

LIFE EXPECTANCY FOLLOWING RADICAL AMPUTATION
FOR CARCINOMA OF THE BREAST: A CLINICAL AND
PATHOLOGIC STUDY OF 218 CASES*

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THE study of these cases was undertaken for the purpose of determining, as nearly as possible, the life expectancy of patients on whom primary radical amputations of the breast have been performed for carcinoma. The factors which seem important in determining the expectancy of life were carefully studied from a clinical and a pathologic standpoint in a series of 218 patients with carcinoma of the breast operated on in the Mayo Clinic. The conclusions reached from the clinical findings and the findings at operation are discussed first, the microscopic picture of the tumors removed and the bearing which these different pictures seem to have on the prognosis are next considered.

It is impossible to foretell the duration of life of all patients with carcinoma of the breast, because the degree of malignancy varies widely, and persons react differently to the disease. For instance, certain types of carcinoma of the breast cause death within a few months after they are recognized, and other types metastasize slowly and do not prove fatal for many years; the latter, however, are rare and constitute only a small percentage of carcinomas of the breast. In the majority of these it is possible to make a fairly accurate prognosis with regard to the duration of life following operation.

It was gratifying to find, from our statistics, that the results obtained from early operations for carcinoma of the breast are probably better than those obtained in operating for any other type of malignant growths, with the exception of basal-cell epitheliomas and epitheliomas of the lip. Patients who apply for treatment may be classed in three groups:

Group 1.—Patients with inoperable growths; growths firmly fixed to the chest-wall; extensive ulcerating growths with metastatic skin nodules; fixed masses in the axilla; extensive involvement of the axillary and supraclavicular glands, or internal metastasis. Operation is of no avail and is probably harmful.

Group 2.—Patients who have removable growths, but in whom, because of the extent of the growth, or the glandular involvement, a cure cannot be expected by operation. Operation is often performed from an humanitarian

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standpoint, without expectation of cure, to relieve future suffering and discomfort.

Group 3.—Patients with removable growths, with or without metastasis in the axillary glands. These patients have a chance for cure through operation. It is the prognosis in this group that we wish to discuss.

By studying the results obtained in 218 cases we found that 51.8 per cent. of the patients operated on, one of each two patients, were living three years after operation. Seventy-five and six-tenths per cent. of the patients without glandular involvement, three of each four patients, were living at the end of three years, and 36.6 per cent. of the patients with glandular involvement, about one of each three patients, were alive at the end of three years. (Table I.)

Thirty-nine per cent. of the patients, about two of each five patients, were alive at the end of five years. Sixty-five and one-tenth per cent. of the patients without glandular involvement, about six of each ten patients, were alive at the end of five years, and 21.9 per cent. of the patients with glandular involvement, about one of each five patients, were alive at the end of five years.

Thirty-six and seven-tenths per cent. of the patients, about one of each three patients, 63.9 per cent. of the patients without glandular involvement, about six of each ten patients, and 18.9 per cent. of the patients with glandular involvement, about one of each five patients, were living from five to eight years after operation.

Of the series of 218 patients, 2.7 per cent. died within six months; 21.1 per cent. died within one year; 34.9 per cent. died within two years; 42.2 per cent. died within three years; 49.1 per cent. died within four years, and 55 per cent. died within five years. Only 2.3 per cent. died after five years. Four and one-tenth per cent. of the patients living from five to eight years after operation have recurrences, and it is probable that these will die from cancer. After eight years the disease rarely recurs.

Carcinomas which developed during pregnancy and during the lactating period invariably proved fatal within five years after operation. Diffuse carcinomas which involved practically the entire breast caused death in every instance within five years; all but one of the sixteen patients with this type of growth died within three years after operation. When the axillary glands were involved, carcinomas around the nipple proved fatal in seventeen of eighteen patients (94.5 per cent.) within five years. Seventeen of twenty patients with ulcerating carcinomas (85 per cent.) were dead at the end of seven years; fourteen died within five years after operation.

Age seems to have a definite bearing on the results to be expected following operation. Forty-one and seven-tenths per cent. of the patients over fifty are alive from five to eight years after operation, while only 31.8 per cent. of those under fifty have lived a corresponding time. The immediate hospital mortality was less than 0.5 per cent.

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In our experience the prognosis has not been affected by the complete removal of small growths for microscopic diagnosis before the radical operation is performed. When local recurrences were found following operation, metastasis was demonstrated in other regions in 60.9 per cent. of the cases, or in six of each ten patients. Nearly all patients who had recurrences following operation died from the disease.

RESULTS OBTAINED IN 218 CASES IN WHICH OPERATION WAS PERFORMED

Of eighty-six patients (39.5 per cent.) without glandular involvement, fifty-five (63.9 per cent.) are alive from five to eight years after operation. Six of the patients had recurrences. Thirty-one (36.1 per cent.) are dead.

Of 132 patients (60.5 per cent.) with glandular involvement twenty-five (18.9 per cent.) are alive from five to eight years after operation; three had recurrences, and 107 (81.1 per cent.) are dead.

TABLE I
*Three, Five, and Eight Year Cures (218 Cases) **

Decades.	Pa- tients.	Alive three years after operation.	Alive five years after operation.	Alive from five to eight years after operation.
20 to 30 With glandular involvement ..	3	0	0	0
Without glandular involvement	1	1	1	1
30 to 40 With glandular involvement ..	16	4	1	1
Without glandular involvement	15	11	9	9
40 to 50 With glandular involvement ..	50	17	10	8
Without glandular involvement	25	20	16	16
50 to 60 With glandular involvement ..	28	10	8	8
Without glandular involvement	31	24	22	22
60 to 70 With glandular involvement ..	26	12	8	6
Without glandular involvement	11	7	6	5
70 to 80 With glandular involvement ..	9	5	2	2
Without glandular involvement	3	2	2	2
		113(51.8%)	85(39 %)	80(36.7%)
Total.... With glandular involvement ..	132	48(36.6%)	29(21.9%)	25(18.9%)
Without glandular involvement	86	65(75.6%)	56(65.1%)	55(63.9%)

* In thirteen cases the exact date of death was un known.

PERCENTAGE OF DEATHS OF PATIENTS UNDER AND OVER FIFTY, WITH AND WITHOUT GLANDULAR INVOLVEMENT

One hundred ten (50.5 per cent.) of the patients operated on were under fifty; sixty-nine (62.7 per cent.) had glandular involvement, and nine (13.0 per cent.) are alive from five to eight years after operation. Forty-one (37.3 per cent.) were without glandular involvement, and twenty-six (63.4 per cent.) are alive from five to eight years after operation.

One hundred eight (49.5 per cent.) were over fifty; sixty-three (58.3 per cent.) had glandular involvement, and sixteen (25.4 per cent.) are alive from five to eight years after operation. Forty-five (41.7 per cent.) were without glandular involvement and twenty-nine (64.4 per cent.) are alive from five to eight years after operation.

PATHOLOGIC FACTORS IN THE LONGEVITY IN CANCER OF THE BREAST

One of the most important questions involved in the entire subject of cancer is: Why do some patients live longer than others with grossly the same or even less local or general cancer? This question was emphasized in the study of a series of cases of gastric cancer,¹ in which it was found that patients with complete involvement of regional lymphatic glands often lived much longer than patients without regional glandular involvement, although as a general rule postoperative longevity is in inverse relation to the amount of glandular involvement. In one series of gastric cancers it was observed that two factors, cellular differentiation and lymphocytic infiltration, apparently play a part in the defensive mechanism against new growths. Thus patients without glandular involvement and with local lymphocytic infiltration lived, on an average, 124 per cent. longer postoperatively than patients without glandular involvement and without local lymphocytic infiltration, and patients with glandular and with local lymphocytic infiltration lived 146 per cent. longer than patients with glandular involvement without lymphocytic infiltration. The average length of postoperative life was increased 7.5 per cent. in the presence of cellular differentiation. When differentiation and lymphocytic infiltration were both present the average length of postoperative life was increased 82 per cent. These data represent averages and do not apply to all specific cases. As general facts, they give some clue to the defensive mechanism of the body against malignant neoplasms.

In the series of 218 cases of mammary cancer here reported it was found that death had occurred in 138. In ninety-one* of these cases complete pathologic material was preserved and studied in detail from the standpoints of cellular differentiation, lymphocytic reaction, fibrosis, and hyalinization (Tables II, III, IV, and V); the two latter possible defensive factors are in greater evidence in mammary cancer than in gastric cancer.

It will be remembered that neoplasia in the breast manifests itself in three reactions—primary, secondary, and tertiary cytoplasia,^{2, 3}—and that these stages are found with or without the presence of partial cellular differentiation, lymphocytic reaction, fibrosis, and hyalinization, the last three of which, we believe, represent either etiologic factors or a defensive mechanism. The conception that the presence of cellular differentiation is unfavorable to the continued growth of cancer cells is based on the unwritten law in general biology that power of cellular reproduction is inversely proportional to cellular differentiation. If this law is correct, cancer cells which show partial differentiation, as in 15 per cent. of the cases of mammary cancer studied, must of necessity grow less rapidly than cancer cells without differentiation.

The following generalizations may be made from the data studied con-

* All pathologic specimens were studied independently of any knowledge of the clinical histories or postoperative mortality. It was not until the pathologic observations were made and recorded that they were assembled with the preoperative and postoperative histories.

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TABLE II
Patients without Glandular Involvement at Operation who died

	Decades												Total		
	30 to 40			40 to 50			50 to 60			60 to 70					
	Years	Months	Days	Years	Months	Days	Years	Months	Days	Years	Months	Days			
Longest.....	4	5	2	5	5	16	4	5	0	3	9	20	5	5	16
Shortest.....	3	0	22	1	2	14	1	1	16	1	8	22	1	1	16
Average.....	3	5	19	3	4	9	2	3	11	2	7	23	2	2	17
Average with local lymphocytic infiltration alone.....	3	5	19	2	1	17	1	1	16	2	7	23	3	3	17
Average with local lymphocytic infiltration, hyalinization and fibrosis.....	3	5	19	1	5	2	1	1	16	2	5	19	3	3	23
Average without local lymphocytic infiltration, hyalinization and fibrosis.....	3	5	19	3	4	9	2	3	11	2	9	23	2	2	19
Average with cellular differentiation.....	3	5	19	4	5	10	2	3	16	2	7	23	2	2	15
Average without cellular differentiation.....	3	5	19	3	2	7	2	2	4	2	7	23	1	2	19
Average with local fibrosis.....	3	5	19	4	1	7	2	2	16	2	7	23	2	2	17
Average without local fibrosis.....	3	5	19	3	2	13	2	2	4	2	5	19	2	2	17
Average with local lymphocytic infiltration.....	3	5	19	3	3	5	3	1	6	2	9	19	2	4	17
Average without local lymphocytic infiltration.....	3	5	19	3	6	13	3	1	4	2	5	27	2	2	16
Average with local lymphocytic infiltration and fibrosis.....	3	5	19	3	3	5	3	1	6	2	9	19	2	4	16
Average without local lymphocytic infiltration and fibrosis.....	3	5	19	3	5	16	3	1	6	2	8	28	2	5	19
Average with local lymphocytic infiltration and hyalinization.....	3	5	19	1	3	2	2	3	6	2	5	23	2	3	15
Average without local lymphocytic infiltration and hyalinization.....	3	5	19	5	5	16	3	5	16	2	7	28	2	5	23
Average with local hyalinization.....	3	5	19	1	3	10	2	5	6	2	8	28	2	3	10
Average without local hyalinization.....	3	5	19	4	5	7	2	1	12	2	5	19	2	2	17

Postoperative life

TABLE III
Patients with Glandular Involvement at Operation who died

	Decades					Total
	20-30	30-40	40-50	50-60	60-70	
Cases.						
Without cellular differentiation	3(100%)	9(90%)	28(90%)	12(92%)	14(100%)	68(91%)
Without local lymphocytic infiltration	1(33.33%)	2(20%)	10(32%)	4(30%)	7(50%)	25(33%)
Without local hyalinization	2(66.66%)	6(60%)	17(54%)	5(37%)	6(42%)	36(48%)
Without local fibrosis	2(66.66%)	3(30%)	9(29%)	3(23%)	6(42%)	23(31%)
With local lymphocytic infiltration and local fibrosis	1(33.33%)	6(60%)	14(45%)	7(53%)	3(21%)	33(44%)
With local lymphocytic infiltration and local hyalinization	1(33.33%)	4(40%)	8(25%)	5(37%)	2(14%)	22(29%)
With local hyalinization and fibrosis	1(33.33%)	4(40%)	14(45%)	8(60%)	7(50%)	37(50%)
With local lymphocytic infiltration, hyalinization and fibrosis	1(33.33%)	4(40%)	8(25%)	5(37%)	2(14%)	22(29%)
Patients who Died and who were without Glandular Involvement at the time of Operation						
Without cellular differentiation	2(100%)	5(100%)	0	2(66.66%)		9(52%)
Without local lymphocytic infiltration	0	2(40%)	6(85%)	2(66.66%)		10(58%)
Without local hyalinization	0	2(40%)	3(42%)	1(33.33%)		6(35%)
Without local fibrosis	0	2(40%)	2(28%)	0		4(23%)
With local lymphocytic infiltration and local fibrosis	2(100%)	1(20%)	1(14%)	1(33.33%)		5(29%)
With local lymphocytic infiltration and local hyalinization	2(100%)	1(20%)	1(14%)	0		4(23%)
With local hyalinization and fibrosis	2(100%)	3(60%)	4(56%)	2(66.66%)		11(64%)
With local lymphocytic infiltration, hyalinization, and fibrosis	2(100%)	1(20%)	1(14%)	0		4(23%)

Total Number of Patients Dead

Without cellular differentiation	77(84%)
Without local lymphocytic infiltration	35(38%)
Without local hyalinization	42(46%)
Without local fibrosis	27(29%)
With local lymphocytic infiltration and local fibrosis	38(41%)
With local lymphocytic infiltration and local hyalinization	26(28%)
With local hyalinization and fibrosis	48(52%)
With local lymphocytic infiltration, hyalinization, and fibrosis	26(28%)

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TABLE IV
Patients with Glandular Involvement at Operation who died

	20 to 30		30 to 40		40 to 50		50 to 60		60 to 70		70 to 80		Total		
	Decades														
	Patients														
	3 10 31 13 14 3 74														
	Postoperative life														
	Years	Months	Days	Years	Months	Days	Years	Months	Days	Years	Months	Days	Years	Months	Days
Longest	3	1	10	4	0	3	5	0	1	5	0	4	8	4	7
Shortest	0	7	0	9	4	18	7	0	4	5	5	2	8	8	5
Average	1	7	21	5	4	16	2	4	14	5	10	9	8	3	17
Average with local lymphocytic infiltration	3	1	0	2	0	1	1	3	8	2	4	2	4	4	11
Average with local lymphocytic infiltration, hyalinization, and fibrosis	1	0	4	1	3	4	2	3	5	2	25	2	8	5	11
Average without local lymphocytic infiltration, hyalinization, and fibrosis	1	7	0	5	5	11	0	4	14	2	25	2	8	5	12
Average with cellular differentiation	1	6	21	5	3	20	4	4	27	4	10	4	8	4	18
Average without cellular differentiation	1	0	4	1	3	8	1	3	12	2	10	2	4	3	15
Average with local fibrosis	1	0	4	1	1	10	1	1	14	2	13	2	8	3	8
Average without local fibrosis	1	7	0	7	4	16	1	5	12	2	15	2	8	5	13
Average with local lymphocytic infiltration	2	0	17	2	4	16	1	2	6	2	7	2	8	5	18
Average without local lymphocytic infiltration	0	7	0	5	4	10	1	4	13	1	5	2	8	5	13
Average with local lymphocytic infiltration and fibrosis	1	1	0	7	2	14	1	4	13	1	21	2	8	5	12
Average without local lymphocytic infiltration and fibrosis	1	7	0	5	3	14	1	2	13	3	29	2	8	5	16
Average with local lymphocytic infiltration and hyalinization	1	0	4	1	3	17	1	2	17	1	25	2	8	5	15
Average without local lymphocytic infiltration and hyalinization	1	7	0	9	5	16	2	3	14	3	25	2	8	5	12
Average with hyalinization	1	0	4	1	2	16	1	2	16	2	14	2	8	6	15
Average without hyalinization	1	7	0	4	2	7	1	3	11	1	12	1	8	6	11

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cerning ninety-one patients who died in the series of 218 patients with mammary cancers:

1. Cellular differentiation occurred in 8.6 per cent.
2. Local lymphocytic infiltration occurred in 62 per cent.
3. Local hyalinization occurred in 54 per cent.
4. Local fibrosis occurred in 71 per cent.
5. Lymphocytic infiltration and fibrosis occurred in 41 per cent.
6. Lymphocytic infiltration and hyalinization occurred in 28 per cent.
7. Hyalinization and fibrosis occurred in 52 per cent.
8. Lymphocytic infiltration, hyalinization, and fibrosis occurred in 28 per cent.
9. The average length of postoperative life of patients with local lymphocytic infiltration alone was 28 per cent. greater than the average length of postoperative life of the ninety-one patients.
10. The average length of postoperative life of patients without local lymphocytic infiltration was 15 per cent. less than the average length of postoperative life of patients with local lymphocytic infiltration.

TABLE V
Postoperative Life of Patients Dead (Ninety-one)

	Years	Months	Days
Longest	7	0	3
Shortest	0	3	5
Average	1	8	24
Average with local lymphocytic infiltration alone	2	2	16
Average with local lymphocytic infiltration, hyalinization, and fibrosis. . . .	2	4	17
Average without local lymphocytic infiltration, hyalinization, and fibrosis. . .	1	4	17
Average with cellular differentiation	2	8	18
Average without cellular differentiation	1	8	22
Average with local fibrosis	1	10	13
Average without local fibrosis	1	3	20
Average with local lymphocytic infiltration	1	7	22
Average without local lymphocytic infiltration	1	10	20
Average with local lymphocytic infiltration and fibrosis	1	8	23
Average without local lymphocytic infiltration and fibrosis	1	8	21
Average with local lymphocytic infiltration and hyalinization	2	4	19
Average without local lymphocytic infiltration and hyalinization	1	8	20
Average with local hyalinization	1	10	14
Average without local hyalinization	1	6	21

11. The average length of postoperative life of the patients with lymphocytic infiltration, hyalinization, and fibrosis was 37.8 per cent. greater than the average length of postoperative life of the ninety-one patients as a group.

12. The average length of postoperative life of patients without lymphocytic infiltration, hyalinization, and fibrosis was 42 per cent. less than the average length of postoperative life of patients with lymphocytic infiltration, hyalinization, and fibrosis.

13. The average length of postoperative life of the patients with cellular

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differentiation was 57 per cent. greater than the average length of postoperative life of the ninety-one patients.

14. The average length of postoperative life of patients with fibrosis was 7 per cent. greater than the average length of postoperative life of the ninety-one patients, and 42 per cent. greater than that of the patients without fibrosis.

15. The average length of postoperative life of patients with lymphocytic infiltration and hyalinization was 44 per cent. greater than the average length of postoperative life of the ninety-one patients.

16. The average length of postoperative life of patients with fibrosis and hyalinization was 1.48 per cent. greater than the average length of postoperative life of the ninety-one patients, and 4.87 per cent. greater than the average length of postoperative life of patients without fibrosis and hyalinization.

CONCLUSIONS

1. The three greatest single factors in increased postoperative longevity of the ninety-one patients with mammary cancers are cellular differentiation, hyalinization, and fibrosis.

2. Lymphocytic infiltration alone does not appear to be the main factor.

3. It appears that while hyalinization and fibrosis play, individually, some part in increasing longevity in cases of cancer of the breast the two greatest known combined factors are cellular differentiation and hyalinization.

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