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FROM THE DEPARTMENT OF RADIATION THERAPY AND ONCOLOGY, MIDDLESEX HOSPITAL, LONDON, ENGLAND.

PRIMARY BREAST CANCER

Complications of axillary management

E. K. YEOH, J. W. DENHAM, S. A. DAVIES and M. F. SPITTLE

Abstract

The complications following surgery and postoperative radiation therapy in the management of the axilla in 187 patients with primary breast cancer treated between 1978 and 1982 have been studied. Although no difference in complication rate could be detected between the three different postoperative radiation schedules utilised there was a strong and positive correlation between complication rate and increasing extent of surgical intervention. When the groups were sub-divided according to the extent of surgery performed, no differences in regional recurrence rates were observed but complication rates (defined as significant lymphoedema of the arm and/or restriction of shoulder movements) were significantly different ($p<0.001$) at 30 months between those who had no surgical intervention (25%), those who had had 'sampling' performed (50%) and those who had had formal dissection performed (84%).

Key words: Breast neoplasms; carcinoma, axillary treatment, complications.

It is well recognised the management of the axilla in breast cancer can result in complications that can compromise arm function sometimes to the extent of interfering with the quality of life. These complications are most commonly manifested in the ipsilateral arm and include lymphoedema, limitation of arm movements and brachial plexus neuropathy. Fortunately these problems have become less common as the Halsted radical mastectomy has been replaced in many centres by other procedures, but their incidence remains significant. Studies assessing the relative contributions of differing degrees of surgical intervention and radiation to these complications are uncommon, which is a surprising and important omission from the literature considering the number of different approaches to the axilla practised today. It is difficult to see how management trends can change in a rational manner if little account is taken of the morbidity rates attributable to different procedures.

The years 1978 to 1982 were associated with an increasing trend towards conservatism in the management of primary breast cancer in Southern England. Although the Patey modified radical mastectomy and simple mastectomy with or without sampling of the axillary contents remained commonly practised procedures, segmental mastectomy with or without axillary sampling was carried out with increasing frequency both at hospitals referring patients to the Radiotherapy Department of the Middlesex Hospital and at the Middlesex Hospital itself. A change in radiation dose fractionation policy for the treatment of patients with early breast carcinoma was proposed in 1980 due to an increasing workload without there being a commensurate rise in treatment equipment, facilities and staff. We therefore had the opportunity not only of studying patients who had had differing degrees of surgical intervention in the axilla but also the chance to compare 3 different radiation shedules.

Material and Methods

The records of all patients registered in 1978 to 1982 as having apparently localised breast carcinoma were reviewed between April and July 1984. A total of 255 patients were registered on our computer registry as having localised breast carcinoma. All the patients were staged according to UICC (1972) criteria and only those patients with T 1,2 and 3 N0 and N1 lesions were included in the present study. Sixty-seven patients were excluded for the following reasons:

1) Advanced regional disease viz., N2 and N3 disease which could cause lymphoedema, restriction of shoulder movements and brachial plexus neuropathy and thus confound the assessment of complications.

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2) Patients who did not receive breast lymph node irradiation because: a) of referral following chest wall recurrence after mastectomy, b) locally advanced (T4) disease in the breast when radiation therapy to the breast was instituted as a toilet procedure often in conjunction with other measures, c) some patients who received adjuvant chemotherapy and in whom radiation therapy was not deemed necessary.

3) Patients who did have lymph node irradiation but who received unconventional dose fractionation regimens for this institution.

Before 1980 patients were treated following primary surgery (modified Patey mastectomy) with megavoltage photons using cobalt teletherapy employing 4 standard fields. The chest wall (or breast) and the internal mammary nodes were encompassed by two opposed tangential wedged fields if the separation between these was less than 23 cm, and treated to a minimum tumour dose of 55 Gy in 27 fractions over 5.5 weeks. If the separation of the tangential fields was greater than 23 cm the internal mammary nodes were included in the third field which consisted of a single anterior field to encompass the supraclavicular and axillary lymph nodes to an applied dose of 55 Gy in 27 fractions over 5.5 weeks. A supplementary posterior axillary field (fourth field) was applied twice a week to bring the midline axillary dose to 55 Gy. After 1980 patients were randomly allocated to receive 42.9 Gy in 13 fractions over 5 weeks or to receive 50 Gy in 25 fractions over 5 weeks, utilising field and dose specifications as before. Patients who had had segmental mastectomies received a supplementary dose of 15 Gy in 5 fractions over one week to the primary excision site either from a short distance cobalt unit or utilising electrons from a Philips SL 75 linear accelerator. In 1981, to further reduce workload on the treatment units, it was decided that all patients who had had primary surgery (modified Patey mastectomy) should receive the 13 fraction 5 week regimen and that only those patients who had had segmental mastectomy should continue to be randomised

A total of 187 patients were therefore eligible for this study. One hundred and ten patients were treated with 55 Gy/27 fractions/5.5 weeks (group I), 27 patients with 50 Gy/25 fractions/5 weeks (group II), and 50 patients with 42.9 Gy/13 fractions/5 weeks (group III). The distribution of T and N stages in these 3 groups is shown in Table 1.

Patients were followed up regularly at 3-month intervals. At each visit evidence of loco-regional recurrence was sought as well as dysfunction of the ipsilateral upper limb. Any degree of lymphoedema was noted and confirmed by measurement 7.5 cm above the olecranon process and the degree of restriction of any shoulder movement recorded (patients were asked to place the palm of their hand on the back of the head and to put the back of their hand on their lumbar spine and finally to raise their arms above their head from the sides of the trunk thereby testing the full range of abduction). Patients were deemed

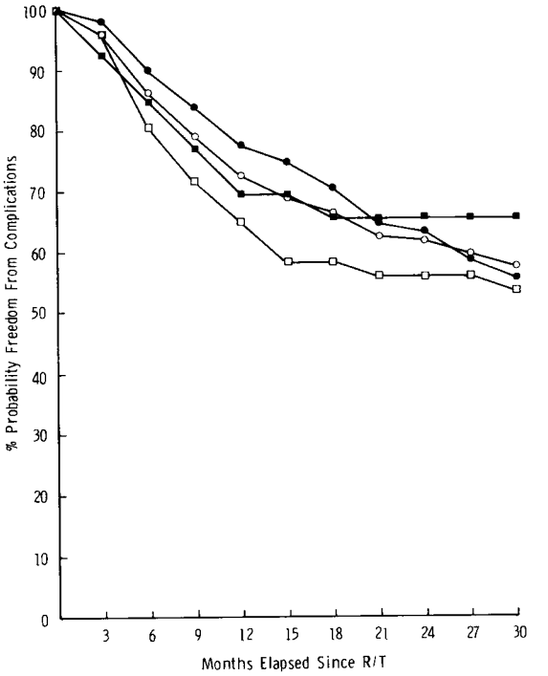

Fig. 1. Probability of freedom from complications according to radiation regimen. Group I (●), group II (■), group III (□), all patients (○). No statistically significant difference.

Table 1

Distribution of T and N stages in patients grouped according to radiation dose regimen

Radiation regimen	No. of cases	T1 or 2	T3	N0	N1
55 Gy/27 fractions/ 5.5 weeks (group I)	110	90	20	56	54
50 Gy/25 fractions/ 5 weeks (group II)	27	20	7	18	9
42.9 Gy/13 fractions/ 5 weeks (group III)	50	41	9	28	22

to have developed these complications only if there was persistence of these abnormalities at 2 successive visits even if clinically insignificant to the patient. For purpose of analysis of the results, lymphoedema and restriction of shoulder movements as defined above were considered together since both are associated with axillary fibrosis and often coexisted in the same patients. Since the period of follow-up varied with the 3 dose fractionation regimens (median 3.24 years for group I patients, 2.68 years for group II and 1.70 years for group III cases), actuarial analysis of complications and regional recurrence was performed using the life table method and the log rank test used to detect differences (8).

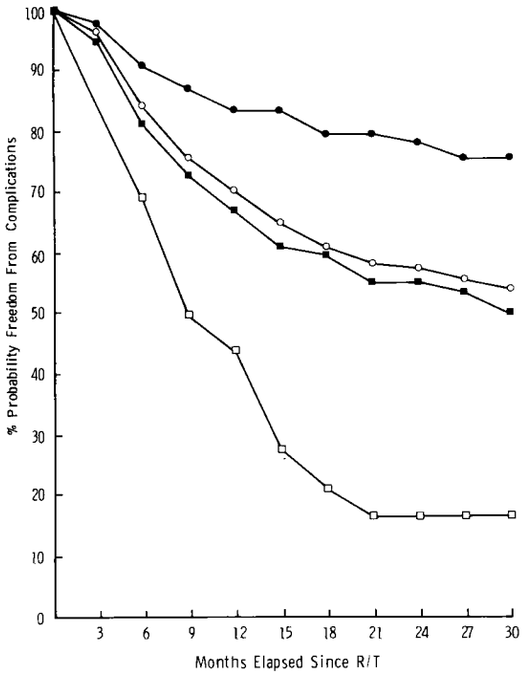

Fig. 2. Probability of freedom from complications according to surgical intervention of the axilla. Axillary dissection (□), axillary sampling (■), no intervention (●). All patients (○). χ^2 = 36.21. DF2 $p<0.001$.

Table 2

Distribution of T and N stages after substratifying according to extent of surgery

Extent of surgery	No. of cases	T1 or 2	T3	N0	N1
Axillary dissection	24	20	4	11	13
Axillary sampling	77	68	9	37	40
No intervention	86	63	23	54	32

Results

From the actuarial analysis the following results were obtained: (1) Forty-six per cent of all the patients developed complications at 30 months (Fig. 1). Although the patients in group II appeared to have the lowest actuarial complication rate, the differences between group II and groups I and III were not statistically significant. This finding was unaltered by the removal from the analysis of 24 patients who had undergone dissection—a factor that might have biased the comparison.

2) When the 187 patients were re-stratified according to the extent of surgery regardless of the radiation dose fractionation regimen they received, highly statistically significant differences in complication rate were revealed (Fig. 2). The 30-month actuarial complication rate increased with the extent of surgery from 25 per cent of those patients who had no axillary intervention to 50 per cent of those who had axillary node sampling and 84 per cent of those who underwent radical axillary dissection. A significantly higher proportion of patients with T3 tumours was present in the group who had no surgical intervention than in the other two axillary groups (Table 2) and therefore a staging bias cannot be held to be responsible for the observed differences in complication rates.

3) The overall 30-month actuarial regional recurrence for the whole series was 2.5 per cent with no significant differences evident between the 3 fractionation regimens to 30 months. Following re-stratification according to extent of surgery, similarly, no significant differences were shown in actuarial recurrence rates according to extent of surgery.

Discussion

Previous investigations have stressed the importance of the size of radiation dose per fraction in the development of late radiation sequelae and the need to reduce total radiation dose when the number of fractions is reduced and therefore dose per fraction is increased (1, 8). However the extent to which surgery of the axillary lymph nodes contributes to the development of late radiation complications was not addressed in these studies. The decision to use 42.9 Gy in 13 fractions over 5 weeks was partly based on its equivalence in NSD terms to 50 Gy in 25 fractions over 5 weeks. This decision was viewed with some trepidation since the risk of extrapolation from 5 fractions per week to 5 fractions per fortnight using the NSD concept was appreciated. However, this analysis has provided welcome reassurance that dramatic and unwelcome differences in biologic effect have not occurred so far, although we would stress that the number of cases in this study is too small to rule out the possibility of a genuine difference. In the Cardiff-St. Mary's trial (6), surgery alone led to a significant incidence of lymphoedema and restriction of elevation of the ipsilateral upper limb. The addition of radiation using a standard fractionation regime appeared to compound the risk of complications of surgery. Similarly, SWEDBORG & WALLGREN (10) have shown that radiation therapy increases arm swelling and decreases arm function whether given before or after surgery. Every patient in the present series however has received radiation so unfortunately it is not possible to directly confirm these findings. However, this study has demonstrated that prior surgery compounds the risk of morbidity occurring after radiation of the axilla. Moreover this study has shown, and not surprisingly, that the *extent* of prior surgical intervention in the axilla is an important factor too.

It has been shown repeatedly that axillary lymph node status is of major prognostic importance (5, 9, 11). A

knowledge of nodal status is therefore of value in deciding those patients likely to benefit from adjuvant chemotherapy (2, 4). However opinion remains divided as to what proportion of the axillary contents require excision in order to establish axillary status with the necessary degree of precision. Some for example would argue that the approximate 10 per cent false negative rate associated with sampling (3, 6) is a worth while trade-off for the lack of morbidity of the procedure. However others would argue that the morbidity associated with dissection is not a great deal higher and that this factor is offset because the need for subsequent irradiation of the axillary contents is obviated. Some adherents of the McWhirter method (simple mastectomy plus chest wall and glandular drainage area irradiation) would argue that the prognostic information which can be derived from a consideration of the size of the primary, its histologic differentiation and hormone receptor status, obviate the need to perform any form of axillary surgical exploration at all. While our data do not help to resolve this dilemma they are consistent with the data from the Cardiff-St. Mary's and Stockholm trials supporting the need for discretion in employing both surgery and radiation to the axilla. In addition our data suggest that the extent of prior surgical intervention must be taken into account when assessing the results of axillary irradiation.

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Request for reprints: Dr E. K. Yeoh, Department of Radiotherapy, Royal Adelaide Hospital, Adelaide, South Australia 5000.

REFERENCES

1. Bates T. D.: A prospective clinical trial of post-operative radiotherapy delivered in three fractions per week versus two fractions per week in breast carcinoma. Clin. Radiol. 26 (1975), 297.
2. Bonadonna G., Rossi A., Valagussa P., Banfi A. and Veronesi U. The CMF programme for operable breast cancer with positive axillary nodes. Update analysis on the disease free interval, site of relapse and drug tolerance. Cancer 39 (1977), 2904.
3. Boova R. S. Bonani R. and Rosata F. E.: Patterns of axillary involvement in breast cancer. Predictability of level dissection. Ann. Surg. 196 (1982), 642.
4. Fisher B., Glass A., Redmond C. et coll.: L-phenyl-alanine mustard (L-PAM) in the management of primary breast cancer. An update of earlier findings and a comparison with those using L-PAM and 5FU. Cancer 39 (1977), 2883.
5. Fisher B., Slack N. H. and Bross I. D.: Cancer of the breast. Size of neoplasm and prognosis. Cancer 24 (1969), 1071.
6. Forrest A. P. M., Roberts M. M., Preece P. et coll.: The Cardiff-St. Mary's Trial. Brit. J. Surg. 61 (1974), 766.
7. Kim J. H., Chu F. C. H. and Hilaris B.: The influence of dose fraction on acute and late reactions in patients with post-operative radiotherapy for carcinoma of the breast. Cancer 35 (1975), 1583.
8. Peto R., Pike M. C., Armitage P. et coll.: Design and analysis of randomised clinical trials requiring prolonged observation of each patient. II. Analysis and examples. Brit. J. Cancer 35 (1977), 1.
9. Schottenfield D., Nash A. G., Robbins G. F. and Beattie E. J.: Ten year results of the treatment of primary operable breast carcinoma. Cancer 38 (1976), 1001.
10. Swedborg I. and Wallgren A.: The effect of pre and post mastectomy radiotherapy on the degree of edema, shoulder-joint mobility and gripping force. Cancer 47 (1981), 877.
11. Valagussa P., Bonadonna G. and Veronesi U.: Patterns of relapse and survival following radical mastectomy. Cancer 41 (1978), 1170.