Combined assessment (aspiration cytology and mammography) of clinically suspicious breast masses

W. F. van Wyk, D. M. Dent, E. Anne Hacking, Genevieve Learmonth, R. E. Kottler, C. Anne Gudgeon, A. Tiltman

We examined the safety and utility of the combined assessment of aspiration cytology and mammography in 705 women who had clinically suspicious or malignant palpable breast masses. Histological assessment confirmed 176 benign and 529 malignant lesions. There were no incorrect (false positive) diagnoses made in the 176 benign masses when combined assessment was used (specificity 1,0; predictive value 0,86); in isolation, however, there was a false positive cytological diagnosis ('papillary carcinoma') and 3 false positive mammographic diagnoses. Benign disease (false negative) was incorrectly diagnosed by combined assessment in 4 of the 529 malignant masses (sensitivity 0,99; predictive value 0,98): cytological diagnoses were of fat necrosis (2) and benign cells on cytospin (1) and aspiration biopsy (1); mammographic diagnoses were of benign disease (2) and normality (2). Indeterminate ('atypical', 'suspicious') diagnoses were problematic and frequent (overall 223 (31,6%), malignant masses 137 (25,9%), benign masses 86 (48,9%); cytology 117 (16,6%), mammography 141 (20%). Thus, with the combined assessment of mammography and cytology in clinically suspicious breast masses, a decisive diagnosis was made in about two-thirds of cases allowing the safe commencement of therapy; the balance of patients required core or excision biopsy.

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Over the last two decades there has been a move away from an initial histological assessment of suspicious breast masses by open biopsy to their investigation by core biopsy,

Departments of Surgery, Radiotherapy, Anatomical Pathology (Cytopathology), Radiology and Pathology, Groote Schuur Hospital and University of Cape Town

W. F. van Wyk, F.C.S. (S.A.)

D. M. Dent, CH.M., F.R.C.S., F.C.S. (S.A.)

E. Anne Hacking, M.MED. (RAD.T.), F.F.RAD.(T.) (S.A.)

Genevieve Learmonth, F.F.PATH. (ANAT.)

R. E. Kottler, M.MED. (RAD.D.), F.R.C.R. (ENG.)

C. Anne Gudgeon, M.B. CH.B.

A. Tiltman, M.D., M.MED. (PATH.)

mammography and aspiration cytology. Numerous publications report the sensitivity, specificity and predictive values of these separate investigations, as well as those of clinical evaluation, usually finding the values of each to be high, but incomplete. In 1976 Kreuzer and Boquoi[1] suggested that clinical examination, fine-needle aspiration biopsy and mammography be combined as a triple assessment, having found an error rate of less than 1% in 602 breast masses so evaluated. While some investigators have found support for triple assessment,[2-6] and acted upon it, others have found the mammographic component unhelpful.[7,8] A recent recommendation, however, was that core or excision biopsy continue to be performed before commencement of therapy, as cytological assessment was insufficiently specific.[9] We have examined the accuracy of combined assessment in our practice.

Patients and methods

This study is a retrospective analysis of the results of investigations performed on 705 women over 30 years of age who presented to this unit between January 1984 and March 1989. Each had a breast mass, which was considered on clinical grounds to be malignant or suspicious of malignancy and each underwent both fine-needle aspiration biopsy and mammography. All had subsequent histological diagnoses made by mastectomy, local excision or Tru-Cut (Travenol) biopsy. Overall, 1 518 women with malignant and 4 986 with benign disease were managed during this period.

Clinical examination

All patients were examined by one of three surgical consultants with a specific interest in breast disease before investigations were performed, and the diagnosis of benign or suspicious/malignant entered on a structured form. The features that suggested malignancy were skin dimpling, oedema, nipple retraction, Paget's disease, regional adenopathy, hardness or shelving, or discrete masses in those patients over the age of 30 years.

Fine-needle aspiration biopsy

The masses were aspirated with a 22-gauge needle, the material smeared onto microscope slides and stained with a modified Papanicolaou technique. The slides were immediately examined by a cytotechnologist and, if acellular, aspiration was repeated. The cytopathological diagnoses were categorised as benign, indeterminate or malignant. The indeterminate category included equivocal or atypical lesions and those suspicious, but not diagnostic, of malignancy.

Mammography

In the initial part of the study standard craniocaudal and lateral views were taken with a Xerographic apparatus (Rank Xerox); this was later replaced with a Senograph film-screen system (CGR) Senographic, Paris). The results were reported as normal, benign, equivocal or malignant; we have combined the normal and benign diagnoses for convenience of analysis.

All cytological and mammographic investigations that produced reports discordant with the final histological findings were reviewed. Any altered diagnoses were not included in the initial analysis but are presented with possible reasons.

Results

On final histological examination 176 masses were found to be benign and 529 masses malignant.

Benign masses (specificity of combined assessment for malignancy)

The combined cytological and mammographic assessments correctly identified 88 (50%) of 176 benign masses, and were indeterminate or discordant in the remainder (Table I). There were no false positive diagnoses when these two investigations were taken in conjunction, and no patient had unnecessary cancer surgery for benign disease. The absolute specificity was 0,5 and the relative predictive value 0,86 (Table II). When cytological findings were analysed in isolation, an incorrect diagnosis of malignancy was made in 1 (0,6%) patient (Case 1, Table III): on cytological review the features remain those of papillary carcinoma (malignant papillary clusters), and inexplicably conflict with the benign (reviewed) histological features. Also, in isolation, 3 (1,7%) mammographic lesions were incorrectly identified as malignant and the features remain suggestive of malignancy on review.

Table I. The mammographic and cytological diagnoses in 176 histologically proven benign lesions

	Mammography			
	Benign	Indeterminate	Malignant	
Cytology				Total
Benign	88	32	2	122
Indeterminate	40	12	1	53
Malignant	0	1	0	1
Total	128	45	3	176

Malignant masses (sensitivity of combined assessment for malignancy)

Combined assessment correctly identified 380 (71,8%) of masses as malignant, made an indeterminate or discordant diagnosis in 145 (27,4%), and missed malignancy in 4 (0,8%) patients (Table IV). The absolute sensitivity of combined assessment was thus 0,72, and the predictive value 0,96 (Table II). In isolation, correct cytological diagnoses were made in 455 (86%) cases, indeterminate diagnoses in 64 (12,1%); benign disease was incorrectly diagnosed in 10 (1,9%) cases (Table III): in 3 instances degenerate cells were seen in cytospins from cysts (review of the material remained unchanged in 2 patients, and missed papillary groups were detected in the 3rd), fat necrosis in 5 and benign cells in 3 instances (cytological review found that in 2 instances the material had been inadequate, and cells suspicious of carcinoma were found in 1). Correct mammographic diagnoses of malignancy were

Table II. Specificity, sensitivity and predictive values of cytological, mammographic and combined assessment

	Benign	Indeterminate	Malignant	Sensitivity		Predictive value	
				Absolute	Relative	Absolute	Relative
Malignant (529)							
Cytology	10	64	455	0,86	0,98	0,92	0,7
Mammography	7	96	426	0,81	0,99	0,95	0,64
Combined	4	149	380	0,72	0,99	0,96	0,98
Benign (176)							
Cytology	122	53	1	0,69	0,99	0,99	0,91
Mammography	128	45	3	0,73	0,98	0,99	0,92
Combined	88	88	0	0,5	1	1	0,86

Absolute calculations exclude indeterminate values and relative calculations include them; diagnostic specificity and predictive value were calculated: true positive tests/true + false positive tests; diagnostic sensitivity and predictive value were calculated: true negative tests/true negative + false negative tests.

Table III. The incorrect cytological and mammographic diagnoses with their reviewed and final histological diagnoses

Case	Age	Final histology	Clinical diagnosis	Cytology		Mammography	
				Initial	Reviewed	Initial	Reviewed
Benign masses							
1.	83	Epithelial hyperplasia	Malignant mass 2 cm	Papillary carcinoma	Ditto	Suspicious opacity	Ditto
2.	59	Granuloma	Malignant mass 2 cm	Inflammatory	Ditto	Malignant opacity	Ditto
3.	70	Intraduct papilloma	Malignant mass 2 cm	Benign	Ditto	Malignant opacity	Ditto
4.	75	Fibrous tissue	Malignant mass 5 cm	Benign	Ditto	Malignant stellate lesion	Ditto
Malignant masses							
5.	50	Lobular & ductal carcinoma *in situ*	Malignant mass 6 cm	Benign cytospin	Ditto	Benign	Suspicious
6.	88	Carcinoma NOS	Suspicious mass 3 cm	Benign (macrophages)	Ditto	Benign	Benign
7.	48	Phyllodes tumour malignant	Malignant mass 4 cm	Benign (fat necrosis)	Ditto	Benign	Suspicious
8.	37	Ductal carcinoma	Malignant mass 1 cm	Benign (fibro-adipose)	Ditto	Benign	Suspicious
9.	49	Ductal carcinoma	Malignant mass 4 cm	Benign cytospin	Ditto	Malignant calcific	Ditto
10.	57	Ductal carcinoma	Malignant mass 5 cm	Benign (fat necrosis)	Inadequate	Malignant opacity	Ditto
11.	83	Ductal carcinoma	Malignant mass 2 cm	Benign (fibroadipose)	Inadequate	Malignant opacity	Ditto
12.	72	Ductal carcinoma	Suspicious mass 3 cm	Benign (fat necrosis)	Ditto	Malignant stellate lesion	Ditto
13.	83	Papillary carcinoma *in situ*	Malignant mass 3 cm	Benign cytospin	Papillary groups	Malignant	Ditto
14.	52	Carcinoma NOS	Malignant mass 3 cm	Benign (fat necrosis)	Suspicious	Malignant stellate lesion	Ditto
15.	32	Carcinoma NOS	Malignant mass 4 cm	Malignant	Ditto	Benign density	Ditto
16.	35	Carcinoma NOS	Suspicious mass 3 cm	Malignant	Ditto	Fribrocystic changes	Ditto
17.	44	Ductal carcinoma *in situ*	Malignant mass 3 cm	Malignant	Ditto	Normal	Normal

NOS = not otherwise specified.

made in 426 (80,5%) patients, indeterminate diagnoses in a further 96 (18,1%) instances and the incorrect diagnosis of benign disease in 7 (1,3%), 3 of which were revised to 'suspicious' on review.

Table IV. The mammographic and cytological diagnoses in 529 histologically proven benign lesions

	Mammography			
	Benign	Indeterminate	Malignant	
Cytology				Total
Benign	4	1	5	10
Indeterminate	0	23	41	64
Malignant	3	72	380	455
Total	7	96	426	529

Overall, an accurate triple assessment (clinical, cytological and mammographic) was made in 468 (66,4%) instances. Indeterminate diagnoses were frequent: 223 (31,6%) patients overall, 86 (48,9%) benign masses, 137 (25,9%) malignant masses, 117 (16,6%) cytological instances and 141 (20%) mammographic instances. Both cytological and mammographic findings were incorrect in 4 (0,6%) instances.

Discussion

In patients with suspicious breast masses, the safety in proceeding to definitive cancer surgery on the results of combined assessment alone — without recourse to excision or core biopsy — relies on the specificity of the combination (i.e. no erroneous diagnosis of malignancy with benign lesions). We found our specificity to be complete, and no patient would have had inappropriate surgery for benign disease. We have thus abandoned open or core biopsy as a routine method of pre-operative diagnosis in suspected breast cancer. Others have evaluated triple assessment, and

have also adopted this approach.[1-6] Kreuzer and Boquoi[1] reported that they were able to reach a decisive pre-operative diagnosis with triple assessment in 40% of 602 cases, finding 1 false positive (duct papilloma) among 355 benign lesions. Hermansen *et al.*[2] found no false positive diagnoses among 115 lesions identified by triple assessment as benign, but placed 42 of these patients in an indeterminate ('suspect') group. Di Pietro *et al.*[5] found no false positive diagnoses in 346 benign masses. Others have evaluated each component of triple assessment separately, have emphasised the value of the cytological component and found no false positive diagnoses.[3,4] Certain authors have been disappointed with the mammographic component, finding it of questionable value,[7] or that it did not augment the clinical and cytological findings,[8] a view which we cannot support on the basis of our data.

An inherent problem in any analysis of a triple assessment is skewing of the data. The clinical component entails the problems of the requisite investigation of most masses in women over 30 years (with overdiagnosis of malignancy or the suspicion thereof, and subsequent low clinical sensitivity).

Unfortunately, a decisive combined assessment was only made in two-thirds of cases; the balance of 32% were indeterminate, and required either core or excision biopsy. This problem was more frequently found in benign (49%) than malignant disease (26%), and occurred despite our immediate reporting of the cytology assessment (and the possibility of repeating it), and the ability to have immediate magnified mammographic views of areas of interest if required. Others have found a significant number of indeterminate diagnoses using combined assessment: Kreuzer and Boquoi[1] had an overall indeterminate rate of 23% finding, as we did, that the problem occurred more with the benign (50%) than the malignant (14%) masses. Others have reported indeterminate combined assessment rates of 35%,[7] 36%,[2] 40%[6] and 41%.[5]

The broad indeterminate band of diagnoses might be refined and narrowed if a stratified approach were adopted, rather than a dichotomous one (benign or malignant) or one with three possibilities, including 'indeterminate', as we used. The Southampton group suggested such an approach:[4,10] they assessed each component of the combined assessment on a 5-point scale: –2 (definitely benign), –1 (probably benign), 0 (inconclusive), +1 (probably malignant), +2 (definitely malignant). Patients with scores between +4 and +6 of the triple assessment were treated with definitive surgery. They were thus able to identify 95% of cancers in a group of young women, where accurate diagnosis can be very difficult. The Nashville group proposed a stratified diagnostic approach to cytological analysis: they categorised their reports into four (benign, suspicious, probable and definite carcinoma), and found no false positives in 62 patients in the 'definite' category, and only 3 in 25 patients in the 'probable' category.[11]

We therefore recommend that women with palpable breast masses that are suspicious of malignancy undergo combined assessment; surgery may be undertaken with confidence and without recourse to core or excision biopsy if there are clinical, cytological and mammographic features of malignancy. In an environment where immediate cytological and mammographic reporting are available, these investigations may be repeated when inadequate, or additional magnified mammographic views may be obtained of suspicious areas during the same consultation. We suggest that core biopsy be performed for discrete masses under the following circumstances: (*i*) when the cytological or mammographic features are indeterminate; (*ii*) in patients with inoperable disease, for histological characterisation; and (*iii*) where the combined assessment is completely negative in a patient over 30 years old.

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