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ORIGINAL ARTICLE

The prevalence and prognostic importance of the androgen receptor in triple-negative breast cancer

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Summary

Purpose: *Triple-negative breast cancer (TNBC) has a significantly more aggressive course, higher recurrence rate, and shorter survival time than the other breast cancer types. The disease has molecular heterogeneity, and in a subset of patients, androgen receptor (AR) expression is present. Our study aimed to demonstrate prevalence of the AR positivity and examine the potential prognostic impact on patient survival.*

Methods: *The study included patients aged >18 years who had a history of triple-negative nonmetastatic breast cancer and were followed-up and treated at Ege University Medical Faculty Hospital between 2005 and 2017. In our study ,staining extent was expressed as a percentage, with ≥1% positivity in stained preparates evaluated as AR positive.*

Results: *36% prevalence rate of AR expression was found in the TNBC group, consistent with previous studies.In our study, although no statistically significant relationship was found between overall and disease-free survival and AR expression in the patients with early-stage TNBC, disease-free survival was significantly longer in the AR-positive group. No significant difference in the number of locally advanced patients was found between the AR-positive and AR-negative groups.*

Conclusion: *Although AR expression was found to have no statistically significant relationship with clinicopathological parameters and survival in the patients with TNBC, a larger series of studies is needed to validate the results of the present study. Furthermore, with the inclusion of AR expression level meaurement in routine histopathological examination in the TNBC group, with an expression rate of 36%, future AR-targeted therapies may show promising effectiveness.*

Key words: *breast cancer, androgen receptor, immunohistochemistry, triple-negative*

Introduction

Triple-negative breast cancer (TNBC) with its distinct biological properties is associated with an aggressive clinical course and a predisposition to premenopausal and younger age groups. Convensional cytotoxic chemotherapy is the essential treatment option with partial benefit. Introducing immunotherapy and targeted treatment to TNBC to achieve higher response rates and survival demonstrated additional benefit in various disease settings.

Although in clinical practice the tumor staining for estrogen receptor (ER), progesterone receptor (PR) and HER-2 define the TNBC patients, it is well demonstrated that the disease has distinct subgroups in molecular analyses. However, to order this molecular analyses to each patient in the clinic is not feasible.

Androgen receptor (AR) is a nuclear steroid hormone receptor family member like ER and PR. By interacting with their corresponding receptors,

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steroid hormone receptors act as transcription factors and trigger gene expression. Androgens are frequently expressed both in normal breast tissue and primary tumors. AR expression was reported in 10-35% of patients in the TNBC group in various studies, most of which reported favorable prognosis in these patients; however, the prognostic role of AR expression is unclear.

Preclinical studies have demonstrated that the AR stimulates the growth of TNBC cell lines and that activating PIK3CA mutations were found more frequently in this patient group [1].

By contrast, patients with AR^- TNBC are more likely to respond to neoadjuvant chemotherapy. In theory, the luminal AR^+ TNBC subtype may mimic luminal A breast cancer that has favorable prognosis despite poor response to chemotherapy [2].

Our study aimed to demonstrate the frequency of AR positivity and examine its potential prognostic impact on nonmetastatic TNBC patients survival in a single center.

Methods

Patient selection

We reviewed the clinicopathological data from the patient medical records with nonmetastatic TNBC who were admitted to the Ege University Medical Oncology Clinic between 2005 and 2017. All the patients with available tumor samples for further AR analysis were included in our study. Patients diagnosed during pregnancy and those who had additional cancer diagnoses were excluded. Disease-associated data were obtained from outpatient clinical files after consent was obtained from the patients or their first degree relatives after death. The patient data were recorded in an SPSS program and the authors declared that no conflict of interest existed.

Clinical and histopathological examinations

Patient staging was based on the TNM classification. The data recorded for each patient included age, body mass index, menopause status, nuclear grade, histological type and grade, Ki-67 index, p53 percentage, AR staining percentage, TNM stage, surgical treatment, adjuvant medical treatment, radiotherapy, and disease-free and overall survival.

Staining of ER and PR <1% was considered negative. Human epidermal growth factor receptor 2 expression (HER2) was reported as negative when it was not detected in immunohistochemical or fluorescence *in situ* hybridization analysis. All tissue samples from 100 cases were fixed in 10% buffered neutral formalin solution and embedded in paraffin. One block that represented the histomorphology best without any bleeding and necrosis area was selected for each patient's tumor AR analyses. Three-micron-thick cross sections were taken from these blocks. Staining was performed on the cross sections with AR primary antibodies in an automatic immunohistochemistry device (Roche, Ventana, Benchmark, XT) in our laboratory. The results were evaluated using Olympus BX51 light microscopy.

AR immunohistochemical evaluation was semi-quantatively performed considering the staining volume and extent. Staining volume was subjectively evaluated as 0=none, 1=low, 2=average, and 3=strong (Figure 1). The extent of staining was expressed as a percentage, with ≥1% positivity in stained preparates evaluated as AR positive.

Statistics

All statistical analyses waere performed using SPSS version 22.0. In addition to the descriptive statistical methods for data evaluation, x^2 test was used for qualitative data comparison. The Mann-Whitney *U* test was used for comparison of data without normal distribution. Disease-free survival (DFS) was defined as the interval between the diagnosis of TNBC to the date of recurrence. Overall survival (OS) was measured from diagnosis to death from any cause.

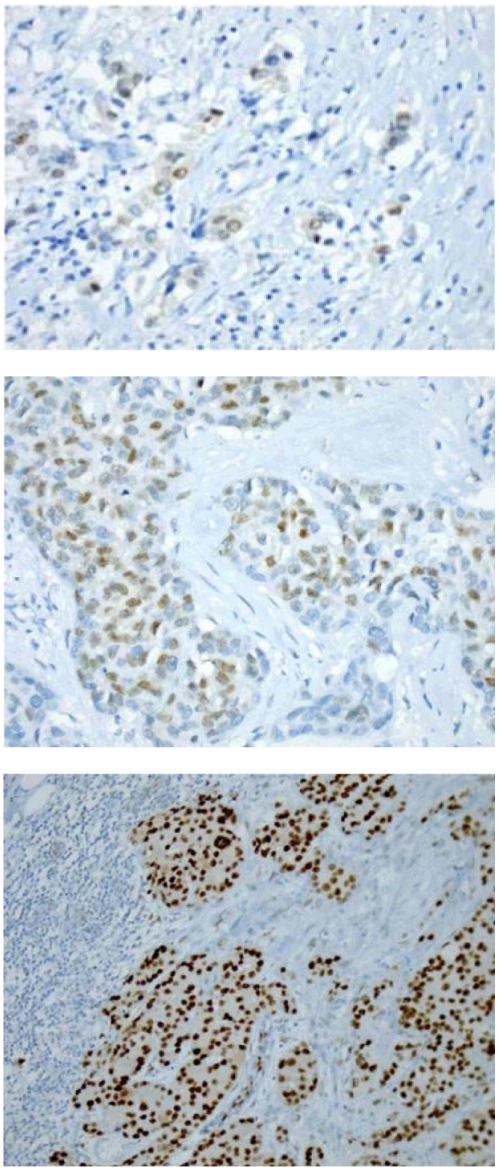

Figure 1. $^+1$, $^+2$, and $^+3$ staining pattern for AR.

Survival duration was estimated using the Kaplan-Meier method, and differences were tested with the log-rank test. The results were evaluated with the 95% confidence interval (CI) and a significance level of $p<0.05$.

Results

By rewieving the medical records of 2,300 patients with breast cancer diagnosed in our unit between 2005 and 2017, we identified 240 patients with TNBC (10.4%). Twenty patients had metastases at diagnosis. Fifty patients did not consent to participation in the study. Eight patients who died from natural causes before follow-up and 12 patients with a concurrent ovarian cancer diagnosis were also excluded. Pathological specimens were unvailable for 29 patients. A total of 100 patients were included in the study after excluding

Table 1. Comparison between AR^+ and AR^- groups

	AR^+ (n=36)		*AR^- (n=64)*		*p*
	Frequency y (n)	*Percentage e (%)*	*Frequency y (n)*	*Percentage e (%)*	
Tumor					0.995
T1	11	30.60	21	32.80	
T2	21	58.30	36	56.30	
T3	3	8.30	5	7.80	
T4	1	2.80	2	3.10	
Node					0.721
N0	21	58.30	39	60.90	
N1	10	27.80	13	20.30	
N2	2	5.60	7	10.90	
N3	3	8.30	5	7.80	
Metastasis					0.735
Bone	4	26.6	11	73.33	
Visseral	10	28.57	25	71.43	
Other	1	14.29	6	85.71	
Stage					0.960
1	7	19.40	11	17.20	
2	22	61.10	40	62.50	
3	7	19.40	13	20.30	
Histological type					0.082
IDC	25	69.40	49	76.60	
ILC	0	0.00	1	1.60	
Apocrine carcinoma	4	11.10	0	0.00	
Medullary carcinoma	2	5.60	6	9.40	
Other	5	13.90	8	12.50	
Chemotherapy					0.231
A	27	75.00	56	87.50	
T	4	11.10	2	3.10	
A+T	5	13.90	5	7.80	
Treatment rejection	0	0.00	1	1.60	
Ki-67, %					0.755
<20	8	22.20	16	25.00	
≥20	28	77.80	48	75.00	
P53, %					0.919
≤10	15	41.70	26	40.60	
>10	21	58.30	38	59.40	
Menopausal status					0.540
Postmenopausal	22	61.10	43	67.19	
Premenopausal	14	38.89	21	32.81	
Mean HG (IQR)	2,63 (2.45-2.82)		2.64 (2.51-2.76)		0.873
Mean NG (IQR)	2.25 (2.04-2.45)		2.45 (2.32-2.58)		0.110
Mean Age (IQR)	51.77 (48.41-55.14)		51.26 (48.21-54.31)		0.830

21 whose tumor tissue specimens were inadequate for further analysis of AR expression.

The median age at diagnosis was 51 years (range, 18-75), and the median tumor size was 3.05 cm (range, 1-13).The patients' characteristics and tumor stage distribution are shown in Table 1.

In 36 (36%) patients the tumor samples were AR^+. During follow-up at 85.17 months, 66% (n = 66) of the patients survived and 34% (n = 34) have died. The 1-year survival rate was 85% for all the patients, and the 5-year survival rate was 66%. In 36 patients, metastasis was seen during follow-up, of whom 41, 55, 22 and 19% had bone, lung, liver, and brain metastases, respectively.

No significant difference was detected between AR positivity and the metastasis location.

The median follow-up period was 85.17 months in the study group . The median OS in AR^+ and AR^- patients was 86.13 months and 84.48 months, respectively (95% CI, log-rank 0.842, p = 0.359). Ten (27.7%) of 36 AR^+ patients and 24 (37.5%) of 64 AR– patients died during their follow-up period .

The median DFS duration was 81.47 months in the AR^+ cases and 76.46 in the AR^- cases (95% CI, log-rank 1.067, p = 0.302). The patients were examined for local recurrence/metastasis formation and no significant difference in median recurrence time based on the DFS of the AR^+ and AR^- patients was noticed (95% CI, p > 0.05). Local recurrence/metastasis occurred in 10 (27%) of the 36 AR^+ patients and 25 (40%) of the 64 AR– patients.

The patients with N0 disease were examined for recurrence. No statistically significant difference in relapse rate was found between the AR^+ and AR^- patients with any lymph node involvement (95% CI, log-rank 3.077, p = 0.07 and p > 0.05, respectively). Relapse was detected in 2 of the 21 AR^+ patients with N0 (9.5%) and 12 of the 39 AR^- patients with N0 disease (30%). A similar examination was performed for the patients with node positive disease. Relapse was detected in 8 of the 15 AR^+ patients with positive lymph nodes and 13 of 25 AR– patients with positive lymph nodes. No statistically significant difference in relapse rate was found between the AR^+ and AR– patients with positive lymph nodes (95% CI, log-tank p 0.001).

Discussion

TNBC has a significantly more aggressive course, higher recurrence rate, and shorter survival time than the other breast cancer types [3,4]. TNBC has been investigated in many research studies owing to its aggressive course and limited treatment options and has been understood to be a heterogeneous disease group [5,6] .

Tumor tissue analyses in previous studies demonstrated basal like subgroups, mesenchymal and luminal like subtype [7]. Basal like subgroups might benefit more from PARP inhibitors whereas mesenchymal subtype could favor from TKI inhibitors [8].Luminal androgen receptor subtype is believed to be driven by hormone mediated signalling of androgen receptor [9]. Though molecular analyses demonstrated distinct types, by recent data, neither applying molecular tests to all TNBC patients nor choosing a therapeutic strategy according to molecular analyses is not yet applicable.

The most important parameter in prognosis determination is cancer stage at the time of diagnosis. Factors such as axillary lymph node metastasis, age, tumor type, tumor diameter, histological and nuclear grades, Ki-67 level, and p53 level are also effective prognostic predictors. However, when these parameters were considered, significant differences were observed in the treatment response and general prognosis among the patients with alike parameters despite applying the same treatment methods This shows that factors beyond well established features might drive the agressiveness of the disease. In recent years, AR expression has been explored among these factors as easily applicable and affordable. As ER and PR expressions are not found in patients with TNBC, AR positivity can be important for determining the prognosis and appropriate treatment option especially in this patient group. Although the prognostic and predictive roles of ER and PR are well known in breast cancer, the prognostic value of AR, which is frequently expressed in both normal breast tissue and primary tumors, has not been completely understood yet. The AR was shown to be expressed in 60%–85% of breast cancers [10-14]. In general, the AR staining prevalence was lower in TNBCs than in other breast cancers [15]. The AR positivity rate was reported to range from 10% to 35% in the TNBC group in different studies and to be a significant predictive factor of good prognosis [10]. Ogawa et al reported that TNBC accounts for 18.5% of all breast cancers, of which 43% are AR positive [14]. In a larger study that included 2,171 invasive breast cancer cases, of which 237 were TNBCs, AR expression was detected in 32% (75/237) [17]. The results of these studies showed notable differences. The cause may be the lack of unique criteria for assessing AR staining results. While some researchers accept >1% nuclear staining for AR staining as positive, others accept 10% [18-22]. Besides, some studies were based on the degree of staining, not the percentage [26].

In our study ,staining extent was expressed as a percentage, with ≥1% positivity in stained pre-

parates evaluated as AR positive. 36% prevalence rate of AR expression was found in the TNBC group consistent with prevous studies.

The TNBC group affects mostly patients aged <50 years and those in their premenopausal period [23,24].

In the study performed by Gazinska et al in TNBC cases, the mean age at diagnosis was 55 years [25]. Consistent with that indicated in the literature, the mean age was 51.7 years in our study.

Of our patients, 45 (45%) were aged ≤50 years. 61.10% (n: 22) of the patients with AR^+ and 67.20% (n: 43) of the AR^- patients were postmenopausal. As postmenopausal patients encounter higher levels of androgen, we consider that AR expression would be different from each other in the pre and postmenopausal period, but no significant statistical difference was found.

The reason for this might be the relative stability of the circulating testosterone levels in the postmenopausal period and also the possible local production of DHT in breast carcinomas.

The incidence of metastasis in early stage TNBC is expected to be higher in the first 5 years and the frequency declines gradually [26]. TNBC showed higher risks of recurrence as visceral organ involvements, including the liver, lung, and brain in the first recurrence [27-30]. The risk of recurrence of TNBC in bone at the initial setting was observed to be rare than that of ER-positive breast cancer. In a study that included 116 patients with TNBC, the most frequent first relapse region was found to be brain involvement and occurred in 46% of the patients during follow-up. However, the most common metastasis site during follow-up period is lung involvement and occurred in 64% [29].

The 1- and 5-year survival rates of the patients with TNBC in our study were 85.5% and 66%, respectively. The findings were in line with those in the literature [3]. During follow-up, 36 patients (36%) of our study group developed metastases. The most common metastases region was lung (55%), followed by bone (41%), liver (22%) and brain (19%).

The ER expression is related to the metastasis location. The risk of clinically significant metastasis is higher for ER-positive tumors in the bone, soft tissue, or reproductive organs, and ER-negative tumors have a higher incidence rates of metastasis in the brain and liver, which are areas related to shorter survival [31]. However, in our study we could not find any relation with AR and metastasis region.

Previous studies demonsrated conflicting relation between AR expression and survival. In a mean follow-up duration of 50 months, Gonzalez-Angulo et al found that AR expression is a significant prognostic factor for general survival and DFS [34].

In the study by He et al, 287 patients with TNBC were followed-up for 72 months on average. The mean 5-year survival was 94.2%; 5-year DFS, 94.2% for the AR^+ group; mean survival rate, 82.3%; and DSF, 74.2% for the AR- group [35].

In the study by Tang et al, 127 patients with TNBC were evaluated, and AR expression was significantly related to both tumor grade and OS and DFS [36].

Several studies have reported no significant difference in DFS or OS between AR^+ and AR^- TNBC [37,38].

Although a statistically significant relationship was not found between OS and DFS in our study, both DFS and OS were observed to be significantly higher in the AR-positive group. Ten out of the 36 AR^+ patients (27.7%) and 24 of the 64 AR– patients (37.5%) died. While the median DFS time of the AR-positive patients was 81.47 months, their OS time was 86.13 months during follow-up. While the DFS time was 76.46 months in the AR-negative group, the mean survival was 84.48 months during follow-up. Again, in a similar study with 84 patients in Turkey, while no relationship was found between OS and DFS, grade 3 tumors were less detected in the AR^+ group [39].

No significant relationship was found between tumor grade and AR expression in our study. In a series published in 2008, the AR positivity rate was significantly higher in smaller carcinomas, tumors without lymph node metastasis, and p53-negative tumors in 227 Japanese patients [16].

The TNBC cases without lymph node involvement were examined for recurrence. Recurrence was detected in 2 of the 21 AR-positive patients (9.5%) and in 12 of the 39 AR-negative patients with N0 disease (30%). Although statistically meaningful difference could not be demonstrated;the recurrence risk seemed to be lower in AR^+ group. However, in locally advanced disease the relapse rate frequency was same.

In the studies by Rakha et al in 282 patients, the incidence rates of high nuclear grade, recurrence, and distant metastasis increased in patients with AR-negative TNBC, especially in locally advanced setting which is contrary to our findings [3].

Our study has some limitations due the retrospective design. As a single center study, our patient number is relatively small and determination of TNBC was accomplished by immunohistochemical methods without any molecular tests to detect subgroups.

Today, AR antagonists are investigated as the new potential target. Understanding the prevalence

of AR expression and its differences among subtypes is important for predicting the group which targeting AR will achieve better response.

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Conflict of interests

The authors declare no conflict of interests.

References

1. Lehmann BD, Bauer JA, Schafer JM et al. PIK3CA mutation in androgen receptor-positive triple negative breast cancer confer sensitivity to the combination of PI3K and androgen receptor inhibitors. Breast Cancer Res 2014;16:406-19.
2. Loibl S, Müller BM, von Minckwitz G et al. Androgen receptor expression in primary breast cancer and its predictive and prognostic value in patients treated with neoadjuvant chemotherapy. Breast Cancer Res Treat 2011;130:477-87.
3. Rakha EA, El-Sayed ME, Green AR, Lee AH, Robertson JF, Ellis IO. Prognostic markers in triple-negative breast cancer. Cancer 2007;109:25-32.
4. Foulkes WD, Smith IE, Reis-Filho JS. Triple negative breast cancer. N Engl J Med 2010;363:1938-48.
5. Koboldt DC, Fulton RS, McLellan MD et al. Comprehensive molecular portraits of human breast tumours. Nature 2012;490:61-70.
6. Lehmann BD, Bauer JA, Chen X et al. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest 2011;121:2750-67.
7. Wang DY, Jiang Z, Ben-David Y, Woodgett JR, Zacksenhaus E. Molecular stratification within triple-negative breast cancer subtypes. Sci Rep 2019;9:19107.
8. Diana A, Carlino F, Franzese E at al. Early Triple Negative Breast Cancer: Conventional Treatment and Emerging Therapeutic Landscapes. Cancers (Basel) 2020;12:819-44.
9. Narayanan R, Dalton JT. Androgen Receptor: A Complex Therapeutic Target for Breast Cancer. Cancers (Basel) 2016 ;8:108-24.
10. Hennighausen L, Robinson GW. Information networks in the mammary gland. Nat Rev Mol Cell Biol 2005;6:715-25.
11. Gonzalez LO, Corte MD, Vazquez J et al. Androgen receptor expression in breast cancer: relationship with clinicopathological characteristics of the tumors, prognosis, and expression of metalloproteases and their inhibitors. BMC Cancer 2008;8:149.
12. Isola JJ. Immunohistochemical demonstration of androgen receptor in breast cancer and its relationship to other prognostic factors. J Pathol 1993;170:31-5.
13. Kuenen-Boumeester V, Van der Kwast TH, van Putten WL, Claassen C, van Ooijen B, Henzen-Logmans SC. Immunohistochemical determination of androgen receptors in relation to oestrogen and progesterone receptors in female breast cancer. Int J Cancer 1992;52:581-4.
14. Moinfar F, Okcu M, Tsybrovskyy O et al. Androgen receptors frequently are expressed in breast carcinomas: potential relevance to new therapeutic strategies. Cancer 2003;98:703-11.
15. Luo X, Shi YX, Li ZM, Jiang WQ. Expression and clinical significance of androgen receptor in triple negative breast cancer. Chin J Cancer 2010;29:585-90.
16. Ogawa Y, Hai E, Matsumoto K et al. Androgen receptor expression in breast cancer: relationship with clinicopathological factors and biomarkers. Int J Clin Oncol 2008;13:431-5.
17. Collins LC, Cole KS, Marotti JD, Hu R, Schnitt SJ, Tamimi RM. Androgen receptor expression in breast cancer in relation to molecular phenotype: results from the Nurses' Health Study. Mod Pathol 2011;24:924-31.
18. Tsutsumi Y. Apocrine carcinoma as triple-negative breast cancer: novel definition of apocrine-type carcinoma as estrogen/progesterone receptornegative and androgen receptor-positive invasive ductal carcinoma. Jpn J Clin Oncol 2012;42:375-86.
19. Pristauz G, Petru E, Stacher E et al. Androgen receptor expression in breast cancer patients tested for BRCA1 and BRCA2 mutations. Histopathology 2010;57:877-84.
20. Chen J, Zhang X, Tian R et al. Expression of androgen receptor in breast carcinoma and its relationship with estrogen receptor, progesterone receptor and HER2 status. Zhonghua Bing Li Xue Za Zhi 2010;39:743-6.
21. Koo JS, Jung W. Clinicopathlogic and immunohistochemical characteristics of triple negative invasive lobular carcinoma. Yonsei Med J 2011;52:89-97.
22. Micello D, Marando A, Sahnane N, Riva C, Capella C, Sessa F. Androgen receptor is frequently expressed in HER2-positive, ER/PR-negative breast cancers. Virchows Arch 2010;457:467-76.
23. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7-34.
24. Rao C, Shetty J, Prasad KH. Immunohistochemical profile and morphology in triple - negative breast cancers. J Clin Diagn Res 2013;7:1361-5.
25. Gazinska P, Grigoriadis A, Brown JP et al. Comparison of basal-like triple-negative breast cancer defined by morphology, immunohistochemistry and transcriptional profiles. Mod Pathol 2013;26:955-66.

26. Liedtke C, Mazouni C, Hess KR et al. Response to neoadjuvant therapy and long-term survival in patients with triple-negative breast cancer. J Clin Oncol 2008;26:1275-81.
27. Lin NU, Vanderplas A, Hughes ME et al. Clinicopathologic features, patterns of recurrence, and survival among women with triple-negative breast cancer in the National Comprehensive Cancer Network. Cancer 2012;118:5463-72.
28. Smid M, Wang Y, Zhang Y et al. Subtypes of breast cancer show preferential site of relapse. Cancer Res 2008;68:3108-14.
29. Lin NU, Claus E, Sohl J, Razzak AR, Arnaout A, Winer EP. Sites of distant recurrence and clinical outcomes in patients with metastatic triple-negative breast cancer: high incidence of central nervous system metastases. Cancer 2008;113:2638-45.
30. Hicks DG, Short SM, Prescott NL et al. Breast cancers with brain metastases are more likely to be estrogen receptor negative, express the basal cytokeratin CK5/6, and overexpress HER2 or EGFR. Am J Surg Pathol 2006;30:1097-1104.
31. Insa A, Lluch A, Prosper F, Marugan I, Martinez-Agullo A, Garcia-Conde J.Prognostic factors predicting survival from first recurrence in patients with metastatic breast cancer: analysis of 439 patients. Breast Cancer Res Treat 1999;56:67-78.
32. Gerratana L, Fanotto V, Bonotto M et al. Pattern of metastasis and outcome in patients with breast cancer. Clin Exp Metastasis 2015;32:125-33.
33. Ahn SG, Kim SJ, Kim C, Jeong J. Molecular classification of triple-negative breast cancer. J Breast Cancer 2016;19:223-30.
34. Gonzalez-Angulo AM, Stemke-Hale K, Palla SL et al. Androgen receptor levels and association with PIK3CA mutations and prognosis in breast cancer. Clin Cancer Res 2009;15:2472-8.
35. He J, Peng R, Yuan Z et al. Prognostic value of androgen receptor expression in operable triple-negative breast cancer: a retrospective analysis based on a tissue microarray. Med Oncol 2012;29:406-10.
36. Tang D, Xu S, Zhang Q, Zhao W. The expression and clinical significance of the androgen receptor and E-cadherin in triple-negative breast cancer. Med Oncol 2012;29:526-33.
37. Astvatsaturyan K, Yue Y, Walts AE, Bose S.Androgen receptor positive triple negative breast cancer: Clinicopathologic, prognostic, and predictive features. PLoS One 2018;8:13-28.
38. Pistelli M, Caramanti M, Biscotti T et al. Androgen receptor expression in early triple-negative breast cancer: clinical significance and prognostic associations. Cancers (Basel) 2014;6:1351-62.
39. Sunar V, T Dogan H, Sarici F et al. Association between androgen receptor status and prognosis in triple negative breast cancer. JBUON 2018;23:1325-30.