Diagnostic Significance of Preoperative Axillary Staging in Breast Cancer

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ABSTRACT

BACKGROUND: The axillary lymph node status is one of the most relevant prognostic factors in breast cancer. The non-invasive investigation of axillary lymph node involvement in the preoperative diagnosis is one of the greatest challenges in the treatment of breast cancer. The aim of our study is to assess the significance of preoperative axillary diagnostics. It will be verified whether the axillary ultrasound, the fine needle aspiration or biopsy of suspicious lymph nodes can safely predict the axillary metastasis.

METHODS: The combination of the clinical examination of the axilla, the axillary ultrasound and ultrasound-guided fine needle aspiration or biopsy were performed for preoperative axillary staging and the planning of further treatment between January 2010 and December 2012 in 586 patients with breast cancer and carcinoma in situ in our hospital.

RESULTS: The axillary ultrasound showed a low positive predictive value (61%). It follows that unsuspicious ultrasound findings can not definitively exclude axillary lymph node metastasis. The sensitivity for the detection of malignancy is only at 62 %, which is why the axillary ultrasound alone has not proven to be sufficiently precise.

The axillary ultrasound in combination with an ultrasound-guided fine needle aspiration or biopsy has shown a sensitivity of 77%. It is easy to perform and, by this method, surgical procedures could be avoided in case of contraindications for sentinel node biopsy or in inoperable patients with breast cancer. Elderly patients with small (<= 2 cm), estrogen receptor-positive and clinically node-negative breast cancer, which will receive endocrine therapy, could be successfully treated without surgical intervention.

CONCLUSION: Our data for preoperative axillary staging have shown that ultrasound-guided fine needle aspiration is a useful and reliable preoperative axillary diagnostic.

INTRODUCTION

The axillary lymph node status is one of the most relevant prognostic factors in breast cancer. Many literature sources indicate the node status as the most important predictive value for the overall survival and metastasis of breast cancer²,⁴. Of prognostic importance in particular is the number of infiltrated lymph nodes. A lymph node involvement of more than four lymph nodes is associated with a poor prognosis.

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described, with survival rates dropping to only 30% when Level III contamination is reached. In the treatment planning of breast cancer, preoperative investigation of axillary lymph node involvement is essential. The concept of sentinel node biopsy has been recognized as a standard strategy for the axillary staging in early stages of breast cancer. Post-operative adjuvant therapy should be selected depending on the number of infiltrated lymph nodes, tumor size, histological grading, vascular invasion, age of the patient and receptor status.

Preoperative diagnostic of axilla:

In the literature, the validity of the clinical examination of the axilla in breast cancer was assessed as limited. Rarely, in 10-50% of cases, can the lymph nodes be detected clinically. The ultrasound has proven to be a useful diagnostic method for the axillary staging. By using ultrasonography in combination with palpation, the sensitivity of detection of axillary lymph node involvement is increased to up to 82% (13). One of the biggest problems of invasive diagnosis of the axilla by sentinel node biopsy is the presence of false-negative results. These lead to axillary dissection not being performed in patients with negative sentinel node biopsy, despite axillary metastases. It has been shown that 1-15% of patients with a negative sentinel lymph node biopsy have infiltrated regional lymph nodes(19). The axillary ultrasound is used worldwide for the axillary staging. It is simple, quick to perform, cheaper than other methods and non-invasive. Because of its relatively low sensitivity, the ultrasound examination is not used routinely and systematically. Because of its ability to reduce the number of false-negative results from the sentinel node biopsy, interest in preoperative sonographic detection of axillary lymph node metastases has increased.

The ultrasound-guided fine needle aspiration cytology or biopsy is a fast and uncomplicated method for the axillary staging. In some locations, this method has replaced the surgical procedure because it is less invasive and more favorable for the treatment planning. Despite increasing evidence-based data that favor not performing the operation in certain cases, many places do not perform percutaneous axillary diagnostics routinely. The sensitivity of fine needle aspiration biopsy is reported in the literature to be between 43% and 94%, with specificity between 96% and 100%. The patients in whom surgery should be avoided are those that can benefit most from a fine needle aspiration or biopsy. Compared to the sentinel node biopsy, the fine needle aspiration or biopsy of axillary lymph node can not replace the axillary dissection, due to the false-negative results and the associated low sensitivity.

For a better staging, patients with negative findings should be evaluated by a sentinel node biopsy. Whether a fine needle aspiration or biopsy should be performed on small tumors is still unclear. Some authors recommend this approach for all patients who are suitable for a sentinel node biopsy, whereas other authors recommend it only in patients with suspicious lymph nodes.

The aim of our study is to assess the significance of preoperative axillary diagnostic. It will be verified whether the axillary ultrasound, the fine needle aspiration or biopsy of suspicious lymph nodes can safely predict the axillary metastasis. The detection rates of the different methods of preoperative axillary staging are analyzed. Furthermore, we investigate whether the ultrasound-guided fine needle aspiration or biopsy of abnormal lymph nodes in breast cancer can reduce the number of false negative or positive results.

PATIENTS AND METHODS

This is a retrospective observational study. This study refers to a database of surveys of a total of 586 patients with primary invasive breast cancer and carcinoma in situ of the breast that were treated between January 2010 and December 2012 in the Clinic of Gynecology, Obstetrics and Reproductive Medicine at the University of Saarland.

The determination of the stage of disease is done by classification according to the UICC TNM classification. 534 of the total 586 patients had invasive breast cancer and 52 had carcinoma in situ. Table 1 shows the tumor characteristics of patients with breast cancer.

297 cases (50.77%) consisted of T1 carcinomas (2 cm or less in greatest dimension), in 157 cases (26.84%) T2 (more than 2 cm but not more than 5 cm in greatest dimension), in 27 cases (4.62%) T3 (more than 5 cm in greatest dimension) and in 29 cases (4.96%) T4 (extension to the chest wall). 400 patients of the total count were node-negative. 28 patients (4.9%) had distant metastases at initial diagnosis; the rest had unsuspicious metastasis staging.

For preoperative assessment of axillary lymph node status, a clinical examination of the axilla, a digital mammogram and an axillary ultrasound
were performed. As an additive method to confirm the diagnosis in unclear axillary findings, an ultrasound-guided fine needle aspiration or biopsy of suspicious lymph nodes was performed. Intraoperatively we performed a sentinel node biopsy with frozen section biopsy and, if appropriate, an axillary lymphadenectomy. Furthermore, a diagnostic staging was performed to exclude distant metastases. This consisted in a liver ultrasonography (or CT abdomen), X-ray examination of the chest (or thoracic CT) and a bone scan.

For statistical data analysis, the SAS program (“Statistical analysis System”), version 9.2 was used.

RESULTS

495 patients (84.76%) had a palpatory unsuspicious axillary finding before the initial therapy.

Preoperative diagnostic of the axilla

169 (29.75%) patients showed malignancy suspicious lymph nodes in preoperative ultrasound examination. The sonographically suspicious lymph node number was assigned to the categories 1 to 4 + (4 or more than 4 suspicious lymph nodes). The ultrasonography showed in 93 cases evidence of one infiltrated lymph node (16.55%), in 12 cases two suspicious lymph nodes (2.14%), in 6 cases 3 suspicious lymph nodes (1.07%) and in 53 cases more than 3 sonographically suspicious nodes (9.43%).

In 118 cases, a preoperative fine needle aspiration or biopsy of abnormal axillary lymph

Table I.
Main clinical-pathological tumor characteristics of 586 breast cancer patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients</th>
<th>Percent</th>
<th>Characteristic</th>
<th>Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Menopausal status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preamenopausal</td>
<td>117</td>
<td>19.97%</td>
<td>Perimenopausal</td>
<td>35</td>
<td>5.97%</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>433</td>
<td>73.89%</td>
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<tr>
<td><strong>Histological diagnosis</strong></td>
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<tr>
<td>Infiltrating carcinoma</td>
<td>532</td>
<td>91.57%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In situ carcinoma</td>
<td>49</td>
<td>8.43%</td>
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<td><strong>Grading</strong></td>
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<tr>
<td>G1</td>
<td>61</td>
<td>11.80%</td>
<td>G2</td>
<td>339</td>
<td>65.57%</td>
</tr>
<tr>
<td>G3</td>
<td>117</td>
<td>22.63%</td>
<td></td>
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<tr>
<td><strong>Tumor size</strong></td>
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<td></td>
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<tr>
<td>T1</td>
<td>297</td>
<td>50.77%</td>
<td>N0</td>
<td>400</td>
<td>68.61%</td>
</tr>
<tr>
<td>T2</td>
<td>157</td>
<td>26.84%</td>
<td>N1</td>
<td>123</td>
<td>21.10%</td>
</tr>
<tr>
<td>T3</td>
<td>27</td>
<td>4.62%</td>
<td>N2</td>
<td>20</td>
<td>3.43%</td>
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<tr>
<td>T4</td>
<td>29</td>
<td>4.96%</td>
<td>N3</td>
<td>13</td>
<td>3.26%</td>
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<td><strong>Nodal involvement</strong></td>
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<tr>
<td>M0</td>
<td>538</td>
<td>95.05%</td>
<td>Negative</td>
<td>436</td>
<td>74.40%</td>
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<tr>
<td>M1</td>
<td>28</td>
<td>4.95%</td>
<td>Positive</td>
<td>89</td>
<td>15.19%</td>
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<td><strong>Her2-neu status</strong></td>
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<tr>
<td>Negative</td>
<td>436</td>
<td>74.40%</td>
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<tr>
<td>Positive</td>
<td>89</td>
<td>15.19%</td>
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<td><strong>ER status</strong></td>
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<tr>
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<tr>
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<td>Positive</td>
<td>370</td>
<td>63.14%</td>
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<td><strong>PgR status</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Negative</td>
<td>213</td>
<td>36.35%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>370</td>
<td>63.14%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Local relapse</strong></td>
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</tr>
<tr>
<td>No</td>
<td>571</td>
<td>97.44%</td>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>2.56%</td>
<td>No</td>
<td>574</td>
<td>97.95%</td>
</tr>
</tbody>
</table>

97.95% | 2.05% |
nodes was performed. It was found that 67 patients (56.7%) had a pathological finding. 31 patients (26.27%) had an unsuspicious finding and in 20 cases (16.94%) could no clear statement be taken by the investigation regarding the nodal involvement.

Postoperative histology of the removed lymph nodes.
541 Patients had a histological surgical clarification of the lymph node status. As part of the axillary staging, first a sentinel node biopsy was performed. If the intraoperative frozen biopsy of the lymph node was positive and the patients did not receive a neoadjuvant therapy, an axillary lymphonodectomy was performed. The histological examination showed positive lymph nodes for 156 (31.90%) patients. The distribution was as follows: 66 patients (13.50%) showed one infiltrated lymph node, 27 two infiltrated lymph nodes (5.52%), 27 three infiltrated lymph nodes (5.52%), 4 four infiltrated lymph nodes (0.82%), 4 five infiltrated lymph nodes (0.82%) and 28 more than five infiltrated lymph nodes (5.69%).

Correlation between the palpatory and the sonographic lymph node status (statistical kappa coefficient of 0.4694, ASE of 0.0408, p < 0.0001).

The clinical and sonographic findings of a total of 561 patients were compared and categorized as unsuspicious or suspicious. In 25 cases no full data were available. Of the 493 cases with clinically unsuspicious lymph node status, the sonography revealed a suspicious finding in 99 cases: in 70 cases one suspicious lymph node, in 8 cases two suspicious lymph nodes, in 4 cases three suspicious lymph nodes and in 17 cases more than three suspicious lymph nodes of the axilla. Of the 68 cases with suspicious lymph nodes on palpation, the ultrasonography showed in 3 cases a normal result.

Correlation between the preoperative palpation lymph node status and invasive determination of lymph node involvement by fine needle aspiration (FNA) or biopsy (USNB) (statistical kappa coefficient of 0.2701, ASE of 0.0576, p < 0.0001).

In the 73 cases with an unsuspicious palpatory finding, the fine needle aspiration or biopsy confirmed the palpatory finding in 28 cases, in 31 cases a pathological cytology or histology was observed, and in 14 cases the result was unclear.

In the 45 cases with suspicious axillary lymph nodes by palpation, the fine needle aspiration cytology or biopsy revealed pathologic findings in 36 cases.

Relationship between the sonographic lymph node status and invasive determination of lymph node involvement by ultrasound-guided fine needle aspiration (FNA) or biopsy (USNB) (statistical kappa coefficient of 0.2074, ASE of 0.0811, p < 0.0001).

Statements on sonography of the axilla and to clarify the lymph node involvement by FNA / USNB could be taken for 117 patients.

There were five cases with normal axillary ultrasound in which a fine needle aspiration or biopsy was performed. All cytologic or histologic findings were negative. In 66 patients with sonographically suspicious lymph nodes, fine needle aspiration or biopsy showed pathologic findings in 35 cases, and 18 cases showed free lymph nodes. 13 cytological or histological findings were unclear.

Ultrasonography showed in 10 cases two suspicious lymph nodes. The fine needle aspiration or biopsy of one or both lymph nodes showed in 4 cases a pathological result and in 3 cases an unsuspicious finding. In the other cases, the material obtained was not representative. In 3 cases with three sonographically suspicious lymph nodes, the fine needle aspiration showed a pathological result in all three patients.

In the 34 cases with more than 3 sonographically suspicious lymph nodes and the presence of the cytologic or histologic findings of fine needle aspiration cytology or biopsy, pathological findings were detected in 24 cases and in 5 cases the result was normal.

Correlation between the clinical palpatory and the postoperative histological lymph node status (statistical kappa coefficient of 0.2701, ASE of 0.0455, p < 0.0001).

Of 423 patients with clinically unsuspicious finding, the histological examination of the lymph nodes showed in 106 cases infiltrated lymph nodes. In 315 cases, the lymph nodes were free of metatases. 2 patients were operated ex domo. In these two cases, the information regarding the nodal involvement was missing.

Of the 54 cases with clinically suspicious lymph nodes, histology showed no metastasis in 17 cases. From these data the following parameters were calculated in order to assess the validity of palpation as a diagnostic procedure: sensitivity: 23%, specificity: 98%, positive predictive value: 85%, negative predictive value: 75%.

Relationship between the sonographic and the postoperative histological lymph node status (statistical kappa coefficient of 0.3027, ASE of 0.0562, p = 0.0620).

Statements about the preoperative sonography and postoperative histology of the lymph nodes
were available for 474 patients.

In 82 patients, one lymph node was assessed preoperatively as suspect. Histology confirmed this suspicion in 51 cases. 31 patients had no infiltrated lymph nodes. In 10 cases with two sonographically suspicious lymph nodes, the postoperative histology showed in 6 cases involved lymph nodes and in 4 cases the patients were node-negative. From 6 cases in which the preoperative sonography revealed 3 suspicious lymph nodes, the histology confirmed the positive findings in half of the cases.

There were 43 cases with sonographically more than three abnormal lymph nodes. The postoperative histology showed 27 patients with infiltrated lymph nodes and in 16 cases the axilla was not metastasized. Of the 333 patients with normal axillary ultrasound examination, the sonographic findings were confirmed in 278 cases. 2 patients were treated ex domo. In 53 cases, lymphatic metastasis was present. A closer examination of these 53 cases revealed that in 19 cases these were micrometastasis of the lymph nodes, and only 8 patients had axillary metastases > 3 mm. For all others, size of the lymph node metastasis was not described. Only 6 patients had more than 2 positive lymph nodes.

These data lead to the following diagnostic value of ultrasonography: sensitivity: 62%, specificity: 83%, positive predictive value: 61%, negative predictive value: 83%.

Correlation between the preoperative cytological or histological outcome of the fine needle aspiration biopsy or axillary lymph nodes and postoperative histologic lymph node involvement (statistical kappa coefficient of 0.5976, ASE of 0.1004, p = 0.0009).

In 104 cases, both an invasive investigation, by means of fine needle aspiration or biopsy of the suspicious lymph nodes, and an operational clarification of nodal status were performed. The cytologic or histologic findings were present in our database. The fine needle aspiration or biopsy of suspicious lymph nodes showed pathologic findings in 58 cases. The postoperative histology confirmed the finding in 44 cases. 14 patients were nodal-negative.

Of 28 cases with normal puncture of the lymph nodes, 13 cases histologically showed infiltrated lymph nodes and in 15 cases no metastasis was found.

There were 18 unclear preoperative cytological or histological findings. The diagnostic significance of axillary lymph node fine needle aspiration or biopsy of the suspect is as follows: sensitivity: 77%, specificity: 51%, positive predictive value: 75%, negative predictive value: 53%.

DISCUSSION

The lymph node status is the most important prognostic factor for the progression of breast cancer. For the assessment of axillary lymph node status, various methods are used. To determine the validity of the diagnostic methods, the important parameters are the sensitivity, specificity, positive predictive value and negative predictive value.

The aim of the study is to identify the diagnostic significance of axillary palpation, ultrasound and fine needle aspiration or biopsy. Each finding was classified as unsuspicious or suspicious of malignancy, and was then compared with the postoperative histologic findings.

Our study was based on a sample population of 586 patients. This number of patients is significantly higher than in most studies published to date. A similar study was conducted in 2012 by Rattay et al. (31), on a total cohort of 348 patients. They showed a sensitivity of axillary ultrasound of 56%, significantly lower than our sensitivity. The specificity of sonography was 90%, positive predictive value 78% and negative predictive value of 76%. The fine needle aspiration of suspicious lymph nodes showed a sensitivity of 76%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 48%. Because of the positive predictive value of fine needle aspiration of 100%, Rattay et al. have recommended avoiding the sentinel node biopsy in favor of immediate execution of the axillary dissection in case of pathological fine needle aspiration. In our study, the positive predictive value of this approach was 75%.

Another study by Park et al. (32), which also examined the axillary ultrasound and fine needle aspiration or biopsy of the suspicious lymph nodes, came to comparable results as our study in the ultrasound examination. However, the fine needle aspiration showed a sensitivity of only 39%, a specificity of 95%, a positive predictive value of 82% and a negative predictive value of 75%. Because of the low sensitivity of the fine needle aspiration, it was not sufficiently accurate in this study.

Comparing our results with the studies of Luparia et al. (33) or Hinson et al. (35), we observe a higher sensitivity in both ultrasound and fine needle aspiration of the axillary lymph nodes (72% for sonography and 88% for the fine needle aspiration, respectively 81% and 82%). However, the patient group was significantly smaller in
these two studies. The authors have recommended the ultrasound-guided biopsy of suspicious lymph nodes as an alternative to preneoadjuvant sentinel node biopsy.

In summary one can say that our results do not greatly differ from the results described in the other studies. Strikingly, however, is that in many studies the axillary fine-needle aspiration or biopsy did not increase the sensitivity of detection of nodal burden\(^\text{(32; 34; 35)}\). Our study showed an increase in sensitivity from 62% to 77% in the cases in which sonography was combined with a fine needle aspiration or biopsy of suspicious lymph nodes.

**Axillary palpation.**

The palpable axillary lymph nodes were often used as the sole criterion in deciding whether a sentinel node biopsy or axillary dissection is conducted, although it is known that the axillary palpation alone has a lower sensitivity than when it is combined with sonography \(^\text{(8)}\). Metastatic lymph nodes are often not palpable and reactive lymph nodes can be estimated as metastasized. Because of the high rates of false-negative and false-positive results, this method was supplemented by ultrasound examination of the axilla.

In our study, the sensitivity of palpation was 23%. The significance of the clinical examination of the axilla is very low. It is an insufficient method for the assessment of axillary lymph node involvement. Surprisingly, a high specificity of palpation of 98% was observed. Of the total of 297 cases with negative histology, axillary status could be evaluated correctly by palpation in 292 cases. With a sensitivity of 23% and a specificity of 98%, the results are in a similar range as the results of other studies\(^\text{(18)}\).

As described, the positive predictive values of palpation of the axilla are in the literature between 61% and 84% and the negative predictive values between 50% and 60%\(^\text{(13; 21; 22)}\). With a positive predictive value of 85% and a negative predictive value of 75%, the significance of the axillary palpation was slightly higher in our study.

**Axillary ultrasound.**

The axillary ultrasound is currently performed additively to mammography and sentinel node biopsy in the diagnosis of breast cancer and lymph node involvement. In our study, in 62% of the cases with preoperatively suspicious lymph node status, the suspicion was confirmed histologically. Out of these 62%, sonographic examination showed one suspicious lymph node in 37.8% of the cases, in 4.2% two suspicious lymph nodes, 2.1% three lymph nodes and in % multiple lymph nodes. 83% of patients with negative lymph nodes were unsuspicious in the preoperative ultrasound examination. With a sensitivity of 62% and a specificity of 83%, the axillary ultrasound showed itself in our evaluation to be moderately sensitive, but quite specific in the diagnosis of axillary lymph node involvement and is therefore well-suited for the preoperative diagnostic of the axilla.

The ultrasound examination of the axilla is usually between 66% and 82%, and the specificity between 44% and 97%\(^\text{(11)}\). From the lymph nodes evaluated during the ultrasound as suspicious, the final histology confirmed in 61% of cases a metastatic infiltration. For the sonographically negative lymph nodes, in 16% of the cases a positive histologic lymph node involvement was found. Because of its relatively low sensitivity, the axillary ultrasound is not appropriate to make an exact statement about the axillary lymph node involvement.

**Ultrasound-guided fine needle aspiration or biopsy of suspicious axillary lymph nodes.**

To optimize the diagnostic axillary, numerous studies have investigated the ultrasound-guided fine needle aspiration or biopsy of axillary lymph nodes. In the literature, the sensitivity of ultrasound-guided fine-needle aspiration or biopsy is usually between 50% and 80%\(^\text{(23-27)}\). In the meta-analysis of Houssami et al. (2011), the sensitivity of the method was 75% and the specificity 98%. 2397 fine needle aspirations or biopsies were performed in 4830 patients, with a median prevalence of lymph node metastasis of 47.2%\(^\text{(27)}\). However, the sensitivity was between 6% and 63% in another study by Leenders et al. (2012). Instead of recruiting only patients with sonographically suspicious lymph node involvement in which a fine needle aspiration or biopsy was performed, all patients with breast cancer were recruited, regardless of the clinical lymph node status\(^\text{(28)}\).

The performing of a fine-needle aspiration or biopsy in the preoperative ultrasoundography has increased the sensitivity of ultrasound examination from 62% to 77%. However, the number of patients who have benefited from the fine needle aspiration or biopsy is low. Only those cases were taken into account where a fine-needle aspiration or biopsy was technically possible and where sufficient material was obtained for a clear diagnosis.
Because of the 14 cases with false-positive result, the specificity in our study was only 51% and was significantly lower than in other studies. The positive fine-needle aspiration cytology has a positive predictive value of 75%. The negative findings are not sufficiently reliable due to the large number of false-negative results (negative predictive value 53%). A negative fine needle aspiration does not exclude an axillary metastasis.

Overview of the sensitivity of the different methods.
In the data of the present work, the sensitivity of palpation of the axilla was 23% and was significantly improved by the ultrasound examination, which increased sensitivity to 62%. Palpation of the axilla revealed 97 false-negative results from a total of 389 investigations. The axillary ultrasound showed in 53 cases false-negative findings, from a total of 331 investigations.

The sensitivity depends on the experience of the examiner. Our results are broadly consistent with the results in the existing literature and show significant benefits by application of ultrasound-guided fine-needle aspiration as part of the preoperative staging of the axilla. The sensitivity was improved by this method and was 77%. It represents a minimally invasive, cheap, easy and not time-consuming method for the evaluation of axillary lymph node involvement, which enables a significant increase in sensitivity.

This raises the question of whether the sensitivity of the axilla stagings could be optimized by other imaging methods. The palpation, mammography, ultrasonography and MRI were compared in a study by Valente et al. (2012). No advantages of MRI regarding the false-negative results were observed\(^\text{29}\). A study by Ueda et al. in 2008, which compared the PET-CT of the axilla with the axillary ultrasound, showed a similar diagnostic significance of both methods for the determination of axillary lymph node involvement\(^\text{30}\).

Another important question is whether an operative staging of clinically and sonographically unsuspicious axilla in the early stages of breast cancer is still necessary. The results of future prospective randomized trials SOUND and INSEMA are expected to clarify this point.

REFERENCES:
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