

Papers

Surgical Resection Plus Tamoxifen as Treatment of Breast Cancer in Elderly Patients: a Retrospective Study

Gabriele Martelli, Daniele Moglia, Patrizia Boracchi, Ivan Del Prato, Emanuele Galante and Giuseppe De Palo

Between March 1982 and May 1989, 151 women with primary breast cancer ranging in age from 70 to 91 years (median 79), were treated with conservative surgical procedure followed by adjuvant tamoxifen. Surgery was performed under local anaesthesia without axillary node dissection. The median duration of follow-up was 60 months (range 36–124). There were six local, six ipsilateral axillary node and six distant relapses. Local recurrences were successfully managed with further surgery whereas axillary node relapses required radiotherapy in 3 cases, surgery in 2 cases and hormonal treatment in 1 case. 2 patients died of progression of disease and one of unrelated conditions. The 5-year relapse-free survival rate was 0.82. This treatment option in elderly patients yields an acceptable local control and reduces the risks of major surgery.

Eur J Cancer, Vol. 29A, No. 15, pp. 2080–2082, 1993.

INTRODUCTION

THE BEST treatment of elderly patients with operable primary breast cancer is currently a matter of intense debate. It has been questioned whether tamoxifen as the sole treatment could be as effective as surgery. In support of this is the fact that breast cancer in the aged tends to be well differentiated, with a greater incidence of oestrogen receptor positivity, thus determining a high responsiveness to anti-oestrogen therapy. An increased operative risk due to concomitant diseases in this age group supports this policy. Conversely, uncontrolled studies so far published [1], in which patients were followed up for at least 5 years, showed that tamoxifen alone did not control local disease in more than 60% of patients, with a high rate of cases that required second-line treatment. Two prospective randomised trials [2–3] compared surgery with tamoxifen in elderly patients. Gazet [2] found no difference in survival between the two groups and concluded that tamoxifen was as effective as surgery. Robertson [3] also showed no difference in survival between wedge mastectomy and tamoxifen, but a significant number of the tamoxifen-treated patients required subsequent surgery because of local progression of disease. Given the uncertainty about optimal treatment for patients over 70, we analysed retrospectively the results of 151 elderly patients with primary breast cancer who underwent surgery and tamoxifen as adjuvant treatment during a 7-year period.

PATIENTS AND METHODS

151 breast cancer patients aged over 70, treated with surgery under local anaesthesia and tamoxifen were selected from the clinical records of the Istituto Nazionale Tumori of Milan in a period between March 1982 and May 1989.

The criteria for eligibility in the analysis were the following: patients aged over 70 with T1–T2–T4b [4] operable breast cancer without palpable nodes in the axilla. Synchronous bilateral carcinomas, previous neoplasms treated in a period less than 10 years from breast surgery, intraductal carcinoma and non-invasive lobular carcinoma were excluded from this analysis.

In all patients, breast cancer was diagnosed by a clinically palpable mass subsequently confirmed by mammography and fine-needle aspiration cytology. Chest X-ray and bone scan were routinely performed to exclude distant metastases.

114 patients underwent wide lumpectomy, 32 patients quadrantectomy and 5 patients total mastectomy, all without axillary dissection. The surgical technique of wide lumpectomy and quadrantectomy has been described previously [5–6]. Total mastectomy constituted excision of the breast leaving the muscles and axilla undisturbed. Tamoxifen was administered as adjuvant therapy after surgery at the dose of 10 mg twice a day, indefinitely. Tumour oestrogen receptors (ER) and progesterone receptors (PgR) were assayed by using the dextran-coated charcoal technique [7] and receptor concentration was evaluated according to Scatchard [8]. Tumours with a receptor concentration below or equal to 10 or 25 fmol/mg cytosol protein were considered, respectively, as ER negative (ER–) or PgR negative (PgR–), whereas tumours with receptor content above such values were considered as receptor positive (ER+, PgR+). All patients were regularly followed-up at 4–6 month intervals and the median follow-up was 60 months (range 36–124). Relapse-free survival time was defined as the time elapsed between the date of surgery and the date of the first unfavourable event (local,

Correspondence to G. Martelli.

G. Martelli, D. Moglia, I. Del Prato, E. Galante and G. De Palo are at the Division of Diagnostic Oncology and Out-patient Clinic, Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan; and P. Boracchi is at the Institute of Medical Statistics and Biometry, University of Milan, Istituto Nazionale Tumori, Milan, Italy.

Revised 25 June 1993; accepted 29 June 1993.

Table 1. Characteristics of the study population

	No. of patients
Total cases	151
Median age (years)	79 (range 70–91)
T1	112
T2	29
T4b	10
Invasive ductal carcinoma	105
Invasive lobular carcinoma	29
Invasive ductal and lobular carcinoma	3
Mucinous carcinoma	5
Papillary carcinoma	5
Tubular carcinoma	1
Other histotypes	3
ER positive	126/133
PgR positive	113/132

axillary and distant relapse, ipsilateral and contralateral breast cancer, second primary) or the date of the last clinical contact. The relapse-free survival curve was estimated by the Kaplan and Meier method [9]. The annual rates for local and axillary relapses were obtained as follows $\hat{\lambda} =$

$$\frac{e}{n \sum_{i=1} t_i}$$

where e = number of events, n = number of patients, t_i = time of follow-up for patient i (in months).

RESULTS

Clinical characteristics of the study population are reported in Table 1. Briefly, clinical stage at presentation showed T1 size in 112 patients, T2 in 29 patients and T4b in 10 patients. Pathological findings demonstrated infiltrating ductal carcinoma in most cases (70%), invasive lobular carcinoma in 19%, ductal and lobular carcinoma in 2% of the cases. Other histotypes accounted for 14 cases (9%). ER and PgR contents were available in 133 and 132 cases, respectively. 126 patients (95%) were ER positive, 113 were PgR positive (86%) and 109 (83%) were positive to both tumour receptors. The 60-month relapse-free survival rate was 0.82 with a 95% confidence interval (0.75–0.89) (Fig. 1).

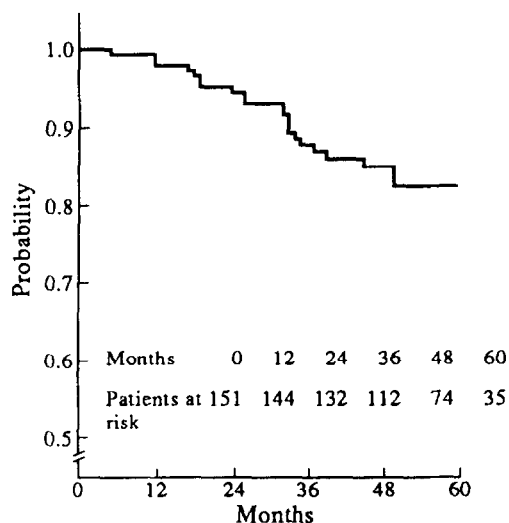


Fig. 1. Relapse-free survival. Whole case series.

Table 2. Relationship between pT and site of recurrence

Pathological stage	Local	Recurrence Ipsilateral axillary node	Distant	Total
pT ₁	5	4	3	12
pT ₂	1	1	2	4
pT ₄	–	1	1	2

Local recurrence occurred in 6 cases (annual rate 1%) at a mean of 39 months (range 12–101). 6 cases (annual rate 1%) developed ipsilateral axillary recurrence within 49 months and 6 patients (annual rate 1%) had distant metastases at a mean time of 28 months (range 25–31). Table 2 shows the relationship between pathological size and site of recurrence. Two ipsilateral (annual rate 0.33%) and three contralateral (annual rate 0.50%) breast cancers were documented at 18, 50, 12, 33, 38 months, respectively, after surgery. A second primary tumour occurred in 2 patients (one colon and one endometrial cancer). All 6 cases with local relapse were managed with further local excision. 1 case subsequently developed distant metastases and died from the disease. In the 6 cases with ipsilateral axillary recurrence, control of disease was achieved with axillary dissection in 2 cases, radiotherapy in 3 cases and further hormonal treatment (megestrol acetate) in 1 case. 1 case died from further progression of disease and 1 from unrelated conditions. The 2 cases with ipsilateral breast cancer were managed with total mastectomy and 1 patient died from a second primary. All 3 cases with contralateral breast cancer were treated with quadrantectomy and 1 patient died from a stroke 4 years after surgery. All 6 patients with distant metastases were treated with a second-line hormonal treatment (aminoglutethimide or megestrol acetate), and radiotherapy was delivered in 2 cases to prevent pathological bone fractures. 4 patients died from disease. Out of the 126 patients who did not develop any recurrence, 23 (18%) died from intercurrent diseases.

DISCUSSION

The results of this retrospective study, the first of a large series of elderly patients treated with wide local excision and adjuvant tamoxifen, showed a locoregional recurrence rate not higher than that reported for patients submitted to more radical surgical approaches [10–12].

Our patient group did not have axillary dissection in the presence of clinically negative nodes, with a very low axillary relapse rate at a median follow-up of 60 months. When examining the value of treating axillary nodes in patients with breast cancer and clinically negative axillary involvement, Fisher *et al.* [13] reported that, out of 40% of the patients treated with simple mastectomy expected to have pathological involvement of the axilla, only 18% developed clinically positive nodes and required a delayed axillary dissection. It is still unclear whether locoregional treatment of the axillary nodes incurs a real advantage in disease-free survival and overall survival in patients with breast cancer. Particularly in the elderly, the importance of axillary dissection is controversial because of an increased death rate due to concomitant diseases, and a high response rate to hormonal therapy.

The low rate of local relapse in the present series represents an interesting and remarkable result. Only 6 women out of 151 (4%) experienced a recurrence of the primary tumour. This

result challenges the usefulness of postsurgical irradiation, particularly in patients generally reluctant to comply with radiotherapy protocols. Such a relapse rate is considerably lower than that observed by Bates *et al.* [14] who compared various surgical treatments followed by adjuvant tamoxifen with tamoxifen only. Two other prospective randomised trials [2–3], comparing surgery with tamoxifen, found a high rate of patients who developed local recurrences after surgery without adjuvant tamoxifen. Reed *et al.* [15] found a locoregional recurrence rate of 35% in patients treated by wide local excision only. The selection of patients for this study included cases with clinical axillary involvement, a large proportion of T2 tumours, and the surgical procedure was probably inadequate to obtain an oncological local radicality. Such a recurrence rate in our series appears to be related to a high hormonal receptor content, a higher proportion of patients (74%) with tumours less than 2 cm in pathological size, and an appropriate conservative approach consisting of a surgical clearance of at least 2 cm from the tumour margins.

Many studies [16–19] concerned with older age groups have shown that tumours rich in oestrogen receptors might be well controlled by tamoxifen for a long period of time, and that in a subgroup of patients, hormonal therapy might be considered an effective alternative treatment. However, since life expectancy in this age group is rather long, tamoxifen as sole therapy should be left only to patients seriously ill or who decline to undergo surgical treatment.

Whether conservative surgery, mainly represented by wide local excision, in day hospital regimen followed by tamoxifen may substitute conventional surgery for elderly patients presenting operable breast cancer is not known. The data of this retrospective study add weight to the view that a subgroup of elderly breast cancer patients, represented by patients with tumours of small size, rich in oestrogen receptors and without clinically axillary involvement, may be satisfactorily controlled by conservative procedure and tamoxifen for long periods.

Furthermore, treatment in a day hospital regimen can improve quality of life, reduce the number of patients requiring hospitalisation, resulting in significant saving in costs, and yield a highly acceptable treatment rate in patients generally reluctant to be hospitalised.

1. Horobin JM, Preece DE, Dewar JA, Wood RAB, Cuschieri A. Long term follow up of elderly patients with loco regional breast cancer treated with tamoxifen only. *Br J Surg* 1991, 78, 213–217.
2. Gazet JC, Markopoulos CH, Ford HT, Coombes RC, Bland JM,

- Dixon RC. Prospective randomised trial of tamoxifen versus surgery in elderly patients with breast cancer. *Lancet* 1988, i, 1679–1681.
3. Robertson JFR, Todd JH, Ellis IO, Elston CW, Blamey RW. Comparison of mastectomy with tamoxifen for treating elderly patients with operable breast cancer. *Br Med J* 1988, 297, 511–514.
4. Hermanek P. and Sabin LH. *TNM Classification of Malignant Tumours*. International Union Against Cancer. Berlin, Springer, 1987.
5. Galante E, Cerrotta A, Martelli G, Del Prato I, Moglia D, Piromalli D. Treatment of breast cancer in elderly women: retrospective analysis of 111 wide lumpectomies performed in a day hospital regimen between 1982 and 1988. *Tumori* 1992, 78, 111–114.
6. Veronesi U, Saccozzi R, Del Vecchio M, *et al.* Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. *N Engl J Med* 1981, 305, 6–11.
7. Ronchi E, Granata G, Brivio M, Coradini D, Miodini P, Di Fronzo G. A double-labeling assay for simultaneous estimation and characterization of estrogen and progesterone receptors using radioiodinated estradiol and tritiated ORG 2058. *Tumori* 1986, 72, 251–257.
8. Scatchard G. The attraction of proteins for small molecules and ions. *Ann NY Acad Sci* 1949, 51, 660–672.
9. Kaplan EL, Meier P. Non parametric estimation from incomplete observations. *J Stat Ass* 1958, 53, 457–481.
10. Robertson JFR, Ellis IO, Elston CW, Blamey RW. Mastectomy or tamoxifen as initial therapy for operable breast cancer in elderly patients: 5-year follow-up. *Eur J Cancer* 1992, 28, 908–910.
11. Toonkel LM, Fix I, Jacobson LH, Bamberg N. Management of elderly patients with primary breast cancer. *Int J Radiat Oncol Biol Phys* 1988, 14, 677–681.
12. Robins RE, Lee D. Carcinoma of the breast in women 80 years of age and older: still a lethal disease. *Am J Surg* 1985, 149, 606–609.
13. Fisher B, Redmond C, Fisher ER. Ten year results of a randomised clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *New Engl J Med* 1985, 312, 674–681.
14. Bates T, Riley DL, Houghton J, Fallowfield L, Baum M. Breast cancer in elderly women: a Cancer Research Campaign trial comparing treatment with tamoxifen and optimal surgery with tamoxifen alone. *Br J Surg* 1991, 78, 591–594.
15. Reed MWR, Morrison JM. Wide local excision as the sole primary treatment in elderly patients with carcinoma of the breast. *Br J Surg* 1989, 76, 898–900.
16. Bradbeer J, Kyngdon J. Primary treatment of breast cancer in elderly women with tamoxifen. *Clin Oncol* 1983, 9, 31–34.
17. Helleberg A, Lundgren B, Norin T, Sander S. Treatment of early localised breast cancer in elderly patients by tamoxifen. *Br J Radiol* 1982, 15, 511–515.
18. Allan SG, Rodger A, Smyth JF, Leonard RCF, Chetty U, Forrest AP. Tamoxifen as primary treatment of breast cancer in elderly or frail patients: a practical management. *Br Med J* 1985, 290, 358.
19. Margolese RG, Foster RS. Tamoxifen as an alternative to surgical resection for selected geriatric patients with primary breast cancer. *Arch Surg* 1989, 124, 548–551.

Acknowledgement—We thank Miss Nicoletta Rossi for her skilled technical assistance.