

COMPARAȚIE ÎNTRE CARACTERISTICILE CLINICO-PATOLOGICE ALE CANCERULUI DE SÂN LA TINERI ȘI VÂRSTNICI

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Rezumat

Introducere: Cancerul mamar este o boală cu diversitate clinică semnificativă, determinată de multiple modificări genetice și evenimente moleculare, având un număr mare de caracteristici descriptive care se corelează cu evoluția bolii.

Scopul studiului de față este compararea caracteristicilor clinico-patologice ale pacienților cu cancer mamar tineri (sub sau egal cu 35 de ani) cu cei în vârstă (peste sau egal cu 70 de ani).

Material și metodă: Am prelucrat datele disponibile a 1334 pacienți cu cancer mamar provenite de la Laboratorul de Anatomie Patologica a Spitalului Clinic Județean Tg.-Mureș, și în final am inclus 42 de pacienți în grupul tânăr, și 128 de pacienți în grupul în vârstă. Am analizat următorii parametri: tipul histologic, dimensiunile tumorii, invazia nodală, gradul histologic și nuclear, prezența sau absența necrozei, fibrozei, a invaziei vasculare și limfovasculare, respectiv statusul receptorilor hormonal.

Rezultate și concluzii: Pacienții tineri au reprezentat 3,82%, iar cei în vârstă 20,91% din populație. Nu au fost diferențe semnificative între cele două grupuri în ceea ce privește dimensiunile tumorii, nr. nodulilor implicați, tipul histologic, gradul nuclear, prezența necrozei, fibrozei, și a invaziei limfovasculare. Diferențele semnificative cu privire la gradul histologic și statusul receptorilor estrogenici au demonstrat că pacienții tineri au cancer mai agresiv și cu dezvoltare mai rapidă. Frecvența mai mare a invaziei nodale și invazia vasculară în cazul grupului mai în vârstă a fost în contradicție cu datele din literatură.

Cuvinte cheie: cancer mamar, caracteristici clinico-patologice

Comparison of clinico-pathological features of breast cancer in the young and old

Abstract

Introduction: Breast cancer is a clinically diverse disease, determined by multiple genetic modifications and molecular events, bearing a large number of descriptive characteristics which correlate with the outcome of the disease.

The aim of the present study is to compare the clinico-pathological features of young (under or equal to 35 years) and old (over or equal to 70 years) breast cancer patients.

Material and methods: We processed the available recorded data of 1334 patients with breast cancer from the archives of the Pathology Department of the Clinical County Hospital Tg.-Mures, and finally included 42 patients in the young age group, and 128 patients in the old age group. Data reviewed included histological type of cancer, tumor size, nodal involvement, histological and nuclear grade, the presence or absence of tumor necrosis, fibrosis, vascular and lymphovascular invasion, and hormone receptor status.

Results and conclusions: Young patients represented 3.82% of the total population, while old patients were 20.91%. There were no significant differences between the two groups concerning tumor size, number of involved nodes, histological type, nuclear grade, presence of necrosis, fibrosis, and lymphovascular invasion. The significant differences in histological grade, and ER status conclusively demonstrated that in case of younger breast cancer patients, the disease is more aggressive and developing more extensively. The higher frequency of node involvement and vascular invasion in the old age group was contradictory to literature data.

Keywords: breast cancer, clinico-pathological features

Introduction

Breast cancer is a clinically diverse disease, determined by multiple genetic modifications and molecular events. Thus, it can be regarded as a heterogeneous group of tumors developing in a similar location, bearing a large number of descriptive characteristics which correlate with the outcome of the disease.

Prognostic factors determine or correlate with the course of the disease, thus supplying information related to the expected disease free survival and overall survival of the patients.

Prognostic factors include tumor size [1], nodal status [2], histological type, histological grade, nuclear grade [3, 4], age of the patient [5], and other histological features like necrosis, vascular invasion, and lymphovascular invasion.

Predictive factors signal the expected behavior and extent of reaction of a disease with certain well

defined characteristics to a determined therapy. The notable predictive factors are the estrogen receptor (ER), which predicts for response to hormonal therapies, progesterone receptor (PR), and expression of the growth factor receptor *cerbB2* (ERBB2, formerly *Her-2/neu*). The hormone receptor status is a double prognostic/predictive factor, signaling poorer prognosis in negative cases, and also providing information for therapeutic decisions in the direction of hormone treatment. *Her-2* positivity is also forecasting a poor clinical outcome, being associated with worse pathological features as well. [6, 7, 8]

The aim of the present study is to compare the clinico-pathological features of two distinct patient populations, located at the two extremities of the human lifespan, specifically young and old patients, establishing trends within the population concerning breast cancer.

Material and method

In this retrospective comparative study we processed the available recorded data of 1334 patients diagnosed with breast cancer between the years 2005 and 2010 from the archives of the Pathology Department of the Clinical County Hospital Tg.-Mures. We established two distinct age categories, one young patient group (under or equal to 35 years of age) and one old patient group (over or equal to 70 years of age). The first group included 51 patients, while the latter 279 patients. We considered only those patients who had complete records, and as a result the final group size was reduced to 42 patients in the young age group, and 128 patients in the old age group. Data reviewed included histological type of cancer, tumor size, axillary lymph node status, histological grade, nuclear grade, the presence or absence of tumor necrosis, fibrosis, vascular and lymphovascular invasion. In addition, we compared the available hormone receptor status of the two age groups.

Statistical analysis was performed using the GraphPad In Stat 3.06 statistic calculation software (GraphPad Software Inc., San Diego, U.S.A.). The p values <0.05 were considered statistically significant, as calculated by the chi-square test, or Fisher's exact test as appropriate.

Results

Considering the whole patient population we examined, the original young age group represented 3.82%, while the original old age group was 20.91% of the total population.

Prognostic factors

Comparing the two groups by tumor size at time of diagnosis there was no real difference between them ($p=0.5471$). In the young age group minimum tumor size was 6mm, the maximum was 195mm, with a mean value across all patients of 32.92mm. The similar values in the old age group were 6mm, 120mm, and 37.05mm respectively (Table I).

Concerning histological types, we noted that invasive ductal carcinoma (IDC) was dominant in both age groups, and invasive lobular carcinoma (ILC) had a slightly higher frequency in the young age group, but there were no significant differences between them ($p=0.237$).

Frequency of occurrence of grade I, II and III in the older age group was 14.06%, 49.22%, and 36.72%, respectively, while in the younger age group the frequencies were 7.14%, 28.57%, and 64.29%, respectively (Figure 1). The difference in distribution was strongly significant ($p=0.007$), with a net superiority of grade III tumors in the young age group (Table II).

Figure 1 Grade distribution across age groups

The number of excised lymph nodes ($p=0.0662$) and the number of metastatic lymph nodes ($p=1.000$) did not show significant differences between the two age groups. Instead the rate of lymph node metastases displayed significant difference, being much more frequent in the old age group (57.81%) than in the young age group (23.81%) (Tables I and II).

| Pathological feature | Young patients (n=42) | | | Old patients (n=128) | | | p value |
|---------------------------|-----------------------|------|-------|----------------------|------|-------|---------|
| | min. | max. | mean | min. | max. | mean | |
| Tumor size (mm) | 6 | 195 | 32.92 | 6 | 120 | 37.05 | 0.5471 |
| Excised lymph nodes (no.) | 4 | 19 | 13.06 | 1 | 36 | 13.15 | 0.0662 |
| Metast. lymph nodes (no.) | 0 | 18 | 3.17 | 0 | 32 | 3.56 | 1.0000 |

Table I Comparison of pathological features

| Pathological feature | | Young patients (n=42) | | Old patients (n=128) | | p value |
|-------------------------|-----------|-----------------------|-------------|----------------------|-------------|---------|
| | | No. of cases | Percent (%) | No. of cases | Percent (%) | |
| Histological type | IDC | 32 | 76.19 | 110 | 85.94 | 0.237 |
| | ILC | 3 | 7.14 | 8 | 6.25 | |
| | Other | 7 | 16.67 | 10 | 7.81 | |
| Lymph node metastases | | 10 | 23.81 | 74 | 57.81 | 0.0002 |
| Histological grade | Grade I | 3 | 7.14 | 18 | 14.06 | 0.007 |
| | Grade II | 12 | 28.57 | 63 | 49.22 | |
| | Grade III | 27 | 64.29 | 47 | 36.72 | |
| Nuclear grade | Grade 1 | 3 | 7.14 | 11 | 8.59 | 0.759 |
| | Grade2 | 27 | 64.29 | 74 | 57.81 | |
| | Grade 3 | 12 | 28.57 | 43 | 33.59 | |
| Necrosis | | 14 | 33.33 | 61 | 47.66 | 0.1115 |
| Fibrosis | | 7 | 16.66 | 35 | 27.34 | 0.2166 |
| Vascular invasion | | 12 | 28.57 | 66 | 51.56 | 0.0122 |
| Lymphovascular invasion | | 4 | 9.52 | 15 | 11.72 | 1.0000 |
| ER positive | | 13 | 30.95 | 70 | 54.69 | 0.0081 |
| PR positive | | 13 | 30.95 | 61 | 47.66 | 0.073 |

Table II Comparison of pathological features II

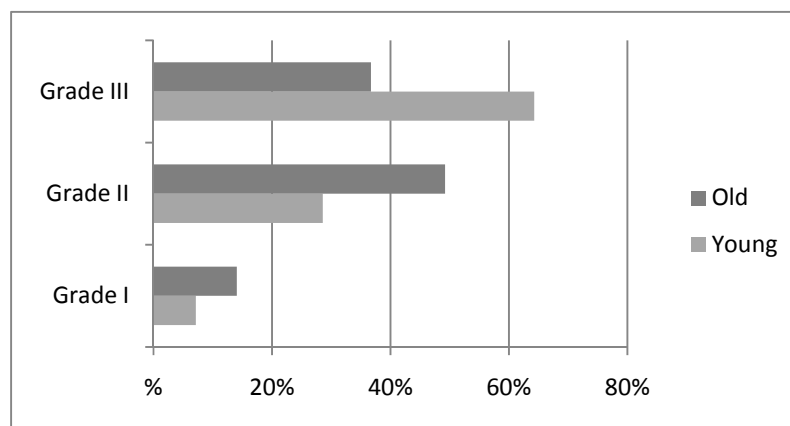


Figure 1 Grade distribution across age groups

I
Distribution of nuclear grades (1, 2, 3) was very similar in the two groups, displaying a p-value of 0.759, with the highest proportion being represented

by nuclear grade 2 in both study groups (64.29% in the young age group, and 57.81% in the old age group).

Tumor necrosis, which is another feature signaling the growth kinetics of the tumor, was present in 33.33% of the young age group, and 47.66% of the old age group, not showing statistically significant difference ($p=0.1115$).

Tumor fibrosis was also slightly more frequent in the older age group compared to the young age group (27.34% vs. 16.66%), but without showing significant differences, that could have been taken into account ($p=21.66$).

Vascular invasion was present in more than half of the old age group patients (51.56%), with a significantly lesser frequency in the young age group (28.57%) ($p=0.0122$). In case of lymphovascular invasion we could not demonstrate a significant difference between the two groups, the ratio of positive cases was low in both (9.52%, and 11.72%, respectively) (Table II).

Predictive factors

Both estrogen receptor (ER) and progesterone receptor (PR) expression was positive in a larger percentage of cases in the old age group (54.69% vs. 30.95%, and 47.66% vs. 30.95%), and this did result in a significant difference between the two age groups in case of ER ($p=0.0081$), but not in case of PR ($p=0.073$) (Table II). Her-2 status was unobtainable for the majority of patients, and as a result we could not establish the ratio of triple negative breast cancer cases, representing a distinct subgroup with poor prognosis.

Discussions

Tumor size and growth rate is one of the most consistent and powerful prognostic factors for distant relapse. Disease recurrence generally increases as tumor size increases. Based on literature data, palpable pathologies are more frequent in the young population, being larger by about 5mm to 10mm than in the old population. [9] In our study there was no significant difference between tumor sizes of the two populations, probably due to the fact that both groups fall outside the regularly screened population.

Most (80% to 90%) primary breast cancers are invasive ductal carcinoma (IDC). Another distinct subtype of breast cancer is invasive lobular carcinoma (ILC), comprising app. 10% of breast cancers. Data suggests that prognosis of IDC is poor, medullary and ILC have moderate prognosis, while mucinous and tubular carcinomas have good prognosis. [10] Our

study showed approximately equal high incidence of IDC in both age groups, as opposed to other data suggesting a significantly higher rate in young patients. [7]

Young patients characteristically have high grade, more aggressive tumors [3, 11], which our results also confirmed.

The absence or presence of axillary lymph node metastasis is also a powerful prognostic factor for primary breast cancer, and a direct relationship exists between the number of lymph nodes and clinical outcome. Several studies reported that younger patients have more nodal involvement, and if they are node-positive, then usually more nodes are involved. However, caution also needs to be exercised, since cancers less than 10mm in young patients are less likely to produce nodal involvement. [3, 12] Our results showed no real difference in terms of number of involved nodes, but a surprising finding was that the older patient group presented a significantly higher nodal positivity, which might be explained by the fact that mean tumor size was in the lower values of the range, thus determining less nodal involvement in the young.

Tumor necrosis, fibrosis and lymphovascular invasion did not show significant differences between the two age groups, although there are studies stating that younger age groups have more frequent necrosis, due to higher kinetics of the tumors.

Breast cancer tumor angiogenesis is an independent prognostic factor, and correlates with the presence of metastases, and consequently a poor clinical outcome. [13] In our study vascular invasion was significantly more characteristic to the old patient group, increasing their risk of developing metastases.

It is established that estrogen and progesterone play a role in the development of breast cancers. Hormone receptor status is classified as one of the main prognostic factors of breast cancer, where negativity is

associated with a poorer prognosis.[11] ER+ tumors usually are better differentiated and have slower progression. Patients with ER- tumors are more likely to present with a higher grade tumor, with more extensive proliferation capabilities, and also they are very likely to be unresponsive to hormonal treatment. [14] As expected, ER+ cases were significantly more

frequent in the old group, confirming the better prognosis of these.

Conclusions

We could not demonstrate significant differences between the two groups as far as tumor size, number of involved nodes, histological type, nuclear grade, presence of necrosis, fibrosis, and lymphovascular invasion is concerned. The significant differences in histological grade, and ER status conclusively demonstrated that in case of younger breast cancer patients, the disease is more aggressive and developing more extensively. The higher frequency of node involvement and vascular invasion in the old age group was contradictory to literature data.

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