

Treatment of Breast Tumors Associated with Pregnancy and Lactation *

B. F. BYRD, JR., M.D., D. S. BAYER, M.D., J. C. ROBERTSON, M.D.,
S. E. STEPHENSON, JR., M.D.

From the Departments of Surgery and of Obstetrics and Gynecology, Vanderbilt University School of Medicine, Nashville, Tennessee

ANY DISCUSSION of management of breast tumors in a pregnant woman will raise a variety of controversies among obstetricians, gynecologists, internists and surgeons. Each physician has his own favorite reference which usually will serve to point out the unfavorable outcome to be expected if the nodule is malignant. Such articles have thus been utilized to justify the decision of the physician who persists in delaying breast biopsy in the pregnant or lactating female. He may hold this position despite the mounting evidence that the ever-present opportunity to improve survival rates in breast cancer lies in early diagnosis and treatment.

One of the early reports concerning the relationship of breast cancer to pregnancy and lactation was made by Harrington,⁷ in 1937. His review covered a group of 88 patients treated at the Mayo Clinic in a 23-year period. He found an over-all five-year survival rate of 5.7 per cent. Haagensen and Stout,⁵ in 1943, found results of treatment so discouraging that they concluded there was no justification for radical mastectomy in the pregnant patient. Later these two authors⁶ reviewed 48 cases seen between 1915-1950 and decided the combination was not a contraindication to operation. In a group of 31 radical mastectomies a five-year survival rate of 32 per cent was found. They found five five-year survivors

among six patients who showed no axillary node involvement at the time of radical mastectomy. Brooks and Proffitt² using the first six cases in the present series interjected some hope into the field. It was their conclusion that such lesions were operable but carried a less favorable prognosis than in the nonpregnant woman. Cheek,⁴ in 1953, surveyed 55 of the nation's leading authorities on breast cancer concerning this problem. This group contributed 151 cases with eight five-year cures (5.3%). White and White¹³ found that breast cancer and pregnancy occurred in 2.8 per cent of breast neoplasms treated. They collected 882 cases from the world literature¹² and found a 21.5 per cent five-year survival in patients with no axillary node involvement and a 6.7 per cent survival in the presence of axillary metastases.

Various ancillary measures have been championed over the years. These have included the immediate emptying of the uterus, sterilization, and preoperative radiation therapy. It has been stated that such patients should avoid future pregnancies. Recently Montgomery^{9,10} has made a strong plea in the obstetrical and gynecologic literature for early diagnosis and treatment of breast lesions in pregnancy or lactation. He has recommended immediate hysterotomy or hysterectomy followed by preoperative radiation therapy to the breast area. He recommends the removal of the lesion of the breast under local anesthesia.

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The wide divergence of opinions in the method of handling this problem and the pessimistic outlook expressed by many authors has prompted us to review the series of pertinent cases at Vanderbilt University Hospital. We have not studied in detail the arguments pro and con on subsequent pregnancies following radical amputation of the breast. We believe these cases have to be individualized especially with respect to moral and religious tenets of patient and husband. This series includes only those tumors occurring during pregnancy or actual lactation.

Incidence

In an analysis of the world literature, White¹³ stated that pregnancy complicated carcinoma of the breast in 2.8 per cent of breast cancer patients. He stated later¹² that breast cancer complicated pregnancy or lactation in three of every 10,000 pregnancies. Last year in the United States there were 4,247,000 live births. From these two figures the magnitude of the problem may be calculated at a minimum of 1,274 new carcinomas of the breast coincident with pregnancy or lactation yearly.

In the present study we have found 29 carcinomas of the breast occurring during pregnancy and lactation. Our total group of 1,162 breast cancers previously reported³ gives an incidence of 2.5 per cent for this particular study. This is comparable to the world incidence as reported by White. Of 134 patients undergoing breast biopsy during pregnancy and lactation, 29 were found to have carcinomas. A pregnant or lactating woman who develops a lump in her breast has a 4.6:1 chance that the tumor is benign. This compares with the ratio of 5.4:1 for all breast tumors removed at the Vanderbilt University Hospital in the last five years.

Clinical Material

In the 35-year period from 1925-1960 we have found 134 pregnant or lactating



Trimester	BENIGN			MALIGNANT		
	1	2	3	1	2	3
	28	22	12	10	4	10
					5	
Total	<u>105</u>			<u>29</u>		

FIG. 1. Breast tumors in pregnancy and lactation.

patients undergoing surgery for a tumor of the breast at the Vanderbilt University Hospital and at St. Thomas Hospital in Nashville. Of this group of patients (Fig. 1) 105 had benign lesions and 29 proved to be carcinomas. There were operations performed during all three trimesters and during lactation. Biopsy was carried out under general anesthesia with the patient prepared to proceed with a radical mastectomy if a malignancy was encountered. There was no maternal fatality in the series. The only fetal mortality (0.75%) occurred in the case of a 43-year-old white woman who was menopausal. She had a negative Hogben test (frog test) on two occasions prior to removal of a cystic lesion of the breast. She aborted spontaneously three weeks post-operatively.

In the 105 benign lesions (Table 1) the largest number were neoplasms, 39 (adenofibroma, lipoma, papilloma, cystosarcoma phylodes). Next most frequent in occurrence was cystic disease and 23 patients had lobular hyperplasia, galactocele or other changes of the breast coincident with pregnancy. There were only seven instances

TABLE 1. *Benign Tumors*

Neoplasms	39
Cystic disease	36
Changes due to pregnancy	23
Inflammation	7
Total	105

TABLE 2. *Method of Treatment*

	5-yr. survival	
Biopsy	1	0
Simple (palliative)	7	1
Radical	21	15 (71.4%)

TABLE 3. *Age and Survival*

Age	No. Patients		No. 5-yr. survivals	
	\bar{s} nodes	\bar{c} nodes	\bar{s} nodes	\bar{c} nodes
20-24	1	1	1	0
25-29	3	1	3	0
30-34	2	7	2	2
35-39	4	5	4	2
40-44	1	1	1	0
45-49	0	3	0	1
Totals	11	18	11	5
		29		16 (55.2%)

of abscess or inflammatory disease. All patients made an uneventful recovery.

Figure 2 shows the age groups of the patients and the trimester in which the lesion was found. The average age in this group of patients was 29.2 years. The parentheses under the lactation column indicate the number of lesions found during pregnancy, in which surgery was delayed until the postpartum period.

The therapy in the 29 malignant lesions was somewhat varied (Table 2). One patient presented with widely disseminated disease and only diagnostic biopsy was performed. This was followed by radiation therapy. This patient survived only two months following biopsy. She expired 14 months following the appearance of the lump. Seven of the patients were treated by what was believed to be only a palliative simple mastectomy. Of the six cases ending fatally in less than five years, one was typical inflammatory carcinoma, the only one in our group. This is a somewhat lower incidence of inflammatory carcinoma associated with pregnancy and lactation than would be expected from published reports.^{1, 6, 9, 13} The average absolute survival in these six cases was 29.5 months and the average survival following surgery was 17.1 months.

The one long-term survivor following simple mastectomy lived 19 years and three months. After a drainage of a breast abscess and biopsy of the abscess wall which revealed a papillary carcinoma, a simple mastectomy was performed. Two years after surgery this patient went through another pregnancy without complication. Seventeen years later she expired following a right cerebral hemorrhage. Autopsy revealed no evidence of residual neoplasm.

The remaining 21 patients were subjected to a classical radical mastectomy. Fifteen (71.4%) of those who were subjected to radical mastectomy were alive at five years. Three have died of their

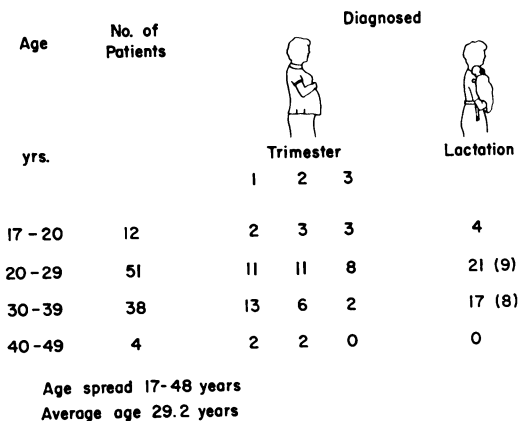


FIG. 2. Occurrence of benign tumors.

disease since their five-year period, at 72 months, 92 months, and 246 months, post-operatively. The remaining patients are apparently well although one developed a carcinoma in the other breast with axillary metastases. This patient is now alive 146 months following her first mastectomy, 91 months following her second mastectomy, and has three additional children. She has no evidence of disease at this time. Two other living patients have had evidence of metastases which have responded to radiation and hormonal therapy. These patients are alive 61 and 198 months, respectively, following their surgery.

In Table 3 the patients with carcinoma are correlated by age and the presence or absence of axillary nodes. The five-year survivors in each age group are shown in relation to axillary node involvement. There have been 16 five-year survivors in the group of 29 patients for an over-all five-year survival rate of 55.2 per cent (Fig. 3).

Of patients who had no axillary node involvement at the time of operation all lived a minimum of five years. Five of 18

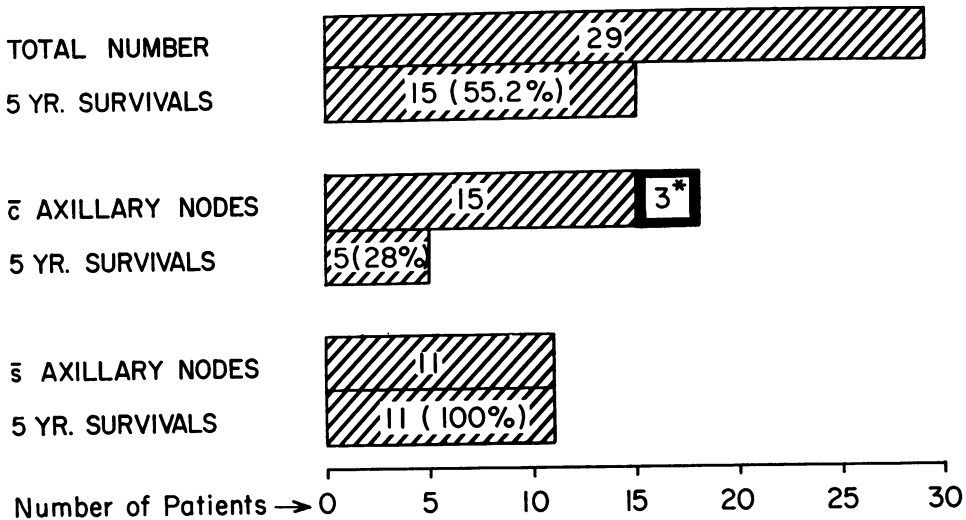
TABLE 4

	Months		
	Average	Mean	Range
Absolute survival (Pre- and postoperative)	108	61	7-409
Postoperative survival	102	61	2-408
Delay in treatment (onset to definitive Rx)	6	3	0-24

patients with axillary metastases (28%) were alive at the end of five years. The average age in this group of patients was 34.0 years. This is slightly older than the average of the benign tumor group.

The absolute survival in the entire group of patients with breast cancer occurring during pregnancy and lactation averaged 108 months with a mean survival of 61 months. The postoperative survival average is 102 months with the same mean survival as before (Table 4).

In the patients with carcinoma the average delay from the detection of a mass to final definitive treatment was six months with a range from two days to 24 months.



* - Axillary and distant met.

FIG. 3. Malignant tumors.

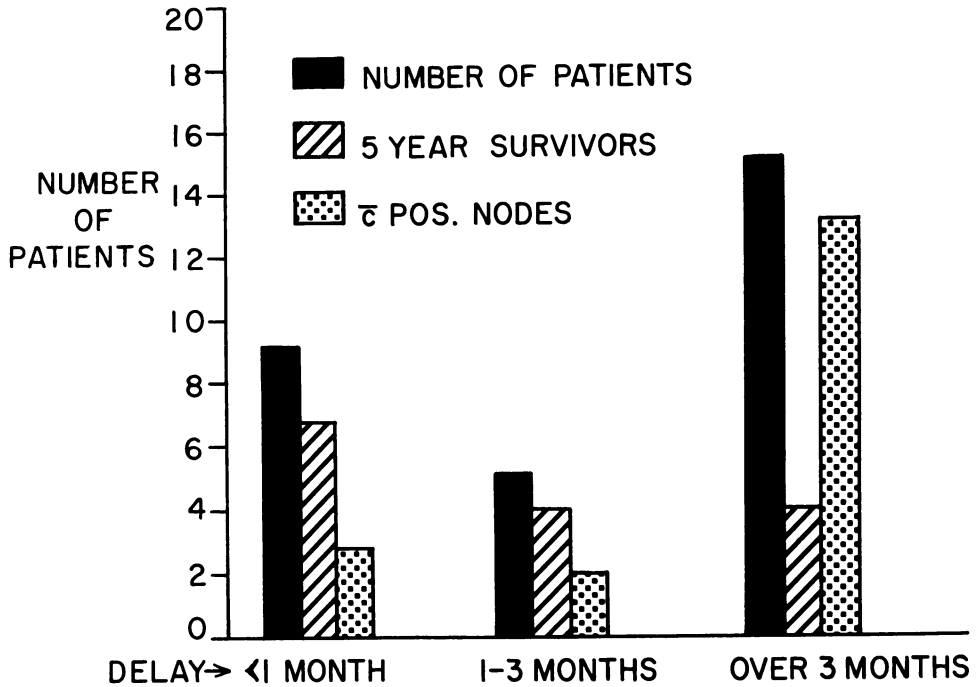


FIG. 4. Delay in relation to survival and axillary nodes.

This delay is of further interest when one compares the average delay of 3.1 months for patients without axillary node involvement to the 7.4 months delay in that group having axillary or distant metastases.

Much has been written concerning the difficulty of establishing the presence of a lump in the rapidly expanding and engorging breast of pregnancy and lactation. Such delays in this small group of patients are actually shorter than in the general group of breast cancers. The delay of 3.1 months in the pregnant woman without axillary nodes compares to 6.4 months in the same over-all age group and the 7.4 months to the 9.1 months with axillary node involvement. The regular visits of the pregnant or post-partum female to her obstetrician thus gives a real opportunity for early diagnosis and treatment that is not customarily available to the medical profession with the nonpregnant female. The difficulty in the current series seems to be a reluctance on the part of the physi-

cian to adequately follow through after he diagnoses a breast tumor. Three-fourths of the delay in the present group of patients was directly related to physician procrastination.

The relation of delay in treatment to survival is also pointed out in Figure 4. When symptoms of a breast tumor had been present less than one month the percentage of axillary node involvement is low and five-year survival is high. With from one to three months delay the number of survivors is markedly reduced. It is in fact equal to the number of patients with axillary node metastases in this series. If the delay is in excess of three months the percentage of five-year survivors is further reduced and most of the patients have metastatic axillary nodes.

Two patients in the group had pregnancy shortened because of the tumor. One had a successful induction of labor at 37 weeks and a second had a caesarean section at 37 weeks. Viable infants were obtained in

each instance. Radical mastectomies were performed six and ten days later respectively. In no instance was pregnancy terminated with death to the fetus in the malignant group.

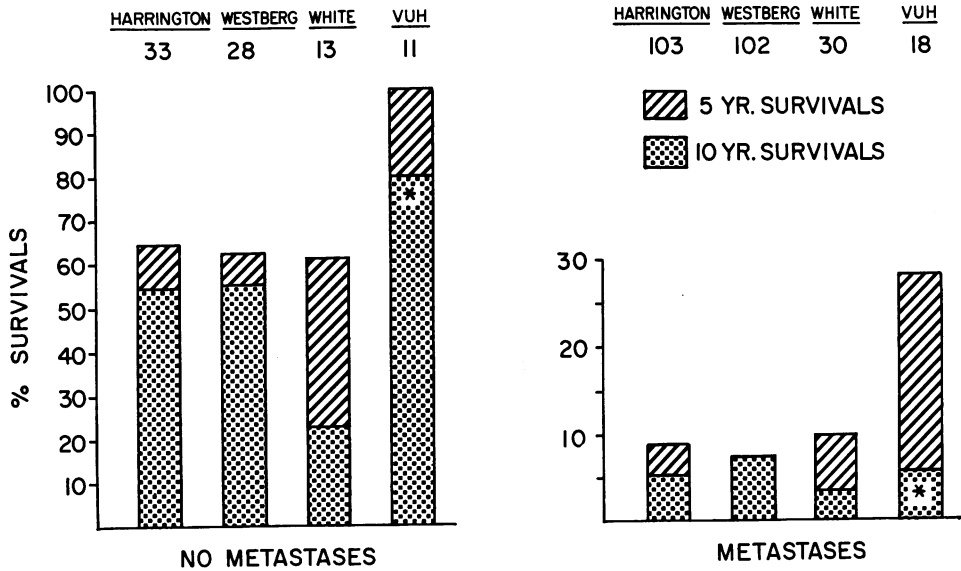
Discussion

Many authors take an especially pessimistic view of the combination of breast cancer and pregnancy or lactation. Though the present series is small it appears that a more enthusiastic approach should be taken to the treatment of these patients. Combined with this approach, we must concentrate our efforts on earlier diagnosis and treatment. Herein lies the only hope in saving this important group of young mothers. A comparison of four reported series¹¹ shows in Figure 5 that satisfactory survival can be obtained at both five- and ten-year periods if no axillary nodes are involved with neoplasm. The survival rates when metastatic nodes are present at the time of surgical treatment leaves much to be desired. The 28 per cent survival rate in this group of patients is appreciably

lower than the five-year survival of 36.5 per cent for the similar portion of the total group of breast cancers previously reported.

Analyzing this group of patients with reference to survival or to complications for mother or fetus, we can find no support for immediate termination of the pregnancy in the first two trimesters as advocated by Montgomery,⁹ Lewison⁸ and others. These figures can only be used to reiterate the belief of White¹⁴ that "abortion cannot be clearly shown to have a favorable effect on the disease." We find no evidence to change our belief stated in a previous paper³ that the pregnant or lactating patient with breast cancer presents no different problem in treatment than her nonpregnant counterpart.

In consideration of termination of pregnancy as a major part of the treatment of breast cancer the third trimester must be studied. The presence of a viable fetus in utero certainly complicates the situation. From a study of premature mortality statistics at the Vanderbilt University Hospital



* Two additional patients living but not 10 years post op.

FIG. 5. Operation after conception.

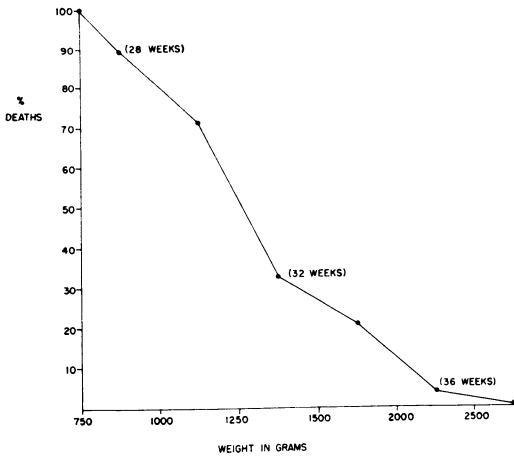


FIG. 6. Premature mortality rates at V. U. H.

(Fig. 6) one sees that the risk of infant death is prohibitively high (over 70%) until after the thirty-second week of pregnancy. One must pass the thirty-sixth week of gestation with an average fetal weight of over 2,500 Gm. before an acceptable risk can be obtained. The pediatric experience also points up the fact that 30 to 40 per cent of infant deaths during the first year of life are from prematurity and the death rate among prematures after this first week is also well above the average for term deliveries. One must also accept the 2.0 per cent infant mortality rate from caesarean section alone. The results of the current study would not suggest that the risks involved with prematurity of the infant are justifiable.

We question whether the psychic trauma associated with the removal of a breast tumor under local anesthesia as recommended by Montgomery¹⁰ is justifiable. Certainly it is more traumatic for the patient to be awake and be aware of the decision of her particular surgeon as to his next step in therapy. This assuredly contributes to more delay in the treatment of the tumor. The present series does not support the contention that general anesthesia should be avoided. Available figures demonstrate that a judicious use of general

anesthesia with the adequate oxygenation made possible by modern-day anesthetic technic does not increase materially the risk to the mother or the fetus.

There is no support from the statistics that the delay caused by interruption of pregnancy and recovery from this procedure, or from preoperative x-ray therapy is justifiable. It seems apparent that the shortest delay possible from the time of suspicion of a breast tumor to final definitive surgical therapy yields the highest salvage. It follows that any delaying ancillary procedure not yet proven to be of definite value in prolonging survival should be avoided.

The only innovation in the current treatment of breast cancer which is not applicable in the treatment of pregnant patients is the use of the chemotherapeutic agents. Since the agents are effective to some extent against malignant cells which are undergoing rapid division and proliferation they may possibly exert the same influence on the rapidly proliferating cells of the fetus. It seems that these agents should be withheld in the pregnant woman until more data is available on their effect on normal but rapidly proliferating cells.

In conclusion, we have reported a series of 134 patients who were operated upon for a tumor of the breast arising during pregnancy or lactation. Of these, 105 were benign lesions; 29 patients having carcinoma of the breast were treated in various fashions without fatality of either mother or fetus.

The results of our evaluation group and of the postoperative course of this group of patients show that the most significant factor in treatment is early diagnosis with radical surgery. There is no apparent loss in this series as a result of an unwillingness to interrupt pregnancy or castrate the mother. With adequate adjunct care concurrent pregnancy does not prevent immediate radical surgery for the patient with breast cancer. Only in this fashion can we

expect to improve the present unsatisfactory survival figures associated with a long delay in treatment.

In the face of general enthusiasm for terminating the pregnancy, we believe the evidence is that the cancer should be terminated.

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