EDITORIAL

It’s Too Soon To Know

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As I read the paper “Sector Resection With or Without Postoperative Radiotherapy for Stage I Breast Cancer: A Randomized Trial,” by Holmberg and colleagues (1), I found myself distressed that it had been accepted for publication, since I believe that it is premature to make the interpretations for which the study was designed and that the authors make. While not changing my view on premature interpretation, I have, on reflection, somewhat modified my opinion as to the appropriateness of publication at this time. The focus of this study is to determine whether, with careful selection of discrete lesions combined with a surgical technique designed to encompass them with pathologically determined free margins, it is possible to spare patients postoperative radiotherapy of the breast and still avoid local recurrence. A second question is whether a difference in the likelihood of local recurrence will result in a concomitant difference in distant metastasis and, ultimately, in survival.

Let us review this study. T1 breast cancers without pathologic evidence of axillary lymph node involvement were included. A variety of criteria were used to assure that the study involved only discrete lesions and was free from multifocal tumors or those with extension to the surgical margins. Only 50% of all patients with stage I breast cancer fulfilled the criteria for inclusion. It is important to note the extent of patient selection because this gives us some evidence of the scrupulousness of the selection technique and, if appropriate, the limitations on the applicability of this technique for all patients. The study began in 1981 and has a mean follow-up time of approximately 33 months in the irradiated group and 29 months in the nonirradiated group. This seems to be too short a period of observation on which to publish any conclusions or recommendations. Despite this very brief follow-up, I am impressed with the high actuarial local recurrence rate in the nonirradiated group (7.6% at 3 yr). There were a total of 15 local recurrences. Eleven of these were in the nonirradiated group, and of the four in the irradiated group, three occurred in patients who did not receive or complete the treatment; therefore, there were 11 in the nonirradiated group and only one in the group actually irradiated. This is quite a large difference! It emphasizes the limitations of the selection techniques and/or the surgical procedure used. The authors interpret this result in a curious way. They believe the recurrence frequency to be low, and indeed it is, by comparison with the results from the B-06 protocol of the National Surgical Adjuvant Breast and Bowel Project (NSABP) (2,3). But the latter study utilized a lesser surgical procedure, did not use such stringent criteria for inclusion, and treated lesions up to 4 cm in size.

Holmberg and colleagues, I believe, have forgotten a basic rule in cancer therapy: “The good news always comes first.” With further time, the number of recurrences cannot decrease. It will either stay the same or, more than likely, increase. Whether this increase will be proportional to the current large differences between groups, only time will tell. If it is proportional to the large differences seen, then clearly the conclusions already suggested should be reconsidered, just as they were in B-06. Such a large number of local recurrences in a mean follow-up time of only 29 months is disturbing and surely does not suggest “that for women with small unifocal tumors without axillary lymph node involvement, a meticulous surgical technique may be an alternative to surgery plus routine radiotherapy” (1). My conclusion, if I were to make any at all at this time, would be that, despite careful patient selection and scrupulous surgical dissection, there have already been 15 local recurrences and a projected rate of such recurrences of 7.6% at 3 years, suggesting that either the method of selection or the surgical technique utilized are not likely to produce sufficient local control so that radiotherapy can be avoided.

We might consider the second question now, i.e., whether a difference in local recurrence affects distant metastases and ultimate survival. There were 11 recurrences in the nonirradiated group and four in the irradiated group, a difference of seven. If this difference were to result in a difference in distant metastases, the most it could account for is a difference of seven. In fact, there were 15 patients with distant metastases in the nonirradiated group and nine in the irradiated group, a difference of six, suggesting, if we are to follow this logic, that the difference of seven in local recurrence might have accounted for the excess of six patients with distant metastases. This number is surprisingly large. The crucial question one might ask is: “Are those the same patients?” Unfortunately the question is not answered, but it is germane to the study. The important point here is that, with such a small number of recurrences, it is impossible to determine whether or not they affect the likelihood of distant metastases. Fortunately, the number of patients who have died of breast cancer is too small to interpret at all. There are only 10 deaths due to breast cancer, six in the nonirradiated group and four in the irradiated group.

This study was designed to determine whether careful selection and detailed surgery could make a difference in local recurrence rate and whether such a difference would affect survival. The data appear to suggest that there is a difference in local control. Whether this difference will persist, become larger, or disappear remains to be seen, and whether such a putative difference might have a concomitant effect on distant metastases is unknown. I am reminded of the title of a song popular during my youth, “It’s Too Soon To Know.” It might even be too soon to publish.

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