Evaluation of the Contralateral Breast

The Role of Biopsy at the Time of Treatment of Primary Breast Cancer

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Ninety-five women who underwent blind contralateral breast biopsy during surgical treatment of a known breast cancer primary were studied prospectively. All biopsies were performed between 1981 and 1989. Patients with palpable or mammographic abnormalities prompting the contralateral biopsy were excluded so that the study sample included only truly blind contralateral biopsies. Only two infiltrating carcinomas were found, resulting in a positive biopsy rate of 2.1% for invasive disease. Three additional biopsies showed only lobular carcinoma *in situ*, a finding that usually does not alter clinical management. One patient with a negative contralateral biopsy developed invasive carcinoma in that breast within 2 years of the biopsy. The authors were unable to identify any subgroup of patients at increased risk of a positive contralateral biopsy. These results suggest that blind biopsy of the contralateral breast performed at the time of the initial treatment of breast carcinoma is not an efficient method of cancer detection. Alternative management strategies are discussed.

A FUNDAMENTAL PRINCIPLE of cancer management is that early detection of malignancy leads to a better chance for successful treatment. Early detection of breast carcinoma has been aided by the identification of high-risk patient populations, which allows for close monitoring of these patients. The highest risk is in patients with a previous history of breast carcinoma; new carcinomas arise in the contralateral breast at an average rate of nearly 1% per year.[1] There is considerable debate as to the appropriate evaluation of patients with a history of breast cancer. In these patients the minimal evaluation of the contralateral breast clearly includes frequent mammography and physical examinations. Because of the highly reported incidence of synchronous breast carcinoma,[2–5] some surgeons have advocated including a blind biopsy in the standard evaluation of the contralateral breast at the time a primary breast carcinoma is diagnosed.

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A question not clearly addressed by the literature, however, is whether such patients, in the absence of any physical or mammographic evidence of malignancy, benefit from a truly blind biopsy of the contralateral breast.

We prospectively studied a series of 95 breast cancer patients treated from 1981 to 1989 whose contralateral breast showed no mammographic abnormality or evidence of malignancy upon physical examination at the time their primary breast carcinoma was diagnosed. These patients underwent blind biopsy of the contralateral breast. Of these 95 biopsies, five yielded positive findings. These included three cases of lobular carcinoma *in situ* (LCIS), and two cases of occult invasive cancer. This represents a 5.3% incidence of clinically occult contralateral breast disease, with a 2.1% incidence of clinically occult invasive malignancy. Of the patients whose blind biopsies were negative, one developed malignancy in the contralateral breast, presenting approximately 2 years after the initial diagnosis. These results suggest that blind biopsy of the contralateral breast at the time of initial management of breast carcinoma is not an effective method of cancer detection and does not warrant the increased morbidity involved in the procedure.

Materials and Methods

Patient Selection

There were surgeons at this institution who routinely performed blind biopsy of the contralateral breast at the time of surgical treatment of a primary breast carcinoma. Blind biopsies routinely performed on 95 patients treated from 1981 through 1989 are included in this study. All patients underwent a preoperative workup, including a

thorough physical examination and bilateral mammography. Patients included in this study had no clinical or mammographic evidence of malignancy in the contralateral breast.

Contralateral Biopsy Technique

The contralateral biopsy was obtained from either the upper outer quadrant of the breast or from a location of mirror image to the primary disease. The percentage of total breast tissue excised varied according to overall breast size, with a maximum of 20% to 25% of the breast parenchyma removed. A minimum sample of 2 cm parenchymal breast tissue was obtained, whenever possible, in a cosmetically acceptable manner. In all cases, the contralateral biopsies were performed with a separate set of instruments.

Pathology

Specimens were sent for permanent section, and results reported using standard histologic categories. These categories included infiltrating ductal carcinoma, ductal carcinoma *in situ*, infiltrating lobular carcinoma, and LCIS.

Treatment and Follow-up

Treatment of the primary breast cancer in these 95 women was based on the standard principles of management. Patients were treated with either modified radical mastectomy or segmental mastectomy with axillary node dissection, depending on the stage of disease, patient preference, and surgeon's recommendation. All patients with stage II or greater disease received standard chemotherapy regimens in the adjuvant setting.

On completion of the study in January 1991, the clinical status of all participants was evaluated by direct physical examination, communication with the patient's primary physician, and chart review.

Results

The 95 patients included in this study ranged in age from 24 to 80 years, with a median age of 48. As indicated in Table 1, 20% of the study patients had a family history of breast cancer; however, none of the patients had a prior breast malignancy. A previous history of fibrocystic breast disease, by findings either on biopsy or physical examination, was present in 37% of the study population. Results of the pathologic examination of the primary tumors (Table 2) demonstrate that the study population is a representative sample of breast cancer patients in the United States, with invasive carcinomas of approximately 75% ductal and 18% lobular histologies.[6] Of the contralateral blind biopsies, 90 had totally benign histology, whereas five (5.3%) showed pathologic changes consistent with malignancy (Table 3). Three patients, however, showed LCIS, and only two patients showed occult invasive malignancy (2.1%). The primary carcinomas in four of these patients were infiltrating ductal carcinomas and one was infiltrating lobular carcinoma (Table 4).

Follow-up was performed on all study patients; the median follow-up was 106 months. The results are shown in Table 5. On completion of the study, 60% of the patients treated were alive with no evidence of disease. One patient who had previously had a negative blind breast biopsy developed a malignancy in the contralateral breast. This patient was initially treated with a modified radical mastectomy for invasive ductal carcinoma with extensive ductal carcinoma *in situ* (stage IIb) and was treated with postoperative chemotherapy. Nineteen months after treatment for her primary tumor, she presented with multiple foci of metastatic disease, including lung, liver, and bone. At this time she was also found to have a malignancy in her contralateral breast, which biopsy showed to be a ductal carcinoma *in situ* similar to her original pathology. This was believed, however, to be a new primary. The patient was treated with chemotherapy and radiation therapy and was lost to follow-up 2 years later.

TABLE 1. *Risk Factors of the Study Population*

Risk Factor	No. of Patients	Incidence (%)
Family history of breast cancer	19	20
Prior fibrocytstic disease	35	37
First pregnancy >30 yr of age	36*	38*

* Data not available for 59 of the 95 patients.

TABLE 2. *Pathologic Findings of the Primary Tumors*

Pathologic Finding	No. of Patients
Infiltrating ductal carcinoma	50
Ductal carcinoma *in situ*	9
Infiltrating ductal with ductal carcinoma *in situ*	22
Infiltrating lobular carcinoma	4
Lobular carcinoma *in situ*	8
Other	2

TABLE 3. *Pathologic Findings of Contralateral Biopsy Specimens*

Pathologic Finding	No. of Patients
Negative	90
Infiltrating ductal carcinoma	2
Lobular carcinoma *in situ*	3

Discussion

We found a 2% incidence of synchronous invasive breast cancer detected by blind breast biopsy, a yield too

TABLE 4. *Profiles of Patients With Positive Biopsy Findings*

Patient	Age	Primary Pathologic Findings	Biopsy Pathologic Findings	Positive Family History	Late First Pregnancy/ Nulliparous	History of Fibrocystic Disease
32	58	DC	DC	+	+	−
41	46	DC	LCIS	−	−	−
46	43	DC	DC	−	+	−
81	57	DC	LCIS	−	+	+
100	46	LC	LCIS	−	+	−

DC, infiltrating ductal carcinoma; LC, infiltrating lobular carcinoma; LCIS, lobular carcinoma *in situ*.

low to advocate blind biopsy as a screening technique, even in this high-risk population. Blind biopsy was negative, however, in one patient, who developed invasive breast cancer within 2 years.

Our results are similar to those found in other studies. In 1977, Urban et al.[2] reported results from 954 contralateral breast biopsies and found that 12.5% of these biopsies contained carcinoma. Fifty-five per cent of these were noninfiltrating carcinomas; the detected incidence of invasive contralateral carcinoma was 5.6%. Of these 954 cases, however, only 301 biopsies were truly blind, that is, performed in the absence of physical examination or mammographic evidence of malignancy. These biopsies were quite extensive, removing 20% to 25% of the breast parenchyma. In this group of 301 truly blind biopsies, five infiltrating and 18 noninfiltrating carcinomas were detected; an incidence of 7.6%, with only 1.7% of all biopsies showing invasive carcinoma. Wanebo et al.[4] evaluated 62 breast cancer patients with contralateral biopsy. Forty of these were blind biopsies, performed to include sampling of the upper outer quadrant and the medial segment of the subareolar duct complex when feasible. Of the patients with no abnormality upon physical examination or mammographic evidence of malignancy, 11% had positive contralateral biopsies, with 80% of these showing *in situ* disease. These results yielded a detection rate of approximately 2% invasive contralateral carcinoma. Two of 49 patients with negative contralateral biopsies developed subsequent invasive carcinomas in the breast on which a biopsy had been performed. Pressman[7] studied 85 patients who underwent contralateral breast biopsies and reported a yield of 12% positive results. All of the lesions detected in this study represented noninvasive disease.

Fenig et al.[8] reported a 3.5% yield of infiltrating carcinomas in 314 blind contralateral biopsies, with noninvasive lesions, mostly LCIS, bringing the total positive biopsy rate to 7.3%. In a series of 321 blind contralateral biopsies, Leis[9] found a 3.1% incidence of invasive carcinomas with noninvasive lesions, bringing the overall positive rate to 7.5%. Other series have found overall positive biopsy rates even more similar to our own. King et al.[10] performed blind contralateral biopsies on 109 patients and found one invasive carcinoma and four noninvasive lesions, for an overall positive biopsy rate of 4.5%, with fewer than 1% invasive lesions. Andersen and Muchardt[11] reported 170 blind contralateral biopsies, with findings of seven contralateral invasive carcinomas in 164 patients with primary ductal histology (4.3%). Three of six patients with primary lobular histology had LCIS on contralateral biopsy. A Mayo Clinic series[12] of 100 blind contralateral biopsies found a 2% rate of invasive carcinoma and no *in situ* lesions.

As summarized above, other large blind biopsy series similar to this study show only a 2% yield of invasive carcinoma, with noninvasive carcinomas, primarily LCIS, accounting for the remaining positive biopsies. Three of the positive contralateral biopsies in our series showed LCIS. This frequency is consistent with other blind biopsy series, in which most positive biopsies showed *in situ* lesions, most of which were LCIS,[2-4,7] and with the same frequency of incidental LCIS in biopsies for palpable or mammographic lesions.[13-15] We believe that, because of our present understanding of its biology and natural history, LCIS requires a different interpretation of contralateral blind biopsy results. It is currently believed that LCIS is a marker of increased risk of breast cancer rather than a precursor to future invasive cancer.[16] In most series, patients with LCIS have a 25% to 30% risk of developing invasive carcinoma over the subsequent 25 years.[6,17-20] One series with shorter follow-up found the risk to be 14%.[14] The mechanism of this increased risk is not known, but appears to be equally distributed over both breasts,

TABLE 5. *Follow-up at Completion of Study* (Median Follow-up: 106 Months)*

Status	No. of Patients
Alive, no evidence of disease	57
Alive with breast cancer	8
Deceased, cause related to breast cancer	11
Deceased, cause unknown	2
Lost to follow-up	17

* Median follow-up: 106 mo.

and is usually manifested as invasive ductal rather than lobular histology.[19,20]

Management options for patients with LCIS include either careful follow-up or bilateral prophylactic mastectomy. Prophylactic mastectomy generally is reserved for women with additional risk factors, such as those with breasts difficult to follow by physical examination and mammography or for those with extreme cancer phobia or significant family history for breast cancer. Most patients are managed with careful follow-up consisting of frequent physical examinations and mammograms, with the goal of detecting new carcinomas at an early and curable stage. This physical examination and mammographic follow-up is already included in the follow-up regimen for women with a diagnosis of invasive breast carcinoma. Thus, the finding of LCIS on a blind contralateral biopsy does not change the management of a patient already known to have invasive carcinoma, except in the few cases where bilateral mastectomy might be considered.

It is appropriate to ask whether there are subgroups of breast cancer patients with sufficient risk of bilateral disease to justify blind biopsy and perhaps result in a higher rate of positive biopsy findings. The highest incidence of multicentric breast malignancy has been reported for lobular carcinoma, with most studies resulting in an incidence of approximately 25%.[6,17] Baker and Kuhajda,[17] however, in a study of 86 patients, concluded that the diagnosis of invasive lobular carcinoma, in spite of its increased multicentricity and bilaterality, is not an indication for blind contralateral breast biopsy. They found that, although 11% of patients had simultaneous contralateral cancers detected by physical examination and mammogram, none were detected by blind biopsy. Of the remaining biopsy-negative patients, 7.8% later developed a contralateral carcinoma. In our series, only one of 12 patients (8.3%) with a lobular histology had a positive contralateral biopsy; this patient's contralateral biopsy showed LCIS (Table 4).

Patient age and stage of primary disease were not found to alter the rate of detection of synchronous contralateral breast cancer by blind biopsy. Pressman[3] reported results of contralateral biopsies in a selected population of 258 patients younger than 65 years of age with tumors smaller than 5 cm and no evidence of axillary metastases. Excluding 11 patients with clinically evident contralateral lesions, he found that 13% of biopsies were positive, but only 1.6% of the total represented invasive disease. Five patients with benign contralateral biopsies subsequently developed invasive carcinomas in the contralateral breast. Although these results are interpreted in support of blind contralateral biopsy in younger stage I patients, this data do not differ appreciably from other blind biopsy series.

In our own series, we were able to look separately at those patients with a positive family history of breast cancer, those with prior fibrocystic disease, and those with late or no childbearing. Only one of 19 patients with a positive family history had a positive blind contralateral biopsy. One of 35 patients with prior fibrocystic disease had a positive contralateral biopsy. Four of five patients with positive contralateral biopsies had had their first term pregnancy after the age of 30 or were nulliparous. This is fairly representative of our study sample, because nearly 60% of all women for whom childbearing data were available had had late or no first pregnancies. Thus, we are unable to identify subgroups of patients likely to benefit from mirror-image biopsy.

It is important to address the efficacy of screening programs in reducing the mortality rate from new or recurrent breast cancer. Few studies have directly addressed screening outcome in patients with previously diagnosed breast cancer. Haagensen et al.[19] used physical examinations at 4-month intervals for women with LCIS and proceeded with radical mastectomy for any invasive cancers detected. It was stated that 30 patients who developed invasive cancer during their follow-up for LCIS were alive and free of disease 1 to 24 years after treatment with radical mastectomy.[19] Outcome of careful follow-up for noninvasive breast cancers treated with wide excision only or wide excision plus radiation therapy will be obtained from the recently closed NSABP-B17 protocol. Screening programs have been shown to reduce breast cancer mortality rate in women with no prior history of breast cancer.[21–27] It seems reasonable to extrapolate this reduction in mortality rate to women with a prior history of breast cancer.

Since its first introduction by Urban et al.,[2] contralateral breast biopsy has been a controversial technique. Much of the confusion results from studies of this question that have included patients whose contralateral breast presents with mammographic or evidence upon physical examination suggesting the need for biopsy. These patients do not pose a dilemma, for they should undergo biopsy even if they were not known to have a primary carcinoma. Although all of the studies presented here clearly indicate the need for close follow-up of the contralateral breast, none of them, including this prospective study, offer support for blind contralateral breast biopsy at the time of initial treatment of a primary breast carcinoma.

Our recommendations for evaluation of patients with newly diagnosed breast cancer include careful bilateral physical examination and mammography before definitive surgical therapy with biopsy of any suspicious areas. We recommend initial postoperative physical examination and laboratory testing every 3 to 4 months, gradually increasing the examination interval to 6 and then to 12 months. Mammograms should be performed initially at 6- to 12-month intervals, then annually. Annual physical examinations, mammography, laboratory tests, chest x-rays, and bone scans, when appropriate, should continue for the rest of the woman's life.

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