THE ADDITIONAL VALUE OF US TO MAMMOGRAPHY IN THE DIAGNOSIS OF BREAST CANCER

A prospective study

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Abstract

Purpose: To assess the additional value of ultrasonography (US) to mammography in the diagnosis of malignant breast tumors.

Material and Methods: Prospectively recorded final assessment categories for mammography and US were compared for 327 (228 palpable and 99 nonpalpable) consecutive malignant tumors confirmed at histology. The additional value of US was assessed for a subpopulation of 71 of these 327 malignancies after excluding mammographically conclusive malignant findings, ductal carcinomas in situ (DCIS), and invasive carcinomas presenting with suspicious microcalcifications, since there is no indication for performing US in these patients.

Results: A total of 267 (82%) of the 327 malignant tumors were correctly diagnosed on both imaging modalities. Mammography correctly diagnosed 41 cancers with false-negative US findings as compared with 11 true-positive US diagnoses of malignant tumors with false-negative findings on mammography (McNemar test p<0.001). US correctly diagnosed ("upgraded") 31 (10%) of the 327 malignant tumors with benign or indeterminate mammographic diagnoses. In the subpopulation, US upgraded 20 (42%) of 48 palpable and 10 (44%) of 23 nonpalpable malignant tumors.

Conclusion: The overall additional value of US to mammography in the diagnosis of breast cancer was rather limited in a population of mixed malignant tumors. Excluding cancers with mammographically conclusive diagnosis and suspicious microcalcifications as well as DCIS from analysis, US correctly upgraded more than 40% of palpable and nonpalpable malignant tumors.

Key words: Breast diseases, neoplasms; US studies; mammography; ultrasonography.

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Ultrasonography (US) has emerged as the most important adjunct to mammography in the diagnosis of breast tumors. Studies comparing the accuracy of mammography and US in patients with palpable malignancies have reported comparable diagnostic performance of the two imaging modalities, with a sensitivity of US in the range of 81 to 97% (3, 9, 17). The detection and characterization of small carcinomas on US is more difficult, the reported sensitivity of nonpalpable malignant tumors being in the range of 45 to 61% depending on the criteria used for a positive US diagnosis (3, 8, 10).

The primary goal of US in patients with a palpable mass is to confirm or exclude the presence of a localized abnormality and, if a lesion is present, to differentiate between a simple cyst and a tumor (5). Recent reports have shown that US also has the potential for differentiation between benign and malignant neoplasms (14, 16, 17). Thus, a further goal of US would be the "downgrading" (increasing the specificity in patients with benign
tumors) or “upgrading” (increasing the sensitivity in patients with cancer) of tumors with indeterminate findings on clinical and mammographic examination. There is in general no indication for performing US in patients with characteristic malignant features on mammography. From the literature, very little is known about the additional value of US as adjunct to mammography in patients presenting with mammographically indeterminate findings.

The aim of this prospective study was to evaluate the diagnostic contribution of US as adjunct to mammography in patients with malignant breast tumors, and specifically to assess the additional diagnostic gain in patients with mammographically indeterminate findings.

**Material and Methods**

Between January 1, 1988 and September 1, 1992 breast US was carried out on 2,985 patients at the Breast Imaging Center (BIC), Department of Radiology, Ulleval University Hospital. The indication for performing US was a palpable lump in 1,877 patients, a localized mammographic density in patients with normal or equivocal clinical findings in 747 patients, and a spectrum of other indications in the remaining 361 patients.

A total of 357 malignant breast tumors were diagnosed at histology. In cases of multifocal malignancies in 1 breast, only the dominant (largest) tumor was recorded and included in the analysis. Of the 357 malignant tumors, 2 patients had isolated lobular carcinoma in situ (LCIS) unassociated with any other malignant diagnosis. As LCIS is considered to have no characteristic imaging features and probably represents a high-risk marker rather than a malignant lesion (15), these 2 LCIS were regarded as incidental findings at biopsy and were excluded from further analysis. Of the remaining 355 malignant tumors, 27 were referred for problem-solving imaging with a complete mammographic examination performed at other institutions, and 1 patient underwent only US at the BIC. Thus, prospectively recorded final assessment categories for mammography and US were available for 327 malignant tumors. The mean age of these patients was 64 years (range 28–92 years). A total of 228 (70%) tumors were palpable and 99 (30%) tumors were nonpalpable. The histologic diagnoses of the 327 malignant tumors are summarized in Table 1.

Mammography was carried out with state-of-the-art equipment (Senographe 600 T, General Electric). Three projections (cranio-caudal, lateral, and oblique views) were performed in most symptomatic patients, and spot compression and/or magnification views were obtained if indicated. Mammographic findings and the final assessment categories were prospectively recorded in the database of the BIC (12). The final assessment categories of the mammographic examination included four diagnostic groups: Normal/definitely benign, probably benign ("follow-up" recommended), indeterminate ("equivocal-suspicious"), and malignant.

US was performed with a 7.5 MHz hand-held, linear-array, real-time transducer (RT 2800, General Electric). The US examination was carried out by a radiologist who was familiar with the clinical and mammographic findings. No acoustic standoff pad was used. In general, only the quadrant of the breast with an abnormality found on clinical or mammographic examination was evaluated.

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<table>
<thead>
<tr>
<th>Pathologic diagnosis</th>
<th>US diagnosis Tumor</th>
<th></th>
<th>US diagnosis Nontumor</th>
<th>Total, n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant</td>
<td>Indeterminate</td>
<td>Benign</td>
<td>Indeterminate</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
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<td>35</td>
<td>6</td>
<td>1</td>
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<tr>
<td>Invasive lobular carcinoma</td>
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<td>4</td>
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<td>0</td>
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<tr>
<td>Ductal carcinoma in situ</td>
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<td>0</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
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<tr>
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<td>5</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Tubular carcinoma</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>Other carcinomas</td>
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<td>0</td>
</tr>
<tr>
<td>Non-carcinomas*</td>
<td>0</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>53</td>
<td>11</td>
<td>4</td>
</tr>
</tbody>
</table>

* Non-carcinomas: 2 non-Hodgkin lymphomas, 1 myeloma, 1 chronic lymphatic leukemia of intramammary lymph node.
Two-by-two table analysis with the prospectively recorded mammographic and US diagnoses of 327 malignant breast tumors

<table>
<thead>
<tr>
<th>Mammographic diagnosis</th>
<th>US diagnosis</th>
<th>Total, n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant tumor</td>
<td>Indeterminate tumor</td>
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<tr>
<td>Probably benign</td>
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</tr>
<tr>
<td>Benign</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>53</td>
</tr>
</tbody>
</table>

Results

Comparison of the mammographic and US diagnoses of the 327 malignant breast tumors is presented in Table 2. Grouping the indeterminate and malignant findings as positive diagnoses, 267 (82%) of the tumors were correctly diagnosed with both imaging modalities. Using this cut-off level for a positive test result, a true-positive mammographic diagnosis was made in 41 cases with false-negative diagnosis on US (Table 2), whereas US correctly diagnosed 11 tumors with false-negative diagnosis on mammography (McNemar test \( p<0.01 \)). A total of 31 tumors (10%) with benign or indeterminate diagnosis on mammography were conclusively diagnosed as malignant on US (Table 2).

Thirty-eight malignant neoplasms were not even recorded as tumors on US, including 15 ductal carcinomas in situ (DCIS) and 15 invasive ductal carcinomas (IDCs) (Table 1). Nine (1 palpable and 8 nonpalpable) of the 15 IDCs presented with suspicious microcalcifications on mammography. Two DCISs and 4 IDCs presenting with microcalcifications were not recorded as malignant on mammographic examination. Indeterminate mass (differentiation between cyst and tumor not possible) was diagnosed in 4 cases. The 6 patients with a nontumor diagnosis on US and a false-negative diagnosis on mammography (Table 2) included 2 palpable retropapillary tumors and 4 nonpalpable...
cancers, which were incidental findings on histology.

A mammographically conclusive malignant diagnosis was made in 250 (77%) of the 327 tumors (Table 2). Furthermore, 2 DCISs and 4 invasive carcinomas with microcalcifications did not have a conclusive malignant diagnosis on mammography. Excluding these 256 tumors from further analysis, a subpopulation of 71 tumors were included for the assessment of the additional role of US as adjunct to mammography. The correlation of clinical findings and US diagnoses of these 71 tumors is presented in Table 3. A total of 44 (92%) of the palpable and 15 (65%) of the nonpalpable tumors were diagnosed as a tumor on US (Table 3). If US is to have an impact on clinical decision making, then it is appropriate to compare the conclusive malignant US diagnoses with the benign or indeterminate mammographic findings. Using this concept, US correctly upgraded 20 (42%) of the 48 palpable and 10 (44%) of the 23 nonpalpable carcinomas presenting with benign or indeterminate findings on mammography (Table 3). Twelve (25%) of the 48 palpable and 9 (39%) of the 23 nonpalpable tumors in the subpopulation were diagnosed as benign tumor or nonneoplastic abnormality on US (Table 3).

Discussion

Mammography often gives a conclusive malignant diagnosis of breast cancer in patients presenting with malignant type microcalcifications or a spiculated mass. However, the mammographic diagnosis is occasionally false-negative, probably benign, or indeterminate in patients with dense breast parenchyma and noncalcified carcinomas manifesting as a round, oval, or lobulated mass. Upgrading on US in these cases means a malignant US diagnosis in patients with benign or indeterminate findings on mammography. The high degree of accuracy in the diagnosis of breast cancer is based on the triple diagnostic, including clinical examination, conventional breast imaging (mammography and US), and needle biopsy. Only patients in whom the results of all three examinations are benign can be observed, obviating the need for open biopsy (2). The result of the needle biopsy, usually fine-needle aspiration cytology (FNAC) in the Scandinavian countries, plays a central role for the decision to perform surgery in a patient with a breast mass. FNAC is, however, an operator-dependent test (4). The additional value of US to mammography in the diagnosis of breast carcinomas is to confirm the presence of malignancy when the other components of the triple diagnostic fail to reveal the true nature of the mass.

No prospective studies have evaluated the additional role of US after excluding mammographically conclusive malignant tumors from analysis, i.e. patients in whom there is no indication for performing US. In a retrospective study, US added valuable additional information to the diagnosis of malignancy with a profit of 10% in patients with cancers (18). One study reported a mammographic sensitivity of 59% (including "suspicious" and "highly suspicious" findings as positive diagnosis) or 72% (including also "benign-appearing" masses as positive findings), as compared with an ultrasonographic sensitivity of 86% and 87%, respectively, using the same criteria (11). Another study reported that US increased the certainty of malignancy over mammography alone in 71 of 125 (57%) malignant lesions (16). These studies can be criticized because US was not compared with high-quality mammography diagnostics, and a disturbing number of carcinomas were classified as mammographically negative or probably benign (6).

In the present prospective study, 250 (77%) had a conclusive malignant diagnosis on mammography, and the sensitivity of mammography was 94% (308 of 327 tumors correctly diagnosed) if indeterminate (suspicious) and malignant findings were grouped as a positive diagnosis (Table 2). Mammography was significantly better than US (McNemar test \(p<0.001\)) in the diagnosis of malignancy for the entire tumor population. A conclusive malignant diagnosis on US was made in 31 (10%) of the 327 tumors with a benign/probably benign or indeterminate mammographic finding. Excluding tumors with mammographically conclusive malignant diagnoses, DCISs and invasive carcinomas with microcalcifications from analysis, US correctly upgraded 20 (42%) of 48 palpable and 10 (44%) of 23 nonpalpable malignant breast tumors (Table 3). However, a total of 4 (8%) of the palpable and 8 (35%) of the nonpalpable malignancies were categorized as a "nonneoplastic abnormality" on US, i.e. a focal lesion that did not meet the criteria of a tumor (Table 3).

A comparison of studies dealing with the additional gain of US as adjunct to mammography is difficult, the problems including study populations, test interpretation bias, criteria for positive mammographic and US diagnoses, and interobserver variation. Masses with stellate or spiculated borders and masses containing suspicious microcalcifications do not require US evaluation (5). The real question is how accurate US is in the differentiation of the mammographically indeterminate mass (7). In daily practice, US should be
carried out with full knowledge of clinical and mammographic findings. Although care is taken to use strict criteria for the classification of US findings, knowledge of mammographic diagnosis can consciously or otherwise bias the interpretation of US. One of the most difficult problems is the lack of standardization of US findings and different criteria applied for a positive US diagnosis. Several studies have classified US findings as “positive” merely if a tumor has been detected. The intention of our classification was to characterize a tumor, and consequently we used more restrictive criteria for a positive US diagnosis (Table 2). Our mammographic assessment categories do not correspond to the final assessment categories of the American College of Radiology’s Breast Imaging Reporting and Data System (BI-RADS) (1, 6).

In conclusion, a moderate additional value of US to mammography was found in a large series of consecutive patients, with an upgrading (conclusive malignant US diagnosis) of 10% of all malignant tumors. Excluding patients in whom there was no indication for performing US, US correctly upgraded 42% of the palpable and 44% of the non-palpable malignancies.

REFERENCES


