

CLINICAL AND PATHOLOGIC CRITERIA AS A BASIS FOR CLASSIFYING CASES OF PRIMARY CANCER OF THE BREAST

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It is only by classifying cases of cancer that comparisons of the results of different therapeutic procedures can be analyzed equitably. There are many reports in the medical literature about the results of treatment of cancer of the breast in which cases are not classified, and therefore unjustifiable conclusions are drawn. Also, in some reports either clinical or pathologic criteria are the basis for statistical analyses. None of these classifications has been entirely satisfactory or generally accepted because of limited applicability.

Classification based solely on histologic criteria, such as one outlined by Ewing¹ or the "grading" plan of Broders,² is unsatisfactory because the histologic structure of most, if not all, of these neoplasms varies in many areas. The histologic name, or grade, given a tumor is subject to individual interpretation of microscopic sections examined but does not describe the whole tumor or the anatomic extent of involvement. Also, patients will survive with cancers considered to be highly malignant from the histology, whereas others will succumb from neoplasms of seemingly low degree of malignancy depending upon anatomic extent of involvement and whether or not the cancers can be eradicated.

Another classification has been based primarily upon pathologic evidence of the presence or absence of metastases in axillary lymph nodes. However, the degree of axillary involvement is most important. Also, there are other clinical and pathologic manifestations of prognostic significance.

Classifications of cases of cancers of the breast based only upon clinical criteria, such as those suggested by Steintal,³ Lee and Stubenbord,⁴ and the American College of Surgeons,⁵ have limited applicability. Physical signs alone may not indicate the extent of involvement. For example, the presence or absence of metastasis to axillary lymph nodes or elsewhere often cannot be settled clinically or even grossly at operation, yet is of considerable prognostic significance. The presence of metastases to axillary lymph nodes can be detected clinically in only about 50 per cent of cases proven to have metastases by microscopic examinations after radical mastectomies.

Another clinical classification of cases designates two groups as "operable" and "inoperable." This method, more than any other, has

been responsible for misunderstandings and controversies about the efficacy of different methods of treatment. These terms are ambiguous; surgeons cannot agree about their definitions because of different interpretations of the clinical signs, sometimes according to estimates of surgical skill. All cancers of the breast are technically "operable," and every Doctor of Medicine is legally qualified to operate. The terms "operable" and "inoperable" should be discarded, and "surgically curable" and "surgically incurable" substituted.

It must be conceded that the anatomic extent of involvement from cancer is the most important factor governing indications for and limitations of therapeutic procedures, curability or incurability, and therefore is the most logical basis for classifying cases. Anatomic extent of involvement can be ascertained best by taking into account all information available from both clinical and pathologic evidence.

When studying a series of cases of cancer of the breast 7 years ago for statistical analyses of the results and comparison of different methods of treatment, I used several of the methods of classification mentioned and found that none were suitable for the reasons indicated. After correlating the clinical findings with the pathologic evidences of extent of involvement, a new classification was developed with the co-operation of Dr. Allen Graham, Director of the Department of Surgical Pathology.

According to this plan cases were divided into three groups, or stages, on the basis of both clinical and pathologic criteria.^{6,7,8} Subsequently, it was found advisable to subdivide the third group to make a fourth for cases having physical or roentgenologic signs of distant metastases when first examined.⁹ The reason for this designation of a fourth group is that the results of operations alone cannot be compared with those of irradiation for patients with distant metastases because operations with the objective to cure are not performed but irradiation may be given for palliation.

In its present improved form the classification being proposed for primary cases of cancer of the breast is arranged as follows:

Group or Stage I

Skin—not involved.

Tumor—localized in breast and movable.

Metastases—none in axillary lymph nodes or elsewhere.

Group or Stage II

Skin—not involved.

Tumor—localized in breast and movable.

Metastases—few axillary lymph nodes involved, no other metastases.

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Group or Stage III

Skin—edematous; brawny red induration and inflammation not obviously due to infection; extensive ulceration; multiple secondary nodules.

Tumor—diffusely infiltrating breast; fixation of tumor or breast to chest wall; edema of breast; secondary tumors.

Metastases—many axillary lymph nodes involved or fixed; no clinical or roentgenologic evidences of distant metastases.

Group or Stage IV

Skin—as in any other group or stage.

Tumor—as in any other group or stage.

Metastases—axillary and supraclavicular lymph nodes extensively involved, and clinical or roentgenologic evidences of more distant metastases.

When this classification was applied to a series of 1000 cases of cancer of the breast, the incidence of each group, or stage, and the 5 year survival rates were found to be approximately as follows:

Incidence	Survival Rates	
	Operations only	Operation and Irradiation
Group I —25%	90%	90%
Group II —25%	50%	65%
Group III—30%	5%	15%
Group IV—20%	5%	10%

This analysis not only proved the applicability and equitability of this classification for statistical comparisons, but also explained the indications for and limitations of different methods of treatment.

Group I—It seldom is possible to distinguish clinically between benign and malignant tumors of the breast that are small, localized, and movable if the skin is normal and no enlarged axillary nodes are palpable. Excision (not incision) and immediate microscopic examinations are indicated. Radical mastectomies may be indicated when tumors are found to be malignant to ascertain whether or not axillary lymph nodes are involved. Every node removed should be examined microscopically.

In 25 per cent of the cases having radical mastectomies, metastases to axillary nodes were not demonstrated. Of these approximately 90 per cent survived 5 years without clinical evidence of cancer whether or not irradiation was given. But about 10 per cent were not cured. Some of these had cancers that did not metastasize to axillary nodes but elsewhere, as may happen especially from inner quadrant tumors which may extend primarily to the parasternal nodes; in others neoplastic

cells may have passed through the axillary nodes to lodge in other regional groups; in a few axillary metastases may have escaped the careful scrutiny of the pathologist.

Since patients without axillary metastases (Group I) rarely develop local recurrences, and since there was no difference in the high percentage of survivals of those having operations alone and those having operation plus irradiation, it was concluded that immediate postoperative irradiation is unnecessary for patients in this category.

Group II—There is adequate statistical evidence that the prognosis is less favorable for patients with small, localized, movable cancers of the breast, without skin or muscle involvement and with metastases in only a few axillary lymph nodes, than for patients with similar tumors but with no axillary extension. In some with small cancers one or two quite large nodes may be palpable and no others involved, but in a majority with few nodes involved the condition cannot be detected clinically but only at operation or by microscopic examination.

These cases are on the borderline between curability and incurability. In our series 25 per cent of the patients having radical mastectomies alone had localized tumors, not involving skin or muscle but with metastases in only a few axillary lymph nodes (Group II). Of those having radical mastectomies alone 50 per cent survived 5 years clinically free from cancer, and 50 per cent died. Very few had local recurrences, but those who died must have had extension beyond the anatomic limits of surgical excision at the time of operation. Since it is impossible to be sure whether or not extension has taken place beyond the axillary lymph nodes when these are involved, it has been concluded that immediate postoperative irradiation should be given routinely. The irradiation may delay neoplastic growth and prolong life although it may not necessarily cure. The possible benefits are indicated by Group II cases of which 50 per cent of those having operations alone survived 5 years, but about 65 per cent of the patients receiving irradiation lived that long, suggesting that the treatment was beneficial.

Group III—The prognosis is less favorable for those with metastases in numerous axillary lymph nodes (Group III) than for those having few nodes involved (Group II). Two types of cases in our series of cancers of the breast were placed in Group III.

In some patients the tumors clinically appeared to be quite localized with little or no involvement of the skin and muscles, few or no palpably enlarged axillary lymph nodes and without evidence of distant metastases, but after operations and microscopic examinations metastases were found in numerous nodes. Many of these patients were obese. Undoubtedly, radical mastectomies were justified yet did

not cure. Some Group III cases had local recurrences, but distant metastases developed sooner or later in all because extension had taken place beyond the axillary lymph nodes and the anatomic limits of surgical removal. Therefore, it was concluded that postoperative irradiation should also be given to patients with metastases in any axillary lymph node.

The second type of case in this category (Group III) had unmistakable physical signs of cancer of the breast but none of distant metastases. These patients are the type about which there is the most disagreement and controversy about "operability" and "inoperability." In our experience they also were incurable; many developed local recurrences and all had distant metastases sooner or later.

These types of cases with numerous axillary nodes involved, with or without clinical evidences of incurability and without demonstrable distant metastases, constituted 30 per cent of our series. Only 5 per cent survived 5 years after operations alone, and none were free from cancer. There is statistical evidence that the average natural duration of life for women with untreated cancer of the breast is about 3 years, and 5 per cent live 5 years.^{6,7} Also there is evidence that a high percentage of patients with the clinical and pathologic manifestations tabulated in Group III, when subjected to radical mastectomies do not live so long as the natural duration of life of untreated cases. This indicates that operations may shorten the lives of some patients. Therefore, it has been concluded that patients with clinical manifestations of incurability should not be subjected to radical mastectomies but should be treated by irradiation alone.

Irradiation may not cure Group III cases, but it may delay extension and prolong the lives and economic usefulness of some. Approximately 15 per cent of the patients in this category survived 5 years, although not cancer free, following operations and postoperative irradiation, whereas only 5 per cent survived as long if operations were the only treatment. It is justifiable to conclude that patients with clinical manifestations of incurable cancer of the breast will survive as long or longer than the average natural duration of life of untreated cases if no operations are performed and irradiation alone is given.

Group IV—All patients with tumors in their breasts, with or without physical signs of cancer, should be examined clinically and roentgenologically for distant metastases in lungs and bones before therapeutic procedures are instituted. Some patients with no, or even minimal, physical signs of cancer have distant metastases, although most patients with metastases will have clinical manifestations of incurability. In our series 20 per cent had distant metastases when first examined. It

is difficult to justify performing radical mastectomies upon patients with distant metastases no matter what may be the condition of the breasts. Irradiation alone should be given for palliation to the breast, regional lymph node groups, and the metastases. Irradiation of the ovaries to inhibit their function has proven to be of benefit in some cases.

Groups III and IV together included approximately 50 per cent of all cases in our series. This observation led to a study of analogous clinical and pathologic manifestations of cancer that they presented. These are tabulated in simple form as the "criteria of incurability" as follows:^{6,7,8}

The skin

Edema ("orange" or "pig skin") of more than slight extent; ulceration of more than slight extent; brawny red and inflamed not obviously due to infection; multiple secondary nodules.

The breast

Diffuse edema; diffuse infiltration; multiple secondary tumors; fixation to chest wall.

Metastases

Axillary lymph nodes numerous, extensively involved and fixed; supraclavicular lymph nodes involved or edema of arm; distant metastases (bones, lungs, or other viscera).

Others who have studied large series of cases of cancer of the breast have found the same relative proportion of incurable cases and similar clinical and pathologic manifestations of incurability.^{9, 10, 11} These criteria of incurability should be sought for, and patients with them should not be subjected to radical mastectomies but should be given irradiation for palliation and prolongation of life and economic usefulness.

It may have been noted that preoperative irradiation has not been discussed. The analysis of our series does not indicate to what types of cases this procedure is applicable.

It seems illogical to give preoperative irradiation to patients with tumors in their breasts who clinically present no manifestations of involvement of skin, muscles, or axillary lymph nodes, and no conclusive evidence of benignity or malignancy. Preoperative irradiation can be of no benefit for benign tumors and is unnecessary for cancers still localized within the anatomic limits of surgical removal. Therefore, it has been concluded that immediate operations are indicated under these circumstances (Groups I or II), with postoperative irradiation for those with metastases in the axillary lymph nodes (Group II).

On the other hand, patients with cancers of the breast that have produced clinical manifestations of incurability have extension beyond

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the anatomic limits of surgical removal (Groups III and IV). No amount of irradiation that can be given by modern technics can minimize this extent of involvement nor bring it within the anatomic limits of surgical removal, although it may delay growth temporarily. In our experience, as has been reported by others, even after seemingly adequate irradiation of cancers of the breast, viable neoplastic cells remained, both in the tumor and in axillary lymph nodes although the tumors and nodes were reduced in size and some neoplastic cells destroyed. Therefore it has been concluded that since patients with the criteria of incurable cancer of the breast have extension beyond the anatomic limits of surgical removal, whether or not irradiation is given, they should not be subjected to radical mastectomies after irradiation, or at any other time, but treated by irradiation alone.

SUMMARY

1. A classification for primary cases of cancer of the breast based on both clinical and pathologic criteria is proposed for statistical reviews and as a basis for determining the indications for different methods of treatment.

2. The clinical and pathologic criteria of incurable cancer of the breast are tabulated.

3. The indications and limitations of operations and irradiation are discussed on the basis of the classification proposed and the criteria of incurable cancer of the breast.

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