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Imaging diagnosis of young women with breast cancer

Melchor Sentís[1]

[1]Corporació Sanitària Parc Taulí, Sabadell (Barcelona), Spain.

Corresponding author:

Melchor Sentís, MD

Breast Radiology Department

UDIAT Centre Diagnòstic

Corporació Sanitària Parc Taulí,

Parc Taulí, S/N

08208-Sabadell (Barcelona). Spain

E-mail: msentis@tauli.cat

Phone: +34 93 723 10 10

Fax: +34 93 717 50 67

Introduction

Breast cancer in young women deserves special consideration as there are complex issues raised by a cancer diagnosis at a young age. Breast cancer in these women may present differently to breast cancer in older women and may be more difficult to diagnose. For women under the age of 40, there are also particular concerns regarding pregnancy, fertility and contraception, sexuality and body image, as well as familial and genetic issues.

Breast tumors in young women tend to be larger (median tumor size 2 cm in young women compared to 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 [1]. Also, breast cancer in young women has a higher mortality and shorter disease free survival than in older women, and is more likely to recur locally or at distant sites after treatment [2].

The diagnosis of breast cancer in young women has limitations in terms of recruitment of patients and how the imaging diagnostic technologies come to them. Basically, there are two large groups of patients: symptomatic patients, in whom the physical examination reveals positive findings, and patients included in high-risk groups who are following protocols for early diagnosis. Recommendations for both groups differ and often overlap one another or are complicated with the recommendations from patients enrolled in clinical studies. The low suspicion of malignancy in young women due to the lower prevalence of cancer and lack of patient stratification according to risk profiles often leads to delays in diagnosis or in the delivery of the most appropriate treatment strategies based on their individual characteristics. Overall, this fact contributes to the worse long-term outcomes observed in this patient group [3].

There are few studies evaluating this situation in depth. Recently, a prospective, multicenter cohort study including 220 young women with breast cancer reported that 80% of patients presented with a self-detected breast abnormality, and most of them

were diagnosed soon after they developed a sign/symptom. However, nearly 25% delayed seeking medical attention and experienced a delay in diagnosis after seeking medical attention [4].

Digital mammography

Young women have a higher breast parenchymal density than older women, making it more difficult to differentiate between tumors and normal breast tissue [5]. According to the results of a study by Harris et al. [6] to determine the appropriate indications for breast imaging in 625 women aged 13-34 years young women, those with indications different from a palpable mass or a suspected abscess, i.e. associated with a very low likelihood of any imaging abnormality, should be followed up clinically rather than be referred for imaging studies.

In recent years, digital mammography has established itself as the most appropriate technique for diagnosing breast cancer, and is gradually replacing analog mammography. In the context of population screening, digital mammography has demonstrated its superior performance by both the easier reading and the improvement in the quality and consistency of images, and is far superior in some situations such as in dense breasts. The Digital Mammographic Image Screening Trial demonstrated that digital mammography had a considerable advantage among women under 50 years of age, perimenopausal, or women with dense breasts [7].

In digital mammography, the process of image acquisition, display (both locally and remotely), and storage are separated, allowing optimization of each step and therefore providing substantial advantages. Transmitted radiation through the breast is absorbed by an electronic detector, a response which is faithful over a wide range of intensities. Once this information is recorded, it can be displayed by using computer image-processing techniques to allow modification of image brightness and contrast settings without the need for further exposure to radiation. The standardization of medical

image formats under the Digital Imaging and Communication in Medicine (DICOM) standard has universalized image quality criteria [8].

Digital mammography has a higher technological development than traditional mammography such as computer-aided diagnosis and detection (CAD) systems, tomosynthesis, telemammography, and an emerging field of future systems based upon administration of contrast and digital subtraction. These techniques are already available in the market and help assess objectively individual risk factors for breast cancer such as breast density [9].

The use of digital mammography in population programs improves detection rates, primarily because of improved contrast resolution and a higher sensitivity for detection of microcalcifications, without the need of increased exposure.

Breast ultrasound

Although mammography is the gold-standard for breast imaging, it is not an optimal screening tool, especially in cases of dense breast parenchyma. Breast ultrasound has not proven its value as a primary screening method for breast cancer, but it represents an additional diagnostic tool for the detection of benign and malignant breast lesions. Thus, this technique is the method of choice for differentiating solid from cystic lesions, for further characterizing mammographic findings and for better identification of palpable breast lesions. Houssami et al. [10] showed that ultrasound was more sensitive than mammography in evaluating breast masses in women younger than 45. Also, ultrasound has been demonstrated to be more sensitive than mammography for screening women with dense breasts, and hence, ultrasound may be particularly useful for surveillance of young women at high risk [11]. Morrow et al. [12] showed that when mammography and ultrasound were performed concomitantly, 37% of imaging studies performed for a palpable breast mass in young women had abnormal findings. Any

suspicious dominant breast mass should be biopsied, even if the imaging studies are negative.

Ultrasound has also a key role in guiding biopsy procedures and in studies to re-evaluate incidental findings on magnetic resonance imaging (MRI). Additionally, it is the method of choice for the initial evaluation of the axilla in patients with a diagnosis of carcinoma [13], and allows the initial characterization of symptomatic lesions in young women.

Current ultrasound-associated developments include the use of contrast media to enhance lesion detectability, Doppler examination and elastography. Additionally, there is a recently developed prototype scanner that allows evaluation of the whole breast and then treating the images obtained in an evaluation console [14].

Breast MRI

For women at increased risk of breast cancer, screening technologies other than mammography may also contribute to the earlier detection of breast cancer, particularly in women under the age of 40 in whom mammography is less sensitive. The American Cancer Society (ACS) guidelines for the early detection of breast cancer state that women at increased risk of breast cancer might benefit from additional screening strategies beyond those offered to women at average risk (i.e. mammography and physical examination), such as earlier initiation of screening, shorter screening intervals, or the addition of screening modalities, including ultrasound and MRI [15].

MRI is the most sensitive technique for the detection and characterization of malignant breast lesions. MRI has demonstrated its high sensitivity and moderate specificity in detecting both invasive carcinoma and carcinoma *in situ* not visible by other modalities, and has become the technique of choice for screening high-risk patients [16]. MRI detects more cancers in high-risk women than mammography, with a sensitivity of 80% compared with 33% for mammography [17].

MRI is now being used for surgical planning in the setting of a known breast cancer, both to evaluate the extent of the disease, and to detect multifocal, multicentric, and contralateral malignancies. Tumor diameter measured by MRI correlates more closely with histologic measurements compared with mammography and ultrasound [18]. MRI could be the preferred technique for the study and pre-treatment of detected lesions and the monitoring of patients in neoadjuvant chemotherapy. In all scenarios, due to its moderate specificity, MRI-guided biopsy methods are essential for proper characterization of lesions detected and only visible on MRI [19].

There are studies demonstrating the usefulness and impact of MRI in the management of local recurrence, the predictive value of MRI in differentiating between recurrence or secondary changes to treatment, and its ability to decrease recurrence rates when used as a method of radiation therapy planning [20].

Conclusions

Many high-risk women develop breast cancer before the age of 40. For these women, cancer risk is managed through vigilant surveillance, in hopes of identifying the disease at an early stage. Traditional surveillance methods for breast cancer include mammography, ultrasound and clinical breast examinations. While mammography is indicated for screening before and after diagnosis and for localization prior to guided biopsy, ultrasound is indicated for diagnosis and characterization of suspected lesions, especially in breasts with dense parenchyma, and for localization of lesions and guided biopsies. There is a need for other promising breast cancer screening techniques in women at high risk of breast cancer such as MRI. This need arises due to follow up after breast surgery when mammograms may be difficult to interpret. MRI may enable the distinction of tumour recurrence from the usual post-operative scarring. The use of MRI in young women with breast cancer has a considerable performance

despite the lack of evidence of improved survival or reduction in the staging of the lesions detected.

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References

1. Foxcroft LM, Evans EB, Porter AJ (2004) The diagnosis of breast cancer in women younger than 40. Breast 13:(4):297-306
2. Nixon AJ, Neuberg D, Hayes DF, Gelman R, Connolly JL, Schnitt S, et al. (1994) Relationship of patient age to pathologic features of the tumor and prognosis for patients with stage I or II breast cancer. J Clin Oncol 12:(5):888-94
3. Barber MD, Jack W, Dixon JM (2004) Diagnostic delay in breast cancer. Br J Surg 91:(1):49-53
4. Ruddy KJ, Gelber S, Tamimi R, Schapira L, Come S, Kereakoglow S, et al. (2009) Presentation of breast cancer in young women. J Clin Oncol (Meeting Abstracts) 27:(15S):6608
5. Di Nubila B, Cassano E, Urban LA, Fedele P, Abbate F, Maisonneuve P, et al. (2006) Radiological features and pathological-biological correlations in 348 women with breast cancer under 35 years old. Breast 15:(6):744-53
6. Harris VJ, Jackson VP (1989) Indications for breast imaging in women under age 35 years. Radiology 172:(2):445-8
7. Pisano ED, Gatsonis C, Hendrick E, Yaffe M, Baum JK, Acharyya S, et al. (2005) Diagnostic performance of digital versus film mammography for breast-cancer screening. N Engl J Med 353:(17):1773-83
8. Lynes J, Riha C (2004) Learning the fundamentals of ... DICOM. Biomed Instrum Technol 38:(1):35-8
9. Pisano ED, Yaffe MJ (2005) Digital mammography. Radiology 234:(2):353-62
10. Houssami N, Irwig L, Simpson JM, McKessar M, Blome S, Noakes J (2003) Sydney Breast Imaging Accuracy Study: Comparative sensitivity and specificity of mammography and sonography in young women with symptoms. AJR Am J Roentgenol 180:(4):935-40

11. Kolb TM, Lichy J, Newhouse JH (2002) Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology 225:(1):165-75

12. Morrow M, Wong S, Venta L (1998) The evaluation of breast masses in women younger than forty years of age. Surgery 124:(4):634-40; discussion 640-1

13. Swinson C, Ravichandran D, Nayagam M, Allen S (2009) Ultrasound and fine needle aspiration cytology of the axilla in the pre-operative identification of axillary nodal involvement in breast cancer. Eur J Surg Oncol 35:(11):1152-7

14. Athanasiou A, Tardivon A, Ollivier L, Thibault F, El Khoury C, Neuenschwander S (2009) How to optimize breast ultrasound. Eur J Radiol 69:(1):6-13

15. Smith RA, Saslow D, Sawyer KA, Burke W, Costanza ME, Evans WP, 3rd, et al. (2003) American Cancer Society guidelines for breast cancer screening: update 2003. CA Cancer J Clin 53:(3):141-69

16. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, et al. (2007) American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. CA Cancer J Clin 57:(2):75-89

17. Kriege M, Brekelmans CT, Obdeijn IM, Boetes C, Zonderland HM, Muller SH, et al. (2006) Factors affecting sensitivity and specificity of screening mammography and MRI in women with an inherited risk for breast cancer. Breast Cancer Res Treat 100:(1):109-19

18. Lehman CD, Gatsonis C, Kuhl CK, Hendrick RE, Pisano ED, Hanna L, et al. (2007) MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med 356:(13):1295-303

19. Kuhl CK, Schrading S, Bieling HB, Wardelmann E, Leutner CC, Koenig R, et al. (2007) MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. Lancet 370:(9586):485-92

20. Whipp E, Beresford M, Sawyer E, Halliwell M (2009) True Local Recurrence Rate in the Conserved Breast after Magnetic Resonance Imaging-Targeted Radiotherapy. Int J Radiat Oncol Biol Phys