Tailoring surgical decisions in breast cancer

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In the last 35 years, advances in our understanding of the natural history of breast cancer have brought about a revolution in the treatment of the disease. Major aspects of the revolution are advances in locoregional treatments; changed timing of treatments; implementation of new techniques to provide more accurate prognoses; and more refined targeting of systemic treatments.

We can also characterise this revolution in terms of a change of attitude: in the 1970s, the approach was to give the maximum tolerated treatment in the hope of arresting the disease. As a result of these advances it is now possible to give the minimum effective treatment, so as to preserve the integrity of the body.

These changes were made possible by studies which demonstrated that conservative treatment is effective [1,2]; that sentinel node biopsy accurately stages the axilla [3,4]; that biopsy of the internal mammary nodes is feasible and can refine the prognosis [5,6]; that a complete radiotherapy course can be given in the operating room, and limited to the tumour area to greatly reduce the dose to important adjacent tissues [7–9]; the preoperative chemotherapy can permit breast conservation in cases of locally advanced disease [10]; and that breast reconstruction techniques can extend indications for conservative surgery, as well as improving cosmetic outcomes [11].

Various trials have demonstrated that survival after conservative surgery plus breast radiotherapy is indistinguishable from that after mastectomy; and although recurrences may increase with some types of conservative surgery, there is still no effect on survival [1,2]. The new paradigm of minimum effective treatment is resulting in better quality of life for treated women, and this is encouraging other women to present for earlier diagnosis and treatment, further improving long-term outcomes.

One of the most exciting conservative approaches in breast cancer surgery is sentinel node biopsy (SNB). Axillary dissection by itself does not improve prognosis, but is important for staging. Ample studies on SNB have shown that histological analysis of the sentinel node provides accurate information for determining the status of the entire axillary region.

In the first series of 376 patients who underwent the sentinel biopsy technique at our institute, the first node draining the tumour area (sentinel node) was identified and removed in 99% following injection of 99Tc-labelled micro-aggregate close to the tumour, and use of a gamma detector during surgery. The patients then underwent complete axillary dissection. The study showed that the sentinel node technique had an overall accuracy of 96.8%, a sensitivity of 93.3% and specificity of 100%.

From 1998 to 1999 we randomised 516 patients in a controlled study comparing SNB with immediate axillary dissection. In the SNB arm, axillary dissection was performed only in cases with a positive sentinel node; those with a negative received no further treatment. After a mean of five years of follow-up there are no differences in the two arms in terms of local recurrence, axillary recurrence, or distant metastases. Because of these studies it is now possible to avoid axillary dissection in many breast cancer patients, greatly reducing the sequelae associated with complete axillary dissection. Currently, patients with early breast cancer who are clinically node negative are managed with SNB; if the sentinel node is tumour free, then axillary lymph node dissection is not performed. It is expected that the indications for SNB will further expand.

More accurate histopathological analysis of the sentinel node has increased the proportion resulting positive for axillary involvement, and it may be that not all should receive axillary dissection. For example, the prognostic significance of the finding of micrometastases only in the sentinel node is currently under investigation. Using a radioactive tracer, it is also possible to identify a sentinel node in the internal mammary chain. This node can be removed during breast surgery with the aid of a probe and analysed to further refine the prognosis.

The current standard of care for early operable breast cancer is quadrantectomy or lumpectomy followed by a 5- to 7-week course of whole-breast radiotherapy. However, there is evidence that it is sufficient just to treat the tumour bed with radiotherapy since that is where most residual tumour cells are located. Using a mobile linear accelerator with a robot arm that delivers an electron beam, the required radiotherapy can be given in a single dose of 21 Gy intraoperatively. It has been shown that this is equivalent to 60 Gy delivered in 30 fractions at 2 Gy/fraction. Intraoperative radiotherapy has the advantages that exposure to the skin and lung is greatly reduced, that chemotherapy, if indicated, no longer delays radiotherapy, while the problem of difficult access to radiotherapy centres is solved. In women previously irradiated for Hodgkin' s disease, intraoperative radiotherapy can be used to avoid repeated irradiation of the whole breast, thereby permitting conservative surgical treatment (otherwise mastectomy would have to be given). In cases where conservative treatment is not feasible, another application of intraoperative radiotherapy is in nipple sparing mastectomy to sterilise the areola-nipple complex (which is at increased risk of harbouring malignant cells) and hence permit immediate breast reconstruction with a prosthesis.

Finally, in the near future, it is expected that assessment of tumour gene expression profiles will allow more precise assignment of the risk of metastasis, allowing more refined tailoring of treatment options (and not simply surgical options) for breast cancer.

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