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ORIGINAL ARTICLE

Hormone sensitivity of primary breast carcinoma

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Summary

Purpose: *This study was designed to evaluate hormonal sensitivity of primary breast cancer by way of determination of estrogen receptors (ER) and progesterone receptors (PR) status as an important prognostic and predictive parameter of breast cancer.*

Methods: *The study enrolled 449 breast cancer patients surgically treated at the Surgical Clinic Nis, in a period covering 3 years, who continued treatment at the Clinic of Oncology, Clinical Centre Nis. All of the patients were divided into 4 groups depending on the positive or negative status of ER and PR, and 2 subgroups, those with positive or negative HER2 status. Standard descriptive statistical parameters were calculated and several types of tests were applied: Student's t-test for paired and unpaired samples, chi-square test, Mantel-Haenszel test, Fisher's test of exact probability and binary logistic regression model.*

Results: *The level of ER and PR status positively correlated with patient age, postmenopausal status, lower clinical stage, lower histologic grade (HG) and nuclear grade (NG) and better prognosis. Amplification/overexpression of HER2 positively correlated with premenopausal status and ER negative breast cancer phenotype. According to the model of binary logistic regression, clinical stage and NG of the breast primary were significantly associated with hormonal sensitivity of the tumor.*

Conclusion: *Measurements of receptor macromolecules in clinical oncology is very important, especially in breast cancer patients. ER and PR analysis is an integral part of breast cancer study since it can provide information essential for both treatment and prognosis.*

Key words: breast carcinoma, estrogen receptors, progesterone receptors

Introduction

Breast carcinoma is the most common malignant neoplasm in women in the Republic of Serbia with great significance because of the continual rise of its incidence and mortality [1]. It is the leading cause of death from malignant diseases, one of the causes of premature death in female population, usually detected in advanced stages and with unfavorable age distribution [1-3].

Prognostic factors used for primary breast cancer can be patient-related (age and menstrual status) and tumor-related: size, histologic type, axillary lymph node status, HG and NG, ER and PR status and proliferative capacity [4]. HER2 receptor and HER2/neu oncogene [5-7] are among the new prognostic factors, thoroughly studied and already in use.

Breast cancer is a prototype of hormone-sensitive tumor, thus ER and PR analysis is an integral part of breast cancer study since it can provide information essential for both treatment and prognosis [8]. High receptor content indicates a positive response to endocrine treatment, i.e. that the breast cancer is hormone-sensitive. Around 70% of all primary breast cancers have positive ER, while 30% are negative in that regard [9]. A positive receptor status correlates with favorable prognostic characteristics: better differentiation, slow growth, hormone sensitivity, a lower percentage of cells in S-phase of the cell cycle, low percentage of aneuploid cells, lower values of oncogene activation and expression, better survival of pre- and postmenopausal patients [10].

ER/PR status is a surrogate marker of the degree of differentiation of breast cancer and it could serve as a predictor of response to hormone therapy and overall post-relapse survival. Expression of ER and PR has

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an important role in the validation of new therapeutic agents and interpretation of clinical results.

Breast tumors with HER2 gene amplification or HER2 protein overexpression on the cell surface, are regarded as HER2-positive tumors [11]. Lots of studies identified the association between amplification and/or overexpression of HER2 and higher tumor grade, low ER/PR content, higher incidence of ductal carcinomas compared to lobular ones, which results in poor prognosis in these patients [12,13].

ASCO recommends that HER2 overexpression should be assessed in each case of primary breast cancer, after the diagnosis or after disease recurrence [14].

In view of breast cancer characteristics and its importance as the cancer most commonly occurring in females in Serbia [2,15,16], this study was designed to evaluate hormonal sensitivity of primary breast cancer by way of determination of ER and PR status as an important prognostic and predictive parameter of breast cancer.

Methods

The study enrolled 449 breast cancer patients surgically treated at the Surgical Clinic, Clinical Centre Nis, in a 3-year period (from January 2003 to December 2005); patients continued adjuvant treatment (chemotherapy, hormonotherapy, trastuzumab) based on tumor biological characteristics, at the Clinic of Oncology, Clinical Center, Nis. Patients with metastatic disease received anticancer treatment (chemotherapy, hormonotherapy, trastuzumab, radiotherapy) based on tumor biological characteristics and tumor spread, at the same Center. All of the patients had histopathologic assessment and diagnosis confirmation at the Institute of Pathology, Clinical Centre Nis. The data were obtained by way of analysis of medical records of the Surgical Clinic and Institute of Pathology, as well as the hospital registry and patient histories at the Clinic of Oncology, Clinical Centre Nis.

All of the patients for whom receptor status was determined (n=440) were divided into 4 groups, depending on the status of ER and PR (Table 1). Data analysis was performed related to hormonal sensitivity; patients were thus divided into 2 subgroups: with hormone sensitive and insensitive disease. At the same time, 2 patient subgroups were analysed: HER2 positive and HER2 negative.

Patients were stratified according to their age, with special selection of those below 40 years of age at the time of diagnosis.

All of the cases were assessed in regard to the clinical tumor stage, defined as operable, locally advanced, or metastatic disease. Patients were also divided into 2 groups according to their menstrual status (pre and postmenopausal).

Table 1. Patient grouping according to steroid receptor status

Hormonal grouping	*ER/PR status Patients, n*
group I	246 with ER+/PR+
group II	65 with ER+/PR–
group III	20 with ER–/PR+
group IV	109 with ER–/PR–

With regard to the type of surgery, patients were divided into 3 groups: those with radical surgery, conservative (sparing) surgery, and biopsy.

Biological characteristics of the tumors were determined by way of the analysis of histopathologic data (histopathologic tumor type, HG and NG). ER, PR and HER2 status were determined immunohistochemically. In cases of HER2++, CICH methodology was utilized. Based on positivity, the following patient groups were identified: those with +(1+) moderate, ++(2+) intermediate, and +++(3+) strong overexpression and/or amplification of HER2. Specific targeted therapy was administered only in 3+ cases. Patients without overexpression and/or amplification were regarded as HER2 negative.

Statistical considerations

Data were processed calculating the standard descriptive statistical parameters (mean value, standard deviation, percent presence). The results were analysed using the appropriate tests, depending on the group size, type of characteristic, and type of distribution. Statistical processing was performed within and between the defined groups.

Several types of tests were applied: Student's t-test for paired and unpaired samples, chi-square test, Mantel-Haenszel test, Fisher's test of exact probability and binary logistic regression model. Differences were considered as statistically significant when $p<0.05$.

Statistical processing was accomplished in Excel 7.0 and SPSS 11.0 in the Windows 98 environment.

Results

Enrolled were 449 patients aged 56±12 years, predominantly urban dwellers (there were no statistically significant differences for these variables among the groups; Table 2).

ER/PR status was determined in 440 (98%) women. Out of the total number of women, ER+/PR+ was observed in 246 (54.7%); ER+/PR- in 65 (14.5%), ER-/

Table 2. Steroid receptors status of primary breast cancer in surgically treated patients

Receptor status	*Patients n (%)*	*Age (years)*	*Place of residence Urban/Rural*
ER+/PR+	246 (54.7)	55.5±11.9	154/92
ER+/PR-	65 (14.5)	57.4±9.02	46/19
ER-/PR+	20 (4.5)	54.2±15.1	9/11
ER-/PR-	109 (24.3)	57.6±11.9	65/44
Undetermined	9 (2.0)	67.4±7.7	4/5
Total	449 (100.0)	56.2±12	278/171

p=nonsignificant

Table 3. Steroid receptors status of primary breast cancer and age structure of the patients

Age groups (years)	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total*
< 39	11 (40.7)	1 (3.7)	7 (26.0)	8 (29.6)	27
40-49	62 (61.4)	10 (9.9)	5 (5.0)	24 (3.7)	101
50-59	80 (55.9)	26 (18.1)	2 (1.6)	35 (24.4)	143
60-69	44 (47.8)	21 (22.8)	3 (4.0)	24 (26.0)	92
70-79	47 (62.6)	7 (9.3)	3 (4.0)	18 (24)	75
80-89	2 (100)	0	0	0	2
Total	246	65	20	109	440

p=nonsignificant

PR+ in 20 (4.5%), and ER-/PR- in 109 (24.3%) women (Table 2). ER+ breast cancer status was 3-fold more common than ER- status.

Most of the patients were aged from 50 to 59, then from 40 to 49, and finally from 60 to 69 years (Table 3). The fewest patients were 80-89 years.

The incidence of receptor status combinations and their trends related to patient age, demonstrated that in patients below 40 years of age hormonal insensitivity predominated (around 30% of all cases). With advancing age, hormonosensitive cancers grew in number while other types diminished (Table 3).

In postmenopausal women ER positivity was very common, in contrast to premenopausal women with predominating ER negativity (Table 4). ER+/PR+ combination was present in 61.3% of postmenopausal women, while 58.9% of premenopausal women had hormono insensitive cancers (ER-/PR-) (Table 4).

Various ER/PR combinations in various histopathologic forms of breast cancer are shown in Table 4.

Ductal invasive carcinoma was the most common histopathologic type in our patients (71.1%), while carcinoma *in situ* and mastitis carcinomatosa were the rarest types (Table 5).

Related to histopathology, hormonosensitivity was identified in 75% of ductal invasive carcinoma, in 77% of lobular invasive carcinoma, 83% of ducto-lobular invasive carcinoma, 67% of carcinoma *in situ*, and 47% of mastitis carcinomatosa cases (Table 5).

The relationship of ER/PR status and HG is shown in Table 6. It may well be observed that most of the patients with HGs 1 and 2 were hormone sensitive, while most of those with hormone insensitive disease had grade 3 disease (Table 6). Variance analysis demonstrated a significant difference in HGs among the patient groups with different receptor status ($F=4.9$, $p<0.05$). *Post hoc* analysis demonstrated statistically significance

Table 4. Steroid receptors status and menstrual status in women operated for breast cancer

Status	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total n (%)*
Postmenopause	200 (61.3)	50 (15.3)	12 (3.7)	64 (19.7)	326 (74.1)
Premenopause	30 (26.3)	10 (8.7)	7 (6.1)	67 (58.9)	114 (25.9)
Total	230 (52.3)	60 (13.6)	19 (4.3)	131 (29.8)	440 (100.0)

p=nonsignificant

Table 5. ER/PR combinations in various histopathologic types of breast cancer

Histology	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total n (%)*
Invasive ductal	175 (55.9)	47 (15)	14 (4.47)	77 (24.7)	313 (71.1)
Invasive lobular	32 (61.5)	7 (13.4)	1 (2.1)	12 (23.0)	52 (11.8)
Invasive ductolobular	43 (64.2)	7 (13.2)	3 (5.6)	9 (17)	53 (12)
Ca *in situ*	2 (66.6)	0	0	1 (33.3)	3 (0.7)
Mastitis carcinomatosa	3 (15.7)	4 (21.0)	2 (10.7)	10 (52.6)	19 (4.3)
Total	246	65	20	109	440

p=nonsignificant

difference between the groups with ER+/PR+ and ER–/PR– (Tukey HSD, p <0.05), confirming the finding of common sensitivity of lower grades and common insensitivity of higher tumor grades. The Mantel-Haenzel test demonstrated that in hormonosensitive tumors HG 2 was significantly more common, and in hormone insensitive disease HG 3 (Hi=8.01, p <0.01). Grade 1 was markedly less common.

The relationship of ER/PR status and NG is shown in Table 7. In the studied patients, NG2 was most common, while NG 1 was significantly less common (Table 7).

In hormone sensitive tumors nuclear grade 2 was the most common (61%), while in hormone insensitive tumors the number of patients with NG 2 and 3 tumors was similar (these grades were the most common in this group; Table 7).

The combinations of receptor status related to clinical disease stage is shown in Table 8.

Variance analysis demonstrated a significant difference in clinical stages among the patients with different receptor combinations (F=3.75, p<0.05). The *post hoc* analysis indicated that the difference among the ER+/PR+ and ER–/PR– groups (Tuckey HSD, p < 0.05) was in favor of ER+/PR+ tumors – operable tumors were predominantly ER+/PR+.

Hormone-sensitive tumors (ER+/PR+, ER+/PR–, ER–/PR+) were operable in 82.2% and locally advanced in 15.1%. Insensitive tumors were operable in 67.9% and locally advanced in 27.5%. The Mantel-Haenzel test confirmed that hormonosensitive tumors were more commonly operable, and less commonly locally advanced compared to insensitive tumors (Hi=8.2 p <0.01). Metastatic tumors did not demonstrate any significant difference in hormonal sensitivity (p=non significant; Table 8).

HER2 status was determined in 94 out of 449 surgically treated patients. Nine of these had weak positivity (+), 10 moderate (++) and there were 75 women with strong positivity (+++). The relationship of HER2 status with strong expression (+++) and menstrual status is shown in Table 9. Statistical analysis demonstrated no significant difference in HER2 positivity related to menopausal status, however it can be observed that HER2 positive women were more commonly premenopausal (61 vs. 39%) and HER2 negative more

Table 6. ER/PR status of breast cancer and histologic grade

Histologic grade	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total n (%)*
1	17 (60.7)	4 (14.2)	2 (7.1)	5 (17.8)	28 (100)
2	173 (61.3)	42 (14.8)	9 (3.19)	58 (20.5)	282 (100)
3	49 (48.1)	11 (10.7)	6 (5.8)	36 (35.3)	102 (100)
Undetermined	7 (25)	8 (28.5)	3 (10.7)	10 (35.7)	28 (100)
Total	246	65	20	109	440

p<0.05

Table 7. ER/PR status of breast cancer and nuclear grade

Nuclear grade	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total n (%)*
1	17 (73.9)	2 (8.7)	2 (8.7)	2 (8.7)	23 (100)
2	153 (60.9)	36 (14.4)	10 (3.9)	52 (20.7)	251 (100)
3	69 (50)	19 (13.8)	6 (4.3)	44 (31.9)	138 (100)
Undetermined	7 (25)	8 (28.5)	2 (7.1)	11 (39.3)	28 (100)
Total	246	65	20	109	440

p<0.05

Table 8. Breast cancer steroid receptors status combinations related to clinical disease stage

Stage	*ER+/PR+ n (%)*	*ER+/PR– n (%)*	*ER–/PR+ n (%)*	*ER–/PR– n (%)*	*Total*
Operable	207 (59.8)	49 (14.1)	16 (4.6)	74 (21.5)	346
Locally advanced	33 (3.7)	13 (16.2)	4 (42.6)	30 (37.5)	80
Metastatic	6 (42.8)	3 (21.4)	0	5 (35.8)	14
Total	246	65	20	109	440

p<0.05

commonly postmenopausal (56 vs. 44%) (Table 9).

The percentage of HER2 positive findings (+++) related to ER status is shown in Table 10. HER2 positive patients were most commonly ER-, while HER2 negative were most commonly ER+ (Mantel-Haenzel test, $p < 0.01$).

In HER2+++ patients ER- tumors were most common (68.3%), while in the HER2 negative group there were 29.5% of ER- tumors (Table 10).

Table 11 displays HER2 status (+++) and clinical stage of primary breast cancer.

Fisher's test of exact probability did not demonstrate significant differences in HER2 distribution among the patient groups with operable and locally advanced carcinoma (Hi=0.23, p=NS). Metastatic cancers were more commonly HER2+++ compared to operable and locally advanced ones, without statistical significance though. It should be noted that the number of patients with determined HER2 status was relatively small for any final conclusion to be drawn (Table 11).

Table 9. HER2 status of primary breast cancer and menstrual status of surgically treated patients

Menstrual status	*HER2 positive (+++) n (%)*	*HER2 negative n (%)*	*Total n (%)*
Premenopause	25 (62.5)	15 (37.5)	40 (100)
Postmenopause	16 (45.7)	19 (54.2)	35 (100)
Total	41	34	75

p=nonsignificant

Table 10. HER2 status of overexpression and/or amplification (+++) related to estrogen receptor level in primary breast cancer

Status	*HER2 positive (+++) n (%)*	*HER2 negative n (%)*	*Total n (%)*
ER positive	13 (35.2)	24 (64.8)	37 (100)
ER negative	28 (73.7)	10 (26.3)	38 (100)
Total	41	34	75

p<0.01

HER2 positive findings related to clinical disease stage were present in 56.2% of operable tumors, in 31.7% of locally advanced disease and in 12.1% of metastatic disease (Table 11).

Table 12 illustrates ER status in patients according to age. There were 70.4% of ER positive patients below 40 years of age, and 75.5% in those over 40.

Fisher's exact test demonstrated a significant difference between ER positive and ER negative tumors in these age subgroups, i.e. ER+ tumors were significantly more common in older women.

The association of all the studied indicators with tumor hormonal sensitivity is shown in Table 13.

The group significance of the model involving all

Table 12. ER status of primary breast cancer according to <40 or >40 years of age

ER status	*<40 years n (%)*	*>40 years n (%)*	*Total n (%)*
ER positive	19 (5.7)	312 (94.3)	331 (100)
ER negative	8 (7.3)	101 (92.7)	109 (100)
Total	27	413	75

p=nonsignificant

Table 13. Association of biological and clinical characteristics of hormone-sensitive tumors

Variable	*OR**	*95% CI[§]*	*p-value[†]*
pT	0.957	0.789-1.160	0.654
pN	1.045	0.917-1.192	0.508
M	1.010	0.797-1.280	0.934
Clinical stage	0.511	0.311-0.839	0.008
Histological grade	0.927	0.532-1.614	0.788
Nuclear grade	0.570	0.402-0.807	0.002
Histopathological type	0.950	0.742-1.217	0.686
HER2 status	0.825	0.575-1.182	0.294
Menopause	1.133	0.565-2.271	0.726
Right/left breast	1.118	0.711-1.761	0.629
Localization in the breast	1.002	0.807-1.245	0.984
Operable carcinoma	1.541	1.028-2.309	0.036
Age	0.987	0.962-1.014	0.351

*odds ratio, [§]95% confidence interval and [†]p-value estimated by binary logistic regression analysis. p: pathological

Table 11. HER2 status and clinical stage of primary breast cancer

Clinical stage	*HER2 positive (+++) n (%)*	*HER2 negative n (%)*	*Not done n (%)*	*Total*
Operable	23 (53.5)	20 (46.5)	303 (87.6)	346
Locally advanced	13 (52)	12 (48)	55 (88.8)	80
Metastatic	5 (71.4)	2 (28.6)	7 (51)	14
Total	41	34	365	440

p=nonsignificant

of the examined factors was Cox & Snell R^2=0.05, with significant association with tumor hormonal sensitivity established only for clinical stage, NG of the primary tumor and tumor operability (Table 13).

Discussion

At the National Cancer Research Centre, according to the hospital registry, the average age at diagnosis of breast cancer patients was 56 years in 2003, with 30% of those below 50 years of age (6% below 40; 24% aged 40-49 years) [1,3]. Our data are very similar: there were 6% of those below 40; 23% of those aged 40-49 years; and 29% of those below 50 years of age. Age structure of breast cancer patients in central Serbia [2] is slightly different though (i.e., there were 27% of those below 50 years of age), but surely indicates younger age at diagnosis when compared to other countries. The average age of breast cancer patients in the U.S.A., Australia, and Slovenia is around 60 years [1] (63 in the USA; 61 in Australia; 61 in Slovenia). According to the data for central Serbia for 2004 [2], breast cancer was diagnosed before 50 years of age in 22% of women (5% below 40; 17% in the age range from 40 to 49 years). In the same year, in Croatia [1] and Great Britain, breast cancer was diagnosed below 50 years of age in 19.5% (4.5% below 40; 15% in the age range from 40 to 49 years).

ER and PR status is an important prognostic and predictive factor in breast cancer. Various studies have reported that around 70% of all breast primaries express ER, while 30% are ER negative [17], which is not much different from our results (ER+ 75%; ER- 25 %). Chariyalertsak et al. have reported a lower percentage of expression (ER+ 36.1%) in Thailand women [18]. Similar results have been obtained in India (ER+ 32%) [19], which has been confirmed by other studies too, reporting a higher percentage of receptor negativity (46.5%). This could be partly explained by more common breast cancer in younger women with higher tumor grade, approximately 10 years younger compared to Western countries [18]. However, the studies in China have reported 73.5% of ER+ women [20].

When the treatment is based on ER and PR content, only 70-80% of those with receptor positive disease will respond positively to treatment; the remaining 20-30% will be resistant. The background of such therapeutic response could be the existence of various ER/PR combinations, i.e. different concentrations of these receptors. In the results published so far by Barnes et al. [19], in the European population there were 50% of ER+/PR+ cancers, 25% were ER-/PR-, 20% were ER+/PR–, and around 5% were ER-/PR+. Our results are similar, except for ER+/PR+ of 55% and ER+/PR– of 15%. There is an unusual result of a study in India [19], reporting a high level of ER–/PR+ (21.1 vs. 5%). This receptor status was present in patients with soft tissue and central nervous system metastases. These data support the fact that this is one biologically and clinically defined subgroup requiring further analyses and assessments.

In our study, ER+/PR+ cancers were present in 55% of women, with even 70.3% in those over 50 years of age, while literature reports give a percentage of 49% (which could be explained by the number of studied patients). ER–/PR– combination was more common in younger patients, which correlates with the literature data [22].

Receptor-positive breast cancers are more common in menopause (80.3%), while receptor-negative cases are commonly encountered in younger age groups (41.2%), which is the result of differences in hormonal status or in biological characteristics of their tumors. More ER-/PR- breast primaries in postmenopause compared to premenopause could be the result of higher estrogen concentrations and better ER saturation with endogenous estradiol [23].

Related to histologic type and invasiveness of breast cancer, according to literature data, lobular carcinoma has different clinical and biologic characteristics compared to ductal carcinoma [24]. In most studies the results of ER and PR were presented related to *in situ* carcinomas, in which the level of ER expression was around 30-80%, and PR around 65%. Both expressions are associated with good nuclear differentiation. Negative ER cases were associated with high HG and NG. Other authors stated that 100% of lobular cancers *in situ* and 80% of ductal cancers *in situ* were ER+ [25].

In numerous studies, ER- breast cancers represent a histopathologically heterogeneous group, generally thought of as cancers with aggressive behavior. Invasive ductal carcinoma belongs to this group in a high percentage. However, it has been demonstrated that this heterogeneous group includes not only aggressive carcinomas, in view of the fact that in around 43% of the cases there are no lymph node metastases [26]. With a small number of cases with carcinoma *in situ* in our study and a larger number of ductolobular cases, our results cannot be taken as statistically significant, however without significant differences from the literature data. Lobular and ductolobular forms of carcinoma express ER+ more than ductal invasive forms. Mastitis carcinomatosa, as a biologically more aggressive form of cancer is more commonly ER- [27]. HG2 was the most common form, and ER+ decreased starting from HG1 (highest) to HG3 (lowest level). ER negativity increased with NG increase.

Operable carcinomas are ER+ in 78.6% compared to ER- with 21.4% operability, while locally advanced cancers are ER+ in 62.5% and metastatic in 64.2%. Data from the literature demonstrate that tumor size does not correlate with ER/PR status [28].

Receptor for human epidermal growth factor (HER2) is also an important prognostic factor in breast cancer. It has been established that there is a significant association of amplification/overexpression of HER2 and low ER and PR concentrations [29-31], which is in concordance with our results. Most of the studies published so far suggest that overexpression of the receptor is associated with poor prognosis in patients with breast cancer [29,31]. However, there are observations that out of all HER2+ breast cancers only a small part (<12%) is activated and only these have poor prognosis, in contrast to the other part of breast cancers with positive HER2, the prognosis of which is similar to HER2 negative cancers [32].

In our study, HER2 status was determined in 20.9% of the cases; out of these, there were 9.6% of cancers with weak expression (1+), 10.6% with 2+, and 79.8% with 3+.

Overexpression and/or amplification was very significant in premenopausal women (62.5%), and associated with ER- phenotype. Patients with HER2 negative receptor had hormonosensitive disease in 64.8%, confirming the literature data, and these patients had better prognosis [33].

HER2 status did not demonstrate any significant association with clinical stage of disease.

According to many studies, breast cancer is much more aggressive in younger patients, it is usually diagnosed in more advanced stages and often requires aggressive therapy. One of the reasons of poor prognosis could be the fact that in these patients receptor-negative breast cancer, unresponsive to hormonal treatment, is more common [22].

In our study there were 27 (6%) women below 40 years of age operated for breast cancer with determined ER/PR status. Out of the total number of patients with measured receptors, 70.3% were with hormonosensitive disease, which is of statistical significance and differs from the results of numerous studies. The reason of such findings could be the relatively small number of studied patients, but also the criteria for receptor positivity determination, subject to modification, with representation only of cancers with significant ER expression in most studies [34]. There are literature data suggesting beneficial effects of hormonal therapy in 10% of receptor-negative carcinomas [35], which is explained by an extra-receptor, insufficiently explained mechanism of action of hormonotherapy.

Conclusion

Breast cancer is the most common malignant disease in women, presenting a special problem in modern oncology due to its incidence and problems related to early diagnosis, appropriate therapy and treatment outcomes.

Measurements of receptor macromolecules in clinical oncology is very important, especially in breast cancer patients. ER and PR analysis is an integral part of breast cancer study since it can provide information essential for both treatment and prognosis. HER2 status is also an important prognostic factor in breast cancer.

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