Clinical Surgery

Outcome in breast molecular subtypes according to nodal status and surgical procedures

Chafika Mazouni, M.D., Ph.D.\textsuperscript{a,*}, Françoise Rimareix, M.D.\textsuperscript{a}, Marie-Christine Mathieu, M.D.\textsuperscript{b}, Catherine Uzan, M.D., Ph.D.\textsuperscript{a}, Céline Bourgier, M.D., Ph.D.\textsuperscript{c}, Fabrice André, M.D., Ph.D.\textsuperscript{b}, Suzette Delaloge, M.D.\textsuperscript{d}, Jean-Rémi Garbay, M.D.\textsuperscript{a}

\textsuperscript{a}Department of Breast Surgery; \textsuperscript{b}Department of Pathology; \textsuperscript{c}Department of Breast Medical Oncology; \textsuperscript{d}Department of Radiotherapy, Institut Gustave Roussy, Villejuif, France

\textbf{KEYWORDS:}
Breast cancer;
Luminal B;
Molecular subtype;
Triple negative

\textbf{Abstract}

\textbf{BACKGROUND:} The purpose of our study was to evaluate the surgical treatment and outcome of breast cancer according to molecular subtypes.

\textbf{METHODS:} We identified 1,194 patients consecutively treated for primary breast cancer from 2004 to 2010. The type of surgery, pathological findings, local recurrence, and distant metastasis were evaluated for 5 molecular subtypes: luminal A and B, luminal HER2 (Human Epidermal Growth Factor Receptor 2), HER2, and triple negative.

\textbf{RESULTS:} Breast-conserving surgery (BCS) was performed more frequently in luminal A (70.6%), triple-negative (66.2%), and luminal HER2 (60.9%) (\(P < .001\)). A sentinel node biopsy was performed more frequently in luminal A (60%) and luminal HER2 (29.3%) types (\(P < .001\)). Among the 791 BCS, positive nodes were observed more often in luminal A (60%) and luminal HER2 (29.3%) types (\(P < .001\)). The number of local recurrences was higher in the node-negative luminal B subtype (3.4%).

\textbf{CONCLUSIONS:} Molecular subtypes exert an impact on BCS and nodal surgery rates. The local relapse rates are influenced by the molecular subtypes according to the nodal status.

\textsuperscript{a}Department of Breast Surgery; \textsuperscript{b}Department of Pathology; \textsuperscript{c}Department of Breast Medical Oncology; \textsuperscript{d}Department of Radiotherapy, Institut Gustave Roussy, Villejuif, France

Breast molecular classification, as described by Perou et al\textsuperscript{1} and Sorlie et al\textsuperscript{2} in the early 2000s, has enhanced our understanding of breast cancer (BC) heterogeneity. Significant differences have been observed in response to treatment and in the long-term outcome of these BC subtypes.\textsuperscript{3} Three levels of evidence I markers,\textsuperscript{4,5} namely the estrogen receptor (ER), progesterone receptor (PR), and HER2 (Human Epidermal Growth Factor Receptor 2) associated with nuclear grading, represent the pivotal factors used to identify BC molecular subtypes.\textsuperscript{6}

Adjuvant systemic therapy has improved in terms of efficacy on prognosis and has limited drugs’ toxicity; different targeting strategies have been initiated during recent years as a result of molecular classification. For instance, triple-negative (TN) tumors identified as being associated with a higher risk of metastatic disease\textsuperscript{7} have been the model chosen for developmental trials of poly (ADP-ribose) polymerase (PARP) inhibitors, antiangiogenics, or molecules targeting epidermal growth factor receptor (EGFR) in the metastatic setting.\textsuperscript{8–10} whereas HER2-expressing tumors are the target of anti-HER2 agents such as trastuzumab or agents targeting the vascular endothelial growth factor, the mammalian target
of rapamycin, and phosphatidylinositol 3-kinase (PI3) kinase pathways.\textsuperscript{11–14}

Will this molecular classification have an impact on the surgical strategy and allow a personalized surgical approach? With regard to locoregional treatment, recent studies have suggested that the molecular subtype exerts an impact on locoregional recurrences even if this risk is strongly dependent on the patient’s age.\textsuperscript{15} In addition, other authors have suggested that the status of nonsentinel nodes is influenced by the molecular subtype.\textsuperscript{16} The purpose of this study was to evaluate the surgical strategy and outcomes according to different BC molecular subtypes and to stratify this analysis according to nodal involvement.

**Patients and Methods**

**Patient selection**

The study cohort consisted of 1,194 consecutive women with clinical stage I or III invasive BC surgically treated through March 2004 to March 2010 at the Institut Gustave Roussy, Villejuif, France. This study was a retrospective chart review. Patients with incomplete data for the ER (n \(=\) 121), PR (n \(=\) 120), and HER2/neu status (n \(=\) 317) and the histologic grade of the primary tumor (n \(=\) 47) were not selected nor were patients with synchronous bilateral BC or synchronous metastasis (n \(=\) 104) or who had received preoperative systemic therapy (n \(=\) 596). BC staging was defined by TNM classification as proposed by the American Joint Committee on Cancer (AJCC) for grouping patients with respect to prognosis.

**Pathology**

Patients were grouped into 5 subgroups according to the BC subtype as previously described\textsuperscript{6,15}: ER positive or PR positive, HER2 negative, and grade 1 or 2 (luminal A); ER positive or PR positive, HER2 negative, and grade 3 (luminal B); ER positive or PR positive and HER2 positive (luminal HER2); ER negative, PR negative, and HER2 positive (HER2 subtype); and ER negative, PR negative, and HER2 negative (triple negative). ER, PR, and HER2 levels were assessed immunohistochemically. Tumors were deemed positive for these receptors if at least 10\% of the invasive tumor cells in a section exhibited nuclear staining. Histologic grading was defined according to the Scarf-Bloom-Richardson system.\textsuperscript{17} HER2 positivity was defined as a 3+ staining intensity score at immunohistochemical analysis for the HER2 protein or for HER2 gene amplification by fluorescence in situ hybridization.

**Treatment**

All patients submitted to breast-conserving surgery (BCS) received whole-breast irradiation. For patients who underwent a mastectomy, chest wall and regional nodal irradiation including the supraclavicular fossa was performed if the patient had \(\geq\) 4 positive lymph nodes or invasive cancer measuring \(\geq\) 4 cm. Indications for adjuvant chemotherapy were in accordance with the St. Gallen guidelines.\textsuperscript{18} Women with ER-positive BC were to receive 5 years of endocrine therapy, which began after the completion of all chemotherapy. After treatment completion, patients were seen every 6 months for the first 5 years and yearly thereafter, with a yearly mammography and a clinical examination at each visit. A bone scan, liver ultrasound, and chest x-ray were not included among the routine follow-up examinations and were performed exclusively in symptomatic cases. The sites of metastases were prospectively recorded.

**Statistical methods**

The chi-square test was used to compare the distribution of baseline characteristics among BC subtypes for categoric factors, whereas the Kruskal-Wallis test was used for continuous variables. The endpoints studied were recurrence-free survival (RFS) and distant metastasis-free survival (MFS) rates. The RFS rate was defined as the time from surgery to the date of any ipsilateral in-breast recurrence (invasive or noninvasive) without evidence of distant metastasis or death from cancer if no earlier recurrence had occurred. The distant MFS time was defined as the time to distant metastasis or death if the latter event occurred before the diagnosis of a distant metastasis. Survival rates were calculated using the Kaplan-Meier method and compared between groups with the log-rank test. A 5\% significance level was used, and all P values were 2 sided. All analyses were performed in R, an open source statistical package (http://www.r-project.org/) using the Design library.\textsuperscript{19}

**Results**

**Patient characteristics and BC subtypes**

The percentage distribution of BC subtypes among the 1,194 patients in the study was as follows: luminal A in 63.2\%, luminal B in 13.8\%, luminal HER2 in 6.9\%, HER2 in 5\%, and TN in 11.1\%. The analysis of patient characteristics and surgical procedures shows significant differences among BC subtypes in terms of age (\(P < .001\)), menopausal status (\(P < .001\)), the rate of BCS (\(P < .001\)), and sentinel node biopsy (SNB) (Table 1). Patients with the HER2 or TN subtypes were younger (\(\leq\) 40 years) than in the other groups. There were also significant differences in the distribution of tumor characteristics including tumor size (\(P < .001\)), grade (\(P < .001\)), and node positivity (\(P < .001\)). BCS was possible in 791 patients (66.2\%). Among these 791 cases, an SNB was performed in 53.1\%. Nodal positivity was observed in 227 patients (28.7\%) and was more frequent in HER2 and luminal B subtypes (\(P < .001\)). Additionally, patients were classified as stage I in 47.2\% (n = 564), stage IIA in 33.8\% (n = 403), stage IIB in 16.6\% (n = 198), and stage IIIA in 2.4\% (n = 29).
Follow-up

At the time of the analysis, 9 of 1,194 patients had developed a local recurrence, 40 patients had developed distant metastases, and 29 had died. In the BCS subgroup, 4 local recurrences and 17 distant metastases were observed.

In the entire group, the 5-year RFS and MFS rates were significantly different according to BC subtypes. The 5-year RFS rates for the following subtypes were 100% for HER2, 99.8% (95% confidence interval [CI], 99.5% to 100%) for luminal A, 98.9% (95% CI, 96.8% to 100%) for luminal B, 98.4% (95% CI, 95.2% to 100%) for luminal HER2, and 97.7% (95% CI, 94.5% to 100%) for TN (P = .003). The 5-year MFS rates for the following subtypes were 91.8% (95% CI, 84.3% to 99.9%) for HER2, 99.1% (95% CI, 98.3% to 99.9%) for luminal A, 98.9% (95% CI, 93.6% to 99.9%) for luminal B, 98.6% (95% CI, 95.9% to 100%) for luminal HER2, and 92.1% (95% CI, 86.9% to 97.6%) for TN (P = .001).

In the total group, the 5-year MFS rates were significantly different according to BC stages, whereas no differences were observed in the 5-year RFS rates. According to stage, the 5-year RFS rates were 99.7% (95% CI, 97.7% to 100%) for stage I, 99.3% (95% CI, 97.3% to 99.8%) for stage IIA, 98.6% (95% CI, 94.3% to 99.6%) for stage IIB, and 100% for stage IIIA (P = .86). According to stage, the 5-year MFS rates were 99.4% (95% CI, 98% to 99.8%) for stage I and 98% (95% CI, 95.6% to 99%) for stage IIA, stage IIB, and stage IIIA (P < .001).

In the univariate analysis, only hormone therapy (HT) (hazard ratio [HR] = 0.16, P = .006) was associated with the RFS rate and not stage, whereas the pathological tumor size (HR = 1.48, P < .001), positive lymph nodes (HR = 3.59, P = .0002), the luminal A subtype (HR = 0.18, P = .002), stages IIB (HR = 6.2, P < .001) and IIIA (HR = 7.8, P = .003), BCS (HR = 0.40, P = .004), chemotherapy (CT) (HR = 10.45, P = .007), and HT (HR = 0.22, P < .001) were associated with the MFS rate. In the multivariate analysis, positive lymph nodes (HR = 4.3, P = .03) and HT (HR = 0.10, P = .02) were associated with the MFS rate.

### Table 1

<table>
<thead>
<tr>
<th>Characteristics of the study population in the different molecular categories</th>
<th>Luminal A (n = 755)</th>
<th>Luminal B (n = 165)</th>
<th>Luminal HER2 (n = 82)</th>
<th>HER2 (n = 59)</th>
<th>TN (n = 133)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>61.3</td>
<td>59.9</td>
<td>56.3</td>
<td>56.5</td>
<td>57.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≤40 years (%)</td>
<td>18 (2.4)</td>
<td>13 (7.9)</td>
<td>7 (8.5)</td>
<td>15 (25.4)</td>
<td>36 (27.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Menopause (%)</td>
<td>568 (75.2)</td>
<td>117 (70.9)</td>
<td>46 (56.1)</td>
<td>38 (64.1)</td>
<td>89 (66.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Family history (%)</td>
<td>248 (32.8)</td>
<td>51 (30.9)</td>
<td>30 (36.6)</td>
<td>12 (20.3)</td>
<td>38 (28.6)</td>
<td>.25</td>
</tr>
<tr>
<td>Mean tumor size (mm)</td>
<td>18.1</td>
<td>24.1</td>
<td>22.6</td>
<td>25.7</td>
<td>22.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>pT &lt;10 (%)</td>
<td>192 (25.4)</td>
<td>14 (8.5)</td>
<td>12 (14.6)</td>
<td>11 (18.6)</td>
<td>13 (9.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>pT &lt;20 (%)</td>
<td>558 (73.9)</td>
<td>87 (52.7)</td>
<td>44 (53.7)</td>
<td>29 (49.2)</td>
<td>65 (48.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>pTNM staging (%)</td>
<td>409 (54.2)</td>
<td>75 (45.7)</td>
<td>63 (78.8)</td>
<td>18 (29.2)</td>
<td>22 (33.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Positive lymph nodes (%)</td>
<td>32 (39)</td>
<td>32 (39)</td>
<td>32 (39)</td>
<td>32 (39)</td>
<td>32 (39)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

pTNM staging = pathological TNM staging.

Prognostic factors in the BCS subgroup

A total of 791 patients underwent BCS, 53.1% of whom underwent an SNB as definitive surgery. Significant differences were observed between subtypes as shown in Table 2. In patients who underwent BCS, younger patients had the TN, luminal HER2, and HER2 subtypes (P < .001). Higher pathological tumor sizes were observed among luminal B and HER2 subtypes (P < .001), and node positivity was more frequent among the luminal B and HER2 subtypes (P = .001). There were also significant differences in tumor size distribution, systemic treatment (P < .001), and distant metastasis (P < .001).

In this BCS group, the 5-year RFS rates for the following subtypes were as follows: 100% for HER2, 100% for luminal A, 98.2% (95% CI, 94.7% to 100%) for luminal B, 100% for luminal HER2, and 100% for TN (P = .05). The 5-year MFS rates for the following subtypes were 88.1% (95% CI, 73.9% to 100%) for HER2, 99.3% (95% CI, 98.4% to 100%) for luminal A, 98.7% (95% CI, 96.2% to 100%) for luminal B, 97.8% (95% CI, 93.6% to 100%) for luminal HER2, and 97% (95% CI, 92.9% to 100%) for TN (P < .001).

According to the univariate analysis, no factor was associated with the RFS rate. The pathological tumor size (HR = 2.15, P = .000723), the luminal A subtype (HR = 0.09,
Gene expression profiling has identified BC subtypes with distinct clinical outcomes.\(^1,2\) The impact of this classification on surgery is less described compared with studies concerning the prognosis of BC. In this retrospective study on a cohort of 1,194 patients, we analyzed surgical outcomes according to the molecular classification of BC. In our series, some subtypes exhibited a higher risk of nodal involvement (ie, luminal B and HER2) and a risk of local relapse (ie, node-negative luminal B).

We observed a higher frequency of SLN procedures for luminal A and luminal HER2 subtypes among the modalities used for breast and axillary surgeries. Consequently, higher rates of positive nodes were observed in luminal B and HER2 tumors. Some recent publications have suggested the role of molecular subtypes in the risk of nodal involvement.\(^16,20–22\) Most of these publications showed a higher risk of positive nodes in HER2-positive tumors or those with a high nuclear grade\(^16,23\) and low nodal involvement with TN tumors.\(^20,21\) However, there is no clear biological explanation for the axillary aggressiveness of HER2 tumors, especially because an interaction with the ER status is often reported.\(^16,24\) Moreover, HER2 overexpression is often associated with a poor histologic grade, a spread to the axillary nodes, and a greater number of involved nodes.\(^25\) Based on tumor biology, Reyal et al\(^16\) proposed a decisional nomogram for predicting the risk of SLN involvement; a limitation of this nomogram is that the PR status was not available in their model.

In the BCS subgroup, a higher prevalence of positive lymph nodes was also observed for luminal B and HER2 tumors, which exhibited aggressive features independently of the tumor size. Interestingly, the rate of positive nodes was previously observed to be inversely correlated with the tumor size and nodal status.\(^22,26\) Thus, for tumors measuring 2 cm or less, patients with basal-like breast cancer had a higher percentage of node-positive tumors than luminal A tumors. However, the equivalent mean tumor size (20 mm) in all subgroups accounts for the absence of a direct interaction with the tumor size in our data.

On the whole, the number of local relapses after BCS was low among the different subtypes but was higher in biologically aggressive tumors such as luminal B and HER2 subtypes. The number of local relapses was higher in the luminal B subtype (3.4%) and luminal HER2 (12.5%) subtypes among patients with node-negative BC. HER2 and luminal B subtypes exhibited the highest rates of distant metastasis (16.7% and 3.4%, respectively). In the 227 women with node-positive tumors, the highest risks were observed for the TN (16.7%), luminal B (13%), HER2 (12.5%), and luminal HER2 (11.1%) subtypes.

### Comments

Gene expression profiling has identified BC subtypes with distinct clinical outcomes.\(^1,2\) The impact of this classification on surgery is less described compared with studies concerning the prognosis of BC. In this retrospective study on a cohort of 1,194 patients, we analyzed surgical outcomes according to the molecular classification of BC. In our series, some subtypes exhibited a higher risk of nodal involvement (ie, luminal B and HER2) and a risk of local relapse (ie, node-negative luminal B).

We observed a higher frequency of SLN procedures for luminal A and luminal HER2 subtypes among the modalities used for breast and axillary surgeries. Consequently, higher rates of positive nodes were observed in luminal B and HER2 tumors. Some recent publications have suggested the role of molecular subtypes in the risk of nodal involvement.\(^16,20–22\) Most of these publications showed a higher risk of positive nodes in HER2-positive tumors or those with a high nuclear grade\(^16,23\) and low nodal involvement with TN tumors.\(^20,21\) However, there is no clear biological explanation for the axillary aggressiveness of HER2 tumors, especially because an interaction with the ER status is often reported.\(^16,24\) Moreover, HER2 overexpression is often associated with a poor histologic grade, a spread to the axillary nodes, and a greater number of involved nodes.\(^25\) Based on tumor biology, Reyal et al\(^16\) proposed a decisional nomogram for predicting the risk of SLN involvement; a limitation of this nomogram is that the PR status was not available in their model.

In the BCS subgroup, a higher prevalence of positive lymph nodes was also observed for luminal B and HER2 tumors, which exhibited aggressive features independently of the tumor size. Interestingly, the rate of positive nodes was previously observed to be inversely correlated with the tumor size and nodal status.\(^22,26\) Thus, for tumors measuring 2 cm or less, patients with basal-like breast cancer had a higher percentage of node-positive tumors than luminal A tumors. However, the equivalent mean tumor size (20 mm) in all subgroups accounts for the absence of a direct interaction with the tumor size in our data.

On the whole, the number of local relapses after BCS was low among the different subtypes but was higher in biologically aggressive tumors such as luminal B and HER2 subtypes. The number of local relapses was higher in the luminal B subtype (3.4%) for node-negative BC, whereas no relapse was observed for the node-negative luminal B and HER2 subtypes. The number of local relapses was higher in the luminal B subtype (3.4%) and HER2 (12.5%) subtypes among patients with node-negative BC. HER2 and luminal B subtypes exhibited the highest rates of distant metastasis (16.7% and 3.4%, respectively). In the 227 women with node-positive tumors, the highest risks were observed for the TN (16.7%), luminal B (13%), HER2 (12.5%), and luminal HER2 (11.1%) subtypes.

### Table 2 Characteristics of the BCS group in the different molecular categories

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Luminal A (n = 533)</th>
<th>Luminal B (n = 98)</th>
<th>Luminal HER2 (n = 50)</th>
<th>HER2 (n = 22)</th>
<th>TN (n = 88)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (years)</td>
<td>62.1</td>
<td>59.7</td>
<td>57</td>
<td>57.2</td>
<td>58</td>
<td>.001</td>
</tr>
<tr>
<td>≤ 40 years (%)</td>
<td>11 (2.1)</td>
<td>6 (6.1)</td>
<td>3 (6)</td>
<td>1 (4.5)</td>
<td>7 (8)</td>
<td>.02</td>
</tr>
<tr>
<td>Menopause (%)</td>
<td>414 (77.7)</td>
<td>74 (75.5)</td>
<td>31 (62)</td>
<td>15 (68.2)</td>
<td>60 (68.2)</td>
<td>.048</td>
</tr>
<tr>
<td>Family history (%)</td>
<td>176 (33)</td>
<td>33 (33.7)</td>
<td>17 (34)</td>
<td>5 (22.7)</td>
<td>29 (33)</td>
<td>.85</td>
</tr>
<tr>
<td>Mean tumor size (mm)</td>
<td>14.9</td>
<td>19.9</td>
<td>17.6</td>
<td>18.9</td>
<td>18.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>pT &lt;10 (%)</td>
<td>159 (29.8)</td>
<td>10 (10.2)</td>
<td>10 (20)</td>
<td>3 (13.6)</td>
<td>12 (13.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>pT &lt;20 (%)</td>
<td>451 (84.6)</td>
<td>63 (64.3)</td>
<td>33 (66)</td>
<td>12 (54.5)</td>
<td>52 (59.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SNB (%)</td>
<td>320 (60)</td>
<td>36 (36.7)</td>
<td>21 (42)</td>
<td>9 (41)</td>
<td>34 (38.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Positive lymph nodes (%)</td>
<td>133 (25)</td>
<td>44 (44.9)</td>
<td>13 (26)</td>
<td>11 (50)</td>
<td>26 (29.5)</td>
<td>.0003</td>
</tr>
<tr>
<td>Adjuvant chemotherapy (%)</td>
<td>171 (32.1)</td>
<td>82 (83.7)</td>
<td>42 (84)</td>
<td>20 (90.9)</td>
<td>78 (88.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hormonal treatment (%)</td>
<td>524 (98.3)</td>
<td>97 (98.9)</td>
<td>50 (100)</td>
<td>2 (9.1)</td>
<td>7 (8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Local relapse (%)</td>
<td>1 (0.2)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (2.3)</td>
<td>.12</td>
</tr>
<tr>
<td>Distant relapse (%)</td>
<td>4 (0.8)</td>
<td>5 (5.1)</td>
<td>1 (2)</td>
<td>2 (9)</td>
<td>5 (5.7)</td>
<td>.001</td>
</tr>
</tbody>
</table>

P = .006, adjuvant CT (HR = 13.8, P = .011), and HT (HR = 0.22, P = .0023) were significantly associated with the MFS rate. In the multivariate analysis, the pathological tumor size (HR = 1.1, P = .09) showed a trend toward prognostic significance for the MFS rate.
often described as a risk factor for local relapse, was underlined. Clearly, after BCS, the risk of local relapse is higher for young women with a luminal B subtype. Moreover, a comparison of long-term outcome using TNM staging system as defined by the AJCC showed that molecular subtypes are more accurate to determine the 5-year RFS rate than the staging system used in this study, which did not show any differences between stages. However, for predicting the 5-year MFS rate, the HR was stronger for staging IIb (HR = 6.2) and IIIa (HR = 7.8) than for luminal A stage (HR = 0.18). Interestingly, the rate of stage IIIa BC was higher in HER2 tumors, whereas stage I tumors were more represented in luminal A tumors as previously reported. In a recent publication, Park et al reported different RFS outcomes as function of stages stratified according to molecular subtypes (hormone receptor positive, HER2, and TN). The authors concluded that in TN tumors, the AJCC TNM staging system was not discriminative to reflect the RFS rate as the other subtypes. In a recent study by Caudle et al in patients receiving neoadjuvant CT and BCS, patients with positive hormone receptor/HER2– and positive hormone receptor/HER2+ subtypes had excellent rates of local-regional RFS regardless of the tumor response to neoadjuvant CT. In contrast, negative hormone receptor subtypes were associated with reduced local-regional recurrence (LRR)-free survival. It should be noted that in their study patients receiving neoadjuvant trastuzumab were excluded.

Future perspectives will likely include evaluating current practice in surgery, particularly the influence of molecular subtypes in the choice of BCS and SNB. With a rate of up to 50% of positive nodes in luminal B and HER2 lesions, the legitimacy of a minimal axillary strategy should be discussed. In particular, the rate of a false-negative sentinel node should be evaluated in terms of molecular subtypes. In an article published in 2011, Reyal et al developed a scoring system to predict the risk of disease in nonsentinel nodes. Alternating nomograms developed to date that include molecular classification is an interesting approach. One limitation of their study is that the PR status was not included in their model. In our series, we used the tumor grade to stratify luminal tumors, but some authors suggest that Ki-67 is an interesting option. However, Ki-67 is not systematically tested in our current practice. Finally, our study represents some preliminary results and requires validation on large external datasets to assess the value in clinical practice of such classification. We also acknowledge that the low number of relapses in the total population might explain the high 5-year RFS rate in HER2 and TN tumors, but also patients who experienced BCS mainly had a small tumor size. Moreover, all patients with HER2 BC were administered trastuzumab, which improved their outcome.

Conclusions

This study showed the importance of molecular subtypes in the surgical approach and the impact on long-term outcome. Local relapse and distant metastasis rates are influenced by molecular subtypes according to the nodal status. A prospective study should be conducted to evaluate the decisional value of molecular types for surgery.

Acknowledgments

The authors thank Lorna Saint Ange for editing.

References


