

Does our better understanding of breast cancer also improve the way we treat it?

Riccardo Ponzone

Division of Gynecological Oncology, Fondazione del Piemonte per l'Oncologia (FPO), Institute for Cancer Research and Treatment at Candiolo (IRC@C), Italy

Corresponding to: Riccardo Ponzone, MD, PhD. Division of Gynecological Oncology, Institute for Cancer Research and Treatment at Candiolo, Strada Provinciale 142, Km 3.95, 10060 Candiolo, Italy. Email: riccardo.ponzone@irc.it.



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The evolution of breast cancer therapy is a paradigm of the application of the scientific method to improve the length and quality of life of our patients (1). Each of the major steps forward that have occurred over the last century was started by the courageous ideas of leading scientists, carried on by the clinical trial machinery with the invaluable help of the patients themselves and finalized by the scientific community with the actual adoption of changes of practice based on the results of such trials.

This precious alliance between patients and clinicians has allowed to refute the *Halstedian* principle of radical surgery with the demonstration that mastectomy and breast conserving surgery (BCS) are associated with the same overall survival (2,3). The paper by Showalter *et al.* (4) confirms that the scientific community actually accepted these results as it shows a progressive decline in the proportion of stage I breast cancer patients from the Surveillance, Epidemiology, and End Results (SEER) database who were treated with mastectomy from 1998 to 2007 in the United States. Nevertheless, looking more in depth to the results of this study, the picture they draw is rather disappointing and clearly indicates that there is still much room for improvement in the way we treat our patients. Indeed, all significant predictors of being treated with mastectomy either cannot be justified by scientific reasons (single/divorced, white race, geographic region, estrogen receptor negativity) or point to the wrong direction (smaller tumor size).

Even more worrying is the under-utilization of radiotherapy (RT) after BCS. In fact, a 20% rate of RT omission is quite high, even in this group of patients at

generally favorable prognosis. No subset of patients has been clearly identified for whom RT can be safely omitted after BCS to date and a recent meta-analysis has confirmed that RT halves the recurrence rates and is also associated with 3.8% absolute reduction of breast cancer deaths (5). Therefore, although the retrospective design and the limited information on tumor and patient characteristics suggest caution when interpreting the results of the study by Showalter *et al.* (4), the lower survival reported in patients submitted to BCS who did not receive RT is not surprising. Moreover, the recognition that BCS is more likely to be performed incorrectly compared to mastectomy is not new. Nattinger *et al.* showed that between 1983 and 1995 the proportion of women undergoing an inappropriate form of BCS (omission of radiotherapy, axillary node dissection, or both) in the SEER database increased from 10% in 1989 to 19% at the end of 1995, while inappropriate forms of mastectomy remained stable at about 2.7% (6).

Other challenges are in front of us when we translate the results of recent randomized trials into everyday clinical practice. The equivalence between sentinel node dissection (SLND) and axillary dissection (AD) in patients with a negative sentinel node has been extensively demonstrated (7). More recently, in the American College of Surgeons Oncology Group (ACOSOG) Z0011 study the omission of AD has proven to be safe even in patients with a positive SNLD, provided that only 1-2 sentinel nodes are positive and radiotherapy is administered after breast conserving surgery (8). The latter study is rapidly changing the practice of many specialists, as well as the recommendations of scientific societies (9,10). Nevertheless,

retrospective studies suggest that the rate of loco-regional relapse is higher in patients with positive as compared to negative SNLD when completion AD is omitted, even if only micro-metastases are found in the sentinel node (11). Furthermore, very little is known on the omission of AD in patients who do not fulfill the entry criteria of the Z0011 study, like those who undergo mastectomy or those with a high risk of positive non-sentinel nodes. Finally, the loss of prognostic information on the total number of metastatic nodes provided by completion AD may alter indications to adjuvant treatments (12), and disorient the physicians towards either the abuse or underuse of radiotherapy and/or chemotherapy (13).

The final message that can be taken from the paper by Showalter *et al.* (4) is that continuous auditing of our clinical practices is essential in order to avoid that potential improvements of patient care based on the results of clinical trials may fail when transferred to the “real world” of our everyday clinical practice. As an example, data from the SEER database show that, although the proportion of women affected by early breast cancer treated with mastectomy decreased from 40.1% to 35.6% between 2000 and 2005, it subsequently increased to 38.4% in 2008 ($P < 0.0001$) (14). Many reasons may explain the very recent rise of mastectomy rates in the United States, such as the diffusion of screening mammography (15) and preoperative magnetic resonance of the breast (16) or the unquestionable appeal of modern nipple-areola sparing mastectomies followed by immediate reconstruction (17). As this is all happening without even a hint of indication that more mastectomies will mean more lives saved, it is vital to avoid that our prejudices may hinder the reality. Otherwise, we will never be able to understand whether the direction that we take will actually benefit the patient or will only satisfy our pride.

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