Do elderly breast cancer patients have poorer survival outcome? "CSC2017 abstract"

Running title Elderly breast cancer patients' survival

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Abstract

Objective

This study is to compare breast cancer in elderly patients to their younger counterparts, and look for factors affecting survival of elderly patients.

Methodology

A retrospective study of breast cancer patients who had surgery in a university hospital from 2000 to 2015 was performed. Stage on presentation, tumor characteristics and modalities of treatment for patients aged 70 and above were compared with those aged below 70. Factors affecting breast cancer specific survival were assessed by multivariate cox regression.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ash.12360

Results

3825 patients with breast cancer underwent surgery during the study period. 510 patients (13.3%) were aged 70 and above. The 5 year overall survival for elderly patients was 76.9%, which was poorer than their younger counterparts 89.5% (p=0.000). By multivariate analysis, use of adjuvant hormonal therapy (p=0.001, HR 0.481), advanced T stage (p<0.05) and advanced N stage (p<0.001) were the independent factors affecting breast cancer specific survival in elderly patients.

Conclusions

Elderly breast cancer patients had worse overall and breast cancer specific survival. Stage on presentation and use of adjuvant hormonal therapy were independent factors affecting the survival in elderly patients. Early diagnosis and comprehensive geriatric assessment to guide the optimal treatment plan would be useful for better survival outcome in elderly breast cancer patients.

Key words

breast cancer, elderly, geriatric, survival, survival outcome

Introduction

Breast cancer is an increasing health burden in Hong Kong (HK). As shown in the latest report published by the HK Cancer Registry, breast cancer is the leading cause of cancer in women and made up to 26.6% of all cancer in women.[1] The lifetime risk of HK women getting an invasive breast cancer is 1 in 16.

Aging is also of public health concern in HK. From the latest published HK population projections, the proportion of the population of age 70 or above was projected to rise from 10.5% to 15.8% in the coming 10 years.[2]

Since there is more breast cancer and there are more elderly, we would expect the number of breast cancer among older patients to increase in time. This postulation was also supported by the data provided by the HK Cancer Registry, which demonstrated that there is a steadily rising trend of patients with carcinoma of the breast diagnosed with increasing age. From 2005 to 2015, around 18% of all breast cancer patients diagnosed in HK were aged 70 or over.[1]

Despite the increasing incidence, the knowledge of the best management for breast cancer in elderly is still limited as fewer studies have been conducted in the older age group as compared to their younger counterparts. A recent local paper concluded elderly patients tend to delay in seeking first medical consultation and receive less aggressive cancer treatment.[3] A number of western studies have shown that tumours in the older aged group

have more favourable histological features.[4,5] However, lower survival rate was observed in the older age group.[6]

To date, the survival of elderly breast cancer patients has not been reported in our locality. The aim of this study is to look at the survival of elderly patients who received treatment in our centre. Moreover we will investigate the factors affecting the survival so as to find ways to improve our health care in order to ameliorate the outcome in older patients.

Methods

We retrospectively reviewed a prospectively collected database, including patients with carcinoma of the breast who received operations in the Division of Breast Surgery, University of HK, from January 2000 to December 2015. The parameters that we recorded included pathological stage, tumour characteristics, modalities of treatment, and survivals. The patients were grouped according to their age on presentation. The study group is below 70 years (the <70 age group) and the comparison group is 70 years or above (the $\geq$ 70 age group).

Comparisons between the two groups were performed by Fisher's exact test or chi square test when appropriate. Kaplan-Meier analysis was used to compare the five year overall and breast cancer specific survivals. Logistic regression analysis was adopted to identify factors affecting the survival. The SPSS version 21 was used for statistical analysis. A p-value of less than 0.05 was considered as statistical significance.

Results

From January 2000 to December 2015, there were 3825 patients with carcinoma of the breast operated in the Division of Breast Surgery, University of HK. 510 patients, which accounted for 13.3% of all patients, were aged 70 or above.

Comparison of pathological stage and tumour characteristics between the <70 age group and the ≥ 70 age group is shown in Table 1. More patients in the older age group presented with T4 (p=0.002) and N3 (p=0.012) diseases. No difference was observed in terms of oestrogen and progesterone receptor status between these two groups. There was less HER2 positive tumours in the older age group (p=0.007).

Table 2 showed the comparison of modalities of treatment between the two groups. More elderly patients had mastectomy performed (14.7%) as compared to their younger counterpart (p=0.000). Only 2.4% of our elderly patients received neoadjuvant chemotherapy (p=0.000), whereas a significant larger portion of elderly patients received neoadjuvant hormonal treatment (p=0.000). For adjuvant treatment, older patients were given significantly less adjuvant radiotherapy (p=0.000) and less adjuvant chemotherapy (p=0.000) compared to the younger age group. 65.9% of elderly patients received adjuvant hormonal treatment (p=0.001).

The five years overall survival for the ≥ 70 age group is 76.9%, which is significantly lower than the < 70 age group 89.5% (p=0.000). (Figure 1) The five years breast cancer specific

survival for the ≥ 70 age group is 82.2%, which is again significantly lower than the < 70 age group 90.3%. (p=0.000). (Figure 2)

Figure 3 showed Kaplan-Meier estimates of overall survival by stage at diagnosis. The curves demonstrated the overall survival for the ≥ 70 age group is significantly lower than the < 70 age group in stage I, II and III diseases at diagnosis respectively (p=0.000), whereas in stage IV disease, the two age groups had no significant difference in overall survival (p=0.299).

A multivariate cox regression analysis was performed to identify independent factors affecting breast cancer specific survival in the ≥ 70 age group. (Table 3) Use of adjuvant hormonal therapy is an independent protective factor [Hazard ratio HR 0.481 (95% confidence interval (CI) 0.309-0.749, p=0.001)]. Larger tumour size [HR 8.509 (95% CI 2.258-32.063, p=0.002) for T3; HR 6.328 (95% CI 1.676-23.883, p=0.006) for T4] and advanced lymph node status [HR 3.956 (95% CI 2.165-7.226, p<0.001) for N2; HR 4.783 (95% CI 2.520-9.081, p<0.001) for N3] are independent adverse factors affecting breast cancer specific survival.

Discussion

There is no universal agreement on the definition of "elderly". The World Health Organization (WHO) used the chronological age of 60 to define the aging population.[7] The HK Special Administrate Region (HKSAR) Government defined HK's elderly population as those aged 65 or above in her population projections report.[2] The chronological age may not be a true reflection of the biological age. However, for simplicity and practicality, chronological age is often adopted to define a target population. In our study, we define "elderly" as those aged

70 years or above, as the age of 70 is currently the most commonly cut-off for the definition of “elderly” within the field of geriatric onocology.[8]

This is the first study looking at the survival outcome of elderly breast cancer patients in our locality. The five year overall and breast cancer specific survivals for older patients were significant worse than their younger counterparts. From the multivariate analysis, we found the reasons were twofold: delayed in presentation and use of adjuvant therapy.

Our study showed more elderly patients presented with larger tumors and more advanced lymph node status. Elderly patients had less HER2 positive, or less aggressive, tumors. Despite having slow growing tumors with more favorable histological features, elderly patients still presented with more advanced stage of disease. This finding is consistent with the results published in the HK Breast Cancer Registry Bulletin[3] - breast tumors were more advanced at presentation in the older population. In their study, 27.5% of the elderly patients waited for more than a year to seek first medical consultation, as compared to 10.8% for patients of all ages. Delayed in presentation and lack of awareness is significantly contributing to the advanced presentation. Attention should be paid to promote breast cancer awareness, not only to the younger age group, but also to the elderly and their caretakers as well.

In our present study, elderly patients received less neoadjuvant chemotherapy, adjuvant radiotherapy and chemotherapy as compared to their younger counterparts. It has been reported that under-treatment is not uncommon in the older age group with breast cancer.[9] There might be several reasons for substandard treatment. Very often, elderly patients were

considered to be frail and with limited life expectancy. Treatment might be perceived to be of doubtful efficacy and uncertain safety in the elderly. Being undertreated, outcomes in the elderly patients would be compromised.

The management in terms of neoadjuvant and adjuvant treatment modalities was difference between the two age groups. In the multivariate analysis, we could only identify the use of adjuvant hormonal therapy as the independent factor in association with the poorer survival in elderly patients.

Use of adjuvant hormonal therapy was shown to be a protective factor affecting survival in our study. However, not all elderly patients with estrogen receptor positive tumors were commenced on adjuvant hormonal therapy. Sometimes it was not prescribed because of accessibility. Sometimes it was omitted as the medication was considered contraindicated because of co-morbidity.

In order to optimize the treatment plan for the elderly, a comprehensive geriatric assessment (CGA) is warranted. The CGA is a quantitative measure of physical and psychosocial functioning of the elderly. Its component may vary but in general contains various domains namely functional capacity, cognition, emotional condition, nutritional status and comorbidity. It is considered as an objective way to determine the life expectancy of the elderly, and has been recommended by the International Society of Geriatric Oncology and the National Comprehensive Cancer Network to be incorporated in treatment planning.[10-12]

Being a retrospective study, this study is limited by inability to provide data on co-morbidity

which was not prospectively collected over the study period.

In conclusion, elderly patients with carcinoma of the breast had poorer overall and breast cancer specific survival outcome as compared to their younger counterparts. Pathological stage and administration of adjuvant hormonal therapy affected the survival outcome in elderly patients independently. The increase of number of geriatric breast cancer patients is imminent and the aim to achieve earlier diagnosis and the introduction of the CGA to guide the treatment plan is likely to result in better treatment outcome in the elderly breast cancer patients.

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Table 1. Comparison of pathological stage and tumour characteristics between the <70 age group and the ≥ 70 age group.

		<70 age group (n=3315)	≥ 70 age group (n=510)	p-value
T stage	T0	609 (18.6%)	69 (13.8%)	0.002
	T1	1533 (46.9%)	217 (43.4%)	
	T2	945 (28.9%)	177 (35.4%)	
	T3	110 (3.4%)	18 (3.6%)	
	T4	75 (2.3%)	19 (3.8%)	
N stage	N0	2102 (63.8%)	353 (70.0%)	0.012
	N1	691 (21.0%)	79 (15.7%)	
	N2	311 (9.4%)	38 (7.5%)	
	N3	193 (5.9%)	34 (6.7%)	
Overall stage	Stage 0	605 (18.4%)	70 (14.0%)	0.143
	Stage I	1049 (31.9%)	172 (34.5%)	
	Stage II	1025 (31.2%)	165 (33.1%)	
	Stage III	475 (14.5%)	76 (15.2%)	
	Stage IV	131 (4.0%)	16 (3.2%)	
ER	positive	771 (25.3%)	115 (23.4%)	0.400
	negative	2277 (74.7%)	376 (76.6%)	
PR	positive	1193 (39.2%)	192 (39.2%)	1.000
	negative	1847 (60.8%)	298 (60.8%)	
HER2	positive	2173 (75.3%)	376 (81.0%)	0.007
	negative	713 (24.7%)	88 (19.0%)	

Table 2. Comparison of modalities of treatment between the <70 age group and the ≥ 70 age group.

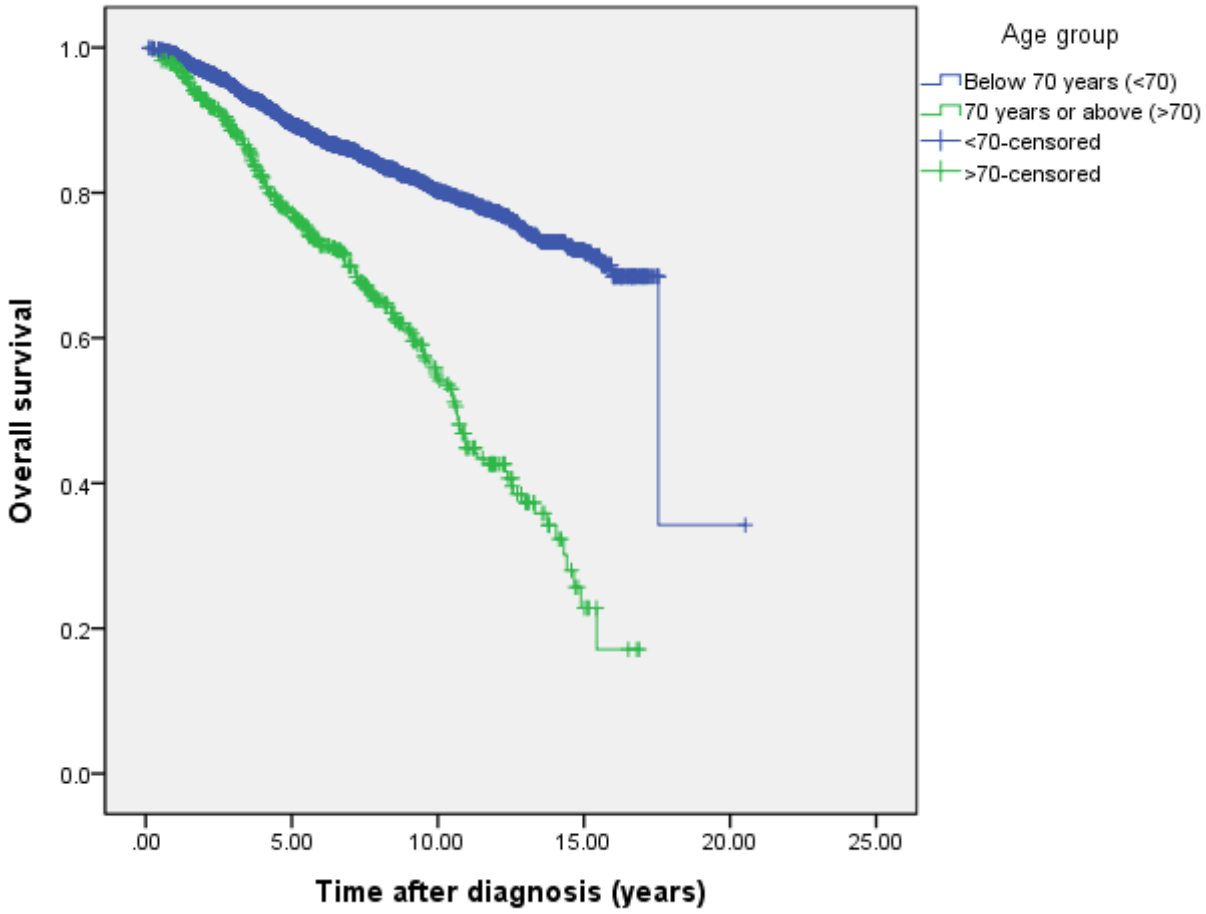
	<70 age group (n=3315)	**≥ 70 age group (n=510)**	**p-value**
Operation			
Mastectomy	2352 (71.0%)	435 (85.3%)	0.000
Lumpectomy	963 (29.0%)	75 (14.7%)	
Neoadjuvant chemotherapy			
Yes	583 (17.6%)	12 (2.4%)	0.000
No	2732 (82.4%)	498 (97.6%)	
Neoadjuvant hormonal therapy			
Yes	124 (3.7%)	66 (12.9%)	0.000
No	3190 (96.3%)	444 (87.1%)	
Adjuvant radiotherapy			
Yes	1775 (53.5%)	135 (26.5%)	0.000
No	1540 (46.5%)	375 (73.5%)	
Adjuvant chemotherapy			
Yes	1513 (45.7%)	37 (7.3%)	0.000
No	1801 (54.3%)	473 (92.7%)	
Adjuvant hormonal therapy			
Yes	1930 (58.2%)	336 (65.9%)	0.001
No	1384 (41.8%)	174 (34.1%)	

Table 3. Multivariate cox regression of breast cancer specific survival in patients aged ≥ 70.

			95% CI for HR	
	p-value	HR	Lower	Upper
Adjuvant hormonal therapy				
Yes	0.001	0.481	0.309	0.749
T stage (Reference: T0/Tis)				
T1	0.713	1.260	0.368	4.320
T2	0.245	2.046	0.613	6.836
T3	0.002	8.509	2.258	32.063
T4	0.006	6.328	1.676	23.883
N stage (Reference: N0/N0(itc)				
N1/N1mi	0.078	1.715	0.941	3.123
N2	<0.001	3.956	2.165	7.226
N3	<0.001	4.783	2.520	9.081

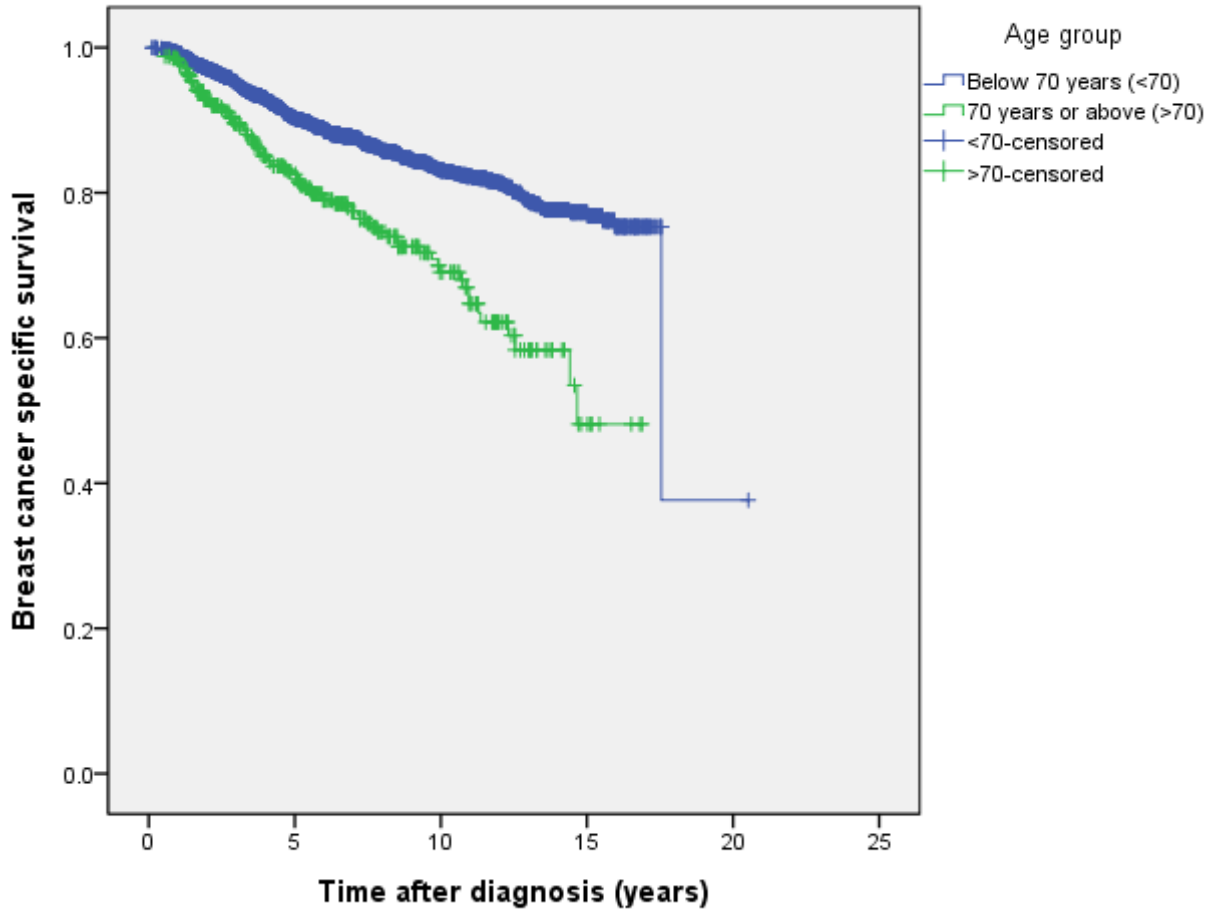
HR hazard ratio, *CI* confidence interval

Figure 1. Overall survival curves of the two groups.



	< 70 age group (n=3315)	**≥ 70 age group (n=510)**	**p-value**
5 year overall survival	89.5%	76.9%	0.000

Figure 2. Breast cancer specific survival curves of the two groups.



	<70 age group (n=3315)	≥ 70 age group (n=510)	p-value
5 year breast cancer specific survival	90.3%	82.2%	0.000

Figure 3. Kaplan-Meier estimates for overall survival by stage at diagnosis: a. Stage I, b. Stage II, c. Stage III and d. Stage IV.