original article

Expression of androgen receptor in invasive ductal breast carcinomas: a clinicopathological study from Jordan

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BACKGROUND: The clinical relevance of androgen receptors (ARs) expressed in breast cancer cells and the suggested prognostic impact has been an area of active research. The prevalence rate of AR expression in breast cancer has never been reported among Jordanian patients.

OBJECTIVE: Determine the expression rate of ARs among invasive ductal breast cancer cases of different stages and molecular subtypes. Also, analyze the relationship between AR expression and clinicopathologic and immunohistochemical criteria, and assess the impact of AR expression on survival.

DESIGN: Retrospective medical record review.

SETTING: Tertiary care hospital in Amman, Jordan.

PATIENTS AND METHODS: Our study comprised only of cases of invasive ductal breast carcinoma of no special type among females from records during a 10-year period between 2006 and 2015. Immunohistochemical staining was considered positive if more than 10% of tumor nuclei showed positive staining.

MAIN OUTCOME MEASURES: The expression rate of ARs and the association of the expression rate with the clinicopathologic features of invasive breast cancer.

SAMPLE SIZE: 293.

RESULTS: Immunohistochemical staining for AR revealed positive staining in 180 (61.4%) cases, including approximately 50% of triple-negative breast cancer cases. AR positivity correlated with estrogen receptor (ER) status (P=.007) and smaller T size (P=.014). However, no significant association was found with any of the other variables. AR expression was positively associated with overall survival (P=.022) in general and in ER-positive cases (P=.012). However, in the multivariate Cox regression model, AR was not independently associated with survival.

CONCLUSIONS: These results were consistent with international reports showing a significant relationship of AR expression with ER status. In addition, AR expression was significantly associated with smaller tumor size. Although AR status was not independently associated with survival, our data suggest AR is a good prognostic factor.

LIMITATIONS: Some clinical data were missing.

CONFLICT OF INTEREST: None.

Breast cancer is the most common malignancy worldwide and the leading cause of cancer-related deaths in women.[1] In Jordan, it is the most common malignancy afflicting women, accounting for 37% of newly diagnosed cancer cases, and is the most common cause of cancer-related deaths per the most recent report provided by the Jordanian Ministry of Health.[2] In a recently published study of 752 patients with breast cancer, 74.3% of breast cancer cases were classified as invasive ductal carcinoma of no special type (IDC-NST), constituting the most common type of breast cancer in Jordan.[3] Most of these tumors were moderately differentiated. Approximately one-third were localized at time of diagnosis, whereas 40% were regionally disseminated, leading to low survival rates among patients.[4]

The etiology of breast cancer involves a combination of genetic, environmental, and hormonal factors that collectively alter normal breast tissue, resulting in neoplastic transformation.[5] Hormonal factors act through complex downstream signaling molecules transmitted through sex steroid receptors and growth factors. The expression of estrogen receptor (ER), progesterone receptor (PR), and the epidermal growth factor receptor-2 (HER-2) in breast cancer has been extensively studied. Targeted therapy against these receptors is now a validated modality of treatment in conjunction with surgery, radiotherapy, and chemotherapy.[6,7]

Another receptor of the nuclear steroid hormone family is the androgen receptor (AR). It functions as an intracellular transcription factor.[8] Binding of specific ligands to the receptor induces conformational changes, dimerization, and subsequent receptor translocation into the nucleus. The dimer then binds to its hormone receptor elements (HRE) within the DNA, resulting in a series of regulatory transcriptional events that function differently in respect to tissue type.[9,10]

Recently, the clinical relevance of this receptor being expressed in breast cancer cells, its role in neoplastic transformation, and suggested prognostic impact has been an area of active research. Many studies reported AR expression in 60% to 80% of breast cancer cases but lower and higher percentages have been described, and these differences can be explained by demographic variations as well as the use of different cutoff points for AR expression intensity.[11-15] Many authors have reported significant associations between AR expression by cancer cells and improved overall survival and disease-free survival.[16-21] In addition, targeted therapy blocking AR receptors is being developed, and researchers are trying to better understand the molecular signaling pathways by which androgens alter the proliferation of cancer cells. It may be the only endocrine therapy available to a subset of patients with the aggressive triple negative tumors that lack the expression of ER, PR, and HER-2/neu, and hence, are unable to respond to targeted therapy.[22] Several clinical trials have also illustrated the activity of anti-androgen therapy for the treatment of AR-positive triple negative breast cancers (TNBC).[23,24]

The prevalence rate of AR expression in breast cancer has never been reported among Jordanian patients. Our study aimed to evaluate the prevalence rate of AR expression in breast cancer cases diagnosed at Jordan University hospital over a 10-year period. We also studied the correlation of AR expression with other clinicopathologic parameters, such as the menopausal status, tumor grade, ER, PR, HER-2/neu expression, T stage, and the presence of distant metastases, in addition to the impact of AR expression on patient survival.

PATIENTS AND METHODS

After the Institutional Review Board approval was obtained at Jordan University Hospital, hematoxylin- and eosin-stained tumor slides, paraffin blocks, and their corresponding ER, PR, and HER-2/neu for all documented cases of IDC-NST of the breast were retrieved from the archives of the Histopathology Department at Jordan University Hospital (JUH). These cases were diagnosed during the 10-year period between 2006 and 2015 and comprised modified radical mastectomy specimens from patients with no previous history or prior neoadjuvant chemotherapy. Clinical information of all cases, including menopausal status and the presence or absence of lymph node involvement or distant metastases, was gathered from patient files.

Morphologic evaluation

One 4-μm-thick section from each submitted paraffin-embedded tissue block was stained with hematoxylin and eosin to verify the presence of IDC and the adequacy of fixation. Cases were classified based on the 2012 WHO classification of breast tumors[25] and staged according to the updated 7th edition of the American Joint Committee on Cancer (AJCC).[26] The modified Bloom-Richardson-Elston (BRE) grading system was used and categorized the cases into low, intermediate, and high grades.

Immunohistochemistry

Immunohistochemical (IHC) staining of AR was performed on 4-μm-thick sections that were added to poly-L-lysine-coated slides that underwent conventional deparaffinization (in incubator for 30 minutes at 70°C),

followed by hydration. Antigen retrieval (20 min; 10 mmol/EDTA buffer, pH 8.0) was done in a microwave, followed by inhibition of endogenous peroxidase activity (hydrogen peroxidase for 5 min). Protein blocker (normal serum) was applied for 5 to 10 minutes, then tapped off, and the excess was wiped away without rinsing. Immunostaining was performed using mouse anti-AR primary antibody (clone AR441) at a 1:50 dilution. The antibody was purchased from Genova Diagnostics (Asheville, NC, USA) and diluted (1:50). This was followed by incubation with a secondary antibody (Super Enhancer) for 20 to 30 minutes. Then, a tertiary antibody (HRP-Polymer) was applied for another 20 to 30 minutes. Addition of chromogen substrate (Leica Biosystems RE 7105, RE 7143) was performed manually by an experienced technician. With each staining run, normal prostatic tissue was used as a positive control. Nuclear staining of AR was considered positive when more than 10% of tumor cell nuclei were stained.

Statistical analysis

Categorical and numerical data were statistically analyzed using IBM SPSS, version 17.0. The Kaplan-Meier method was used to analyze survival. Statistical significance was established when *P* value was equal to or less than .05.

RESULTS

We identified 293 cases of IDC-NST that ranged between 22 and 79 years of age, with a mean age of 50 years, and almost half were premenopausal (**Table 1**). In addition, approximately 50% of the tumors were of T2 size, relative to almost 27% with T1, 12% with T3, and 7% with T4. Positive lymph node involvement was indicated for 64.5% of cases, and 15.7% were metastatic. As for receptor biomarkers, staining for ER, PR and HER-2/neu was 83.4%, 75.8%, and 22.5% of cases, respectively. Some data was missing and excluded from the analysis (**Table 1**). Positive staining for AR was detected in 61.4% of cases. AR expression was significantly associated with ER status (*P*=.007), in which 65.3% of AR-positive cases were also ER-positive relative to 44.7% of cases. In addition, AR-positive cases tended to be of significantly smaller tumor size. For example, 70.8% of T1 cases were AR-positive, whereas 67.7% of T4 cases were AR-negative (*P*=.014. Interestingly, AR expression was higher in tumors without lymph node involvement and in non-metastatic tumors, although this did not reach statistical significance. **Figures 1A and 1B** show cases of positive and negative nuclear staining for AR.

In addition, there was no significant association between the expression of AR with other clinicopathological features of the tumors, including menopausal status (*P*=.402) and histologic grade (*P*=.809) (**Table 1**). In addition, positive AR expression was not associated with expression of either PR (*P*=.232) or HER-2/neu overexpression (*P*=.968). Approximately 48% of triple-negative breast cancer cases were AR-positive with a lack of association with AR status (*P*=.075).

The data were analyzed further to correlate AR expression with clinicopathological and immunohistochemical features of breast cancer cases according to ER status. As shown in **Table 2**, AR expression was significantly associated only with smaller tumor size (*P*=.043) in patients with ER-positive but not ER-negative tumors. ER expression with clinicopathological and and immunohistochemical factors such as age, menopausal status, TNM stage, PR and HER2/neu status were also correlated (**Table 3**). Only in tumors lacking the expression of AR was the expression of ER associated with tumors of lower histological grade (*P*=.031)

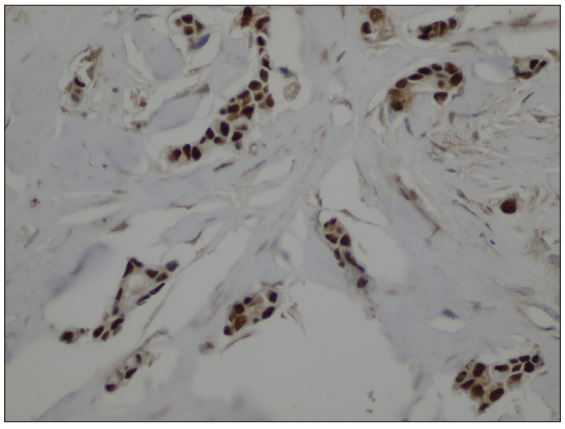

Figure 1A. Case of IDC-NST with positive nuclear staining for AR (400×).

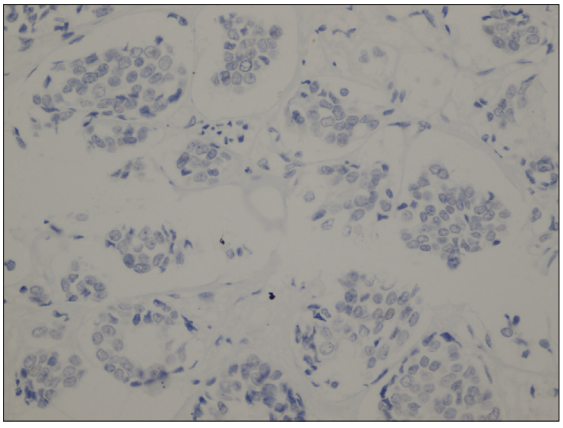

Figure 1B. Case of IDC-NST with negative nuclear staining for AR (400×).

Table 1. Association of AR expression in breast cancer cases with clinicopathological and immunohistochemical features (n=293).[a]

Variable		No. of cases (%)	AR expression		*P* value
			Positive n (%)	Negative n (%)	
		293 (100%)	180 (61.4%)	113 (38.6%)	
Age (years)	<40	32 (10.9%)	21 (65.6%)	11 (34.4%)	.875
	40-55	125 (42.7%)	76 (60.8%)	49 (39.2%)	
	>55	136 (46.4%)	83 (61.0%)	53 (39.0%)	
Menopausal status	Pre	149 (50.9%)	90 (60.4%)	59 (39.6%)	.402
	Post	144 (49.1%)	90 (62.5%)	54 (37.5%)	
Primary tumor size (T) (n=265, 90.4%)	T1	72 (27.2%)	51 (70.8%)	21 (29.2%)	**.014**
	T2	144 (54.3%)	87 (60.4%)	57 (39.6%)	
	T3	31 (11.7%)	15 (48.4%)	16 (51.6%)	
	T4	18 (6.8%)	6 (33.3%)	12 (66.7%)	
Lymph node involvement (n=256, 87.4%)	Negative	91 (35.5%)	59 (64.8%)	32 (35.2%)	.158
	Positive	165 (64.5%)	95 (57.6%)	70 (42.4%)	
Metastasis (n=153, 52.2%)	Negative	129 (84.3%)	77 (59.7%)	52 (40.3%)	.150
	Positive	24 (15.7%)	11 (45.8%)	13 (54.2%)	
TNM stage group (n=136, 46.4%)	I	18 (13.2%)	14 (77.8%)	4 (22.2%)	.074
	II	56 (41.2%)	29 (51.8%)	27 (48.2%)	
	III]	38 (27.9%)	26 (68.4%)	12 (31.6%)	
	IV	24 (17.7%)	11 (45.8%)	13 (54.2%)	
Histological grade (n=285, 97.3%)	Grade 1	35 (12.3%)	23 (65.7%)	12 (34.3%)	.809
	Grade 2	153 (53.7%)	92 (60.1%)	61 (39.9%)	
	Grade 3	97 (34.0%)	58 (59.8%)	39 (40.2%)	
Lymphovascular invasion (n=282, 69.3%)	Positive Negative	121 (42.9%) 161 (57.1%)	71 (58.7%) 102 (36.4%)	50 (41.3%) 59 (63.6%)	.425
ER status (n=283, 96.6%)	Positive	236 (83.4%)	154 (65.3%)	82 (34.7%)	**.007**
	Negative	47 (16.6%)	21 (44.7%)	26 (55.3%)	
PR status (n=273, 93.2%)	Positive	208 (76.2%)	131 (63.0%)	77 (37.0%)	.232
	Negative	65 (23.8%)	37 (56.9%)	28 (43.1%)	
HER2/neu status (n=275, 93.9%)	Positive	62 (22.5%)	38 (61.3%)	24 (38.7%)	.968
	Equivocal	13 (4.7%)	8 (61.5%)	5 (38.5%)	
	Negative	200 (72.7%)	126 (63.0%)	74 (37.0%)	
TNBC (n=281, 95.3%)	Negative	250 (89%)	159 (63.6%)	91 (34.4%)	.075
	Positive	31 (11%)	15 (48.4%)	16 (51.6%)	

[a]Some information was not available for certain criteria and, hence percentages are calculated per cases with available data and missing data were excluded from analysis occurred at random and did not bias the results. Statistical analyses by Pearson's chi-squared test.

Table 2. Association of AR expression cases with clinicopathological and immunohistochemical features of breast cancer cases according to ER expression status.

	ER-positive tumors			ER-negative tumors		
	AR-positive	AR-negative	*P* value	AR-positive	AR-negative	*P* value
Age (years)						
<40	17 (70.8)	7 (29.2)	.665	3 (60)	2 (40)	.692
40-55	65 (67.0)	32 (33.0)		10 (40)	15 (60)	
>55	72 (62.6)	43 (37.4)		8 (47.1)	9 (52.9)	
Menopausal status						
Pre	75 (67.0)	36 (37.9)	.350	13 (41.9)	18 (58.1)	.413
Post	79 (63.7)	45 (36.3)		8 (50.0)	8 (50.0)	
Primary tumor size (T)						
T1	45 (76.3)	14 (23.7)		4 (40.0)	6 (60.0)	
T2	74 (61.7)	46 (38.3)	.043	12 (52.2)	11 (47.8)	.364
T3	12 (52.2)	11 (47.8)		3 (37.5)	5 (62.5)	
T4	6 (42.9)	8 (57.1)		0 (0.0)	3 (100)	
Lymph node involvement						
Negative	53 (70.7)	22 (29.3)	.096	5 (35.7)	9 (64.3)	.409
Positive	80 (60.6)	52 (39.4)		13 (44.8)	16 (55.2)	
Metastasis						
Negative	71 (62.8)	42 (37.2)	.100	6 (40.0)	9 (60.0)	.669
Positive	10 (45.5)	12 (54.5)		1 (50.0)	1 (50.0)	
TNM stage group						
I	14 (87.5)	2 (12.5)		0 (0.0)	2 (100)	
II	27 (54.0)	23 (46.0)	**.035**	2 (33.3)	4 (66.7)	.327
III	23 (67.6)	11 (32.4)		3 (75.0)	1 (25.0)	
IV	10 (45.4)	12 (54.6)		1 (50)	1 (50)	
Histological grade						
Grade 1	21 (70.0)	9 (30.0)	.540	2 (50.0)	2 (50.0)	.242
Grade 2	77 (61.1)	49 (38.9)		12 (57.1)	9 (42.9)	
Grade 3	49 (67.1)	24 (32.9)		7 (31.8)	15 (68.2)	
Lymphovascular invasion						
Positive	59 (62.1)	37 (37.4)	.398	9 (40.9)	13 (59.1)	.999
Negative	92 (68.1)	43 (31.9)		9 (40.9)	13 (59.1)	
PR status						
Positive	128 (64.0)	72 (36.0)	.295	3 (37.5)	5 (62.5)	.999
Negative	21 (75.0)	7 (25.0)		16 (43.2)	21 (56.8)	
HER2/neu status						
Positive	23 (79.3)	6 (20.7)	.103	15 (46.9)	17 (53.1)	.500
Equivocal	7 (87.5)	1 (12.5)		1 (20.0)	4 (80.0)	
Negative	121 (63.4)	70 (36.6)		4 (50.0)	4 (50.0)	

Data are number (percentage).Statistical analyses by Pearson's chi-squared test.

Table 3. Association of ER expression with clinicopathological and immunohistochemical features of breast cancer cases according to AR expression status.

	AR-positive tumors			AR-negative tumors		
	ER-positive	ER-negative	*P* value	ER-positive	ER-negative	*P* value
Age (years)						
<40	17 (85.0)	3 (15.0)	.741	7 (77.8)	2 (22.2)	.235
40-55	65 (86.7)	10 (13.3)		32 (68.1)	15 (31.9)	
>55	72 (90)	8 (10)		43 (82.7)	9 (17.3)	
Menopausal status						
Pre	75 (85.2)	13 (14.8)	.184	37 (67.3)	18 (32.7)	**.027**
Post	79 (90.8)	8 (9.2)		45 (84.9)	8 (15.1)	
Primary tumor size (T)						
T1	45 (91.8)	4 (8.2)	.443	14 (70.0)	6 (30.0)	.657
T2	74 (86.0)	12 (14.0)		46 (80.7)	11 (19.3)	
T3	12 (80.0)	3 (20.0)		11 (68.8)	5 (31.2)	
T4	6 (100)	0 (0)		8 (72.7)	3 (2.9)	
Lymph node involvement						
Negative	53 (91.4)	5 (8.6)	.235	22 (71.0)	9 (29.0)	.364
Positive	80 (86.0)	13 (14.0)		52 (76.5)	16 (23.5)	
Metastasis						
Negative	71 (92.2)	6 (7.8)	.621	42 (82.4)	9 (17.6)	.345
Positive	10 (90.9)	1 (9.1)		12 (92.3)	1 (7.7)	
TNM stage group						
I	14 (100)	0 (0.0)	.615	2 (50)	2 (50)	.173
II	27 (93.1)	2 (6.9)		23 (85.2)	4 (14.8)	
III	23 (88.5)	3 (11.5)		11 (91.7)	1 (8.3)	
IV	10 (90.9)	1 (9.1)		12 (92.3)	1 (7.7)	
Histological grade						
Grade 1	21 (91.3)	2 (8.7)	.757	9 (81.8)	2 (18.2)	**.031**
Grade 2	77 (86.5)	12 (13.5)		49 (84.5)	9 (15.5)	
Grade 3	49 (87.5)	7 (12.5)		24 (61.5)	15 (38.5)	
Lymphovascular invasion						
Positive	59 (86.8)	9 (13.2)	.448	36 (73.5)	13 (26.5)	.821
Negative	92 (91.1)	9 (8.9)		43 (76.8)	13 (23.2)	
PR status						
Positive	128 (97.7)	3 (2.3)	**<.01**	72 (93.5)	5 (6.5)	**<.01**
Negative	21 (56.8)	16 (43.2)		7 (25.0)	21 (75.0)	
HER2/neu status						
Positive	23 (60.5)	15 (39.5)	**<.001**	6 (26.1)	17 (73.9)	**<.001**
Equivocal	7 (87.5)	1 (12.5)		1 (20.0)	4 (80.0)	
Negative	121 (96.8)	4 (3.2)		70 (94.6)	4 (5.4)	

Data are number (percentage).Statistical analyses by Pearson's chi-squared test.

and in menopausal patients (*P*=.027). Regardless of the AR expression status, ER was significantly associated with expression of PR and absence of HER2/neu expression (*P*<.001 for each).

Forty deaths occurred among 144 patients who completed the 5-year follow-up. In the overall survival analysis, a significantly favorable prognosis (*P*=.022) was observed in AR-positive cases in comparison to AR-negative cases (**Figure 2A**). After stratifying these cases according to ER status, AR expression was also positively associated with overall survival (*P*=.012) in the ER-positive group (**Figure 2B**), but not in ER-negative tumor cases (*P*=.987) (**Figure 2C**). In the multivariate Cox regression models for overall survival, statistical significance of AR expression disappeared when adjusting for the clinicopathological parameters previously discussed (data not shown).

DISCUSSION

The prevalence of AR expression, its biological role, and prognostic significance in breast cancer are well established.[16,27-30] For example, a significant association between AR expression with decreased recurrence rate among all breast cancer types and better overall survival in ER-positive tumors has been reported.[17] Other studies have suggested considering AR expression as an independent prognostic factor from tumor size, stage, and grade.[31-33] In a study analyzing 678 cases of breast cancer, 396 of which were of the non-basal triple negative subtype, AR expression was associated with better overall patient survival and was inversely associated with tumor grade.[34] Thus, the determination of AR expression appears to be a promising approach to achieve better understanding of breast cancer. This study aimed to determine the prevalence rate of AR expression in breast cancer in association with immunohistochemical and clinicopathological criteria.

Studies have reported a prevalence rate ranging between 40% and 80%.[17,19,35,36] In 2010, Castellano et al reported an expression rate of 70.9% among 859 ER-positive tumors.[32] Another study by Agrawal et al demonstrated an AR expression rate in 43.7% of 96 cases of predominantly ER-positive invasive breast carcinomas.[19] In Korea, the percentage was close to 58% among 931 patients.[26] Higher rates of expression reaching 80% were reported by two other studies.[37,38] Our study demonstrates an expression rate of 61.4%, which is in agreement with other studies.

We also studied the association between AR receptor expression and other hormones. AR was expressed in 88% of ER-positive tumors in comparison to only 12% of ER-negative tumors. Many studies have reported that

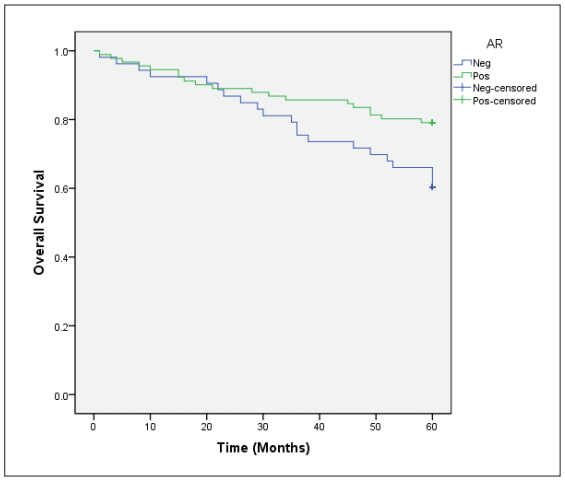

Figure 2A. Overall survival according to AR expression in general (*P*=.022 for AR-positive vs AR-negative cases).

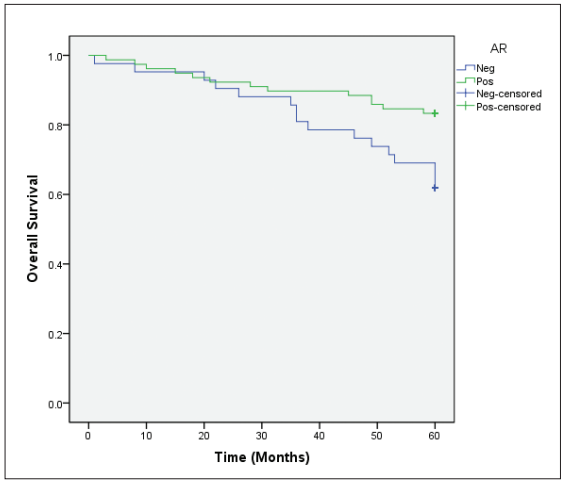

Figure 2B. Overall survival according to AR expression in the ER-positive group (*P*=.012 for AR-positive vs AR-negative cases).

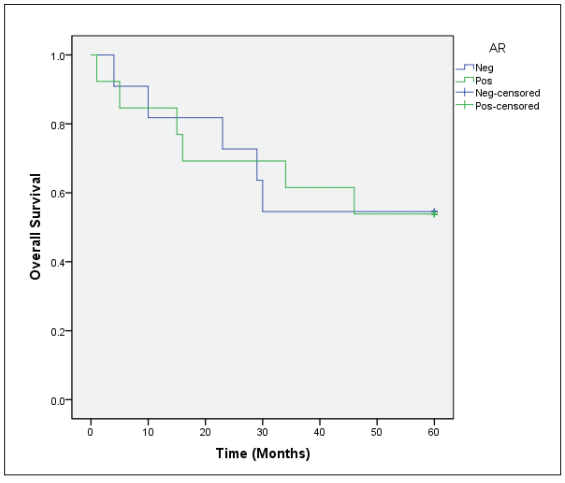

Figure 2C. Overall survival according to AR expression in the ER-negative group (*P*=.987 for AR-positive vs AR-negative cases).

AR expression was higher in ER-positive tumors compared to ER-negative tumors.[18,37-39,41] These included two studies from Egypt.[39,41] AR was expressed among 95% of ER-positive tumors in comparison to only 10% of estrogen-negative tumors in another study.[40] This positive relationship was also linked with a more favorable prognosis among ER-positive patients.[11]

We found no association between AR and PR or HER-2/neu expression status (*P*=.968 and *P*=.226, respectively). In contrast, AR expression correlated with PR positivity and HER-2/neu negativity in many studies.[18,31,41,42] The low sample number could be a factor in our findings.

We found that 48.4% of TNBCs expressed AR, which was higher than the 30% reported by Farag et al from Egypt.[43] These tumors are generally more aggressive than their ER-positive counterparts, with higher rates of relapse in the early stages and decreased overall survival rates.[44,45] International studies reported variable expression rates.[46-48] A more recent study reported an expression rate of 24.8% among TNBCs, and an even lower expression rate in African American women.[34]

A significant relationship was found between AR expression and the histologic grades of tumors. Many studies have found that AR expression correlates with a lower overall tumor grade.[26,36,37,41] Lower grade tumors tend to have better prognosis, and hence, the expression of AR can serve as a good prognostic indicator. We found no significant association between tumor grade and AR expression. However, AR was expressed more frequently in grade I tumors (65.7%) as compared to grade III tumors (59.8%).

No significant association was observed between menopausal status and AR expression in our study. In an Egyptian study, a significantly increased expression of AR in postmenopausal patients was found.[41] Patients whose tumors expressed AR were more likely to have a longer disease-free survival than those with AR-negative tumors.[49] Similar results were reported in another study in which researchers found a significant association between high AR expression and distant metastasis-free survival among 250 cases of invasive breast carcinoma.[18] Although we found no significant association between AR expression and the presence of distant metastasis or lymph node metastasis, AR-positive tumors tended to be negative for both criteria. It is possible that inclusion of more samples could reveal a positive association.

A functional relationship has previously been reported between ER and AR whereby AR has an antagonistic effect to ER.[33] In fact, the potential therapeutic effects of aromatase inhibitors may be due to both a reduction in estrogen levels and an increase in inhibitory AR signaling pathways.[50] In support of the latter observation is a large retrospective study that demonstrated a prognostic and predictive role of AR in the subset of ER-positive tumors.[32] However, in ER-negative tumors, the situation is different as there is no benefit of endocrine therapy, and tumors have a poor prognosis.[51] The lack of ER expression in breast cancer cells switches the inhibitory effect of AR to that of an oncogenic role, at least in cell lines.[52] Taken together, AR expression could be an additional significant factor for endocrine therapy for ER-positive cancers. For that reason, we analyzed the prognostic significance of AR according to ER expression status and vice versa. In ER-positive tumors, AR expression was significantly associated only with smaller tumor size as reported in a previous study.[16] However, there was no significant correlation with other clinicopathologic parameters, such as lymph nodal involvement, distant metastases, tumor histologic grade, and menopausal status. On the other hand, in patients with ER-negative cancer, AR expression was not statistically related to any clinicopathologic parameter in parallel with the latter study.[16]

Regardless of the AR expression status, ER status is significantly associated with expression of PR and absence of HER2/neu expression. A study on the expression of ARs in primary breast cancer and the relationship of ER, AR, and HER2/neu expression showed that AR was expressed significantly in correlation with HER-2/neu overexpression in ER-negative tumors, but not in ER-positive tumors.[48]

We showed an important implication of AR in prognosis. In univariate survival analyses, AR was generally a significant factor for overall survival outcome. This was also found in the ER-positive subgroup. However, the prognostic significance of AR disappeared in multivariate analyses. These findings were consistent with previous reports.[16,32,40] One limitation of this study was that some patient files had missing data. In conclusion, AR expression appears to be a prognostic factor, as it is associated with lower tumor grade and well-differentiated histologic type. This observation is consistent with what has been reported previously. These findings substantiate previous findings that AR is a good prognostic indicator. The high prevalence of AR expression in breast cancer is consistent with studies that support the use of anti-androgen therapy as beneficial in increasing survival. More studies among Jordanian breast cancer patients are needed to assess the actual rate of AR expression, not only in a single histologic subtype, but in other subtypes as well.

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