4%)] while lower frequency to be HER-2 positive (15.5%). Most of cases (88%) underwent upfront surgery, modified radical mastectomy (MRM) was the main procedure. The overall survival (OS) rate for the whole study group at 5 years was 70.7% with median OS 87.1 months, while the DFS rate at 5 years was 81.6% after exclusion of the 21 patients who had metastasis at diagnosis. Expression of ER and PR was related with better survival.

Conclusion: Breast cancer in elderly patients in our study tends to be diagnosed at a later stage with best outcome with hormone receptor positive women and further studies are needed to evaluate better management.

Key Words: breast cancer - elderly patients - survival- adjuvant

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Introduction:

Carcinoma of the breast is one of the most prevalently diagnosed cancers and the 5th cause of cancer-related deaths with approximately 2.3 million new cases worldwide in accordance with the GLOBOCAN 2020 data [1].

In Egypt, breast carcinoma is considered to be the most prevalent carcinoma in females accounting for 37.7% of their whole number with 12,621 new cases in 2008. It is also the main cause of cancer-related mortality representing 29.1% of their collective number with 6546 deaths. [2].

Around 50% of breast carcinomas arise in females at the age of 65 years or older and 35% happen after the age of 70 [3].

Age is the most essential factor predisposing for occurrence of breast cancer [4].

Coinciding with a rising susceptibility to breast cancer, increasing age also is linked to higher risks for other health morbidities [5].

Elder women have tumors expressing more ER and PR and less HER-2 compared to younger patients. Tumor size and nodal involvement increase with age allocated to delayed diagnosis and aggressiveness as

well [6]. Elderly breast cancer (EBC) patients are underrepresented in clinical trials and their treatments are mainly assumed from trials in younger cases [7].

Aimed to assess the clinical presentation and pathological parameters and their correlation with treatment outcome of breast cancer in elderly patients (above 65 years) treated at Medical Oncology Department, NCI, Cairo, Zagazig University Hospitals, and Meet Ghamr Oncology Center during the period between January 2012 to December 2016).

Methodology:

Retrospective study was carried out based on medical records of elderly females with breast cancer who were treated in National cancer institute, Cairo University, Zagazig University Hospitals, Medical Oncology department and Meet-Ghamr oncology center in the period between January 2012 and December 2016 to study the clinical and pathological features of breast cancer in this group of patients and its impact on survival including DFS and OS rates.

After authorization, the following data were collected for every case if possible: age, date of diagnosis, history of OCP, family history, laterality, ECOG performance status and TNM stage, metastatic sites if any, histologic type and grade, estrogen, progesterone and Human Epidermal Growth factor receptors-2 (HER-2) receptor status, and treatments utilized [8].

Statistical analysis

Data management and analysis was done using Statistical Package for Social Sciences (SPSS) vs. 25. Numerical data were reviewed for normality and were statistically described as means (standard deviations). Categorical data were expressed as numbers and percentages. Survival analysis was performed using Kaplan-Meier method comparing two or more survival curves using log rank test with Bonferroni adjustment when necessary. All statistically significant factors on Kaplan-Meier analysis entered the multivariate Cox regression analysis using forward likelihood-ratio (LR) method for variable selection. Overall survival rates (OS) were computed from the date of diagnosis to the date of death or last follow-up. Disease free survival rates (DFS) were calculated from the date of start of treatment to the date of loco-regional or metastatic recurrence whichever comes first. Patients presented with metastasis at diagnosis were excluded from DFS analysis (n=21). Hazard ratios were calculated for significant factors in the last step of cox-regression with 95% confidence interval estimates. All tests were 2 tailed and P-value ≤ 0.05 was considered statistically significant.

Results:

A total of 343 patients were included in the last analysis with mean age 68.8 years (ranging between 65 and 80 years), most of them (56.3%) had ECOG II and (35.2%) ECOG I PS. The majority of patients (85.1%) had negative family history of breast carcinoma and about (82.8%) of them had negative history of taking OCP. Co-morbidities were noted in (57.4%) of cases; hypertension (46.4%), diabetes (30%) and cardiac diseases (11.4%) were the most frequently reported diseases, other medical disorders as renal, hepatic and respiratory diseases were reported with lower frequencies.

Our patients had comparable figures for right and left breast involvement, and were more likely to have IDC (75.2%) rather than ILC (7.6%).

Most of the studied group present at later stage with relative proportions of stage I, II, III and IV (15.2%), (44.8%), (34%), and (6%), respectively.

Most of the tumors were T2 lesions (61.8%), with positive LN involvement [N1 (24.5%), N2 (16.9%), N3 (15.2%)] and of grade II & grade III (77%), (11.7%) respectively with higher frequency to be hormone receptor positive [ER-positive (79.6%), PR-positive (76.4%)] while lower frequency to be HER-2 positive (15.5%).

At diagnosis 21 patients (6%) had distant metastasis at diagnosis, lung metastasis had the highest frequency (3.4%) followed by bone (1.7%) and then liver (0.9%).

Among the 343 patients, 339 (98.8%) patients underwent surgery while 4 patients (0.2%) did not undergo any surgery. Modified radical mastectomy (MRM) was the main performed surgery (73.2%) followed by CBS (22.4%).

About (43.1%) of the patients received postoperative radiotherapy while (8.2%) of them received radiotherapy as palliative intent.

Chemotherapy was given as neoadjuvant therapy in 41 (12%) patients and as adjuvant therapy in 210 (61.2%) patients. Anthracyclins was the commonest chemotherapy used in both settings.

Hormonal treatment was administered to 270 patients. Aromatase inhibitors was the most commonly used hormonal therapy and was received by 223 (82.6%) patients followed by tamoxifen in 47 (17.4%) patients.

The overall survival rate for the whole study group at 3 years and 5 years was 78.8% and 70.7% respectively with median OS 87.1 months, while the DFS rate at 3 and 5 years was 85.9% and 81.6% respectively after exclusion of the 21 patients who had metastasis at diagnosis.

Performance status of the patients significantly affected the overall survival at 3 and 5 years, where patients with ECOG I had better survival rates than those with ECOG II and III with p value (p= 0.035).

Regarding the correlation between the pathological characteristics of the tumors and 3&5 overall survival rates, tumors with lower stage had better survival than those with higher ones; T0-1 stages were associated with the best survival (p= 0.0001). T2-3 lesions had better survival than T4 lesions (p= 0.0007). N0-1 stages had better 3 and 5 years OS rates with statistically significant difference than those with more advanced stages (p= 0.041).

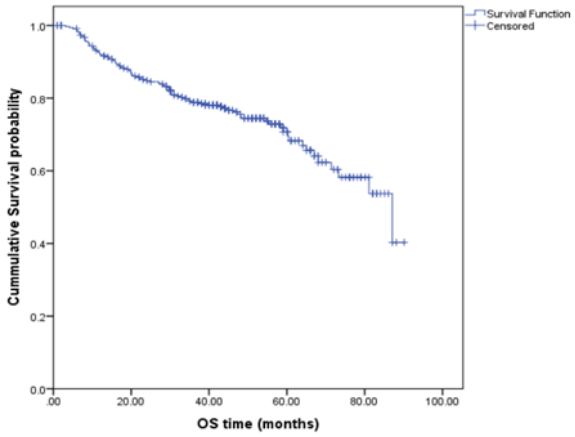

Figure (1): OS for the whole group (n=343)

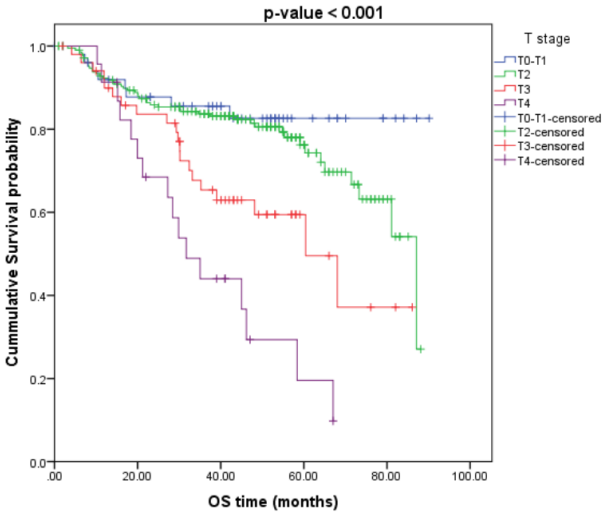

Figure (2): OS in relation to T Stage

Expression of ER and PR was associated significantly with better survival (p value: 0.004, 0.007 respectively). While the pathological type, grade and presence of metastasis on diagnosis did not affect the 3 and 5 years overall survival.

As regard different treatment modalities, patients who underwent CBS had no significant difference on survival as compared to those who underwent MRM. Also receiving post-operative radiotherapy did not confer survival benefit. Neoadjuvant use of anthracyclins and/or Taxanes was accompanied with poorer overall survival (P= 0.001) due to associated comorbidities and chemotherapy related toxicities. On the other hand, adjuvant hormonal therapy was associated with better overall survival (p= 0.001) despite the type of hormonal therapy used.

The DFS at 3&5 years was better for the patients with tumors with lower T and N stages with significant P value (p=0.001and 0.04) respectively. However, pathological type, grade and presence of metastasis on diagnosis did not affect the 3 and 5 years DFS. Expression of ER and PR was associated significantly with better survival (p = 0.04, 0.037 respectively) while amplification of Her-2 receptors was associated with lower DFS rates with significant p value (p= 0.021).

Regarding different treatment modalities, patients who underwent CBS had non-inferior DFS as compared to those who underwent MRM (p= 0.011).

Despite the 3 and 5 years DFS was better with receiving post-operative radiotherapy; it was not statistically significance. Both neoadjuvant & adjuvant chemotherapy administration of anthracyclins and/or Taxanes is related to poorer DFS rates (p= 0.041). On the other hand, hormonal treatment administration was interrelated with better DFS rates (p= 0.001).

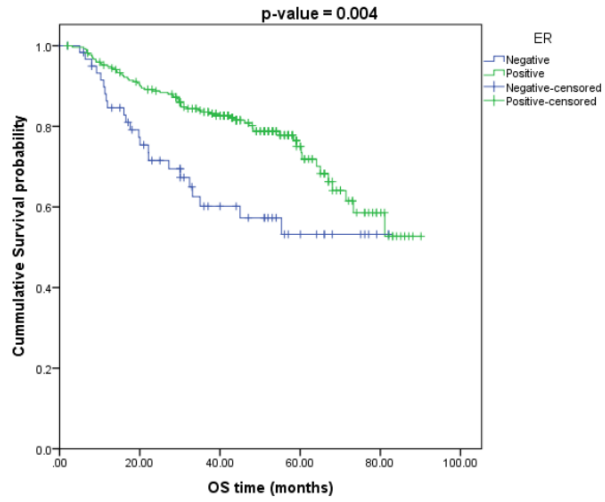

Figure (3): OS in relation to ER status

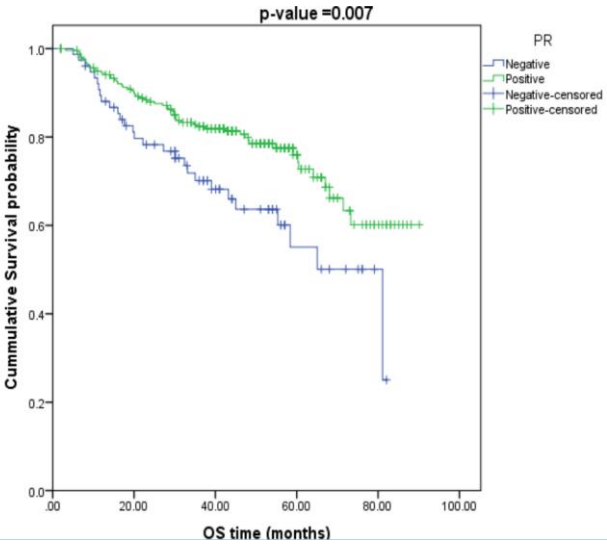

Figure (4): OS in relation to PR status

Table 1. Clinical characteristics of elderly breast cancer patients

		n	(%)
Age (years), mean ± SD		68.8±4.3	
Marital status	Single	2	(0.6)
	Married	285	(83.1)
	Divorced	4	(1.2)
	Widowed	52	(15.2)
Family history	Negative	292	(85.1)
	Positive	51	(14.9)
OCP history	Negative	284	(82.8)
	Positive	46	(13.4)
	Unknown	13	(3.8)
ECOG	1	121	(35.3)
	2	193	(56.3)
	3	29	(8.5)

Discussion:

The prevalence of carcinoma of the breast in the geriatric women is high; with higher life expectancy, screening and treatment procedures are evolving for this group. In 2016, the incidence of breast carcinoma in elderly females aging more than 65 years was 436.9 per 100,000 per year. About greater than 50% of breast cancer cases are diagnosed at the age more than 60 years [9].

Clinical presentation differs among the elderly patients. Some cases are more probably to present later with breast cancer owed to lack of awareness [10].

Some reports show the elderly group present with more favorable features of malignancy than their younger counterparts [11].

The mean age of the study group was 68.8 years ranging between 65 and 80 years and most of them were married (83.1%), which is comparable to data in other studies [12],[13].

The majority of our patients (85%) had negative family history for breast cancer, similar to data reported by other studies.[14].

We did not report strong association between taking OCP and the incidence of breast cancer in elderly patients which came in hand with data presented in other studies [14],[15].

About 56.3% of our patients were of ECOG II, 35.3% of them were of ECOG I and only 8.5% were of ECOG III, compared to results noted by Ibrahim et al., where 65% of the patients in their study were of ECOG II and only 8% was ECOG III. While, Pavei et al., found that more than 80% of their patients were of ECOG I [16],[17].

The most common reported histologic type among our patients was IDC (75.2%) then ILC followed by other types that came in line with results published by Grumpelt et al. [18].

The majority of the included patients had tumors of histological grade II (77%) in agreement with results reported by Pavei et al. but not with Lodi et al. who reported that most of the cases had grade I tumors [17],[19].

Most of the studied cases present at stage II and III (4.8%), (34%), and (6%), respectively in consistency with other studies [19].

Regarding TNM staging, most of the patients had tumors of T2 stage (61.8%), while T1 and T3 had the same prevalence rate (14.9%). Similar to these results, T2 had the highest prevalence among elderly cases in a study by Sierink et al. [20].

Most of the included patients had relatively high incidence of lymph node involvement and low incidence of distant metastasis N0 (41.1%), M0 (94 %) respectively which was comparable to figures in a study conducted by Sierink et al. [20].

Overall, aging was associated with grade II lesions, relatively average size (T1, T2) with more nodal involvement, lower incidence of metastasis and higher expression of ER and PR and low expression of HER-2. In line with data reported by Lodi et al. [19].

Metastasis was found in a low rate (6 %) of patients mainly in the lung (3.4%) at time of diagnosis which was consistent to data reported by Cortadellas et al. [21].

Performance status by ECOG was the only significant predictor for 5-OS in the current study, which comes in line with data reported by Phua et al. [22].

Pathological type and grade did not affect the 3 and 5 years patient survival in line with results by Crystal et al. [23].

TN staging was considered as significant predictor as T0-1 stages had better survival significantly and T2-3 had better survival than T4. N0-1 had better 3 and 5 years survival rates with statistically significant

difference. In concordance with results presented by Grumpelt et al. [18].

Expression of ER and PR was associated significantly with better survival that comes in line with results reported by Vazquez et al., while there was no statistically significant difference of HER-2 expression on overall survival which comes in line with Crystal et al. [24],[23].

Using post-operative radiotherapy did not improve the 3 and 5 years OS, in agreement with Crystal et al., [23].

Neoadjuvant chemotherapy use of anthracyclins and/or Taxanes was associated with poorer overall survival, which was similar to data presented by Crystal et al. [23].

Disease free survival rate (DFS) at 3 years was 85.9% and at 5 years was 81.6%. Similar results were reported by Reddy et al. [25].

Histological type and grade did not affect DFS rates in our study. Crystal et al., reported that histological type was not a significant predictor for DFS rates while the histological grade was a significant one [23].

TN staging was considered significant predictor for DFS rates as T0-1 had better DFS rates and N0 followed by N2 had better DFS rates, in agreement with Crystal et al. [23].

The study had some limitations as lack of randomization and being retrospective. Another limitation is absence of control group including young age breast cancer patients.

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