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Papers

Breast Conservation is the Treatment of Choice in Small Breast Cancer: Long-term Results of a Randomized Trial

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From 1973 to 1980, 701 women with small breast cancer (less than 2 cm in diameter) were randomized into two different treatments. 349 patients received classic Halsted mastectomy and 352 patients received quadrantectomy, axillary dissection and radiotherapy on the ipsilateral breast. 24.6% of the patients in the mastectomy group and 27.0% of the patients in the conservation group had axillary metastases. Overall 10 year survival was 76% in the Halsted patients and 79% in the quadrantectomy patients; 13 year survival was 69% and 71%, respectively. No differences were observed after analysis by site and size of the primary tumour and age of the patients. Patients with positive axillary nodes had consistently better survival curves in the quadrantectomy group compared with the Halsted group (not significant). Among the quadrantectomy patients there were 11 local recurrences (with 4 deaths) while among the Halsted patients, 7 had local recurrences (5 deaths). There were 19 cases of contralateral breast carcinomas in the quadrantectomy group and 20 in the Halsted group. At 16 years from the beginning of the trial no evidence of oncogenic radiation risk was observed. In patients with small size carcinomas total mastectomy should have no role.
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INTRODUCTION

CONSERVATION of the breast in patients with small size breast cancer is much debated. At the Milan Cancer Institute from 1973 to 1980, we did a randomized trial of patients with small breast carcinomas, comparing the classic Halsted mastectomy with radiosurgical treatment to conserve the breast. Early results, which showed the validity of the conservative treatment, were reported in 1981 [1] and updated in 1986 [2]. The impact on breast cancer treatment was considerable but slow since, in the opinion of many surgeons, the results needed longer follow-up. It was suggested that patients might have unfavourable events many years after the operation, that the number of women who, after conservative treatment, would need salvage mastectomy for a local recurrence should be evaluated and that to evaluate any oncogenic risk of breast irradiation a very long follow-up is required.

For these reasons, all the patients who participated in the trial were carefully followed up so that, 16 years from the beginning of the study, we present a final assessment of the results.

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PATIENTS AND METHODS

Patients (less than 70 years old) with clinical and mammographic evidence of a breast carcinoma of less than 2 cm in diameter and without palpable axillary nodes were eligible for the trial. Eligible patients had an excisional biospy in the operating theatre under general anaesthesia and, if the diagnosis of a carcinoma of less than 2 cm was confirmed at frozen section examination, the patients were randomized to the Halsted mastectomy or to the conservative procedure. The conservation treatment was defined as 'quadrantectomy', which removes the primary tumour with a 2–3 cm margin of normal mammary tissue *en bloc* with the overlying skin and the underlying muscular fascia. Axillary dissection was total in all cases and was done in continuity with the quadrantectomy when the primary carcinoma was in the outer-upper quadrant. All patients in the quadrantectomy group had, within a month after surgery, radiotherapy to the ipsilateral breast (50 Gy with high energy plus 10 Gy as a boost with orthovoltage). Quadrantectomy plus radiotherapy was called QUART.

From 1973 to 1975 all cases with positive axillary nodes of both arms were randomized into no further treatment and adjuvant radiotherapy on supraclavicular and internal mammary nodes. From January 1976, all cases with axillary metastases

Table 1. Patients' characteristics

	Halsted	QUART
No. of patients	349	352
Mean age (yr)	51	50
Size <1 cm	44.4%	46.0%
Axillary metastases	24.6%	27.0%
>3 positive nodes	5.7%	5.1%

were treated with CMF (cyclophosphamide, methotrexate, fluorouracil) for 12 months.

Life tables were calculated by the actuarial method and the curves were compared by the log-rank test after adjustment for nodal involvement and for adjuvant therapy.

RESULTS

The two series of patients had similar characteristics without significant differences (Table 1).

There were 7 local recurrences in the Halsted group and 11 in the QUART group. Another 9 patients in the QUART group developed a second new ipsilateral carcinoma in the treated breast. There were 20 contralateral carcinomas among the Halsted patients and 19 among the QUART patients.

The local recurrences in the conservative group were all treated by total mastectomy, with the exception of 1 case who was treated with a new breast resection. Out of the 11 patients who developed a local recurrence in the conservative group, 4 died of the disease, while 7 are living without evidence of disease 10–15 years after the first operation. Out of the 7 patients who had a local recurrence after Halsted mastectomy, 5 died of disseminated disease, 1 is alive with disease and 1 is free of disease 14 years from primary surgery.

Table 2. 10 and 13 year survival (95% CI) by size of primary carcinoma

Size of primary carcinoma	No.*	10 year survival (%)	13 year survival (%)
≤1 cm			
Halsted	155	80 (74–86)	69 (60–78)
QUART	162	81 (75–87)	76 (69–83)
>1 cm			
Halsted	171	72 (65–79)	67 (59–75)
QUART	157	78 (71–85)	67 (57–77)

*In 56 cases, size was not available.

Table 3. 10 and 13 year survival by site of primary carcinoma

Site of primary carcinoma	No.	10 year survival (%)	13 year survival (%)
External quadrants			
Halsted	218	79 (73–85)	71 (64–78)
QUART	211	79 (73–85)	73 (66–80)
Internal/central quadrants			
Halsted	131	72 (64–80)	66 (56–76)
QUART	141	79 (72–86)	67 (57–77)

Overall survival of the women treated with Halsted mastectomy or with quadrantectomy, axillary dissection and radiotherapy was similar, with a non-significant advantage for QUART (Fig. 1). 10 year survival for the Halsted and QUART patients was 76% (95% CI 72–80%) and 79% (75–83%), respectively. Corresponding figures at 13 years were 69% (63–75%) and 71% (65%–77%).

To identify any differences in subsets of patients, survival was evaluated according to size and site of the tumour, age of the patients and axillary nodal status (Tables 2–5 and Figs. 2–6). There were no statistically significant differences in survival between the two treatments. When the analysis was done by axillary nodes status, the QUART group had persistently better survival in patients with positive nodes, both at 10 and 13 years from treatment. The difference, however, was not statistically significant. In patients with positive axillary nodes, radiotherapy to the supraclavicular and internal mammary nodes did not improve survival compared with no treatment.

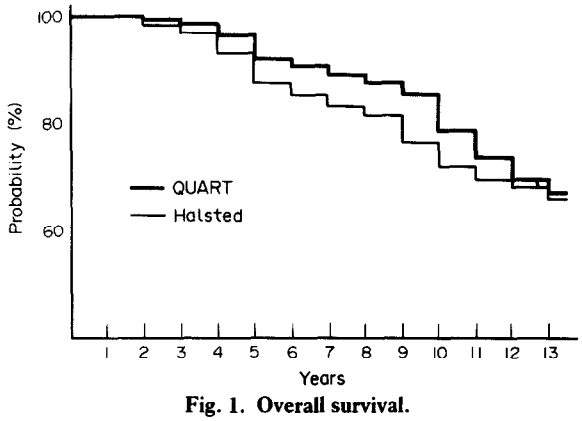

Fig. 1. Overall survival.

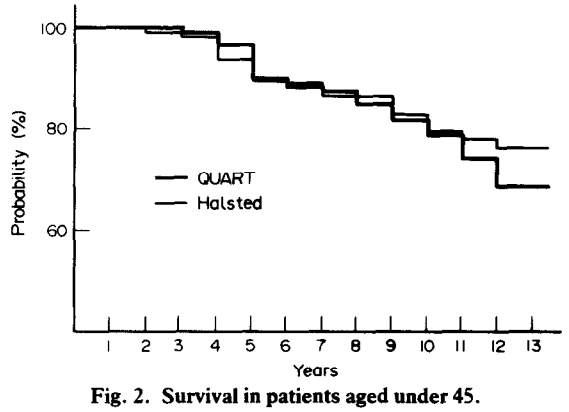

Fig. 2. Survival in patients aged under 45.

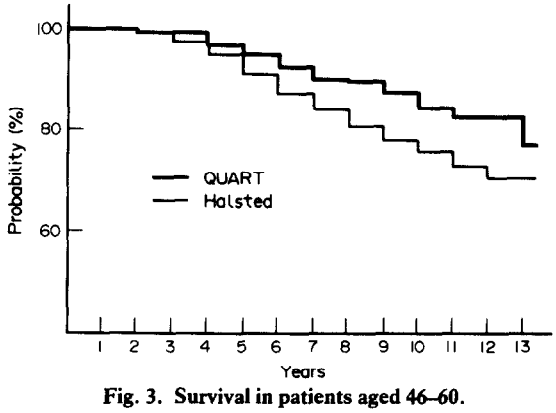

Fig. 3. Survival in patients aged 46–60.

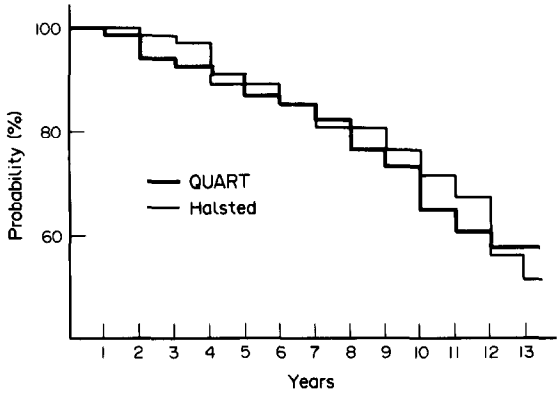

Fig. 4. Survival in patients aged over 60.

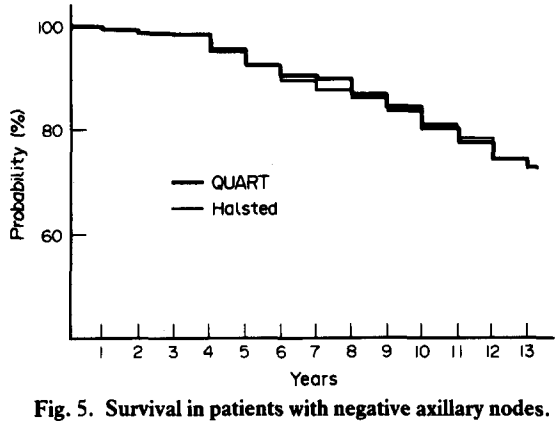

Fig. 5. Survival in patients with negative axillary nodes.

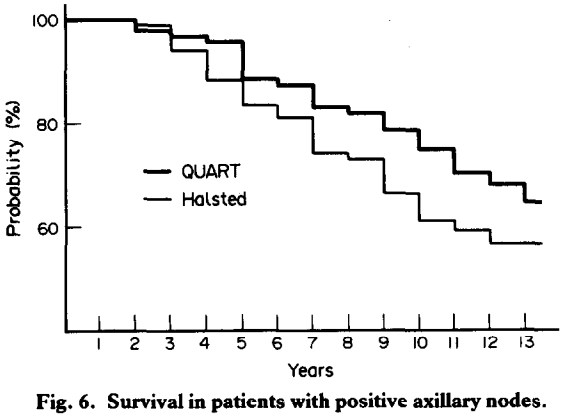

Fig. 6. Survival in patients with positive axillary nodes.

DISCUSSION

The 13 year survival data of small breast cancer show that QUART, a conservative treatment, gave identical results to those of Halsted mastectomy. Subdivision of the patients by size of tumour, site and age did not reveal any difference between the treatments. Any doubt that breast conservation treatments might induce late, unforeseen and unfavourable results should now be put aside. On the contrary, QUART was superior to Halsted mastectomy in patients with positive axillary nodes, without being statistically better.

The risk of late oncogenic action of radiotherapy is, from these data, non-existent. There were 9 new ipsilateral cases in the heavily irradiated breasts whilst in the contralateral breasts there were 19 cases. It appears therefore that breast irradiation, at the doses we used, might perhaps protect the breast either by destroying occult foci of *in situ* carcinomas or by inactivating any proliferative precancerous lesions. During the heavy

Table 4. 10 *and* 13 *year survival by age*

Age	No.	10 year survival (%)	13 year survival (%)
<45			
Halsted	115	80 (73–87)	77 (69–85)
QUART	124	79 (72–86)	69 (60–78)
46–60			
Halsted	159	76 (69–83)	71 (64–78)
QUART	159	85 (79–91)	77 (69–85)
>60			
Halsted	75	72 (62–82)	52 (36–68)
QUART	69	65 (54–76)	58 (45–71)

Table 5. 10 *and* 13 *year survival by axillary nodal status*

Node	No.	10 year survival (%)	13 year survival (%)
Negative			
Halsted	263	81 (76–86)	73 (67–79)
QUART	257	81 (76–86)	73 (67–79)
Positive			
Halsted	86	61 (50–72)	57 (45–69)
QUART	95	75 (66–84)	65 (53–77)

irradiation on the operated breast in the QUART group, the contralateral breasts received a low dose of scattered irradiation. The dosage was calculated to be from 0.5 Gy in the lateral part to 5–15 Gy in the medial part [3]. 19 carcinomas appeared in the contralateral breasts of the QUART patients, no different from the number of new carcinomas (20) that appeared in the contralateral non-irradiated breasts of the Halsted patients. This indicates that low-dose irradiation is not oncogenic, at least in a population of adult women.

We therefore conclude that QUART is safe and that traditional mastectomy in small breast carcinomas should have no role.

Quadrantectomy involves extensive breast resection including the overlying skin. Whether the quadrantectomy, radiotherapy or axillary dissection may be subtituted by a less aggressive local treatment is unknown. Many trials are in progress to evaluate reduction of the surgical excision, the need for immediate radiotherapy compared with delayed radiotherapy only in cases of local recurrence, the indications for the type of the boost, and the maximum size of the primary carcinomas for which breast conservation is indicated. The results will provide new information in a field that has changed the image of breast cancer, by greatly reducing women's fear of a scaring mutilation.

1. 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.
2. Veronesi U, Banfi A, Del Vecchio M *et al.* Comparison of Halsted mastectomy with quadrantectomy, axillary dissection, and radiotherapy in early breast cancer: long-term results. *Eur J Cancer Clin Oncol* 1986, **22**, 1085–1089.
3. Zucali R, Luini A, Del Vecchio M *et al.* Contralateral breast cancer after limited surgery plus radiotherapy of early mammary tumors. *Eur J Surg Oncol* 1987, **13**, 413–417.