Male Breast Cancer:

A Clinicopathologic Study of 97 Cases

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From 1949 through 1976, 97 men have been treated at Memorial Hospital for primary operable breast cancer. Seven per cent had intraductal carcinoma. Of the patients with invasive carcinoma 30% were pathologic stage I, 54% stage II, and 16% stage III. Fourty-six per cent had pathologically negative axillary lymph nodes. The most common type of tumor was infiltrating duct carcinoma. Fourty per cent of the patients had microscopic gynecomastia. None of the eight patients with intraductal or intracystic carcinoma died of cancer. Survival of the entire group of men with invasive carcinoma was 40% after ten years. The ten year survival for men with negative nodes was 79%, for men with positive nodes 11%. Comparison with a series of 304 women with breast cancer operated on at Memorial Hospital in 1960 revealed no difference with regard to incidence of positive axillary lymph nodes or stage of disease. There was, however, a significantly lower survival rate for men. This poorer prognosis was limited to those men with pathologically positive axillary nodes.

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CANCER OF THE MALE BREAST is an uncommon disease occurring 1% as often as cancer of the female breast.[8] Each year in the United States at least 600 new cases are diagnosed and 250 men die of the disease.[17] Holleb, Robbins, and others from Memorial Hospital as well as authors from other institutions have discussed the presenting symptoms, prognosis, patterns of metastases, treatment, and possible etiologies of this disease.[3–5,8,10,20,21] In order to identify those factors which influence survival and to determine the frequency of gynecomastia in this disease, we have analyzed the records of all men treated for breast cancer at Memorial Hospital from 1949 through 1976. From this group we selected for study only those men with operable disease whose initial treatment was at this hospital.

Materials and Methods

From 1949 to 1976, 97 men were treated at Memorial Hospital for primary operable carcinoma of the breast. Some of these patients had a biopsy performed elsewhere, but in all cases the initial definitive surgical treatment was at this institution. Patients with clinical evidence of distant metastases or supraclavicular lymph node involvement at the time of presentation have been excluded.

Pathologic specimens were reviewed and classified by one of us (PPR) without knowledge of the prior pathology report except that all patients were said to have had breast cancer. Material from all but 19 of the 97 patients was available for rereview. Slides for all 97 patients in the report had previously been reviewed at this institution at the time of initial treatment.

Assessment of the presence or absence of gynecomastia was based on the examination of samples of uninvolved breast tissue available for review. The number of slides or amount of tissue varied considerably among the cases. To be recorded as having gynecomastia it was necessary that there be multiple ducts with papillary epithelial hyperplasia with at least some stromal proliferation. Stromal proliferation alone was never the basis for a diagnosis of gynecomastia. These features were felt to be distinctive from senile atrophy.

The TNM staging was based on the size of the primary tumor as measured by the pathologist, and from either the clinical or pathological extent of axillary

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TABLE 1. *Operations Performed to Treat Primary Breast Cancer in Men*

	Radical Mastectomy	Modified Radical Mastectomy	Simple Mastectomy
Invasive Carcinoma	73/89 82%	8/89 9%	8/89 9%
Intraductal Carcinoma	2/8 25%	4/8 50%	2/8 25%

nodal metastases (see appendix). In some cases, when the initial excisional biopsy was performed at another hospital, the size of the tumor was not known. These patients could not be staged. Survival rates were calculated from the initial date of treatment by the life table method.[1] 95% confidence limits were calculated using the method of Greenwood.[2]

Follow-up was obtained by direct contact with the patient or his family. The cause of death of patients was obtained from autopsy reports and death certificates when available, or by correspondence with the hospital and physician caring for the patient at the time of his death. Patients dead of other causes, lost to follow-up, or alive at last follow-up within less than ten years after surgery were removed from risk during the midpoint of the year when they were last seen. Patients with recurrent cancer when last seen were considered to have died of disease at that date. Except for routine chest x-rays further postoperative evaluation was performed only in those patients whose physical findings or symptoms suggested recurrence.

The data on staging and survival of women with breast cancer was obtained from a recent study of 304 women treated at Memorial Hospital in 1960.[16] Statistical significance of selected observations was tested by the method of CHI square. Differences were considered to be significant when $p < .05$.

Results

The median age of the men in this series was 65 years. Eighty-nine had invasive carcinoma and eight had intraductal or noninvasive carcinomas. There were five patients with bilateral breast cancer, one of whom had synchronous cancer in both breasts. Of the group with invasive carcinoma, 82% were treated by radical mastectomy, 9% by modified radical mastectomy, and 9% by simple mastectomy. At least 13 of these patients, ten of whom had axillary metastases, received postoperative radiation therapy. Simple mastectomy was limited to those patients who were high operative risks because of other serious concurrent disease. Patients with intraductal carcinoma were usually treated with less extensive operations (Table 1).

The clinical assessment of axillary lymph node metastases could be compared to pathologic findings in 85 patients. Errors were common. The clinical impression was correct in 63 (74%) of the patients, falsely negative in 15 (18%) and falsely positive in seven (8%). Of the 89 men with invasive carcinoma 41 (46%) had pathologically negative nodes, 15 (17%) had metastases only in level I lymph nodes, and 25 (28%) had metastases in levels II and/or III (Table 2). Axillary metastases were found in 12 of 34 (35%) of men with primary tumors 2 cm or less in diameter and 23 of 31 (74%) of those with tumors larger than 2 cm.

TABLE 2. *Frequency and Extent of Axillary Lymph Node Metastases Based on Pathologic Evaluation in Men and Women with Invasive Breast Cancer*

	Total	Negative	Positive at level I* only	Positive at levels II and/or III*	Unknown†
Men	89	41 (46%)	15 (17%)	25 (28%)	8 (9%)
Women‡	304	147 (48%)	59 (19%)	98 (32%)	—

* Level I consisted of the nodes adjacent to the breast, lying lateral and inferior to the pectoralis minor muscle. Level II nodes were situated behind the pectoralis minor muscle. Level III nodes were at the apex of the axillary dissection, medial and superior to the pectoralis minor muscle.

† Patients treated by simple mastectomy.

‡ From Schottenfeld et al.[16]

Of the 89 men with invasive carcinoma, 12 with negative nodes could not be clinically staged because the size of the primary tumor was not known. An additional eight patients treated by simple mastectomy could not be staged pathologically because the axillary lymph nodes could not be microscopically examined. Of the 69 patients who could be staged, 21 (30%) were classified pathologic stage I, 37 (54%) stage II and 11 (16%) stage III (Table 3).

The most common histologic type of breast cancer in men was infiltrating ductal carcinoma (IFDC) (Table 4). Of the 68 patients with this type of carcinoma 31 (46%) did not have areas of intraductal carcinoma (IDC) recognizable in the tumor. Among our patients with male breast carcinoma we also found four cases of intracystic papillary carcinoma (Fig. 1), one colloid carcinoma, one tubular carcinoma, and four cases of

TABLE 3. *Comparison of Stage of Disease in Groups of Men and Women with Breast Cancer at Memorial Hospital*

	Stage I		Stage II		Stage III	
Men (clinical)	25/77	32%	41/77	53%	11/77	14%
Men (pathologic)	21/69	30%*	37/69	54%	11/69	16%
Women (clinical)†	66/304	22%	176/304	58%	62/304	20%
Women (pathologic)†	55/304	18%*	187/304	62%	62/304	20%
Men ≤ 65	9/33	33%	18/33	55%	6/33	18%
Men > 65	12/36	33%	19/36	53%	5/36	14%

* $p < .05$.

† From Schottenfeld et al.[16]

TABLE 4. *Comparison of Pathologic Types of Breast Carcinoma in Groups of Men and Women at Memorial Hospital*

Type of carcinoma	Men	Women*
Intraductal (ID)	4† 5%	3.8%
Intraductal and Infiltrating duct (ID + IFDC)	37‡ 47%	64%
Infiltrating duct (IFDC)	31§ 40%	15%
Intracystic papillary	4 5%	
Colloid	1 1%	1.4%
Tubular	1 1%	
Not reviewed	19	15% (Other)

* From Rosen et al.[12]

† Includes one case of papillary intraductal carcinoma.

‡ Includes 4 cases with Paget's Disease and 2 with papillary carcinoma.

§ Includes one infiltrating terminal ductal, one poorly differentiated, and one duct carcinoma with apocrine metaplasia.

Paget's disease. This series did not include any examples of medullary or lobular carcinoma.

Forty per cent of the 70 patients from whom sufficient material was available for review had microscopic evidence of gynecomastia (Fig. 2). We could not compare the prevalence of clinical gynecomastia in all hospitalized patients with that pathologically identified in breast cancer patients because the pertinent information was not indicated in every chart. There was no significant difference in the prevalence of gynecomastia diagnosed in patients over or under the age of 65. The presence or absence of microscopic gynecomastia was independent of the proportion of intraductal carcinoma present, the stage of disease or the pathologic extent of axillary metastases.

Areas of intraductal carcinoma within infiltrating duct carcinomas were more often found in patients with less advanced lesions. Of the 33 patients with ID + IFDC in whom the pathologic stage was known, 13 were stage I. Only three of 21 patients without an intraductal component to their tumor were in stage I (Table 5). Similarly there was a significantly greater percentage of patients with negative axillae in the ID + IFDC group than in the group with IFDC alone (Table 5).

Life table analyses of survival are summarized in Table 6. No patient with purely intraductal or cystic papillary carcinoma died of breast cancer. Therefore survival figures are calculated only for those patients with invasive carcinoma who were treated by radical or modified radical mastectomy. For this group of patients the five year and ten year survivals are 72% and 40% respectively. In men with no axillary metastases the five and ten year survivals were 90% and 79% respectively. However, after ten years only 11% of men with positive axillary nodes had survived.

Men with pathologic stage I disease had 100% five and 89% ten year survival rates. Men with pathologic stage II disease had five and ten year survivals of 63% and 12%. Because of the small number of men with stage III disease, survival figures in this group were not meaningful. There was no difference in the observed survival between men greater or less than 65-years-old.

Men with pathologic stage II breast cancer were further subdivided to better understand their low sur-

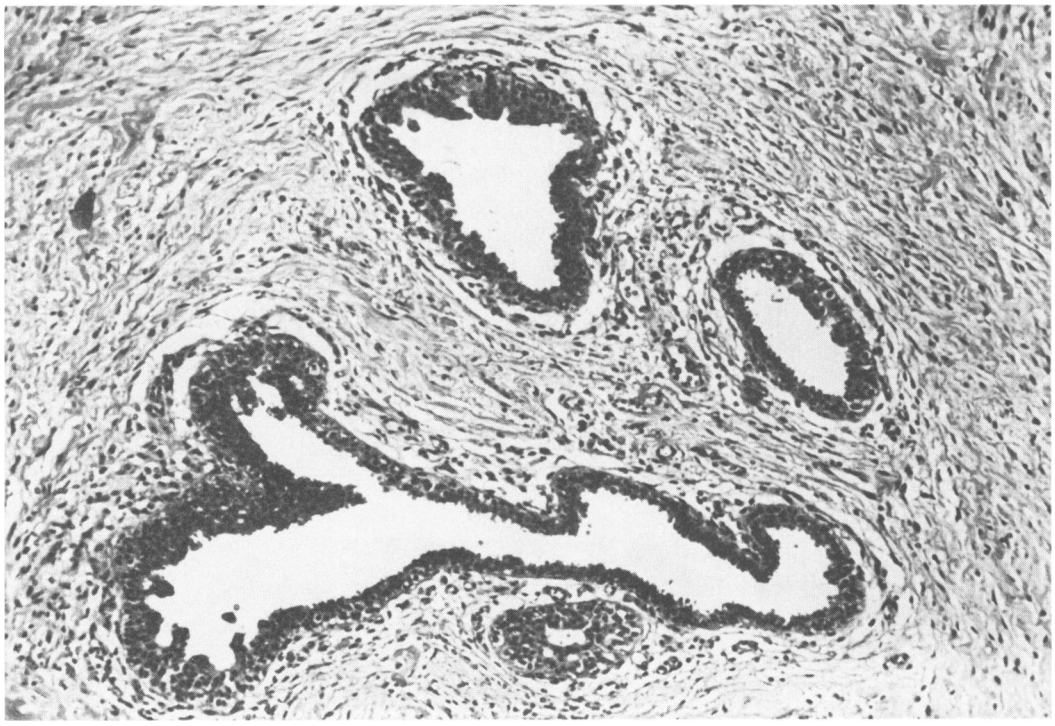

FIG. 1. Photomicrograph of part of a cystic papillary carcinoma. Wall of the cystic tumor is in lower part of this field.

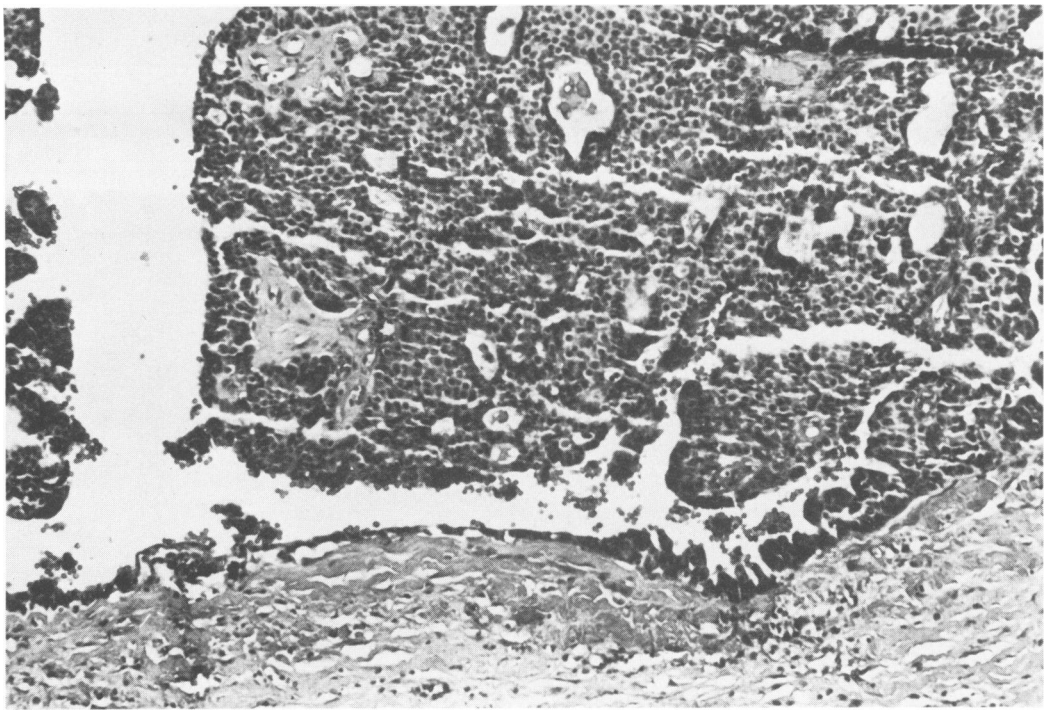

FIG. 2. Gynecomastia in the breast of a patient with carcinoma. This was not clinically evident. Note slight papillary proliferation of ductal epithelium, edema of periductal connective tissue with infiltrate of lymphoid cells.

vival. Among the six patients with T2N0 disease there were only two deaths after ten years. All eight of those men with T1N1 disease had died of cancer within ten years. Of the 37 men in pathologic stage II, six had T2N0 disease and ten had T1N1 disease.

The median time interval from diagnosis to recurrence was 24 months (range 1–120 months). The median survival after recurrence was 22 months (range 0–108 months). There was an encouraging trend towards earlier diagnosis and treatment. Prior to 1960 only 17 of 39 men (44%) were treated within three months of the onset of symptoms and in 16 of 39 (41%) therapy was delayed for more than one year. Since 1960 only 12 of 58 (21%) have delayed treatment for more than one year and 35 of 58 (60%) were treated within three months of initial symptoms.

Discussion

Many authors have emphasized that men develop breast cancer at a later age than women.[5,6,8,23] The median age of men in our series was 65 years. This was 11 years older than the mean age of 54.1 years seen in women with breast cancer at Memorial Hospital.[16] Because of this and because men die at a younger age than women we chose to analyze our data by the life table survival method. This allowed adjustment for deaths due to other causes and the comparison of two or more groups of different age dependent expected mortality.

Several authors report equal survival rates for men and women with breast cancer.[6,8,19,23] In those studies, however, ten year follow-up was not obtained. We found that although there was no difference between survival of men and women at five years, men had a poorer prognosis at ten years (Table 6). The 40% survival reported in this series was significantly less than the corresponding 62% survival for all women with breast cancer at ten years.[16] The five and ten year survival in men with no axillary metastases was similar to that found in women. However, the 11% ten year survival of men with pathologically positive axillary nodes was worse than the 43% survival of women with axillary involvement ($0.02 < p < 0.05$). Similarly, while men and women with pathologic stage I disease had a good prognosis, the 12% ten year survival of men with pathologic stage II disease was worse than that in women with stage II disease.

We observed a particularly poor prognosis for men with T1N1 disease. A similarly poor prognosis for women has been reported.[16] There seemed to be fewer men in stage II who had T2N0 disease (6/37) and more with T1N1 (10/37) than in a similar population of women (72/197 and 25/197 respectively). This, however, was

TABLE 5. *Relationship of Extent of Disease to Pathologic Type in Men with Breast Cancer*

	Pathologic Stage			Lymph Node Status*	
	I	II	III	Neg.	Pos.
ID + IFDC	13	17	3	19	16
IFDC	3	14	4	8	18

* $p < .001$.

TABLE 6. *Comparison of Survival at Five and Ten Years (in Per Cent) in Groups of Men and Women Treated for Breast Carcinoma at Memorial Hospital**

	Five Years				Ten Years			
	Men		Women†		Men		Women†	
	Number‡ at risk	Survival	Number at risk	Survival	Number§ at risk	Survival	Number at risk	Survival
Axillary nodes Neg. (pathologic)	41	90 ± 11	147	86 ± 6	17	79 ± 18	126	71 ± 7
Axillary nodes Pos. (pathologic)	40	59 ± 18	157	59 ± 8	16	11 ± 13	92	43 ± 8
Axillary nodes Neg. (Clinical)	48	75 ± 14			22	48 ± 16	179	72 ± 3‖
Axillary nodes Pos. (Clinical)	33	55 ± 22			10	12 ± 15	112	38 ± 5‖
Stage I (Pathologic)	21	100	55	91 ± 8	10	89 ± 21	50	82 ± 10
Stage II (Pathologic)	37	63 ± 19	187	87 ± 5	15	12 ± 15	163	68 ± 7
Stage III (Pathologic)	11	45 ± 29	62	51 ± 12	5	25 ± 16	32	35 ± 12
Total	81	72 ± 11	304	73 ± 5	33	40 ± 14	221	62 ± 5

* Includes all patients with invasive carcinoma who were treated with mastectomy and axillary lymph node dissection.
† From Schottenfeld et al.[16]
‡ Alive at beginning of year one.
§ Alive at beginning of year six.
‖ Derived from Schottenfeld et al[16], Figure 1.

probably an artifact due to the 12 men with negative axillary nodes in whom the size of the primary tumor was not known. If many of these were T2N0, their inclusion would have resulted in a population similar to the women.

The 40% survival of men in this series was about the same as the 35% survival reported by Crichlow.[5] He attributed this low survival in part to the advanced age and possible delay in diagnosis of men with breast cancer. Slack, in a review of 56 cases treated from 1960 to 1968[19] attributed the poorer prognosis for men with breast cancer to a higher frequency of stage II and III disease. He observed that men and women had similar survivals after adjusting for stage of disease. Langlands et al.[9] in a report of 88 patients found more than 60% of men to have stage III disease. However, we could not relate the poor survival of men to a high proportion with advanced disease. In our series, by either pathologic or clinical criteria the percentage of men with stage I disease was greater than the percentage of women with stage I disease (Table 3). In addition, there was no difference in survival between men greater or less than 65-years-old.

The most important factor determining prognosis was the presence or absence of axillary lymph node metastases. After ten years only 11% of patients with pathologically positive axillary nodes survived. Crichlow[5] made a similar observation. Only 4% of his patients with positive nodes survived ten years. The percentage of men with positive axillary nodes was the same as for women (Table 2). Therefore the low survival of men with breast cancer was due to other factors that increased the lethality of cancers metastatic to axillary nodes, not to a predominance of advanced disease. This difference was seen only in those patients with stage II disease. The prognosis of men and women with stage III disease was equally poor.

Analysis of these survival figures emphasized two points. Reliable data are only obtained by following patients for at least ten years. Secondly, because of the frequency of errors in the clinical evaluation of axillary lymph nodes and the poor prognosis for patients with axillary nodal metastases, clinical staging may give rise to misleading results (Table 6). Evaluation of the treatment for male breast cancer should be based on pathologic staging only.

The reason for the lethal nature of stage II cancers in men may be related to their central location. The extent of axillary nodal involvement is similar in men and women (Table 2). Handley[7] showed that in women, cancers in a central position had a poor prognosis, possibly because of the high frequency of internal mammary lymph node metastases. This may partially explain the poor prognosis we observed in men in whom breast cancer almost always occupied a central position.[4,11] We were unable to evaluate internal mammary metastases since these lymph nodes were not biopsied in any of our cases.

Eighty-seven per cent of the cancers seen in this series were infiltrating duct carcinomas. This is similar to what has previously been reported.[4,8,11,20,21] Silverberg and Chitale[18] described an increasing frequency of lymph node metastases in women with ductal carcinoma as the percentage of intraductal carcinoma decreased and the infiltrating component increased. We observed a similar pattern in men. There was a higher incidence of stage I disease and negative nodes in those men whose tumors contained intraductal elements. Al-

though Silverberg and Chitale demonstrated a decreased survival in women in whom 90–99% of the tumor was IFDC we were not able to confirm this in men. As others have noted, papillary carcinoma in this series had a better prognosis than infiltrating duct carcinoma.[8,11,20]

Clinical gynecomastia has rarely been associated with breast cancer in men.[3,5,8,10] On the other hand, microscopic gynecomastia characterized by fibroepithelial proliferation and lymphocytic infiltration, occurs in 3% of all men at autopsy.[14] Scheike and Visfeldt[15] have reported microscopic gynecomastia to be present in 21 of 79 cases of male breast cancer. Only one of their patients had clinical gynecomastia. We found 40% of our patients to have microscopic gynecomastia. Although these areas usually featured papillary epithelial hyperplasia none showed transition from gynecomastia to carcinoma. Scheike and Visfeldt claimed that patients with gynecomastia were younger than patients without gynecomastia, but we were unable to confirm this. The prevalence of gynecomastia was similar in the groups younger and older than 65. There seemed to be no relationship between gynecomastia and the extent of disease or survival. The high incidence of gynecomastia suggested that it might be a premalignant condition, but we were unable to find conclusive evidence to prove this.

Adequate treatment of male breast cancer should include mastectomy and axillary lymph node dissection Treatment of internal mammary lymph nodes by either resection or radiation may be indicated for certain patients. Because of the poor prognosis of men with axillary nodal involvement, adjuvant therapy should be considered. The role of adjuvant systemic chemotherapy in this group of men should be subjected to clinical trial. In view of the high frequency of estrogen binding positive carcinomas in men[12] adjuvant hormonal therapy may prove more effective than it appears to have been in women.

Appendix

Summary of TNM Staging

T: *Primary Tumor*
- T1 Tumor ≤2 cm. in its greatest dimension
- T2 Tumor 2 cm. ≤ 5 cm. in greatest dimension
- T3 Tumor >5 cm. in greatest dimension
- T4 Tumor of any size with direct extension to skin or chest wall

N: *Regional lymph nodes*

CLINICAL
- N0 No palpable axillary nodes
- N2 Palpable axillary nodes

PATHOLOGIC
- N0 No metastases to axillary nodes
- N1 Metastases present in axillary nodes

M. *Distant Metastases*
- M0 None present
- M1 Present

Clinical or Pathologic Stage Grouping
- Stage I—T1N0M0
- Stage II—T1N1M0
  T2N0M0
  T2N1M0
- Stage III—T3 with any N M0
  T4 with any N M0

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