Triple assessment is not necessary in most young women referred with breast symptoms

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ABSTRACT

INTRODUCTION A palpable lesion in the breast is usually subjected to triple assessment (clinical examination [CE], imaging and core biopsy [CB] or fine needle aspiration [FNA]) to minimise the risk of missing breast cancer. However, breast cancer is rare in young women, and triple assessment (especially CB) is invasive and expensive. Our aim was to see whether CB/FNA could be avoided in young women with benign findings on CE and imaging.

METHODS This study analysed data from a prospectively entered database on female patients aged under 25 years who attended a rapid diagnosis breast clinic over a 68-month period.

RESULTS Among 10,301 patients seen, 955 females (9.3%) were aged <25 years. The most common presenting complaint was a lump, followed by pain and nipple discharge. CE was normal or revealed benign findings in all except 15 patients, in whom it was indeterminate. Ultrasonography was performed in 692 patients (72%) and was normal ($n=289$) or benign ($n=382$) in all except 21 patients, in whom it was indeterminate. In six patients, both were indeterminate. A total of 317 patients (35%) had triple assessment: FNA in 106, CB in 239 and both in 9 cases. No cancers were diagnosed.

CONCLUSIONS It would appear safe to omit FNA/CB in patients aged under 25 years when clinical and ultrasonography findings are normal or benign. This approach would have avoided needle biopsies in all but 30 patients (3%) in the study.

KEYWORDS

Breast disease – Neoplasm – Fine needle biopsy – Large core needle biopsy

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The gold standard approach to assessing a patient presenting with a palpable breast lesion is triple assessment, which consist of clinical examination (CE), imaging (mammography, ultrasonography or both) and a core biopsy (CB) or fine needle aspiration (FNA). Triple assessment is used because it has the lowest risk of missing a breast cancer^{1,2} but it is expensive and invasive, and it may not be necessary in all females presenting to a breast clinic.

Increasing breast awareness has resulted in more and more women (especially young women) presenting to breast clinics for assessment for a real or perceived breast problem. Despite being the most common cancer in women with a lifetime risk of 1 in 8, breast cancer is still rare in those aged <25 years. Among 41,259 malignant breast neoplasms diagnosed in female patients in England in 2010, only 25 (0.06%) were in those aged under 25.³ We reviewed our experience with females in this age group presenting to a breast clinic to study the need for needle biopsies in this population.

Methods

We identified all female patients referred to a rapid diagnosis breast clinic over a 68-month period between May 2005 to December 2010, who were aged <25 years at the time of

attendance, from a prospectively entered database. The database was interrogated to gather details of presenting complaint, the assessment process and the outcome. CE, imaging and histology/cytology results were graded on a scale of 1–5 as per the recommendation of the UK National Health Service Breast Screening Programme (Table 1).⁴ All patients had a CE. Following this, some underwent ultrasonography. Mammography was not used in this age group. CB or FNA were carried out when considered necessary by the examining clinician or the radiologist performing the ultrasonography. CB was done under ultrasonography guidance and FNA was done either clinically or under ultrasonography guidance.

Patients were given the results of the CE and ultrasonography on the same day. FNA/CB findings were given 3–4 days later by telephone and/or letter. All patients with a benign diagnosis were discharged but when considered clinically necessary or on patient request, a follow-up appointment or surgical excision of the lesion was arranged.

Results

Among 10,301 patients seen during the study period, 955 were females aged <25 years at the time of attendance. The median age was 21 years (range: 8–24 years). Four

Table 1 Reporting categories of non-operative diagnostic procedures as used by the UK National Health Service Breast Screening Programme⁴

Clinical examination		Ultrasonography		Core biopsy		Fine needle aspiration	
P1	Normal	U1	Normal	B1	Normal	C1	Inadequate
P2	Benign	U2	Benign	B2	Benign	C2	Benign
P3	Uncertain	U3	Indeterminate, probably benign	B3	Uncertain	C3	Atypical, probably benign
P4	Suspicious	U4	Suspicious	B4	Suspicious	C4	Suspicious
P5	Malignant	U5	Highly suspicious of malignancy	B5	Malignant	C5	Malignant

patients (<1%) were aged <10 years, 45 (5%) were aged 10–14, 315 (33%) were aged 15–19 and 591 (62%) were aged 20–24. Patients were referred by general practitioners in the community either routinely ($n=748$, 78%) or urgently ($n=197$, 21%) and others ($n=10$, 1%) were referred by other specialties in the hospital such as the emergency department. The most common presenting complaint was a perceived lump ($n=762$, 80%), followed by pain ($n=184$, 19%), nipple discharge ($n=44$, 5%) and others ($n=55$, 6%). Some patients had multiple complaints such as pain and a lump.

Triple assessment results

Results of triple assessments are presented in Table 2. The CE was graded as normal or benign (P1 or P2) in 938 cases (98%) and indeterminate (P3) in 17 (2%). Two of these 17 patients only had skin lesions rather than breast lesions. Another 17 patients underwent needle tests following CE

without ultrasonography. These 17 patients and the two patients with indeterminate skin lesions are not discussed any further. In total, 692 patients (72%) had ultrasonography; this included all 15 patients with an indeterminate CE. Ultrasonography was normal or benign in all except 21 patients, in whom it was indeterminate (U3 in 20 and U4 in 1).

Six patients with an indeterminate CE (all P3) also had indeterminate ultrasonography (all U3); all had ultrasonography guided CB, which was normal (B1) in two and benign (B2) in four patients. Among the other nine P3 patients, ultrasonography was U1 in three and U2 in six patients; three patients had no biopsies, two had benign (C2) FNA and four had benign (B2) CB.

Among patients with abnormal ultrasonography but normal or benign clinical findings ($n=15$), one lesion was a cyst and the remaining 14 patients had a CB that was either normal (B1) or benign (B2) including the single U4 lesion, which was graded B2 on CB.

Table 2 Outcome of triple assessment

Mode of assessment	<i>n</i>
Clinical examination total	955 (100%)
P1	262 (27%)
P2	676 (71%)
P3	15 (2%)
Ultrasonography total	692 (72% of total)
U1	289 (42%)
U2	382 (55%)
U3	20 (3%)
U4	1 (0.1%)
Triple assessment total	317 (33% of total)
FNA total	88
C1	47 (53%)
C2	41 (47%)
CB total	221
B1	13 (6%)
B2	202 (91%)
B3	6 (3%)
FNA + CB total	8
B1 + C1	2
B1 + C3	1
B2 + C1	2
B2 + C2	3

FNA = fine needle aspiration; CB = core biopsy

Outcomes

The final diagnoses were fibroadenoma ($n=248$, 26%), mastalgia ($n=102$, 11%), breast cyst ($n=38$, 4%), fibrocystic and other non-specific benign breast changes ($n=171$, 18%), and normal breasts ($n=281$, 29%). The diagnoses in the remaining 115 patients (12%) ranged from skin lesions and breast asymmetry to sebaceous cysts and abscesses. No breast cancers were diagnosed.

Among the 955 patients, 848 (89%) were discharged following the visit, 52 (5%) had a follow-up visit arranged and 46 (5%) had the breast lesion excised surgically. Others were referred to other specialties such as plastic surgery, the genetics clinic or underwent non-breast related investigations. None were diagnosed with breast cancer at our institution within one year of the initial visit.

Discussion

Breast cancer is rare in those aged <25 years with an estimated annual age adjusted incidence of 5.2 cases per million.⁵ Despite this, increasing media attention on breast cancer and increasing breast awareness among young women (combined with possible unwillingness or lack of success in reassuring these females or their parents in primary care) may be reasons for a large number of young women being sent for specialist opinion.

There are national guidelines in the UK to assist in the referral process^{6,7} but this study reveals that 21% of these young female patients were referred urgently as suspected cancers (all had P1 or P2 on CE) and 29% had normal breasts. This suggests education at primary care level may reduce this problem. Being referred on the 'two-week wait' cancer pathway induces patient and parental anxiety, and places avoidable stress on the system as these patients have to be seen by the hospital as a priority.

Breast cancer, however, is still the most commonly diagnosed malignancy in young women and delay in diagnosis has been reported in this age group; the priority therefore remains that no cancers are missed.⁵ Triple assessment has been in clinical practice for over 30 years and it has proven its value in this regard (with sensitivity approaching 100%) but it is expensive and invasive. We wanted to address the question of whether it is safe to omit FNA or CB in young women when clinical and ultrasonography findings are either normal or benign.

The CE component of the triple assessment appears to have the least sensitivity in the diagnosis of carcinoma and the sensitivity decreases with decreasing age, presumably owing to more glandular rather than fatty breasts in younger women.⁸ On the other hand, over the years, advances in ultrasonography have improved the quality of imaging significantly, and sonography can now be used to accurately classify solid breast lesions as benign with a negative predictive value of 99.5% and a sensitivity of 98%.⁹

There are now also dedicated breast radiologists in most breast units in the UK and elsewhere who perform a large number of breast ultrasonography scans, which should improve its accuracy. In a large study of women aged <30 years, no malignancies were seen in 666 patients where the ultrasonography was reported as BI-RADS® (Breast Imaging Reporting and Data System; American College of Radiology, Reston, VA, US) category 1, 2 or 3.¹⁰ However, one should consider biopsy in a young woman who is known to have or at a high risk of carrying a mutation (owing to family history of such a mutation, or a strong family history of breast or ovarian carcinoma) that increases the risk of breast cancer such as *BRCA1*.

Although the risk is very small (one recent study estimates the risk of breast cancer in *BRCA1* mutation carriers aged 20–29 years at 8.7 per 1,000),¹¹ there are reports suggesting that cancers occurring in these women may exhibit benign ultrasonography features.¹² Similar caution may have to be exercised in those where the lump increases in size following an initial 'benign' assessment.

Although there were over 1,200 breast cancers diagnosed at our institution during the study period, none were found in patients aged <25 years and reviewing the reports on cancers diagnosed in those under the age of 25 suggests that a dual assessment (CE and ultrasonography) is unlikely to miss a cancer in this age group. The numbers of cancers were small in all studies owing to its rarity in young patients. The most common solid lump in this age group is a fibroadenoma. In one study, one case out of 357 ultrasonography diagnoses of fibroadenoma proved to be malignant on histology.¹⁵ However, on reviewing the imaging, the authors noted

that even that single case would have been classified as suspicious by today's standards.

In another study with 7 malignant breast neoplasms diagnosed in women aged 25 years and under during a 15-year period, 5 had ultrasonography and all 5 lesions were either indeterminate or malignant on ultrasonography.¹² In another study spanning 70 years in the same age group, 11 out of 12 patients diagnosed with breast cancer had at least 1 suspicious feature on clinical history, examination or imaging.⁵ Out of 3,334 cases of breast cancers seen in a UK general hospital over 17 years, only 1 patient who had bilateral breast cancer was aged <25 years; she had a genetic susceptibility to the disease.¹⁴

Conclusions

Limiting CB and/or FNA to only those patients with abnormal CE and/or ultrasonography would spare the discomfort and cost associated with a percutaneous needle biopsy in women aged under 25 years. Exceptions would include those patients with a genetic susceptibility to breast cancer.

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