Mastectomy with axillary clearance versus mastectomy without it

Late results of a trial in which patients had no adjuvant chemo-, radio- or endocrine therapy

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Objective. Long-term outcome of comparison of mastectomy with axillary clearance to mastectomy without it.

Design. Second analysis of a terminated prospective randomised trial.

Setting. The Breast Clinic, Groote Schuur Hospital, Cape Town.

Patients. Ninety-five women aged under 76 years with stages 1 and 2 (T1-2 N0-1 M0) breast cancer.

Interventions. Radical mastectomy (mastectomy and formal axillary dissection with pectoral muscle excision) or simple mastectomy (mastectomy without axillary dissection if nodes were not clinically palpable, or local excision of the nodes if they were).

Outcome measures. Loco-regional recurrence and survival.

Results. Whereas initial analysis at 40 months had showed more axillary recurrences ($P = 0.056$) in the simple mastectomy group (leading to the termination of the trial), this difference has disappeared at 10 years ($P = 0.113$). There was no difference in rate of recurrence at all other sites, time to recurrence, or survival rates at 40 months or at 10 or 25 years.

Conclusions. Full axillary clearance offered no better long-term loco-regional control or survival. Early analysis and marginally significant differences in axillary recurrence prompted premature termination of this trial.

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A longstanding and continuing debate[1-3] in the surgical management of operable breast cancer is whether routine axillary clearance is necessary or not. Over the past 30 years many prospective randomised trials have attempted to address this question, and these are the subject of a recent meta-analysis.[4] The Groote Schuur Hospital trial compared the option of axillary clearance to nothing (if nodes were not palpable), or node picking (if they were), in women undergoing mastectomy. Three years after its inception, however, the trial was terminated because the authors '. . . felt very disturbed about this high rate of (axillary) recurrence (in the group without axillary clearance)'.[5] This trial has been quoted frequently in overviews, including the recent one,[4] and we therefore believe that a final report is necessary. Of interest is the fact that the trial was conducted without the possible confounding factors of radiotherapy or adjuvant chemo- or endocrine therapy. We are also in a position to reflect on whether the trial was not in fact terminated prematurely.

Patients and methods

The trial was conducted at the Groote Schuur Hospital Breast Clinic, where all patients were followed up and where all data were available for analysis. Women were eligible if they were younger than 76 years, had stages 1 or 2 (T1-2 N0-1 M0) breast cancer, and were fit for surgery. Randomisation took place on receipt of the intra-operative frozen section diagnosis, and was by blind selection from a pre-prepared pool of the two treatment possibilities. No attempt was made to balance the sequence of randomisation into smaller groups.

There were two surgical groups: 'radical' (43 women), who underwent radical mastectomy (mastectomy, axillary clearance and excision of the pectoral muscles), and 'simple' (52 women), who underwent mastectomy alone if nodes were not clinically palpable, or with local excision of enlarged nodes, but without formal block excision, if they were. The two groups appeared comparable (Table I). Twenty-five patients in the simple mastectomy group had palpable axillary nodes and underwent node excision, and in 16 of these cases the nodes were found to contain malignant cells. No adjuvant radiotherapy or chemo-endocrine therapies were given. Patients were given combinations of radiotherapy and dromostanolone (Masteril) on relapse. Patients were entered into the trial between September 1968 and December 1971. Initial analysis (and termination) was at 40 months; final follow-up and re-analysis was in June 1995. Three analyses are presented: at 40 months, and 10 and 25 years.

Table I. Comparability of the radical and simple mastectomy groups

	Radical (43 patients)	Simple (52 patients)
Age (yrs) (median, range)	53 (31 - 69)	54 (23 - 75)
Stage		
T1	5	8
T2	37	39
T3	1	4
N0	21	27
'Node picking'	–	25*
Pathological N1	22	16*

* Twenty-five patients were thought to be node-positive on clinical grounds, but this was confirmed in only 16 of them.

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Results

Recurrence (Table II)

By 40 months 5 patients in the simple mastectomy group had developed axillary recurrence (3 after node picking and 2 in the undisturbed axilla), whereas none in the radical group had developed recurrence. This was marginally significant ($P = 0.056$). Surgical resection was not possible in any of these cases.[5] By 10 years the axillary recurrence rates were not significantly different ($P = 0.113$). All other sites of recurrence, the time to recurrence, and rate of development of distal metastases, at both 40 months and 10 years, were not different. There was only 1 recurrence after 10 years (in a skin flap in a patient in the radical group).

Table II. Comparison of the sites of recurrence, time to recurrence and development of metastases (analysis at 40 months in brackets, followed by the 10-year analysis)

	Radical (43 patients)	Simple (52 patients)	P^*
All loco-regional	(9) 11	(16) 19	(0.274) 0.27
Scar	(3) 4	(4) 6	(0.609) 0.510
Flap	(1) 2	(3) 3	(0.397) 0.595
Axilla	(0) 2	(5) 8	(0.056) 0.113
Supraclavicular	(3) 3	(2) 2	(0.424) 0.424
Median months to recurrence	25	18	
Distant metastases	11	13	0.569

* Fisher's exact test, one-tailed *P*-value.

Mortality (*Table III, Fig. 1*)

There was no significant difference in survival rate between the two groups at 10 years (log rank test: $\chi^2 = 1.8188$ (1 df); $P = 0.1775$). Between 10 and 25 years there were 3 further deaths related to breast cancer: the patient with recurrence in the skin flap mentioned above died shortly after, and 2 further patients developed contralateral disease at 11 and 12 years. There were 11 non-cancer-related deaths in the prolonged follow-up period.

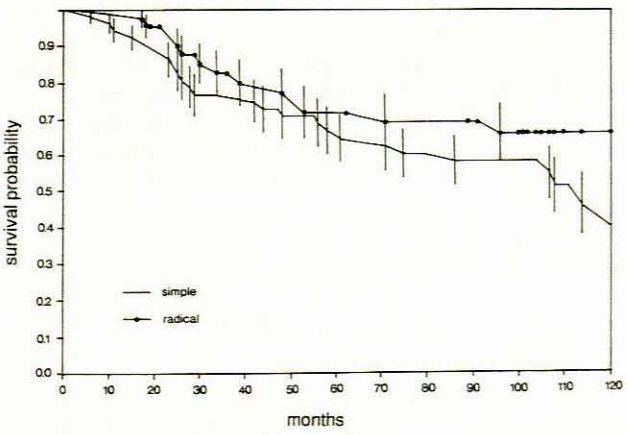

Fig. 1. Comparison of survival rates of the radical and simple mastectomy groups (log rank test: $\chi^2 = 1.8188$ (1 df); $P = 0.1775$).

Table III. Comparison of survival data for radical and simple mastectomy at 10 years

	Radical	Simple
Dead from disease	13	22
Dead from other causes	8	8
Alive with disease	0	1
Alive free from disease	3	1
Lost to follow-up	19 (104)*	20 (108)
Mean survival (months)	85	79
5-year survival (%)	71	65

* Median months after which patients were lost to follow-up in brackets.

Discussion

The issues at stake are whether formal axillary clearance affects local recurrence or survival after mastectomy for breast cancer. Our patients with un- or partially dissected axillae had a higher axillary recurrence rate initially, but this difference became insignificant with time. Local control was achieved by radiotherapy after recurrence. It could be expected that axillary recurrence would be higher in the patients without axillary dissection: this has been the case in other similar trials, where adjuvant radiotherapy or chemotherapy have not confounded the issue.[6,7] It would also be expected, and has been found, that the rate of axillary recurrence is higher when the undissected axilla has not received radiotherapy.[8] Meta-analysis of all trials that have examined the role of axillary dissection has not found that this improved survival, however.[4] Indeed, Devitt[9] suggested that 'axillary lymph node metastases are an expression of a bad prognosis rather than a determinant'. It would therefore appear that survival is no longer part of the axillary dissection debate; instead, the debate would appear to revolve around harms, benefits and costs of prophylactic axillary dissection or radiotherapy, or subsequent axillary treatment only for that proportion of women who relapse. These are probably matters of personal choice, for both doctor and patient.

We must conclude that this trial was terminated prematurely: the axillary recurrence rate in the simple mastectomy group, which so disturbed the trialists, was only marginally significant ($P = 0.056$) at 40 months when they terminated the trial, and became quite insignificant ($P = 0.113$) at 10 years. All other comparisons showed no differences. With the wisdom of hindsight we can caution that while trials should be analysed repeatedly during their progress, any differences that could lead to termination of the trial should be markedly significant before such a decision is taken.

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