Advances in Modern Oncology Research
 doi: 10.30564/amor.v4i5.187

ORIGINAL RESEARCH ARTICLE

Surgical Procedures, Pathological Features and Prognosis in Young Women with Breast Cancer in China – a Single Institute Experience

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Abstract: Objective: To compare the differences in surgical procedures, pathological features and prognosis between young and elderly women with breast cancer in China. Methods: A retrospective study compared the data of surgical procedures, pathological features and prognosis of 61 cases of young females (≤ 40 years) and 507 cases of elderly females (> 40 years), treated in our department from August 2011 to July 2018. This data was analyzed using SPSS 23.0 program. Results: 10.74% of total cases, in this period of time, involve young females. In terms of surgical procedures, 24.59% of young patients underwent breast conserving surgery (8.48% elderly, respectively), and 13.11% underwent reconstruction surgery (1.18% elderly, respectively), with statistically significant differences existing between the two groups (P < 0.05). Progesterone receptor (PR) expression in young women was significantly higher than in elderly females (P < 0.05). There were no significant differences between the two groups in the proportion of invasive ductal carcinoma (IDC), axillary lymph node metastasis (ALNM), expression of estrogen receptor (ER), human epidermal growth factor receptor-2 (HER-2) and Ki-67, but the lymphatic metastasis stage showed an increasing rate with younger age. No significant difference was found in 3-year disease-free survival (DFS) and overall survival (OS). Conclusion: The selection rate of breast conserving and reconstructive surgery in young women with breast cancer is significantly higher than that in elderly women. The younger the patient, the more frequently the PR positive expression, and the more likely ALNM to occur. The 3-year prognosis of the young and elderly patients is similar.

Keywords: Breast neoplasm; young women; surgical procedures; pathological features; prognosis

Received: 12th February 2019; Accepted: 3rd April 2019; Published Online: 17th April 2019

1. Introduction

Breast cancer is the most common malignancy in women worldwide, accounting for 25.1% of all cancers, with a mortality rate of 12.9 (per 100,000)\(^1\). In China, the crude incidence rate of female breast cancer patients was 32.43 per 100,000 and about 55,500 women died of breast cancer in 2010\(^2\). With improvement in detection rate and constant follow-up, the average age of diagnosis of breast cancer has come forward, so that young breast cancer now attracts more attention. In developed countries, 6-10% of breast cancers are diagnosed under the age of 45, while in developing countries the rate can be as high as 20%\(^3\).

At present time, the definition of young breast cancer remains unclear. In this paper, according to the recommendation of the European Society of Breast Cancer experts, the definition of young breast cancer is defined as "no older than 40 years"\(^4\). Female breast cancer patients admitted to our department from August 2011 to July 2018 were taken as the research objects to explore the surgical procedures, pathological features and prognosis of young
female with breast cancer.

2. Methods

2.1 Research Subjects

Included subjects: Female breast cancer patients admitted to department of breast surgery, Shanghai East Hospital during August 2011 to July 2018 (total of 568 cases), and matching the following conditions: 1) breast cancer diagnosed by pathology, including all pathological types; 2) surgery performed right after diagnosis and no other neoadjuvant treatment performed; 3) complete immunohistochemical results. Excluded subjects: 1) patients who gave up surgery after diagnosis or did not have surgery in our department; 2) patients who could not perform surgery immediately, and received neoadjuvant treatment; 3) incomplete immunohistochemical results.

2.2 Classification Methods

Surgical classification includes: 1) Mastectomy (simple, modified radical, nipple and areola sparing); 2) breast conserving surgery (expanded lumpectomy, expanded lumpectomy plus sentinel lymph node biopsy, expanded lumpectomy plus axillary lymph node dissection); 3) mastectomy plus reconstruction. The pathological classification is recommended according to the 2018 Breast Cancer Diagnosis and Treatment Guidelines of Chinese Society of Clinical Oncology [5]: 1) pathological pattern was referred to World Health Organization (WHO) breast cancer classification (2012); 2) the positive threshold of estrogen receptor (ER) and progesterone receptor (PR) was set at 1%; 3) HER2 negative was defined as HER2(-~+) or HER2(2+) and FISH (-), and HER2 positive was defined as HER2(3+) or HER2(2+) and FISH (+); 4) Ki-67 < 15% defined as low expression, > 30% as high expression, and 15%-30% as critical interval.

2.3 Statistical Methods

SPSS 23.0 program was used for statistical data processing; x±s selected for measurement data; frequency (%), chi-square test and P value were selected for counting data.

3. Results

3.1 Age

A total of 568 female breast cancer patients were admitted to our department from August 2011 to July 2018, with an average age of 55.73 ± 12.56 years old and a median age of 56 years old. Among them, 61 patients were less than or equal to 40 years old (10.74%), while 507 cases older than 40 years old (89.26%).

3.2 Age and Surgical Options

Among of the 61 young patients, 38 (62.30%) underwent mastectomy, 15 (24.59%) breast conserving surgery, and 8 (13.11%) mastectomy plus reconstruction surgery (7 implants and 1 latissimus dorsi flap combined with implant). Among the 507 elderly patients, 458 (90.34%) underwent mastectomy, 43 (8.48%) breast conserving surgery, and 6 (1.18%) mastectomy plus reconstruction surgery. The difference was statistically significant (P < 0.05). See Table 1.

3.3 Age and Pathological Features

3.3.1 Age and Clinicopathologic Features

Forty-eight patients (78.69%) had the feature of IDC in the young group compared to 368 patients (72.58%) in the elderly group, and 27 patients (45%) were with ALNM in the young group compared to 165 patients (33.74%) in the elderly group, presenting no significant difference between the two groups (P > 0.05). However, the lymphatic metastasis stage showed an increasing rate with younger age. See Table 2, Figure 1.

3.3.2 Age and Immunohistochemical Features

The expressions of ER, PR, HER-2 and Ki-67 in the two groups were compared respectively. The results showed that the positive expression rate of PR in the
young group was 81.97%, and in the elderly group was 66.67%, with significant difference (P < 0.05). The differences of the expression rate of ER, HER-2 and Ki-67 between the two groups were not statistically significant (P > 0.05). See Table 2.

Table 2. Comparison of pathological features between the young and elderly female

<table>
<thead>
<tr>
<th></th>
<th>Young Group N(%)</th>
<th>Elderly Group N(%)</th>
<th>χ²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48 (78.69)</td>
<td>368 (72.58)</td>
<td>1.035</td>
<td>0.309</td>
</tr>
<tr>
<td>No</td>
<td>13 (21.31)</td>
<td>139 (27.42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LNM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>33 (55.00)</td>
<td>324 (66.26)</td>
<td>3.625</td>
<td>0.305</td>
</tr>
<tr>
<td>N1</td>
<td>16 (26.67)</td>
<td>86 (17.57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>7 (11.67)</td>
<td>53 (10.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td>4 (6.67)</td>
<td>26 (5.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncertain</td>
<td>1</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>50 (81.97)</td>
<td>373 (73.57)</td>
<td>2.020</td>
<td>0.155</td>
</tr>
<tr>
<td>Negative</td>
<td>11 (18.03)</td>
<td>134 (26.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>50 (81.97)</td>
<td>338 (66.67)</td>
<td>5.888</td>
<td>0.015</td>
</tr>
<tr>
<td>Negative</td>
<td>11 (18.03)</td>
<td>169 (33.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HER-2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>43 (76.79)</td>
<td>332 (66.26)</td>
<td>0.500</td>
<td>0.479</td>
</tr>
<tr>
<td>Positive</td>
<td>13 (23.21)</td>
<td>127 (25.73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncertain</td>
<td>5</td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ki-67</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15%</td>
<td>14 (22.95)</td>
<td>116 (22.88)</td>
<td>0.485</td>
<td>0.784</td>
</tr>
<tr>
<td>15%-30%</td>
<td>19 (31.15)</td>
<td>179 (35.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 30%</td>
<td>28 (45.90)</td>
<td>212 (41.81)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Lymph node biopsy/dissection was not performed in one young patient and 18 elderly patients with invasive tumor.
b. FISH detection was not performed in 5 young patients and 48 elderly patients with HER2 (2+).

3.4 Age and Prognosis

The median follow-up time for all patients was 40 months. Among 61 cases of young patients, 51 women were followed up, with a loss rate of 16.39%. During follow-up, local recurrence or metastasis occurred in 7 patients (13.73%) and 4 patients died (7.84%). The rate of disease-free survival of young patients was 86.27% and overall survival was 92.16%. Among 507 cases of elderly patients, 415 women were followed up, with a loss rate of 18.15%. During follow-up, local recurrence or metastasis occurred in 32 patients (7.71%), 11 patients (2.65%) died of breast cancer and 18 patients (4.34%) died of other reasons. The rate of disease-free survival of elderly patients was 87.95% and overall survival was 93.01%. See Table 3.

Table 3. 3-year DFS and OS of two groups

<table>
<thead>
<tr>
<th></th>
<th>DFS</th>
<th>P value</th>
<th>OS</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>young</td>
<td>86.27%</td>
<td>0.730</td>
<td>92.16%</td>
<td>0.822</td>
</tr>
<tr>
<td>elderly</td>
<td>87.95%</td>
<td></td>
<td>93.01%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>87.77%</td>
<td></td>
<td>92.92%</td>
<td></td>
</tr>
</tbody>
</table>

4. Discussion

The average age of diagnosis of breast cancer in China is nearly 10 years earlier than in European countries and America[6]. The incidence of young breast cancer in European countries and America remains at 4-5%[7], but China has reached 12.5%[8]. In this study, the proportion of young breast cancer patients aged less than or equal to 40 years also reached 10.74%. The median age of breast cancer patients admitted to our department was 56 years old, slightly higher than counted in 2008[9]. The long-term outcome of young breast cancer is generally poor[10,11], which is contradictory to the life expectancy of this group. Therefore, optimizing the treatment of breast cancer in this group of patients remains crucial.

Young patients should actively accept surgical treatment because of less systemic diseases and more tolerance to surgical trauma. Every patient has an individual surgery plan. According to the previous studies[12,13], young patients usually present with larger tumor diameters and higher clinical stage, resulting in fewer patients choosing breast conserving surgery. However, in this study, the proportion of young patients receiving breast conserving surgery was significantly higher than that elderly patients. Racio[14] pointed out that before deciding on the surgical approach, young women wanted to obtain information such as surgical side effects, postoperative recurrence risk, cosmetic feature, quality of life influence and so on. Therefore, in addition to the objective consideration of tumor growth, there are two main factors influencing the decision-making of whether young women receive breast conserving surgery: their own needs and demand for cosmetic feature and quality of life.

Age may be an independent risk factor affecting the prognosis of breast cancer[15,16]. Whether young patients undergoing breast conserving surgery will increase the risk of recurrence and metastasis has been a controversial concern. However, recent studies suggest that compared with conserving surgery, mastectomy does not provide more benefits for young patients in terms of DFS and
that case, the young patients may have early lymphatic involvement is an independent factor for OS, and even the conserving group shows a better outcome[17,18]. The negative effects of mastectomy such as appearance loss, decreased sexual behavior, and long-term psychological problems[19,20] lead to more young women choosing conserving surgery, except a few patients who choose mastectomy because of the rejection to radiotherapy after breast conserving surgery. Breast conserving surgery can be considered as the first choice for patients who meet the indications for breast conserving surgery, as well as the patients who meet the indications for radiotherapy.

In this study, there was also a significant difference in the proportion of patients receiving breast reconstruction between the two groups, as other scholars reported[21]. Breast reconstruction is mainly aimed at patients who do not meet the requirements of breast conserving surgery and have a strong demand for personal image. Although, the safety of reconstructive surgery for young patients has been confirmed[22], the side effects and complications of breast reconstruction, such as implant tolerance[23], postoperative infection and skin flap necrosis, will greatly affect the comprehensive outcome. In order to reduce postoperative complications and improve satisfaction, we need to fully inform the advantages and disadvantages of different reconstruction methods before surgery, including breast symmetry, postoperative recovery time, possible complications and so on[24]. Factors such as cancer stage, age, BMI, smoking history and radiotherapy history were combined to determine the timing of reconstruction[25]. Ensure operative techniques, such as blood perfusion of autograft, preserving the fat outside of the breast fascia to reduce the necrosis of the skin flap, the selection of auxiliary tissue. In conclusion, the surgeon should fully consider the surgical conditions, fully inform of the surgical risk, and help the patients make right decisions.

In addition to variation in surgical options, we also observed differences in the pathological features of young patients. The prognosis of breast cancer is closely related to the invasion and metastasis ability of tumor cells, so lymph node involvement is an independent factor for OS and DFS[26]. In spite of no significant difference, between the two groups of female patients, in the rate of ALNM, and DFS[27,28]. The reason may be that our sample size is so small that the difference does not reach statistical significance. In that case, the young patients may have early lymphatic metastasis, rapid tumor progression, late clinical staging, and poor prognosis. We need to be more alert to reduce the misdiagnosis and missed diagnosis rate, to provide early treatment and strengthen postoperative comprehensive treatment.

PR is a ligand-dependent transcription factor of the nuclear/steroid hormone receptor family, is induced by the binding of estrogen (E2) to ER, and PR positivity is considered as proof of the integrity of the E2-ER response pathway[29]. In this study, the PR positive expression in the young group was significantly higher than in the elderly group, therefore suggesting a higher sensitivity to endocrine therapy, as well as promoting prognosis. However, the role of PR in breast cancer remains controversial. On the one hand, PR can inhibit the proliferation of tumor cells by inactivating the cycling-dependent kinase pathway and inducing cell death, and PR is an important predictor of long-term benefits of endocrine therapy for ER+ patients[30]. On the other hand, PR is usually divided into two types: PR-A and PR-B. According to recent reports, in Luminal breast cancer, PR-A can promote tumor invasion and metastasis by inhibiting estrogen regulation of key microRNAs[31], and high PR-A/PR-B ratio may be associated with poor prognosis[32]. Due to the lack of detection of independent expression of two types, the specific significance of the high positive rate of PR in young patients in this study needs further discussion, and the detection of PR typing and targeted anti-progesterone therapy may be the direction of further research in the future.

In combination with previous researches[33-36], the correlation between age and various pathological characteristics is still not clear, which this may be due to inconsistency in research group, detection technology, boundary criteria and other aspects. Therefore, different scholars hold different opinions of the treatment of young breast cancer. Higher rate of lymphatic metastasis may lead to poor prognosis. We should pay more attention to the postoperative adjuvant treatment, especially in endocrine therapy targeted at progesterone receptor.

The young patients in reproductive stage should be informed more carefully before receiving treatment. Embryo and oocyte cryopreservation, ovarian tissue cryopreservation and gonadotropin-releasing Hormone (GnRHa) are four main strategies for fertility preservation. Embryo and oocyte cryopreservation techniques is recommended worldwide[37]; but in China, due to the limitations of economic and technological popularization, GnRHa is generally the first choice. In addition, young breast cancer requires multidisciplinary guidance, including oncology, surgery, radiology, rehabilitation, psychology and fami-
ly planning, etc. Doctors should develop individualized treatment programs for patients.

The results of our study showed that there was no significant difference in 3-year DFS and OS between the two groups, which was inconsistent with the general view that the prognosis of breast cancer in young women is poor. The reason may be that our follow-up time is too short, according to which the outcome of the prognosis has not reached a statistical difference. However, at present, we believe that the prognosis at all ages is similar within 3 years after surgery.

This study has some other limitations, including the following aspects: 1) this study is a retrospective analysis, partial data loss may cause bias; 2) FISH test was launched in our hospital after 2014, therefore the test not used in 53 patients with HER2 (2+); 3) secondary detection was not performed in all patients whose Ki-67 is between 15% and 30%. 4) The study was conducted in surgery department. We have not collected data on patients receiving adjuvant treatment in internal medicine. To sum up, we need to further sort out and analyze the data to verify the accuracy of the results of this study.

5. Conclusion

The selection rate of breast conserving and reconstructive surgery in young women with breast cancer is significantly higher than that in elderly women. The younger patient, the more frequently the PR positive expression, and the more likely ALNM to occur. The 3-year prognosis of the young and elderly patients is similar.

References


