

THE TEN-YEAR SURVIVORS OF RADICAL MASTECTOMY

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A YEAR ago a paper¹ was presented to this Association containing the results of the operative treatment of carcinoma of the breast from 1913 to 1932, inclusive, and it has seemed desirable to present a further study restricted to the group of ten-year survivors of 1913 to 1923, inclusive. In this period of eleven years 115 patients were operated upon or, if incomplete operations are excluded, the number is 108. Of these twenty-eight have survived for periods of from ten to twenty years. The percentage of survivors of the ten-year period is just over 25 and it is interesting to see that the modern surgical results of different operators do not depart far from 25 per cent. for ten-year cures.

The surgeon, and particularly the friends of the patient, wish to know at the termination of the operation what the outlook is for life and health and in this paper we consider so far as possible the factors bearing on the prognosis, based on the work of others and a consideration of these twenty-eight cases.

Early Operation.—If treatment is neglected, the patients face a mortality rate of 100 per cent. Hence the sooner treatment is instituted the better the prognosis. This point needs no elaboration. But the practical point really is how are we to get the patients for earlier operation. There is considerable debate as to whether as a result of the campaign of publicity the patients are coming earlier than they did fifteen or twenty years ago. On this subject there is no unanimity of opinion. McCarty² has discussed this subject, using as evidence the size of the tumors of patients appearing at the clinic now and fifteen years ago. According to him, accurate measurements show no evidence that the size of the tumors coming to the clinic is less than in former years. Our own impressions are the same, based on the percentage of patients showing lymph-node involvement at the time of operation. This seems the more remarkable when one compares carcinoma of the breast with some other surgical diseases. For instance, our operations for acute appendicitis are now very largely performed within twenty-four hours of the appearance of symptoms. Twenty years ago this was certainly not the case. In looking over the list of thirteen carcinomas of the breast operated on within the last year, we find that ten of the thirteen showed glandular metastases. One patient had bilateral carcinoma; another carried the disease during the nine months of pregnancy; a third had a sloughing tumor scarcely suitable for palliative surgery; a fourth sought operation when axillary nodes were detected, no tumor having been detected in the breast; a fifth had a large tumor with involved glands and peau d'orange over the growth. Perhaps two

cases might be spoken of as fairly early. The cases of 1913 could have made no worse showing. Sometimes the delay is to be credited to the patient and perhaps necessarily as in the case in which the patient felt an axillary mass but could detect none in the breast. The physicians come in for their share of criticism. We do not blame them for their inability to diagnose early carcinomas especially when their type of practice leads them to see breast tumors infrequently, but what is shocking is that the physician, knowing himself inexperienced, is willing to assume the responsibility for observing these patients over varying periods until the diagnosis becomes conclusive. It may be that they go to their text-books of surgery and see pictures showing swollen arms, large and ulcerated tumors, carcinoma en cuirasse in general terminal conditions, the text-book not even mentioning that the breast cancers with which we can best surgically contend will show nothing in a picture. Strange to say, the private patients are not as a class arriving much earlier than the clinic ones. Some of the early cases come from the clinics and are discovered by the younger men of either medical or surgical training who have been disciplined in the making of routine thorough examinations. Another cause of delay is due to the submission of some of the cases to a trial of radiotherapy.

Functional Activity of the Breast.—At times it has been tacitly assumed that functional activity of the breast is detrimental and may in some way be concerned in the origin of a breast cancer. Lane-Clayton³ has investigated the subject statistically. She says: "We may therefore conclude that the fertility of the patients in the present investigation is definitely lower than for non-cancerous patients." Summers⁴ believes that carcinoma of the breast is proportionately more common in single than in married women of the cancer age and presents evidence based on a consideration of statistics showing the number of single and married women over thirty-five years of age in Pennsylvania. He has compared these with the deaths in the state from breast cancer and finds the single patients contributing a disproportionately large number of the total deaths. Among our twenty-eight survivors of operation 50 per cent. are known to have been single or married and childless and information is lacking regarding some of the rest. The statistics mentioned and our own would suggest that the child-bearing group has an advantage from the standpoint of tendency to breast cancer.

Prognosis as Related to Age of Patient.—There is a rather fixed belief that cancer in general proves more malignant in young persons than in those of later years and this has been maintained in particular of cancer of the breast. Some evidence has been presented to that effect but it has seemed to me that the anecdotal method has been depended upon to a large extent instead of statistical evidence. Sistrunk and MacCarty⁵ divided their 218 cases into those over fifty years of age and those under fifty years of age and they give a survival value of from five to eight years among the older group as 41.7 per cent. while the survivors under fifty years for a corresponding time was 31.8 per cent.—a very noticeable difference. Major

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Greenwood⁶ has analyzed 273 cases with regard to age, dividing the patients into ten-year groups beginning at twenty-five years, and he finds no great difference in the length of life among the younger, his conclusion being: "It will be seen that either there is no significant relation of age at onset and duration of life or at least these data are not numerous enough to establish it." Lane-Clayton³ has studied 2,006 cases and divides her subject into those under forty, forty to fifty-nine, and sixty or over and concludes: "The results obtained in this large series of cases show that the statement commonly made that the prognosis is worse in the young is erroneous." Lewis and Rienhoff⁷ also have divided their patients, numbering 573, into decades and find the ten-year survivors in each decade about the same except that those from seventy to seventy-nine have done better than the other groups as regards survival. Table I is based on an analysis of the twelve youngest

TABLE I

	Age	Node In- volvement	Grade	Duration of Life
Case 1.....	L 32	Yes	I	17 years
Case 2.....	L 26	No	I	8½ years
Case 3.....	L 28	No	II	7 years
Case 4.....	D 28	Yes	III	1 years
Case 5.....	D 31	Yes	III	3¼ years
Case 6.....	D 33	No	II	8 years
Case 7.....	D 28	Yes	II	2¼ years
Case 8.....	D 29	Yes	I	9½ years
Case 9.....	D 30	Yes	II	3½ years
Case 10.....	D 32	No	II	4 years
Case 11.....	D 33	No	III	1¾ years
Case 12.....	D 32	Yes	I	4 years
Average.....				5.83 years

Fifty-one cases with ages from fifty to fifty-nine lived 4.9 years average to date. Nine cases still living.

patients in my series of 230 operative cases. It shows three patients still living and an average length of life for the group up to date of 5.83 years. For comparison, fifty-three patients with ages of fifty to fifty-nine had an average length of life of 4.9 years. Nine of these patients are still living. We are not then quite in a position to compare averages in the two groups because some patients in each are still living. The former group of patients is too small to make a determination of the median length of life in the two groups of cases of much value. The median length of life for the fifty- to fifty-nine-year patients is just over 2.5 years, while seven of the twelve in the younger group have survived four years. These younger victims of cancer, then, have varied in grade of malignancy, lymph-node involvement and duration of life as have the older patients but in average and median duration of life have behaved as well or better than the older patients.

It is further of interest to note that the ten-year survivors have averaged but 48.5 years of age at the time of operation while the average for a series

of 200 patients operated upon was fifty-two. Hence the patients who have survived the longest have had an average age at operation distinctly less than the average age of all the patients afflicted with carcinoma of the breast. It is worthy of mention that there is considerable discrepancy in various groups of statistics as to the age of the beginning of symptoms of carcinoma of the breast. Daland,⁸ in his series of 100 untreated patients, gives 57.5 years as the age of onset of the disease. He mentions, however, that a series of figures of fifteen surgeons gives 50.1 as the average age of onset. The average age at the time of operation in our 230 cases has been fifty-two years. It is notoriously difficult in an individual case to obtain even an approximate idea of the duration of the disease. Our point is that the average age of our ten-year survivors is 48.5 at the time of operation, which is distinctly lower than the average age of onset of the disease as arrived at in the various statistical reports. The range of age of our ten-year survivors has been from twenty-nine to sixty-nine, and by no manipulation of the facts and figures can one arrive at the impression that the prognosis is worse in the younger cases.

Involvement of Axillary Nodes.—Next to early operation the question of axillary-node involvement would seem to be of most importance in estimating the prognosis. In our cases the glands have been involved in 67.3 per cent. Table II brings out the importance of gland involvement very clearly.

TABLE II

Prognosis as Related to Axillary Nodes

33 patients without nodes
19 surviving ten years or over—57½ per cent
1 has since died
77 patients with glands
9 surviving ten years or over—11.7 per cent
3 have since died of cancer

Of the nineteen survivors without glands all but one are now living from ten to twenty years while of the nine survivors with glandular involvement, four have since died and three of them from cancer. Harrington⁹ reports from The Mayo Clinic in a series of 2,557 cases that 52.9 per cent. of the patients without nodes were living ten years after operation while of those with nodes only 14.6 per cent. survived for ten years. There is no definite way of determining the average period intervening between the onset of cancer in the breast and the involvement of axillary nodes. There is no doubt, however, that individuals vary greatly in this respect. Sometimes six months has been suggested as an average time between onset and gland involvement. One thing is clinically quite certain that involvement of glands bears no definite relation to the size of the tumor. It does not depend on whether the tumor is mainly scirrhous, or medullary nor do I think that the size of the individual cells of the tumor bears any definite relation to the time of gland involvement. The largest individual cells can easily enough be transported through the lymphatics.

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Biopsy in Relation to Prognosis.—In neglected cases, diagnosis is easy. Clinical diagnosis early in the disease is notoriously difficult. We do well to learn early in our career that we are unable to make positive diagnoses in early cases though diagnosis is of the utmost importance. In the earliest cases we have only the age of the patient and the possible skin retraction to guide us. The importance of the former is that few breast masses except carcinomata begin after the age of forty-five. We are not in position to let time decide the question nor should we do radical mastectomies on innocent growths, hence the necessity of biopsies—and by this I mean only biopsies made with the stage set for the radical operation. As time has gone on we have felt more and more the need of making the pathologist an integral part of our operating-room team. The macroscopical appearance of the tumor is usually sufficient but certainty is what is needed; hence the necessity for confirmation of clinical opinion based on frozen section diagnosis. Sometimes it is suggested that the prognosis is impaired by biopsy. On the other hand, Eggers¹⁰ has maintained that the prognosis is improved if a discreet tumor is first widely excised preparatory to proceeding with a radical mastectomy. He thereby hopes to forestall dissemination during the manipulation incident to mastectomy. Assuming that we must do biopsies, we have to consider three procedures: incision of the tumor, wide excision, and simple mastectomy. All three of these have been resorted to one or more times in our ten-year survivors. The total number of biopsies on these ten-year cases has been 50 per cent. We would not advise incision even though the wound edges are immediately cauterized nor do we like simple mastectomies as it seems to complicate a subsequent radical operation more than a generous removal of the tumor would do. Experience with biopsies has not led to the conclusion that any harm has resulted from its employment and it seems as if it must be resorted to in all but the perfectly clear cases. Biopsy with an intervening period of days or weeks before radical mastectomy is done is undesirable from more than one standpoint.

The Pathology of the Tumor.—We have been accustomed to say that prognosis depends in large measure on the morphology of the tumor though nowadays we prefer to speak of the biology rather than the morphology, a consideration of the morphology being used to foretell the biology replacing the static term by a dynamic one. In past years it must be admitted that such terms as "medullary," "adenomatous" or "scirrhous" as applied to tumor have had no prognostic importance, neither were they related in any regular way to early or late lymph-node involvement. Greenough¹¹ has classified cases according to these characters and found them of no prognostic significance. On the other hand, the terms "gelatinous," "papillary" or "cystic" as applied to the tumor would suggest a malignancy below the average. In our twenty-eight patients surviving ten to twenty years, three are recorded as gelatinous carcinoma, one is now living, one lived ten years, another sixteen. And there are records of twenty and more years of survival. There was one of the sweat-gland type, the patient still living and well. The terms

“papillary” and “cystic” recur frequently in the reports, and “scirrhous” does also. Different portions of the same tumor may show widely different morphological appearances. On the other hand a metastasis in the glands may closely reproduce the characteristics of an original tumor. This brings up the subject of tumor grading, a subject which is still under investigation. The comparative factors are still only partly established. We have been fortunate in having the series of breast carcinomas graded by Dr. Cushman W. Haagenson, of the Institute of Cancer Research, New York. He graded the tumors of about 200 patients on whom I have operated and whose clinical history is known up to date but the grading has been done without knowledge of the clinical result till after the grading was complete. Table III shows

TABLE III
Grade of Malignancy—Ten-Year Survivors

Grade I	17 cases
Grade II	8 cases
Grade III	1 case
Not graded	2 cases
	28 cases
Total	28 cases

especially the frequency of Grade I of malignancy and that one patient who survived eighteen years and has died of apoplexy was in the third grade of malignancy with nodes involved. Table IV shows the factors which were considered in the grading and, though Haagenson’s own paper on the grading of these tumors should be referred to as giving the details of the methods, and

TABLE IV
A Plan for the Histological Grading of Carcinoma of the Breast
By Dr. C. W. Haagenson¹³

Cell morphology	{	Size of cells.	
		Size of nuclei.	
		Variation in size and shape of cells.	×
		Hyperchromatism.	
	{	Number of mitoses (average number per high-power field, 10 by 40 magnification, Zeiss).	×
Manner of growth of cells	{	Papillary character (papillary adeno-carcinoma arising in a cyst formed in a duct).	×
		Adenoid arrangement of cells (for form acini).	×
		Comedo character (growth mainly within ducts, often with central necrosis of cells).	×
Reaction of stroma	{	Secretory activity of cells (vacuoles in cytoplasm).	
		Fibrosis.	
		Hyaline degeneration.	
		Gelatinous degeneration.	×
	{	Lymphocytic infiltration.	

The characters marked × are found to be the most important ones in prognostic grading.

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their results, we have marked those which he has found most significant. It will be noticed that it is the characteristics of the tumor-cells rather than the reactions of the stroma which are of greater weight.

Among the twenty-eight survivors there have been nine patients who during their subsequent course have had recurrences. Four of these patients have died from carcinoma. To illustrate, a comparatively small group of patients who develop here and there metastases, usually near the first operative field, are then operated on from time to time for recurrences before exhaustion, ulceration, sepsis or internal metastases terminate the case. Only one patient of the group has died from intercurrent disease. She has succumbed within the past month, eighteen years after operation, at the age of seventy-six, from apoplexy. With few exceptions minor operations for local recurrences have accomplished little though one patient has survived her secondary operation for a tumor near the scar for ten years. It seems better to use radium or X-ray in such cases.

Bilateral Tumors.—There is something intriguing about the group of bilateral carcinomas. They occur in about 6 per cent. of breast cancer patients or, otherwise stated, they constitute about 9 per cent. of the total recurrences. It has impressed me that they belong to two groups. The first and larger is the group in which the carcinoma by permeation passes the middle line of the body to involve breast, skin, fascia and nodes of the opposite side—one or all. These tumors are clearly dependent upon the first tumor. The second group is no doubt smaller and impresses one as being composed of cases in which the patient develops a new tumor. Among our twenty-eight patients, four have developed tumors of the opposite breast with characteristics that make one think of new tumor. Sampson Handley¹² has called attention to cases in which the glands of the opposite axilla were involved without involvement of the opposite breast. Moreover, there is no group of so-called “trunk lymphatics” connecting the two breasts. In fact, we think of the lymphatics of the middle line of the torso as similar to the blood-vessels crossing the middle line and being in the main inconspicuous. The conditions which suggest that the second tumor is unrelated to the first are: First, the long interval between the first and second tumor; second, that there has been no evidence of recurrence on the side of the first operation; third, that the tumor at its origin has developed in mammary-gland tissue rather than in the subjacent fascia or lymph-nodes. One patient was seen eleven years after operation with a carcinoma of the opposite breast which spread to skin and axillary nodes and developed a local en cuirasse appearance. Another patient sixteen years after operation for a small carcinoma with a single axillary gland involved has four months ago been operated on by Dr. Jonathan Wainwright for a tumor fairly circumscribed in the opposite breast. Multiple carcinomata are now not infrequently recognized and they might be still more common were we more often successful in curing the first. It is a fairly general rule that locations in the body which are frequently the seat of primary growths are not the usual seat of meta-

stases and vice versa. For instance, we should not expect a carcinoma of the breast to metastasize to the lip or uterine body. A mention of two illustrative cases may not be amiss. A patient operated upon for carcinoma of the breast and with no signs of local recurrence died five years later following hysterectomy for carcinoma circumscribed in the uterine fundus. A patient with carcinoma of the cervix was operated upon seventeen years ago by abdominal hysterectomy and has this winter succumbed to thoracic metastases following a local removal of a carcinoma of the breast a year and a half previously. Moreover, though no great importance is attached to the observation, it may be said that the grading of the tumors and the characteristic microscopical picture has not always been the same in the first and second tumors.

It is difficult if not impossible to prove that carcinoma of the second breast is not a metastasis but when the interval is long and there is no sign of local recurrence, the presumption seems to favor the view of a second primary tumor. The fact that animals can be immunized to transplantable tumors would suggest that the factors of bodily resistance and perhaps a local susceptibility of tissue should be considered in these cases.

Summary.—The average age at which women are attacked with cancer of the breast has been variously stated at anywhere from forty-five to fifty-seven and a half years of age. The modal age of onset (Lewis and Rienhoff), that is, the year in which the greatest number of cases occur, is forty-seven, which probably is not very different from the average age of onset of the same cases as will be seen from an inspection of their graph. The average age of our cases at the time of operation is fifty-two years.

The average expectation of life if carcinoma of the breast is untreated is thirty-eight months (Greenwood) or forty months (Daland). The median duration of life (the time at which half the patients are living half dead) is less than this, and according to Daland is thirty months. The median duration of life following operation is scarcely three years though the average is considerably longer.

The abrupt fall in the percentage of survivors in the first, second and third years following operation is due largely to the lateness of operation with gland involvement of many of the cases and to some extent is due to the elimination of patients of higher grade of malignancy. About 40 per cent. of cases operated upon may be expected to live for five years and 25 per cent. for ten years. The deaths between the five- and ten-year period are mainly carcinoma and to a very small extent from intercurrent disease. If a patient survives for five years from the date of operation, her expectation of living five more is $62\frac{1}{2}$ per cent., and if her nodes are not involved at the time of operation, her expectation is even greater.

The group of five- and ten-year survivors will contain some cases of each grade of malignancy and some patients with glandular involvement but the favorable results will be largely confined to the patients with Grade I tumors

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as regards malignancy and who, at the time of operation, were without involvement of axillary nodes.

The younger patients, contrary to common belief, do quite as well following operation as the average patient. A few of the oldest develop a very slowly advancing type of carcinoma.

Biopsies must be done on early cases of carcinoma to prevent us from doing too much or too little for breast tumors.

Grading of tumors has developed a prognostic significance.

Gland involvement is still our most reliable factor in determining the prognosis, which is not very different from saying that the early cases do better than the later ones.

Patients may develop multiple malignant tumors either simultaneously or in sequence and it is quite likely that some of the late carcinomas of the second breast are not recurrences but new tumors.

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