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Special Paper

Ten Year Results of a Randomised Trial Comparing Two Conservative Treatment Strategies for Small Size Breast Cancer

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We report the 10-year results of a randomised clinical trial in which two different breast conservation treatment strategies were compared in women with small, non-metastatic primary breast cancer: quadrantectomy, axillary dissection and radiotherapy (QUART) versus tumorectomy and axillary dissection followed by external radiotherapy and a boost with ^{192}Ir implantation (TART). No second surgery was given to women with affected surgical margins. Axillary node positive women received adjuvant medical therapy. From 1985–1987, this trial accrued 705 patients, 360 in the QUART and 345 in the TART arm. Crude cumulative incidence curves for intrabreast tumour recurrence (IBTR) and metastases as first events and mortality curves in each of the two treatment arms were computed. A crude cumulative incidence curve of IBTR as a second event (in women who had already had a local recurrence) was also computed. The two groups were compared in terms of hazard for IBTR, metastases or death occurrence by using Cox regression models, both with and without adjustment for patient age, tumour size, number of metastatic axillary nodes and histology. Possible interactions between the aforementioned prognostic factors and the type of surgery were also investigated. The two groups were well matched for baseline patient and tumour characteristics, the only exception being resection margins, which were more often positive in the TART group. At the Cox model, a significant difference between groups was detected for IBTR ($P < 0.0001$), but not for distant metastases and overall survival. In particular, 5- and 10-year estimates of crude cumulative incidence of IBTR were 4.7 and 7.4% in the QUART group, and 11.6 and 18.6% in the TART group. The difference was not substantially affected by patient or disease characteristics. Likewise, the status of resection margins in women who underwent TART treatment did not significantly influence the risk of occurrence of IBTRs. Finally, the rate of second IBTR occurrence was relatively high, when compared with the rate of IBTR occurrence as first event. In summary, the results of this trial show that a better local control of the disease can be obtained with the more extensive surgical resection, i.e. QUART. © **1998 Elsevier Science Ltd. All rights reserved.**

Key words: breast conservation surgery, breast neoplasms, randomised clinical trials
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INTRODUCTION

AFTER SHOWING that disease free survival (DFS) and overall survival curves of patients with small size breast carcinomas treated with conservative surgery overlap those of mastectomised patients, a second generation of trials was started in the

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mid-1980s aimed at identifying the most suitable kind of treatment for both local control and cosmetic results. In this context, from 1985–1987, at the Istituto Nazionale per lo Studio e la Cura dei Tumori (INT) of Milan, a randomised clinical trial was carried out comparing two treatment options: quadrantectomy, axillary dissection and radiotherapy (QUART) versus tumorectomy and axillary dissection followed by external radiotherapy and a boost with ^{192}Ir implantation (TART). Preliminary results have already been published [1]. In this paper updated results after some 10 years of follow-up are reported. In particular they concern:

(1) the comparison of the two treatments in terms of first event occurrence, intrabreast tumour recurrences (IBTR), distant metastases and overall mortality, after making allowance for the impact of well-known prognostic factors;
(2) investigation of the possible effect of margin involvement on the risk of IBTR in women undergoing TART;
(3) the presence of possible first order interaction of surgical treatments with age at surgery, tumour size, axillary lymph nodes status and histology. Namely, assessment of treatment-nodal status interaction enabled the investigation of the possible effect of adjuvant chemotherapy on the protection of the residual gland from the risk of local relapse;
(4) the estimate of crude cumulative incidence for second IBTR in women who received second sparing surgery at the time of first IBTR.

PATIENTS AND METHODS

This trial accrued 705 patients, 360 in the QUART and 345 in the TART arm (Figure 1). The study design was described in detail elsewhere [1]. Briefly, the study population comprised women with non-metastatic, unilateral breast cancer up to 2.5 cm in diameter at gross pathological investigation. Excluded were women over 70 years of age, with non-infiltrating or Paget carcinoma and those who had already had malignant tumours.

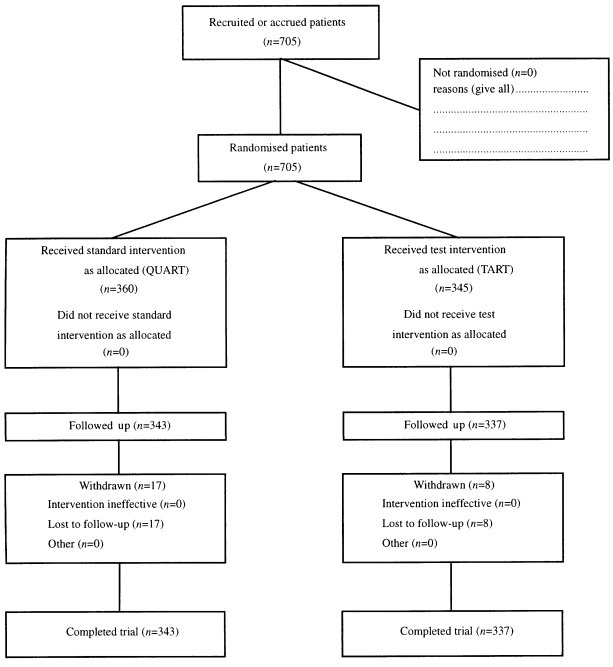

Figure 1. Flow chart of the progress of patients through the trial. (Adapted from Begg C, Cho M, Eastwood, S, *et al.* Improving the quality of reporting the randomised controlled trials: the CONSORT statement. *JAMA* 1996, 276, 637–639).

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 randomised to one of the two treatments before surgery. Uncertain cases were randomised after a frozen section examination. In both cases, to enter a new patient surgeons had to call the data manager by telephone, who held a computer-generated randomisation list.

Quadrantectomy was performed by removing the primary tumour with at least 2 cm of normal mammary tissue around the lesion, together with a portion of overlying skin and the underlying pectoral fascia. Axillary dissection was total, with removal of lymph nodes of the three levels up to the apex. Whenever the tumour was located in the upper-outer quadrant, the skin incision was prolonged so as to perform axillary dissection in continuity. External irradiation with a 6 MeV linear accelerator began 4–6 weeks after surgery. The breast was treated with two opposite tangential fields (total 50 Gy given in 5 weeks with a daily target dose of 2 Gy) soon followed by a boost of 10 Gy in five fractions to the tumour bed with an orthovoltage unit or electrons.

Tumorectomy consisted of a limited excision of the primary tumour with a margin of 1 cm or less of normal tissue. Axillary dissection was carried out with a separate incision, whatever the site of the tumour and was total. Patients received both external and interstitial radiotherapy. External irradiation began 4 weeks after surgery and the technique was the same as that used after quadrantectomy. The difference was the total dose (45 Gy) given over 5 weeks with a daily dose of 1.8 Gy. After 2–3 weeks, wires of ^{192}Ir were implanted interstitially to give a boost of 15 Gy directly to the tumour bed. This higher dose to the tumour bed through interstitial modality was considered adequate to control the risk of local recurrences after the more conservative surgery. In any case, radiation treatment was designed in order to give the same dose of 60 Gy to the diseased breast in both groups.

Most patients with positive axillary nodes were treated with adjuvant medical therapy: premenopausal women and postmenopausal patients negative for oestrogen receptors received chemotherapy (cyclophosphamide, methotrexate and 5-fluorouracil (CMF) combination, with or without doxorubicin), whereas postmenopausal women positive for oestrogen receptors received tamoxifen for 2 years.

Patients were checked at quarterly intervals for the first 5 years and subsequently on a 6-monthly basis. Mammography, chest X-ray and bone scan were performed annually. As of 31 December 1996, the median follow-up time was 113 months. At this date, almost all tumour relapse free patients were making regular follow-up visits. For all patients vital status was ascertained through regular follow-up or by a search for death certificates.

Statistical analysis

Main patient and tumour characteristics for the QUART and TART groups were described by means of contingency tables.

The primary outcome measure was intrabreast tumour recurrence (IBTR), defined either as any homolateral relapse of breast cancer at the mammary gland parenchyma or as a cutaneous or subcutaneous recurrence within 2 cm from the surgical scar. Other outcomes considered were regional or distant metastasis, contralateral breast cancer, other tumours and death from any cause. Time to occurrence of the above mentioned events was computed from the date of surgery.

Crude cumulative incidence curves for IBTR and metastases as first events were computed as described by Marubini and Valsecchi [2]. Contralateral breast cancer, other primary tumours and death for non-neoplastic reasons were considered as competing events. The same approach was adopted for obtaining the crude cumulative incidence curve of IBTR as a second event in women who had already had a local recurrence (in the latter case, however, time to occurrence of IBTR was computed from the date of the first event). First-event incidence and all-cause mortality curves were estimated according to the Kaplan–Meier approach [3].

Table 1. *Patient and tumour characteristics*

	QUART *n* (%)	TART *n* (%)
Age (years)		
≤ 35	16 (4.4)	16 (4.6)
36–45	95 (26.4)	92 (26.7)
46–55	136 (37.8)	136 (39.4)
56–65	92 (25.6)	89 (25.8)
> 65	21 (5.8)	12 (3.5)
Menopausal status		
Premenopause	186 (54.9)	182 (56.7)
Menopause	153 (45.1)	139 (43.3)
Not reported	21	24
Tumour site (quadrants)		
Lateral	243 (67.5)	220 (63.8)
Medial/Central	117 (32.5)	125 (36.2)
Tumour size (cm)		
≤ 0.5	15 (4.2)	13 (3.8)
0.6–1.0	70 (19.5)	84 (24.6)
1.1–2.0	219 (61.0)	203 (59.5)
> 2.0	55 (15.3)	41 (12.0)
Not reported	1	4
Focality		
Monofocal	348 (96.7)	335 (97.1)
Multifocal	12 (3.3)	10 (2.9)
Histology		
IDC	244 (67.8)	219 (63.7)
ILC	75 (20.8)	70 (20.3)
EIC	22 (6.1)	37 (10.8)
Others	19 (5.3)	18 (5.2)
Not reported	0	1
Resection margins		
Negative	168 (95.5)	237 (83.7)
Positive	8 (4.5)	46 (16.3)
Not reported	184	62
Tumour receptors		
ER-PgR –	53 (16.4)	50 (15.9)
ER-PgR +	23 (7.1)	14 (4.5)
ER + PgR –	50 (15.5)	48 (15.3)
ER + PgR +	197 (61.0)	202 (64.3)
Not reported	37	31
Positive axillary nodes		
0	240 (66.7)	225 (65.2)
1–3	88 (24.4)	86 (24.9)
4–9	24 (6.7)	19 (5.5)
≥ 10	8 (2.2)	15 (4.3)

IDC, infiltrating duct carcinoma; ILC, infiltrating lobular carcinoma, associated or not with an infiltrating ductal component; EIC, infiltrating duct carcinoma with extensive intraductal component; ER = oestrogen receptors; PgR = progesterone receptors; negative (–); positive (+).

The study had been designed to detect a doubling in the hazard of IBTR occurrence from an anticipated 4 events/1,000 women-years at risk with QUART to 8 events/1,000 women-years at risk in the TART arm. The available sample size and the median follow-up time achieved yielded a power of approximately 90% for a two-sided test at the 5% significance level.

QUART and TART patients were compared in terms of hazard of first event occurrence, IBTR, metastases and mortality by using Cox regression models, after verifying the proportional hazard assumption by means of log-minus log-survival plots [4]. All patients were included in the analysis according to the intention-to-treat principle. The analyses were carried out both with and without adjustment for the following known prognostic factors: patient age, tumour size, number of metastatic axillary nodes and histology. Based on past experience [5] these factors were categorised as shown in Table 1 and entered into Cox models by means of 0–1 indicator variables. Tumour histology in particular was classified as infiltrating duct carcinoma, infiltrating lobular carcinoma, associated or not with an infiltrating ductal component, infiltrating carcinoma with extensive intraductal component, according to the definition given by Schnitt and colleagues [6] and other histotypes. For each outcome event considered, results of the analysis are reported as unadjusted and adjusted hazard ratio estimates for TART versus QUART patients, the corresponding 95% confidence interval (CI) and *P* value by the Wald test [2].

To investigate the role of IBTR in predicting the occurrence of metastases, a Cox time-dependent model was fitted. In the latter, distant recurrences observed as first or second event after IBTR were considered, whereas local recurrence was entered into the model by means of a time-varying indicator variable.

Possible interactions between surgical treatment and prognostic factors in terms of IBTR occurrence were also investigated. According to the literature, several statistical methods have been developed for such an evaluation. Here we adopted the empirical Bayesian method described by Dixon and Simon [7, 8], implemented by the SAS™ macro kindly supplied by the above mentioned authors. This method requires binary covariates; accordingly, prognostic factors were categorised as shown in Table 7.

RESULTS

A flow diagram of patient participation is reported in Figure 1. As the total number of conservative treatments carried out at our Institute was some 450/year, the available sample represents some 52% of the target population. Out of the 415 women alive with no neoplastic event during the study, only 25 (6%) were lost to follow-up, 17 (7%) and 8 (4%) in the QUART and TART groups, respectively, 52–112 months after surgery.

The two groups were well matched for baseline patient and tumour characteristics (Table 1) as well as adjuvant treatments administered to node-positive women (Table 2). The only exception was the frequency of positive resection

margins, which was obviously higher in the TART group. According to the criteria presently adopted at the INT, women without menses for at least 1 year were classified as postmenopause. Discrepancies with the figures reported in the first paper [1] depend on the different criteria previously adopted. Negligible discrepancies regarding some of the remaining characteristics are due to extensive data checking carried out when the MI2 trial data were included in a clinical database specifically devoted to breast conservation surgery [9].

The number of first events observed are reported in Table 3. Intralymphatic vascular IBTRs, 1 in the TART and 1 in the QUART group, were regarded as distant metastases. The relative cumulative incidence curves are drawn in Figure 2. At the Cox model, the two treatment groups showed a significant difference ($P = 0.02$) both with and without adjustment for prognostic factors (patient age, tumour size, number of metastatic axillary nodes and histology).

As regards the single events, attention was focused on IBTR and metastases.

Intrabreast tumour recurrences

The main features and treatments adopted for the IBTRs recorded in the two treatment groups are described in Tables 4 and 5, respectively.

Table 2. Adjuvant therapy administered to node positive women (120 patients in each treatment arm)

Adjuvant treatment	QUART *n* (%)	TART *n* (%)
Chemotherapy	78 (65.0)	86 (71.7)
Tamoxifen	30 (25.0)	27 (22.5)
Tamoxifen + chemotherapy	1 (0.8)	0 (0.0)
None	11 (9.2)	7 (5.8)

Table 3. Number of first events

First event	QUART *n*	TART *n*	Total *n*
IBTR	25	63	88
Metastasis	73	60	133
Contralateral breast cancer	18	22	40
Other tumour	15	4	19
NED death	1	9	10
Total	132	158	290

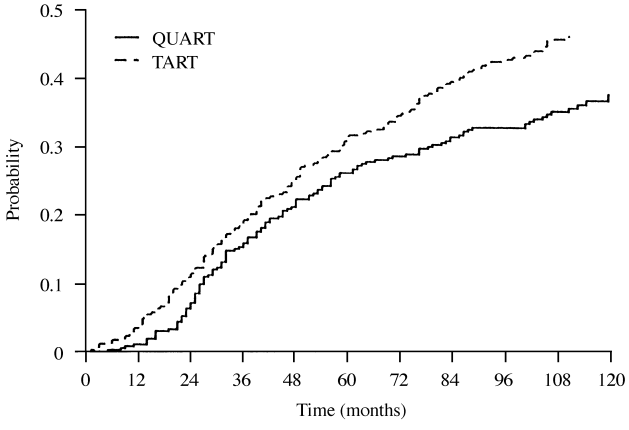

Figure 2. First event incidence curves in the two treatment arms ($P = 0.02$, Cox model).

Crude cumulative incidence curves in the two study arms are shown in Figure 3. 5- and 10-year estimates (and corresponding standard errors) were 0.047 (0.011) and 0.074 (0.015), in the QUART group, and 0.116 (0.017) and 0.186 (0.021) in the TART group. In Figure 4 the crude cumulative incidence curve for TART women was divided according to the status of resection margins. The curve for the subgroup with positive margins was somewhat higher than that of patients with negative margins. The two curves, however, tended to converge at 108 months and the difference between them was not statistically significant by the Gray test ($P = 0.2865$). 5- and 10-year incidence estimates were 0.152 and 0.245 in TART women with positive margins, 0.106 and 0.176 in TART women with negative margins.

Table 4. Main features of intra-breast tumour recurrences (88 women overall, 25 in the QUART and 63 in the TART arm)

	QUART *n* (%)	TART *n* (%)
Tumour site		
Surgery area (≤ 2 cm)	18 (72.0)	52 (82.5)
Not surgery area	7 (28.0)	11 (17.5)
Tissue		
Skin	2 (10.0)	1 (1.7)
Parenchyma	18 (90.0)	56 (94.9)
Both	0 (0.0)	2 (3.4)
Not reported	5	4
Tumour size (cm)		
≤ 0.5	5 (31.3)	11 (22.9)
0.6–1.0	2 (12.5)	7 (14.6)
1.1–2.0	6 (37.5)	25 (52.1)
> 2.0	3 (18.8)	5 (10.4)
Not reported	9	15
Number of lesions		
Single	15 (78.9)	46 (80.7)
Multiple	4 (21.1)	11 (19.3)
Not reported	6	6
Histology		
IDC	8 (40.0)	26 (44.1)
ILC	5 (25.0)	12 (20.3)
EIC	4 (20.0)	15 (25.4)
DCIS	3 (15.0)	2 (3.4)
Other	0 (0.0)	4 (6.8)
Not reported	5	4

IDC, infiltrating duct carcinoma; ILC, infiltrating lobular carcinoma, associated or not with an infiltrating ductal component; EIC, infiltrating duct carcinoma with extensive intraductal component; DCIS, duct carcinoma *in situ*.

Table 5. Treatments performed in relation to breast tumour recurrences (88 women overall, 25 in the QUART and 63 in the TART arm)

	QUART *n* (%)	TART *n* (%)
Surgery		
Resection	7 (28.0)	10 (15.9)
Quadrantectomy	1 (4.0)	25 (39.7)
Mastectomy	17 (68.0)	28 (44.4)
Adjuvant therapy		
Chemotherapy	0 (0.0)	1 (1.7)
Hormone therapy	6 (27.3)	14 (23.7)
None	16 (72.7)	44 (74.6)
Not reported	3	4

The results obtained for IBTR with the Cox model (Table 6) were highly significant ($P < 0.0001$). Adjusted and unadjusted hazard ratio (TART/QUART) estimates overlapped and denoted approximately a 3-fold increase in the hazard of occurrence of the event for TART women.

Finally, hazard ratio estimates and posterior credibility intervals obtained with the Bayesian analysis are reported in Table 7. The estimates in the distinct subsets considered, little differed from those obtained for the whole series. There was, therefore, no clear evidence of possible qualitative or quantitative variation of treatment effect in different patient subgroups. It is worth noting that the value of HR = 2.562 is slightly lower than the frequentist estimates reported in Table 6; this finding partly reflects the 'shrinkage' effect of the Bayesian approach and partly the difference between the underlying models.

Table 6. *Results of the Cox model, in terms of hazard ratio (HR) estimates for the TART versus QUART group, corresponding* 95% *confidence intervals (CI) and* P *levels*

Outcome	Analysis*	HR	95% CI	*P*
IBTR	Unadjusted	2.810	1.768–4.467	< 0.0001
	Adjusted	2.752	1.727–5.384	< 0.0001
Metastases	Unadjusted	0.904	0.642–1.272	0.5620
	Adjusted	0.907	0.642–1.282	0.5802
Mortality	Unadjusted	1.112	0.802–1.542	0.5247
	Adjusted	1.134	0.812–1.582	0.4603

*See text for explanation.

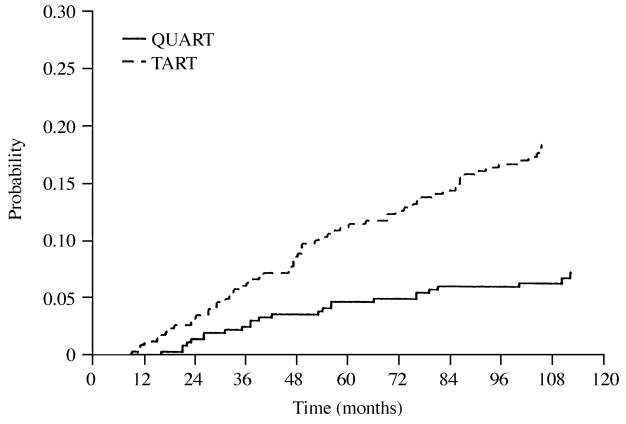

Figure 3. Crude cumulative IBTR incidence curves in the two treatment arms.

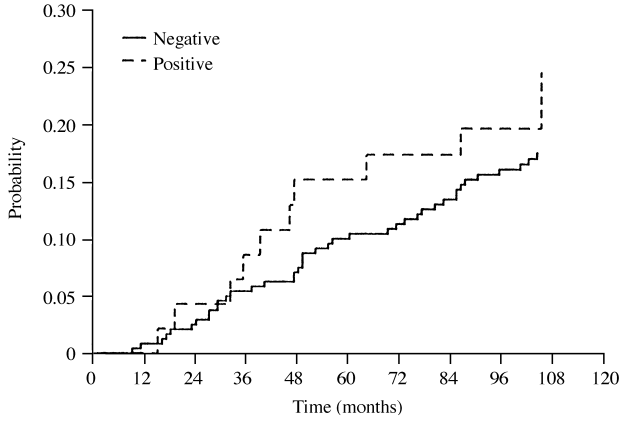

Figure 4. Crude cumulative IBTR incidence curves in the TART treatment arm according to surgical resection margins.

Distant metastases

Crude cumulative incidence curves for metastases are reported in Figure 5. No significant difference was detected (Table 6). The time-dependent Cox model showed that IBTR was able to predict significantly metastases (HR: 3.54, $P = 0.0001$), a finding in accordance with our previous results [5].

Survival

144 deaths were recorded, 70 in the QUART and 74 in the TART group. Only 1 and 9 deaths, respectively, were not preceded by tumour recurrence. All-cause mortality curves are plotted in Figure 6. 5- and 10-year mortality estimates were 0.089 (0.015) and 0.209 (0.024) in the QUART group and 0.104 (0.017) and 0.212 (0.023) in the TART group. Results of the Cox model (Table 6) were not statistically significant and hazard ratio estimates were close to one, thus showing no substantial difference in patient survival between the two arms.

Table 7. *IBTR hazard ratio (HR) posterior means and corresponding* 95% *confidence intervals (CI) obtained with the Dixon and Simon Bayesian approach* [7, 8] *in the whole series and in the distinct subsets considered*

Category	HR	95% CI
Overall series	2.562	1.554–4.246
Age (years)		
≤ 55	2.428	1.473–3.963
> 55	2.630	1.389–7.149
Tumour size (cm)		
≤ 1	2.667	1.449–7.250
> 1	2.430	1.459–4.027
Nodes		
N −	2.627	1.562–4.600
N +	2.425	1.260–4.486
Histology		
EIC	2.547	1.278–5.960
Other	2.545	1.543–4.238

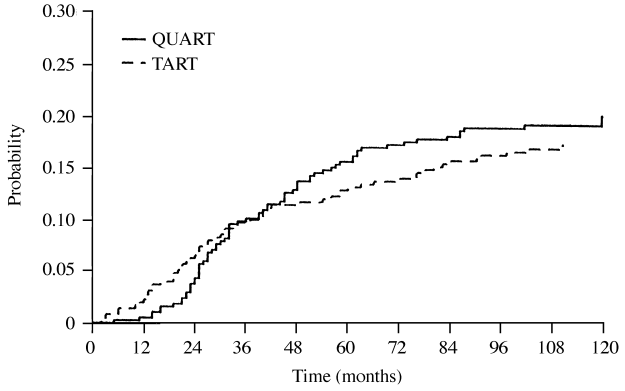

Figure 5. Crude cumulative metastases incidence curves in the two treatment arms.

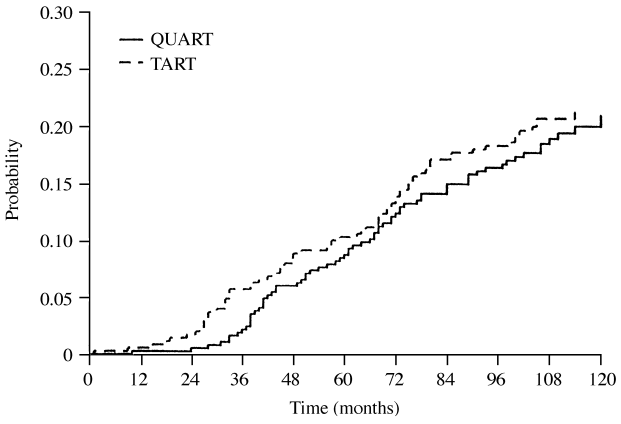

Figure 6. All cause mortality curves in the two treatment arms.

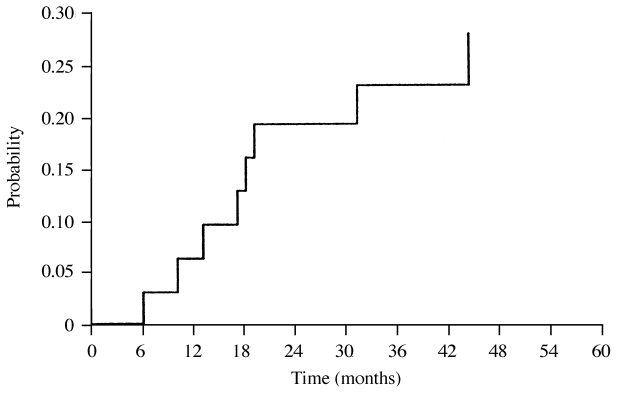

Figure 7. Crude cumulative incidence curve for second IBTR in women who received breast sparing surgery at the time of first IBTR.

Second intrabreast tumour recurrences

Of the 88 women who experienced IBTR, 12 patients had a second local recurrence. In particular, two recurrences occurred in 2 women of the QUART group, one of whom had received breast sparing surgery (resection or quadrantectomy) for the first recurrence, whereas the other had received mastectomy. The remaining 10 recurrences were recorded in TART women, all treated with breast sparing surgery for the first recurrence.

Due to the limited information available, QUART and TART cases were pooled so as to estimate the risk of second local recurrence. Crude cumulative incidence of second IBTR and annual rates of event occurrence ($\times 100$ women-years at risk) were computed separately for women who had received breast sparing surgery or mastectomy at the first IBTR. The crude cumulative incidence curve of second IBTR in women who received breast sparing surgery for first IBTR is plotted in Figure 7. No such curve is presented for women who received mastectomy, since only one event was observed. The annual rates (and corresponding 95% CI) were 7.8 (4.3–14.1) after conservative surgery and 0.7 (0.1–4.7) after mastectomy. For comparison, annual rates of first IBTR occurrence were 0.9 (0.6–1.4) in the QUART group and 2.6 (2.1–3.4) in the TART group.

DISCUSSION

Tables 1 and 2 show that the two treatment groups differed significantly only for the frequency of positive resection margins, which were much more frequently involved in the TART than in the QUART group. The crude cumulative incidence curve of IBTR as first event (Figure 3) was significantly higher in the TART than in the QUART group showing that the IBTR risk was nearly 3-fold for more sparing treatment (Table 6). When the crude cumulative incidence of the TART group was divided according to the status of resection margins (Figure 4), it was found that both patients curves with positive or negative margins were above those estimated for QUART women as a whole (Figure 3). For comparison, 5- and 10-year incidence estimates were 0.152 and 0.245 in TART women with positive margins, 0.106 and 0.176 in TART women with negative margins, versus the figures of 0.047 and 0.074 in the QUART group. As regards the impact of IBTR on the appearance of distant metastases, the time-dependent Cox model showed that IBTR, as first event, had a statistically significant role in predicting distant metastases with a hazard ratio comparable to those previously published [5, 10].

The IBTR hazard ratio (TART/QUART) was found to be stable across the dichotomous prognostic factors considered in Table 7. This suggests that in terms of local recurrences QUART performs favourably regardless of the category to which the patients belong. As all N^+ patients received adjuvant treatment, namely some two thirds underwent chemotherapy (Table 2), it could be argued that adjuvant chemotherapy did not protect the residual gland from the risk of local relapse.

In terms of metastasis occurrence and all causes mortality, the two surgical treatments appeared to give comparable results (Figures 4 and 5, Table 6).

One important result in patients treated with TART is the limited difference in terms of local recurrences between cases with positive as opposed to negative margins. This finding focuses once again on the issue of the diagnostic reliability and clinical relevance of margin assessment. It has been repeatedly stated that negativity of margins is not an indicator of low risk of local recurrence [11]. In the NSABP B06 trial [12], cases with negative margins treated with lumpectomy showed a local recurrence rate of more than 40%. The present updated analysis of Milan II trial data shows that among patients with pathologically negative margins 41 had a local recurrence, underlining that margin negativity should not reassure the surgeon. Conversely, the data presented here show that the finding of positive margins is likewise not an important indicator of additional risk compared with the negative margin cases (Figure 4). Recent results published by Cage and colleagues [13] also show that the presence of 'focally positive' margins is not a bad prognostic factor and only a very extensive invasion of the margins increases the rate of recurrence to 28% (14/50).

The limited effect of margin involvement on the local recurrence risk may be due to both technical reasons, as the pathologist draws samples from the surface of the tumour specimen haphazardly and to biological reasons, as the spread of cancer cells is very often discontinuous. Moreover, the definition of margin positivity does not consider that cancer cells may be 'close to the margin', a condition which does not have a clear prognostic connotation according to different pathologists. Finally, in the case of a positive margin it is objectively difficult for the pathologist to distinguish between

the interstitial spread of the primary carcinoma and a separate focus in a multifocal carcinoma.

In his editorial, Fisher [14] argued that the higher incidence of local recurrences in the TART group could be due to the lack of "re-resection in an effort to obtain tumour free margins", contrary to the NSABP policy and to less aggressive radiation therapy. However, the first point seems questionable, on the grounds of the above considerations on the limited effect of margin involvement. As for radiation therapy, this was equivalent in the two groups in terms of total dose, maybe with a slight disadvantage in the TART arm in relation to the 2–3 week time interval between external and interstitial irradiation. However, in our opinion, such a delay was insufficient to explain the observed between-group difference in local control of disease.

The annual rates of second local recurrence for patients who received re-excision or mastectomy for the first IBTR were 7.8 and 0.7, respectively. It is widely accepted that local recurrence is a psychological trauma for patients, particularly if it happens after two operations. Therefore, in treating small breast cancers it seems sensible to adopt a strategy implying conservative breast surgery with sufficient margins of healthy tissue like quadrantectomy followed by radiotherapy, which has proved [9] to have a cumulative 10-year IBTR incidence less than 8% in routine practice, while in the case of local recurrence, the option of mastectomy can be considered by the surgeon and discussed with the patient, especially when the recurrence occurs early after surgery.

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