Androgen Receptor Score of Expression and its Correlation with Prognosis in Triple Negative Invasive Breast Cancer

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Abstract

Introduction: **Androgen receptor (AR) is thought to play a crucial role in determining the prognosis of breast cancer patients. No published research that studied score of AR expression and its impact on prognosis. Aim: to correlate the score of expression of AR with the clinicopathological features of triple negative breast cancer patients.** ***Methods:*** **Retrospective-prospective cohort (historical cohort) study of 30 files of breast cancer patients; classified/stratified and tested for Androgen Receptor score of expression, considering time to tumor progression (TTP) as primary end point, and overall survival (OS) as second end points.** ***Results:*** **with a mean follow-up period of 66 months (about 5.5 years), AR intermediate expression (score5) had the best prognosis in triple negative breast cancer female patients; for both TTP and OS (100% had TTP to the 12th year and 100% had OS to the 14th year).** ***Conclusion:*** **Androgen receptor intermediate expression had the best prognosis in triple negative invasive breast cancer female patients. We recommend testing androgen receptors in breast cancer patients whenever feasible; to keep it as a possible target (if positive) in case of failure of the approved lines of treatment.**

Key words: Overall survival, Time to Tumor Progression, Androgen Receptor

Introduction, Aim and Rationale

Breast cancer is the most common cancer in women both in the developed and less developed world. Androgen receptor is a member of the nuclear steroid hormone receptor family, which also includes ER and PR. Steroid hormone receptors are critical components of signaling pathways and play a crucial role as transcription factors regulating gene expression. Although ER and PR are widely recognized for their prognostic and predictive roles in breast cancer, the biological role of androgen receptor in breast cancer is still emerging. (1)

In 2013, Tiffany A. Traina and colleagues experienced bicalutamide as an anti-androgen in treating triple negative androgen receptor positive breast cancer patients; as a phase II trial. AR was expressed in 12% of patients with ER/PgR-negative breast cancer screened for this trial. The CBR of 19% observed with bicalutamide shows proof of principle for the efficacy of minimally toxic androgen blockade in a select group of patients with ER/PgR-negative, AR-positive breast cancer. (2)

In 2014, a case report was published and mentioned the role of bicalutamide in the treatment of a patient with metastatic

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breast cancer with chest wall lesions –as a clinical trial- after progression following many lines of treatment. After 4 months of treatment, the patient achieved a complete clinical response according to RECIST criteria for at least 12 months after starting treatment. (3).

In 2015, another case report was published. It was about an old-aged (91 years old) from South Asia. She was unfit for any chemotherapy line of treatment. Flutamide, an antiandrogen was prescribed, well tolerated and resulted in good response for at least 1 year and 10 months. (4)

No study had been done to test whether the degree/score of androgen receptor expression differ in prognosis among different subtypes of breast cancer.

Aim and rationale: This study is done to evaluate the expression of Androgen receptor and to correlate its degree of expression with the different clinicopathological features for breast cancer patients; to be able to bring new option of treatment and new hope and of course; for better lifestyle for breast cancer patients attending Clinical Oncology and Nuclear Medicine department at Suez Canal University Hospital.

Subject & methods

It was a Retrospective-Prospective Cohort Study (to study the correlation between score/degree of androgen receptor expression and the clinicopathological features and prognosis for simple random sample from all triple negative invasive breast cancer patient attending clinical oncology and nuclear medicine department in Suez Canal university hospital in period from January 2015 until December 2019. Patients with unknown hormonal receptors status and patients who refuse to participate in the study were excluded.

When diagnosed as breast cancer patient, the patient is referred to our clinical oncology and nuclear medicine department to start the plan of management. Routinely, the paraffin block is requested to test for hormonal receptors namely: Estrogens-Receptor, Progesterone-Receptor and HER-2neu. Then, the patient will be asked whether to accept or to refuse testing for the Androgen Receptor using his/her same initial paraffin block without any new tissue biopsy. Result of the Androgen receptor expression was correlated to the patient clinicopathological data already present in the patient archive file records in the department.

Data was collected and coded then entered as a spread sheets using SPSS. Patients were categorized into groups having the same clinicopathological features and treatment received; in order to avoid cofounding. Data was analyzed using SPSS. Data are presented as tables and graphs, t test was used to compare between quantitative data expressed as mean and standard deviation. P value < 0.05 was considered as significant. Kaplan Meier curves were used to estimate survival.

Concerning ethical considerations, Data was collected from archive files in Suez Canal University hospital clinical oncology department (SCUCOD). Approval of the staff responsible in the SCUCOD and approval of the Ethics committee in the Faculty of Medicine- Suez Canal University were obtained before starting field work. Confidentiality was maintained. The patient had the right to accept or to refuse participating in the study. The study

had no harm on the patient; and no invasive maneuver. The patient had the right to cancel his participation in the study at any time and without giving any excuse.

Results:

A mean of 162 patients per year attended clinical oncology department in Suez Canal University hospital, in the period between January 2015 and December 2017. Hence, the sample size was calculated to provide 95% confidence interval and to ensure reliability of Data.

107 female patients with breast cancer were tested for androgen receptor on their paraffin block. Regarding molecular classification; 43 patients were hormonal receptor (HR) positive, HER2Neu negative. 39 had ER, PR +VE/HER2Neu –ve; while 4 had ER +ve, PR and HER2Neu –ve. 30 patients were triple negative, 24 patients were HER2Neu positive while only 10 patients had triple positive breast cancer.

Here, we study only triple negative patients. 30 patients' files were included and studied. 30 paraffin blocks – corresponding to each of the 30 patients/files were tested for androgen receptor expression via immunohistochemistry.

Sections from the selected paraffin blocks were cut into 4 micrometers thick sections for immunohistochemical (IHC) staining. Slides were prepared and incubated with primary anti-AR antibody (Lot and Company). This was followed by incubations with the propriate secondary antibody (Lot and Company). All slides are lightly counterstained with hematoxylin for 30s prior to dehydration and mounting.

Immunohistochemical scoring

Invasive tumor cells with nuclear reaction to AR antibody were considered positive. Semi-quantitative analysis of stained tissue sections was performed through modified Allred scoring system guidelines **. Positive cells were counted in 3 different high-power fields (hpf) (400x) *(Figure 1)* and the average number was calculated. Individual scores of the percentage of positive cells (0–5) and the staining intensity of the cytoplasm (0–3) were summed up to obtain the final grades. The percentage of positive cells was set as follows: 1-less than 10 positive cells; 2- from 10 to 20 of positive cells; 3-from 20 to 50 positive cells; 4-from 50 to 70 positive cells; and score 5-more than 70 positive cells. The staining intensity of positivity in the cytoplasm was scored as: 1-weak; 2-moderate; and 3-strong.

Final score was calculated by the sum of number of positive cells in HPF and the intensity of staining of the cytoplasm. Final score of Zero is considered negative. Final score of 3 in addition to Zero is considered low.

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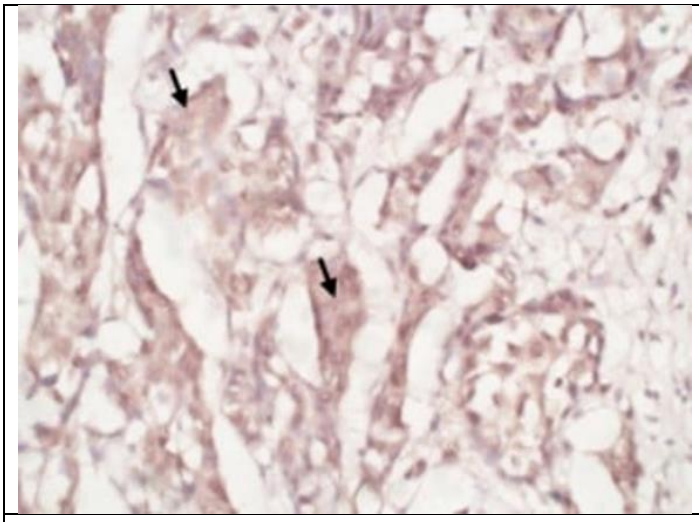
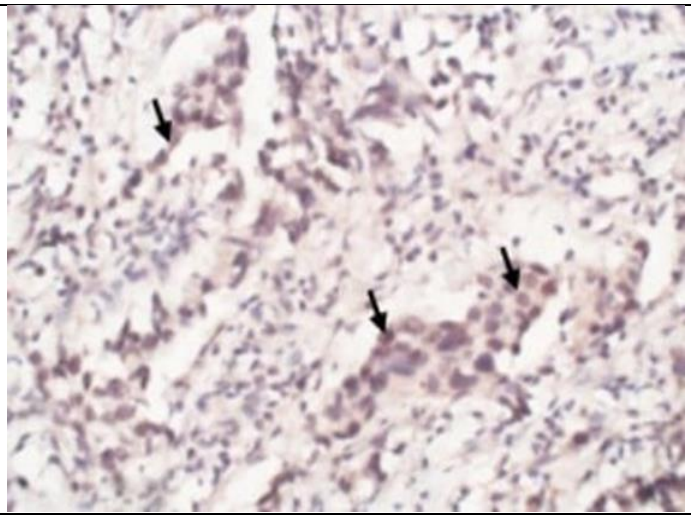
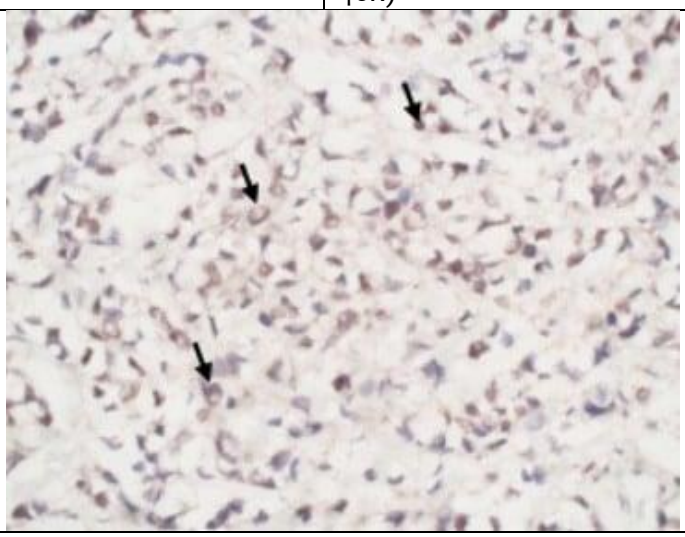


Grade I invasive ductal carcinoma tumor cells showing strong nuclear and cytoplasmic reaction to AR (Black arrows) (IHC, 40x)



Grade II invasive ductal carcinoma tumor cells showing moderate nuclear reaction to AR (Black arrows) (IHC, 40x)



Grade III invasive ductal carcinoma tumor cells showing moderate nuclear reaction to AR (Black arrows) (IHC, 40x)

Figure 1: Androgen receptor expression with Hematoxylin and Eosin staining

Androgen receptor degree of expression was estimated by the number of positive cells per high power field plus the intensity of its staining; both yielding a final score.

Final score of androgen receptor expression in our study ranged from 0 then 3 to 8. Score was defined as follows:

0 → Negative/ No androgen receptor expression
3 → Low positive expression
4 → Low to intermediate expression
5 → Intermediate expression
6 → Intermediate to high expression
7 → High expression
8 → Highest / Very high expression

Patients' characteristics including demographic, different clinic-pathological data are summarized in the table below. *(Table 1)*

Table 1: Triple negative breast cancer female patients clinicopathological data.		
Comparison 3 triple negative	Number	Percentage
Age at diagnosis	30	100%
Younger than 35	3	10%
36-50 years	11	36.7%
Older than 50 years	16	53.3%
Menopausal status at diagnosis	30	100%
Premenopausal	19	63.3%
Postmenopausal	11	36.7%
Body Mass Index at diagnosis	30	100%
Obese	14	46.7%
Overweight	16	53.3%
Co-morbidities	30	100%
No history of any chronic illness	14	46.7%
Diabetes mellitus	6	20%
Hypertension and diabetes mellitus	10	33.3%
Presenting symptom	30	100%
Breast lump	30	100%
Side	30	100%
Right breast	6	20%
Left breast	24	80%
Operation	30	100%
Modified Radical Mastectomy	20	66.7%
Conservative breast surgery	5	16.7%
Biospy as locally advanced	5	16.7%
Histopathological Subtype	30	100%
Invasive ductal carcinoma	28	93.3%
Metaplastic carcinoma	2	6.7%
Grading	30	100%
Grade 1	3	10%
Grade 2	16	53.3%
Grade 3	11	36.7%
Tumor Size	30	100%
T1	3	10%
T2	14	46.7%
T3	6	20%
Locally advanced T4	7	23.3%
Nodal Status	30	100%
N0	8	26.7%
N1	6	20%
N2	8	26.7%
N3	8	26.7%
Distant Metastasis	30	100%
M0	24	80%
M1	6	20%
Extranodal Extension	30	100%
No	15	50%

Positive	8	26.7%
Unknown as no surgery/ lymph node dissection done	7	23.3%
Surgical margins	30	100%
Free	23	76.7%
Unknown as no surgery done	7	23.3%
Multicentricity	30	100%
No multicentricity	23	76.7%
Unknown/ no surgery done	7	23.3%
Multifocality	30	100%
No multifocality	23	76.7%
Unknown/ no surgery done	7	23.3%
Early versus advanced	30	100%
Early	10	33.3%
Locally advanced	6	20%
Advanced metastatic	6	20%
Resectable advanced	8	26.7%
Neoadjuvant chemotherapy if any	30	100%
No	24	80%
Yes	6	20%
Regimen of neoadjuvant chemotherapy if any	30	100%
None received	24	80%
3 FEC	3	10%
3 Vinorelbine/ Cisplatin	3	10%
Adjuvant Chemotherapy	30	100%
No adjuvant chemotherapy	2	6.7%
6 FEC	8	26.7%
4 AC then 12 Paclitaxel weekly	2	6.7%
4 AC then 4 Paclitaxel every 3 weeks	6	20%
4 FEC then 4 Paclitaxel/ Carboplatin	6	20%
3 Vinorelbine/ Cisplatin	6	20%
Post-operative Radiotherapy	30	100%
No adjuvant radiotherapy	8	26.7%
50Gy/25#	19	63.3%
45Gy/18#	3	10%
Androgen Receptor Expression Final Score	30	100%
0	3	10%
3	3	10%
4	3	10%
5	5	16.7%
7	5	16.7%
8	11	36.7%

Cross Correlation of different scores/degrees of androgen receptor expression against multiple variables are illustrated below in the following Kaplan Meier survival Curves. Scores 0 to 8 against many variables tested separately

to avoid confounding. Variables: Age, Menopausal status, body mass index, early versus advanced stage. Time to Tumor Progression and Overall Survival: Generally: (Figure 2)

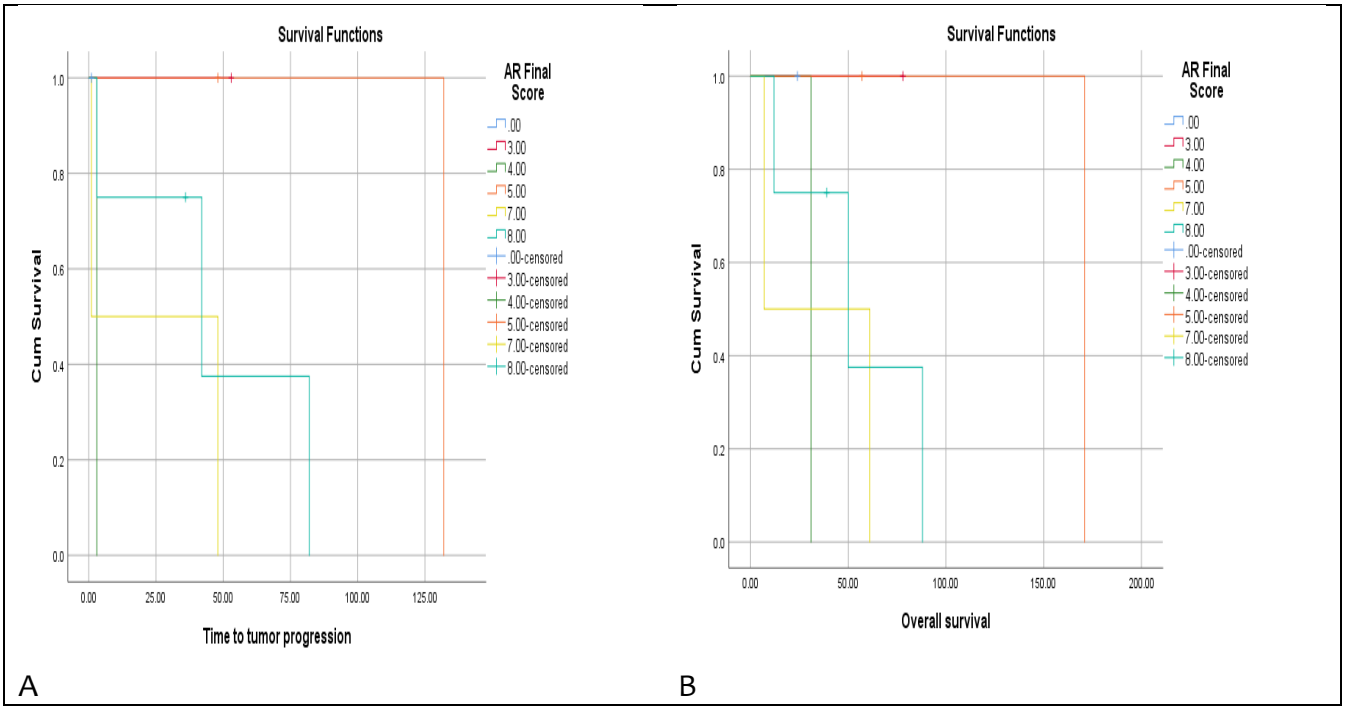


Figure 2: Time to tumor progression and overall survival in triple negative patients generally.

The Kaplan-Meier curve *(Figure 2-A)* shows time to tumor progression when comparing the levels of androgen receptor expression in **triple negative** patients **generally**; as follows:
Score 5: 100% → 135 months
Score 4: 100% → 4 months… 75% → 33 months… 38% → 85 months.
(with overall maximal standard error: 0.354)

The Kaplan-Meier curve *(Figure 2-B)* shows the overall survival in **triple negative** patients **generally**; as follows:
Score 5: 100% → 170 months
Score 4: 100% → 30 months
Score 8: 100% → 15 months… 75 % → 50 months… 38% → 90 months
Score 7: 100% → 10 months… 50% → 65 months (with maximal standard error: 0.354)
With body mass index: (Figure 3)

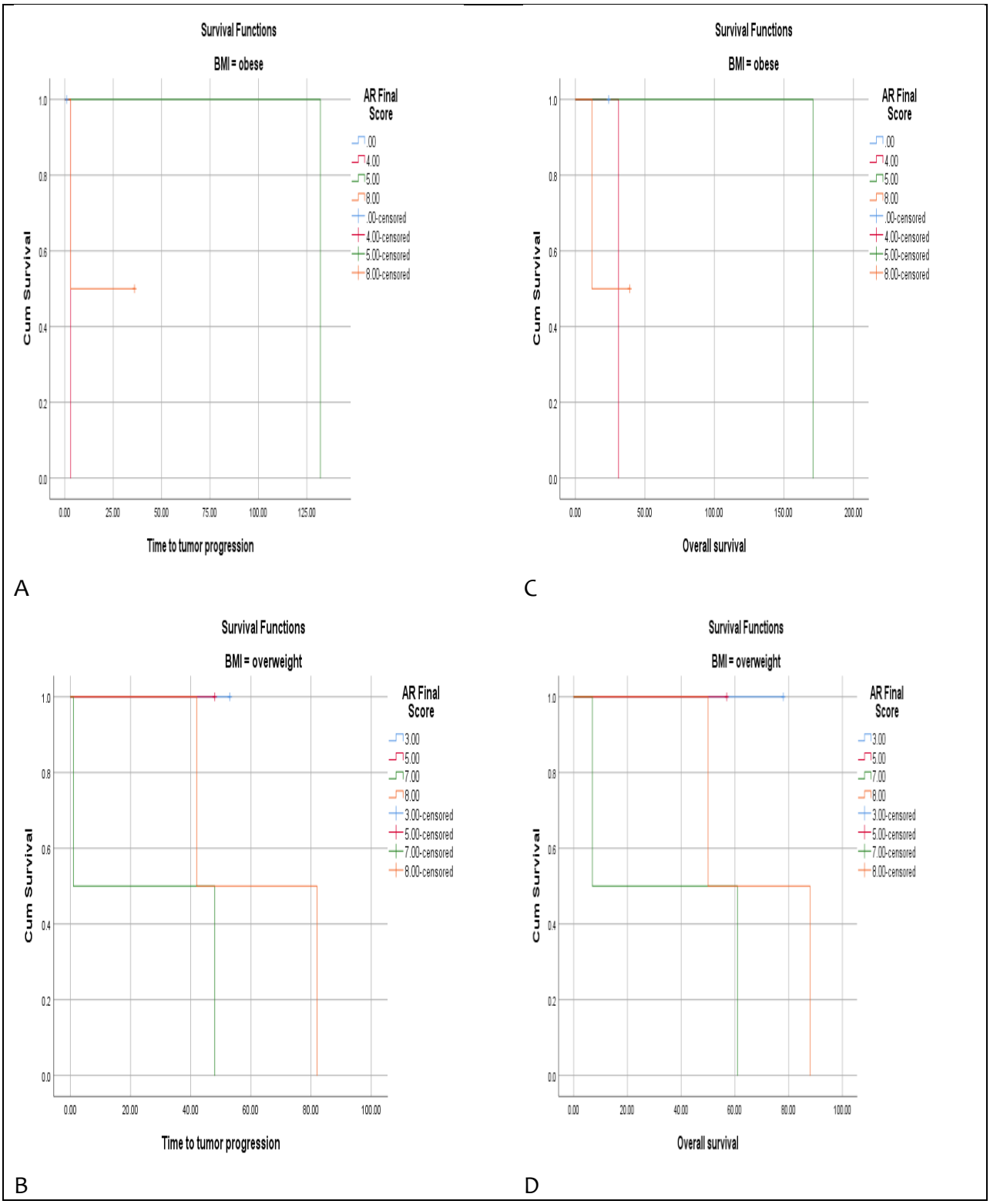
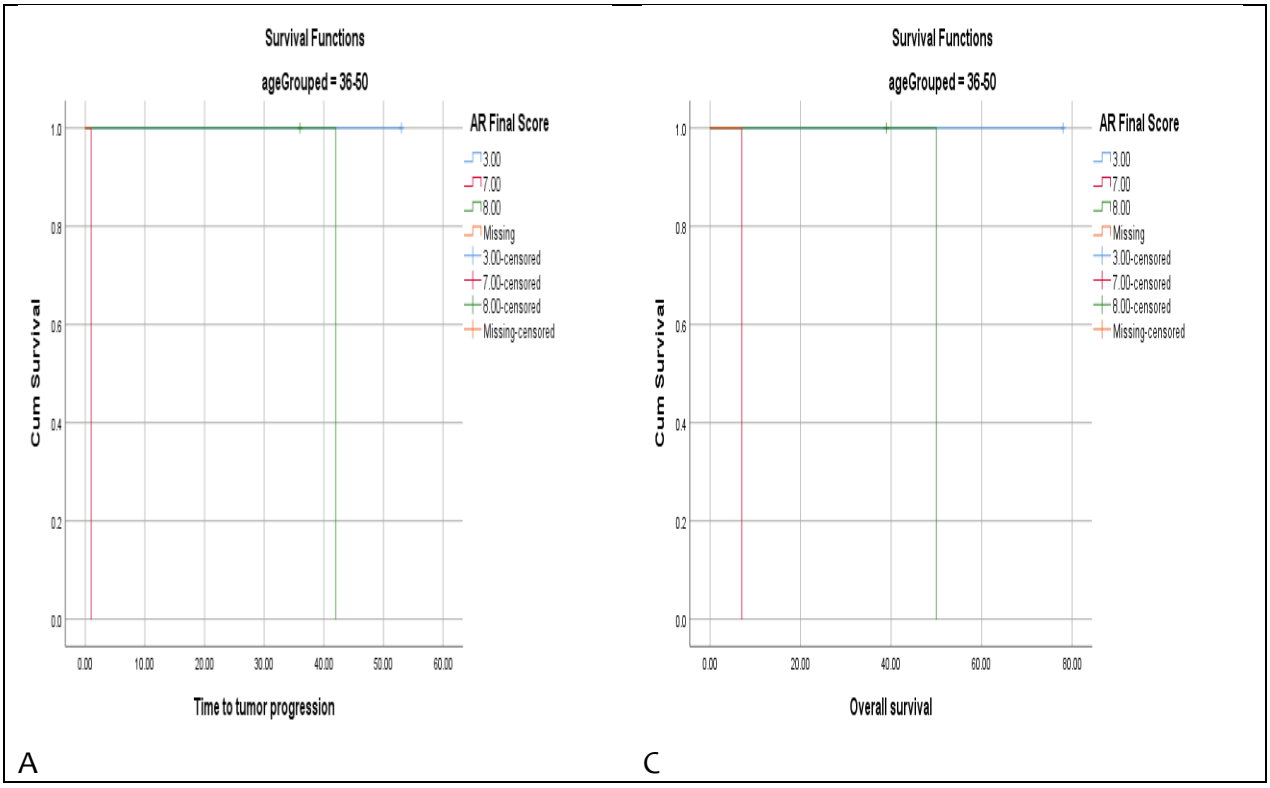


Figure 3: Time to tumor progression and overall survival in triple negative patients plotted against body mass index status.

The Kaplan-Meier curve *(Figure 3-A)* shows time to tumor progression when comparing the levels of androgen receptor expression in **obese triple negative** patients as estimated by body mass index (BMI); as follows:
Score 5: 100% → 135 months
Score 8: 100% → 4 months… 50% → 30 months
Score 4: 100% → 4 months.
(with overall maximal standard error: 0.500)
The Kaplan-Meier curve *(Figure 3-B)* shows time to tumor progression when comparing the levels of androgen receptor expression in **overweight triple negative** patients as estimated by body mass index (BMI); as follows:
Score 3: 100% → 52 months
Score 5: 100% → 48 months
Score 8: 100% → 42 months… 50% → 82 months
Score 7: 100% → 3 months… 50% → 48 months.
(with overall maximal standard error: 0.500)
The Kaplan-Meier curve *(Figure 3-C)* shows the overall survival in **triple negative obese** patients as estimated by Body Mass Index (BMI); as follows:
Score 5: 100% → 170 months
Score 4: 100% → 30 months
Score 8: 100% → 15 months… 50% → 40 months
(with maximal standard error: 0.354)
The Kaplan-Meier curve *(Figure 3-D)* shows the overall survival in **triple negative overweight** patients as estimated by Body Mass Index (BMI); as follows:
Score 3: 100% → 78 months
Score 8: 100% → 50 months … 50% → 88 months
Score 5: 100% → 56 months
Score 7: 100% → 15 months… 50% → 62 months (with maximal standard error: 0.354)
With age group: (Figure 4)



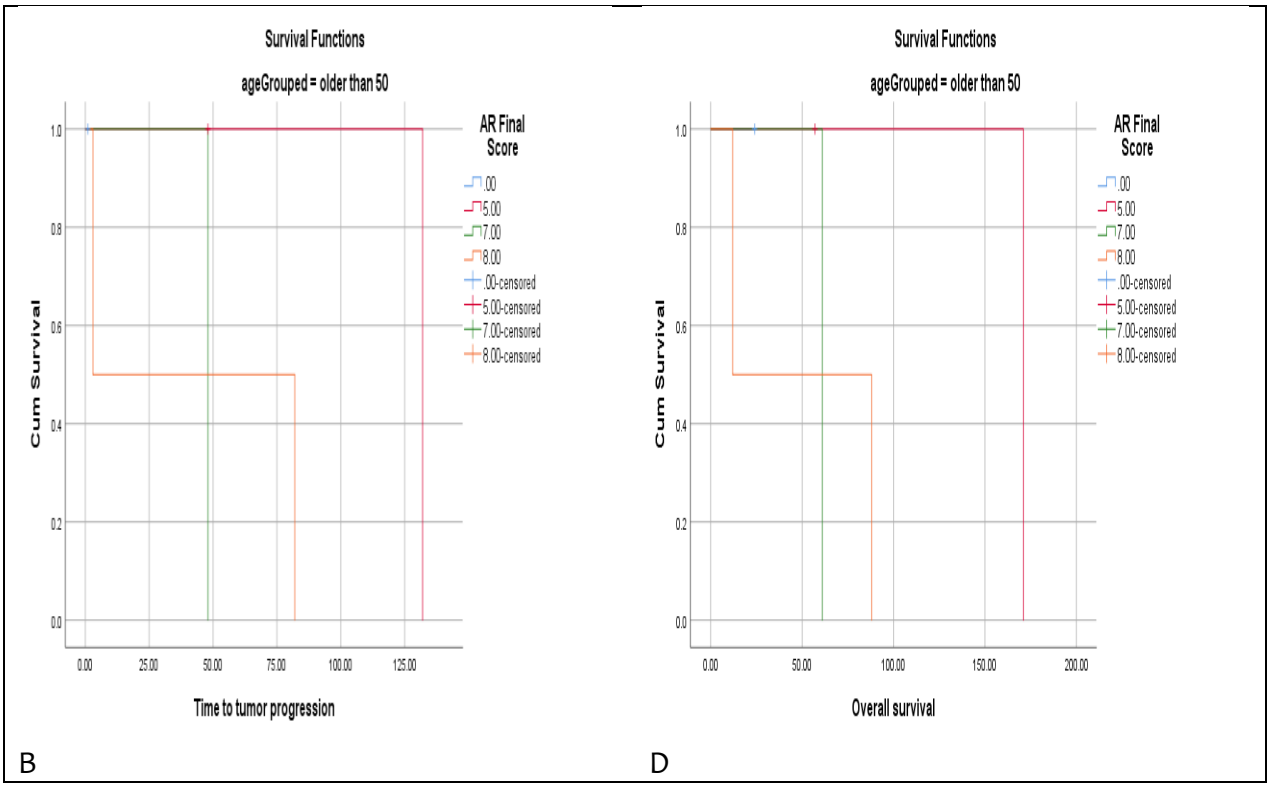


Figure 4: Time to tumor progression and overall survival in triple negative patients plotted against age group.

The Kaplan-Meier curve *(Figure 4-A)* shows time to tumor progression when comparing the levels of androgen receptor expression in **triple negative** patients with regard to **age 36 to 50 years;** as follows:

Score 3: 100% → 57 months
Score 8: 100% → 45 months
Score 7: 100% → 4 months.
(with overall maximal standard error: 0.000)

The Kaplan-Meier curve *(Figure 4-B)* shows time to tumor progression when comparing the levels of androgen receptor expression in **triple negative** patients with regard to **age older than 50 years;** as follows:

Score 5: 100% → 135 months
Score 7: 100% → 48 months
Score 8: 100% → 4 months… 50% → 85 months.
(with overall maximal standard error: 0.500)

The Kaplan-Meier curve *(Figure 4-C)* shows the overall survival in **triple negative** patients aging 36 to 50 years; as follows:

Score 3: 100% → 78 months
Score 8: 100% → 50 months
Score 7: 100% → 20 months
(with maximal standard error: 0.000)

The Kaplan-Meier curve *(Figure 4-D)* shows the overall survival in **triple negative** patients aging **older than 50 years;** as follows:

Score 5: 100% → 170 months
Score 7: 100% → 60 months
Score 8: 100% → 15 months… 50 % → 85 months
(with maximal standard error: 0.354)

With menopausal status: (Figure 5

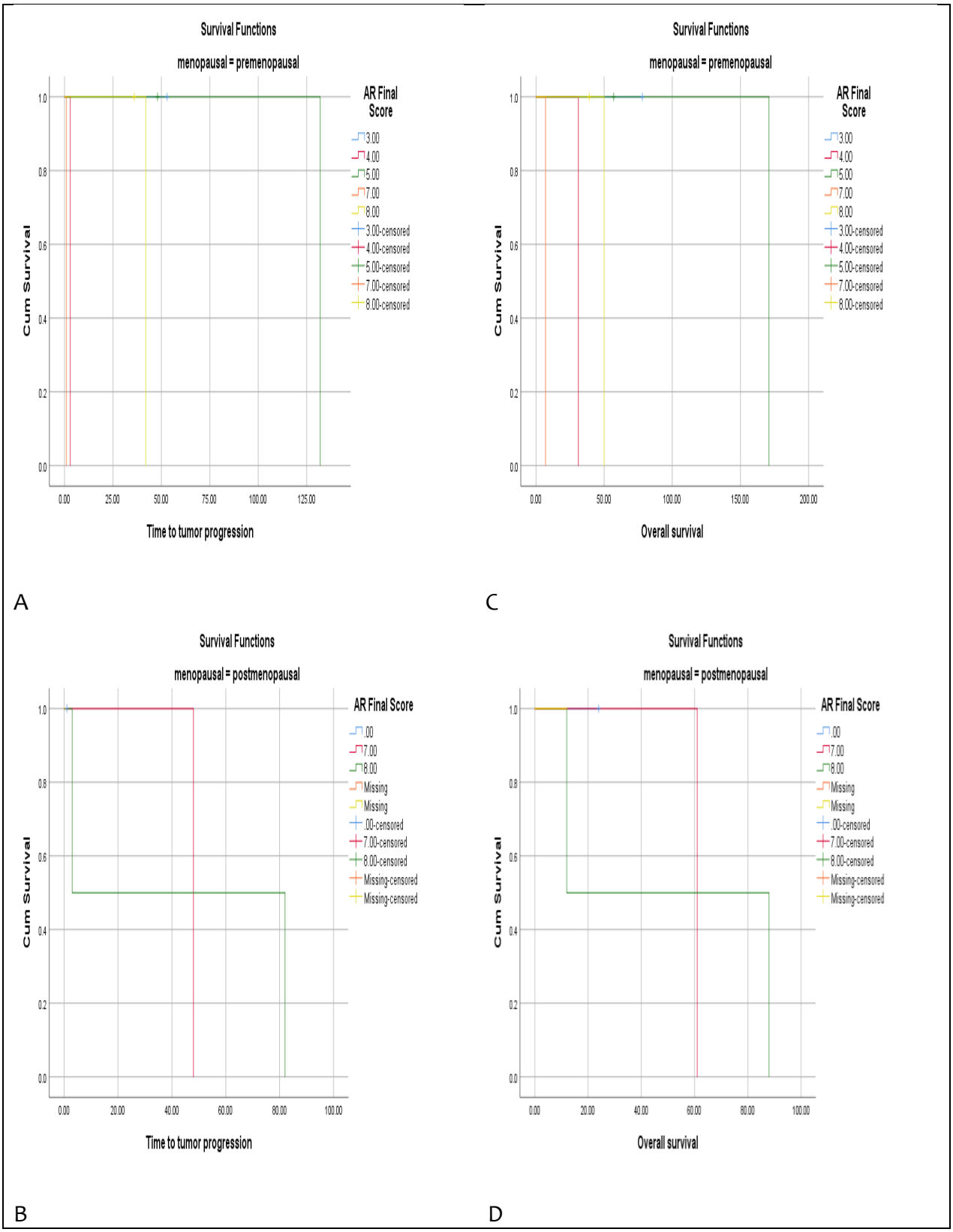
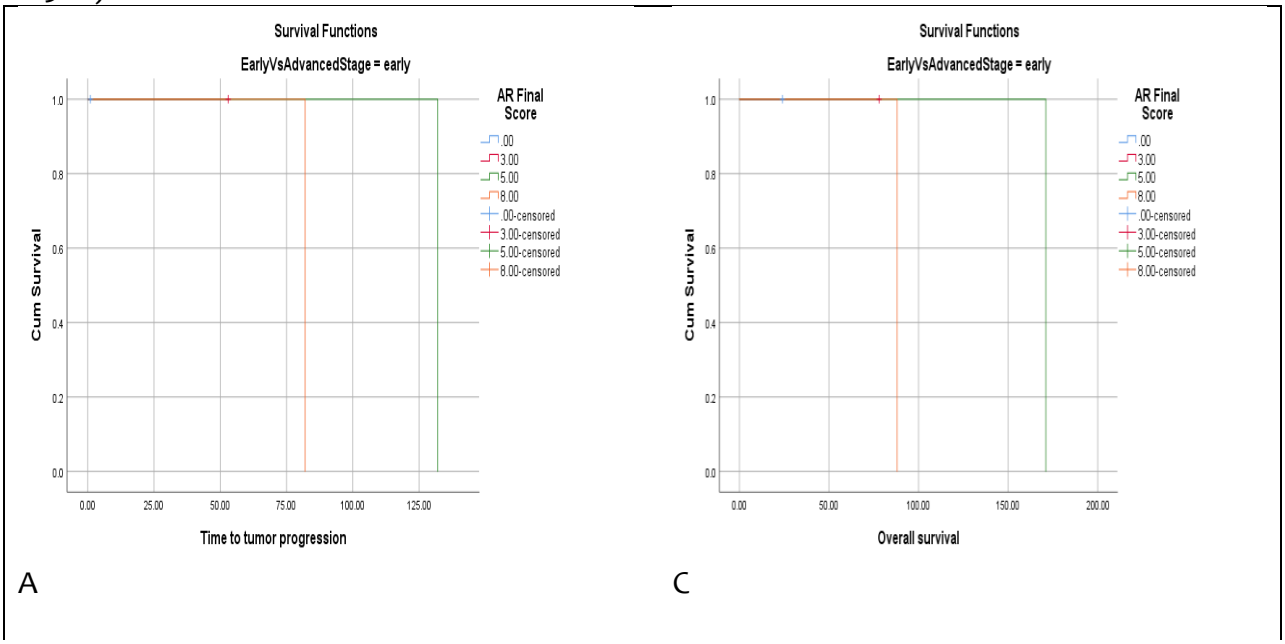
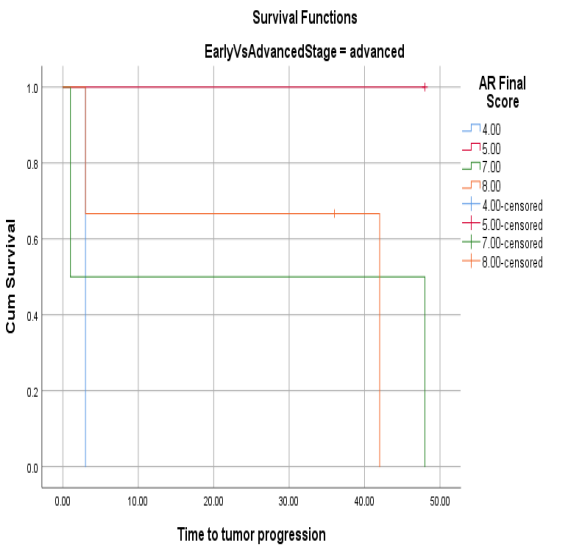


Figure 5: Time to tumor progression and overall survival in triple negative patients plotted against menopausal status.

The Kaplan-Meier curve *(Figure 5-A)* shows time to tumor progression when comparing the levels of androgen receptor expression in **premenopausal triple negative** patients; as follows:
Score 5: 100% → 135 months
Score 8: 100% → 42 months
Score 4: 100% → 5 months.
(with overall maximal standard error: 0.000)
The Kaplan-Meier curve *(Figure 5-B)* shows time to tumor progression when comparing the levels of androgen receptor expression in **postmenopausal triple negative** patients; as follows:
Score 7: 100% → 48 months
Score 8: 100% → 4 months… 50% → 82 months
Score 0: 100% → 2 months.
(with overall maximal standard error: 0.500)

The Kaplan-Meier curve *(Figure 5-C)* shows the overall survival in **triple negative premenopausal** patients; as follows:
Score 5: 100% → 170 months
Score 3: 100% → 35 months
Score 8: 100% → 50 months
Score 4: 100% → 35 months
Score 7: 100% → 8 months
(with maximal standard error: 0.000)
The Kaplan-Meier curve (Figure 5-D) shows the overall survival in **triple negative postmenopausal** patients; as follows:
Score 7: 100% → 62 months
Score 0: 100% → 25 months
Score 8: 100% → 35 months… 50 % → 88 months (with maximal standard error: 0.354)





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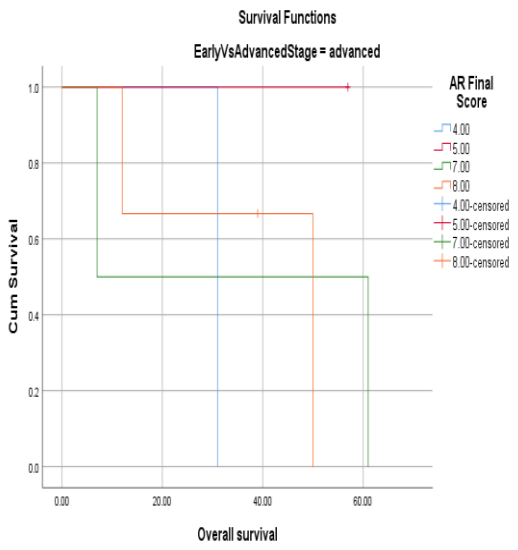

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Figure 6: Time to tumor progression and overall survival in triple negative patients plotted against stage.

The Kaplan-Meier curve (*Error! Reference s ource not found.*) shows time to tumor progression when comparing the levels of androgen receptor expression in **triple negative** patients with regard to **early stage**; as follows:

Score 5: 100% → 140 months
Score 8: 100% → 85 months
Score 3: 100% 54 months.
(with overall maximal standard error: 0.000)

The Kaplan-Meier curve (*Error! Reference s ource not found.*) shows time to tumor progression when comparing the levels of androgen receptor expression in **triple negative** patients with regard to **advanced stage** ; as follows:

Score 5: 100% → 47 months
Score 7: 100% → 2 months… 50% → 47 months
Score 8: 100% → 4 months… 67% → 42 months.
(with overall maximal standard error: 0.667)

The Kaplan-Meier curve (*Error! Reference s ource not found.*) shows the overall survival in **triple negative** patients with **early stage**; as follows:

Score 5: 100% → 170 months
Score 8: 100% → 83 months
Score 3: 100% → 75 months
Score 0: 100% → 25 months (with maximal standard error: 0.000)

The Kaplan-Meier curve (*Error! Reference s ource not found.*) shows the overall survival in **triple negative** patients with **advanced stage**; as follows:

Score 5: 100% → 56 months
Score 7: 100% → 8 months … 50% → 62 months
Score 4: 100% → 32 months
Score 8: 100% → 13 months… 68% → 50 months (with maximal standard error: 0.354)

Summary and Statistical significance for Time to Tumor Progression and Overall Survival:

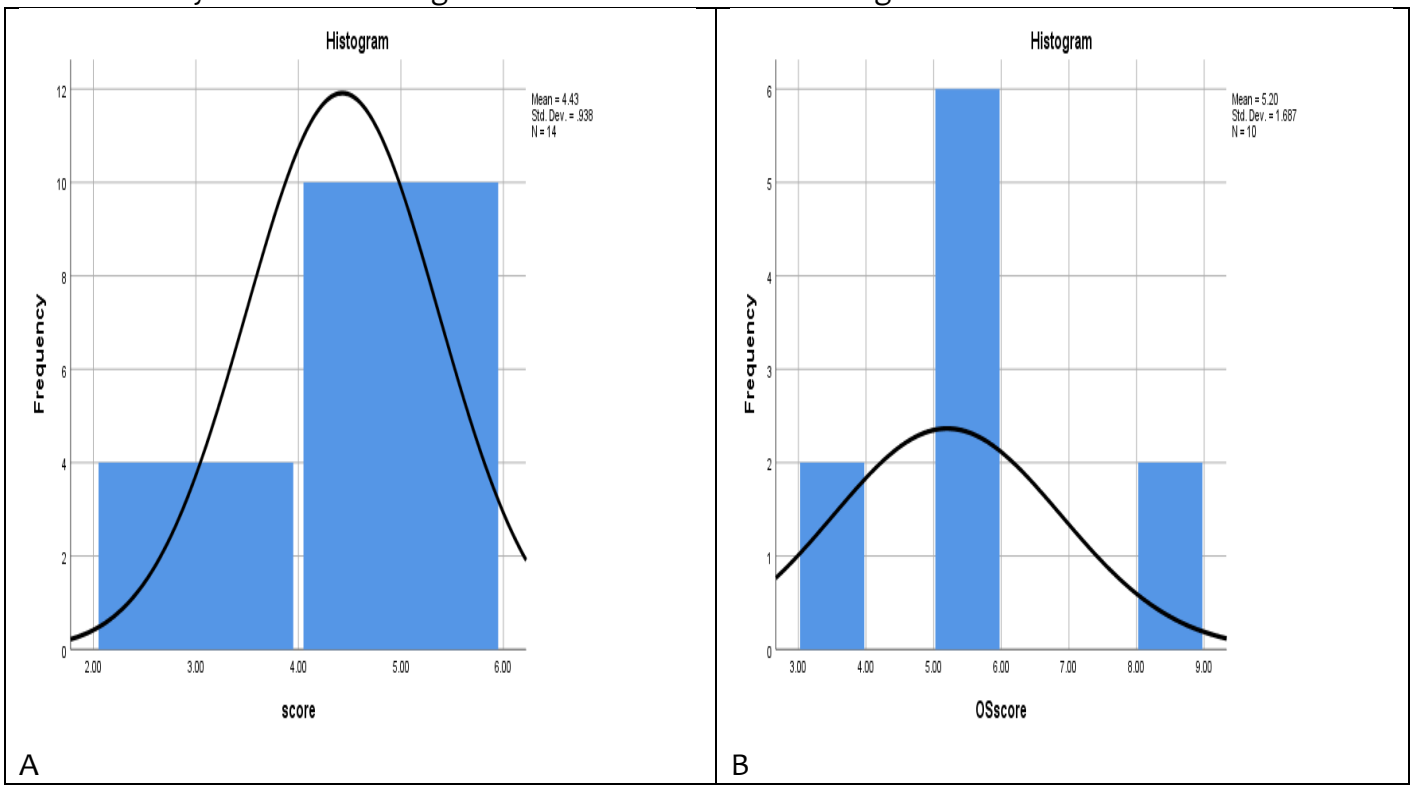

Figure 7: Score 5 as degree of androgen receptor expression is the predominant with best time to tumor progression (TTP) and Overall survival (OS) in all triple negative patients.

The histogram *(Figure 7-A)* shows that score 5 as degree of androgen receptor expression is the predominant and has the best time to tumor progression (TTP) in all triple negative patients in our study. Z score = -15.51. P-Value is < .00001. (statistically significant)

The histogram *(Figure 7-B)* shows that score 5 as degree of androgen receptor expression is the predominant and has the best overall survival (OS) in all triple negative patients in our study. Z score = -4.172. P-Value is 0.7078. (statistically not significant)

Discussion

Androgen receptors have recently become one of the vital areas of research in breast cancer worldwide. It emerged at first on the way to search for a new target therapy for triple negative breast cancer; to find any possible long-term maintenance treatment that would importantly also ensure an average quality of life.

After some surprising promising results reported by some studies and case reports, a new way of curious thinking suggested searching for its role in all breast cancer patients including and/or other than triple negative breast cancer patients.

Hence, in our study, we included all breast cancer female patients; female patients to avoid confounding higher androgen levels in male breast cancer patients than those in females.

Sample size was calculated based on the total number of breast cancer patients treated in our Suez Canal University

Clinical Oncology Department. 810 breast cancer patients attended in the period from January 2005 to December 2017 (mean= 162 per year). Sample was defined by keeping a 95% confidence interval; is able to reliably represent the study population.

When running across the literature, during the years of our study, several scientific papers were published about the role of androgen receptors in breast cancer. Those papers are from different countries, with different ethnic races, and with different results concerning the role of androgen receptors in the prognosis of breast cancer. Therefore, still many research be needed to define its role.

30 female patients with breast cancer were tested for androgen receptor on their paraffin block. Patients were randomly selected keeping in mind to respect the inclusion and exclusion criteria.

Clinicopathological data was collected from their confidential files in our department file archive. Androgen receptor was tested on their paraffin blocks by immunohistochemistry. Androgen receptor degree of expression was estimated by the number of positive cells per high power field plus the intensity of its staining; both yielding a final score.

Final score of androgen receptor expression in our study ranged from 0 then 3 to 8. Score was defined as follows:

0 → Negative/ No androgen receptor expression
3 → Low positive expression
4 → Low to intermediate expression
5 → Intermediate expression
6 → Intermediate to high expression
7 → High expression
8 → Highest / Very high expression

Androgen receptor was tested on 107 randomly chosen paraffin blocks (but after been reassured that they are fulfilling the inclusion and excluding the exclusion criteria). 30 patients with triple negative breast cancer had positive androgen receptor expression and were studied.

Kuenen-Boumeester V, Moinfar F, Vera-Badillo FE found –in different years- that Androgen receptor (AR) is expressed in 70% to 90% of primary breast cancers, a frequency that is comparable to or higher than that of either ER or PR. [5] [6] [7]

In our studied patients, 102 out of 107 patients (95.3%) had postive androgen receptor expression and 5 patients (4.7%) had negative androgen receptor expression.

This result comes in agreement with what was stated by Kuenen-Boumeester V, Moinfar F, Vera-Badillo FE.

This result was in contradiction with what was stated by Younes and colleagues in Menoufia where only 37.04% were immunoreactive to AR. [8].

Park S in 2010 reported that AR incidence of expression in TNBC, had a wide range (6.6% to 75%) (Significant variability in the reported literature). [9].

In our study, among triple negative female breast cancer patients, 27 out of 30 (90%) patients had positive androgen receptor staining of patients.

Our study results is in contradiction with the conclusion of Park S.

This heterogeneity primarily results from variability among reported studies in terms of the number of patients included and the cutoff used for AR positivity (≥1% or >10%). The source of primary antibody and methodology of testing are other reasons for variability among different studies. Another possible reason for the

variability could be the confounding effects of patient selection in prospective studies.

Traina TA and colleagues had studied patients with triple-negative breast cancer (TNBC) that have tumors expressing androgen receptor (AR) that may benefit from an AR inhibitor. This phase II study evaluated the antitumor activity of enzalutamide in patients with locally advanced or metastatic AR-positive TNBC. AR was expressed in 12% of patients with ER/PgR-negative breast cancer screened for this trial. The CBR of 19% observed with bicalutamide shows proof of principle for the efficacy of minimally toxic androgen blockade in a select group of patients with ER/PgR-negative, AR-positive breast cancer. [10]

In our study, intermediate degree of androgen receptor expression (score 7) had the best time to tumor progression (P-Value <0.00001) (statistically significant) and the best overall survival in triple negative breast cancer patients (P-Value: 0.7078) (statistically insignificant)

Arce-Sallinas C and colleagues had published a case report in 2014 of a 55 years old female patient with androgen receptor positive triple negative breast cancer with chest wall satellite nodules recurrence who received Bicalutamide after failure of many lines of treatment. She had complete tumor clinical response 4 months after treatment with Bicalutamide 150mg orally daily. [11]

Nakajima M and colleagues had published another case report of a 91 years old female patient with apocrine breast cancer. Her treating oncologists found that surgery under general anesthesia and hospital care would worsen the patient's general status. Tumor was tested negative for ER, PR, and HER2Neu and the Ki67 index was 10-20%. Androgen receptor was tested in a way to find any effective alternative treatment that would be less damaging than chemotherapy. Androgen receptor was tested positive and anti-androgen therapy "Flutamide 250mg daily dose." was prescribed. The patient received the treatment for more than 1 year and 10 months; with marked shrinkage of the tumor and with no obvious adverse effects. [4]

In the study (sponsored by Pfizer) "Safety Study of Enzalutamide (MDV3100) in patients with Incurable Breast Cancer" was not completed; as 15 and 75 patients did not complete the intended course in stage 1: Dose Escalation and stage 2: Dose Expansion respectively. Patients did not complete due to disease progression, adverse event, withdrawal by patient or other. [12]

Our study results relatively came in agreement with what Traina TA, Arce-Sallinas C and Nakajima M and their colleagues had stated and suggested that androgen receptor can be a possible therapeutic target. Our study results were in contradiction with the study of Pfizer.

Conclusion

Androgen receptor intermediate expression had the best prognosis in triple negative invasive breast cancer female patients. We recommend to test for androgen receptor in breast cancer patients whenever feasible; to keep it as a possible target (if positive) in case of failure of the approved lines of treatment.

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Appendix/Abbreviations

AC	Adriamycin-cyclophosphamide
AIs	Aromatase Inhibitors
AR	Androgen Receptor
BC	Breast Cancer
BMI	Body mass index
C	Cyclophosphamide
CI	Confidence Interval
ER	Estrogen Receptor
FEC	5fu-epirubicin- cyclophosphamide
gr	Grade
Gy	Gray
Her-2	Human Epidermal Growth Factor Receptor-2
HR	Hormonal receptor
IDC	Invasive Ductal Carcinoma
IHC	Immunohistochemistry
ILC	Invasive Lobular Carcinoma
MRM	Modified Radical Mastectomy
OS	Overall Survival
Pfs	Progression-free survival
PgR/PR	Progesterone Receptor
RT	Radiotherapy
SCUCON	Suez Canal University center of Oncology and Nuclear Medicine
TTP	Time to Tumor Progression