To the Editor:

I have read with great interest the controversy on operable breast cancer in a series of articles by Drs. Anglem, Leber and Crile in the November/December 1973 issue of Ca–A Cancer Journal for Clinicians, pages 330-340. As a researcher who has been interested in statistical data analysis for some time, I find the claims of these authors highly misleading and even erroneous. Further, I am surprised that even though the authors are involved in experimental study and claim to have collected statistical data, they are apparently unfamiliar with the basic techniques of statistical data analysis and design of experiments.

The controversy centers around the superiority of the method of treatment for operable breast cancer for which a 10-year survival rate is the only criterion. Putting aside the bias which may exist in their experiments (which may be discussed more appropriately by a clinician), I would like to comment on the inadequacy of the criteria used. Consider an experimental study where there are only two patients, A and B. Patient A is treated with simple mastectomy and patient B with a modified radical mastectomy. If after 10 years, patient A survives and B does not, the 10-year survival rate for simple mastectomy is 100 percent and for modified radical mastectomy, zero percent. This immediately indicates that erroneous conclusions can be drawn if the treatments are compared based on percentages alone—the underlying reason being that the decision is based on too few samples. In the above example, although simple mastectomy was found to be superior for the two patients, we are essentially interested in determining how these techniques will compare for patients operated on in the future. In such problems, the techniques of statistical inference are useful where one tries to infer generalities from specific observations.

Let us now examine Table 1 from Drs. Anglem’s and Leber’s article which reports the 10-year survival rates for Dr. Crile’s 226 patients with breast cancer, operated on between 1955 and 1959.

Based on the 10-year survival rates as given in Table 1, it has been claimed that simple mastectomy is a superior technique over modified radical mastectomy. For convenience, the data in Table 1 is presented below in a slightly different fashion in Table 2.

| Author | Method of Treatment          | Number of Cases | Surviving 10 Years |
|--------|------------------------------|-----------------|--------------------|
| Crile  | Simple Mastectomy            | 133             | 41%                |
| Crile  | Modified Radical Mastectomy  | 93              | 30%                |

All Cases 36.5%

| Method of Treatment          | 10-year Survival |
|------------------------------|------------------|
|                              | Yes   | No   | Total |
| Simple Mastectomy            | 55    | 78   | 133   |
| Modified Radical Mastectomy  | 26    | 65   | 93    |

Total 83 143 226
Once the above data has been obtained, we are interested in testing the hypothesis that the two variables—method of treatment and 10-year survival—are independent. If method of treatment is independent of 10-year survival, then the proportion of patients who did survive 10 years after simple mastectomy should be the same as the proportion of patients who also survived 10 years after modified radical mastectomy. The procedure is to study the sample proportions and determine whether or not they are "significantly" different. The statistic used to compare the proportions is a Chi Square ($X^2$) statistic.

Simple computations show the hypothesis of independence is accepted (computed $X^2 = 2.98$, critical $X^2 = 3.84$ at five percent level of significance). In other words, we do not have sufficient evidence to say that the 10-year survival of a patient is dependent on whether the patient undergoes simple mastectomy or modified radical mastectomy.

My purpose in writing is to emphasize the increasing importance and application of statistics in medicine, which is evident from the numerous articles published not only in medical journals, but also in computer and engineering publications. Valuable classical statistical methods have been adapted for use in medical research and a quick perusal of the many available tests in biostatistics indicates that the repertoire of the statistically conscientious, working medical researcher is substantial indeed. Finally, I strongly believe that there is a substantial need for more rigorous and cautious analysis of medical data.

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To the Editor

I enjoyed the interchange with Drs. Anglemi and Leber in the November/December 1973 issue of *Ca—A Cancer Journal for Clinicians*. I’d like to point out, however, that when I mentioned a 12 percent difference in survival between patients who received no treatment and those who underwent the most radical treatment, I was referring not to the treatment of the breast, but rather to the axillary nodes. The remark was perhaps written unclearly and was open to misrepresentation. I certainly believe that surgery significantly improves the patient’s prognosis.

George Crile, Jr., M.D.
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To the Editor:

From recent electron microscopy, mammography, whole and bilateral organ and other investigations, it could be implied that the natural history of epithelial breast carcinoma, like any other epithelial structure, progresses sequentially from proliferation to dysplasia, to in situ, to microinvasion and then eventually to the clinically familiar macroroinvasion. This natural growth, like cancer of the uterine cervix, may span twenty years or more, as shown by backtracking, kinetic or biomathematical studies and clinical observations.

It is well known that extirpation of the so-called Clinical Stage I primary lesions has resulted in prolonged short-term survivorship but paradoxically the mortality ratio has not changed since Halsted’s time. Apparently, we have been uncovering the disease in its earlier phases, thus improving immediate survival time, but not early enough to catch the disease at a pre-seeding stage to ensure permanent cure.

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