Mammography and ultrasound usefulness for breast cancer diagnosis in elderly women with and without symptoms: our experience

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Aims and objectives

The risk of breast cancer increases with age Fig. 1 on page 3, thus more than 30% of breast cancers are diagnosed in women 70 years old or older [1]. Even though the American Cancer Society recommends that screening mammography should continue as long as a woman is in good health and is expected to live 10 more years or longer, the U.S. Preventive Service Task Force recently stated that the current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older [2].

The goals of treatment in old patients are typically different than in young patients. In most cases breast cancer in old, healthy women should be considered more as an inconvenience than a threat to their lives (in particular in the frequent cases of favorable molecular profile) [3]. Nonetheless, even in elderly patients, a significant percentage of tumors possess an aggressive biological phenotype, affecting relapse-free and overall survival [4]. The diagnosis of such a tumor in an old woman can be particularly critical, since many of these patients have comorbidities that result in loss of function potentially compromising their breast cancer care. Chemotherapy treatment of old patients with advanced disease is problematic, while surgery, radiation therapy and hormonal therapy have improved breast cancer care for the elderly, but require a diagnosis at an early stage to be useful [5]. Thus, for reasons different than in young women, and specifically to have the chance to use effective and less-aggressive therapies, achieving an early diagnosis is relevant even in old women.

In this clinical scenario, it is well known that screening mammography has sensitivity and specificity higher in old women than in young women [6].

The purpose of our work was to evaluate the usefulness of screening with mammography and ultrasound in elderly women, retrospectively assessing all the women aged 70 years or older who received a diagnosis of breast cancer in a six months' period in our Institute, comparing clinical features, histologic presentation, dimensions at mammography and ultrasound between patients with and without symptoms.
**Fig. 1:** The risk of breast cancer increases with age. Adapted from Howlader N, et al. (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda

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Methods and materials

This retrospective study was performed in a university referral hospital for breast diseases. All the women aged 70 years or older who received a diagnosis of breast cancer in the period from the 1\textsuperscript{st} January 2015 to the 30\textsuperscript{th} June 2015 in our Institute were included. The whole sample was splitted in two groups, one composed by symptomatic patients, the other by asymptomatic (screening) patients.

Mammography examinations were performed with digital systems (SD and 3DL, Giotto IMS, Bologna, Italy), and included cranio-caudal and medio-lateral oblique views of both breast. Ultrasound examinations were obtained using different systems (LogiQ E9, GE Healthcare, Little Chalfont, UK; MyLab Class C, Esaote, Firenze, Italy; iU22, Philips, Eindhoven, The Netherlands), all equipped with 7-15 MHz linear probes.

Clinical data, mammography and ultrasound examinations available were assessed by two radiologists with more than 10-years experience in breast imaging, in consensus, according to ACR BI-RADS lexicon, fifth edition. In all patients the presence or absence of symptoms (palpable mass, ulcerated lump, sore nodule, nipple discharge) was assessed. Histologic features of each cancer were considered. Readers assessed if the disease was unifocal, multifocal, multicentric or bilateral. The maximum diameter of the lesion of each patient was measured (of the greatest one in case of multifocal or multicentric disease), both on mammography and ultrasound examinations. Mammographic features were recorded: mass, asymmetry, architectural distortion, microcalcifications. Ultrasound features too were assessed: mass, ultrasound inhomogeneity.

The previously reported features (histologic features, unifocality, multifocality, multicentricity, bilaterality of disease and maximum diameter with both mammography and ultrasound) were compared between the group of symptomatic and asymptomatic patients. T-test and chi-square test were used; results were considered statistically significant if the p value was less than 0.05. Statistical analysis was performed with the software program MedCalc, v. 9.1.0.1.
Results

In the period from the 1\textsuperscript{st} January 2015 to the 30\textsuperscript{th} June 2015, 67 women aged 70 years or older with a newly diagnosed breast cancer were identified. The mean age of patients was 77.1 years (range 70 - 91 years). Of these patients, 28 were asymptomatic (41.8%, mean age 75.3 years), while 39 had symptoms (58.2%, mean age 78.3 years): 33 were affected by a palpable mass, 1 by an ulcerated lump, 3 by a sore nodule and 2 by a pathologic nipple discharge Fig. 2 on page 7.

The more frequent histological diagnosis was invasive ductal carcinoma (48/67, 71.6%), followed by invasive lobular carcinoma (9/67, 13.4%), in situ ductal carcinoma (3/67, 4.5%) and other, less frequent, histological subtypes. In detail, in asymptomatic patients, the histological diagnosis was: in 19 cases (67.9%) invasive ductal carcinoma, in 5 cases (17.9%) invasive lobular carcinoma, in 1 case (3.6%) mucinous carcinoma, in 3 cases (10.7%) in situ ductal carcinoma. In symptomatic patients, the histological diagnosis was: in 29 cases (74.4%) invasive ductal carcinoma, in 4 cases (10.3%) invasive lobular carcinoma, in 1 case ductal-lobular invasive carcinoma (2.6%), in 1 case (2.6%) mucinous carcinoma, in 1 case intraductal papillary carcinoma (2.6%), in 2 cases (5.1%) papillary carcinoma, in 1 case apocrinous invasive carcinoma (2.6%). The distribution of histological subtypes was not significantly different between asymptomatic and symptomatic patients (p=0.0791) Fig. 3 on page 7.

The disease was unifocal in 46/67 patients (68.7%), multifocal in 16/67 patients (23.9%) and multicentric in 5/67 patients (7.5%); cases of bilateral disease were not found. Among asymptomatic patients, 19/28 were affected by unifocal disease (67.9%), 7/28 by multifocal disease (25%) and 2/28 by multicentric disease (7.1%). Among symptomatic patients, 27/39 were affected by unifocal disease (69.2%), 9/39 by multifocal disease (23.1%) and 3 by multicentric disease (7.7%). The distribution of unifocal, multifocal and multicentric disease was not statistically different between asymptomatic and symptomatic patients (p=0.1991) Fig. 4 on page 8. The case of a patient 83 years old with a palpable lump (multifocal disease with node metastasis, IDC G3 pT2 N2a) is shown in Fig. 6 on page 8 Fig. 7 on page 9.

The mean diameter of breast cancers assessed with mammography was 20.3 mm. In symptomatic women it was 23.5 mm and in asymptomatic patients it was 16.3 mm (difference: 7.2 mm; 95% CI of the difference: 2.5 mm / 12 mm; p=0.0036). The mean diameter of breast cancers assessed with ultrasound was 19.8 mm. In symptomatic women it was 22.8 mm and in asymptomatic patients it was 14.9 mm (difference: 7.9 mm; 95% CI of the difference: 3.5 mm / 12.4 mm; p=0.0007) Fig. 5 on page 8.

With respect to mammography, it was not performed in 6 patients with symptoms and in 3 asymptomatic women, due to the clinical status. It was negative (false negative result) in 4 patients with symptoms and in 1 asymptomatic woman. The most frequent
presentation pattern of breast cancer was the presence of a mass, both in symptomatic (26/29 - 89.6%) and in asymptomatic (17/24 - 70.8%) patients. Parenchymal distortions were present in 3 symptomatic patients (3/29 - 10.3%) and in 2 asymptomatic patients (2/24 - 8.3%). In patients without symptoms 3 cases of breast cancer were identified as a microcalcifications cluster (3/24 - 12.5%), while 2 cases were identified as density asymmetries (2/24 - 8.3%); none of the cases of breast cancer in symptomatic patients was identified because of microcalcifications cluster or density asymmetries.

With respect to ultrasound, it was not available in 1 patient with symptoms and in 4 asymptomatic women. In 61 cases a mass was found (38/38 - 100% - cases of patients with symptoms and 23/24 - 95.8% - cases in patients without symptoms), in 1 (asymptomatic) patient an ultrasound inhomogeneity.
**Fig. 1:** The risk of breast cancer increases with age. Adapted from Howlader N, et al. (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda

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<table>
<thead>
<tr>
<th>Current Age</th>
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<th>20 Years</th>
<th>30 Years</th>
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<tbody>
<tr>
<td>30</td>
<td>0.44</td>
<td>1.87</td>
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<tr>
<td>40</td>
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<td>50</td>
<td>2.28</td>
<td>5.53</td>
<td>8.75</td>
</tr>
<tr>
<td>60</td>
<td>3.46</td>
<td>6.89</td>
<td>8.89</td>
</tr>
<tr>
<td>70</td>
<td>3.89</td>
<td>6.16</td>
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</tbody>
</table>

**Fig. 2:** Rate of symptoms. White: palpable mass, green: sore nodule, blue: nipple discharge, Yellow: ulcerated lump.

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**Fig. 3:** Histologic classification in women with and without symptoms.

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<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Symptomatic (39)</th>
<th>Asymptomatic (28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal cancer</td>
<td>29 (74.4%)</td>
<td>19 (67.9%)</td>
</tr>
<tr>
<td>Invasive lobular cancer</td>
<td>4 (10.3%)</td>
<td>5 (17.9%)</td>
</tr>
<tr>
<td>Ductal-lobular invasive cancer</td>
<td>1 (2.6%)</td>
<td>-</td>
</tr>
<tr>
<td>Mucinous cancer</td>
<td>1 (2.6%)</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Papillary cancer</td>
<td>2 (5.1%)</td>
<td>-</td>
</tr>
<tr>
<td>Invasive apocrine cancer</td>
<td>1 (2.6%)</td>
<td>-</td>
</tr>
<tr>
<td>In situ ductal carcinoma</td>
<td>-</td>
<td>3 (10.7%)</td>
</tr>
<tr>
<td>Intraductal papillary carcinoma</td>
<td>1 (2.6%)</td>
<td>-</td>
</tr>
</tbody>
</table>

**Fig. 4:** Unifocal, multifocal, multicentric and bilateral disease in women with and without symptoms.

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<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Symptomatic (39)</th>
<th>Asymptomatic (28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unifocal</td>
<td>27 (69.2%)</td>
<td>19 (67.9%)</td>
</tr>
<tr>
<td>Multifocal</td>
<td>9 (23.1%)</td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Multicentric</td>
<td>3 (7.7%)</td>
<td>2 (7.1%)</td>
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<tr>
<td>Bilateral</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Fig. 5:** Measures with mammography and ultrasound in women with and without symptoms.

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<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Symptomatic</th>
<th>Asymptomatic</th>
<th>All</th>
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<tbody>
<tr>
<td>Mammography</td>
<td>23.5 mm</td>
<td>16.3 mm</td>
<td>20.3 mm</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>22.8 mm</td>
<td>14.9 mm</td>
<td>19.8 mm</td>
</tr>
</tbody>
</table>
Fig. 6: Mammography examinations of a patient 83 years old with a palpable lump (multifocal disease with node metastasis, IDC G3 pT2 N2a)

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Fig. 7: Ultrasound examination of a patient 83 years old with a palpable lump (multifocal disease with node metastasis, IDC G3 pT2 N2a)

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Conclusion

In our experience, the mean diameter of breast cancers in symptomatic patients was superior than in screening patients, and the difference was statistically significant. Moreover, the mean diameter found in symptomatic patients, both with mammography and ultrasound, correspond to a T2 stage according to TNM, while the mean diameter found in screening patients correspond to a T1 stage. Thus, the difference found is not only statistically, but also clinically significant. This finding is concordant with previously published papers [5] [7] [8], and is crucial in elderly women, since early stage lesions are associated with improved prognosis and can often avoid chemotherapy: a great therapeutic advantage in a group of women with a very high rate of comorbidities [9] [10].

Screening women were 3 years younger than symptomatic ones, on average. Since we had not available reliable information about previous examinations, we cannot argue anything. However, it is interesting that screening patients, compared to symptomatic ones, could benefit of the diagnosis in advance.

The distribution of histological subtypes was not statistically different in the two groups. However, we found 3 in situ ductal carcinomas among screening patients (10.7%) and only 1 intraductal papillary carcinoma among symptomatic patients (2.6%): as it is already known [11], the detection rate of in situ carcinomas is higher when screening mammography is performed. Obviously, a higher rate of in situ breast cancers result in a reduction of systemic therapies.

Unexpectedly, the distribution of unifocal, multifocal and multicentric disease was comparable and non-statistically different between symptomatic and screening patients. However, it is known that the clinical and prognostic significance of multifocal and multicentric disease is not fully understood. Intuitively, it would seem that the presence of more than one synchronous unilateral tumor would portend a worse prognosis when compared with unifocal counterparts. However, while studies have consistently shown a correlation between multifocality and multicentricity and the rate and extent of lymph node metastases [12], the literature is divided on whether there is a corresponding impact on survival outcomes [13]. In the absence of compelling evidence to dictate otherwise, the convention according to the current TNM-staging guidelines has been to stage and treat multifocal and multicentric patients according to the diameter of the largest lesions, without taking other foci of disease into consideration, and according to the extent of lymph node involvement [14].

We had 4 false negative mammographic examinations in symptomatic patients, while only in 1 woman without symptoms mammographic examination was false negative: in all false negative cases, breast density was increased (BIRADS C or D) and accounted for the wrong diagnosis.
Our study has some **limitations**: mainly, it is retrospective, the sample size in relatively small, mammography or ultrasound were not available in all cases. Moreover, in our clinical activity ultrasound is performed always after mammography, thus its diagnostic performance is increased in our study.

In **conclusion**, in our experience screening with mammography and ultrasound in elderly women is useful, since it results in a diagnosis at an earlier stage and, as a consequence, it gives the chance to use effective and less-aggressive therapies, with positive effects on the quality (but possibly also on the quantity) of life.
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