Breast cancer in women under 35 years old: clinical, radiological, ultrasound and MRI findings correlated to pathological-biological factors

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Purpose

Although breast cancer in young women is a relatively uncommon condition (approximately 7% of all breast cancer are diagnosed before the age of 40 years, and less than 4% of female cases are diagnosed under the age of 35 [1]), there has been a dramatic increase in the number of breast cancers diagnosed in premenopausal women in many parts of the world [2].

The diagnosis of breast cancer in young women may be challenging because of: 1) baseline dense breast tissue (which can obscure the radiological features of early breast cancer), 2) lack of routine breast screening for these population, 3) shorter tumor doubling times, and 4) different and atypical tumor presentations compared with older women. [1-2]

For these reasons, breast imaging may be less reliable, and radiologists may have a lower index of suspicion, in this age group, all of which may contribute to a delay in diagnosis. [3-8]

Breast cancers in women under the age of 40 years tend to be larger (median tumour size 2 cm in young women vs. 1.5 cm in older women), more advanced at diagnosis (more likely to be lymph node positive) and more aggressive (less well differentiated) than breast cancer in older women. [9-10]

Furthermore, breast cancer in young women is often associated with a positive family history of breast and/or ovarian cancer and with risk gene mutations, particularly BRCA gene germ line mutations. [11-12]

Cancer in young women also has a higher mortality and shorter disease free survival than in older women, and is more likely to recur after treatment both locally and at distant sites. [13-14] Considering that screening mammography is not recommended for young women, most breast cancers are diagnosed by detection of a palpable mass. [15-16]

Recent advances in breast imaging technologies may contribute to early detection of breast cancer in young women. Even if the usefulness of mammography in women under 35 years old is controversial, mainly because of the great density of the glandular parenchyma and radio-sensitivity [15-22], digital mammography was shown to provide improved detection of breast cancers compared with conventional film screen mammography among women younger than age 50 years [23]. In fact, initial reports described how approximately 60% of breast cancer cases in younger women were not detected through mammograms. However, recent studies reported that mammography was able to detect as many as 90% of the breast cancer cases in women under 35 years old, despite 40-70% with dense parenchyma. This increase in sensitivity may be due to technical improvements in the mammographic equipment. [15-22]
On the other hand, *ultrasound* has been considered the method of choice for symptomatic young women. The higher percentage of glandular tissue and the presence of a palpable mass favor the sensitivity of this method. [24-26] Houssami et al. demonstrated that ultrasound has a significantly greater sensitivity than mammography (84 and 76% respectively) in symptomatic women who are 35 years old or younger. [27]

A combination of the two imaging tests, *mammography and ultrasound*, is therefore often used to maximize imaging accuracy. [28]

In addition, several prospective studies have shown that *breast magnetic resonance imaging (MRI)* can find breast cancers in young, high-risk women more frequently, at smaller sizes, and at earlier stages than does clinical examination, mammography, or breast ultrasound. [29-31] The American Cancer Society currently recommends breast MRI as an adjunct to screening mammography in women at markedly increased risk for breast cancer. [32] Moreover, MRI can play an important role in preoperative planning and some BIRADS MRI features can be used to predict breast cancer prognosis. [1]

The purpose of our study was to evaluate clinical and radiological findings of breast cancer in young women under 35 years old, the problems encountered in the diagnosis and to determine whether pathological and biological factors could be correlated.
Methods and Materials

We performed a retrospective review of a consecutive series of women under 35 years old with breast cancer, who were seen in our Institute between January 2009 and July 2012. A total of 47 women with breast cancer were identified.

For all these patients clinical characteristics, radiological features (mammography, ultrasound, MRI), pathological and biological factors were retrospectively reviewed.

Clinical evaluated data were age, presence of symptoms at diagnosis (asymptomatic, palpable mass and others) and family history of breast cancer (first relatives or no).

Mammography was performed with a FFDM unit (Lorad Selenia, Hologic, Bedford, MA). Breast Imaging Reporting and Data System (BI-RADS) classification was taken from the original report. Breast density grades were also taken from the original report and were determined according to BI-RADS.

Ultrasound examination was performed with dedicated high-resolution units (Technos MPX Esaote, Hitachi Logos Hi Vision or Esaote My Lab Twice) with linear array probes between 10-18 MHz. A radiologist with prior knowledge of clinical and/or mammographic features performed examination procedures. The findings were classified by the authors according to BI-RADS ultrasound categories.

MRI images were acquired with a 1.5 T MRI scanner (Achieva Intera, Philips) with a seven-channel dedicated breast coil. The dynamic study was performed with three-dimensional T1-weighted gradient recolled echo (GRE) acquisition in the axial plane (TR/TE: 5.18/2.52 ms; matrix 352 x 352; field of view 340 x 340 mm; slice thickness 1.8 mm; acquisition time less than 70 sec) obtained before and for five times after intravenous bolus injection of 0.2 ml/kg body weight Gd-BOPTA at a rate of 2 ml/sec, followed by 20 ml saline solution flush. Breast Imaging Reporting and Data System (BI-RADS) MRI classification was taken from the original report.

The histopathology was reported according to the WHO classification. The tumour grade (G) was evaluated according to Elston and Ellis. The estrogen receptor (ER) and the progesterone receptor (PgR) status, and the expression of Ki-67 were determined. HER2/neu was evaluated immunocytochemically.
Results

The mean age of patients at breast cancer diagnosis was 32.2 years (range 26-35 y).

Presence of symptoms at diagnosis (38/47 women were symptomatic at diagnosis [Fig.1-4]) and family history are shown in Table 1.

\[\text{Table 1.}\]

\begin{tabular}{|c|c|c|}
\hline
\multicolumn{2}{|c|}{Number of patients} & \% \\
\hline
\textbf{NO FAMILY HISTORY OF BREAST CANCER} & 15/47 & 31,9 \\
\hline
\textbf{FAMILY HISTORY OF BREAST CANCER} & 17/47 & 36,2 \\
\hline
First-degree relatives & 12/47 & 25,6 \\
Other relatives but no first-degree relatives & 5/47 & 10,6 \\
Maternal side only & 11/47 & 23,4 \\
Paternal side only & 4/47 & 8,5 \\
Both sides & 3/47 & 6,4 \\
Unknown & 15/47 & 31,9 \\
\hline
\textbf{PRESENCE OF SYMPTOMS AT DIAGNOSIS} & 38/47 & 80,9 \\
\hline
Palpable mass & 36/47 & 76,6 \\
Other symptoms & 2/47 & 4,3 \\
\textbf{ASYMPTOMATIC} & 9/47 & 19,1 \\
\hline
\end{tabular}

Fifty-one cancers were diagnosed in 47 patients. Breast cancer mean size was 23.5±16.8 mm.

37/47 patients had dense breasts, while 10/47 patient had no dense breasts.

Mammography detected 41/51 lesions (80.4%) and ultrasound 47/51 (92.2%). Considering the 41 mammographic lesions, 24/41 were masses with or without microcalcifications, while 8/41 were microcalcifications alone.
MRI detected all lesions, which were mainly mass-like lesions (41/51); only 10/51 were non-mass lesions.

The most frequent histological type was invasive ductal carcinoma (29/51) and CDIS was found in 5/47 (10.6%) women. Tumor characteristics at diagnosis are shown in Table 2,3.

**Table 2.**

<table>
<thead>
<tr>
<th>TUMOR TYPE</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infiltrating ductal carcinoma</td>
<td>29/51 (56.9%)</td>
</tr>
<tr>
<td>Infiltrating lobular carcinoma</td>
<td>1/51 (2%)</td>
</tr>
<tr>
<td>Infiltrating ductal+lobular carcinoma</td>
<td>1/51 (2%)</td>
</tr>
<tr>
<td>Infiltrating ductal carcinoma + DCIS</td>
<td>8/51 (15.7%)</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>5/51 (9.8%)</td>
</tr>
<tr>
<td>Others</td>
<td>7/51 (13.7%)</td>
</tr>
</tbody>
</table>

**TUMOR GRADE**

<table>
<thead>
<tr>
<th>NODE POSITIVE</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>22/51 (43.1%)</td>
</tr>
<tr>
<td>Yes</td>
<td>29/51 (56.9%)</td>
</tr>
</tbody>
</table>

**Table 3.**

<table>
<thead>
<tr>
<th></th>
<th>ER</th>
<th>PgR</th>
<th>Ki-67</th>
<th>Her2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>#25</td>
<td>&gt;25</td>
</tr>
<tr>
<td>Mammographic features</td>
<td>0-1</td>
<td>2-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Masses (24/41)</td>
<td>17</td>
<td>7</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Microcalcifications (8/41)</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
Luminal A (*ER*+ e/o *PgR*+ *HER2*-) phenotype cancers (24/51) were mainly mass at mammography and MRI.
Fig. 1: 26 years old woman with lump in the left breast: mammography shows a mass in the upper-outer quadrant

Fig. 2: 26 years old woman with lump in the left breast: mammography shows a mass in the upper-outer quadrant

Fig. 3: 26 years old woman with lump in the left breast: ultrasound confirms a mass in the upper-outer quadrant

**Fig. 4:** 26 years old woman with lump in the left breast: also MRI demonstrates the mass lesion in the upper-outer quadrant

Conclusion

In our study, the vast majority of patients under 35 years old still detected their tumors on self-examination, as reported in other studies [1-2]. The large median tumor size and the high proportion of patients with axillary node involvement reflect the shortcomings and/or the lack of current screening recommendations.

To implement breast cancer surveillance in young women could be helpful in earlier detection, even if symptoms are the most frequent presentation feature.

The retrospective nature of our study does not allow us to prove that earlier detection would have been achieved through screening. However, our results show that most breast cancers arising in women age 35 and younger are detectable using currently available imaging technologies.

Ultrasound can be considered the most appropriate initial imaging test for symptomatic young women, but mammography is useful to confirm suspicious findings, also considering the benefits due to the introduction of digital mammogram technology.

MRI still remains the most sensitive modality, useful for treatment planning, therapeutic options and eventually to predict breast cancer prognosis and not only for high risk women.
References


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