

The efficacy of early cystoprostatectomy is not in question [6, 7] but most surgeons have avoided this route, no doubt questioning its justification in older patients whose chance of remaining progression-free after 5 years is perhaps 60% [2].

Not surprisingly, the divergence of opinion is founded on uncertainty. Because of the relative scarcity of T1 G3 disease there have been no large series reported, so the crucial questions remain unanswered: what is the true risk of progression? Are some forms of the disease more at risk than others? To what extent do conservative treatments reduce the risk?

The report in the current issue of the *European Journal of Urology* from the Dutch South East Urological Oncology Group on 121 patients with T1 G3 bladder cancer — twice the size of any previously reported study — is therefore welcome. Interesting points emerge but, frustratingly, the answers to the above questions remain elusive. The superficial recurrence rate following TUR alone in T1 G3 disease is confirmed as approaching 80%. Adjuvant therapy with intravesical agents or radiotherapy has a modest effect on reducing recurrence rate, and this benefit may be durable. The only independent determinant of recurrence is the presence of multiple and multifocal tumours at the outset. Whereas the progression rate was fairly high in patients with recurrent disease, 43%, the overall progression rate was only 25% after a median follow-up period of 4 years. Of those who died, only 36% did so from bladder cancer. These figures give little support to the early cystectomists. Performing radical surgery on patients with recurrent disease seems justifiable. It will not obviate disappointments however. A report from Uppsala described a series of patients who progressed from superficial disease where 43% showed progression at first recurrence [8].

Presumably because progression was a relatively uncommon event in the current series, Mulders *et al.* have not performed a multivariate analysis on this end point. Gloomily they point out that treatment had no influence on rate of progression. Was

treatment not determined by severity of disease? They claim not, which is surprising since a recent survey in the U.K. [5] found that whereas 86% of urologists would treat with TUR alone when a single tumour was present, 37% would choose this treatment when there were multiple tumours and only 17% when there was associated carcinoma *in situ* — a condition which was present in 24% of the Dutch pT1 G3 patients. Also, as only 17 of their patients received radiotherapy, it is to be expected that the trend towards the lower progression rate in this group was not significant. The point is well made, however, that apart from an unacceptably aggressive policy of early radical surgery, there is no certain way of saving lives in T1 G3 transitional cell carcinoma of the bladder.

In the past, clinical uncertainty has been an important impetus to recruitment into randomised trials. Let us hope that current and future studies addressing the question of management of this dangerous condition will be supported.

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Breast Conservative Surgery: Towards More Personalised Treatments

A. Costa and A. Filiberti

INTRODUCTION

A CENTURY after the publication of Halsted's paper on mastectomy, the approach to primary breast cancer treatment has dramatically changed as a result of two "conceptual revolutions" in the 1970s. The first concerns the biological concept of breast

Correspondence to A. Costa at the Breast Cancer Division, European Institute of Oncology, via Ripamonti 435, 20141 Milan, Italy.
A. Filiberti is at the Psychological Division, National Cancer Institute, via Venezian 1, 20133 Milan, Italy.
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cancer as a systemic disease involving a complex spectrum of host-tumour interrelations. This is in stark contrast to the concepts of Halsted's thesis, and was proposed by Fisher in 1970 [1, 2]. This new concept ushered in the era of combined treatments for breast cancer, providing a rationale for adjuvant chemotherapy and other systemic approaches. The second major innovation, developed in Europe and at the Milan Cancer Institute since 1968, was the idea of preserving the breast in patients with small tumours. This hypothesis was verified in the first randomised trial (1973) to address the issue and the results were published by Veronesi *et al.* in 1981 [3]. The new technique

was called quadrantectomy, and its main characteristic is the radial direction of the incision so that resection can encompass the whole ductal tree of the gland. The Veronesi procedure includes a total axillary dissection, and is followed by irradiation of residual mammary tissue and the scar. The results of the Milan study were subsequently confirmed by other investigators [4-6] who used different techniques (segmental mastectomy, lumpectomy, tumorectomy) all followed by radiotherapy.

Conservative surgery has proven to be as effective as mastectomy in terms of survival and disease-free interval. Mastectomy is, therefore, a procedure no longer supported by biological and clinical evidence [7].

DIFFERENT PROCEDURES OF BREAST CONSERVATIVE SURGERY (BCS)

The most important issue to be addressed in BCS is the quantity of breast tissue (mammary gland and skin) to be removed. The quadrantectomy proposed by Veronesi and colleagues [8] is a considerably more extensive operation than the lumpectomy reported in the study by Fisher's group [9]. The question is whether this difference has implications for the rate of local recurrence, as this unfavourable event is always very distressing for the patient and for her physician, although it has not been demonstrated to affect survival adversely [10]. A randomised study comparing quadrantectomy with a much less extensive procedure called "tumorectomy" followed by intensive, partly intestinal radiotherapy was conducted at the same Milan institute in the 1980s [11]. Survival was similar in the two groups of patients, but there were significantly more local recurrences among those treated with tumorectomy and radiotherapy.

Another important variable is radiotherapy. In an attempt to reduce the length and intensity of treatment, the role of surgery without radiotherapy has been explored. However, both major studies in this field [12, 13] have shown that, in young women, limited surgery offers only incomplete protection against local recurrence, and that postsurgical radiotherapy is essential. Similar results are obtained in intraductal carcinoma, where breast irradiation is also more appropriate than lumpectomy alone [14].

In contrast, in older women, a more extensive operation such as quadrantectomy may be sufficient to prevent local recurrence without a need for radiotherapy, whereas this may not be true for a simpler operation such as lumpectomy [13].

In conclusion, while it is now widely accepted that mastectomy and BCS followed by radiotherapy provide comparable and adequate degrees of local control in the management of early breast cancer, the issues of how to avoid local failures and of how to involve the patient in the decision are yet to be fully addressed. In our opinion, the two problems are interrelated, since the fear of recurrence is one of the major factors influencing the decision of both physician and patient about the type of surgery.

PSYCHOLOGICAL ASPECTS

A number of studies have tried to compare the emotional adjustment to mastectomy and to breast-preserving techniques and, although most data indicate that different procedures do not necessarily lead to significant differences in the overall psychological adjustment of the patient, BCS appears to be a better option with regard to body image and sexuality [15, 16]. In almost all papers on BCS, however, the authors refer to lumpectomy as a standard technique, and not to other procedures like quadrantectomy or segmentectomy, and this may have affected some of their conclusions, since the significant

difference between the two main techniques is that cosmetic results are better in patients with lumpectomy, but local recurrence is less frequent in patients with quadrantectomy [17]. In fact, Margolis reported that the most important psychological factor affecting a woman's choice of lumpectomy and radiotherapy is a degree of anticipated concern about adverse effects on her body image [18]. Alternatively, despite the apparent cosmetic advantage of saving the breast, concerns about recurrence and death may influence women to choose mastectomy [19]. These patients feel that removal of the whole breast will give greater protection against recurrence, but it has never been demonstrated by scientific observation or shown by clinical experience that the fear of recurrence decreases over the years in a patient who underwent ablative surgery. Clinical practice shows how distressing the scar of mastectomy is, and how hard it is to see the outcome of this operation for the first time.

Fallowfield and colleagues report that the burden experienced by breast cancer patients from either mastectomy or BCS is similarly rated [20]. Since we share Fisher's opinion, that "mastectomy is a procedure no longer supported by biological and clinical evidence" [7], we feel that such a generic message may have negative consequences on breast cancer management because it might encourage those doctors who prefer ablative surgery to avoid offering patients the option of BCS, even in cases with small tumours. We would like to stress that the nature of the psychological investigation can be very important in influencing the results of these studies. For example, Fallowfield and colleagues stated that both psychiatric morbidity (anxiety and depression) and the overall psychological adjustment (including sexuality and body image) are similar in both groups, but they used only a single self-reported item on the Rotterdam checklist to rate sexual function. We are convinced that not only the fear of local recurrence but also sexual aspects deserve far more attention.

SHOULD THE PATIENT DECIDE?

In a recent comment in this journal, Morris stressed the need for patients to be fully involved in making the decision about the type of surgery [21]. A few studies have shown that offering a choice of surgery did not have any adverse effects on patients, and those who were involved in decision-making experienced less anxiety and depression postoperatively than those who were not offered a choice [15, 20]. However, a potential problem with offering a choice of treatment is that patients may assume responsibility for the outcome of the chosen treatment [20]: patients who develop local recurrences after a conservative operation may feel they made the wrong decision or, as Morris suggested, those who elected to have a mastectomy may, in the longer term, wish they had undergone BCS.

Our opinion is that the debate on whether to involve the patient in the decision on the kind of surgery is too limited, especially if the discussion is on the choice between ablation and conservation. We agree with Fisher when he says that "patient autonomy will not be compromised and paternalism will not be resurrected" if physicians tell patients that, in almost all cases, mastectomy is no longer justifiable [7].

Of course, if women who are offered a choice are told that the tumour could recur locally in 2% of mastectomy-treated breasts and in 15% of breasts treated with wide excision and radiotherapy, as in the Wolberg study [22], then the issue will be biased by the doctor's form of presentation. However, if it is accepted that BCS combined with radiation therapy provides equivalent survival along with superior cosmetic results, then

the real problem is to identify the optimal breast conservation technique.

The extent of surgery of the two main breast-saving procedures, lumpectomy and quadrantectomy, differs considerably, and in the future, it will be important to identify markers contained within the tumour, and be able to predict which patient will have recurrences and which patient with ductal carcinoma *in situ* will have an invasive or a metastatic disease [23]. The Council on Scientific Affairs of the American Medical Association recently stated that the optimal technique for providing local control has not been established by randomised clinical trials [24], and that particularly lacking are data to determine the minimal tumour-free margin required in BCS. However, when it states that "curvilinear incisions that follow skin crease lines are preferred to radical incisions", the Council implicitly excludes quadrantectomy from the group of possible BCS techniques, since this procedure is generally performed with a radial incision to remove an extensive portion of tissue, following the mammary gland tree structure which radiates from the nipple to the periphery. Alternatively, quadrantectomy complies with the other recommendation of the AMA ("skin flaps should be centred over the tumour to be excised and should be thick"), since the European procedure includes a portion of skin overlying the tumour and the underlying fascia [3, 6].

CONCLUSIONS

The treatment choice for early breast cancer should no longer be between mastectomy and BCS, but among different therapeutic approaches, all of which are breast-saving procedures. Simple lumpectomy gives the best cosmetic results, but insufficient protection from local recurrences, even if followed by radiation therapy. Although it is accepted that local failures do not necessarily determine or indicate a fatal prognosis, they remain a very distressing event for the patient, and the risk should be as low as possible. Quadrantectomy has been shown to be a safer procedure as regards local relapse, but in some cases, e.g. tumours in the upper inner quadrants of small breasts, it gives unsatisfactory cosmetic results [25]. The extent of quadrantectomy might be reduced in the future by the use of primary (preoperative) chemotherapy [26], and cosmetic results improved by separate incisions for the removal of the quadrant and the axillary dissection.

Further efforts are needed to abandon over-mechanistic approaches, to identify innovative staging systems [27], and to increasingly personalise breast cancer treatment by actively involving the patient in decisions about the best possible treatment modality for her individual and specific situation.

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