

## ORIGINAL ARTICLE

# Breast cancer in women under 40 years of age

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## Summary

**Purpose:** It is widely believed that breast cancer in young women is characterized by a relatively unfavorable prognosis and unusual pathological features. The aim of this study was to investigate clinicopathological and biological characteristics in young patients with breast cancer.

**Methods:** The study enrolled 1029 consecutive female breast cancer patients who were admitted to the Clinical Centre Nis between July 2002 and December 2008.

**Results:** 91 (8.8%) patients were under and 938 (91.2%) were over 40 years. The mean age was 35.9 years for those under 40 years and 58.3 for those older than 40 years. In both patient groups, left breast was most commonly involved; the most common primary tumor site was the upper lateral quadrant; the most common histological type was ductal carcinoma; histological and nuclear grade 2 was most common. In the younger group of patients, the proportion of patients

with T3 and T4 disease was higher (13.0 vs. 9.3% and 16.5 vs. 12.0%), the number of patients with histological and nuclear grade 3 disease was higher (27.5 vs. 24.7% and 37.4 vs. 33.2%), the proportion of patients with 4-9 and >10 positive lymph nodes was higher (22.6 vs. 18.3% and 7.1 vs. 4.0%), and the percentage of family history of breast cancer was higher (5.5 vs. 3.1%), without statistically significant differences between the two age groups. Patients in the younger age group exhibited higher estrogen (ER)/progesterone (PR) receptor negativity (32.6 vs. 24.4%) ( $p < 0.05$ ).

**Conclusion:** Although uncommon, breast cancer in young women is worth special attention. The underlying causes of the disease must be investigated in large population-based studies in the future.

**Key words:** biological characteristics, breast carcinoma, clinical characteristics, pathological characteristics, young women

## Introduction

Breast cancer is the most common type of cancer among women. Its incidence is low at young age, but it is widely believed that the clinical and pathological profile of breast cancer in young women is significantly different than in older patients, with a predominance of unfavorable prognostic parameters. These patients usually have a poorer prognosis [1]. It has been reported that younger patients have more metastatic axillary lymph nodes and higher incidence of local recurrences than older patients [2]. Some authors reported that breast cancer in younger women was of higher grade, higher proliferation fraction, had more vascular invasion, and expressed less ER and PR positivity compared to tumors in older women [3,4]. Women under 40 had a low-

er 5-year overall survival [5] and more common family history of breast cancer compared to older ones [6].

Some authors have accepted patients under 40 years as young, while some others have considered patients under 35 years as young patients. According to different authors, the incidence of breast cancer in women under 35 years is between 2.7-12.5% [7,8]. The incidence is also low among those under 40 years. The highest incidence reported in the literature is 28% [8] and 42.5% [9].

In view of breast cancer characteristics and its importance as the cancer most commonly occurring in females in Serbia [10,11], we performed a retrospective review of young female breast cancer patients admitted at the Clinical Centre Nis, to assess clinicopathological and biological characteristics that may influence the clinical outcome and prognosis.

## Methods

The study enrolled a total of 1029 female breast cancer patients surgically treated at the Surgical Clinic, Clinical Centre Nis, from July 2002 to December 2008. All patients had histopathologic assessment and diagnosis confirmation at the Institute of Pathology, Clinical Centre Nis. Patients were put on adjuvant treatment (chemotherapy, hormonotherapy, trastuzumab) based on tumor biological characteristics, at the Clinic of Oncology, Clinical Center Nis, while those with metastatic disease received anticancer treatment (chemotherapy, hormonotherapy, trastuzumab, radiotherapy) based also on tumor biological characteristics and tumor spread, at the same Center. The data were obtained by way of analysis of medical documentation of the Surgical Clinic and Institute of Pathology, as well as the hospital registry and patient records at the Clinic of Oncology, Clinical Centre Nis. Patients under 40 years of age at the time of breast cancer diagnosis were considered as young.

### Statistical considerations

Data were processed calculating the standard descriptive statistical parameters (mean value, standard deviation (SD), percent presence). The results were analysed using the appropriate tests, depending on the group size, type 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, Fisher's test of exact probability. Differences were considered as statistically significant when  $p < 0.05$ .

Statistical processing was accomplished in Excel 7.0 and SPSS (version 11.0).

## Results

In total, there were 91 patients (8.8%) treated for breast cancer aged below 40 years (range 23-70) ( $X \pm SD = 35.9 \pm 4.3$ ) (Table 1). There were 938 elderly patients (91.2%) treated for breast cancer with age range from 41 to 85 years, ( $X \pm SD = 58.3 \pm 10.3$ ; Table 1).

In both patient groups, left breast was most commonly involved: 53.8% (49 patients) and 52.6% (493 patients) in younger and older groups, respectively. In both patient groups, the most common primary tumor site was the upper lateral quadrant, while lateral medial quadrant was the most common primary tumor site in patients below 40 years of age ( $p < 0.05$ ), and central

**Table 1.** Clinicopathological characteristics

Characteristics	Age <40 years Patients		Age ≥40 years Patients	
	n	%	n	%
Number of patients	91	8.8	938	91.2
Histological type				
Ductal	65	71.4	684	72.9
Lobular	12	13.2	111	11.8
Ductal-lobular	13	14.3	112	11.9
Ca <i>in situ</i>	1	1.1	9	1.0
Mastitis carcinomatosa	0	0	22	2.3
T stage				
Tis	1	1.1	8	0.9
T1	23	25.3	290	30.9
T2	40	44.0	440	46.9
T3	12	13.0	87	9.3
T4	15	16.5	113	12.0
Histological grade				
1	3	3.3	66	7.0
2	63	69.2	640	68.2
3	25	27.5	232	24.7
Nuclear grade				
1	3	3.3	54	5.8
2	54	59.3	573	61.1
3	34	37.4	311	33.2
Family history*				
Positive	5	5.5	29	3.1
Negative	85	94.5	909	96.9

Non-significant for all parameters

\*Patients who had at least one first-degree relative with breast cancer

and upper medial quadrant sites were more common in older women ( $p < 0.05$ ; Table 2).

Histological breast cancer types were similar in both groups. The most common histological type was ductal carcinoma (71.4 vs. 72.9%; Table 1).

The distribution of T stages was similar in both groups. T2 and T1 stages were most common findings in both age groups. The proportion of patients with T3 and T4 disease was higher in the younger group, but the difference was not statistically significant (Table 1).

In 84 (92.3%) younger patients and 872 (93.0%) older patients pN status was determined. The proportion of patients with 0 and 1-3 positive lymph nodes was higher in the older age group, while there were more patients with 4-9 and >10 positive lymph nodes in the younger age group, although the difference between the two age groups was not statistically significant (Table 3).

Histological and nuclear grade 2 was most common (Table 1). The number of patients with histological and nuclear grade 3 disease was higher in the younger age group, but this difference did not reach statistical significance.

Similarly, the rate of a positive family history did not differ significantly among the two groups (5.5 vs 3.1%; Table 1).

**Table 2.** Primary tumor site

Site	Age <40 years		Age ≥40 years		Total	
	Patients, n	%	Patients, n	%	Patients, n	%
Central	9	9.9	176	18.8*	185	18.0
ULQ <sup>1</sup>	49	53.8	518	55.2	567	55.1
UMQ <sup>2</sup>	7	7.7	151	16.1*	158	15.4
LLQ <sup>3</sup>	7	7.7	49	5.2	56	5.4
LMQ <sup>4</sup>	15	16.5*	37	3.9	52	5.0
Axilla	2	2.2	2	0.2	4	0.4
Areolar	2	2.2	5	0.5	7	0.7
Total	91	100.0	938	100.0	1029	100.0

\*p&lt;0.05

<sup>1</sup>upper lateral quadrant, <sup>2</sup>upper medial quadrant, <sup>3</sup>lower lateral quadrant, <sup>4</sup>lower medial quadrant**Table 3.** Lymph node status

Number of lymph nodes	Age <40 years		Age ≥40 years		Total	
	Patients, n	%	Patients, n	%	Patients, n	%
0	35	41.7	402	46.1	437	45.7
1-3	16	19.0	218	25.0	234	24.5
4-9	19	22.6	160	18.3	179	18.7
>10	6	7.1	35	4.0	41	4.3
Unknown	8	9.5	57	6.5	65	6.8

Non-significant for all parameters

**Table 4.** Receptor status

Receptor status	Age <40 years		Age ≥40 years		Total	
	Patients, n	%	Patients, n	%	Patients, n	%
ER+/PR+	35	39.3	515	55.9	550	54.5
ER+/PR-	3	3.4	137	14.9	140	13.9
ER-/PR+	22	24.7	44	4.8	66	6.5
ER-/PR-	29	32.6*	225	24.4*	254	25.1

\*p&lt;0.05

There were 89 patients (97.8%) below 40 years of age with determined ER/PR status and 921 women (98.2%) in those over 40. Various ER/PR combinations in the two groups of patients are shown in Table 4. Hormonal insensitivity was higher in the younger age group (32.6 vs. 24.4%). The difference between the two groups was statistically significant (p<0.05).

## Discussion

The incidence of breast cancer in women below 40 years of age is lower. In the USA approximately 2.7% of breast cancer are younger than 35 years [7]. According to Kothari et al. [12], women under the age of 35 years comprise 5% of breast cancer cases. El Saghier et al. reported an incidence of 8.1% in women with breast cancer below 35 years [13]. According to Han et al., the percentage of breast cancer under the age of 40

was 28.5% [8]. Dirier et al. reported extremely high incidence of breast cancer in women under 40 years old (42.5%) [9]. As authors suggested, this might be a result of a younger population pyramid of the country. In our group of patients the incidence of breast carcinoma in women below 40 years of age was 8.8%. This data is less favorable compared to the data for Central Serbia (5%), Croatia and Great Britain (4.5%) [10,14].

In our study, in both patient groups, left breast was more commonly affected, while tumors were most commonly situated in the upper lateral quadrant [12,15].

It is widely believed that breast cancer in young women is characterized by a relatively unfavorable prognosis and unusual pathological features. Young patients have larger tumor sizes, more positive lymph nodes, more negative hormone receptors and higher tumor grades than older patients [9,13,16,17]. According to Dirier et al. [9], in younger patients, when T stages were taken into account, the number of patients with

T4 tumors was greater in younger age group, although, similar to other studies, the difference between the younger and older age groups was not statistically significant [13]. As authors suggested, the delay in seeking medical help and consequently delayed diagnosis might contribute to the higher incidence of initially metastatic tumors at presentation in the younger group. In our study, T2 and T1 stages were most common findings in both age groups. The proportion of patients with T3 and T4 disease was higher in the younger group, but the difference was not statistically significant.

In our study, in both patients groups, histological and nuclear grade 2 was most common. Similar to the results of a recent study [9], in our study the number of patients with histological and nuclear grade 3 disease was higher in the younger age group, but this difference did not reach statistical significance.

Similar to other reports, we did not find a significant difference among the two age groups in terms of the number of positive lymph nodes [8,9,13]. Fowble et al. reported a poorer prognosis in lymph node-negative stage I and II young patients [18]. On the contrary, Han et al. reported that lymph node negativity did not affect the prognosis in a negative way [8]. Dirier et al. [9] also noticed that lymph node status did not affect prognosis.

Similar to other reports, in our study women under 40 had more frequently family history of breast cancer compared to older ones [6,9], but without reaching statistically significant difference.

Out of the total number of 1010 patients with measured receptors (98.2%), we found an ER/PR positivity of 67.4% in younger patients and 75.6% in the older patients with breast cancer, which is of statistical significance. Dirier et al. [9] found an ER positivity of 51.9% in younger patients and 62.9% in the older patients with breast cancer. They calculated the PR positivity as 54.8% and 48.9% in younger and older patients, respectively. Chow and Ho [19] reported ER positivity in 53% of premenopausal and in 61.6% of postmenopausal women with breast cancer. In the same study PR positivity was 51.5% and 46.2% in pre- and postmenopausal patients, respectively [19]. According to El Saghir et al. [13], 71.6% of women under the age of 35 years had positive hormone receptors while 78.5% of those older than 50 had positive hormone receptors. McAree et al. [20] found that 76.8% and 39.3% of women with breast cancer under 40 years of age were ER and PR positive, respectively. According to the literature data, one of the reasons of unfavorable prognosis of breast cancer in younger patients could be the fact that in these patients receptor-negative breast cancer unresponsive to hormonal treatment is more common [4].

## Conclusion

Young age remains a controversial issue as a prognostic factor in breast cancer. Debates include patients from different parts of the world. Although uncommon, breast cancer in young women is worth paying special attention due to the unique and complex issues that are raised. The underlying causes of the disease must be investigated in large population-based studies in the future.

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