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Original Scientific Paper

INDEPENDENT FACTORS FOR POOR PROGNOSIS IN YOUNG PATIENTS WITH STAGE I-III BREAST CANCER

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SUMMARY – Breast cancer is the most common malignancy in the population of women under 40 years of age. Young age is an independent factor for poor prognosis. In this research, we tried to establish other factors for poor prognosis in stage I-III breast cancer. The following parameters were observed: tumor size, lymph node status, histologic grade, hormonal receptor status, Ki-67 prognostic index, Her2 neu status, histologic type of the tumor, local recurrence and metastases. Logistic regression was used to evaluate the effect of specific factors on the probability of lethal outcome and development of distant metastases. Our patients showed a predominance of T1 tumor (49.4%), had positive lymph nodes (62%) and most of them were pN1 (61.2%). Up to one-third of patients had triple negative status. Ki-67 proliferation index was high (25%). Multicentric tumor was detected in 23% of patients. There was no difference in overall survival between the two types of surgical procedures. Patients with pN0 status had better overall survival. Breast cancer in the population of young women has a more aggressive nature. Study results indicated positive lymph node status as an independent factor for poor prognosis of stage I-III breast cancer.

Key words: *Breast cancer; Young women; Multivariate analysis; Independent risk factor*

Introduction

Breast cancer represents a global public health issue. It is the most common malignancy and mortality factor in the population of women. Due to the expansion of novel therapeutic options, from surgical and oncologic perspective, and with greater potential for recovery, breast cancer is one of the most researched malignancies in the past twenty years. Young women with breast cancer are considered to be those under 40 years of age[1,2]. In this population, breast carcinoma represents the most common malignant disease with highest mortality, although breast cancer accounts for 6% of the total number of cancer cases[3]. Numerous clinical studies have confirmed that breast cancer in young women has a higher histologic grade, unfavorable hormonal status, and overall higher death rate compared to the older population of women[4-6]. Young age is an adverse prognostic factor in primary breast cancer. Various studies found young women to have worse outcomes than older patients[7,8]. Young age is also an independent risk factor for disease-free survival (DFS) and overall survival (OS) in women with operable breast cancer[9,10]. In the group of young women, there are limited data on prognostic factors. Only a few studies recognize nodal status, estrogen receptor status and molecular subtype as independent factors for poor survival[11,12].

We recognized young age as an independent factor for poor prognosis but also wanted to establish other possible independent factors for DFS and OS in the group of young women with breast cancer from our population.

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Patients and Methods

This was a retrospective study. Data were collected from medical charts of young female patients having undergone surgical treatment at the Department of Surgery, Osijek University Hospital Centre, Osijek, Croatia, during the 2002-2010 period. Study patients were under 40 years of age at the time of surgery. Data on the following parameters were collected: tumor size, lymph node status, histologic grade, hormonal receptor status, Ki-67 prognostic index, Her2 neu status, histologic type of tumor, local recurrence, metastases, and outcome (alive or death). All patients included in the study had complete medical documentation. Those with incomplete documentation and data were excluded from the study. All study patients had stage I-III tumor. Patients who had positive distant metastasis (M) at the time of diagnosis were not included in the study. All patients were monitored during routine and urgent checkups. All patients included in this study were monitored for 5-13 (median 8.7) years. We collected data on 79 young female patients, median age 37 (range 33-39) years.

Breast tissue was fixed, embedded in paraffin and cut into 5-μm sections. After that, it was stained and observed under a microscope. Hormonal status, Her2 neu status and Ki 67 were determined by immunochemical staining. Among patients with Her2 neu 2+, the FISH method was performed to determine whether the patient was Her2 neu positive or negative. Histologic grading of breast carcinoma was performed by Elston and Ellis method. We used the TNM (tumor-nodes-metastases) classification of the American Joint Committee on Cancer Staging System for Breast Cancer, 2010[13,14].

Local recurrence is defined as recurrence in the field of mastectomy or in the original tumor location for breast conserving resection. Local recurrence was diagnosed pathologically after surgical biopsy. Metastases are defined as recurrence of the tumor in distant organ during regular or urgent follow up examinations using abdominal ultrasound, lung radiography, bone scintigraphy, surgical biopsy, computed tomography (CT), magnetic resonance imaging (MRI) and positron emission/computed tomography (PET/CT) scans. Outcome was defined as the patient being dead or alive at the end of the follow up period.

Table 1. Study parameters in young women with breast cancer

Affected side, n (%)	
right	40 (50.6)
left	39 (49.4)
Histologic type, n (%)	
ductal invasive	56 (70.9)
lobular invasive	11 (13.9)
other	12 (15.2)
Tumor size (T), n (%)	
T1 ≤2 cm	39 (49.4)
T2 >2 cm, ≤5cm	30 (38)
T3 >5 cm	7 (8.9)
T4 any size with skin or chest wall spread	3 (3.8)
Positive lymph nodes, n (%)	49 (62)
Lymph nodes status, n (%)	
1-3 lymph nodes	30 (61.2)
4-9 lymph nodes	13 (26.5)
≥10 lymph nodes	6 (12.2)
Estrogen status, n (%)	
negative	36 (45.6)
positive	43 (54.4)
Progesterone status, n (%)	
negative	35 (44.3)
positive	44 (55.7)
HER2 neu status, n (%)	
negative	60 (75.9)
positive	19 (24.1)
Triple negative, n (%)	25 (32.1)
Ki67, median (25%-75%)	25 (11-48)
Type of surgical procedure, n (%)	
modified radical mastectomy	52 (65.8)
breast conserving resection	27 (34.2)
Multicentric tumor position, n (%)	18 (23.1)
Histologic grade, n (%)	
I	13 (16.5)
II	43 (54.4)
III	23 (29.1)
Local recurrence, n (%)	MRM 0 (0) BCR 3 (3.8)
Metastases, n (%)	21 (26.6)
Outcome, n (%)	
alive	64 (81)
dead	15 (19)

Table 2. Impact of parameters on prediction of lethal outcome (univariate regression analysis)

Variable	β	p	Odds ratio (OR)	95% confidence interval
Age	-0.025	0.75	0.975	0.84 -0.94
Histology type				
ductal invasive		0.84		
lobular invasive	-1.003	0.36	0.367	0.04-3.15
other	-0.087	0.91	0.917	0.17-4.89
Tumor size T (cm)	0.079	0.54	1.083	0.837-1.40
Lymph nodes status				
pN0		0.04		
pN1	2.178	0.03	8.8	1.012-76.9
pN2	2.556	0.03	12.89	1.27-130.5
pN3	3.367	0.01	29	2.3-373.7
Estrogen				
negative				
positive	-1.073	0.04	0.342	0.105-0.812
Progesterone				
negative				
positive	-0.785	0.18	0.456	0.145-1.44
HER2 neu				
negative				
positive	-0.288	0.68	0.750	0.188-2.9
Ki-67 (%)	0.019	0.03	1.019	0.797-0.97
Type of surgery				
BCR				
MRM	0.875	0.21	2.4	0.614-9.4
Multicentric position				
no				
yes	1.041	0.09	2.833	0.845-9.49
Triple negative				
no				
yes	0.783	0.18	2.187	0.691-6.92
Histology grade				
I		0.89		
II	0.229	0.79	1.257	0.232-6.8
III	0.424	0.64	1.528	0.252-9.3
Local recurrence				
no				
yes	2.271	0.07	9.692	0.82-114.9
Metastases				
no				
yes	22.119	0.997	4.0x109	0

BCR = breast conserving resection; MRM = modified radical mastectomy

Statistical analysis was performed with SPSS 13.0 (Chicago, IL, USA) software. Logistic regression (univariate and multivariate) was used to evaluate the impact of several factors on the probability of negative outcome in study subjects.

Table 3. Impact of parameters on prediction of lethal outcome (multivariate regression analysis)

Variable	β	p	Odds ratio (OR)	95% confidence interval
Lymph nodes status				
pN0		0.04		
pN1	2.016	0.09	7.509	0.707-79.770
pN2	3.433	0.01	30.97	2.044-468.9
pN3	3.579	0.01	35.83	2.339-548.8
Estrogen positive	-1.856	0.14	0.156	0.013-1.871
Progesterone positive	0.677	0.57	1.968	0.191-20.296
Ki-67 (%)	0.019	0.17	1.019	0.992-1.048
Local recurrence				
yes	2.240	0.12	9.398	0.553-159.78
Constant	-3.843	0.005	0.021	

Results

Data were collected on 79 patients, median age 37 (range 33-39) years (Table 1). There were no significant differences according to the side operated on. Invasive ductal carcinoma was the most common histologic type of tumor (70.9%). Invasive lobular carcinoma was the second most common type (13.9%).

Regarding the size of the tumor, most patients had T1 and T2 (87.4%) tumor size, with a predominance of tumor size ≤2cm (49.4%). The majority of patients had positive lymph nodes (62%), most of them with pN1 status (1-3 positive nodes; 61.2%). There were no significant differences in estrogen or progesterone status. The majority of patients were her2 neu negative (75.9%) and up to one-third of patients had triple negative immunohistochemical status. Ki-67 proliferation index was rather high (25%; interquartile range 11% to up to 46%). We found a high incidence of multicentric tumors (n=18, 23.15%) in our group of young women. More than one-half of patients were histology grade II (54.4%) (Table 1).

Modified radical mastectomy was the preferred type of surgical procedure, performed in 65.8% of patients. Only three patients developed local recurrence. They all were primarily treated with breast conserving resection.

At the end of follow up, metastases were detected in 26.6% of patients and 15 (19%) of them died (Table 1).

Effect of parameters on predicting lethal outcome

Logistic regression was used to estimate the potential impact of specific factors on the possible lethal outcome in the study group of patients. The model contains fourteen parameters: age, histologic type, tumor size, lymph node status, estrogen status, progesterone status, Her2 neu, Ki-67, type of surgical procedure, multicentric position, triple negative status, histology grade, local recurrence, and metastases (Table 2).

From the predictor variables that showed statistical significance, and exclusion of variables that did not change the probability (P) model by 20%, the following five variables were selected for the model on which to apply multivariate logistic regression: estrogen and progesterone positive status, lymph node status, Ki-67, and local recurrence. The model was statistically significant, χ^2=20.4 (df=7, p=0.005), and explained between 22.7% (after Cox & Snell) and 36.6% (after Negelkerke) of variance for death outcome, and accurately classified 86.1% of cases. The strongest independent factor for death outcome was lymph node status (Table 3).

Effect of parameters on predicting development of metastases

The probability of developing distant metastases in the study sample was evaluated by screening for the specific factors applying the logistic regression methods. The model contains thirteen parameters: age, histologic type, tumor size, lymph node status, estrogen status, progesterone status, Her2 neu, Ki-67, type of surgical procedure, multicentric position, triple negative status, histology grade, and local recurrence (Table 4).

Four predictor variables that showed statistical significance were chosen for the model on which multi-

Table 4. Impact of parameters on prediction of metastasis development (univariate regression analysis)

Variable	β	p	Odds ratio (OR)	95% confidence interval
Age	-0.157	0.03	0.855	0.745-0.981
Histology type				
ductal invasive		0.81		
lobular invasive	-0.674	0.42	0.510	0.099-2.614
other	-0.556	0.51	0.574	0.110-2.989
Tumor size T (cm)	0.048	0.70	1.049	0.823-1.337
Lymph nodes status				
pN0		0.04		
pN1	1.350	0.06	3.857	0.927-16.048
pN2	1.727	0.04	5.625	1.097-28.83
pN3	2.890	0.006	18	2.26-143.3
Estrogen				
negative				
positive	-0.905	0.08	0.404	0.145-1.128
Progesterone				
negative				
positive	-0.708	0.17	0.493	0.179-1.356
HER2 neu				
negative				
positive	0.651	0.25	1.917	0.633-5.802
Ki-67 (%)	0.007	0.52	1.007	0.987-1.027
Type of surgery				
BCR				
MRM	-0.671	0.25	0.511	0.164-1.592
Multicentric position				
no				
yes	1.386	0.015	4	1.305-12.256
Triple negative				
no				
yes	0.370	0.49	1.448	0.508-4.128
Histology grade				
I		0.60		
II	0.756	0.37	2.129	0.410-11.057
III	0.878	0.33	2.406	0.419-13.832
Local recurrence				
no				
yes	22.37	0.99	5.2 x109	0

BCR = breast conserving resection; MRM = modified radical mastectomy

variate logistic regression was applied. These variables were found to be predictors for metastasis development: age, lymph node status, estrogen status and multicentric position. The model was statistically significant, χ^2=20.1 (df=5, p=0.001), and explained between 22.5% (after Cox & Snell) and 32.7% (after Negelkerke) of variance for metastasis development, and accurately classified 78.5% of cases. The strongest independent factor for metastases was lymph node status (Table 5).

Table 5. Impact of parameters on prediction of metastasis development (multivariate regression analysis)

Variable	β	p	Odds ratio (OR)	95% confidence interval
Lymph nodes status				
pN0		0.07		
pN1	1.626	0.04	5.086	1.020-25.349
pN2	1.995	0.06	7.354	0.953-56.729
pN3	3.523	0.02	33.874	1.718-667.8
Estrogen positive	-1.52	0.03	0.219	0.054-0.885
Age	-0.160	0.05	0.852	0.723-1.003
Multicentric position, yes	0.719	0.39	2.052	0.054-0.885
Constant	3.854	0.18	47.1	

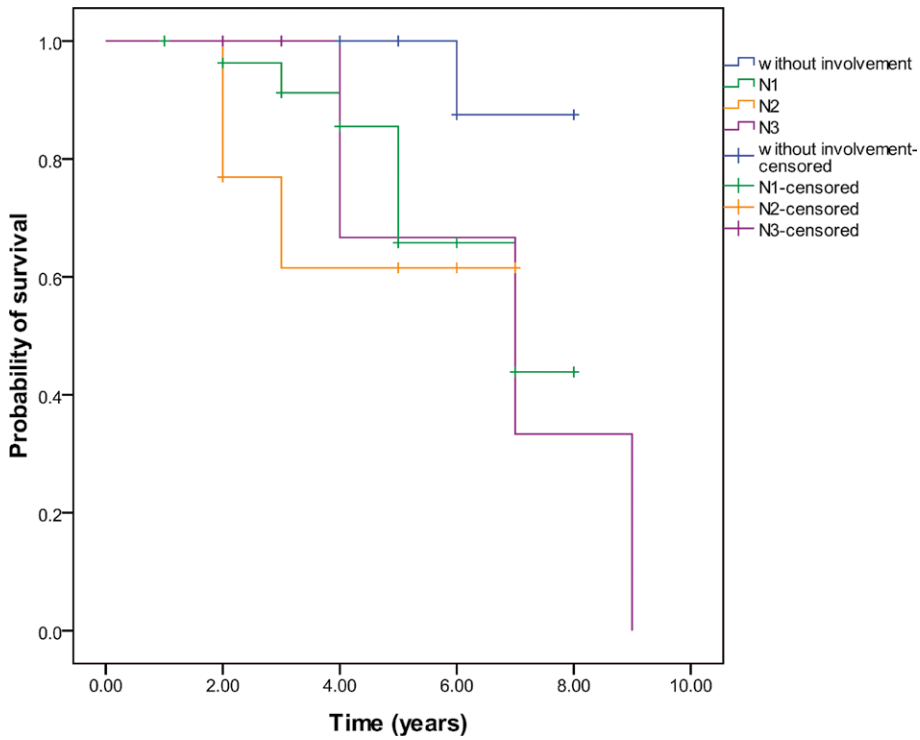

Fig. 1. Kaplan-Meier's analysis of survival with lymph node involvement.

Kaplan-Meier's analysis of survival

Kaplan-Meier's analysis of survival was applied in patients with distant metastases. Patients without positive lymph node (n=8) had OS at 7.8 years (95% CI 7.3-8,2). Patients with N1 (n=27) had OS at 6.5 years (95% CI 5,6-7,4). Lowest OS was recorded in patients with N2 (n=13), at 5.2 years (95% CI 3.8-6.7). Patients with N3 (n=3) had OS at 6.7 years (95% CI 3.8-9.5). Patients with positive N had poor OS, but without differences according to the number of positive nodes (Mantel-Cox test, p=0.08) (Fig. 1).

The mean survival period in our group of young patients was 7.3 years (95% CI 6.6 to 8.1). Survival time of patients operated on with modified radical mastectomy with axillary dissection was 6.8 years (95% CI 5.7 to 7.8), and of patients operated on with breast conserving resection 7.3 years (95% CI 6.6-8), with no significant difference (Mantel-Cox test, p=0.13) (Fig. 2).

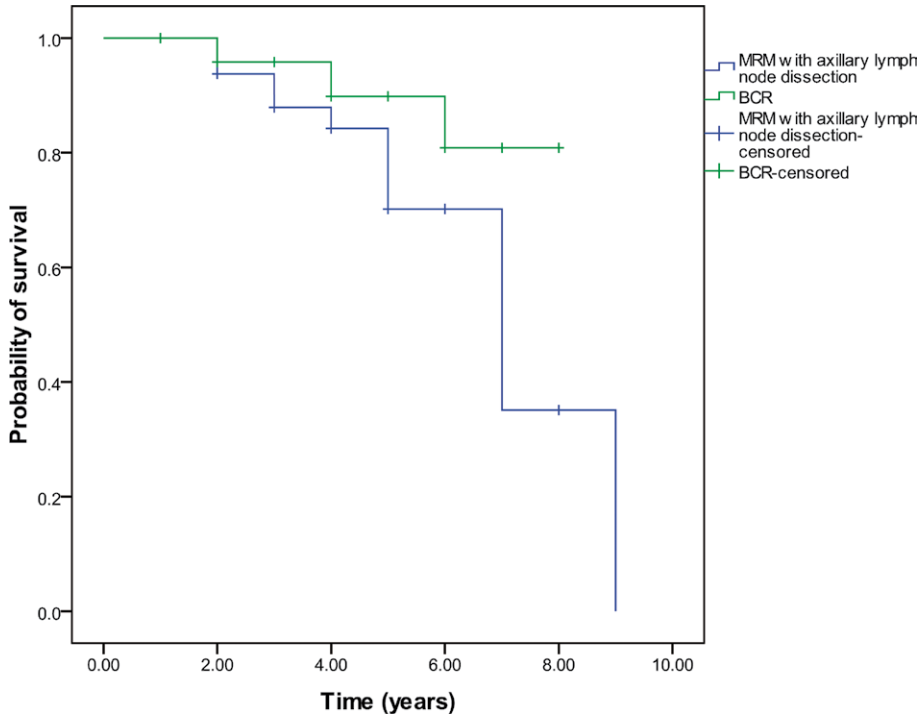

Fig. 2. Kaplan-Meier's analysis of survival with type of surgical procedure.

BCR = breast conserving resection; MRM = modified radical mastectomy

Discussion

Breast cancer in the population of young women accounted for only 5%-7% of all breast cancer patients[3]. In Far East countries, the incidence of breast cancer in young patients was found to be twofold that in developed countries[10]. Breast cancer among young women is considered to have a more aggressive nature and higher tumor grade with more vascular invasion than breast cancer in older women[4]. When compared to older women, breast cancer in younger women tends to have a worse prognosis in terms of OS and DFS[9,10]. Young age has been identified as an independent factor for poor prognosis[9,15].

In our sample, we found invasive ductal carcinoma as the most frequent histologic type of tumor. The second most common type was invasive lobular carcinoma. Among other different studies, Rosenberg *et al.* in their case-control study confirmed invasive ductal carcinoma as the most frequent one, and invasive lobular carcinoma as the second most common[16,17]. We found a predominance of tumors smaller than 5 cm, especially T1, which is consistent with the findings reported by Colleoni *et al.*[18]. Prognostic value of tumor size is independent of the state of lymph nodes. Patients with small tumors have better prognosis[19,20]. The prognosis of multicentric tumor is worse than for solid tumors of similar size (often axillary metastases)[21]. Multicentric cancer has worse biologic behavior with frequently present multiple foci and therefore should be considered in planning adjuvant treatments[22]. We found a rather high proportion of multicentric breast cancer.

Positive axillary lymph nodes have been considered as the most important prognostic factor for poor prognosis of breast cancer patients[19]. We found the majority of our patients to have positive lymph nodes. Our positive lymph node patients had worse OS and DFS (positive distant metastases) than lymph node negative patients, however, without difference between pN1-pN3 lymph node status. This is somewhat different from the findings reported from one study, which established difference in OS between pN1 and a greater number of lymph nodes involved[23]. Tai *et al.* also report on difference in prognosis within pN1 group between 1-2 and 3 lymph nodes involved[24]. Our findings might be somewhat imprecise due to the small sample size.

Triple-negative breast cancer is more aggressive, more likely to metastasize, and has more frequent recurrences after treatment. This is visible in the first 5 years after treatment. Generally, triple negative breast cancer has poor prognosis and higher mortality rate compared to other molecular subtypes[25]. In our study sample, up to one-third of patients were triple negative. Studies emphasize that the Ki-67 index ≥20 is a poor prognostic sign. Breast cancer patients with high Ki-67 had a significantly worse prognosis due to local recurrence, distant metastasis and poor OS[26,27]. In our study, Ki-67 was found to be 25%, which is a high value pointing to poor prognosis of the disease in our group of young women.

When compared with modified radical mastectomy, breast conserving surgery is similar in OS and the chance for distant metastasis development. Of course, breast conserving resection must be combined with radiotherapy. Breast conserving resection has more local recurrences; all local recurrences in our sample were in the breast conserving resection group. We proved that there was no difference between these two surgical procedures in OS, which is consistent with recent literature[28,29].

On statistical analysis, we identified local recurrence, hormone receptor status, lymph node status and Ki-67 index as predictors of poor OS. Lymph node status, hormone receptor status and multicentric position were predictive of developing distant metastases. However, lymph node status was an independent factor for both OS and DFS. Other authors recognize hormone receptor status and lymph node status as predictors of poor prognosis[11,12].

Conclusion

Breast cancer in the population of young women has a more aggressive nature, positive lymph nodes, often triple negative molecular subtype, high Ki-67 index, multicentric tumor position and distant metastases. These are predictors of poor prognosis, but positive lymph node status is an independent prognostic factor for OS and DFS.

References

1. Collins LC, Marotti JD, Gelber S, Cole K, Ruddy K, Kereakoglow S, Brachtel EF, Schapira L, Come SE, Winer EP, Partridge AH. Pathologic features and molecular phenotype by patient age in a large cohort of young women with breast cancer. Breast Cancer Res Treat. 2012 Feb;131(3):1061-6. doi: 10.1007/s10549-011-1872-9. Epub 2011 Nov 13.
2. Zhou P, Recht A. Young age and outcome for women with early-stage invasive breast carcinoma. Cancer. 2004;101: 1264-74.
3. Brinton LA, Sherman ME, Carreon JD, Anderson WF. Recent trends in breast cancer among younger women in the United States. J Natl Cancer Inst. 2008 Nov 19;100(22):1643-8. doi: 10.1093/jnci/djn344. Epub 2008 Nov 11.
4. Walker RA, Lees E, Webb MB, Dearing SJ. Breast carcinomas occurring in young women (<35 years) are different. Br J Cancer. 1996;74:1796-800.
5. Chung M, Chang HR, Bland KI, Wanebo HJ. Younger women with breast carcinoma have poorer prognoses than older women. Cancer. 1996;77:97-103.
6. Gajdos C, Tarrter PI, Bleiweiss IJ, Bodian C, Brower ST. Stage 0 to stage III breast cancer in young women. J Am Coll Surg. 2000;190:523-9.
7. Fowble BL, Schultz DJ, Overmoyer B, Solin LJ, Fox K, Jardines L, Orel S, Glick JH. The influence of young age on outcome in early stage breast cancer. Int J Radiat Oncol Biol Phys. 1994 Aug 30;30:23-33.
8. Nixon AJ, Neuberg D, Hayes DF, Gelman R, Connolly JL, Schnitt S, Abner A, Recht A, Vicini F, Harris JR. Relationship of patient age to pathologic features of the tumor and prognosis for patients with stage I or II breast cancer. J Clin Oncol. 1994 May;12:888-94.
9. Han W, Kim SW, Park IA, Kang D, Kim SW, Youn YK, Oh SK, Choe KJ, Noh DY. Young age: an independent risk factor for disease-free survival in women with operable breast cancer. BMC Cancer. 2004 Nov 17;4:82.
10. Kataoka A, Iwamoto T, Tokunaga E, Tomotaki A, Kumamaru H, Miyata H, Niikura N, Kawai M, Anan K, Hayashi N, Masuda S, Tsugawa K, Aogi K, Ishida T, Masuoka H, Iijima K, Kinoshita T, Nakamura S, Tokuda Y. Young adult breast cancer patients have a poor prognosis independent of prognostic clinicopathological factors: a study from the Japanese Breast Cancer Registry. Breast Cancer Res Treat. 2016 Nov;160:163-72. doi: 10.1007/s10549-016-3984-8. Epub 2016 Sep 19.
11. van der Hage JA, Mieog JS, van de Velde CJ, Putter H, Bartelink H, van de Vijver MJ. Impact of established prognostic factors and molecular subtype in very young breast cancer patients: pooled analysis of four EORTC randomized controlled trials. Breast Cancer Res. 2011 Jun 24;13(3):R68. doi: 10.1186/bcr2908.
12. Filleron T, Dalenc F, Kramar A, Spielmann M, Levy Ch, Fumoleau P, Canon J-L, Martin A-L, Roché H. Prognostic factors of young women (≤35 years) with node positive breast cancer: possible influence on post-therapeutic follow-up. Bull Cancer. 2013 Jul-Aug;100(7-8):22-9. doi: 10.1684/bdc.2013.1791.

13. Singletary SE, Allred C, Ashley P. Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol. 2002;20(17):3628-36.
14. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;17(6):1471-4. doi: 10.1245/s10434-010-0985-4.
15. Chen HL, Zhou MQ, Tian W, Meng KX, He HF. Effect of age on breast cancer patient prognoses: a population-based study using the SEER 18 database. PLoS One. 2016 Oct 31;11(10):e0165409. doi: 10.1371
16. Rosenberg LU, Magnusson C, Lindström E, Wedrén S, Hall P, Dickman PW. Menopausal hormone therapy and other breast cancer risk factors in relation to the risk of different histological subtypes of breast cancer: a case-control study. Breast Cancer Res. 2006;8(1):R11-10.1186/bcr1378.
17. Bertheau P, Steinberg SM, Cowan K, Merino MJ. Breast cancer in young women: clinicopathologic correlation. Semin Diagn Pathol. 1999 Aug;16(3):248-56.
18. Colleoni M, Rotmensz N, Robertson C, Orlando L, Viale G, Renne G, Luini A, Veronesi P, Intra M, Orecchia R, Catalano G, Galimberti V, Nolé F, Martinelli G, Goldhirsch A. Very young women (<35 years) with operable breast cancer: features of disease at presentation. Ann Oncol. 2002;13:273-9.
19. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status and survival in 24,740 breast cancer cases. Cancer. 1989;63:181-7.
20. Michaelson JS, Silverstein M, Wyatt J, *et al*. The prediction of breast cancer survival from tumor size. Cancer. 2002;95:713-23.
21. Rezo A, Dahlstrom J, Shadbolt B, Rodins K, Zhang Y, Davis AJ, *et al*. Tumor size and survival in multicentric and multifocal breast cancer. Breast. 2011 Jun;20(3):259-63. doi: 10.1016/j.breast.2011.01.005.
22. Neri A, Marrelli D, Megha T, Bettarini F, Tacchini D, De Franco L. Clinical significance of multifocal and multicentric breast cancers and choice of surgical treatment: a retrospective study on a series of 1158 cases. BMC Surg. 2015 Jan 14;15:1. doi: 10.1186/1471-2482-15-1.
23. Fisher B, Bauer M, Wickerham DL, *et al*. Relation of the number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. Cancer. 1983;52:1551-7.
24. Tai P, Yu E, Joseph K. Prognostic significance of number of positive nodes: a long-term study of one to two nodes *versus* three nodes in breast cancer patients. Int J Radiat Oncol Biol Phys. 2010;77:180-7. doi: 10.1016/j.ijrobp.2009.04.073.
25. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, *et al*. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res. 2007;13(15 Pt 1):4429-34.
26. Abubakar M, Orr N, Daley F, Coulson P, Ali HR, Blows F, *et al*. Prognostic value of automated KI67 scoring in breast cancer: a centralised evaluation of 8088 patients from 10 study groups. Breast Cancer Res. 2016;18(1):104. doi: 10.1186/s13058-016-0765-6.
27. Munzone E, Botteri E, Sciandivasci A, Curigliano G, Nole F, Mastropasqua M, Rotmensz N, Colleoni M, Esposito A, Adamoli L. Prognostic value of Ki-67 labeling index in patients with node-negative, triple-negative breast cancer. Breast Cancer Res Treat. 2012;134:277-82. doi: 10.1007/s10549-012-2040-6.
28. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, *et al*. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002;347(16):1227-32.
29. Fisher B, Jeong JH, Anderson S, Bryant J, Fisher ER, Wolmark N. Twenty-five-year follow-up of a randomized trial comparing radical mastectomy, total mastectomy, and total mastectomy followed by irradiation. N Engl J Med. 2002;347:567-75.

Sažetak

NEOVISNI ČIMBENICI ZA LOŠU PROGNOZU KOD MLADIH BOLESNICA S RAKOM DOJKE I.-III. STADIJA

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Rak dojke je najčešći zloćudni tumor u populaciji žena u dobi ispod 40 godina. Mlada dob je neovisan čimbenik za lošu prognozu. Željeli smo utvrditi i druge čimbenike loše prognoze kod raka dojke I.-III. stadija kod mlade populacije žena. Uzeli smo u obzir sljedeće parametre: veličinu tumora, stanje limfnih čvorova, histološki stupanj, status hormonskih receptora, Ki-67 prognostički indeks, HER2 neu status, histološki tip tumora, lokalni recidiv i razvoj udaljenih metastaza. Logistička regresija korištena je za procjenu utjecaja čimbenika na vjerojatnost smrtnog ishoda i razvoja udaljenih metastaza. Naše bolesnice imale su većinom tumor T1 (49,4%), pozitivne limfne čvorove (62%), a većina njih bile su pN1 (61,2%). Do jedne trećine bolesnica imale su trostruko negativan hormonski status. Ki-67 indeks proliferacije bio je visokih 25%. Našli smo učestalost multicentričnog tumora kod 23% bolesnice. Nije bilo razlike u preživljenju između dviju vrsta kirurškog zahvata. Bolesnice sa statusom limfnih čvorova pN0 imale su bolje preživljenje. Rak dojke kod mlade populacije žena ima agresivniju prirodu. Rezultati istraživanja ukazali su na pozitivan status limfnih čvorova kao nezavisan čimbenik za lošu prognozu raka dojke I.-III. stadija.

Ključne riječi: *Karcinom dojke; Mlade žene; Multivarijatna analiza; Nezavisni čimbenik rizika*