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Androgen Receptor and its Prognostic Correlation with Age and Menopausal Status Among Female Patients with Invasive Breast Cancer

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Abstract

Introduction: High AR expression often correlates with postmenopausal status and increasing age. Obesity and weight gain are associated with increased risk of postmenopausal breast cancer, with AR potentially driving tumor progression in these environments.

Patients and methods: We aimed to correlate the score of expression of androgen receptor with the clinicopathological features of the different hormonal profiles of invasive breast cancer Egyptian patients. Retrospective-prospective cohort (historical cohort) study of 107 files of breast cancer patients; classified/stratified and tested for Androgen Receptor score of expression, considering Time to Tumor Progression (TTP) as primary end, and Overall Survival (OS) as second end point.

Results: With a mean follow-up period of 66 months (about 5.5 years), Androgen receptor intermediate expression has the best prognosis in patients older than 50 years (TTP: 100% of patients → 13 months… 70% → 135 months) (OS: 100% → 50 months… 75% → 140 months) (P-Value 0.001423). Low level of androgen receptor expression (score 3) is significantly associated with best prognosis in all overweight patients (TTP: 100% → 53 months) (OS: 100% → 78 months) (P-Value 0.000177). Intermediate level of androgen receptor expression (score 5) is insignificantly associated with best prognosis in patients younger than 35 years, patients aging 36 to 50 years; premenopausal patients, postmenopausal patient's obese patients, overweight patients; patients with average Body Mass Index (BMI)and underweight patients.

Conclusion: Androgen receptor intermediate expression has the best prognosis in patients older than 50 years. Low level of androgen receptor expression (score 3) is significantly associated with best prognosis in all overweight patients. Intermediate level of androgen receptor expression (score 5) is insignificantly associated with best prognosis in patients younger than 35 years, patients aging 36 to 50 years; regardless of the menopausal status & Body Mass Index (BMI) status of patients.

Keywords: Overall Survival (OS); Time to Tumor Progression (TTP); Androgen Receptor (AR).

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Introduction and rationale

The Androgen Receptor (AR) is the most widely expressed steroid receptor in breast cancer, appearing in approximately 60% to 90% of cases. Its role is complex and often "dichotomous," meaning it can either inhibit or promote tumor growth depending on the hormonal landscape of the body [1].

The function of the AR is heavily influenced by the presence or absence of estrogens, which changes drastically during menopause [2]. In premenopausal women, AR typically acts as a tumor suppressor. It competes with the Estrogen Receptor (ER) for binding sites on the DNA, effectively "putting the brakes" on estrogen-driven cell proliferation [3]. After menopause, ovarian estrogen production drops. Androgens (from the adrenal glands) become the primary source for estrogen via aromatization in peripheral tissues. In this low-estrogen environment, AR can sometimes "mimic" ER or cooperate with other growth signals, potentially promoting tumor progression [2,4].

AR expression levels and their prognostic value vary across different age groups. In Older Patients (≥50-51 years), high AR expression is strongly correlated with a favorable prognosis, especially in ER-positive cases. In these patients, AR is associated with lower-grade, less aggressive tumors and longer disease-free survival. However, in younger patients (<50 years), the protective effect of high AR expression is less pronounced or statistically insignificant. Younger women more frequently present with "Triple-Negative" or basal-like subtypes, where the role of AR is still being debated, though a specific "Luminal Androgen Receptor" (LAR) subtype exists in this category as well [2].

Obesity significantly alters the hormonal "soil" in which a tumor grows, impacting AR signaling. In obese individuals, dysfunctional fat tissue secretes higher levels of androgens and inflammatory markers (adipokines). Adipose tissue contains the enzyme aromatase, which converts androgens into estrogens. In obese postmenopausal women, this leads to higher circulating estrogen, which may override the AR's inhibitory effects [5].

Subjects and 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 confounding.

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.

Most of the patients were between 36 and 50 years old at diagnosis; (n=49) with a percentage of 45.8%, followed by patients older than 50 years old (n=39) with a percentage of 36.4%. To be noted, the number of patients below 35 years old in our study is 19 (representing 17.8% of our total number of patients); showing how much the disease could affect young women.

Premenopausal patients were much more than postmenopausal female breast cancer patients in our study; with a percentage of 68.2% and 31.8% respectively.

According to the Body Mass Index (BMI), overweight patients represented the majority (n=48) with a percentage of 44.9%; followed by obese ones (n=42) with a percentage of 39.3%.

Most of the patients had no history of any chronic illness (n=73) with percentage of 68.2% of the total number of patients included in our study.

107 patients' files were included and studied. 107 paraffin blocks - corresponding to each of the 107 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. Semiquantitative 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) 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

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: Clinicopathological characteristics of All patients included in the study.

Comparison	Number	Percentage
Age at diagnosis	107	100%
– Younger than 35	19	17.8%
– 36-50 years	49	45.8%
– Older than 50 years	39	36.4%
Menopausal status at diagnosis	107	100%
– Premenopausal	73	68.2%
– Postmenopausal	34	31.8%
Body Mass Index at diagnosis	107	100%
– Obese	42	39.3%
– Overweight	48	44.9%
– Average	10	9.3%
– Underweight	7	6.5%
Co-morbidities	107	100%
– No history of any chronic illness	73	68.2%
– Hypertension	12	11.2%
– Diabetes mellitus	5	4.7%
– Hypertension and diabetes mellitus	17	15.9%
Presenting symptom	107	100%
– Breast lump	105	98.1%
– Easy fatigability	2	1.86%
Side	107	100%
– Right breast	39	36.4%
– Left breast	68	63.6%
Operation	107	100%
– Modified Radical Mastectomy	80	75%
– Conservative breast surgery	17	15.9%
– Biopsy as metastatic	5	4.5%
– Biopsy as locally advanced	5	4.5%
Histopathological Subtype	107	100%
– Invasive ductal carcinoma	100	93.2%
– Invasive lobular carcinoma	3	2.8%
– Metaplastic	2	1.86%
– Medullary	2	1.86%
Grading	107	100%
– Grade 1	10	9.1%
– Grade 2	80	75%
– Grade 3	17	15.9%
Tumor Size	107	100%
– T1	20	18.2%
– T2	60	56.8%
– T3	17	15.9%
– Locally advanced T4	10	9.1%

Nodal Status	107	100%
– No	34	31.8%
– N1	24	22.7%
– N2	17	15.9%
– N3	32	29.5%
Distant Metastasis	107	100%
– M0	97	90.9%
– M1	10	9.1%
Extranidal Extension	107	100%
– No	56	52.3%
– Positive	41	38.6%
– Unknown as no surgery/ lymph node dissection done	10	9.1%
Surgical margins	107	100%
– Free	97	90.0%
– Unknown as no surgery done	10	9.1%
Multicentricity	107	100%
– No multicentricity	91	85.3%
– Multicentricity	6	5.6%
– Unknown/ no surgery done	10	9.1%
Multifocality	107	100%
– No multifocality	100	93.5%
– Multifocality	3	2.8%
– Unknown/ no surgery done	4	3.7%
Early versus advanced	107	100%
– Early	49	45.5%
– Locally advanced	12	11.4%
– Advanced metastatic	10	9.1%
– Resectable advanced	36	34.1%
Neoadjuvant chemotherapy if any	107	100%
– No	88	82.2%
– Yes	19	17.8%
Regimen of neoadjuvant chemotherapy if any	107	100%
– None received	88	82.2%
– 3 FEC	2	1.9%
– 3 FEC then 3 Vinorelbine/Cisplatin	4	3.7%
– 3 FEC then 3 Docetaxel	2	1.9%
– 2 CMF	2	1.9%
– 3 Vinorelbine / Cisplatin	3	2.8%
– 2 Docetaxel / Gemcitabine	3	2.8%
– 2 Docetaxel / Gemcitabine the 2 Vinorelbine/ Cisplatin	3	2.8%
Estrogen Receptor	107	100%
– Positive	54	50.5%
– Negative	53	49.5%
Progesterone Receptor	107	100%
– Positive	51	47.7%
– Negative	56	52.3%
HER2Neu	107	100%
– Negative	73	68.2%
– Positive	34	31.7%
Molecular group	107	100%
– ER, PR+ve, HER2neu –ve	39	36.4%
– Triple positive	10	9.3%
– ER, PR –ve, HER2neu +ve	24	22.4%
– Triple negative	30	28.0%
– ER +VE, PR, HER2Neu -ve	4	3.7%
Adjuvant Chemotherapy	107	100%
– No adjuvant chemotherapy	2	1.9%
– 6 FEC	44	41.1%
– 4 AC then 12 Paclitaxel weekly	7	6.5%
– 4 AC then 4 Paclitaxel every 3 weeks	7	6.5%
– 4 FEC then 4 Paclitaxel/ Carboplatin	10	9.3%
– 4 AC then 4 Paclitaxel/ Trastuzumab and Trastuzumab continued for 1 year	24	22.4%
– 3 Paclitaxel/ Carboplatin	3	2.8%
– 3 Vinorelbine/ Carboplatin	10	9.3%

Post-operative Radiotherapy	107	100%
– No adjuvant radiotherapy	15	14%
– 50Gy/25#	87	81.3%
– 45Gy/18#	5	4.7%
Hormonal Treatment and/or maintenance Capecitabine	107	100%
– No hormonal treatment	31	28.9%
– Letrozole	20	18.7%
– Capecitabine alone	20	18.7%
– Letrozole + Capecitabine	2	1.86%
– Tamoxifen	24	22.4%
– Tamoxifen for 2 years then Letrozole	9	8.4%
– Bicalutamide + Capecitabine	1	0.93%
Androgen Receptor Expression Final Score	107	100%
– 0	5	4.7%
– 3	12	11.2%
– 4	5	4.7%
– 5	24	22.4%
– 6	12	11.2%
– 7	22	20.6%
– 8	27	25.2%

The above-mentioned table (Table 1) represents patients' characteristics as follows:

- Most of the patients were between 36 and 50 years old at diagnosis; (n=49) with a percentage of 45.8%, followed by patients older than 50 years old (n=39) with a percentage of 36.4%. To be noted, the number of patients below 35 years old in our study is 19 (representing 17.8% of our total number of patients); showing how much the disease could affect young women.
- Premenopausal patients were much more than postmenopausal female breast cancer patients in our study; with a percentage of 68.2% and 31.8% respectively.
- According to the Body Mass Index (BMI), overweight patients represented the majority (n=48) with a percentage of 44.9%; followed by obese ones (n=42) with a percentage of 39.3%.
- Most of the patients had no history of any chronic illness (n=73) with percentage of 68.2% of the total number of patients included in our study.
- The vast majority of the patients presented complaining of breast lump, with a minority had started to seek medical advice complaining of easy fatigability; with a percentage of 98.1% versus 1.86% respectively.
- Left sided breast cancer (n=68) was more than right sided breast cancer (n=39); with a percentage of 63.6% versus 36.4% respectively.
- 80 patients (75%) did Modify Radical Mastectomy (MRM). That denotes that still organ preservation protocols have to be searched for and found.
- Invasive ductal carcinoma was the most common histopathological subtype among our patients (n=100) with a percentage of 93.2%. Invasive lobular carcinoma, metaplastic carcinoma and medullary carcinoma were also present but less commonly.
- Intermediate grade (Grade II) carcinoma affected 80 patients (75%); followed by grade III (n=17) with a percentage of 15.9%
- Concerning tumor size, most of the patients (n=60) had T2 carcinoma; with a percentage of 56.8%., followed by T1, T3 and T4; with percentages of 18.2%, 15.9% and 9.1% respectively.
- We had two opposite poles/peaks in positive lymph nodes affected, N0 and then N3, 31.8% versus 29.5% of total number of patients respectively.
- Patients had distant metastasis at diagnosis; with a percentage of 9.1%.
- Extranidal extension was positive in 41 patients (38.6%), negative in 56 patients (52.3%) and unknown in 10 patients who didn't do any surgery because they were metastatic from the start and didn't respond to treatment.
- All the patients who did mastectomy had free surgical margins.
- Multicentricity was found in 6 patients (5.6%), while multifocality was found in 3 patients (2.8%).
- 45.5% of the patients (n=49) had early breast cancer, followed by respectable advanced stage breast cancer (n=36), then locally advanced (n=12) and finally advanced metastatic from the start (n=10); whose percentages 34.1%, then 11.4% and finally 9.1%.
- 88 patients (82.2%) didn't receive neoadjuvant chemotherapy; while 19 patients (17.8%) did. The most commonly used regimen was Vinorelbine combined with Cisplatin; either 3 cycles only, or 3 cycles following 3 cycles 5-Fluorouracil/ Epirubicin/ Cyclophosphamide (FEC), or 2 cycles following 2 cycles Docetaxel/Gemcitabine.
- Estrogen Receptor (ER) and Progesterone Receptor (PR) were positive in about half of the patients (n=54) (50.5%) and (n=51) (47.7%) respectively.
- HER2Neu was positive in 34 patients (31.7%).
- 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.

- The regimen FEC was the most commonly received adjuvant chemotherapy protocol in the form of 6 cycles, followed -in frequency- by 4 cycles Doxorubicin/Cyclophosphamide then 4 cycles Paclitaxel/Trastuzumab and Trastuzumab continued for 1 year (n=24) (28.9%).
- 87 patients (81.3%) received post-operative radiotherapy (50Gy/25#).

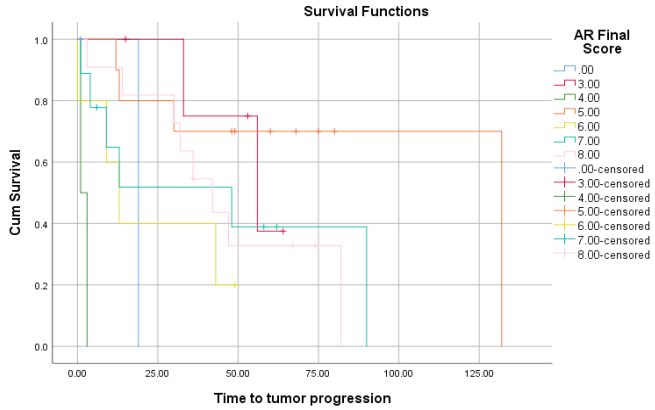

Figure 1: Time to tumor progression in all patients generally.
This Kaplan-Meier curve (Figure 1) shows time to tumor progression when comparing the levels of androgen receptor expression in all patients generally; as follows:

- Score 5: 100% of patients survived for → 15 months… 80% of patients survived for → 30 months … 70% of patients survived for → 135 months.
- Score 3: 100% → 35 months… 75% → 55 months
- Score 0: 100% → 20 months
- Score 8: 90% → 20 months… 80% → 30 months… 35% → 80 months
- Score 7: 65% → 20 months… 50% → 48 months… 38% →90 months
- (With overall maximal standard error: 0.354)

With body mass index

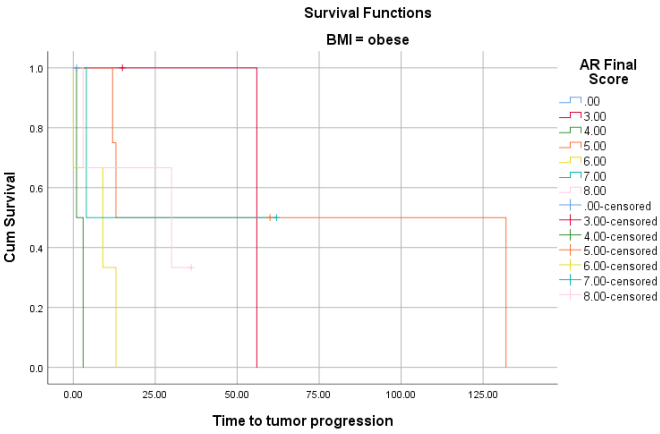

Figure 2: Time to tumor progression in all obese patients.
This Kaplan-Meier curve (Figure 2) shows time to tumor progression when comparing the levels of androgen receptor expression in all obese patients as calculated by body mass index (BMI); as follows:

- Score 3: 100% of patients survived for → 55 months.
- Score 5: 100% of patients survived for → 15 months… 50% of patients survived for → 135 months.
- Score 7: 50% → 60 months.
- Score 8: 70% → 30 months.

(With overall maximal standard error: 0.354).

- Tamoxifen was the most commonly used adjuvant hormonal treatment (n=24) (22.4%). Anastrozole was surprisingly not received by any of our patients.
- Positive androgen receptor was present in the vast majority of our patients (n=102) (95.3%). 27 patients were tested highly positive; final score= 8 (25.2%), and 22.4% scored 5 as final score (intermediate).

Time to Tumor Progression (TTP)

Generally:

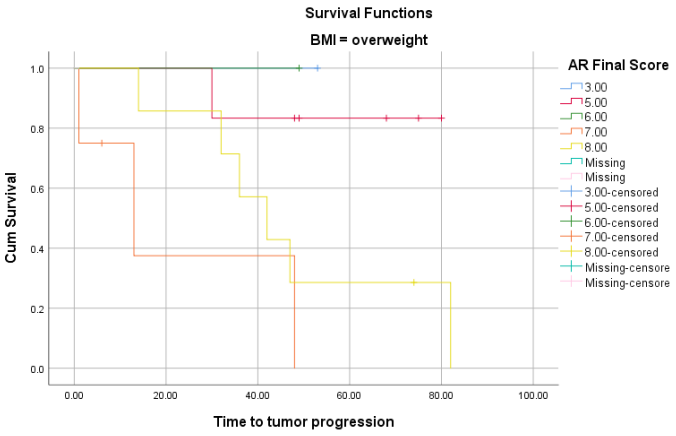

Figure 3: Time to tumor progression in all overweight patients.
This Kaplan-Meier curve (Figure 10-3) shows time to tumor progression when comparing the levels of androgen receptor expression in overweight patients; as calculated by body mass index (BMI) as follows:

- Score 3: 100% → 53 months
- Score 6: 100% → 50 months
- Score 5: 100% → 30 months… 83% → 80 months
- Score 8: 85% → 33 months… 30% → 83 months.

(With overall maximal standard error: 0.833)

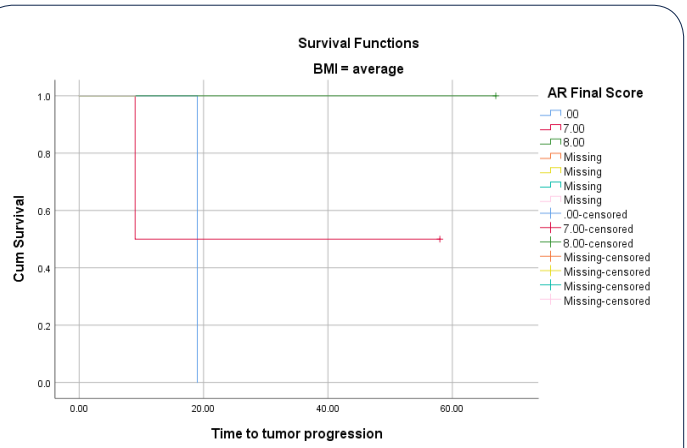

Figure 4: Time to tumor progression in all average-weight patients.
This Kaplan-Meier curve (Figure 10-4) shows time to tumor progression when comparing the levels of androgen receptor expression in all patients with regard to average Body Mass Index (BMI); as follows:

- Score 8: 100% → 65 months
- Score 7: 100% → 10 months… 50% → 58 months
- Score 0: 100% 18 months.

(With overall maximal standard error: 0.500)

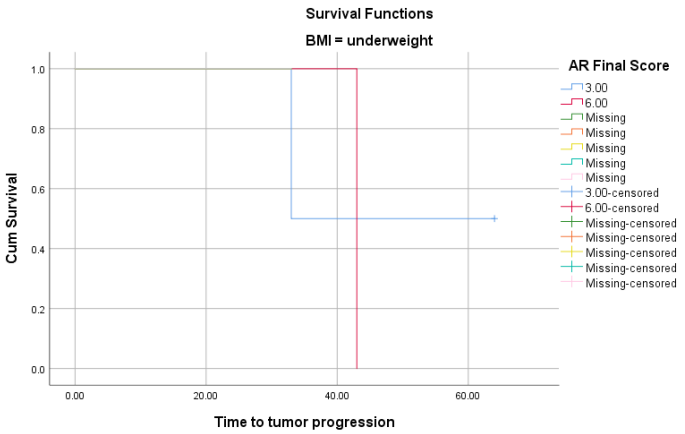

Figure 5: Time to tumor progression in all underweight patients.

This Kaplan-Meier curve (Figure 5) shows time to tumor progression when comparing the levels of androgen receptor expression in underweight patients as calculated by Body Mass Index (BMI); as follows:

- Score 6: 100% → 45 months
- Score 3: 100% → 33 months… 50% → 65 months.

(With overall maximal standard error: 0.500)

With age group

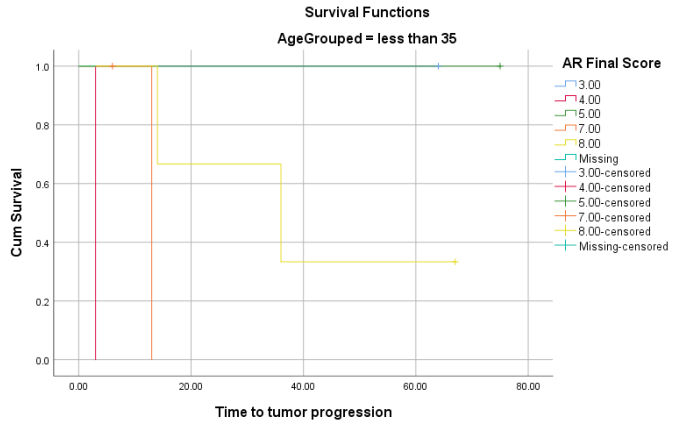

Figure 6: Time to tumor progression in all patients with age less than 35 years.

This Kaplan-Meier curve (Figure 6) shows time to tumor progression when comparing the levels of androgen receptor expression in all patients with regard to age less than 35 years; as follows:

- Score 5: 100% → 75 months
- Score 8: 100% → 15 months… 68% →37 months… 37% → 65 months.

(With overall maximal standard error: 0.667)

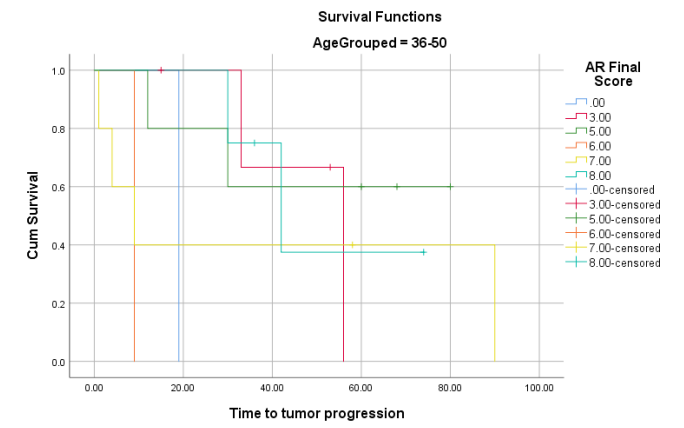

Figure 7: Time to tumor progression in patients with age 36 to 50 years.

This Kaplan-Meier curve (Figure 7) shows time to tumor progression when comparing the levels of androgen receptor expression in all patients with regard to age 36 to 50 years; as follows:

- Score 3: 100% → 32 months… 67% → 55 months
- Score 8: 100% → 30 months… 75% → 44 months… 38% → 75 months
- Score 5: 100% → 13 months… 80% → 30 months… 60% → 80 months.

(With overall maximal standard error: 0.800)

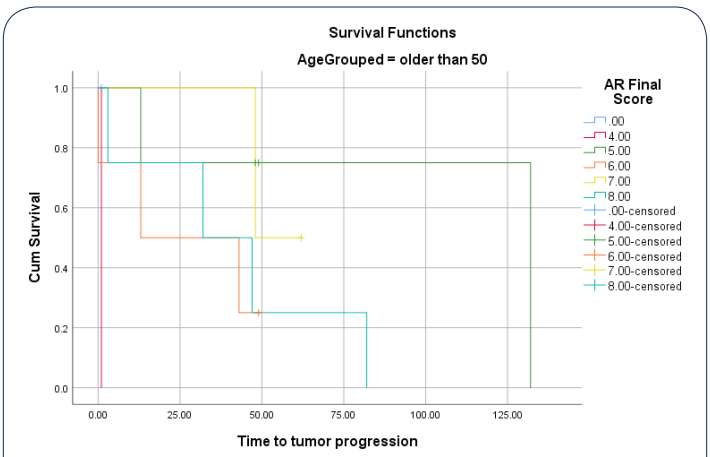

Figure 8: Time to tumor progression in all patients with age older than 50 years.

This Kaplan-Meier curve (Figure 8) shows time to tumor progression when comparing the levels of androgen receptor expression in all patients with regard to age older than 50 years; as follows:

- Score 7: 100% → 48 months… 50% → 60 months.
- Score 5: 100% → 13 months… 70% → 135 months.
- Score 8: 100% → 5 months… 70% → 35 months… 50% → 47 months… 27% → 85 months.

(With overall maximal standard error: 0.750)

With Menopausal status

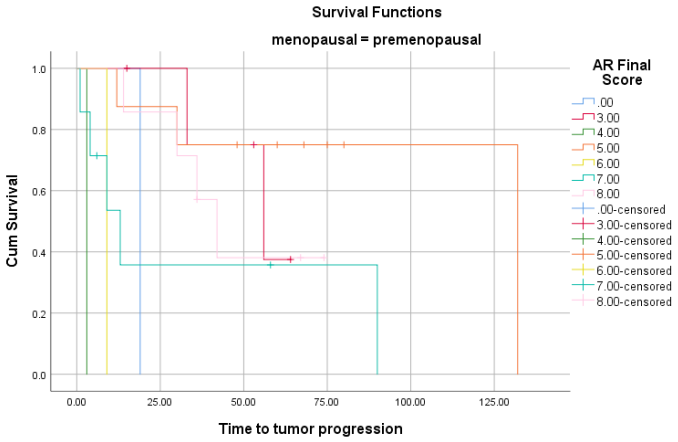

Figure 9: Time to tumor progression in all premenopausal patients.
This Kaplan-Meier curve (Figure 9) shows time to tumor progression when comparing the levels of androgen receptor expression in all premenopausal patients; as follows:

- Score 3: 100% → 35 months… 75% → 53 months… 48% → 67 months.
- Score 5: 100% → 13 months… 88% → 30 months… 75% → 135 months.
- Score 8: 100% → 15 months… 70% → 35 months… 38% → 74 months.

(With overall maximal standard error: 0.875)

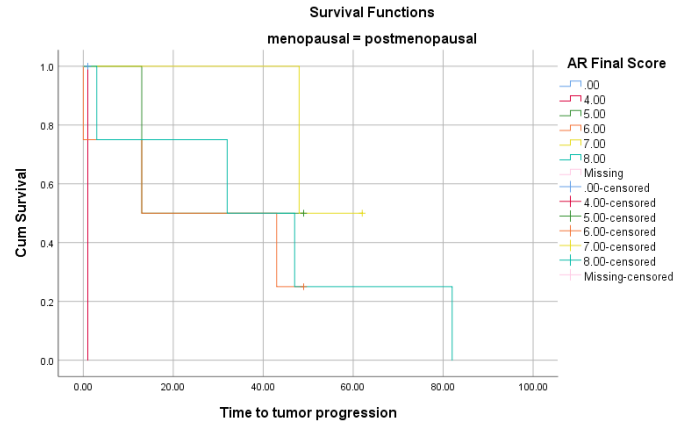

Figure 10: Time to tumor progression in all postmenopausal patients.
This Kaplan-Meier curve (Figure 10) shows time to tumor progression when comparing the levels of androgen receptor expression in all postmenopausal patients; as follows:

- Score 7: 100% → 48 months… 50% → 61 months
- Score 5: 100% → 13 months… 50% → 49 months
- Score 8: 100% → 4 months… 75% → 32 months… 50% → 47 months… 25% → 84 months.

(With overall maximal error: 0.750)

Overall Survival

Generally:

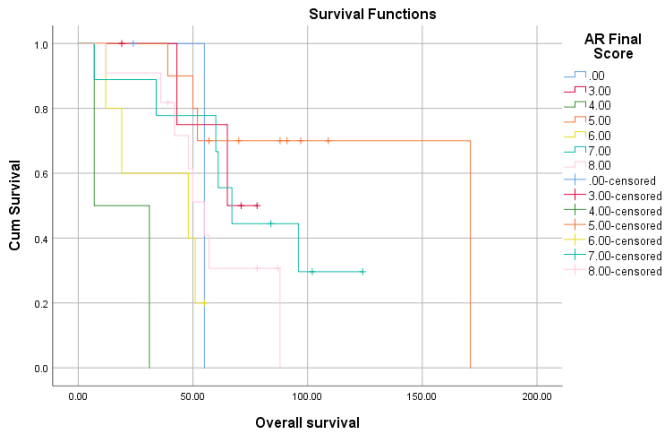

Figure 11: Overall survival of all patients generally.
This Kaplan-Meier curve (Figure 11) represents the overall survival of all patients with various degrees of expression of androgen receptor as follows:

- Score 5: 100% of patients survived for → 37 months… 90% of patients survived for → 50 months … 70% of patients survived for → 170 months
- Score 0: 100% → 55 months
- Score 3: 100% → 42 months … 75% → 70 months… 50% → 80 months
- (With maximal standard error: 0.354)

With body mass index

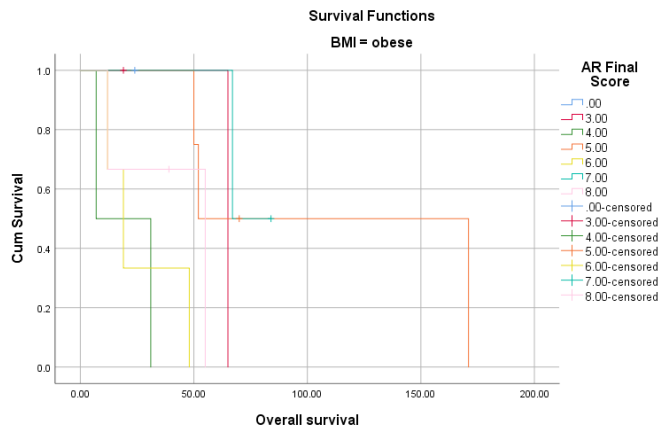

Figure 12: Overall survival in all obese patients.
This Kaplan-Meier curve (Figure 12) shows the overall survival when comparing the levels of androgen receptor expression in all obese patients (as estimated by Body Mass Index "BMI"); as follows:

- Score 5: 100% → 50 months… 50% → 170 months
- Score 7: 100% → 70 months… 50% → 80 months
- Score 3: 100% → 68 months.

(With maximal standard error: 0.354)

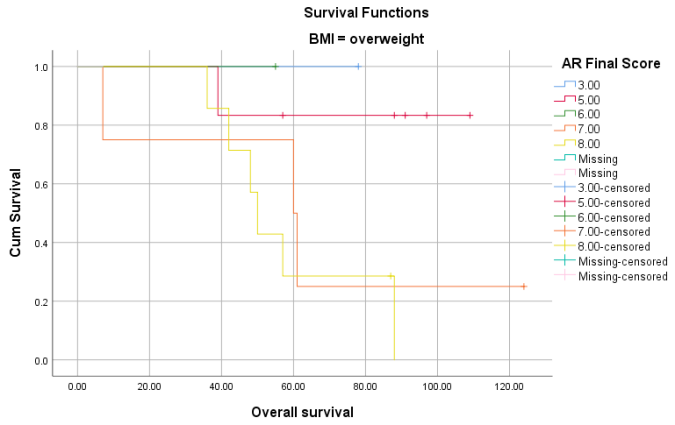

Figure 13: Overall survival in all overweight patients.

This Kaplan-Meier curve (Figure 13) shows the overall survival when comparing the levels of androgen receptor expression in all overweight patients (as estimated by Body Mass Index "BMI"); as follows:

- Score 3: 100% → 78 months
- Score 5: 100% → 40 months… 83% → 110 months
- Score 7: 100% → 7 months 75% → 60 months… 27% → 125 months.

(With maximal standard error: 0.250)

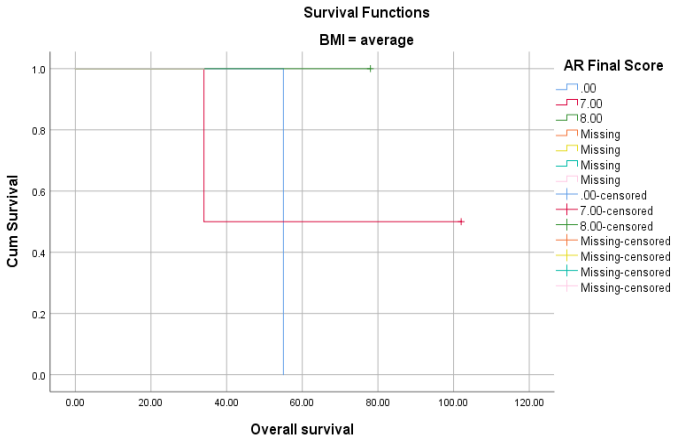

Figure 14: Overall survival in all patients with average Body Mass Index.

This Kaplan-Meier curve (Figure 14) shows the overall survival when comparing the levels of androgen receptor expression in all patients with average Body Mass Index (BMI); as follows:

- Score 8: 100% → 78 months
- Score 0: 100% → 55 months
- Score 7: 100% → 37 months… 50% → 105 months.

(With maximal standard error: 0.354)

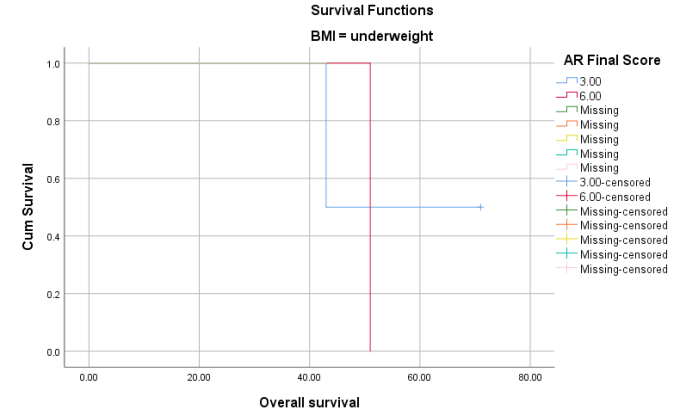

Figure 15: Overall survival in all underweight patients.

This Kaplan-Meier curve (Figure 15) shows the overall survival when comparing the levels of androgen receptor expression in all underweight patients (as estimated by Body Mass Index "BMI"); as follows:

- Score 6: 100% → 53 months
- Score 3: 100% → 43 months… 50% → 73 months

(With maximal standard error: 0.354)

With age group:

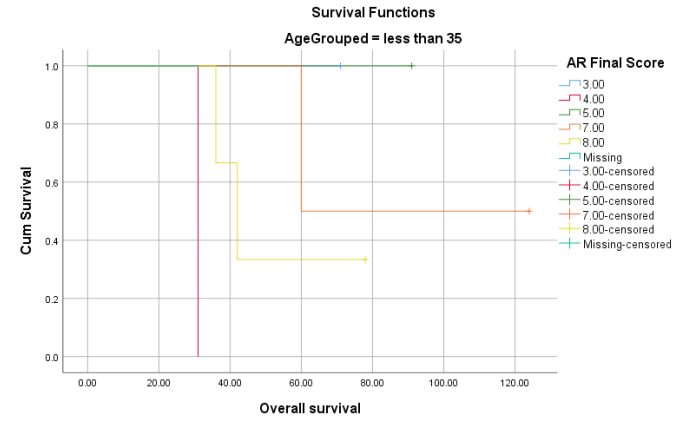

Figure 16: Overall survival in all patients with age less than 35 years.

This Kaplan-Meier curve (Figure 16) shows the overall survival when comparing the levels of androgen receptor expression in all patients with regard to age less than 35 years; as follows:

- Score 5: 100% → 92 months
- Score 7: 100% → 60 months… 50% → 125 months
- Score 8: 100% → 35 months… 70% → 42 months… 35% → 78 months
- Score 4: 100% → 30 months

(With maximal standard error: 0.354)

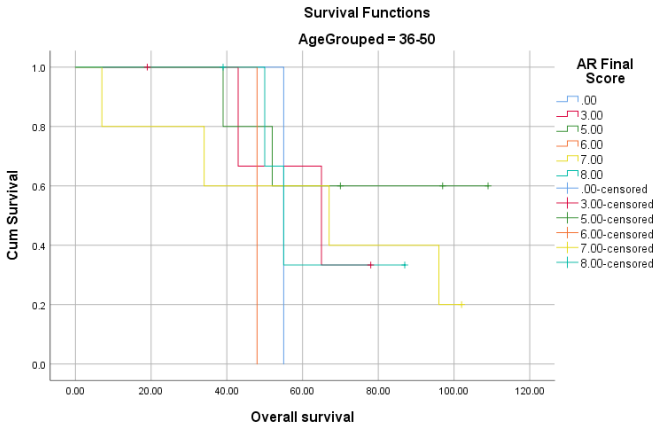

Figure 17: Overall survival in all patients with age 36 to 50 years.

This Kaplan-Meier curve (Figure 17) shows the overall survival when comparing the levels of androgen receptor expression in all patients with regard to age 36 to 50 years; as follows:

- Score 5: 100% → 92 months
- Score 7: 100% → 60 months… 50% → 125 months
- Score 8: 100% → 35 months… 70% → 42 months… 35% → 78 months
- Score 4: 100% → 30 months

(With maximal standard error: 0.354)

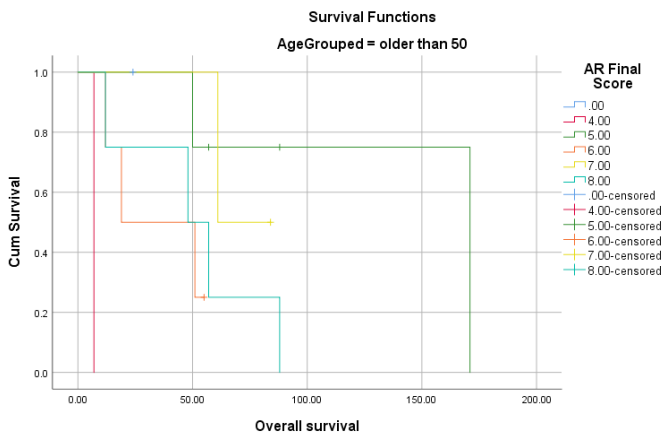

Figure 18: Overall survival in all patients with age older than 50 years.

This Kaplan-Meier curve (Figure 18) shows the overall survival when comparing the levels of androgen receptor expression in all patients with regard to age older than 50 years; as follows:

- Score 7: 100% → 68 months
- Score 5: 100% → 50 months… 75% → 140 months
- Score 8: 100% → 13 months… 75% → 48 months… 50% → 58 months… 28% → 85 months
- Score 6: 100% → 17 months… 50% → 50 months

(With maximal standard error: 0.354)

With menopausal status:

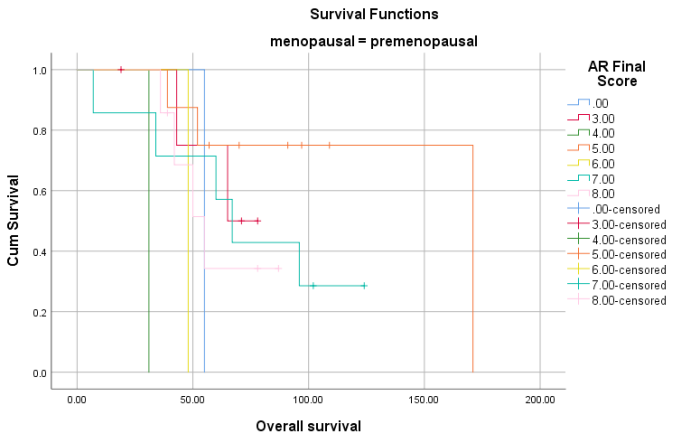

Figure 19: Overall survival in all premenopausal patients.

This Kaplan-Meier curve (Figure 19) shows the overall survival when comparing the levels of androgen receptor expression in all premenopausal patients; as follows:

- Score 5: 100% → 45 months… 75% → 170 months
- Score 0: 100% → 60 months
- Score 6: 100% → 49 months

(With maximal standard error: 0.250)

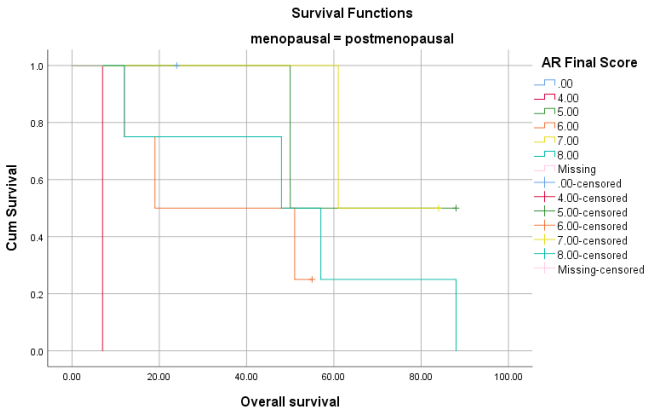

Figure 20: Overall survival in all postmenopausal patients.

This Kaplan-Meier curve (Figure 20) shows the overall survival when comparing the levels of androgen receptor expression in all postmenopausal patients; as follows:

- Score 7: 100% → 62 months… 50% → 90 months
- Score 5: 100% → 50 months… 50% → 92 months
- Score 8: 100% → 16 months… 75% → 57 months… 25% → 88 months
- Score 6: 100% → 16 months… 50% → 50 months

(With maximal standard error: 0.354)

Relation of androgen receptor degree of expression with different factors

Age group: Less than 35

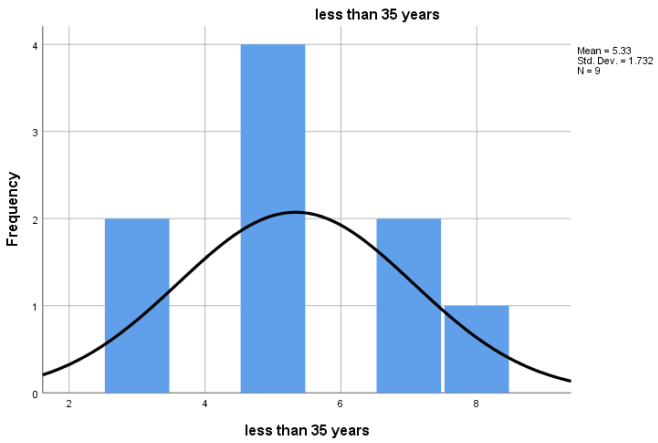

Figure 21: Score 5 degree of androgen receptor expression is the predominant and has the best prognosis in all patients younger than 35 years.

This histogram (Figure 21) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all patients younger than 35 years in our study. Z score = 0.533. P-Value is .594034. (Statistically not significant)

36-50 years

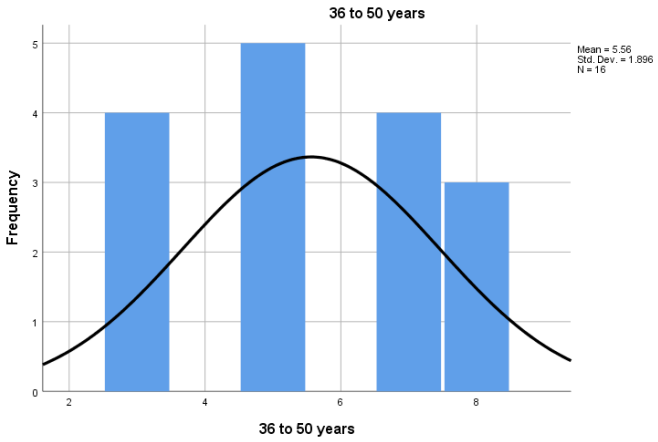

Figure 22: Score 5 androgen receptor expression has the best prognosis in all patients aging 36 to 50 years.

This histogram (Figure 22) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all patients aging 36 to 50 years in our study. Z score = 1.1814. P-Value is .237444. (Statistically not significant)

More than 50 years

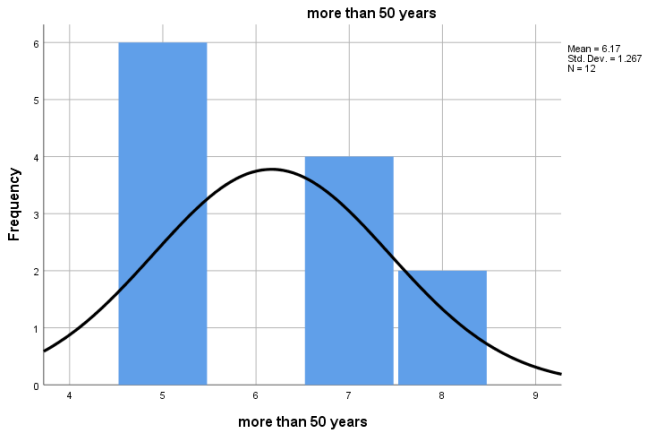

Figure 23: Score 5 degree of androgen receptor expression again is the predominant and has the best prognosis in all patients older than 50 years.

This histogram (Figure 23) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all patients older than 50 years in our study. Z score = 3.19. P-Value is .001423. (Statistically significant).

Menopausal status: Premenopausal.

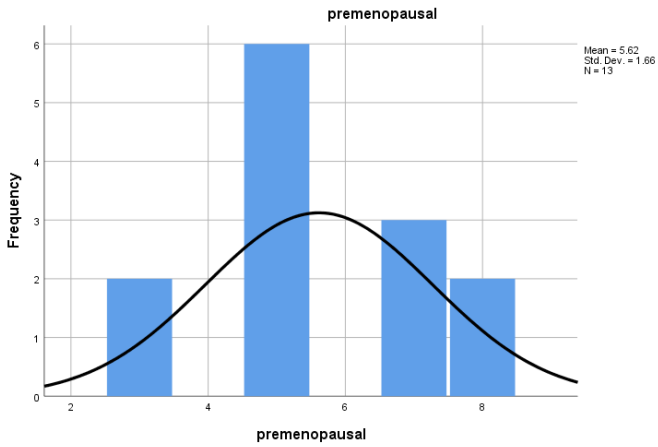

Figure 24: Score 5 as degree of androgen receptor expression is the predominant in all premenopausal patients.

This histogram (Figure 24) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all premenopausal patients in our study. Z score = 1.346. P-Value is .178109. (Statistically not significant)

Postmenopausal

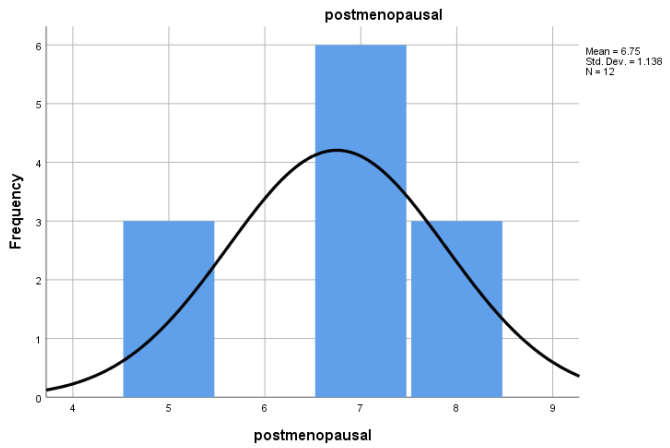

Figure 10-119: Score 7 as degree of androgen receptor expression is the predominant and has the best prognosis in all postmenopausal patients.

This histogram (Figure 10 119) shows that score 7 as degree of androgen receptor expression is the predominant and has the best prognosis in all postmenopausal patients in our study. Z score = 0.761. P-Value is .446657. (Statistically not significant)

Body Mass Index (BMI)

Obese

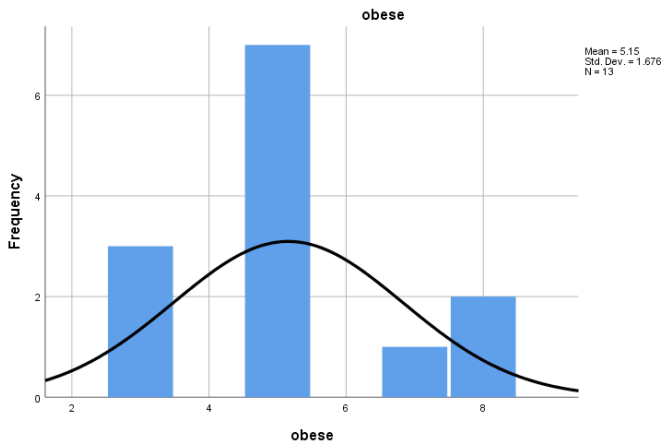

Figure 25: Score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all obese patients.

This histogram (Figure 25) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all obese patients in our study. Z score = 0.322. P-Value is .746695. (Statistically not significant)

Overweight

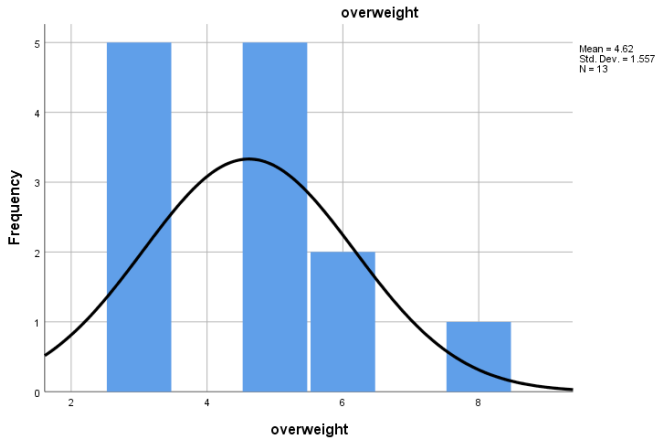

Figure 26: Scores 3 and 5 as degree of androgen receptor expression are the predominant and have the best prognosis in all overweight patients.

This histogram (Figure 26) shows that score 5 as degree of androgen receptor expression is the predominant and has the best prognosis in all overweight patients in our study. Z score =-0.8799. P-Value is .378859. (Statistically not significant)

This histogram (Figure 26) shows that score 3 as degree of androgen receptor expression is the predominant and has the best prognosis in all overweight patients in our study. Z score = 3.751. P-Value is .000177. (Statistically significant)

Average

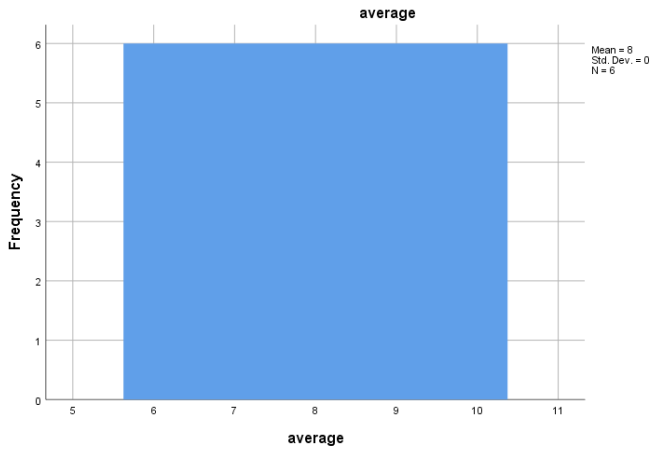

Figure 27: Score 8 as degree of androgen receptor expression is the predominant and has the best prognosis in all patients with average body mass index.

This histogram (Figure 27) shows that score 8 as degree of androgen receptor expression is the predominant and has the best prognosis in all patients with average Body Mass Index (BMI) in our study. Z score = 0. P-Value is 1. (Statistically not significant)

Underweight

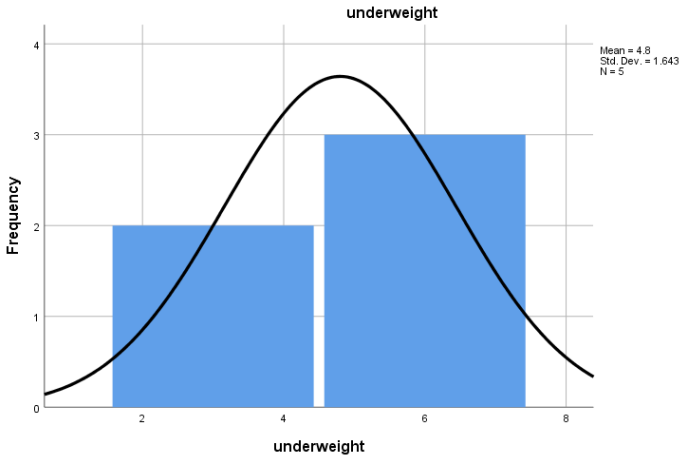

Figure 28: Score 6 as degree of androgen receptor expression is the predominant and has the best prognosis in all underweight patients. This histogram (Figure 28) shows that score 6 as degree of androgen receptor expression is the predominant and has the best prognosis in all underweight patients in our study. Z score = -1.633. P-Value is .102469. (Statistically not significant)

Discussion

Concerning age,

- Shuai Xu and colleagues studied breast cancer patients in the United States aged 20 to 49 years. An increase in breast cancer incidence rates among young US women and age-related crossover between non-Hispanic White and Black women were observed.
- In our study, most of the patients were between 36 and 50 years old at diagnosis; (n=49) with a percentage of 45.8%, followed by patients older than 50 years old (n=39) with a percentage of 36.4%. The number of patients below 35 years old in our study was 19 (representing 17.8% of our total number of patients).
- That showed how much the disease could affect young women.
- Younes SF and colleagues in Menoufia in 2016 had found that AR immunoreactivity was significantly correlated with older age (p=0.03).
- In our study, intermediate androgen receptor expression (score 5) was the predominant and had the best prognosis in all patients older than 50 years. (P-Value: 0.0014) (statistically significant).

Our study results came in agreement with what was stated by Younes SF and her colleagues. Concerning menopausal status.

- Younes SF and her colleagues stated that AR immunoreactivity was significantly correlated with post-menopausal status (p=0.001).
- In our study, intermediate androgen receptor expression (score 5) was the predominant and had the best prognosis in premenopausal and postmenopausal status with no statistical significance.

Our study results relatively came in agreement with what was stated by Younes SF and her colleagues. Concerning Body Mass Index (BMI).

Nelson Rangel and his colleagues in 2021 had searched for the associations between obesity and androgen receptor signaling. They had stated that among the adipocyte-secreted factors, altered adiponectin and leptin levels have been shown to be independently associated with breast cancer development. Leptin functions were clearly pro-tumorigenic. Invalid source specified.

- In our study, high androgen receptor expression (score 7) had the best prognosis in all overweight patients (P-Value: 0.00017) (statistically significant).
- Our study came in agreement with what was stated by Nelson Rangel and his colleagues.

Conclusion

Intermediate level of androgen receptor expression (score 5) was significantly associated with best prognosis in patients older than 50 years.

Low level of androgen receptor expression (score 3) was significantly associated with best prognosis in all overweight patients.

Intermediate level of androgen receptor expression (score 5) is insignificantly associated with best prognosis in patients younger than 35 years, patients aging 36 to 50 years; regardless of the menopausal status & Body Mass Index (BMI) status of patients.

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