Breast Cancer in Young Women: Is It Different? A Single-Center Retrospective Cohort Study

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ABSTRACT

INTRODUCTION: Breast cancer (BC) is one of the commonest cancers among women worldwide. Differences regarding tumor biology, presentation, genetics, and molecular subtypes may contribute to the relatively poorer prognosis among younger women. Limited information exists regarding pathologic characteristics and long-term outcomes among this group.

METHODS: This retrospective cohort study included 695 BC patients diagnosed over a 10-year period and investigated the clinicopathological characteristics and long-term disease outcomes among patients diagnosed at age less than or equal to 40 years compared with older ones. Cox regression analysis was performed, and Kaplan-Meier curves were generated to assess overall survival (OS).

RESULTS: Compared with the younger patients (⩽40 years) estrogen receptor (ER) and progesterone receptor (PR) expression was mainly positive in older patients (>40 years) (76.2% vs 61.3% and 64.2% vs 49.6%, respectively). The most common molecular subtype in both age groups was luminal B (44.1% in older and 40.3% in younger). A clinical complete remission after neoadjuvant therapy was observed more frequently in older patients (76.7%; N = 442) in comparison with the younger patients (66.4%; N = 79) ($P = .018$). Recurrence and disease progression were significantly more likely to occur among younger patients accounting for 12.6% and 29.4% of the cases, compared with 6.3% and 18.2% in older patients ($P = .016$ and $P = .006$, respectively). The overall mortality was 132 (19%) of 695, with 88% cancer-related deaths. Estrogen receptor and PR expression ($P \leqslant .001$ and $P = .003$, respectively), molecular subtype ($P = .002$), tumor grade ($P = .002$), and N stage ($P = .038$) were the variables that were found to be significantly influenced by age. The OS was not statistically different among 2 age groups, but younger patients with luminal A molecular subtype showed significantly poor outcome ($P = .019$).

CONCLUSION: Overall survival in women diagnosed with BC at age less than or equal to 40 years is not significantly worse than older patients. However, among patients with luminal A subtype, younger women had relatively poor survival. Further research is needed to understand this age-based disparity in outcomes.

KEYWORDS: Breast cancer, long-term outcomes, clinicopathological characteristics, overall survival

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Introduction

Breast cancer (BC) is the most prevalent malignant tumor among the younger women worldwide.[1] There exists a controversy regarding the definition of younger age with some studies defining it as less than 35, 40, or 45 years; however, most studies choose 40 years as a reasonable cutoff point for this category.[1-3] In women less than 40 years of age, BC is the leading cause of cancer-related mortality, which is expected to rise in the next few years.[2] Approximately 4% to 5% of all newly diagnosed BC patients in the United States are women below 40 years of age, whereas 13% of Asian BC patients are in this age category.[2]

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According to the Saudi National Cancer Registry, BC accounts for 30.1% of all cancers reported in women with a median age at diagnosis of 50 years and accounted for 30.9% to 40.1% of all cancers affecting the young women.[4]

Breast cancer diagnosis at a young age has been reported to be an independent risk factor of death or recurrence[5-7] and is associated with a poor prognosis.[8] It is controversial whether the poor prognosis reflects delay in diagnosis or differences in tumor biology, but there is accumulating evidence that biological differences may play an important role.[9] Nevertheless, it has been established that BC is more histologically aggressive in young women compared with their older counterparts.[2,3] Differences in tumor biology and BC presentation among younger women could even vary among different races.[10] Apart from the tumor biology, the poor outcome may be a result of lack of access to health care and delayed diagnosis among vulnerable young patients.[11,12]

Whether the different age frequencies could also alter the prognosis in different BC molecular subtypes and had been a subject of recent research. A worse relapse-free survival (RFS) has been reported in hormone receptor-positive (estrogen receptor [ER]-positive or progesterone receptor [PR]-positive) BC among younger age group (<40 years) compared with the older ones.[13,14] Certain other studies found a worse overall survival (OS) among young patients (<40 years) in the triple-negative breast cancer (TNBC) subtype.[6] Conflicting data exist on the impact of age on local recurrence (LR). Increased rates of LR among younger women have previously been attributed to a higher prevalence of unfavorable histological features and a higher incidence of positive margins.[15] Contrary to this, age less than 35 years was found to be an independent risk of LR after adjustment for pathologic and treatment variables.[16] Most randomized trials (RCTs) have not found an impact of age on LR after mastectomy, but some have reported an association between younger age and an increased risk of LR after mastectomy.[3] A Danish cohort study reported a higher incidence of LR post-treatment in women less than 35 years of age compared with those aged 45 to 49 years, without any increase in the relative risk of death after therapeutic treatment compared with mastectomy in any age group.[17] Both National Surgical Adjuvant Breast and Bowel Project (NSABP) B24 trial and European Organisation for Research and Treatment of Cancer (EORTC) study reported an increased risk of LR among younger age group.[18,19] Overall, these observations suggest that younger age is a poor prognostic factor but should not be used as a sole reason for mastectomy.[8,20]

Breast cancer among young women is a crucial problem, and limited information exists regarding the diagnosis, presentation, and pathologic characteristics of the disease in this age group. Smaller studies of the Saudi local population have revealed that younger women are more likely to present with a palpable mass, ER-/PR-negative, and/or human epidermal growth factor receptor 2 (HER2)-positive, and poorly differentiated tumors with more advanced disease at the time of presentation.[21] Whereas another study revealed no clear difference between young (25-35 years) and very young (≤25 years) women.[22]

The primary objective of this study was to investigate the long-term disease outcomes (disease-free survival and OS) among a cohort of young (age ≤40 years) BC patients compared with older ones (>40 years). The secondary objectives were to evaluate the disease characteristics, tumor stage, and disease presentation in younger age group as compared with the older group.

Materials and Methods

Patient sample

This was a retrospective cohort study which included young female BC patients over a 10-year period (January 2007 to December 2017) at King Abdulaziz Medical City Riyadh, Saudi Arabia.

Inclusion and exclusion criteria

All women with BC diagnosed at our center irrespective of their age (both ≤40 and >40 years of age) were included in this study. Only those patients for whom the data were not available or had data missing for most variables were excluded.

Statistical data and analysis

Demographic and clinicopathological tumor data, disease presentation, time from presentation to diagnosis and initiation of therapy, disease characteristics, treatment pattern, and localized and systemic therapy were also collected. Tumor stage was established using Tumor, Nodes and Metastasis (TNM) staging classification eighth edition, and[23] OS was calculated from the date of diagnosis until the date of last follow-up. Cox regression analysis was performed, and Kaplan-Meier curves were generated to assess OS among the 2 groups, that is, ≤40 years versus >40 years. Cross tabulation was used to assess the difference in clinicopathological parameters among the 2 age groups. A test with a *P* value of less than or equal to .05 was considered statistically significant.

Treatment methods

Patients with locally advanced disease (T2/3, N1, M0) received neoadjuvant chemotherapy (NAC) along with adjuvant chemotherapy and the protocol followed was mainly anthracyclin/taxane in sequence of 4 cycles adriamycin/cyclophoshamide or 5-flouriuracil/epirubicin/cyclophosphamide, followed by 4 cycles of Taxotere plus anti-HER2 for patients with HER2-positive BC. In addition, most patients with hormone-positive cancers were treated with tamoxifen and few with luteinizing hormone-releasing hormone agonist plus an aromatase inhibitor.

Ethics approval and consent

The study was approved (RC 19/237/R) by the Institutional Review Board of King Abdullah International Medical

Research Center, Riyadh Saudi Arabia. The study was a retrospective cohort study that involved review of medical record data collected over a 10-year period, and hence, the informed consent was exempted.

Results

A total of 695 BC cases were included in this study. Baseline characteristics are summarized in Table 1. Out of these 695 cases, 82.9% were greater than 40 years of age (N = 576) and 17.1% were less than or equal to 40 years (N = 119). The mean age was 51.9 years. The most common morphological type identified was invasive ductal carcinoma (IDC) (91.4%) compared with only 8.6% cases were invasive lobular carcinoma (ILC). Grades 2 and 3 had equal incidence with both being identified in 41.6% of patients. Most of the patients (49.4%) had their tumor on the left breast whereas in only 2.7% cases it was bilateral. The most commonly identified TNM stages were tumor stage T2 (N = 384; 55.3%), nodal stage N0 (N = 309; 44.5%), and metastatic stage M0 (N = 583; 84.0%). Clinical stage II was most frequent and was recognized in 51.4% of the cases. Most of the tumors were ER-positive (73.3%), PR-positive (61.7%), and/or HER2-negative (73.4%). The most common BC subtype was luminal B, followed by luminal A and TNBC (43.5%, 30.9%, and 15.3%, respectively). In total, 50.8% of patients underwent neoadjuvant therapy, and 58.0% underwent radiation therapy as well. Most of the patients had no lymphovascular invasion (N = 609; 87.6%). Patients who underwent mastectomy comprise of 44.9%; lumpectomy was done in 25.8% of patients; and 28.5% did not undergo any surgical procedures. Mortality of BC patients in this study was 132 (19%) of 695; of these, 88.8% were cancer-related deaths.

Most of the patients had complete clinical remission (N = 521; 75%); 26.6% developed metastasis (N = 185); in 20.1%, there was disease progression (N = 140); and recurrence was observed in 7.3% of the cases (N = 51). The mean percentage of Ki67 was 30.4%. The mean survival time was 5 years.

Table 2 shows the difference among clinicopathological parameters among the 2 age groups (younger: ⩽40 years and older: >40 years). The variables that were found to be significantly influenced by age were ER and PR expression ($P \leqslant .001$ and $P = .003$, respectively), molecular subtype ($P = .002$), tumor grade ($P = .002$), and N stage ($P = .038$).

Patients greater than 40 years of age had ER-positive expression in 76.2% of the cases compared with 61.3% of the cases who were less than or equal to 40 years. Younger group had more ER-negative tumors (38.7%) compared with the older ones (23.8%). Progesterone receptor expression was mainly positive in patients greater than 40 years of age (64.2% vs 49.6%). In contrast, it was mainly negative in patients less than or equal to 40 years (50.4% vs 35.8%).

The most common molecular subtype in both age groups was luminal B with an incidence of 44.1% in the older age group and 40.3% in the younger age group. A greater number of luminal A tumors were seen in patients greater than 40 years

Table 1. Baseline characteristics.

VARIABLE (N, %)	CATEGORY	N = 695
Age (y)	>40	576 (82.9)
	⩽40	119 (17.1)
Morphology	IDC	635 (91.4)
	ILC	60 (8.6)
Grade	1	117 (16.8)
	2	289 (41.6)
	3	289 (41.6)
Laterality	Right	333 (47.9)
	Left	343 (49.4)
	Bilateral/Paired	19 (2.7)
T stage	1	155 (22.3)
	2	384 (55.3)
	3	115 (16.5)
	4	41 (5.9)
N stage	0	309 (44.5)
	1	223 (32.1)
	2	126 (18.1)
	3	37 (5.3)
M stage	0	583 (84)
	1	111 (16)
Clinical stage	I	109 (15.7)
	II	357 (51.4)
	III	117 (16.8)
	IV	112 (16.1)
ER	Negative	183 (26.3)
	Positive	512 (73.7)
PR	Negative	266 (38.3)
	Positive	429 (61.7)
HER2	Negative	510 (73.4)
	Positive	185 (26.6)
Molecular subtype	HER2-enriched	72 (10.4)
	Luminal A	215 (30.9)
	Luminal B	302 (43.5)
	Triple-negative	106 (15.3)
Neoadjuvant	No	342 (49.2)
	Yes	353 (50.8)

(Continued)

Table 1. (Continued)

VARIABLE (N, %)	CATEGORY	N = 695
LVI	0	609 (87.6)
	1	86 (12.4)
Radiation	No	292 (42)
	Yes	403 (58)
Type of surgery	None	198 (28.5)
	Lumpectomy	179 (25.8)
	Mastectomy	312 (44.9)
	Mastectomy/Lumpectomy	6 (0.9)
Status	Alive	563 (81)
	Dead	132 (19.0)
Cause of death	Cancer	103 (88.8)
	Noncancer	13 (11.2)

Abbreviations: IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; LVI, lymphovascular invasion.

of age (33% vs 21%), whereas triple-negative tumors were more prevalent among the younger age group (23.5% vs 13.5%). Compared with the older age group, more tumors among younger patients were HER2-enriched (15.1% vs 9.4%).

Most of the patients who were greater than 40 years had grade 2 tumors (N = 251; 43.6%) followed by grade 3 tumors (N = 222; 38.5%). In contrast, most of the patients who were less than or equal to 40 years had grade 3 tumors (N = 67; 56.3%), followed by grade 2 tumors (N = 38; 31.9%).

N0 is the predominant stage in both age groups, constituting 46.2% of the cases (N = 266) in patients greater than 40 years, and 36.1% (N = 43) in patients aged less than or equal to 40 years, followed by N1 (32.3% vs 31.1%), N2 (16.3% vs 26.9%), and then N3 (5.2% vs 5.9%) in both age groups (>40 years vs ⩽40 years). N2 was significantly more prevalent among younger age group.

In the older age group, clinical stage II was found in 52.1% of cases, stage 1 in 16.7%, and stages 3 and 4 were found in 15.6% of the cases each. In comparison, most cases among the younger age group were stage 2 (47.9%), followed by stage 3 (22.7%), stage 4 (18.5%), and stage 1 (10.9%) with an insignificant *P* value of .12. Human epidermal growth factor receptor 2 expression was negative in 74.5% of older cases and in 68.1% of the younger cases (*P* = .15).

Tumor stage (T) was not significantly different among both age groups (*P* = .97), but T2 remained the most common stage in both groups constituting 54.9% of the older category and 57.1% of the younger category, followed by T1 (22.6% vs 21.0%), T3 (16.7% vs 16.0%), and T4 (5.9% vs 5.9%) in both age groups (>40 years vs ⩽40 years). Age was also found to be a significant factor for the choice of systemic therapy (*P* = .054), as more younger patients underwent neoadjuvant therapy (58.8%) in contrast to older (50.9%) ones. Radiation therapy does not appear to be influenced by age (*P* = .839). The choice of surgery was not influenced by age as well, with mastectomy being the most common surgical procedure among both age groups (44.8% of old vs 45.4% of young) (*P* = .728). Mortality seems to be higher among patients less than or equal to 40 years of age (22.7%) in comparison with patients who were greater than 40 years (18.2%) with a *P* value of .26. Cancer-related deaths constituted 95.8% of the younger cases, compared with 87.0% in older group (*P* = 0.22). Most cases in both age groups (>40 years vs ⩽40 years) did not develop metastasis (84.5% vs 81.5%) with a *P* value of .42.

Table 3 describes the difference in disease progression, remission, recurrence, and metastasis stratified by age groups. The younger age group (⩽40 years) was significantly more likely to develop metastasis (37.8%) in comparison with the older age group (24.3%) (*P* = .002). Liver metastases were found in 20.2% of younger patients in comparison with only 7.1% of the older age group (*P* ⩽ .001). Brain metastasis was more common among younger patients (9.2%; N = 11) compared with 3.1% (N = 18) of the older patients (*P* = .002). For the 2 groups (>40 years vs ⩽40 years), no statistically significant difference was observed for lung (10.2% vs 14.3%) and lymph node metastasis (5.0% vs 6.7%) with the *P* values of .198 and .455, respectively, whereas axillary metastasis was significantly more common among younger patients (1.7% vs 5.9%), with *P* = .008. The most common site for metastasis was in bones, with significantly more (25.2%) cases aged less than or equal to 40 having bone metastasis compared with 14.6% in cases greater than 40 years (*P* = 0.004).

A clinical complete remission after neoadjuvant therapy was observed more frequently in patients older than 40 years (76.7%; N = 442) in comparison with the younger patients (66.4%; N = 79) (*P* = .018). Recurrence and disease progression were significantly more likely to occur among younger patients accounting for 12.6% and 29.4% of the cases, compared with 6.3% and 18.2% in older patients (*P* = .016 and *P* = .006, respectively).

Although the patients who were older than 40 years of age were observed to have a better OS in comparison with younger patients (Figure 1), the OS was not statistically different among 2 age groups (⩽40 years vs >40 years) (*P* = .569). But the OS in each molecular subtype stratified by age (Figure 2) revealed luminal A molecular subtype to be the only subtype with significantly poor outcome in younger age group compared with the older one (*P* = .019).

Discussion

Breast cancer is one of the most common malignant tumor among women worldwide[3] with an increase in incidence

Table 2. Association between clinicopathological parameters and age category.

VARIABLE	CATEGORY	AGE CATEGORY (Y)				*P*
		>40		⩽40		
		N	%	N	%	
Morphology	IDC	523	90.8	112	94.1	.24
	ILC	53	9.2	7	5.9	
Grade	1	103	17.9	14	11.8	.002
	2	251	43.6	38	31.9	
	3	222	38.5	67	56.3	
T stage	1	130	22.6	25	21.0	.97
	2	316	54.9	68	57.1	
	3	96	16.7	19	16.0	
	4	34	5.9	7	5.9	
N stage	0	266	46.2	43	36.1	.038
	1	186	32.3	37	31.1	
	2	94	16.3	32	26.9	
	3	30	5.2	7	5.9	
M	0	486	84.5	97	81.5	.42
	1	89	15.5	22	18.5	
Clinical stage	I	96	16.7	13	10.9	.12
	II	300	52.1	57	47.9	
	III	90	15.6	27	22.7	
	IV	90	15.6	22	18.5	
ER	Negative	137	23.8	46	38.7	<.001
	Positive	439	76.2	73	61.3	
PR	Negative	206	35.8	60	50.4	.003
	Positive	370	64.2	59	49.6	
HER2	Negative	429	74.5	81	68.1	.15
	Positive	147	25.5	38	31.9	
Molecular subtype	HER2-enriched	54	9.4	18	15.1	.002
	Luminal A	190	33.0	25	21.0	
	Luminal B	254	44.1	48	40.3	
	Triple-negative	78	13.5	28	23.5	
Neoadjuvant	No	293	50.9	49	41.2	.05
	Yes	283	49.1	70	58.8	
Radiation	No	243	42.2	49	41.2	.84
	Yes	333	57.8	70	58.8	

(Continued)

Table 2. (Continued)

VARIABLE	CATEGORY	AGE CATEGORY (Y)				*P*
		>40		⩽40		
		N	%	N	%	
Type of surgery	None	163	28.3	35	29.4	.73
	Lumpectomy	149	25.9	30	25.2	
	Mastectomy	258	44.8	54	45.4	
	Mastectomy/lumpectomy	6	1.0	0	0.0	
Status	Alive	471	81.8	92	77.3	.26
	Dead	105	18.2	27	22.7	
Cause of death	Cancer	80	87.0	23	95.8	.22
	Noncancer	12	13.0	1	4.2	

Abbreviations: IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; LVI, lymphovascular invasion.

Table 3. Difference in disease progression, remission, recurrence, and metastasis stratified by age groups.

	>40Y				⩽40Y				*P*
	NO		YES		NO		YES		
	N	%	N	%	N	%	N	%	
Metastasis			140	24.3			45	37.8	.002
Bone metastasis	492	85.4	84	14.6	89	74.8	30	25.2	.004
Liver metastasis	535	92.9	41	7.1	95	79.8	24	20.2	<.001
Brain metastasis	558	96.9	18	3.1	108	90.8	11	9.2	.002
Lung metastasis	517	89.8	59	10.2	102	85.7	17	14.3	.198
Lymph node metastasis	547	95.0	29	5.0	111	93.3	8	6.7	.455
Supraclavicular metastasis	574	99.7	2	0.3	118	99.2	1	0.8	.431
Axillary metastasis	566	98.3	10	1.7	112	94.1	7	5.9	.008
Breast local recurrence	566	98.3	10	1.7	117	98.3	2	1.7	.96
Clinical complete remission	134	23.3	442	76.70	40	33.6	79	66.40	.018
Recurrence	540	93.8	36	6.30	104	87.4	15	12.60	.016
Disease progression	471	81.8	105	18.20	84	70.6	35	29.40	.006

among younger women in certain parts of the world. Young female patients present a serious concern in diagnosis and adequate management of the disease in developing countries.[24] According to the Saudi National Cancer Registry, BC accounts for about 30.9% of all cancers reported in women.[25] Some factors may indicate poor prognosis in BC such as onset at younger age, triple-negative cancer, higher grade, and lymphovascular invasion.[26–28] Thus, our study aimed to compare the difference in prevalence, mortality, cancer types, hormonal receptors, and metastasis rates between old (>40 years) and young (⩽40 years) female BC patients.

It is well established that BC in younger women differs greatly from that of older women. There was a debate in several prior studies whether that difference resulted from biological factors or it was just a matter of a delay of diagnosis and treatment.[29] Although it is true that delay in diagnosis and seeking for medical attention are some of the important factors affecting prognosis, but it was found that there are many biological factors that exist in young patients and are absent from older ones.[3,29] For instance, BC in younger women is more likely to have a triple-negative nature, higher grade, Ki-67 positivity, and lymphovascular invasion.

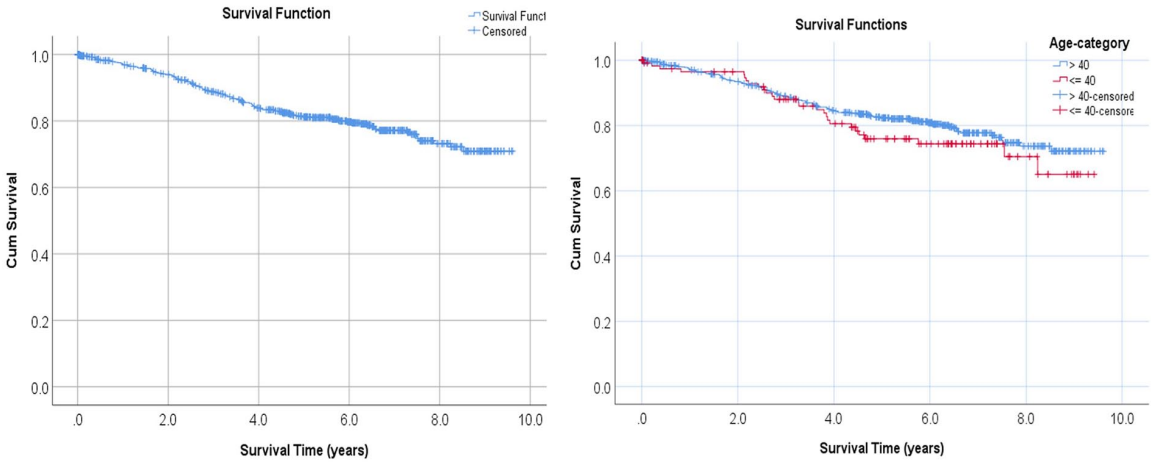

Figure 1. Cox regression analysis and Kaplan-Meier curves for overall survival of the whole cohort as well as stratified by the age. Survival curves by molecular subtype and age group.

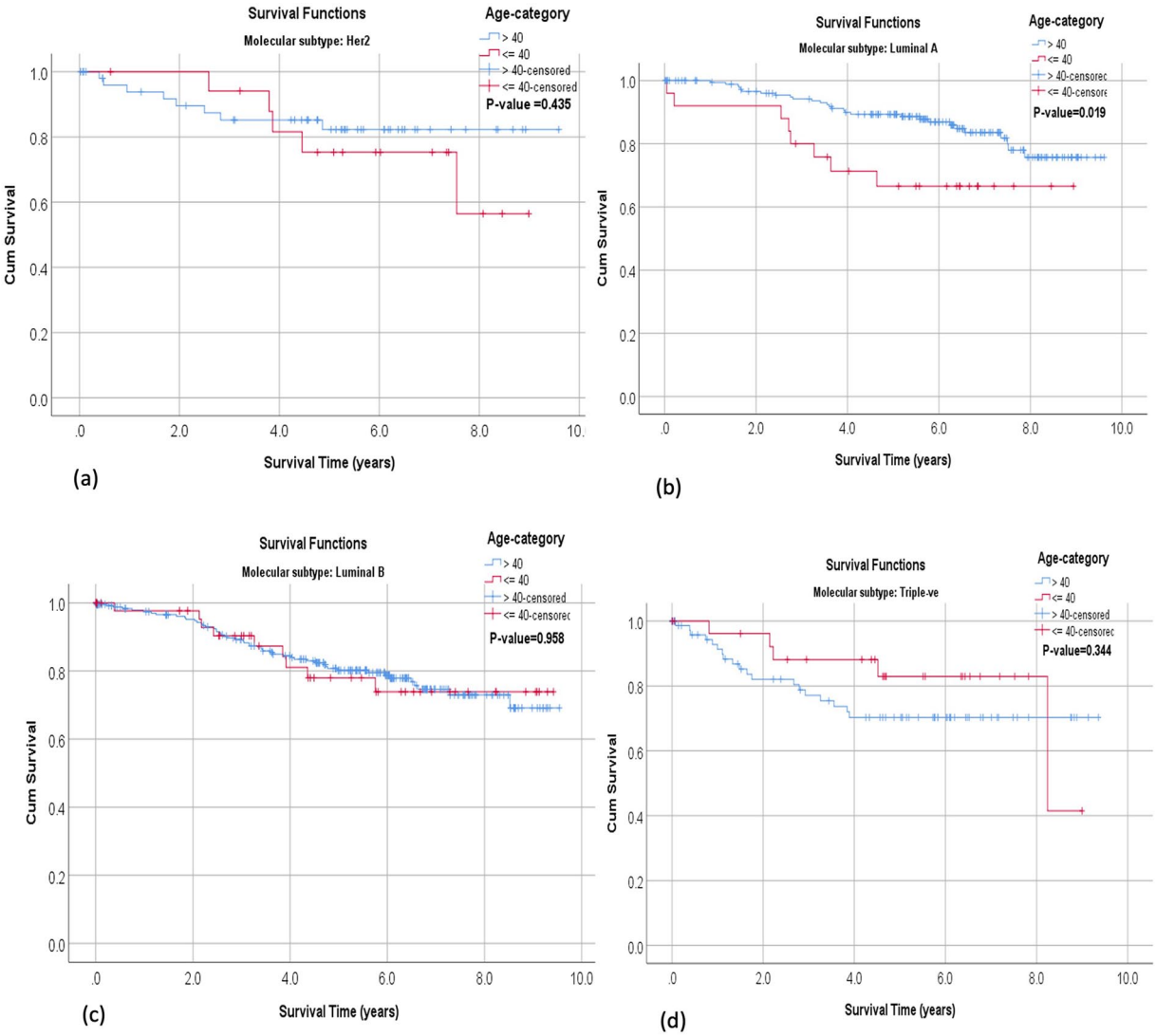

Figure 2. Cox regression analysis and Kaplan-Meier curves for overall survival stratified by the molecular subtype and: (a) HER2, (b) Luminal A, (c) Luminal B, (d) Triple negative.

However, both T (tumor size) and N (nodal status and the number of nodes involved) in staging were reported to be similar in both older and younger women.[3] Findings of our study strengthen their findings of no significant difference in tumor size among both groups, but contradict the nodal status, with significantly more N2 and N3 cases among younger patients compared with older ones in our cohort.

Accordingly, a difference in survival rate should be expected. Recent studies have found that survival rates in younger patients were worse than survival rates of elderly patients whether it was a receptor-positive (ER- or PR-positive) or receptor-negative patients.[30,31] On the contrary, various studies reported contrary to this, thus highlighting the conflicting nature of the findings among different cohorts. Our findings of no significant difference in OS between younger and older groups of BC patients are in line with findings reported by Alabdulkarim et al[32] with similar survival rates among the 2 groups. Apart from strengthening each other's results, the similarity in findings from both these studies involving young BC patients from the same region and their contradiction with what has been reported by most studies from west raises the prospect of exploring the personal, environmental, and demographic influences along with the parameters related to tumor biology. Interestingly, the incidence of BC among young women is quite high among the local population but we observed that OS remains similar to older cases, which may be because of the fact that approximately 1 of 3 of the population represented by this cohort are youth.

Certain other studies found a worse OS among young patients (<40 years) in the TNBC subtype.[6] In our study, we did report a poor OS among younger patients with luminal A subtype of BC but not with the TNBC. This finding is well supported by Partridge et al[33] who also reported an association of worse survival with young BC patients with luminal A subtype and not for those with TNBC. In line with our findings, Sheridan et al[34] also reported poor survival among young (<40 years) luminal BC patients and reported no difference in OS for both age groups of TNBC patients.

Moreover, several studies have found that recurrence rates are higher in women younger than 30 years.[35,36] This study reported a statistically significant increased risk of recurrence among younger group (twice as many younger cases developed recurrence compared with older), which supports the findings of earlier studies. A study has also found association between younger age and a high recurrence risk score on Oncotype Dx analysis.[37] We also report a significantly higher risk of metastasis among younger cases. It is still not well understood whether the risk of recurrence and metastasis is because of the biological factors stated earlier or younger age is a risk factor itself.[30]

Our observation of a significantly increased likelihood of younger patients receiving NAC is in line with the study by Zouzoulas et al[38] who also reported the use of NAC in 1 of 3 of their younger cases. Despite the increased use of NAC in younger patients, both these studies reported a higher mortality rate for the young. This could well be because of the aggressive nature of disease in these younger patients that fulfills the criteria for administering NAC. The higher mortality could even be a result of noncompliance to treatment among younger cases compared with the older ones as reported by Hershman et al.[39] In addition, recent data have suggested that there may be differences in the tumor genomics of young women with hormone receptor-positive BC which may confer more poor outcomes and further research in this area is necessary including potentially targeting these differences with treatment.[40,41]

The importance of our study comes from the lack of data related to BC among young women in the Middle East. Although there were multiple previous studies from this region, they all had the same problem—a small population sample. For example, a study in 2012 found that younger BC patients were more likely to have ER-/PR-negative, and/or HER2-positive, and low-grade tumors with more advanced disease at the time of presentation.[21] Furthermore, we also used the most recent and precise definition for younger age group, which has consensus of various international societies on BC and thus brought homogeneity and minimized the variation in interpretation of our results.

The retrospective nature was one of the limitations of this study as it can cause a statistical bias. Our main limitation was that it was a single-center study, and as would be anticipated, there were substantially fewer young patients compared with older patients, as patients aged 40 years at diagnosis and younger were only 17.1% of the whole sample.

Conclusions

The long-term OS in younger patients was not significantly worse than older patients except for luminal A subtype. Hormone receptor expression (negative ER and PR), molecular subtype, tumor grade 3, and nodal stage 3 were significant factors that could contribute to more disease progression (recurrence and metastasis) and less clinical remission among younger patients. Further research is needed to understand why young women far worse after a diagnosis of a luminal A–like BC.

Author Contributions

OA, AA, and AP contributed to the conception and design of the study. AA, AO, DM, MAZ, LAR, NA, FA, and GA conducted the literature review. OA, AA, and GA collected and organized the data. EM performed the data analysis, and all authors contributed to interpretation. AO, OA, AA, and GA conceived the initial draft, and all authors revised it. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Ethics Approval

The study was approved by the Institutional Review Board of King Abdullah International Medical Research Center, Riyadh Saudi Arabia (grant no RC 19/237/R). The study was a retrospective cohort study that involved review of medical record data collected over a 10-year period, and hence, the informed consent was exempted.

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