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The Value of Clinical Breast Examination, Imaging, and Fine Needle Aspiration and the Challenge of Diagnosing Breast Cancer in a Low Resource Setting: A Hospital-Based Analytical Study in Yaounde

C. E. Ebong[1,2], N. J. D. Kemfang[1,3], E. Atenguena[1,3], F. Essiben[1,2], J. H. Fouedjio[1,2], A. Ngassam[4], S. Nyada[1,4], N. F. Mangala[5], A. N. Ngalame[6], J. T. Fouogue[7], S. Dohbit[1,8]

[1]Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon
[2]Central Hospital of Yaoundé, Yaoundé, Cameroon
[3]General Hospital of Yaoundé, Yaoundé, Cameroon
[4]Gynecological Endoscopic Surgery and Human Reproduction Teaching Hospital of Yaoundé, Yaoundé, Cameroon
[5]Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon
[6]Gyneco-Obstetric and Pediatric Hospital of Douala, Douala, Cameroon
[7]Faculty of Medicine and Pharmaceutical Sciences of the University of Dschang, Dschang, Cameroon
[8]Faculty of Health Sciences, University of Buea, Buea, Cameroon
Email: cliford.ebong@fmsb-uy1.cm

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Abstract

Background: Breast cancer is the most common cancer in the world, as well as in Cameroon, where it represents about 20.1% of all cancers recorded in 2020. The number of pathologists in the country is as few as seven for a population of about 26 million. The diagnostic performances of diagnostic modalities other than histology—clinical breast examination (CBE), imaging and fine needle aspiration and cytology (FNA)—in our context are not known. **Study Objectives:** Our objectives were to estimate the proportions of cases managed with mammography, breast ultrasound and FNA and to estimate the sensitivity, specificity, positive and negative predictive values, and accuracy of CBE, mammography, breast ultrasound and FNA; using histology as reference. **Study Methodology:** The study was cross-sectional and analytical, and was carried out at the Yaoundé General Hospital. It lasted twelve months, April 2015 through March 2016 and covered the period January 2010 to February 2016. Using histology as reference, we calculated measures of diagnostic accuracy for all four modalities using the statistical methods of Galen and Gambino. **Results:** We recruited 107 cases, 105 females (98.1%) and 02 males. We had 112 breast lumps, 106 malignant (94.6%) and 6 benign. The mean

lump size was 61.1 mm. The most frequently used diagnostic tool after CBE was FNA (49.1%), while the diagnostic accuracies were 76.8%, 79.1%, 82.9%, and 82.0% for CBE, breast US, mammography and FNA. **Conclusion:** The four baseline diagnostic modalities for breast cancer are used sub-optimally and FNA appears to be the most commonly used in our setting after CBE. We recommend that FNA should be considered for diagnosis as appropriate but a negative result should not stop the quest for histological elimination of presence of malignancy.

Keywords

Breast Cancer, Lump, Clinical Breast Examination, Breast Ultrasound, Mammography, Fine Needle Aspiration, Accuracy, Cameroon

1. Background and Rationale

Breast cancer is the most common cancer in the world, with over 2 million new cases in 2020 [1]. This is also the case in Cameroon, where it represents about 20.1% of all cancers recorded in 2020, with about 4170 new cases [1] [2]. As with other cancers, early diagnosis and prompt management are strong determinants of a better prognosis.

The diagnosis of breast cancer is classically based on the triplet: clinical breast examination (CBE), imaging (breast ultrasound and mammography) and pathology (cytology and histology) [3]. A common approach to clinically and/or radiologically suspicious breast masses, in our context, is to do a fine needle aspiration and cytological analysis (FNA). The reported specificity of FNA is about 97% and may reach 100% when FNA is in agreement with clinical assessment and imaging [3] [4]. Its reported accuracy is as high as 76% to 96% [5] [6]. Consequently, a lesion positive for malignancy on FNA may be managed as such, especially if this is concordant with the initial assessment. In such cases and if indicated, commonly, oncological surgery would be done (like tumorectomy and radical mastectomy), and the material sent for detailed study to help determine further management (histological type and grade, stage, surgical margins, and immunohistochemistry).

When FNA is discordant with initial assessment, a biopsy is done in many centers for histological analysis prior to treatment. This is because of the relative simplicity and safety of FNA cytology when compared to core or excision biopsies [5]. This approach, however, requires that the FNA and cytology have adequate accuracy. FNA and cytology require a high level of skill and this determines their accuracy. Unfortunately, we found no studies done to determine the accuracy of FNA in the diagnosis of breast cancer in our setting.

The contribution of the other diagnostic modalities: CBE and imaging, to the process of rational decision making for management is also of paramount importance. A well-done CBE would be exact (accurate result), with respect to the diagnosis of malignancy, in about 75% of cases of breast lump [3]. Mammogra-

phy has a reported sensitivity of 70% - 97% for breast cancer and may reveal infraclinical lesions (microcalcifications) [3] [7]. Its reported specificity, however, is relatively modest (64.5%) [8]. A meta-analysis of studies done to evaluate the sensitivity of breast ultrasound in the diagnosis of breast malignancy reported a sensitivity of 89.2% [9]. Meanwhile, for women aged below 45 years, the sensitivity of breast ultrasound is reported to be about 13.1% higher than that of mammography [10]. Data about the value of all these diagnostic modalities were lacking in our setting.

Histology, the "Gold standard" for the diagnosis of breast lumps, is based on the study of a tissue specimen for analysis of both architectural and cytological patterns [11]. The specificity and positive predictive value of core biopsy may be as high as 100% [11]. However, false negative rates may be as high as 6.1% (1.7%, 8.9% and 13% for ultrasound-guided, stereotactic-guided and clinically guided procedures respectively) [12].

There are about 25,000 new cases of cancer in Cameroon each year, 80% diagnosed by histology, 10% by cytology, and 10% clinically. The estimated availability of pathologists in 2016 was 0.28/1 million inhabitants [13], that is about seven for a population of 26 million. These pathologists are mostly available in big cities, with most health districts—even those in which some oncologic surgery is done—having no pathologist [14]. The cost of pathological analysis and the challenges of transportation of biopsies, especially for semi-urban and rural health districts, and health areas within them, is a major deterrent to pathological diagnosis. To alleviate this situation, even telepathology has been considered [14].

In this context—where it is not always possible to perform "true cut" and incisional biopsies prior to surgical and other management of breast lumps—there is a real need to evaluate the diagnostic performance of the other more available modalities of diagnosis, especially considering that they generally tend to be operator and equipment dependent.

2. Study Goal and Objectives

General objective: to assess the contribution of CBE, imaging and FNA cytology in the diagnosis of breast cancer in Yaoundé.

Specific objectives:

- Estimate proportion of cases managed with mammography, ultrasound and FNA.
- Estimate the specificity, sensitivity, positive and negative predictive values and accuracy of CBE, mammography, ultrasound and FNA cytology; using histology as reference, at the Yaoundé General Hospital.

3. Study Methodology

The study was cross-sectional and analytical, and was carried out at the Yaoundé general hospital, a reference in the management of breast cancer. It lasted twelve months, April 2015 through March 2016. All files available for patients with

breast lump managed at the Yaoundé general hospital during the period January 2010 to February 2016, and who had a definitive histological diagnosis were included.

Sampling was consecutive and exhaustive. The minimum sample size was 97 for a confidence level of 95%, margin of error 10% and population size of 10 million, using the online sample size calculator (available at: https://www.qualtrics.com/blog/calculating-sample-size/). The files of all cases of breast lump managed in the service were included and studied. Files that did not have a clear definitive histological diagnosis were excluded. Information from the files was used to fill a case report form with the following sections; patient identification, relevant past history, clinical evaluation, imaging report, cytology and histological diagnosis.

Lumps were considered suspicious for malignancy on CBE when at least one of the following features was present: ipsilateral lymphadenopathy (axilla, breast, supraclavicular), lump adherence, and local breast skin changes. For mammography and breast ultrasound, the Breast Imaging Reporting and Data System (BI-RADS) of the American College of Radiology (ACR), as reported by the radiologists, was used to classify lumps as malignant (ACR 4 - 5), or benign (ACR 1, 2 and 3) [15]. Lesions that were ACR 0 and ACR 6 were excluded in the analysis for imaging. All FNA cytology reports that confirmed malignancy or were suspicious for malignancy were considered positive for malignancy. Patients whose results showed an inadequate FNA sample were excluded.

A data sheet was created with CSPRO 6.1 and data were entered. Analyses were done using SPSS 20, aided by Excel 2010 software. Using the biopsy result as reference, the patients were classified as true positive, true negative, false positive and false negative with respect to their clinical, imaging or cytological diagnoses. The sensitivity, specificity, positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy were then calculated using the statistical methods of Galen and Gambino [16].

Ethical considerations were addressed by anonymizing all data collected from patient files. We presented the study protocol to the Yaoundé general hospital's management and obtained a written approval.

4. Results

We recruited 107 cases, 105 of them females (98.1%) and 02 males. There were 112 lumps, 106 of them malignant (94.6%) and 6 benign.

4.1. Baseline Characteristics of Patients

Table 1. Baseline characteristics and prevalence of some risk factors.

Characteristic	Category	Number	Proportion (%)
Age range	<40 years	37	35.2
	≥40 years	68	64.8

Continued

Sex	Female	105	98.1
	Male	2	1.9
Menopause	Yes	41	43.6
	No	53	56.4
	Not specified	11	/
History of breast disease (benign or cancer)	Yes	4	4.5
	No	84	95.5
	Not specified	19	/
Family history of breast cancer	Yes	4	4.3
	No	88	95.7
	Not specified	15	/

Female patient parity range was 0 to 10 with a mean of 3.57 ± 0.24 births. All males were aged above 40 years. The prevalence of some risk factors for breast cancer was: 43.6% for menopause, 4.5% for history of breast disease and 4.3% for family history of breast cancer.

4.2. Characteristics of Breast Lumps

Of the 112 lumps, 68 (61%) were in the left breast and 37% of lumps were in the upper outer quadrant.

Table 2. Clinical characteristics of lumps.

	Lumps with specified size	Mean lump size (mm)	Presence of other breast signs	Presence of lymphadenopathy
Right breast	42	59.17 ± 4.59	21	24
Left breast	59	62.71 ± 4.97	35	35
Total	101	61.1 ± 4.76	56 (50%)	59 (52.7%)

Lump size was not specified in 11 cases. One patient had a submandibular and 03 had supraclavicular lymph nodes in addition to axillary nodes. One or more "other breast signs" including; "peau d'orange", ulcer, retraction and fixed lump were present in 56 cases (50% of lumps).

4.3. Frequency of Use and Performance of Diagnostic Modalities in the Diagnosis of Breast Cancer

Table 3. Frequency of use of Clinical Breast Examination (CBE), mammography, breast ultrasound, and Fine Needle Aspiration (FNA).

Diagnostic test	Number of cases	Proportion (%)
CBE	112	100
Breast ultrasound	45	40.2

Continued

Mammography	50	44.5
FNA cytology	55	49.1

CBE criteria were applied to all 112 lumps. FNA was done in 49.1% of cases, mammography in 44.5% and breast ultrasound in 40.2%.

Table 4. Comparison of results of Clinical Breast Examination (CBE), ultrasound, mammography and Fine Needle Aspiration (FNA) with biopsy results.

Diagnostic modality	Opinion	Final classification of case (Biopsy)		Total
		Malignant lesion	Benign lesion	
CBE	Malignant	82	2	84
	Benign	24	4	28
Ultrasound	Malignant	31	3	34
	Benign	6	3	9
Mammography	Malignant	33	0	33
	Benign	7	1	8
FNA cytology	Malignant	46	0	46
	Benign	11	4	15

Of the 84 lesions considered malignant on CBE, 82 were confirmed on histology while 2 were benign (false positives). Of 28 lumps considered benign, 24 turned out to be malignancy after biopsy (false negatives).

Table 5. Diagnostic performance of CBE, ultrasound, mammography and FNA.

Modality	Sensitivity	Specificity	PPV	NPV	Accuracy
CBE	77.4%,	66.7%	97.6%	14.3%	76.8%
Breast US	83.8%,	50%	91.2%	33.3%	79.1%
Mammogram	82.5%	100%	100%	12.5%	82.9%
FNA	80.7%	100%	100%	26.7	82.0%

CBE: Clinical Breast Examination; FNA: Fine Needle Aspiration; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

5. Discussion

The profile of our patients reflects the general trend seen in breast cancer, which is essentially the woman's disease, and occurrence increases with age. As such, just close to 2% of our patients were males and 2/3 of cases were aged 40 years and above (Table 1). The world health organization estimates that only 0.5% - 1% of cases occur in males [17]. The majority of breast lesions (61%) were in the left breast and the preferred location in the breast for these lumps was the upper outer quadrant with 37% of lumps (Table 2). These results go in line with literature which reports about 40% - 50% of lesions in this area of the breast [18].

The mean lump size of 61.1 ± 4.76 mm reflects late presentation of patients. This is further supported by the high prevalence of lymphadenopathy (52.7%) and other breast signs (50.0%). Worthy of note, however, is that the study was done at a tertiary reference center, which contributes to this situation as patients usually have to transit through other levels of care, sometimes with undue delays in referral, as well as delays in relation to difficult financial access to care.

The diagnostic value of CBE is high firstly because it is applicable to all patients, as we did (**Table 3**). We used the presence of at least one objective element of suspicion (presence of local skin changes, lump adhesion, and/or ipsilateral lymph-adenopathy), firstly because many cases did not have a clear clinical diagnosis spelt out in their records, and secondly because many referred cases came with investigations already done that could influence the clinical diagnosis made. The sensitivity was high, that is, 77.4% (**Table 4**) and this is consistent with figures reported in the literature (88.9%) [3] [19]. A very low sensitivity (6%) was reported by one study, carried out in a high resource setting, in which CBE was used alongside magnetic resonance imaging for screening in a high-risk group [20]. Only cases that were diagnosed as positive for malignancy on CBE and negative on magnetic resonance imaging were considered in the study, hence the great difference in sensitivity for CBE compared to our finding. The NPV of CBE in our study was very low (14.3%). This was likely influenced by the low number of negative cases in our sample, but also probably because we did not include other aspects that increase clinical suspicion of malignancy like advanced age, menopausal status, history of breast disease, family history of breast cancer, increased lump size and irregular surface [3]. Even though these arguments are integrated in routine clinical practice for diagnosis, cutoff points are not clear. The high diagnostic accuracy of CBE that we observed (76.8%) is also consistent with literature (75%) [3]. However, diagnosis of cancer by CBE in our study may have been facilitated by late presentation, as reflected by the large mean lump size and high prevalence of lymphadenopathy (**Table 2**).

None of the paraclinical modalities of diagnosis studied achieved 50% usage in our sample (**Table 3**). Fine Needle Aspiration (FNA) cytology was found to be the most commonly used diagnostic modality (49.1%) outside CBE. The high accuracy of 82.0% observed is consistent with literature, which reports it at 76% - 96% [5] [6]. FNA and mammography shared an impressive 100% specificity and Positive Predictive Value (PPV) for diagnosis of malignancy (**Table 5**). Reported PPVs are 89% for Mammography [8] and 94.8% for FNA [21]. The high number of positive cases in the study sample probably contributed to an increase in our PPVs (**Table 4**).

Ultrasound and mammography were the most sensitive tools (83.8% and 82.5% respectively), with figures that agree with those reported in the literature, highlighting their value as screening tests. The reported sensitivity of mammography may be as high as 70% - 97% and that of breast ultrasound is 89.2% from a meta-analysis of studies in settings similar to ours [3] [9] [19]. This study,

however, did not include the assessment of infraclinical lesions where mammography is all-powerful.

The Negative Predictive values (NPVs) were low for all diagnostic modalities studied here (12.5% - 33.3%). The 26.7% NPV value of FNA was particularly of concern, highlighting the need to consider the possibility of malignancy even with negative FNA. However, the low number of negative cases for malignancy (5.4%) in the study sample may have contributed to the low NPVs [21] [22]. Even though figures of NPV reported earlier were relatively low, with the introduction of ultrasound guidance, more recent figures are as high as 95.4% and improve when the proportion of negative cases increases (in BI-RADS categories 2, 3, and 4A and in patients younger than 50 years) [21].

In this study, the reference test was biopsy and, when surgery was done, the detailed pathology report of the resected lesion was used to back up any core biopsy done earlier. This is because it is recognized that core biopsy may have a false negative rate as high as 6.1% [12]. However, we noted no discordance between core biopsy report and the detailed pathology report after lesion resection.

The main limits of this study stem from the fact that it was carried out at a tertiary referral level using results from different specialists working in their different health facilities. The patients were not subjected to doing all tests and the choices made by the treating physicians may have been influenced by some factors. The number of benign lesions was consequently low and this expectedly contributed to lower the negative predictive values.

6. Conclusions

The four baseline diagnostic modalities for breast cancer (CBE, ultrasound, mammography and FNA) are used sub-optimally and FNA appears to be the most commonly used in our setting after clinical examination.

When compared with biopsy results, the most sensitive modalities are ultrasound and mammography while the most accurate are mammography and FNA. However, the negative predictive value of FNA is low in our context.

We therefore recommend mammography and/or ultrasound, as appropriate with respect to breast density, after CBE for breast lumps, in our setting. FNA should be considered as appropriate but a negative result should not stop the quest to rule out the presence of malignancy by histology.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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