

Revisiting surgical management of breast cancer in a geriatric population

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SUMMARY

OBJECTIVE: Breast cancer is a leading cause of death not only in the young population but also in the elderly. There are no consensus treatment guidelines for elderly breast cancer patients. We purposed to discuss surgical treatment options for breast cancer cases over 80 years concerning morbidity and mortality.

METHODS: This retrospective study includes 58 patients over 80 years of age at the time of surgery for breast cancer between 2006 and 2017. A sum of 58 cases (54 females and 4 males), over 80 years of age, with an average age of 84.5 ± 4.07 (80–94) years were included in the study. The modified radical mastectomy was the most common surgical modality in 30 (51.7%) cases, and the axillary intervention was performed on 41 (70.7%). Axillary dissection and sentinel lymph node biopsy were performed for 30 (51.7%) and 11 (18.9%) cases, respectively.

RESULTS: Minor and major complications were observed in 8 (13.8%) cases. The average follow-up period of the patients was 37.5 (1–120) months. During the follow-up period, breast cancer-related mortality was observed in 9 (15.52%) cases. No statistical differences were detected in mortality with/without axillary intervention and chosen surgical modality.

CONCLUSIONS: Comorbidity, the American Society of Anesthesiologists score, and life expectancy should be considered in the management and surgical planning of patients over 80 years of age with breast cancer. Minimally invasive approaches should be preferred for the elderly whenever feasible and applicable in the light of oncologic surgery principles in order to reduce complications and mortality rates.

KEYWORDS: Breast. Breast cancer. Geriatrics. Elderly. Pathology.

INTRODUCTION

Increasing life standards, widespread screening tests, and improved treatment options lead to an increased length of human life worldwide. The number of elderly people is estimated to be more than double by 2040 to 1.3 billion and 14% of the world population will be of pensionable age. The United Nations definition of “very old population” is the proportion of the elderly in a country that exceeds 10% of the total¹.

Breast cancer is the most common cancer in the world and one of the leading causes of cancer death in women, accounting for 23% of total cases and 14% of all cancer-related mortalities². The most common type of cancer in women in our country is breast cancer. According to 2014 data, a sum of 16,646 women were diagnosed with breast cancer within 1 year and one out of every four women was diagnosed with that².

The median age is defined as 60 years, and over 40% of women with newly diagnosed breast cancer are aged 65 years or older. The risk is present in 15 out of 1000 women in the

fifth decade and 43 out of 1000 women in the age range of 70–80. Even though about two-fifths of breast cancer is seen over the age of 65, no standard consensus on breast cancer treatment in elderly cases has been reported³. Hutchins et al.⁴ demonstrated that only 9% of those over 65 years were represented in cancer studies. We purposed to describe the general characteristics of elderly breast cancer cases over 80 years and discuss surgery for elderly over 80 with breast cancer whose numbers are increasing in society.

METHODS

This retrospective study includes the medical data of 58 patients who had been operated on for breast cancer diagnosis at the age of 80 years and older in our Department between 2006 and 2017. The patients' data were evaluated regarding the age, sex, breast cancer type, tumor size, tumor spread, surgical approach, axillary intervention, anesthesia, complication, hormonal status

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of the tumor, neoadjuvant and adjuvant treatment, follow-up period, recurrence status, and mortality. Descriptive statistics for continuous variables in our study were expressed as the mean±standard deviation, and categorical variables were expressed as numbers and percentages. The Kolmogorov-Smirnov test was applied to test the normal distribution of continuous variables. The distributions of nonparametric variables were compared using the Kruskal-Wallis test and Mann-Whitney U test, chi-square test, and Fisher's exact test was used to determine the relationship between categorical variables. The Kaplan-Meier test was performed for survival. Statistical significance was accepted as $p < 0.05$. A statistical package program SPSS (IBM SPSS for Windows, version 24) was used for the calculations.

RESULTS

Of 58 patients diagnosed with breast cancer, 54 (93.1%) were female and 4 (6.9%) were male, and the mean age was 84.5 ± 4.07 (80–94) years. The mean tumor diameter was 32.6 ± 2.66 (8–100) mm, and 51 (87.9%) cases were diagnosed by physical examination and 7 (12.1%) by breast ultrasonography and mammography. Axillary lymph nodes were clinically detected in 14 (24.1%) of the cases while not in 44 (75.9%). Notably, 53 (91.4%) cases had undergone surgery under general anesthesia and 5 (8.6%) were under local anesthesia. The American Society of Anesthesiologists (ASA) scores of the patients were as follows: 38 patients had ASA-2, 18 had ASA-3, and 2 had ASA-4 without perioperative mortality. The demographic and clinical data of the patients are given in Table 1.

The modified radical mastectomy (MRM) was performed for 30 (51.7%) of 58 cases, while the segmental mastectomy for 11 (19%), simple mastectomy for 6 (10.3%), mastectomy with sentinel lymph node biopsy (SLNB) for 4 (6.9%), and breast-conserving surgery (BCS) with SLNB for 7 (12.1%). The axillary intervention was performed on 41 (70.7%) while not on 17 (29.3%) patients. SLNB was performed on 11 (26.8%) of 41 with axillary intervention. The remaining 30 (73.2%) underwent axillary dissection (AD) without SLNB. The axillary interference was completed to levels I-II AD due to the metastatic lymph nodes detection in the axilla of 4 (36.4%) of 11 patients who underwent SLNB. The metastatic lymph nodes were positive in 23 (56.1%) of 41 with the axillary intervention and in 19 (63.3%) of the cases who had AD.

Histopathologically, breast cancer was revealed as the invasive ductal cancer in 41 (70.7%) cases while invasive lobular cancer in 7 (12.1%), mucinous cancer in 3 (5.2%), and papillary carcinoma in 3 (5.2%), apocrine cancer in 1 (1.7%), neuroendocrine cancer in 1 (1.7%), medullary cancer in 1

(1.7%), and adenoid cystic carcinoma in 1 (1.7%) case. The presence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor (Her2/Neu) was analyzed in 49 (84.5%) of the 58 patients; however, 9 (15.5%) patients' data were not available. ER (+) was found in 35 (71.4%) patients, ER (–) in 14 (28.6%), PR (+) in 29 (59.2%), PR (–) in 20 (40.8%), Her2/Neu (+) in 21 (42.9%), and Her2/Neu (–) in 28 (57.1%) patients.

The analysis of chemotherapy (CT), radiotherapy (RT), and hormone therapy (HT) treatments in the postoperative period revealed that 14 (28.57%) of 49 patients were treated without any treatment and 35 (72.43%) were treated with one or several cycles of CT, RT, and HT treatments. Of 49 patients whose data were obtained, 11 (22.4%) received CT, 6 (12.2%) RT, and 31 (63.3%) HT. In detail, 5 (10.2%) patients received CT and HT, 4 (8.16%) patients received RT and HT, and 2 (4.08%) patients received RT, CT, and HT. Only 4 (8.16%) cases received CT and 20 (40.81%) received HT. Only two cases received CT as neoadjuvant therapy.

The average follow-up period was 37.5 (1–120) months and the disease-free survival time of the operated patients was 36.6 (1–120) months. Recurrence was observed in 3 (5.2%) of 58 patients. No significant difference was revealed in the effect of the axillary intervention and surgical modalities on disease-free survival. During follow-up, 14 (24.14%) of 58 patients died: 9 (15.5%) were due to breast cancer, and 5 (8.6%) were due to other causes. The average life span was 44.11 (12–85) months for those who died due to breast cancer, while 51 (3–120) months for those who died from other causes. No statistical differences were detected in mortality with/without axillary intervention and chosen surgical modality.

DISCUSSION

The incidence of breast cancer increases with age and peaks in the oldest-old group of patients. Despite this, there is no standard approach to managing breast cancer in the elderly. In the treatment strategy of elderly patients, some factors are different from younger ones. All elderly should undergo a pretreatment evaluation, including age and comorbidities, threatening their health and life expectancy, which may have a decisive impact on surgery⁵.

Chronological age, per se, is not an appropriate criterion on which to decide the treatment strategy. Instead, biological age, which reflects the presence of comorbid diseases, and the general fitness or health of a patient should be considered. Comorbidities increase with age, and cancer patients in their 70s may be expected to have at least three comorbid conditions^{5,6}. Regardless of the age, the greater

Table 1. The demographic characteristics, diagnostic and surgical modalities, histopathologic evaluations, and survival of the cases.

Age (years)	84.5±4.07 (80-94)		
Sex, n (%)	Female: 54 (93.1)		
	Male: 4 (6.9)		
Diameter of the tumor (mm)	32.6±2.66 (8-100)		
Clinical axillary lymph nodes, n (%)	(+): 13 (22.4)		
	(-): 44 (75.9)		
	Unknown: 1 (2.7)		
Diagnostic method, n (%)	CE: 51 (87.9)		
	Screening: 7 (12.1)		
Neoadjuvant treatment, n (%)	(+): 2 (3.4)		
	(-): 56 (96.6)		
Type of anesthesia, n (%)	Local: 5 (8.6)		
	General: 53 (91.4)		
Axillary intervention, n (%)	Yes: 41 (70.7)		
	No: 15 (25.8)		
	Unknown: 2 (3.5)		
Sentinel lymph node biopsy, n (%)	Malignancy (+): 4 (36.4)		
	Malignancy (-): 7 (63.6)		
Axillary dissection, n (%)	Malignancy (+): 19 (63.3)		
	Malignancy (-): 11 (36.7)		
Surgical modalities, n (%)	MRM	30 (51.7)	
	Segmental mastectomy	11 (19.0)	
	Simple mastectomy	6 (10.3)	
	Mastectomy+SLNB	4 (06.9)	
	BCS+SLNB	7 (12.1)	
Postoperative complication, n (%)	SLNB	Minor: 1 (14.3)	Major: 0 (0.0)
		Minor: 5 (71.4)	Major: 1 (14.3)
	AD	Minor: 0 (0.0)	Major: 0 (0.0)
		Minor: 0 (0.0)	Major: 0 (0.0)
	No intervention		
Histopathology, n (%)	Invasive ductal carcinoma	41 (70.7)	
	Invasive lobular carcinoma	7 (12.1)	
	Mucinous carcinoma	3 (5.2)	
	Papillary carcinoma	3 (5.2)	
	Apocrine carcinoma	1 (1.7)	
	Neuroendocrine carcinoma	1 (1.7)	
	Medullary carcinoma	1 (1.7)	
	Adenoid cystic carcinoma	1 (1.7)	
Receptor status, n (%)	ER	35 (71.4) (+)	14 (28.6) (-)
	PR	29 (59.2) (+)	20 (40.8) (-)
	Her2/Neu	21 (42.9) (+)	28 (57.1) (-)
Adjuvant treatment, n (%)	CT	11 (22.4) (+)	38 (77.6) (-)
	RT	6 (12.2) (+)	43 (87.8) (-)
	HT	31 (63.3) (+)	18 (36.7) (-)
Recurrence, n (%)	3 (5.2) (+)		
	55 (94.8) (-)		
Causes of death, n (%)	Breast cancer	9 (15.5)	
	Other causes	5 (8.6)	
Disease-free survival (month)	36.6 (1-120)		
Mean follow-up time (month)	37.5 (1-120)		

CE: clinical examination; SLNB: sentinel lymph node biopsy; MRM: modified radical mastectomy; BCS: breast-conserving surgery; AD: axillary dissection; ER: estrogen receptor; PR: progesterone receptor; Her2/Neu: human epidermal growth factor receptor 2; CT: chemotherapy; RT: radiotherapy; HT: hormone therapy.

the number of additional diseases, the greater the likelihood of death due to non-breast cancer causes⁷. No matter how the chronological age of breast cancer patients is advanced, an important part of them dies from breast cancer. Besic et al.⁸ reported that 31% of cases, over 80 years, died from breast cancer during the mean follow-up period of 5.3 years. In the United Kingdom, breast cancer-related mortality in women aged 80 years or older was 39% between 1999 and 2009⁹. In our study, 15.5% of patients died due to breast cancer during the mean follow-up period of 37.5 months.

In the elderly, the biological features of breast cancer are more innocent than the younger patient. Breast cancer in elderly women expresses ER and/or PR more often than in younger and tumors show lower proliferative indices and less HER2 overexpression¹⁰. In the present study, ER (+) was detected in 71.4% while PR (+) in 59.2%, and Her2/Neu (+) in 42.9%. Although the tumor's biological features are better than those of younger people, the prognosis of breast cancer is worse in older patients. The screening of breast cancer in the elderly is still controversial, and there is no consensus on annual mammography screening¹¹. The breast cancers were revealed by clinical examination and imaging in 82 and 18%, respectively⁸.

Blair et al.¹² examined 2947 cases in order to investigate the treatment of breast cancer over 80 years and reported the 2169 surgical approach (mastectomy or BCS) as the most common choice of treatment. No specific recommendations in the literature regarding the extent of surgery in breast cancer cases over 80 years¹³. Surgical treatment extends from local excision to segmental resection, quadrantectomy, and total or partial removal of the mammary gland and axillary lymph nodes, id est, MRM, or BCS¹⁴. In the present study, 51.7% of the 58 had MRM, while 19% had a segmental mastectomy, 10.3% simple mastectomy, 6.9% mastectomy+SLNB, and 12.1% BCS+SLNB.

German pathologist Rudolf Virchow's hypothesis revealed that breast cancer is primarily spread on axillary lymph nodes and passes through other places when the lymph nodes are filled with the tumor¹⁵. AD demonstrates the status of the lymph nodes and helps determine the adjuvant treatment and control the disease. Lymphedema may cause many morbidities, such as pain, paresthesia, limitation of limb movements, altered quality of life, and weakness¹⁶. Lymph node involvement is a

major prognostic factor in breast cancer, even in the elderly. The presence of axillary metastasis suggests a reduction in disease-free survival and overall survival rates¹⁷. Histopathologic examination of lymph nodes after AD in approximately 70% of patients with T1/T2 tumors exhibits negative¹⁸. In the axillary SLNB negativity estimation model based on the criteria of patient age, tumor diameter, and palpability, 5% of the cases had positive SLNB even in the lowest risk group. Regardless of the age of the patient, it is important to at least stage the axillary with SLNB in all cases where it is thought that adjuvant systemic therapy will be determined^{19,20}.

CONCLUSIONS

The elderly population is increasing rapidly all over the world and the incidence of breast cancer is also increasing in them. Providers should consider their additional diseases, ASA score, and life expectancy while planning the surgical approach. Similar surgical modalities may be administrated to the elderly like the younger in case of possessing healthy status. Ad hoc elderly with severe comorbidities and limited life expectancy, avoiding surgery may be useful. Of note, minimally invasive techniques should be applied to the elderly as much as possible in order to attenuate morbidity and even mortality. *Nulla tenaci invia est via.*

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AUTHORS' CONTRIBUTIONS

TK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft. **IS:** Investigation, Methodology, Software, Supervision, Visualization, Writing – original draft, and Writing – review & editing. **IA:** Investigation, Methodology, Validation, Visualization, Writing – original draft. **SV:** Investigation, Validation, Visualization. **DS:** Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing.

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