

Quadrantectomy versus Lumpectomy for Small Size Breast Cancer

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Between 1985 and 1987 quadrantectomy plus external radiotherapy and lumpectomy plus external and interstitial radiotherapy were compared in a randomized trial of patients with small carcinomas of the breast. Quadrantectomy involves excision of 2–3 cm of normal tissue around the tumour plus the removal of a sufficiently large portion of overlying skin and underlying fascia whilst lumpectomy removes only the tumour mass with a narrow margin of normal tissue. Patients in both groups also received total axillary dissection. 705 cases were evaluable, 360 quadrantectomies and 345 lumpectomies. No differences in distant metastases and survival were observed in the two groups. However, lumpectomy patients had a much higher frequency of local recurrences (7.0 vs. 2.2%). Since a local recurrence needs a second operation and creates severe psychological distress to the patient, conservative surgical procedures should include generous excision of normal tissue around the primary carcinoma plus intensive postoperative radiotherapy.

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INTRODUCTION

FOR patients with small carcinomas, appropriate breast preserving treatments have the same efficiency as mastectomy. The conservative approach, although generally accepted, is not free from criticism. The main reason for uncertainty is the fear of increased incidence of local recurrences, which might impose the psychological distress of a second operation on patients. After the first trials [1–5], a second generation of trials are in progress to identify the most appropriate type of treatment that leads to firm local control and good cosmetic results. Many variables are being tested, such as the extent of normal breast tissue to be excised around the tumour, the amount of overlying skin to be removed, the timing of radiotherapy, the breast volume to be irradiated, the need for and type of boost and the role of preoperative chemotherapy.

A randomized trial was done at the Milan Cancer Institute in 1985–1987 to compare classic quadrantectomy, axillary dissection and radiotherapy (QUART) with a more limited treatment, consisting of a tumorectomy followed by external radiotherapy and a boost with ^{192}Ir implantation (TART).

PATIENTS AND METHODS

Eligibility

Patients with breast cancer measuring up to 2.5 cm in the maximum diameter at gross pathological examination were studied. Patients older than 70, with non-infiltrating lesions, or with a history of a malignant tumour were ineligible.

Randomization

If the mammographic and clinical aspects were consistent with the diagnosis of a primary breast carcinoma of less than 2.5 cm and if cytological examination after a fine-needle biopsy revealed malignant cells, the patient was randomized to one of the two treatments. Uncertain cases were randomized after a frozen section examination.

Treatment of the primary

The two treatments were QUART or TART. QUART [1, 4] consists of a large resection of the quadrant harbouring the primary carcinoma, with at least 2 cm of normal tissue surrounding the tumour, and included removal *en bloc* of a large portion of overlying skin and the underlying fascia of the major pectoralis muscle. Dissection of the axilla is complete, with removal of all the lymph nodes of the three levels up to the apex of the axilla. When the primary carcinoma was located in the upper-outer quadrant, quadrantectomy and axillary dissection were done *en bloc*. Irradiation with a cobalt unit or a 5 MeV linear accelerator was started 4–6 weeks after surgery. The breast was treated with two opposing tangential fields (total 50 Gy given in 5 weeks with daily target dose of 2 Gy) followed by a boost of 10 Gy in five fractions to the tumour bed with an orthovoltage unit.

TART consisted of excision of the primary tumour with a margin of normal breast tissue of 1 cm. The overlying skin was not removed, except for a very thin portion for histological examination. Axillary dissection was done with a separate incision and was total. Radiotherapy was both external and interstitial. External irradiation was started 4 weeks after surgery and the technique was the same as that given after quadrantectomy in equipment, field arrangements and volume irradiated. The difference was the total dose (45 Gy) given over 5 weeks

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with a daily dose of 0.9 plus 0.9 Gy. After 2–3 weeks wires of ^{192}Ir were implanted interstitially to give a boost of 15 Gy directly to the tumour bed.

A total dose of 60 Gy was thus given to both groups of patients. Nodal sites were never irradiated.

Pathology

The breast specimen was examined and the primary carcinoma and the extent of the normal tissue removed around the tumour in all directions were measured. The intraductal component was assessed in all patients. The resection margins of most of the specimens from TART patients and from 176 QUART patients were evaluated for positivity of cancer cells.

When the margins were positive no further resection was done. Since, in TART, lumpectomy is by definition cytoreductive only and the main curative treatment is radiotherapy, there was no reason to change our policy according to positivity or negativity of resection margins. This information was therefore recorded mainly to assess its predictive value and to calculate the percentage of radioresistant cases.

The primary carcinomas of both groups were analysed for peritumoral lymphatic invasion and for oestrogen and progesterone receptors (ER and PR) and the proliferation index was evaluated by tritiated thymidine uptake (TLI).

Follow-up

The patients of both groups were followed up with a quarterly clinical examination and an annual mammography, chest X-ray and bone scan.

Adjuvant treatments

Patients with positive axillary nodes received adjuvant systemic treatments, consisting of cyclophosphamide, methotrexate and fluorouracil (CMF) or CMF plus doxorubicin in premenopausal women and tamoxifen in postmenopausal women with ER positive carcinomas. 17 postmenopausal patients with ER negative tumours did not receive adjuvant treatments.

RESULTS

705 patients were evaluable. 360 were treated with QUART while 345 received TART. The two groups had similar characteristics (Table 1). Different adjuvant treatments were equally distributed (Table 2).

Cosmetic results

A sample of 148 consecutive patients (75 QUART and 73 TART, done 18–24 months previously) was evaluated for cosmetic results. The patients had a frontal photograph and the images were analyzed by computer to assess symmetry: height

Table 1. Patients' characteristics

	TART	QUART
No. of patients	346	360
Average age (S.D.)	50 (9)	50 (9)
Premenopause (%)	54.0	50.7
External quadrants (%)	65.0	69.0
Size <1 cm (%)	27.0	23.0
Ductal infiltrate (%)	62.0	67.5
Positive axillary nodes (%)	34.4	32.8
>3 positive nodes (%)	10.5	9.0

Table 2. Adjuvant treatments in node positive patients

Adjuvant	TART (n = 119)	QUART (n = 118)
CMF	55	49
CMF + doxorubicin	31	31
Tamoxifen	26	29
None	7	10

of the nipples, height of the inferior profiles of the breasts and distance of the nipples from the median line. Lumpectomy had cosmetic advantage compared with quadrantectomy (Table 3).

Local recurrences

Local failures sited in the area of previous surgery (i.e. cutaneous, subcutaneous or parenchymal lesions) that appeared within 3–5 cm from the line of quadrantectomy and lumpectomy scars, respectively, were considered as true local recurrences. At the time of the last review (May 1990) there were 8 local recurrences in the QUART group and 24 in the TART group. The median time of appearance from surgery was 32.5 and 25.9 months, respectively. Histological review of the primary carcinoma showed that out of the 24 TART cases who had a local recurrence, 6 were originally infiltrating carcinomas with an extensive intraductal component. Out of the 28 QUART cases, 1 had a multicentric intraductal component.

The resection margins of 283 TART specimens were evaluable. 46 cases (16%) had positive margins and 6 of these patients had local recurrences. 13 of 237 cases with negative margins had local recurrences. Of the 176 QUART specimens evaluated, 7 (3%) had positive margins and no recurrences; 4 patients out of the 169 with negative margins had a local recurrence.

10 of the patients with local recurrence in the lumpectomy group were treated with quadrantectomy and 14 had total mastectomy. Of the 8 cases of local recurrence in the QUART group, 6 had total mastectomy and 2 partial resection.

No differences were found in the rate of recurrences in the lumpectomy patients according to the size of the primary carcinoma. 7 (7.5%), 8 (7.7%), and 9 (7.6%) cases had a primary tumour under 1, 1.1–1.5, or 1.6–2.5 cm, respectively. The same applied to the presence or absence of axillary metastases: 17 (7.9%) patients were node negative and 7 (6.0%) were node positive.

2 of the 25 TART cases had distant metastases: 22 patients are free of disease at an average of 40 months from primary surgery. The 8 QUART cases are free of disease (average 31 months).

Table 3. Cosmetic results

	Quadrantectomy (n = 75)	Lumpectomy (n = 73)
>3 cm in height between nipples	16 (21%)	5 (7%)
>3 cm in height between inferior profiles of breasts	8 (11%)	2 (3%)
>1.5 cm in length between median line and nipples	13 (17%)	4 (5%)

New ipsilateral and contralateral carcinomas

A malignant nodule that appeared in the same breast distant from the original carcinoma (at least 3 cm from the quadrantectomy scar and 5 cm from the lumpectomy scar) was defined as a new primary carcinoma. 8 new primaries were observed, 3 in the QUART group and 5 in the TART group. 12 QUART and 14 TART cases had new contralateral carcinomas.

Distant metastases

Distant metastases occurred in 36 cases in the quadrantectomy group and in 35 cases in the lumpectomy group (not significant). The distribution by site in the two groups was similar.

DISCUSSION

With a proper amount of normal tissue removed *en bloc* with a portion of the overlying skin and the underlying muscular fascia (quadrantectomy), the rate of local recurrences was 1.1% whilst with lumpectomy, in which the excision of normal breast tissue is narrower (1 cm), the rate was (7.2%). These results were not unexpected. Holland *et al.* [6] showed that the risk of leaving cancer cells in the operated breast was inversely related to the extent of normal breast tissue removal around the tumour. With 1 cm of normal tissue resected, the probability of cancer foci (invasive or non-invasive) remaining in the breast was about 59%, whilst with 3 cm, the probability fell to 17%. Radiotherapy is certainly capable of destroying a high proportion of residual cancer cells, greatly reducing the risk of local recurrences. But 20–25% of cases will be radioresistant.

Is a higher rate of local recurrences an acceptable price for better cosmetic results? Local recurrence is a psychological trauma to patients. Their hope for cure is undermined by the new event and intense anxiety may reappear. Because of our improved surgical technique, quadrantectomy may offer cosmetic results that, although inferior to those usually obtained with lumpectomy, are generally well accepted by patients. Since local recurrences are in many cases treated with mastectomy, an excessive number of salvage operations would frustrate the original objective of conservation. Thus we feel that any radiosurgical procedure that results in an elevated rate of local recurrences should be discouraged.

Does the high rate of local recurrences have any influence on the appearance of distant metastases and on prognosis? In an early trial on breast conservation [7] an excess of local-regional recurrences in patients treated conservatively resulted in an increased risk of distant spread of the disease and in poorer long-term survival compared with patients treated with Halsted's mastectomy. However, many of the recurrences were not at the site of the breast resection but at the axilla, since axillary nodes had not been surgically removed and were left for radiotherapy at a dosage that we would consider inadequate today. In contrast, the more recent NSABP trial report [5], which also showed in one of the arms (breast resection without radiotherapy) a considerable excess of local recurrences, did not show any difference in the rate of distant metastases and in survival.

Our data, although preliminary, show that local recurrences do not influence the appearance of distant metastases. Survival of the two groups of patients was identical (Fig. 1). Our recent review of 1232 patients treated with quadrantectomy plus radiotherapy reached the same conclusion, in that the survival

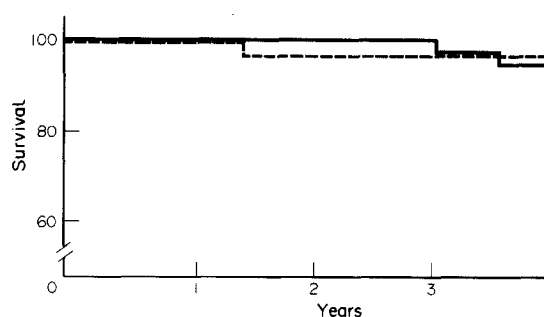


Fig. 1. Overall survival. Solid line = QUART, broken line = TART.

of the 39 patients who had a local recurrence (3% of the total) was similar to that of the patients who had no local failure [8].

We looked at the predictive value of the pathological evaluation of the margins of the resected specimen. In the lumpectomy group, out of 46 patients with positive margins there were 6 cases of local recurrences. However, 13 local recurrences occurred among the 237 patients who had negative margins. Thus pathological positivity of resection margins as a predictor of recurrence, although important, is far from accurate.

In the subgroups of women with metastatic axillary lymph nodes, there was no statistical difference in terms of local relapses. This result could infer that adjuvant chemotherapy did not protect the residual gland from the risk of local relapse. However, this demands for further and more cautious analysis because in a previous review of 871 women treated by QUART, local recurrences were more frequent in node negative women [9].

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