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Diagnostic strategies in non-palpable breast lesions

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Abstract

The number of non-palpable breast lesions is growing. Needle-localised breast biopsy (NLBB) is the gold standard for evaluating these lesions. Cost-saving techniques and less invasive alternatives such as core-needle biopsy (LCNB) and fine-needle aspiration (FNA) have emerged. The aim of this study was to find out if the lesions of patients who were sent directly for surgery to undergo a NLBB differed from lesions of patients who were send for a non-operative procedure. Furthermore, if a benign result was obtained, we assessed the total and kind of subsequent diagnostic procedures that were undertaken. A retrospective study on 718 women with 749 non-palpable breast lesions was performed. In 58% of women with non-palpable breast lesion, a non-surgical procedure was chosen. Lesions sent directly for surgery were more frequently not visible on ultrasound (62%) and mainly consisted of micro-calcifications only (56%). In 45%, this primary surgical approach could have been avoided. If the non-operative procedure showed a non-malignant result, 41% of these women received an additional surgical diagnostic procedure. These figures obtained from routine daily practice show the importance of protocols in order to standardise diagnostic procedures and prevent unnecessary surgery.

Keywords: Breast; Non-palpable; FNA; Core; Biopsy; Microcalcifications; Ultrasound

1. Introduction

Screening by mammography in cases with a family history for breast cancer and nationwide screening programmes have led to an increase in the number of non-palpable breast lesions and therefore in the number of interventions required to further assess the abnormalities detected [1]. Needle-localised open breast biopsy (NLBB) is considered the gold standard procedure for the diagnosis of non-palpable breast lesions [2]. NLBB is an invasive procedure with high costs and for most of the patients a traumatic experience, sometimes with poor cosmetic results in cases of benign disease [3].

In the past, non-operative image-guided techniques such as fine-needle aspiration (FNA) and large-core needle biopsy (LCNB) have been advocated as alternatives to surgery in order to obtain an ultimate diagnosis. For guidance, ultrasound or stereotaxis are used. When stereotaxis is used for guidance, two systems are available. A system that can be placed on to a normal upright mammography unit (the so-called 'add on equipment') or specially constructed prone equipment to be used independently from a mammography unit. Compared with NLBB, image-guided FNA and LCNB have advantages. They are less invasive than surgery, do not deform the breast, cause minimal to no scarring on subsequent mammograms and can be performed quickly. Women who have image-guided diagnostic interventions may suffer less surgical procedures and have a lower cost of diagnosis [4]. However, these image-guided techniques also have some disadvantages compared with NLBB. Their main disadvantage is that they are probably less reliable compared with NLBB. This is certainly the case when ultrasound-guided FNA

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is used for the assessment of lesions consisting of microcalcifications only on mammography [5]. Stereotactic 14-gauge large-core needle biopsy also has recognised limitations in the assessment of lesions that consist of microcalcifications only [4,6]. Furthermore, it is unclear what the diagnostic strategies should be in cases when the LCNB or FNA reveals a benign lesion. The second disadvantage is the initial expense of the prone stereotactic equipment. Therefore, it is not widely available in Europe. Ultrasonography is available in every hospital, but the main disadvantage of sonographic guidance is that the lesion must be sonographically evident to undergo ultrasound-guided biopsy. Thus, ultrasound-guided diagnostic interventions may not be feasible for calcifications and small solid masses that are sonographically not visible [7]. The choice between the different diagnostic strategies, image-guided diagnostic intervention or NLBB is made depending on the image characteristics (including ultrasound), availability of equipment and experienced personnel. The aim of this study was to find out if lesions of patients who were sent directly for surgery differed from the lesions of patients who were sent for a non-operative procedure. If a benign result was obtained, we assessed the total and kind of subsequent diagnostic procedures. We present herein the results of 718 women with non-palpable lesions, diagnosed in a day-care setting in three Dutch hospitals.

2. Patients and methods

In this study, all patients were included with non-palpable lesions. All of these lesions were classified as non-benign (probably benign, suspect malignant and malignant). Patients were referred for an additional intervention procedure in order to get an ultimate diagnosis. We included all patients referred for such a procedure in a defined calendar period at three different hospitals in The Netherlands: The University Medical Centre, Nijmegen (UMCN), the Antoni van Leeuwenhoek Hospital, Amsterdam (AvL) and the University Medical Centre, Utrecht (UMCU). These three hospitals were chosen because of their different strategies and their large experience in diagnostic work-up for patients referred with non-palpable breast lesions. In these hospitals, there was no defined assessment protocol for non-palpable lesions. In the UMCN, both ultrasound and a stereotactic add-on device were available. In the AvL, only ultrasound was available, while in the UMCU, both ultrasound and a stereotactic prone table were available. During the study period of 1996–1999, only 7.5 MHz transducers were used. Patients were identified by means of the hospital registry. In all three hospitals, we used the central computer system of the hospital registration to obtain the records of all patients, and looked for patients who underwent a NLBB or an image-guided breast intervention. Because in the AvL a computerised data system was available after 1997, we decided to define a different calendar period for this institution (1997–1999), in order to prevent incorrect inclusion of patients. A total of 237 women were identified in the UMCN (January 1996–September 1999), 279 women in the AvL (January 1997–December 1999) and 202 (January 1996–December 1999) in the UMCU. These 718 women had 749 non-palpable mammographically-suspect lesions. We collected records of all radiological and pathological breast-examinations. The following data were abstracted: patient characteristics, imaging technique at first examination, mammographical lesion characteristics, ultrasound lesion characteristics, biopsy method (NLBB, FNA, LCNB), pathological lesion characteristics, therapeutic excision, imaging follow-up after diagnosis.

Firstly, we assessed what percentage of lesions a non-operative diagnostic procedure was performed for and we set out to study the characteristics of this group by comparing them with those who were sent immediately for NLBB. Secondly, we assessed the total number and kind of diagnostic procedures following the primary procedure for those cases that did not show malignancy. Data were administered and analysed using the Statistical Package for the Social Sciences 8.0 (SPSS Inc., Chicago, IL, USA).

3. Results

In Table 1, the characteristics of the patients ($n = 718$) and of the breast lesions ($n = 749$) are presented. The mean age of the patients was 54.7 years (range 21–85 years). Two hundred and eight (28%) lesions were screen-detected. Of all of the 749 lesions, 729 (97%) were examined by mammography: 223/729 (31%) showed microcalcifications only, 433/729 (59%) showed a mass (including densities, densities with microcalcifications and spiculated masses), and 56/729 (8%) were not visible by mammography (these lesions were detected with ultrasound). In 3% ($n = 20$), no mammography result was available. In these 20 lesions, mammography was performed in another hospital or in the Dutch national screening programme. These patients received no repeated mammography, only additional ultrasound was performed. The mean diameter of the lesions (according to the radiological examinations) was 13.9 mm. Malignancy was finally diagnosed in 367 (49%) lesions of which 100 (27%) were Ductal Carcinoma *In Situ* (DCIS) and 267 (73%) were invasive carcinoma.

To see which percentage of all of the non-palpable lesions would qualify for an ultrasound or stereotactic-guided procedure, we compared the mammography

with the ultrasonography results of the initial imaging (Table 2). Ultrasound was performed in 567 lesions. In 78% (442/567), the lesion was visible on ultrasound. Ultrasonography was not performed in 182 of the 749 (24%) lesions. Most of these cases (133/182 = 73%) showed only microcalcifications on mammography. However, in 20 cases out of 90 (22%) with microcalcifications only on mammography, where ultrasound was actually performed, a lesion was found. Mammographical masses were seen as a solid lesion on ultrasound in 319 out of 389 cases (82%). Thus, most of the non-palpable lesions could have been assessed primarily by a non-surgical procedure. One could emphasise that lesions that consist of microcalcifications only would be better assessed directly by NLBB, since a large-core needle procedure has a lower sensitivity in these types of lesions. There were 223 of these lesions. If all of these lesions had undergone ultrasound, we assume that 22% were visible (Table 2: 20 out of 90), leaving 174 lesions undetected. This assumption reveals that 174 lesions should be assessed primarily by NLBB.

To examine the characteristics of patients (lesions) that were sent directly for a NLBB, we compared the group of lesions sent directly for surgery with the group that were first approached by a non-operative procedure (Table 3). In the non-operative group of 433 lesions, 242 underwent FNA, 128 LCNB with ultrasound guidance and 63 a stereotactic-guided LCNB. The remaining 316 lesions were sent directly for surgery. Thus, 42% of all non-palpable lesions were removed directly by a surgeon and in these cases no prior image-guided diagnostic procedure was performed. This percentage was 37% in the UMCU (79/211), 51% in the UMCN (129/255) and 38% (108/283) in the AvL. These lesions that were directly operated upon showed more frequently on mammography microcalcifications only (56% versus 11% in the non-operative group) and also more frequently, lesions that were not sonographically evident

Table 1
Characteristics of the study population

	Total population	UMCU	UMCN	AvL
Number of patients	718	202	237	279
Number of lesions	749	211	255	283
Mean age (range) (years)	54.7 (21–85)	52.8 (24–85)	54.8 (26–84)	55.9 (21–83)
Reason for examination (%)				
Screen-detected lesions	208 (28)	56 (27)	90 (35)	62 (22)
Family history of breast cancer	98 (13)	27 (13)	49 (19)	22 (8)
History of breast cancer	136 (18)	33 (16)	39 (15)	64 (23)
Other[a]	155 (21)	58 (27)	54 (21)	43 (15)
Unknown	152 (20)	37 (18)	23 (9)	92 (33)
Mammography (%)	729 (97)	208 (99)	245 (96)	276 (98)
Only microcalcifications	223 (31)	63 (30)	73 (30)	87 (32)
Density with microcalcifications	85 (12)	18 (9)	33 (13)	34 (12)
Density	252 (35)	72 (35)	81 (33)	99 (36)
Spiculated lesion	96 (13)	22 (11)	32 (13)	42 (15)
Focal asymmetry	3 (0.5)	1 (0.5)	2 (1)	0
Architectural distortion	12 (2)	1 (0.5)	9 (4)	2 (1)
Not visible	56 (8)	31 (15)	15 (6)	10 (4)
Unknown	2 (0.5)	0	0	2 (1)
Ultrasonography (%)				
Number (% of lesion per clinic)	567 (76)	135 (64)	202 (79)	230 (81)
Solid	410 (72)	110 (81)	128 (63)	172 (75)
Both solid and cystic	16 (3)	6 (4)	7 (3)	3 (1)
Not described	16 (3)	1 (1)	8 (4)	7 (3)
Not visible	125 (22)	18 (13)	59 (29)	48 (21)
Radiological diameter of lesion				
No. of cases known (%)	450 (60)	84 (40)	169 (66)	197 (70)
mm (S.D.)	13.9 (11)	10.9 (5)	16.3 (13)	13.0 (10)
Malignant lesions (histology)[b]	367 (49)	84 (40)	126 (49)	157 (55)
DCIS	100 (27)	26 (31)	33 (26)	41 (26)
Invasive carcinoma	267 (73)	58 (69)	93 (74)	116 (74)

S.D., standard deviation; DCIS, Ductal Carcinoma *In Situ*.

[a] Includes: palpable lesion somewhere else in the breast(s), follow-up for benign condition in the past, pain, hormone replacement therapy.

[b] Histology report from surgical specimen (gold standard).

(62% versus 4% in the non-operative group). However, a comparable proportion of these lesions were malignant in both groups (51% versus 47%). In the NLBB group, 21 high-risk lesions (ADH,LCIS) were found (7%). In the non-operative group, 16 lesions with suspect cytology, high-risk or malignant histology were not confirmed by the gold standard for various reasons (e.g. treatment in another hospital, brain metastasis, systemic therapy).

To assess the number and type of additional diagnostic procedures for lesions with a benign or non-conclusive pathology report after the primary diagnostic procedure we studied the strategies followed (Table 4). For NLBB, a total of 133 lesions with a benign or non-conclusive pathology report were noted, these numbers were 146 and 66 for FNA and LCNB ultrasound-guided, respectively. In six out of 133 (5%) primary NLBB procedures, the lesion was not removed. In 2 cases, a second NLBB was performed to remove the lesion and in 4 cases the lesion was left in place and the lesion was checked with follow-up by imaging. Primary non-malignant FNA required an additional invasive intervention in 58% of the cases (85/146). In a further 27% of cases (39/146), a mammographical follow-up strategy

Table 2
Comparison of ultrasound and mammographical images of 749 non-palpable lesions

Mammographical image	Ultrasound image					
	Solid	Both solid and cystic	Not described	Not visible	Ultrasound not performed	Total
Only microcalcifications	15 (7)		5 (2)	70 (31)	133 (60)	223 (100)
Density + microcalcifications	48 (56)	2 (2)	2 (2)	20 (24)	13 (15)	85 (100)
Density	198 (79)	12 (5)	4 (2)	17 (7)	21 (8)	252 (100)
Spiculated lesion	73 (76)		1 (1)	12 (13)	10 (10)	96 (100)
Focal asymmetry	1 (33)			2 (67)		3 (100)
Architectural distortion	8 (67)			3 (25)	1 (8)	12 (100)
Not visible	50 (89)	2 (4)	2 (4)		2 (4)	56 (100)
Unknown	1 (50)		1 (50)			2 (100)
Mammography data not available (not performed)	16 (80)		1 (5)	1 (5)	2 (10)	20 (100)
Total	410 (55)	16 (2)	16 (2)	125 (17)	182 (24)	749 (100)

Numbers in parentheses are percentages.

Table 3
Comparison of patients with a non-surgical approach (FNA and LCNB) with patients with a primary surgical diagnosis

	Non-surgical approach (FNA, LCNB) $n=433$	Primary NLBB $n=316$	Total
Mean age (years)	54.3	55.1	
Non-surgical approach			
Ultrasound-guided FNA	242 (56)		
Ultrasound-guided LCNB	128 (30)		
Stereotactic-guided LCNB	63 (15)		
Mammography performed	417 (96)	312 (99)	729
Microcalcifications only on mammography	47 (11)	176 (56)	223
All other lesions	370 (89)	136 (44)	506
Ultrasound performed	394 (91)	173 (55)	567
Not visible on ultrasound	17 (4)	108 (62)	125
Visible on ultrasound	377 (96)	65 (38)	442
Classification after imaging	433	316	749
Probably benign	166 (38)	87 (28)	253
Suspect malignant	235 (54)	202 (64)	437
Malignant	26 (6)	13 (4)	39
No classification	6 (1)	14 (4)	20
Malignant lesions (gold standard)	205 (47)	162 (51)	367
DCIS	30 (15)	70 (43)	100
Invasive carcinoma	175 (85)	92 (57)	267

FNA, fine-needle aspiration; DCIS, Ductal Carcinoma *In Situ*; LCNB, large-core needle biopsy; NLBB, needle-localised open breast biopsy. Numbers in parentheses are percentages.

Table 4
Number and type of diagnostic procedures after primary diagnosis, in cases of a non-conclusive or benign pathology report

Primary pathology report: non-conclusive or benign		Additional diagnostic procedure						Total of patients that needed more than one procedure
		NLBB	FNA	LCNB ultrasound	LCNB stereotactic	Follow-up imaging	Unknown	
Primary procedure	*n*							
NLBB	133	2[a] (2)				4[a] (3)		2 (2)
FNA	146	53 (36)	15 (10)	16 (11)	1 (1)	39 (27)	30 (21)	85 (58)
Non-conclusive	70	32 (46)	10 (14)	13 (19)	1 (1)	17 (24)	10 (14)	56 (80)
Benign	76	21 (28)	5 (7)	3 (4)		22 (29)	20 (26)	29 (38)
LCNB US-guided	66	33 (50)		1 (2)		14 (21)	12 (18)	34 (52)
Non-conclusive	5	4 (80)					1 (20)	4 (80)
Benign	61	29 (48)		1 (2)		14 (23)	11 (18)	30 (49)

NLBB, needle-localised open breast biopsy; FNA, fine-needle aspiration; LCNB US-guided, large-core needle biopsy ultrasound-guided.
Numbers in parentheses are percentages.
[a] Lesion not removed on primary NLBB.

was chosen. For ultrasound-guided LCNB, these percentages were 52 and 21%, respectively. During the calendar period of this study, all patients who underwent a stereotactic-guided LCNB also underwent a NLBB. The additional NLBB performed during this period was part of a study protocol to test the validity of LCNB [8]. Therefore, stereotactic-guided LCNB procedures are not included in Table 4.

4. Discussion

The diagnostic procedure of first choice was non-operative in 58% of all non-palpable breast lesions (433/749). Ultrasound-guidance was used in 370/433 lesions (85%) and stereotactic-guidance in 63/433 lesions (15%). Of all of the lesions, 42% were sent immediately for surgery to get an ultimate diagnosis (316/749). If we assume that 78% of lesions that consist of microcalcifications only are not detectable by ultrasound and, furthermore, that LCNB is not the method of first choice for these types of lesions, a total of 174 lesions should have been assessed directly by NLBB [4,6,9]. However, 316 lesions were assessed primarily by NLBB, resulting in 45% unnecessary NLBBs. In cases where a percutaneous biopsy reveals a benign lesion, surgery is prevented for these women. Furthermore, cases of malignancy percutaneous biopsy decrease the number of surgical procedures required and give significantly better sentinel node mapping compared with patients who underwent a prior surgical excision [4,10]. Yet, the lesions that went directly for surgery had characteristics that were different from the group that had a non-operative diagnostic procedure. They were more frequently not visible on ultrasound (62%) and mainly consisted of microcalcifications only (56%). A limitation of LCNB is its accuracy at predicting invasion when DCIS is found on core biopsy. A meta-analysis of LCNB showed that infiltrating carcinoma was found in 15% of the surgically removed areas diagnosed as DCIS on LCNB [11]. It is likely that these known limitations (besides the availability of dedicated equipment) directed the choice for performing a NLBB as the first choice procedure.

When the primary diagnostic procedure (NLBB, FNA and LCNB) showed no malignancy, the total number and type of additional diagnostic procedures differed per primary strategy. NLBB showed in 2% the need for an additional invasive intervention. The figures for FNA (58%) and ultrasound-guided LCNB (52%) were much higher. Up until now, these figures have received little attention.

Surgical NLBB was by far the most frequently performed additional diagnostic procedure. After primary non-malignant FNA, NLBB was performed in 62% of the cases (53/85) and after primary ultrasound-guided LCNB in 97% (33/34) of cases as an additional diagnostic procedure.

Surgery was performed in 50% (33/66) of the non-malignant lesions that were diagnosed with ultrasound-guided LCNB. This figure is high compared with the literature. A study on the use and cost-effectiveness of ultrasound-guided LCNB showed an additional surgical biopsy in 19% (18/95) of the lesions where no malignancy was found on LCNB [12]. The primary use of FNA avoided surgery in 64% (93/146) of the cases. In the literature this figure ranges from 49.5 to 77.3% [13,14].

The high percentage of additional diagnostic procedures in cases of a benign result after the initial non-operative diagnostic procedure needs attention. Our figures represent daily practice, the routine of diagnostic procedures in three outstanding clinics, and therefore do not resemble results obtained under ideal study circumstances. The advantage of performing non-operative

diagnostic procedures to get an ultimate diagnosis is diminished when in a large proportion of cases with a benign result, additional surgery is performed. Performing additional diagnostic surgery is aggravating for the women involved and is expensive. The initial high expense of the stereotactic equipment indicates a small cost-effective balance. Cost-saving procedures can therefore become cost-enlarging.

In The Netherlands, the most recent guidelines for the diagnosis of non-palpable breast lesions were published in 2000. Our study results reflect the period (1996–1999) before these new guidelines were implemented. In the Dutch guidelines for the screening and detection of breast cancer (2000), it is stated that non-palpable lesions should undergo pre-operative sampling in at least 70% of cases. The 58% non-surgical diagnostic procedures we found in this study implicate further implementation of image-guided sampling procedures. Furthermore, the amount of additional diagnostic surgery in cases of a benign result after FNA or LCNB should be reduced.

In conclusion, we found that in only 58% of women with non-palpable lesions was a non-surgical diagnostic procedure chosen. In cases of a non-malignant result, 41% (86/212) of these women received an additional surgical diagnostic procedure. Clear guidelines but, preferably, defined assessment protocols should standardise the diagnostic procedures to prevent unnecessary surgery.

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