Pregnancy Subsequent to Mastectomy for Cancer of the Breast

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ONE of the most fascinating and yet frustrating aspects of mammary cancer research and therapy has been the reaction of this malignant lesion to the addition or subtraction of estrogenic hormones. There is no doubt that growth of this tumor can be influenced by altering its hormonal environment. Some tumors, however, thrive with added estrogen while others regress. On occasion, estrogen administration causes both regression and increased growth of the same lesion at different periods. The clinician is left with many theories as to the cause and effect relationship of hormone to tumor growth, and with catch phrases such as "hormone dependent," but with little knowledge on which to base therapeutic decisions.

In spite of this lack of clear-cut information, advice must be given to patients. One such decision deals with advice to the young woman who has undergone mastectomy for mammary cancer. Should further pregnancies be discouraged or permanently prevented? Should she be castrated by either surgical or radiotherapeutic means? If pregnancy should ensue, is therapeutic abortion indicated?

Answers to these questions depend upon answers to a more basic question; i.e. Is the survival of patients successfully treated for cancer of the breast significantly altered by subsequent pregnancy? This paper presents data which will help answer this question.

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Materials and Methods

A large series of patients who have become pregnant following mastectomy for mammary cancer is collected with difficulty. This stems from the limited incidence of breast cancer at the child-bearing age, and reluctance of patients to bear children following mastectomy. A meaningful number must, therefore, be gleaned from a large group of patients.

The 7,381 cases collected by the Committee for the Study of Delay in Breast Cancer in Philadelphia County provides such a group. These patients were unselected and were treated in all hospitals in the area by many surgeons, using a variety of technics. This assortment of patients and therapeutic approaches creates drawbacks to critical analysis. The advantage is, however, a cross section of results in an urban community, containing many hospitals, and influenced to some extent by five medical schools and one school of osteopathy.

Of the 7,381 patients, 593 were 40 years of age or under when treated. Of these, 40 became pregnant subsequent to mastectomy. Follow-up information is complete for these 40 patients. Only 32, however, who were treated more than five years prior to this study, are available for 5-year survival statistics.

One troublesome obstacle to critical analysis is the self-selective nature of the study group. To compare, for instance, survival rates for all patients with cancer of the breast who are under the age of forty

TABLE 1. *Survival in Years*

Years	Living	Dead
1	0	1
2	0	2
3	0	1
4	0	4
5	21	0
6–10	3	0
Total	24	8

Survival of 32 patients who experienced one or more pregnancies following mastectomy for carcinoma of the breast.

TABLE 2. *Five year Survival By Clinical Stage*

Stage	Survived	Died
I	22	2
II	2	5
III	0	1
Total	24	8

Five-year survival according to clinical stage of disease. Patients were staged by American System developed by the Joint Committee on Cancer Staging and End Results Reporting.

who did not become pregnant with those who did, is not helpful. The nature of the disease is such that patients with advanced or aggressive neoplasms do not become pregnant. They are eliminated either by death or recurrent tumors.

To obviate this bias of selection, a control group was obtained by selecting two matched control patients for each study patient. Each control was matched with its counterpart in the study group according to the following criteria:

1. Clinical stage of disease.
2. The presence or absence of histologically positive axillary lymph nodes.
3. Age of patient (within 2 years).
4. Initial survival after mastectomy. (Each control must have survived at least as long after mastectomy as its match in the study group survived prior to pregnancy.)
5. Random selection of matched controls. (The two matched controls for each study patient were selected at random from those who qualified according to the above requirements.)
6. Three patients in the study group were living and well for 5 years after mastectomy before becoming pregnant. Because pregnancy obviously could not have affected five-year survival in these individuals, they are not considered when five-year survival of the study group is compared with that of the matched controls (Table 4). All remaining study patients conceived within five years of mastectomy.

Because of diverse staging technics used by the reporting institutions, the records of all patients were reviewed and the lesions reclassified according to the American System developed by the Joint Committee on Cancer Staging and End Results Reporting. Although there are some disadvantages to retrospective staging, the records were sufficiently complete to make this classification obvious in most cases.

Results

The absolute 5-year survival for 32 patients who were treated 5 or more years prior to the study was 75 per cent (Table 1). Three of the 24 survivors have lived for more than 10 years. Of the eight who died, the cause of death was carcinoma in all but one who died from subacute bacterial endocarditis and no residual carcinoma was found at autopsy.

It is apparent from Tables 2 and 3 that the two characteristics of greatest prognostic significance are the clinical stage of the lesion and the presence or absence of involved axillary lymph nodes. Of 24 patients with Stage I tumors, 22 (92%) survived 5 years. Only two of seven patients with Stage II lesions survived 5 years. Long-term survival could not be expected in one patient with a Stage III lesion, and we eliminated this case from the matched control series in Table 4.

In this series of 32 patients, 19 had no histological evidence of metastatic disease in axillary lymph nodes (Table 3). All but one (95%) lived 5 years or more. Of 13 in whom positive nodes were found, six (46%) survived.

The significance of these figures is better appreciated when the study group is compared with the matched controls (Table 4). Of 17 patients in the study group classified as clinical Stage I and free of axillary nodal metastases, 16 survived 5 years. Five with Stage I lesions had positive nodes and four survived. This is an unusually high 5-year survival even for Stage I lesions. It is more significant, however, when compared to the matched control series in which only 24 of 34 Stage I patients with negative nodes and six of 10 Stage I patients with positive nodes survived 5 years. Superficial comparison of these figures might seem to indicate that patients who became pregnant following mastectomy could anticipate longer survival than matched controls. Statistical analysis, however, would not substantiate such a claim. If one assumes that matched controls were truly comparable to study patients, these figures indicate that pregnancy does not adversely affect survival.

For individuals with Stage II lesions (all of whom had positive axillary nodes), the number of patients is too small for statistical significance. It is interesting, nevertheless, that there is little difference in 5-year survival between the study and control patients in this small series.

It is not possible to determine the effect (if any) of pregnancy on the growth of residual cancer following mastectomy. Of eight patients who did not live 5 years, one survived for one year, two for 2 years, one for 3 years, and four for 4 years. All but three conceived between the second and third postoperative years.

To determine the effect of pregnancy, it might be more meaningful to know the length of life after pregnancy than after mastectomy. Table 5 compares continued survival of the study group after pregnancy with that of the control series after its matching date. While the study patients appear to have a somewhat better 4 and 5-year survival rate after pregnancy than the controls, one would be reluctant to suggest that pregnancy confers some beneficial effect upon patients with surgically treated cancer of the breast. There is, however, no evidence of any adverse effect of pregnancy on survival.

Eleven patients had more than one pregnancy following mastectomy (Table 6). Eight survived 5 years and three died. The significance of this is difficult to interpret because of the obvious element of natural selection. A certain period of longevity is an obvious prerequisite to multiple pregnancies.

TABLE 3. *Five-year Survival and Nodal Metastases*

	Survived	Died
Negative Nodes	18	1
Positive Nodes	6	7

Five-year survival of patients with histological evidence of axillary nodal metastases compared to those without nodal involvement.

TABLE 4. *Survival—Study Group Vs. Matched Controls*

Stage and Nodes	Study Group	Control
I Negative	16/17	24/34
I Positive	4/5	6/10
II Positive	1/6	4/12

Comparison of 5-year survival of study patients with that of matched control series. Each group subdivided according to clinical stage of primary lesion and presence or absence of histologically positive axillary nodes. In each fraction, the numerator represents 5-year survivors and the denominator total patients in group.

Discussion

Several authors reported survival statistics on patients who have developed cancer of the breast during pregnancy or lactation.[3] Few, however, report the courses

TABLE 5. *Survival after Pregnancy*

Years after "Pregnancy"	Study Group			Control Group		
	Subjects at Risk*	Number Survived	Per Cent Survived	Subjects at Risk	Number Survived	Per Cent Survived
<1 year	32	24	75	64	39	61
1	32	24	75	61	36	59
2	32	24	75	59	34	58
3	32	24	75	49	30	61
4	32	24	75	35	17	49
5 or more	29	21	72	23	7	26

Survival after pregnancy. "Pregnancy" equals date of delivery for study group and the matching date for the control series.

* In this table, subjects were considered to be "at risk" whenever the interval between pregnancy (either real or corresponding control date) and the end of the study period was long enough that the patient could have survived. For example, a patient whose date of pregnancy was exactly 3 years prior to the end of the study would be "at risk" for 3 years but not for 4 years. Where such an individual died within the first 3 years, one might argue that she should be counted as a death for the 4-year period but this would not be valid. Patients still alive at 3 years could not be included in a 4-year period and, therefore, all patients whose date was only 3 years prior to the end of the study must be excluded for the fourth year.

of patients who have become pregnant following definitive surgical treatment. Bunker[1] reported 31 patients who conceived 34 times subsequent to mastectomies, with a 5-year survival of 77.4 per cent. Holleb[2] reported 52 patients in this category with an overall 5-year survival of 52 per cent. White[4] collected from the literature 269 patients who conceived following mastectomy. Fifty-nine per cent of these survived 5 years and 47 per cent for 10 years.

The significance of these uncontrolled, retrospective studies is limited. A prospective study, on the other hand, presents a logistical dilemma which is prohibitive. Any protocol for such an investigation would have to consider not only the variables intrinsic to the neoplasms but also the uncertainties of conception and pregnancy. Even with complete cooperation of institutions and patients, prospective randomization would be formidable.

TABLE 6. *Survival and Multiple Post-operative Pregnancies*

	5-Year Survival	Died
One Pregnancy	16	5
Multiple Pregnancies	8	3

Five-year survival of patients having single pregnancy after mastectomy compared to those having multiple pregnancies.

A controlled, retrospective analysis, therefore, seems to be reasonable. The only objection is the question of comparability between the control and study groups. Although controls were matched by what appeared to be reasonable criteria, it is possible that hidden factors were not taken into consideration. The unusually high rate of survival for the patients with Stage I lesions, for example, suggests some natural selection which was not matched in spite of precautions. We do not suggest that pregnancy has a beneficial effect on post-mastectomy patients. Such a claim could not be substantiated, nor does it seem reasonable on the basis of known facts regarding the behavior of this tumor.

It has been demonstrated that insofar as this study can be controlled, there is no evidence to indicate that pregnancy should be avoided following mastectomy for carcinoma of the breast in patients with clinical Stage I lesions, with or without axillary metastases. For Stage II lesions, the same conclusion is suggested but lacks statistical substantiation because of the small numbers in this group.

Conclusions

1. Following radical mastectomy for Stage I mammary carcinoma, survival time is unaffected by subsequent pregnancy. We interpret this to mean that if the cancer is completely excised, subsequent pregnancy is not deleterious. This study has not clearly established the effect of pregnancy on the course of patients with residual tumors.

2. In assessing the effects of multiple postoperative pregnancies, the only valid conclusion seems to be that successful completion of one pregnancy without evidence of recurrent disease gives no guarantee of cure. Pregnancy, therefore, as a "provocative test" of a successful mastectomy is not satisfactory.

3. In advising young women who have had mastectomies for cancer of the breast the evidence indicates that if the lesion is clinical Stage I, there is no reason to believe survival will be prolonged by oophorectomy, tubal ligation, or avoidance of pregnancy. Should pregnancy ensue, there is no indication for therapeutic abortion unless some other clinical evidence influences one's judgment.

Summary

From a series of 7,381 patients with cancer of the breast collected by the Committee for the Study of Delay in Breast Cancer in Philadelphia County, 40 patients became pregnant following operative treatment of the breast lesions. Of these, 32 were available for 5-year survival studies. This retrospective study was controlled by the selection of two matched controls for each patient in the study group. All patients were staged according to the American System, developed by Joint Committees on Cancer Staging and End Results Reporting.

Insofar as this study can be controlled, there is no evidence in patients with clinical Stage I lesions, of an adverse effect of pregnancy on 5-year survival following mastectomy.

It is concluded that for young patients with clinical Stage I lesions there is no indication to advise avoidance of pregnancy after mastectomy for mammary carcinoma.

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