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Dear Editor:

We were very much pleased by the paper "Survival Following Locoregional Recurrence After Breast Conservation Therapy for Cancer" by Stotter et al., vol. 212, no. 2, pp 166–172. It is certainly difficult to believe that a local recurrence after breast-conserving treatment (BCT) for breast cancer would not bear the inherent risk of metastases and subsequent death, just like a second primary. Until now, only one empirical study has confirmed the hypothesis that, in the long run, survival after local recurrence would be impaired.[1]

We want to make some remarks with regard to the methods applied.

(1) No distinction was made between local (confined to the breast), locoregional (in both breast and lymph nodes), and regional (localized only in the lymph nodes) recurrences. This is certainly not appropriate, because the essential difference between mastectomy and BCT is the possibility of recurrence in the preserved breast. Regional recurrences are not more frequent after breast-conserving treatment than after mastectomy. The treatment of the axilla is the same in both treatment modalities. It would have been more appropriate to perform this procedure for local and locoregional recurrences only. Now the relative survival deficit after BCT due to locoregional recurrence in comparison with mastectomy is probably overestimated.

(2) The validity of the exponential model applied (also known as the DEALE) is not shown. This model, using a decreasing exponential function for survival, assumes that the hazard rate is constant.[2,3] This is probably not the case in breast cancer, especially not in the first 5 to 10 years after diagnosis.[4] Furthermore, Beck et al. showed that a decreasing exponential survival function to estimate the life expectancy (which is the inverse of the hazard rate) only was valid in diseases with hazard rates exceeding 0.1 per year; otherwise mortality will be overestimated.[2] It is possible to compute the yearly mortality forces or hazard rates from the monthly values mentioned in the paper of Stotter et al. simply by multiplying them by a factor of 12. The yearly hazard rates, recalculated in this way, equal approximately 0.01 per year for stage 0 patients, 0.032 per year for stage I patients, 0.05 per year for stage II patients, and 0.11 per year for stage III patients. Thus, the real survival deficit due to local recurrences will be somewhat lower than suggested in the paper.

(3) The really important point is not whether the survival deficit exists, but whether it is clinically important, if it exists. This might be explored by a clinical decision analysis, in which mathematical models can be applied to model the possible survival deficit, but also other factors, such as age of the patient and quality of survival, can be integrated to come to a balanced judgment about the potential impact of the local recurrence risk on the lives of breast cancer patients.

References

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Dear Editor:

We would like to thank Drs. Verhoef and Stalpers and Prof. van Daal for their interest in our paper.

Taking their points in sequence:

(1) In the part of our paper in which we compared the outcome in those of a cohort of patients with locoregional recurrence with the rest, we were able to take into account the site (breast and/or axilla) and extent of recurrence because we had that detailed information about our patients' recurrences. Thus, in our mathematical model, we apportioned a hazard for locoregional recurrence according to its "stage." A smaller hazard was apportioned for a small breast recurrence not involving skin, and a larger hazard as tumor size increased, if poor-prognosis local features were present, and particularly if lymph nodes were involved (even if no breast recurrence was evident). When assessing the results of published trials, such detail was not possible because the precise location and extent of locoregional recurrences have not been included in the publications.

(2) Gore et al. showed that hazard rates for treated breast cancer patients are higher for higher-stage disease, increase during the first 1 to 4 years, and then decline and converge on a constant level. The initial rise was negligible for small tumors, however, the hazard rate being essentially constant with time, indicating that the exponential curve is a good approximation in early-stage disease. The exponential model was chosen mainly for its simplicity, however. Our calculations then could be simple and, although the choice of curve influences the details of the predictions, it does not alter the overall pattern. We hoped thereby that our potential audience would not be put off: we wanted to obtain the attention of a wide range of clinicians, including those unfamiliar with such use of mathematical formulae and detailed statistical analysis. Our purpose was to reopen the issue of local recurrence and its possible impact on survival. Choosing the most accurate mathematical form to model the survival curve was considered less important than getting the overall message across.

If the choice of the exponential curve has led to an overestimate of the hazard related to locoregional recurrence, our ignoring second and subsequent recurrences will have led to underestimation. The two may well balance out.

(3) We agree with the final points. We did not intend our paper to indicate that breast conservation treatment for early breast cancer should be eschewed. We are suggesting a small risk affecting a minority of patients. It will regularly be outweighed in the older patient, the unfit, and particularly in the woman keen to preserve her breast.

Reference

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