

Breast Cancer Survival Rate; Clinico-Pathological Correlation in Duhok

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Abstract

Background: Breast cancer (BC) is a common cause of cancer related death, yet the efforts to follow-up patients in developing countries are humble. This study aims to establish a primary percentage of the 7-year BC survivors in Duhok province and correlate it to the age and the main histopathological features at time of diagnosis; including the tumor size and the status of the lymph nodes (LNs).

Material and method: A total of sixty BC patients were included in this follow-up study, all of them were diagnosed in the histopathological department of the central lab in Duhok before 2013. The survival rate was estimated by contacting the survived patients or the families of the late BC patients.

Results: The study reported 7-year survival rate of 30%. Mortality was significantly higher in patients younger than 40 years and in patients equal or older than 50 years. Most of the patients (86.7%) had tumor size equal or greater than 2cm at time of diagnosis. Mortality was significantly higher when the tumor size was greater than 5 cm. About 78.3% of the patients had positive LNs. Mortality in these patients was only slightly higher (70.2%) than those presented with negative LNs (69.2%).

Conclusion: The high percentage of mortality in the first 7-years and the high percentages of patients presented with large tumor size and positive LNs at time of first diagnosis require a special attention and further follow-up studies.

Keywords: Breast Cancer, Survival, Age, Tumor Size, Lymph Nods.

Introduction:

All over the world, BC represents the commonest cancer in females. It brings about the highest cancer related mortality rate in women [1, 2]. In 2017, it had been estimated that 30% of all newly diagnosed cancers among women in the United States of America (USA) were BC cases [3]. Despite the great improvement in the database studies of cancers worldwide, there is an obvious limited knowledge about the survivors of BC in certain developing countries and their appropriate clinical and pathological features. Studies suggested that the incidence and prognosis of BC differ according to the age and ethnicity [4, 5]. Some researches found that BC in female patients has a relatively good outcome and prognosis when compared with other cancers [6, 7]. Furthermore, in recent decades there was an obvious improvement in BC survival [7]. However, different prognostic factors may play role in the outcome of this heterogeneous cancer including; in addition to the age and ethnicity, the size of the tumor, the grade, the LNs involvements, the hormonal receptor status and the presence of vascular invasion or metastasis [8, 9].

According to our knowledge the survival rate had not been studied or even estimated in this region.

The present study aims to estimate a primary percentage of the 7-year survival rate among BC cases and to assess the relation between these survivors and their age, tumor size and LNs involvement at time of diagnosis.

Materials and Methods:

This is a follow up study included 60 BC patients, their data were retrieved from the archives of the pathology department of Duhok central laboratory before 2013. The study was conducted from April 2019 to September 2019 and the ethical approval was obtained from Research Ethics Committee in Duhok, and permissions were taken from all survived patients or the families of the late BC patients. The cases were divided into two groups; those who survived for more than 7 years, and those who deceased before that period. The age of the patient at time of first diagnosis and the pathological parameters of both groups were analyzed. These parameters included: tumor size and the number of lymph nodes involved by the malignancy. Then these data were analyzed by t-test to compare the results by using IBM SPSS software version 22. Chi-square (χ^2) tests was used to compare between proportions, P values ≤ 0.05 were considered statistically significant.

Including criteria:

1. Breast cancer cases diagnosed before 2013
2. Patient's reports included the tumor size and the status of the lymph nodes.

Excluded criteria:

1. Any patient died from other cause (other than the breast cancer) during the first 7 years.
2. Patients who could not be contacted personally or by the families of the deceased.

Results:

This study found that only 18 BC patients out of the 60 studied patients (30%) survived more than 7 years, the other 42 patients (70%) deceased before that period. The age of all patients ranged from 25 to 79 years, with a mean age of 45.5 years. The highest percentage was between 40-49 years (43.4%) as shown in Table 1. The mean age of those who survived was 44.56 years, while that of the deceased was slightly higher (45.95 years). No statistical significance was seen between the mean ages of both groups

Table 1: The breast cancer survivors and deceased in relation to the age of the patient

Age by years		7-year survival	Deceased	Total	P-Value
<40		3 (21.4%)	11 (78.6%)	14 (100%)	0.001
	20-29	0 (0%)	2 (3.3)	2 (3.3%)	
	30-39	3 (5%)	9 (15%)	12 (20%)	
40-49		11 (42.3%)	15 (57.7%)		0.1
		11 (18.4%)	15 (25%)	26 (43.4%)	
≥50		4 (20%)	16 (80%)	20 (100%)	0.04
	50-59	2 (3.3%)	11 (18.3%)	13 (21.6%)	
	60-69	2 (3.3%)	4 (6.7%)	6 (10%)	
	70-79	0 (0%)	1 (1.7%)	1 (1.7%)	
Total		18 (30%)	42 (70%)	60 (100%)	

Mortality was significantly higher in patients younger than 40 years (78.6% in relation to 21.4%) and those who were equal or more than 50 years, (80% in relation to 20%) whereas, the difference was not significant in patients age group 40-49 years (57.7% in relation to 42.3%).

Most of the patients at time of the diagnosis had tumor size equal to or greater than 2cm (86.7%). Mortality was significantly higher when the tumor size was greater than 5 cm but not when the tumor size 2-5cm. Unexpectedly in the eight patients presented with tumor less than 2 cm, seven died and only one survived as seen in Table 2. They were from different age groups (30, 31, 45, 49, 53, 58 and 60) with a mean age of 46.6 years. The age of the survived patient was 40 years.

Table 2: The breast cancer survivors and deceased in relation to the tumor size

Tumor size	Survivors	Deceased	Total	P-Value
< 2cm	1 (1.7%)	7 (11.6%)	8 (13.3%)	0.02
2-5cm	10 (16.7%)	18 (30%)	28 (46.7%)	0.1
> 5cm	7 (11.6%)	17 (28.4%)	24 (40%)	0.01
Total	18 (30%)	42 (70%)	60 (100%)	

The lymph nodes involvement at time of diagnosis was seen in 47 out of the 60 patients (78.3%). More than half of the patients had more than 3 positive lymph nodes (31 out of the 60 = 51.7%). In the small group of patients presented without LNs at time of diagnosis death was relatively high (69.2%). Death in those presented with LNs was only slightly higher (70.2%) and the difference was statistically insignificant as seen in Table 3. Among patients with LNs involvements death was higher in patients who had three LNs or less (87.5%) than those who had more than three LNs (61.3%), however this difference was statistically insignificant.

Table 3: The breast cancer survivors and late in relation to the lymph nodes involvement

LN	Survivors	Late	Total	P-Value
Negative LNs	4 (30.8%)	9 (69.2%)	13 (100%)	0.3
Positive LNs	14 (29.8%)	33 (70.2%)	47 (100%)	
1-3	2 (12.5%)	14 (87.5%)	16 (100%)	
> 3	12 (38.7%)	19 (61.3%)	31 (100%)	
Total	18 (30%)	42 (70%)	60 (100%)	

* Chi-square (x2) tests

Discussion

Less than one third of the studied BC patients in Duhok survived for more than 7 years and the mortality rate was 70%. This result differs from many other results all over the world or even opposite to some of them, especially in developed countries. In a study carried out in France in 2017, the BC survival rate was 78 % at 10 years [10]. In USA the survival rate was near that of France but started to improve even more over several decades [7]. Howlader et al, reported an increase in the 5-year survival rate among females diagnosed between the years 1975 and 1979 from 74.6% to 90.6% for those diagnosed in 2006 [11]. In China, the reported 5-years survival rate was 80.9% [6].

This wide variation in the reported survival rate in our study and those reported in developed countries can be partly explained by the early diagnosis due to improved screening and by the advanced methods of treatment. DeSantis et al stated that [Breast cancer mortality rates are decreasing in most high-income countries. In contrast and of concern are the increasing incidence and mortality rates in a number of countries, particularly those undergoing rapid changes in human development] [12].

However, other factors including the ethical variation may be added to the explanation. Some authors reported a higher mortality rates from BC among Asian-Indian BC patients than that of the African-descent patients [13]. Furthermore, other study carried out in 2012 reported a 42% higher mortality rate due to BC in black females than white females, even after the adjustments of other factors including the hormone receptor status, the subtypes, and the socioeconomic status [14].

In the current study the mean age of all patients at time of diagnosis was 45.5 years. Although the mean age of the survivors (44.56 years) was lower than deceased (45.95 years), this difference was of no statistical significance. However, mortality was significantly higher in patients younger than 40 years and those who were 50 years or more. In 2013 a study carried out in Kurdistan included 324 BC patients, their mean age was found to be 46.8 years, which was slightly higher than the mean age of this study [15]. In Egypt they found that the very young patients with BC have special characteristics including advanced presentation, aggressive biologic behavior and less survival rate [16]. In agreement with our results, a study carried out by Johansson et al at 2019 found that young females had double BC mortality when compared to female age between 50-59 years [17]. Similarly Chen et al found that middle aged BC patients had better prognosis than young and elderly patients and that an age group of 60 years and more represents an independent poor prognostic factor [18].

In this study patients also had special characteristics; in addition to the low mean age, most patients had tumor size equal to or greater than 2cm at time of the diagnosis. Moreover, large number of the studied females (78.3%) had lymph nodes involvement at time of diagnosis. The very small number of patients with tumor less than 2 cm made the statistical correlation unreliable. However, from the eight patients presented with tumor less than 2 cm, seven died and only one survived. This unexpected finding needs further investigations; like the standardization of hormonal or HER2 status. Vaz-Luis et al found a relative high mortality in patients with a mass less than 2cm, negative LNs and positive HER2 [19]. In USA the 5-year survival rate for stage IV BC was below 20% [7]. In general there is a worldwide increase in incidence of BC among young females with more LNs invasion and worse prognosis at that age [20] although some research showed that elderly women had poorer prognosis than younger patients [21, 22].

Finally, the understanding of the complicated prognostic factors for BC is not completed yet. Foulkes et al questioned [how much we truly understand about the apparently simple relationship between tumour size, axillary lymph node status, and survival], they require re-evaluation of some of the diagnosed BC cases at small sizes [23].

One of the weakness points of this study was the small number of patients presented with tumor size less than 2 cm, which made the analysis of the data and the explanation of results in this group difficult. Larger follow up studies for BC patients are required in this region, with more relations to other prognostic factors like the hormonal status and the type of treatment.

Conclusion

The high mortality rate and the high percentages of patients presented with large tumor size and positive LNs at time of first diagnosis, in addition to the significantly higher mortality in patients younger than 40 years and older than 50 years, require a special attention and further follow-up studies.

References

1. Stewart BW, Wild CP. World Cancer Report 2014. Geneva, Switzerland: WHO Press; 2014.
2. Bansal C, Pujani M, Sharma KL, Srivastava AN, Singh US. Grading systems in the cytological diagnosis of breast cancer: a review. J Cancer Res Ther. 2014; 10:839–45.

3. Siegel RL, Miller KD, Jemal A. Cancer Statistics. CA Cancer J Clin. 2017; 67:7–30.
4. Liu P, Li X, Mittendorf EA, Li J, Du XL *et al.* Comparison of clinicopathologic features and survival in young American women aged 18-39 years in different ethnic groups with breast cancer. Br J Cancer. 2013; 109(5):1302–9.
5. Biffl WL, Myers A, Franciose RJ, Gonzalez RJ, Darnell D. Is breast cancer in young Latinas a different disease. The American Journal of Surgery. 2001; 182:596–600.
6. Allemani C, Weir HK, Carreira H, Gonzalez RJ, Darnell D. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2) Lancet. 2015; 385:977–1010.
7. Chen L, Linden HM, Anderson BO, Li CI, Harewood R, Spika D *et al.* Trends in 5-year survival rates among breast cancer patients by hormone receptor status and stage. Breast Cancer Res Treat. 2014; 147(3): 609–16.
8. Goldhirsch A, Glick JH, Gelber RD, Coates AS, Thürlimann B *et al.* Panel members. Meeting highlights: international expert consensus on the primary therapy of early breast cancer. Ann Oncol. 2005; 16:1569–83.
9. Zheng YZ, Wang L, Hu X, Shao ZM *et al.* Effect of tumor size on breast cancer-specific survival stratified by joint hormone receptor status in a SEER population-based study. Oncotarget. 2015; 6:22985–95.
10. Cowppli-Bony A, Colonna M, Ligier K, Jooste V, Defossez G *et al.* Descriptive epidemiology of cancer in metropolitan France: incidence, survival and prevalence. Bull Cancer. 2019; 106:617–34.
11. Howlader N, Noone AM, Krapcho M *et al.* SEER Cancer Statistics Review, 1975–2011. 2014 http://seer.cancer.gov/csr/1975_2010/. Accessed 14 August 2014.
12. DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO *et al.* International Variation in Female Breast Cancer Incidence and Mortality Rates. Cancer Epidemiol Biomarkers Prev. 2015; 24:1495–1506.
13. Brown CR, Hambleton IR, Hercules SM, Alvarado M, Unwin N *et al.* Social determinants of breast cancer in the Caribbean: a systematic review. Int J Equity Health. 2017; 16:60.
14. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA *et al.* Breast cancer statistics, 2015: convergence of incidence rates between black and white women. CA Cancer J Clin. 2016; 66: 31- 42.
15. Yalda MI. Estrogen and Progesterone Receptors (ER and PR) Status of Breast Cancer Cases in Kurdistan and Their Correlation with Pathologic Prognostic Variables. Medical Journal of Babylon-e: 2013; 10(1): 75-84.
16. Farouk O, Ebrahim MA, Senbel A, Emarah Z, Abozeed W *et al.* Breast cancer characteristics in very young Egyptian women ≤ 35 years. Breast Cancer. 2016; 8:53–8.
17. Johansson A, Trewin CB, Hjerkind KV, Ellingjord-Dale M, Johannesen TB *et al.* Breast cancer-specific survival by clinical subtype after 7 years follow-up of young and elderly women in a nationwide cohort. Int J Cancer. 2019; 144:1251-61.

18. Chen HL, Zhou MQ, Tian W, Meng KX, He HF. Effect of age on breast cancer patient prognoses: a population-based study using the SEER 18 database. PLoS One. 2016; 11: e0165409.
19. Vaz-Luis I, Ottesen RA, Hughes ME Mamet R, Burstein J et al. Outcomes by tumor subtype and treatment pattern in women with small, node-negative breast cancer: A multi-institutional study. J Clin Oncol. 2014; 32:2142-50,
20. Dobi A, Kelemen G, Kaizer L, Weiczner R, Thurzo L *et al.* Breast cancer under 40 years of age: increasing number and worse prognosis. Pathology oncology research: POR. 2011; 17(2):425–8.
21. Schonberg MA, Marcantonio ER, Li D, Li D, Silliman RA, Ngo L *et al.* Breast cancer among the oldest old: tumor characteristics, treatment choices, and survival. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2010; 28(12): 2038–45.
22. Yancik R, Wesley MN, Ries LA, Havlik RJ, Edwards BK *et al.* Effect of age and comorbidity in postmenopausal breast cancer patients aged 55 years and older. Jama. 2001; 285(7):885–92.
23. Foulkes W. Size surprise? Tumour size, nodal status, and outcome after breast cancer. Current Oncology. 2012; 19(5):241–3.